Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals

Second Edition

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Editors

EXTRAS ONLINE

Springer

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2nd ed. 2017

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ISBN 978-3-319-46540-1 e-ISBN 978-3-319-46542-5
DOI 10.1007/978-3-319-46542-5

Library of Congress Control Number: 2017943687

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG Switzerland
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

A few pioneer neurophysiologists, surgeons, anesthesiologists, and researchers from many disciplines and countries gave birth to the field of intraoperative neuromonitoring over 40 years ago when together they realized that there was a need and a means for providing better patient care. Their interest and efforts resulted in numerous subsequent international meetings, spawned the establishment and growth of various professional societies, and ignited a growing interest in IOM. All of this would not have occurred without the contributions and support of countless individuals who dedicated a significant part of their professional lives and resources to the field of IOM. It is to these various pioneers and individuals that we dedicate this book.

Foreword to First Edition: Orthopedic Spine Viewpoint

We began our Case Western Reserve University (CWRU) efforts to develop a system for monitoring spinal cord function during scoliosis corrective surgery in the late 1960s. It was prompted by the risks to the spinal cord as a result of using Harrington Rods for curvature correction. From the very beginning, we approached it as a team effort. University Hospitals and CWRU had the expertise to tackle this difficult challenge, but they had to be pulled together. A young neurosurgeon by the name of Jerald *Brodkey* had some experience with a technique of summating distal peripheral nerve stimulations as they were expressed over the cortex, a process reported by Dawson in the 1950s. At the same time there was a very bright, young master's biomedical engineer, Richard *Brown* working in the CWRU biomedical engineering laboratories of Drs. Victor Frankel, MD, PhD and Al Burstein, PhD. Fortuitously, Richard's undergraduate degree was in electrical engineering and he had some free time available to work on the spinal cord monitoring project (which became his PhD thesis!).

The approach taken in the laboratory was to study the effect of graduated weights applied directly to the thoracic spinal cord of dogs for varying periods of time on the ability of the cord to transmit trains of stimuli from the distal extremities to the cortex. In the course of these studies it also became apparent that pressure, time, and blood pressure were all critical variables. Then available commercial neuromonitoring systems were used, but from the beginning Rich Brown recognized that they would not work in the highly electrically charged environment of an operating room (OR). Thus began his creation of a stand alone, portable spinal cord monitoring system capable of accurately recording the very small cortical signals generated in the hostile atmosphere of the OR. Thus "Big Blue," as Rich would call it, came to be originally equipped with four channels, but soon expanded to eight with all data stored on tape for later analysis. "Real-time" record assessment was done by holding up a base line printout up to the light with the current record printout superimposed to visually determine latency and amplitude changes. Appropriate filtering, stimulus rates, stimulus configuration, and voltages along with Rich's primary passion, patient safety, were all factors to be sorted out. "Warning signs" of changes in latency and amplitude were part of

the equation with the 10 and 50% guidelines becoming evident even then. From the beginning, Rich's goal was to produce a system that would prove both reliable and provide valid data – causes he championed his entire career – later holding all systems to the same fire he held his own.

Once the system had proven to be effective in the laboratory by sorting out the amounts of weight over what periods of time that correlated clinically with the presence or absence of clinical neurological deficits, it was time to take it to the OR. It was strongly suspected that the more complex anesthesia used in humans would have significant effects on the cortex and hence the records. Accordingly, the next challenge was to have an anesthesiologist who would help the team sort out this piece of the puzzle. Betty *Grundy* , MD, was the person who enthusiastically joined the team and in her own right added a great deal of knowledge to the process of making spinal cord monitoring a viable clinical tool in the OR. She also became a voice within the anesthesia profession that meticulous anesthesia protocols had to be followed for spinal cord monitoring to be effective. Along the way, Rich became quite knowledgeable regarding the various anesthetic agents used in spinal surgery to the extent that he was a frequent presenter to anesthesia grand rounds on the subject of their effects on cortical function. The final addition to the team was Marianne *Wilham* , RN, the primary orthopedic OR nurse for the spinal surgical team and a critical person in maintaining a constant process in the OR. She and Rich also became quite adept at dealing with teenage patients and parents as they went through pre-operative spinal cord monitoring testing and the next day trip to the OR for surgery.

Together this team meticulously developed protocols and systems that seemed to provide the most consistent and reliable approach to intraoperative spinal cord monitoring using Somatosensory Cortical Evoked Potentials (SSEPs). Early in this process, several significant and revealing cases were performed that were encouraging and confirmed the value of Rich Brown's "Big Blue" and the future of SSEPs. It should be noted that the "Wake-Up Test" of Stagnara came into vogue about the same time as the CWRU work, and it was adopted by the Case Team as a way to verify the findings of the intraoperative changes seen in monitoring. One early case was a patient with scoliosis and diastomatomyelia. It was elected to do the Harrington spinal corrective surgery before removing the diastomatomyelia. Each time the Harrington distraction was applied, the signals deteriorated and after removal returned. The case was aborted with no neurological deficits. The

diastomatomyelia was removed and the subsequent spinal corrective surgery went forward without incidence. Other early cases included a patient with cervical spinal cord abscess in which artificially raising the blood pressure temporarily restored SSEP responses and the clinical function. There was also a case of cervical spinal cord hemangioma dissection that was performed successfully under the protective umbrella of SSEPs. Thus, these early anecdotal experiences became convincingly indicative of the potential for intraoperative spinal cord monitoring to make a great contribution to the safety of patients undergoing major corrective spinal surgery. This monitoring tool also proved to be one of the critical factors contributing to the development of more and more powerful and corrective spinal implant systems that could be applied in a safe manner.

It turns out that during the same time period, Dr. Tetsuya Tamaki and a team of Japanese researchers including an anesthesiologist, Dr. K. Shimoji, were independently working on a method for intraoperative spinal cord monitoring using spinal – spinal evoked potentials. Before long there was communication between the Case Team and Dr. Tamaki's team to the extent that a series of international spinal cord monitoring conferences were held, the first being in Cleveland, Ohio, in 1977. At this first meeting, Dr. Vernon Nickel, a highly respected orthopedic surgeon remarked to the gathering, "One day intra-operative spinal cord monitoring will be as accepted and used as the EKG." One of the key individuals in this movement to develop intraoperative spinal cord monitoring was a neurosurgeon, Dr. J. Schramm, from Germany. The list of participants continued to grow both in the United States and throughout the world in great measure because of the encouraging and engaging efforts of Rich Brown whose nature was to share his ideas and expertise freely with all who took an interest. Again this welcoming approach was grounded in Rich's passion for rigorous process, analysis, expertise, and training. Similarly he was cautious and scientifically reluctant to prematurely declare SSEPs as the "Gold Standard" for monitoring spinal cord function replacing the tried and true "Wake-Up Test". As a final note, Rich never "went commercial" with his system and expertise, but rather directed his efforts into organizing the experts in the field and establishing standards of nomenclature, processes, and technical training. He was an energetic founding member and later a president of the American Society of Neurophysiologic Monitoring to which he remained committed and focused until his untimely death.

All who have gone before would applaud this valuable book, and in particular Rich Brown, PhD, who very early on recognized the critical role that anesthesia and anesthesiologists would play in the development and practice of intraoperative spinal cord monitoring.

And the rest is history.

Clyde L. Nash Jr.
Cleveland, OH
September, 2011

Foreword to First Edition: Peeling Back the Onion Skin Layers

"As natural selection works solely by and for the good of each being, all corporeal and mental endowments will tend to progress towards perfection."
(Charles Darwin: The Origin of The Species, XV, 1859)

My! How times have changed! As I write this, I am looking at a copy of an anesthetic record from June 14, 1968. Being a perpetual "pack rat," I made it a habit over the years to file cases of interest and needless to say, accumulated quite a library over the past 50 years. This case, (Fig. 1), is that of a 3-month-old baby with a diagnosis of cranial synostosis with orbital compression and the operative procedure was in three stages, the final one occurring 2 months later and involved a ventricular peritoneal shunt using the-then relatively new silastic Holter valve. In this sick and lethargic baby, local anesthetics (carbocaine) supplemented with sedation were used over the period of 3 h and 50 min. Specific monitors included a blood pressure cuff and temperature probe. For neuromonitoring, we considered ourselves "advanced" as we employed a unit that we nicknamed the "bullet" or "torpedo," since it had a cylindrical shape with a diameter of about 6 in. and a length of 1.0 foot! One end had a transparent viewplate with the tube containing a cathode ray tube and the electronics for a one-channel electrocardiogram, lead II, and another single channel for an electroencephalogram lead, using a parietal presentation. Since explosive agents were in use at that time, the "bullet" had an explosion proof casing and elevated on a tripod above the 5 foot explosive level. So now we were able to visualize the EEG, EKG, and measure the heart rate with clicks triggered by the Q-T complex. If we now move 16 years to 1994, we can note the emergence of a neuromonitoring culture as demonstrated by the book edited by Peter Sebel and William Fitch, *Monitoring the Central Nervous System* [1]. There, 21 authors discussed a range of topics which are extraordinary when compared to the availability of neuromonitoring facilities in the 1960s. In this time period the horizon of neuromonitoring is expanded to not only include physiochemical topics as cerebral blood flow *and metabolism* , ICP, and EEG, but critical aspects relating to memory, recovery from anesthesia, cognitive factors, and brain death. Fast forward to today and to the wonderful effort made by the authors of the present-day book to present a sophisticated

review of the great advances in neuromonitoring and its application to patient care as well as increasing our understanding of the complexities not only of the central nervous system but the incredible relationships among electrodynamic and electrochemical signaling that lead to cognitive changes which may affect modalities such as pain. Similarly, the effects of our monitoring efforts may be in themselves modified by the clinical medium of anesthesia and cause a shift in the paradigm, which in a sense involves monitoring the monitors and helps to eliminate false assumptions [2, 3]. The expertise and experience of the authors contribute greatly to a sense of true security that these methodologies have been tested by those knowledgeable in their field. Further cementing the link between development and application are the hard-nosed Case-Based Presentations of practitioners often highlighting those on both sides of the procedure table. This type of hegemony is critical for carrying out many of these procedures. This book has important source material even for those not directly connected with the many procedures listed in the Table of Contents, for many of the authors are not only capable as practitioners, but have had a primary role in developing the many neuromonitoring techniques listed.

[redacted]

ANESTHESIA RECORD

DATE 6-14-68 [redacted] UNIT NO. [redacted]

NAME [redacted] AGE 3 Mos WEIGHT 7.9 #/4

DIV. 7W RISK II HEMO GLOBIN Hct 41% URINE neg BL. PRES.

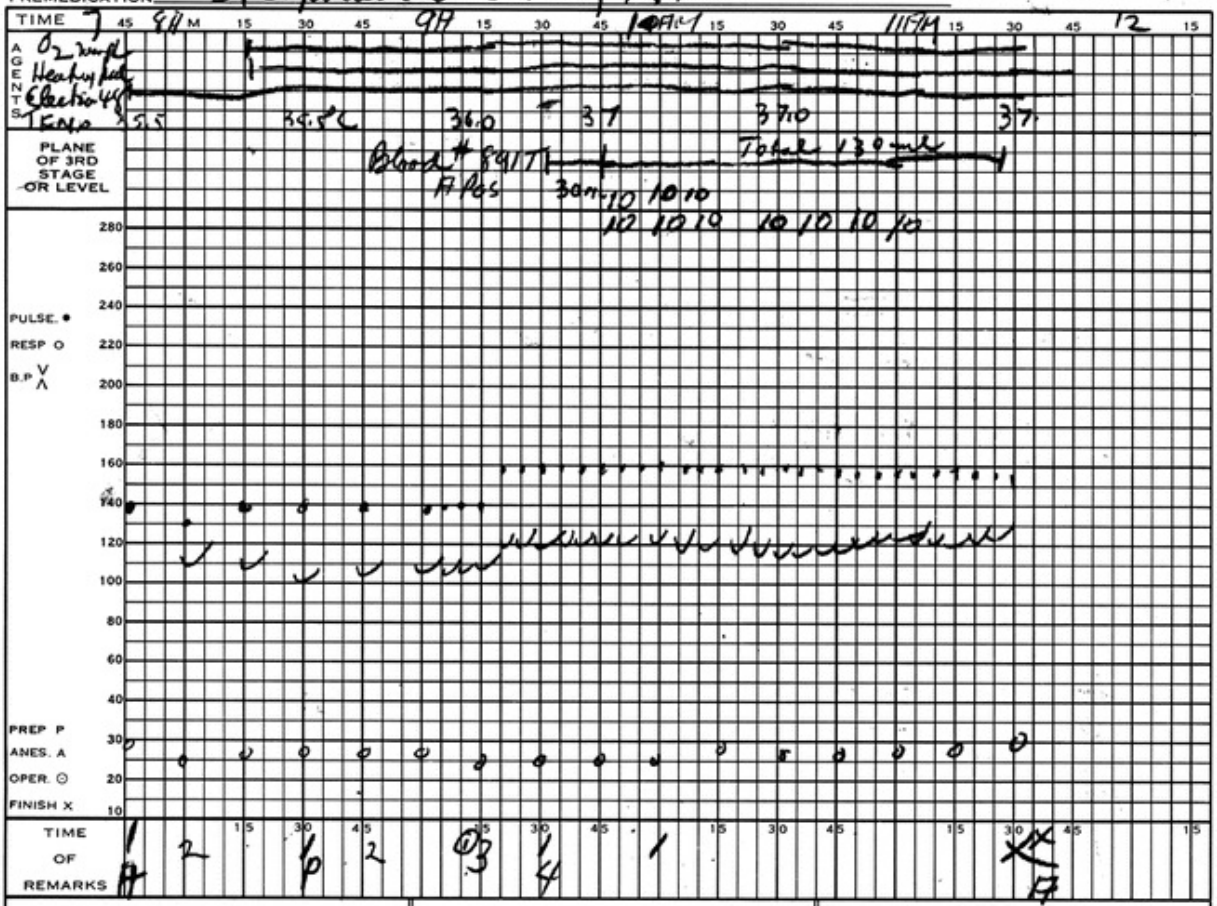
PREOPERATIVE DIAGNOSIS Cranial Synostosis & orbital compression

POST OPERATIVE DIAGNOSIS As above

OPERATION Craniotomy & orbital decompression, left

PREMEDICATION Scopolamine 0.1 mg I.V.

PREMEDICATION
SATISFACTORY ☐
OVERMEDICATED ☐
UNDERMEDICATED ☐
REMARK



REMARKS
1. Demerol, 5 mg I.V.
2. Vistaril, 5 mg I.V.
3. Seconal, 5 mg I.V.
4. Start Whole blood # 6917 TYPE A Rh Pos

McGEE, ATHENS, O. K74895X

ANESTHETIC AGENTS Cyclocaine, 50 mg

ANES. METHODS Local Infiltration & I.V. Succinylcholine

FLUIDS Electrolyte #4, 250 ml; whole blood, 130 ml

SURGEONS Yasbin, Weiss, Lopez ANESTHETISTS All

ANES. TIME 3'50"
OPER TIME 2'20" No
RECOVERY ROOM
P. O. CONDITION good

FORM B38-A REV.

Fig. 1 A 1968 record of a pediatric case with the anesthesia provided by the author. Total monitoring included systolic blood pressure, temperature, heart rate, lead II of the EKG, and one EEG lead

Before terminating this Preface, I must take a moment to pay homage to one, who, in many ways is regarded as the "Mother" of neuromonitoring in the anesthesia and neurological community, namely, Betty Grundy, MD. I have known Betty for more than 40 years and can attest to how hard she has worked to bring electrophysiological monitoring into the operating room and clinical arena as well as educating a whole host of superb clinicians and those doing research in this area.

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Maurice S. Albin
Birmingham, USA

September, 2011

Foreword to First Edition: Neurosurgeon's Viewpoint

I am honored to have been invited to provide a foreword to this important volume. As a practicing cerebrovascular surgeon, I have a unique perspective on the field of neuromonitoring as I function somewhat as a "consumer" of these very valuable resources. Vascular surgeons are charged with exposing the brain, retracting brain tissue, reconstructing complex vascular anatomy, temporarily interrupting cerebral blood flow, and performing complex revascularizations. Not infrequently our target organ is already diseased and dysautoregulated at the time we expose it. While we have marvelous technologies to allow us to perform computerized image guidance, highly magnified 3-dimensional views, and microsurgical instrumentation that allows extraordinary things to be done, we perform this invasive maneuvers blinded as to how the brain is tolerating these actions. Neuromonitoring, when performed by skilled technologists and physicians with high expertise in the interpretation of data provide the surgeon with actionable information that can prove lifesaving.

From my perspective, one of the most interesting aspects of contemporary neuromonitoring lies in the domain of systems-based practice and communication. The surgeon often feels like a pilot of an aircraft in which he or she has certain control capabilities but because the door is closed behind the pilot, he or she has essentially no knowledge of what is happening in the rest of the aircraft. It is critical that in our surgical environments the "door" remains open and that the key human elements have professional confidence in each other and communicate openly. At the start of the procedure, everyone responsible including the physicians, technologists, and nurses must understand the nature of the planned procedure, important details about the patient, the general phases of the operation expected, and when the critical moments will be occurring. As each stage of the procedure unfolds, the entire team must be aware of those transitions. When an unexpected anomaly develops, a rapid assessment of its significance must be performed followed by direct communication with the surgeon. A timely but deliberate discussion of the options to be considered and which one to be pursued assures the optimal environment for the patient's successful outcome.

It cannot be over emphasized that successful surgical neuromonitoring

requires a coordinated team effort. The critical elements obviously include in-depth knowledge of the principles of neuromonitoring and technical proficiency. Yet, without a full understanding of the patient's physiologic state prior to surgery and the unique aspects of patient positioning, abnormal data may be misinterpreted. The principles of the planned surgical procedure must be understood by all team members and constant communication must occur among the key participants to assure that proper perspective of the environment is obtained prior to the announcement of an abnormal finding.

Clearly this book will be a significant benefit to surgeons, technologists, neurophysiologists, anesthesiologists, and neurologists. The information contained in these chapters will empower the surgical team members with the knowledge needed to interpret unexpected changes and to react quickly and appropriately. This book will be an important reference for all members of these teams and hopefully enhance our ability to provide safe procedures with optimal outcomes.

H. Hunt Batjer
Chicago, IL
September, 2011

Preface to Second Edition

Intraoperative monitoring (IOM) of the nervous system continues to play a key role for safeguarding neurological function during surgery and interventional procedures when the nervous system is at risk for injury. For many procedures, it has been integrated as a key component of decision making and a variety of studies have shown a clear association of its use with improved outcomes. The utilization of monitoring continues to evolve as monitoring techniques are improved and developed and their contributions to improved patient care are better understood. As such, we are pleased to present this second edition which reflects these changes.

We continue to be grateful to the many past and present pioneers in the field who have laid the groundwork for modern day monitoring and who continue to fuel the evolution of its techniques and applications. Anesthesiologists have played a key role in this evolution with improvements in neuroanesthesia and their interface with monitoring. In this capacity, we wish to celebrate the life and acknowledge the key role of Maurice Albin, who passed in 2016. We are honored that Dr. Maurice Albin wrote the anesthesiologist viewpoint foreword to the first edition of this book. Similarly, many surgeons and interventionists have expanded the role of monitoring into existing and innovative new procedures. Finally, many neurophysiologists have also expanded our understanding of the role of monitoring and have developed enhanced techniques to meet the needs of various procedures. We owe a great deal of gratitude to all of these individuals as these developments have been included in this new expanded text.

As with the first edition of the book, the major theme of this edition is to emphasize the roles of all members of the procedure team cooperatively working together to provide the patient with the most effective techniques for ensuring an optimal outcome. Since this involves education across specialty boundaries, this book continues to take a holistic approach by discussing modalities and their application during various procedures. The second edition now has five news, key learning points, questions and answers and has expanded the learning opportunities to online resources including videos and hyperlinks to PubMed so as to enhance the text content. We are grateful to the publisher and the electronic resources that are available to include these

additions. We hope you will find that they are helpful in your patient care and eagerly look forward to further advancements in monitoring techniques and their improved understanding and application.

The international reach of the first edition of this book included both English and Chinese. With this edition, it has been expanded to include the Japanese and Korean languages as well. We are honored and grateful.

Antoun Koht
Tod B. Sloan
J. Richard Toleikis
Chicago, IL, USA, Aurora, CO, USA, Chicago, IL, USA

Preface to First Edition

Intraoperative monitoring of the nervous system (IOM) has become common place in orthopedics, neurosurgery, otologic surgery, vascular surgery, and other procedures. In addition to the improvement in patient outcome which has been observed in several circumstances, the monitoring has been incorporated into the management of surgical procedures where the nervous system is at risk. The use is being fueled by the understanding that functional knowledge of the nervous system is an important partner to structural knowledge and both contribute to the quality of care and patient safety.

IOM is more than just a tool like fluoroscopy, intraoperative MRI, or CT scanning which gives a structural view of the patient's anatomy. IOM provides a means for assessing the nervous system function and determining how the surgical, anesthetic, and physiological environment are impacting this function. Pamela Prior expressed it well in 1985 when she said "routine clinical monitoring of ECG, arterial pressure and blood-gas tensions only indicates the adequacy of factors supporting brain function. The EEG and evoked potentials are more valuable because they can monitor continuously the end result at a neuronal functional level."[1] This "window to the nervous system" allows all of us to bring our own contributions to help our patients have the best possible outcomes. The prompt diagnosis of circumstances unfavorable to the nervous system will enable timely adjustment of the pharmacologic and physiologic environment to augment surgical decision.

IOM has evolved in the last 30 years from the lonely somatosensory evoked potentials (SSEP) modality that was used during spine surgery to now include; MEPs, both free running and triggered EMG, D waves, the H reflex, and other monitoring modalities. This expansion was not restricted to spine surgery but extended to other surgeries including those of the head and neck. The addition of IOM multimodalities allowed a more comprehensive assessment of the nervous system while adding restraint on the anesthetic technique. The optimal anesthetics for one modality is often not the same as that for others, thus a very delicate anesthetic balance is needed and complete cooperation between the IOM team and the anesthesiologist is invaluable.

This team effort is the key to the best patient outcome. Clearly the monitoring is helpful to the surgeon, but it is equally valuable to the anesthesiologist. In that respect, IOM allows the anesthesiologist to see the

impact of the anesthetic and physiologic management on the functional integrity of the nervous system. For example, there is a growing appreciation that a blood pressure which might be appropriate for one patient may not be adequate for another. Further complicating factors are the aging patients with increased comorbidities and the more complex surgical procedures with increasing neurological trespass. IOM can help the anesthesiologist insure that the environment of the nervous system is optimal for the individual and to adjust the patient's physiology as needed when the surgical procedure places an additional stress on the nervous system.

This interplay of anesthesia, physiology, and surgery is what makes IOM different from the use of these techniques for diagnostic assessment of pathology in the nervous system. The situation is dynamic with a constantly shifting equilibrium of the effects of the procedure, the drugs given, and the physiological milieu. This is why IOM, like monitoring of blood pressure, heart rate, oxygenation, etc., must be done constantly to identify changes that allow rapid correction while adverse neurological circumstances are still reversible. Some of that reversibility will be contained in the surgical maneuvers, but changes in the management of the anesthesia, physiology, and positioning of the patient can mitigate some of the adverse effects of the procedure.

Well recognized by anesthesiologists, each patient is different, not only in their pathology and comorbidities, but also in how they will react to anesthesia and the surgical procedure. Each patient therefore presents a different problem. An injury could develop and progress without the surgeon's, proceduralist's, or anesthesiologist's knowledge. This is where IOM can become valuable to identify functional changes in the nervous system which will not be observed in structural studies or reflected in other means of traditional monitoring.

To make the team effort most effective, each member of the team needs to understand each other's roles. Like an interlocking crossword puzzle, the interface of each other's contribution is made stronger when each one knows about the other and the more effective the team becomes. This book is designed to help all members of the operative team to better understand what each member of the team is doing. It is not designed to provide technical details since there are many excellent papers and books on that subject. Rather we have sought to allow everyone an opportunity to gain insights into each of the operative components.

Many of the early applications of IOM were developed in the 1970s by surgeons, neurophysiologists, anesthesiologists, and other researchers both in the USA and Japan, as they recognized that the development of aggressive treatment programs carried a high risk of secondary spinal cord damage and that there was a need to develop methodologies for defining and evaluating spinal cord function. Among these were Clyde Nash, MD, and Richard Brown, PhD, who pioneered the use of SSEPs during Harrington distraction of the spine in patients with scoliosis [2]. This advance from the intraoperative wake-up test of Vauzelle and Stagnara would become increasingly important as procedures presented multiple possible injurious steps [3]. In patients with many significant comorbidities, a one-time clinical assessment which was used in healthy young patients with scoliosis is not applicable. The pioneers of IOM not only developed the techniques for monitoring, but they designed and built equipment to meet the specific challenges present in the operating room that were not encountered in the diagnostic laboratory. They also recognized the importance of the team effort and that such things as blood pressure management during distraction of the spine was essential for overcoming the effects of the procedure [2]. With an awareness that others were beginning to address the need for monitoring spinal cord function, Clyde Nash and Jerald Brodkey invited participants from throughout the world and hosted the first two symposia on spinal cord monitoring which were held in Cleveland in September 1977 and St. Louis in January 1979. These were followed by a series of International Symposia on spinal cord monitoring, the first of which was held in Tokyo, Japan, in 1981 and was hosted by Dr. Tetsuya Tamaki. Three years later, Dr. Johannes Schramm hosted the Second International Symposium held in Erlangan, Germany (1984). The Third and Fourth Symposia were later held in Annapolis, Maryland (in 1986) and Niigata, Japan (in 1989), and were hosted by Drs. Thomas Ducker and Richard Brown and by Dr. Koki Shimoji, respectively. Special thanks to these early pioneers who recognized the importance of this new technology and worked to strengthen it and expand its usage. Subsequent to the International Symposia came the formation of the American Society of Neurophysiologic Monitoring (ASNM) in 1989, and also the advent of the International Symposia on Intraoperative Neurophysiological Monitoring in Neurosurgery held in New York and hosted by Drs. Vedran Deletis and Fred Epstein (1998–2006). From these latter symposia came the formation of the International Society of

Intraoperative Neurophysiology (ISIN) in 2006.

IOM has evolved from the early days. Some of the techniques currently used are refinements of the early techniques while others are completely new. The monitoring professionals have recognized that the changes in neurophysiology that result from anesthesia and surgery are different from those seen in the laboratory which makes diagnostic approaches less applicable. Further, IOM must be done with constant, rapid updates to provide timely information about the state of the nervous system. This evolution in techniques has been accompanied with the development of a new field of intraoperative neurophysiology with professionals who have dedicated their career to IOM. The backgrounds of these individuals are as diverse as the techniques currently being employed. Some come from the logical pioneering fields of orthopedic surgery, neurosurgery, neurology, and anesthesiology. But a whole new field of intraoperative neurophysiology has developed with individuals bringing to bear their knowledge of intraoperative neurophysiology with the many allied medical fields to provide focused IOM care. These individuals have been responsible for many developments in the field and are key to the current utilization of monitoring for providing excellent patient care.

Many of the early developments of IOM can also be attributed to anesthesiologists. Recently, Tamaki (orthopedic surgeon) wrote an article about the history of EP monitoring and credited Shimoji (anesthesiologist) with introducing epidural evoked potential monitoring in 1971 [4]. Betty Grundy, MD, as an anesthesiologist involved in the early applications of IOM recognized this in 1982 when she wrote about the application of auditory evoked potentials in surgery on the brainstem in the *Journal of Neurosurgery* "we wanted early indication of deteriorating function so that we could intervene to prevent permanent injury. We therefore selected an approach similar to that used for intraoperative monitoring of other physiological parameters such as heart rate or arterial blood pressure, attempting to correct undesirable trends as soon as these could be identified with certainty" [5].

Dr. Grundy went on to bring IOM into anesthesiology; her landmark article in Anesthesiology in 1983 was a call for anesthesiologists to take an active role in the team. She noted that "the hope is that deteriorating neurologic function will be detected early so that the surgeon and/or anesthesiologist can intervene to optimize function and minimize the possibility of permanent damage to the nervous system" [6]. Dr. Grundy was

to further stress that role when she wrote in 1984 “the anesthesiologist has important responsibilities in facilitating the electrophysiological monitoring. A multiplicity of factors under their control of the anesthesiologist can alter evoked potentials” [7]. Her early experience noted the interaction of anesthesia, physiology, and the nervous system which supported her recommendations for anesthetic and physiological management; without IOM many unfavorable interactions would have gone unrecognized. These observations are still echoed today.

As IOM techniques and applications have evolved, some advancements have come from anesthesiologists. In particular, the anesthetic techniques and physiological management that supports IOM, and which have been refined from observations made by IOM, have also improved patient care. Many anesthesiologists remain actively involved in IOM and are contributors to this book.

As the field of IOM has developed, the cadre of IOM professionals that has emerged to provide the best neurophysiological monitoring has been a distraction from the integral role of anesthesiologists in the IOM team. As such, this book is devoted to restoring that role by focusing on the knowledge and experience gained by anesthesiologists and professionals who are part of the IOM team. Our goal is to facilitate the most effective team effort by expanding the interface of knowledge between the surgical, anesthesiological, and neurophysiological members.

The first section describes the different techniques used in monitoring. The goal is to provide insight into the anatomy, physiology, and techniques so that the information provided by their use can be placed in the context of the surgical, anesthetic, and physiological management.

The second section seeks to provide basic aspects of anesthetic management. Not only will this be helpful to anesthesia providers seeking to refine their choice of medications, but it also will be helpful to practitioners in other specialties to understand the challenges inherent in the anesthetic management. Some anesthesiologists are concerned about anesthesia without muscle relaxants while other members of the team may be concerned about any use of muscle relaxants. The contributions of the authors will be helpful to reassure both that it is possible to meet this need and successfully obtain optimal signals which will enable the team to effectively monitor the patients and for the surgeon to make the best decision.

Finally, the book provides case examples of specific types of procedures

where IOM has become a routine part of the management. In each case the chapter provides an overview of the anatomy, neural physiology, and pathology which is central to the procedure. Understanding this allows each member of the team to understand how the procedure, anesthesia, physiology, and IOM come to bear on the risks of the procedure and outcome. In each case, the authors have also presented some examples of typical IOM changes in these cases. This allows discussion of the differential diagnosis of the effects which could cause these changes. In that respect, the emphasis has been on non-surgical effects to allow better insight into the ways that the management of anesthesia, positioning, and physiology can contribute to improved outcome.

We have assembled a prestigious group of contributors who are all actively involved in the team efforts of IOM during various surgical procedures. Each has contributed their knowledge and experience to improve all of our effectiveness in these procedures. Hopefully, by sharing our knowledge and experience we can make the fabric of our team efforts stronger and provide the best possible care of our patients.

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Acknowledgment

We want to acknowledge our families; (TS) Celia, Wendy, and Heather; (JRT) Sandra, Jennifer Anne, Matthew, Jason, and Jennifer Rachel; (AK) Sonia, Yara, John, and Alexander who have provided love, support, and understanding during many late hours of monitoring and without which the creation of this book would not have been possible.

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Section I
Monitoring Techniques

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_1

1. Somatosensory-Evoked Potentials

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Keywords Somatosensory-evoked potentials – Anatomy – Vascular supply – Methods – Stimulation – Recording – Intraoperative variables – Pharmacology – Physiology

Key Learning Points

- The ultimate goal of intraoperative SSEP monitoring is to ensure maintenance of neurologic integrity throughout a procedure with resultant improved outcome and decreased morbidity.
- General consensus is that standard SSEP recording monitors solely the

dorsal column pathway, which mediates mechanoreception and proprioception. However, other pathways may contribute to somatosensory function, including the dorsal spinocerebellar tract, the anterolateral columns, the postsynaptic dorsal column pathway, and the vagus nerve.

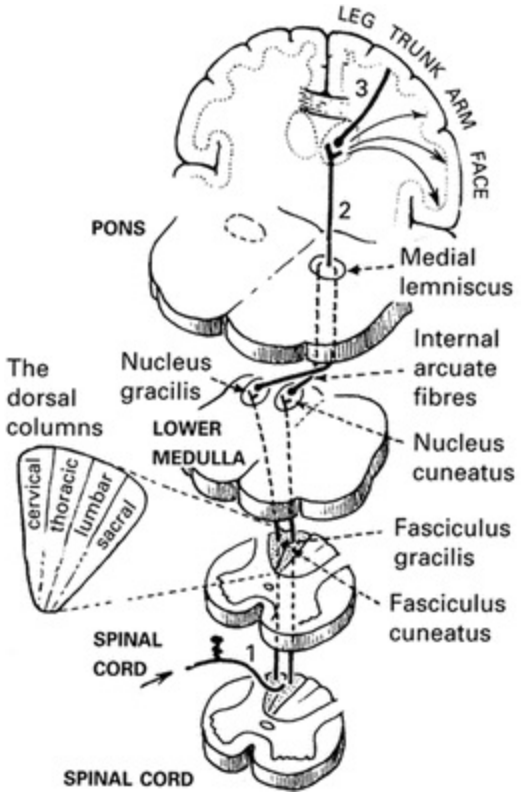
- Stimulation and recording are the two major technical aspects of SSEP monitoring; understanding the parameters that affect each is critical to successful intraoperative SSEP monitoring. Stimulation parameters include electrode type, electrode placement, stimulus intensity, stimulus duration, stimulus rate, and unilateral versus bilateral stimulation. Recording parameters include electrode type, electrode placement (recording montage), and specific equipment parameters, which include channel availability, filters, averaging, and time base.
- Most anesthetic agents have detrimental effects on SSEPs, while a select few actually have beneficial effects. In general, cortical effects are more pronounced than peripheral effects.
- Several physiologic variables can affect the success or failure of SSEP monitoring, including patient temperature, blood pressure, hemoglobin levels, intracranial pressure, oxygenation, and ventilation.
- Reproducible baseline waveforms are crucial in SSEP monitoring. Evidence-based recommendations on when to intervene when SSEP monitoring is altered from baseline are difficult to provide due to the low specificity of SSEP monitoring. However, general consensus is that a 50 % amplitude reduction and 10 % increase in latency, not attributable to anesthetic or physiologic causes, are significant changes that warrant intervention.

Intraoperative application of evoked potentials has evolved during the past 30 years, and somatosensory-evoked potential (SSEP) monitoring is the method most commonly employed [1]. The ultimate goal of intraoperative SSEP monitoring is to ensure maintenance of neurologic integrity throughout a procedure with resultant improved outcome and decreased morbidity. The premise of evoked potentials is simple. When neural tissue is stimulated, either by true sensory or artificial electrical stimulation, ascending electrical impulses—or volleys—are sent through synapses via neural pathways. Depending on stimulation site and recording location, there is characteristic

waveform morphology of the volley. Near-field potentials result when the neural impulse passes immediately beneath the reference electrode. Far-field potentials result from impulses distant to the recording electrodes. SSEPs are, in general, mixed-field potentials [2]. The value of intraoperative SSEP monitoring is derived from consistency—reproducible, recognizable waveforms—such that meaningful conclusions can be extrapolated from data for surgical guidance. An appreciation of the anatomy and the technical aspects of SSEPs is required for this consistency and successful intraoperative employment.

Anatomy and Vascular Supply

The somatosensory system consists of the dorsal column–lemniscal pathway (Fig. 1.1), or posterior column pathway, and the spinothalamic pathway. The former pathway mediates mechanoreception and proprioception, whereas the latter mediates thermoreception and nociception. The general consensus is that standard SSEP recording monitors solely the dorsal column pathway. However, other pathways may contribute to somatosensory function, including the dorsal spinocerebellar tract, the anterolateral columns, the postsynaptic dorsal column pathway, and the vagus nerve [1, 3].



DORSAL COLUMN PATHWAY

1. Fibres enter in the root entry zone and run upwards in the *dorsal columns* to the *lower medulla* where they terminate in the *nucleus gracilis* and *nucleus cuneatus*.
2. *Second order neurons* decussate as the *internal arcuate fibres* and pass upwards in the *medial lemniscus*. Maintaining a *somatotopic arrangement*, they terminate in the ventral posterolateral thalamus.
3. *Third order neurons* arise in the thalamus and project to the *parietal cortex*.

Fig. 1.1 The dorsal column pathway . (*1*) Fibers enter in the root entry zone and run upward in the dorsal columns to the lower medulla where they terminate in the nucleus gracilis and nucleus cuneatus. (*2*) Second-order neurons decussate as the internal arcuate fibers and pass upward in the medial lemniscus. Maintaining a somatotopic arrangement, they terminate in the ventral posterolateral thalamus. (*3*) Third-order neurons arise in the thalamus and project to the parietal cortex (from Lindsay and Bone [83]; with permission)

The pathway of the dorsal column–lemniscal tract begins with peripheral receptor stimulation of a first-order neuron in the dorsal root ganglia. This afferent volley is sent via the ipsilateral posterior spinal cord to the medullary nuclei to synapse on second-order neurons. These second-order neurons decussate in the medulla as the internal arcuate fibers and ascend in the medial lemniscal pathway to third-order neurons in the ventroposterior nuclei of the thalamus, maintaining a somatotopic arrangement. Projections from the thalamus proceed to the sensorimotor cortex, where further synapsing occurs. Synapses are believed to be the site of action for inhalational anesthetics; thus, the early SSEP response is minimally affected by inhalational anesthetics. However, as the volley ascends the dorsal column–lemniscal pathway and more synapses occur en route to the cortex, cortical SSEPs are increasingly susceptible to the effects of inhalational anesthetics (see Chap. 19 for more discussion of anesthesia) [1, 4, 5]. Perfusion to the dorsal

column–lemniscal pathway usually comes from the posterior spinal arteries in the spinal cord. The posterior spinal artery originates from the vertebral arteries and travels bilaterally the length of the spinal cord in the posterior lateral sulci, supplying the posterior one-third of the spinal cord, including the posterior horns as well as the dorsal column–lemniscal pathway [6]. The anterior spinal artery, also arising from the vertebral arteries, supplies the anterior and anterolateral two-thirds of the spinal cord, including the anterior horns, spinothalamic tracts, and corticospinal tracts. However, there is a great degree of individual variability in origin of vascular supply for both the posterior and anterior spinal arteries, with each being supported by a varying number of radicular arteries, particularly in the thoracic spinal cord. Chapter 40 ("Electrophysiological Monitoring During Thoracic Aortic Aneurysm Surgery") discusses blood supply of the spinal cord in greater detail.

As the dorsal column–lemniscal pathway ascends to the medullary nuclei of the brainstem, perfusion comes from both the vertebral artery and perforating branches of the basilar artery. While the somatosensory cortex maintains somatotopic arrangement, blood supply is divided into the anterior and middle cerebral artery. The anterior cerebral artery supplies the cortex representing the lower extremity while the middle cerebral artery supplies the cortex supplying the face, head, neck, trunk, and upper extremity.

Venous drainage is provided by a large venous network encircling the spinal cord. This network flows to either the median posterior or anterior spinal veins. Venous blood then flows through numerous radicular veins and ultimately to the azygous and pelvic venous systems [6, 7].

Methods

As mentioned, the foremost goal of SSEP monitoring should be consistency. Achieving this consistency requires manipulation of the two major technical aspects of acquiring SSEPs: stimulation and recording. The following recommendations are based largely on published guidelines from "Intraoperative Monitoring Using Somatosensory Evoked Potentials: A Position Statement by the American Society of Neurophysiological Monitoring" [1].

Stimulation

In order to achieve consistent intraoperative SSEP monitoring , adequate stimulation must be applied. Stimulation parameters include electrode type, electrode placement, stimulus intensity, stimulus duration, stimulus rate, and unilateral versus bilateral stimulation. The specific hardware and software employed for stimulation and recording exists in a variety of commercially available units [1, 2, 8–10].

The first step to meaningful intraoperative SSEP monitoring is stimulating appropriate nerves for a given operation. In general [1, 8, 9], nerves chosen for intraoperative monitoring should be below, with recording sites above, the area at risk from surgery such that the monitored pathway travels through the neural area at risk. For example, during corrective thoracic scoliosis surgery, monitoring solely upper extremity SSEPs would be insufficient as the lower extremity dorsal column tract through the spinal cord would be missed. For this example, it would be useful to monitor the upper extremity SSEPs for position-related injury. The upper extremity SSEPs would also provide useful information for interpreting the lower extremity SSEPs. In this case, a significant amplitude reduction throughout all waveforms is more likely to be related to anesthetic or physiologic parameters than if the amplitude change occurred in just the lower extremity SSEPs.

From a hardware standpoint , successful SSEP monitoring begins with proper electrode selection. Stimulation electrode options include bar electrodes, EEG metal disk electrodes, subdermal needle electrodes, and adhesive surface electrodes. While each has advantages and disadvantages, adhesive surface electrodes are typically used intraoperatively as they are noninvasive and adhere reliably throughout the dynamic intraoperative period (including patient position changes and patient edema). Subdermal needle electrodes are also commonly used by many providers, especially when stimulation must occur within the sterile field as they can be placed intraoperatively in a sterile fashion by the surgeon. Subdermal needle electrodes are also recommended in cases where stimulation needs to occur closer to the nerve (e.g., obese or edematous patients).

Correct placement of stimulation electrodes with respect to the nerve is also critical to adequate stimulation and subsequent stable SSEPs. Placement is dependent on both the electrode being used and the nerve being stimulated (e.g., surface electrodes are generally placed 2–3 cm apart, whereas subdermal needles are placed 1 cm apart) [1, 2, 8–10].

For upper extremity SSEPs, frequently used peripheral nerves include the median nerve (C5-T1) at the wrist and the ulnar nerve (C8-T1, ± C7) at the wrist or elbow. For median nerve stimulation, the cathode is placed over the median nerve 2–4 cm proximal to the wrist crease, and the anode is placed 2–3 cm distal over the median nerve (Note: The cathode is the proximal electrode connected to the negative pole of the stimulator; the anode is the distal electrode connected to the positive pole; this convention is used to avoid a phenomenon known as anode blocking). For ulnar stimulation at the wrist, the cathode is placed 2–4 cm proximal to the wrist crease and the anode is placed 2–3 cm distal, both over the ulnar nerve. Ulnar nerve stimulation at the elbow begins by locating the ulnar groove. The cathode is then placed 2 cm proximal to the elbow crease at the ulnar groove, while the anode is placed 2–3 cm distal over the ulnar nerve. For these mixed nerves, corresponding muscle twitch (i.e., thumb adduction) with stimulation confirms appropriate electrode placement [1, 8–10].

Lower extremity peripheral nerves commonly used for intraoperative monitoring include the posterior tibial nerve (L4–S3) at the ankle and the peroneal nerve (L4–S2) at the head of the fibula. For posterior tibial nerve stimulation, the cathode is placed between the medial malleolus and the Achilles tendon, just proximal to the malleolus; the anode is placed 2–3 cm distal over the posterior tibial nerve as it courses around the medial malleolus. For peroneal nerve stimulation, the cathode is placed just medial to the head of the fibula. The anode is placed 2–3 cm distal. For these mixed nerves, corresponding muscle twitch (i.e., plantar toe flexion with posterior tibial nerve stimulation and eversion of the foot with peroneal nerve stimulation) with stimulation confirms appropriate electrode placement [1, 8–10].

The electrical stimulus applied during SSEP monitoring is a series of square-wave pulses, with durations of 0.1–0.3 ms, at a given intensity [1, 3, 8, 9]. When stimulating mixed sensory and motor nerves, the stimulus intensity is adjusted to elicit a minimal twitch of the distal muscles innervated by the peripheral nerves. In purely sensory nerves, stimulation intensity two to three times the sensory threshold is recommended [2]. Typical intraoperative stimulation intensity ranges from 10 to 50 mA. However, stimulation intensity up to 100 mA may be required intraoperatively to elicit a reproducible, recognizable waveform, as there may be underlying pathology in addition to the deleterious effects of anesthetics on SSEPs [1].

Possible tissue damage from repeated high current at the stimulation sites warrants consideration, but the literature contains no evidence to support this concern as long as stimulation is within parameters on commercially available instruments for SSEP monitoring [1]. Use of constant current stimulation is recommended to compensate for any change in contact resistance. This compensation is limited by the maximum output voltage of the stimulator. With constant current stimulation, the output of the stimulator is current-limited when contact resistance is excessive. Most instruments designed for SSEP monitoring have a built-in warning for this [1, 8, 9].

The frequency of stimulation generally ranges from 2 to 5 Hz [1, 8–10]. To decrease noise with averaging, the rate of stimulation should not be an integer multiple of the line power supply frequency (50 or 60 Hz), the most common noise frequency . When excessive noise occurs, small changes in the stimulus rate may improve the SSEP quality [1, 11].

Stimulation can be unilateral or bilateral. Simultaneous bilateral stimulation can enhance SSEPs, while potentially masking unilateral changes. To effectively and simultaneously monitor both sides of an extremity pair, interleaved unilateral (alternating left and right) stimulation is recommended [1].

Recording

In conjunction with adequate stimulation , appropriate recording techniques must be employed to achieve consistent intraoperative SSEP monitoring. Recording parameters include electrode type, electrode placement (recording montage), and specific equipment parameters, which include channel availability, filters, averaging, and time base.

As with stimulating electrodes , a variety of recording electrodes are available, each with attendant advantages and disadvantages. For intraoperative SSEP recording, subdermal needles and metal disk electrodes are used most frequently. Subdermal needles are placed quickly, though they must be secured with tape or surgical staples to prevent dislodging. Metal cup electrodes take longer to secure and require conductive gel or paste. Corkscrew electrodes, like subdermal needles, are quickly placed and have the advantage of being fairly secure. For direct cortical recording, as employed during corticography, strip or grid array electrodes are used [1, 10, 12, 13]. A ground electrode is placed between the stimulation sites and

recording electrodes, usually on the shoulder [3].

As mentioned previously, recording sites for intraoperative monitoring should be proximal to the surgical area at risk, with stimulation sites distal. As the neural volley ascends the dorsal column–lemniscal pathway, different generators of the potential are recorded by various recording electrodes.

Recording electrical activity requires measurement of voltage between two electrode sites, an active electrode and a reference electrode. These electrode pairs are called recording montages , denoted by: active electrode–reference electrode. In general, one cortical montage and one subcortical montage are used to record the ascending neural volley for intraoperative SSEPs. Scalp electrode locations for recording are based on the 10–20 International System of EEG electrode placement (Fig. 1.2). An additional recording site, distal to the stimulation site but proximal to the surgical site, is often used to verify peripheral conduction [1].

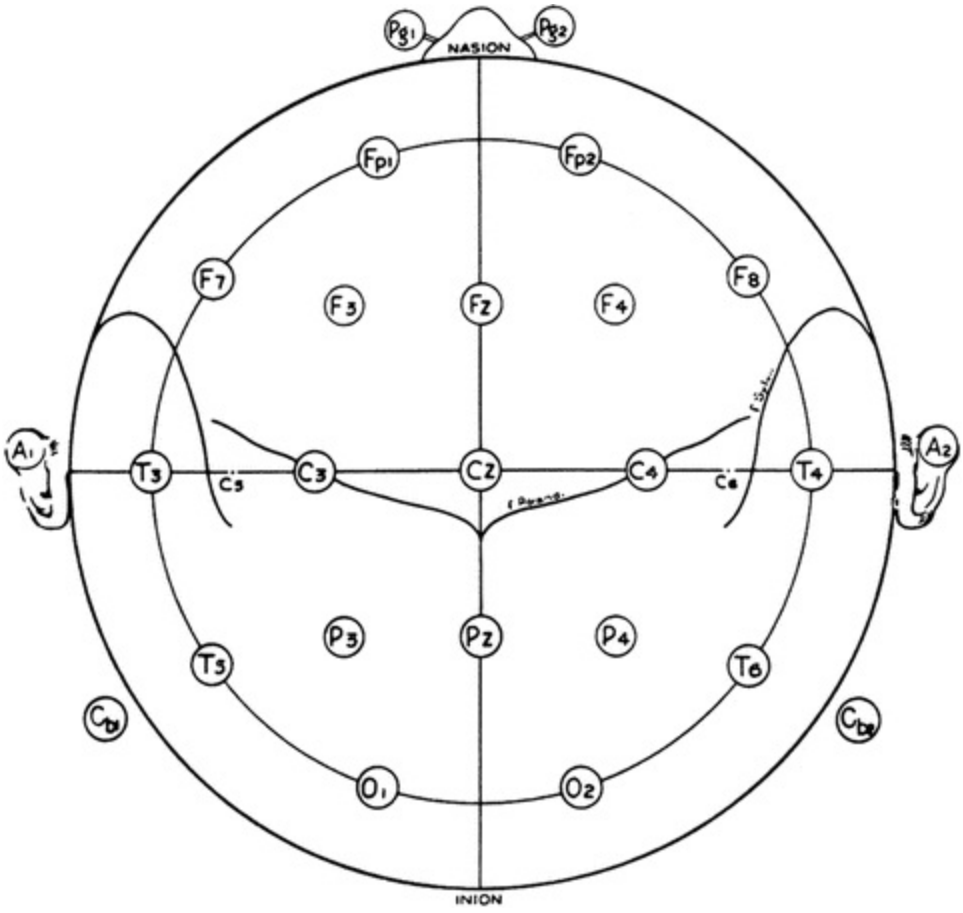


Fig. 1.2 10–20 International System of Electrode Placement. A single plane projection of the head, showing all standard positions and locations of the rolandic and Sylvian fissures. The outer circle was

drawn at the level of the nasion and inion. The inner circle represents the temporal line of electrodes. This diagram provides a useful stamp for the indication of electrode placements in routine recording. "CP" and "FP" locations are midway between the designated "C" and "P" or "C" and "F" locations, respectively, "c" and "i" indicate respective locations contralateral or ipsilateral to the side of stimulation, respectively (from Klem et al. [84]; with permission)

A recording from a given montage for a specific stimulated peripheral nerve has a characteristic waveform distribution measured in amplitude (microvolts) and latency (milliseconds). This is recorded on a graph of voltage (microvolts) versus time (milliseconds) and represents the SSEP. In general, this characteristic morphology is from synapses at sites along the neural pathway. These sites are referred to as the generators of the waveform. Waveforms are labeled "N" and "P" to represent the polarity of the signal (generally negative is up, positive is down, although the specific convention used may vary by individual) followed by an integer to represent the poststimulus latency of the wave in normal adults. For example, for cortical recording from median nerve stimulation, characteristic peaks N20 (a negative, or upward, deflection at about 20 ms) and P22 (a positive, or downward, deflection at about 22 ms) define the amplitude of the waveform (Figs. 1.3 and 1.4). The generators of these peaks are thought to be the thalamus and somatosensory cortex [1, 9].

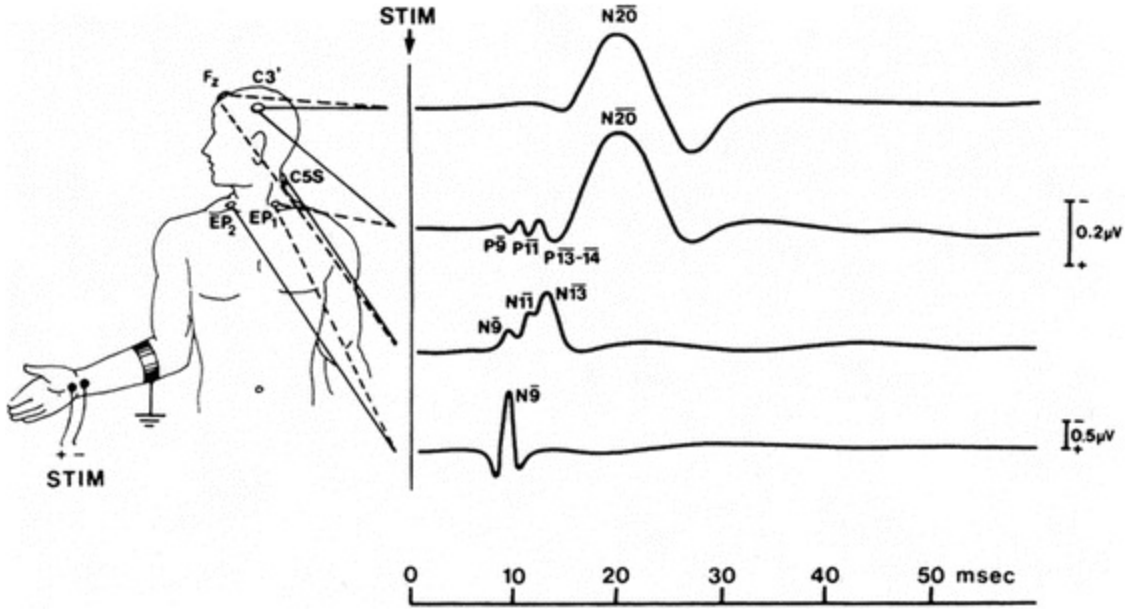


Fig. 1.3 Schematic diagram of normal SSEPs to arm stimulation . Tracings are obtained from the regions identified on the anatomic model (from Misulis and Fakhoury [2]; with permission)

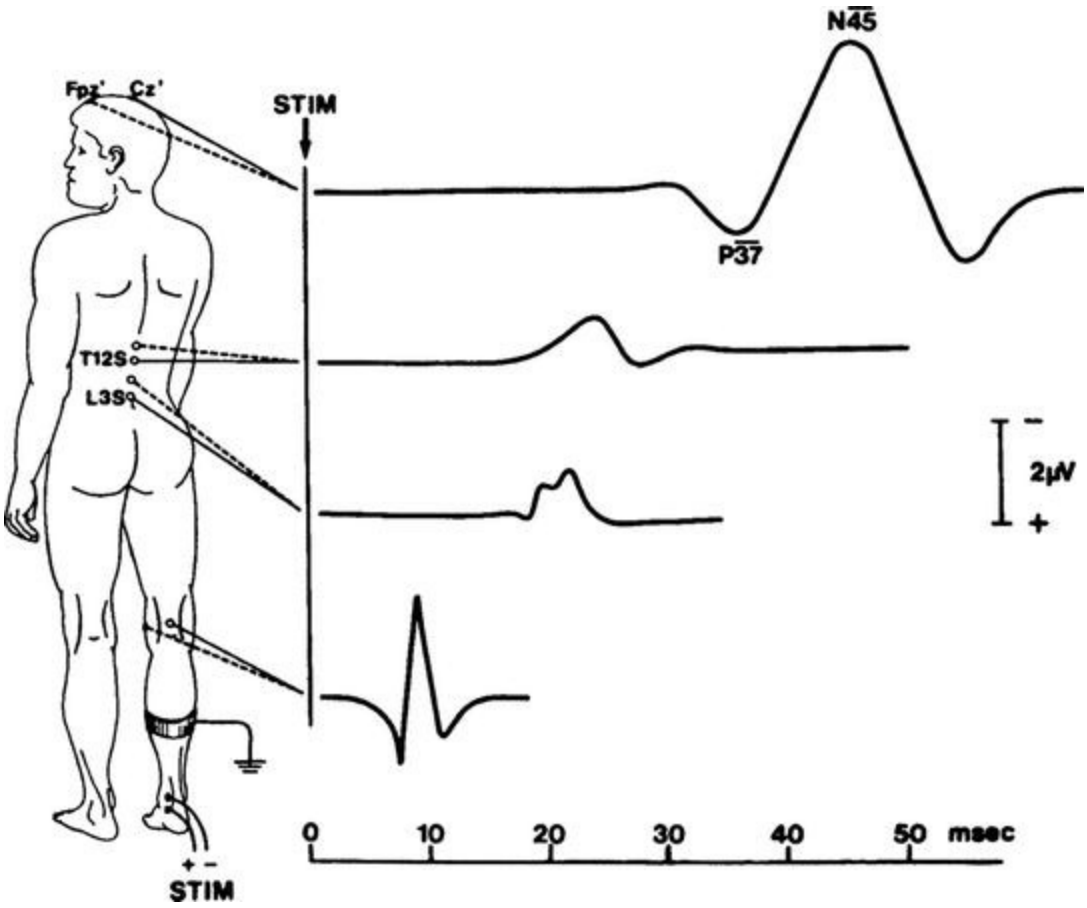


Fig. 1.4 Normal posterior tibial nerve SSEPs. Traces from bottom to top show popliteal fossa potential, lumbar potential, low thoracic potential, and scalp potential (from Misulis and Fakhoury [2]; with permission)

Table 1.1 is not meant to be an exhaustive list of possible recording montages for upper extremity and lower extremity peripheral nerve stimulation. However, it is meant to assist with understanding evoked potentials and provide a background for intraoperative monitoring.

Table 1.1 Neural generators for median and tibial nerve SEP generators[a]

Median nerve SEP generators				**Tibial nerve SEP generators**			
Label	**Generator**	**Common channels used**	**Alternate labels**	**Label**	**Generator**	**Common channels used**	**Alternate labels**
N9	Brachial plexus	EPi-EPc	Erb's	Popliteal	Tibial nerve action potential	Popliteal	
N11	Spinal nerve root	Crv-Fpz		N23	Dorsal horn interneurons	T12-iliac cr.	Lumbar point

N13a	Dorsal horn interneurons	Crv6-Fpz	Cervical, subcortical	P31	Medulla	Crv-Fpz, Mast-Fpz	Cervical subcortical
N13b	Dorsal column	Crv2-Fpz	Cervical, subcortical	N34	Primary sensory cortex	Cc-Fpz	N37
P13	Spinomedullary junction	Crv-Fpz, Mast-Fpz	Cervical, subcortical	P38	Primary sensory cortex	Ci-Fpz, Cz′-Fpz, Ci-Cc, Cz′-Cc	P39, P40, cortical
P14	Lemniscal paths, cuneate nucleus	Crv-Fpz, Mast-Fpz	Cervical, subcortical	N38	Primary sensory cortex	Cc-Fpz	
N18	Brainstem/thalamic	Ci-noncephalic					
N19	Primary sensory cortex	Cc-Fz, Cc-Ci	N20, cortical				
P22	Primary motor cortex	Cc-Fz, Cc-Ci					

[a]From Minahan and Mandir [82]; with permission

For upper extremity peripheral nerve stimulation, there are several montages commonly used for cortical recording. The responses recorded are most likely generated by the thalamus and somatosensory cortex. Since cortical responses are characteristically sensitive to general anesthetics, and because patients in the operating room may have underlying neurologic injury, different montages may be used to enhance cortical response amplitude. Montages include CPc–2 cm posterior to CPc (contralateral cortex to the stimulus; i.e., CP3 for right arm stimulation and CP4 for left arm stimulation), CPc–Fz (midline frontal electrode), CPc–FPz, and CPc–CPi (cortex ipsilateral to the stimulus) [1, 3, 10].

For subcortical recording of upper extremity peripheral nerve stimulation, response generators vary with the montage used and include the spinal cord, the cervicomedullary junction, higher parts of the brainstem, and the thalamus. Common montages include CPi–Erbc (Erb's point contralateral to the stimulus), CvN (posterior spinal cervical electrode over the Nth cervical spinous process, typically C6 or C7)–Fz, Fz–A1A2 (linked ear electrodes), Cz–A1A2, and FPz–A1A2 [2, 3, 10].

Cortical recording of stimulation of lower extremity peripheral nerves represents generators of the neural volley in the somatosensory cortex. Recording montages used include CPz–2 cm posterior to Cz, CPz–Fz, CPz–

CPc, and FPz–Cz [2, 3, 10].

The generator source(s) of far-field subcortical potentials from lower extremity peripheral nerve stimulation are thought to lie in the brainstem. Recording montages to acquire these potentials include CPi–A1A2, CvN–Fz, and FPz–A1A2 [2, 3, 10].

Peripheral recording of the nerve volley distal to the stimulation site but proximal to the surgical site can confirm the conduction of the peripheral stimulus. For lower extremity SSEPs, this site is the ipsilateral popliteal fossa —one electrode at the popliteal fossa (4–6 cm above crease) and the other placed 2–4 cm proximal. For upper extremity SSEPs this site is the ipsilateral Erb's point (2 cm above the midpoint of the clavicle and at the posterior border of the head of the sternocleidomastoid muscle) referenced to the contralateral Erb's point or a scalp electrode, often Fz [1, 3, 10].

After acquisition of the evoked potential, some signal manipulation is required to distinguish the evoked potential from background noise such as spontaneous EEG activity, ECG activity, muscle activity, or 60 Hz noise. Amplifiers are used to increase the size of the biologic signal, while filters are used to reduce noise. The signal is averaged over repeated stimuli to increase the signal-to-noise ratio [1].

Filters should be set to provide quality potentials with the least amount of averaging. Low frequency (high pass) filter and high frequency (low pass) filter settings are combined to eliminate components of the acquired potential outside the range of the evoked potential being studied. For most instruments, the standard settings are 20 Hz for the low frequency filter and 3000 Hz for the high frequency filter. Maintaining standard settings allows a laboratory to make meaningful comparisons for any given patient to laboratory normals [1].

However, since intraoperative potentials are also compared to a patient's baseline recorded earlier in the case, other suggested settings specific to either cortical or subcortical potentials have been suggested. For cortical potentials, these suggested filter settings are 1–30 Hz for the low frequency filter and 250–1000 Hz for the high frequency filter. For subcortical potentials, 30–100 Hz and 1000–3000 Hz are suggested, respectively. To improve cortical SSEPs, setting the high frequency filter as low as 300–500 Hz may help decrease artifact as the relative frequency content of cortical potentials is lower than subcortical potentials. The 60-Hz rejection filter should be reserved as a last resort to improve SSEPs as it can cause "ringing

artifact” [1, 8–10].

Recorded potentials are averaged over repeated stimuli to increase the signal-to-noise ratio. Guidelines have suggested acquiring 500–2000 trials per averaged response [1, 8, 9]. However, the signal-to-noise ratio and need for prompt intraoperative reporting may dictate the number of trials averaged. The optimal choice of montage allows the largest signal-to-noise ratio , which minimizes the number of averages needed and the acquisition time of a response [12–15]. In addition, in a rare patient, the somatosensory fibers are uncrossed such that the ipsilateral and contralateral cortex need to be evaluated for the maximal amplitude [16].

The timebase (milliseconds) for waveform display also needs to be appropriate for the given potential. Generally, this means 50 ms for upper extremity potentials and 100 ms for lower extremity potentials [1]. Also, in the presence of underlying abnormal neurologic function and subsequent increased latency of SSEPs, the timebase may need to be increased to adequately acquire and display the evoked potential.

Intraoperative Variables Affecting SSEPS: Pharmacology and Physiology

In addition to the stimulation and recording parameters discussed earlier, pharmacologic and physiologic variables can also significantly affect the reliable recording of evoked potentials. Understanding how these variables influence the process is essential to successful intraoperative SSEP monitoring.

Anesthetic drugs have various effects on SSEPs . While the mechanisms of action for specific anesthetic drugs differ along with each drug’s effect on SSEPs (i.e., some drugs enhance SSEPs, while most decrease SSEPs), all anesthetics share a general mechanism of action by either altering the function of synapses or axonal conduction to change neuronal excitability (see Chap. 19) [4, 5]. As the number of synapses in a pathway increases, the effect of a given anesthetic drug on the SSEP is more pronounced. Therefore, cortical potentials are more sensitive than subcortical, spinal, or peripheral nerve recordings to anesthetic effects [1, 4, 17]. This includes both deleterious and augmentative effects on SSEPs.

Inhalational Anesthetics

Halogenated inhalational agents produce a dose-related reduction in amplitude and increase in latency of SSEPs. This SSEP decrement is more pronounced for cortical recordings than subcortical, spinal, or peripheral recordings· [1, 4, 17].

Nitrous oxide decreases cortical SSEP amplitude and increases latency [18, 19]. This effect is synergistic with halogenated inhalational agents and most intravenous anesthetics [1, 4, 17, 19, 20]. For example, with equipotent doses, nitrous oxide combined with halogenated agents produces a greater decrease in amplitude and increase in latency of the cortical SSEP [15, 19]. As with halogenated agents, the effect on subcortical and peripheral SSEPs is minimal [1, 4, 17, 19].

Intravenous Anesthetics

In general, the intravenous drug effects on SSEPs are less than those from inhalational agents. With the exceptions of etomidate and ketamine, minimal effects on cortical SSEPs are seen with low doses of intravenous anesthetics. Moderate reduction in amplitude and increase in latency are seen with higher doses, again with the exceptions of etomidate and ketamine. Most intravenous agents have negligible effects on subcortical SSEPs. The following provides details for specific intravenous anesthetic effects on SSEPs.

Barbiturates produce a short-term dose-dependent reduction in amplitude and increase in latency of cortical SSEPs, with little effect on subcortical and peripheral SSEPs [1, 4, 17, 21]. Specifically, the SSEP decrement for induction doses of thiopental lasts less than 10 min [20–23]. Infusion of methohexital as part of a total intravenous general anesthetic has been shown to provide excellent conditions for SSEP monitoring [24]. Even at doses causing coma, barbiturates allow the monitoring of cortical SSEPs [1, 4, 21, 25–28].

Propofol influences SSEPs in a similar manner to that of barbiturates but with desirable rapid emergence after prolonged infusion. As a one-time induction dose, there is no change in amplitude for cortical and subcortical SSEPs from median nerve stimulation, but there is a mild increase in cortical latency [21, 29]. Propofol induction and infusion causes cortical amplitude

reduction with recovery after infusion termination [4, 30]. Propofol has no effect on epidural-evoked potentials [4, 31]. Combined with opioids, propofol produces less cortical amplitude depression than nitrous oxide or midazolam [1, 21, 32–35]. Compared to equipotent doses of halogenated agents [1, 3] or nitrous oxide [1, 36], the amplitude decrement is less with propofol. As part of a balanced total intravenous anesthetic, propofol is compatible with intraoperative monitoring of SSEPs [1, 4, 21, 33, 37, 38].

Etomidate and ketamine are unique in that they increase cortical SSEP amplitude. Etomidate produces a marked increase in cortical amplitude and a mild increase in cortical latency [1, 4, 17–22, 37]. Etomidate's effects on subcortical amplitude vary from no change to mild reduction [1, 4, 17, 20–22, 37, 38]. Despite this potential for subcortical SSEP amplitude reduction and variable peak specific effects on latency, infusion of etomidate as part of a total intravenous general anesthetic has been used to improve cortical SSEPs [4, 39, 40], even when intraoperative monitoring was otherwise unobtainable [4, 39]. Etomidate has the drawback of adrenal suppression.

Ketamine increases cortical SSEP amplitudes with no change in cortical latency or subcortical potentials [1, 4, 21, 41, 42]. The addition of nitrous oxide [4, 41] or enflurane 1.0 MAC [4, 43] to a ketamine anesthetic decreases SSEP amplitude by approximately 50 %. However, ketamine has been used successfully as part of a balanced anesthetic with midazolam and nitrous oxide for intraoperative SSEP monitoring during spine surgery [21, 44] and is an acceptable component of total intravenous anesthesia (TIVA) for SSEPs [1, 3]. Drawbacks to ketamine include hallucinations, long half-life with subsequent prolonged emergence, sympathomimetic effects, and increased intracranial pressure in the setting of intracranial pathology.

The alpha-2 agonists clonidine and dexmedetomidine are anesthetic agents with a broad spectrum of applications. Adjuvant clonidine [21] and dexmedetomidine [21, 45–47] use is compatible with intraoperative SSEP monitoring.

In general, systemic opioids mildly decrease cortical SSEP amplitude and mildly increase latency with minimal effect on subcortical and peripheral potentials [1, 4, 19, 21]. Bolus dosing of opioids has a greater impact on SSEP changes than continuous infusion [1]. Therefore, opioid infusions are an important component of anesthesia for intraoperative SSEP monitoring. Remifentanil is often used as it has a short context sensitive half-time and promotes rapid emergence. Neuraxial opioids, excluding meperidine, have

minimal or no effect on SSEPs [4, 17, 21, 48–51]. The decreased cortical amplitude and increased cortical latency seen with subarachnoid meperidine [21, 48] is likely secondary to its local anesthetic-like qualities. Neuraxial opioid-only techniques can augment analgesia without affecting intraoperative SSEP monitoring.

Benzodiazepines have mild depressant effects on cortical SSEPs [1, 4, 21]. In the absence of other agents, midazolam causes mild to no depression of cortical SSEPs, a moderate increase in N20 latency, and minimal to no effects on subcortical and peripheral potentials [1, 4, 20, 52]. Used as an intermittent bolus or continuous infusion (50–90 μg/kg/h) to promote intraoperative SSEP monitoring [1], midazolam is useful to promote amnesia with TIVA and to ameliorate hallucinations with ketamine [17].

Droperidol, a sedative-hypnotic used in neuroanesthesia, has minimal effects on SSEPs [1, 4, 17]. Concern for QT prolongation is a consideration.

Neuromuscular blocking agents commonly used during general anesthesia do not directly affect SSEPs. However, by decreasing electromyographic artifact and/or interference from muscle groups near recording electrodes, neuromuscular blockers may increase the signal-to-noise ratio and improve the quality of SSEP waveforms [4, 21, 53].

Perioperative infusion of systemic lidocaine is used to decrease postoperative pain. Infusion of relatively high-dose lidocaine has been shown to decrease cortical SSEP amplitude and increase latency [54], while lower infusion rates have been shown to have no effect [55].

Summarizing pharmacologic effects, intravenous anesthetic agents are more compatible with intraoperative monitoring of SSEPs than inhalational agents. While inhalational agents have been used in low dose combined with other intravenous agents, TIVA is preferred for consistent intraoperative SSEP monitoring in patients with small-amplitude SSEPs. Also, motor-evoked potentials (MEPs) are frequently paired with intraoperative SSEP monitoring and are extremely sensitive to inhalational agents, often requiring TIVA. TIVA can be any combination of intravenous drugs for end-effects of hypnosis, amnesia, analgesia, optimal surgical conditions (i.e., an immobile patient), and quick metabolism for an immediate postoperative neurologic examination. A typical infusion combination is propofol and remifentanil with intermittent midazolam, with or without muscle relaxant. However, as mentioned previously, various other hypnotic and opioid drugs may be used. To help ensure amnesia, a monitor of anesthetic depth may be useful (see

Chap. 19 for additional information about anesthesia considerations).

The physiologic milieu of an intraoperative patient is very dynamic and can affect SSEP amplitude and/or latency.

Temperature

Changes in body temperature affect SSEPs . Mild hypothermia increases cortical SSEP latency but has little effect on cortical amplitude and subcortical or peripheral responses [1,]. Mild hypothermia (down to 32 °C) may even be associated with increased cortical amplitudes [56–58]. With profound hypothermia, cortical SSEPs disappear. Subcortical, spinal, and peripheral responses may remain with increased latency, but they also disappear at lower temperatures [1, 59]. Rewarming improves the latencies but not in the reverse trajectory as cooling [1, 21]. Mild hyperthermia (39 °C) is associated with a decrease in cortical and subcortical latencies with no change in amplitudes [21, 60].

Similar to core temperature, local temperature changes at anatomic sites can affect SSEPs. For example, temperature changes at the surgical site from surgical exposure or cold irrigation in the surgical field can affect SSEPs. Also, stimulating an extremity exposed to cold intraoperative temperatures, with or without cold intravenous fluid infusing, may affect SSEPs [4].

Tissue Perfusion

Changes in blood pressure can affect tissue perfusion and thus can affect SSEPs. If perfusion is insufficient to meet basic metabolic demands of the tissue, cortical SSEP amplitude begins to diminish. With normothermia, this occurs when cerebral perfusion decreases to about 18 cm^3/min/100 g of tissue [1, 4, 17, 61–63]. Further reductions in perfusion below approximately 15 cm^3/min/100 g of tissue can cause loss of cortical SSEPs [1, 4, 51, 53, 61–63]. Subcortical responses are less sensitive to reductions in tissue perfusion.

Regional ischemia, with or without any degree of systemic hypotension, can be caused by local factors that can affect SSEPs. Examples include spinal distraction, surgical retractor-induced ischemia, position ischemia, tourniquet-induced ischemia, ischemia from vascular injury, and vascular clips (either temporary or permanent) [4, 64–66].

Oxygen delivery is affected by changes in hematocrit , which alters oxygen-carrying capacity and blood viscosity. Primate data reveal that in general, mild anemia produces an increase in SSEP amplitude. Primate data also reveal that reductions in hematocrit beyond mild anemia cause further SSEP amplitude reduction and increase in SSEP latency [4, 21, 67, 68].

Oxygenation/Ventilation

Variations in both oxygen and carbon dioxide levels can affect SSEPs. Mild hypoxemia does not affect SSEPs [4, 69]. A decrease in SSEP amplitude was reported as a manifestation of intraoperative hypoxemia [70]. Up to a $PaCO_2$ of 50 mmHg, hypercarbia has no effect on human SSEPs [21, 71]. Cortical amplitude augmentation and a mild decrease in latency occur with hyperventilation in awake volunteers [21, 69]. However, in isoflurane-anesthetized patients, hypocapnia to 20–25 mmHg caused no change in amplitude and a mild decrease in latency [21, 72].

Intracranial Pressure

Increased intracranial pressure decreases amplitude and increases latency of cortical SSEPs [4, 59]. As intracranial pressure increases, there is pressure-related cortical SSEP decrements and concurrent loss of subcortical responses with uncal herniation [4].

Other Physiologic Variables

A multitude of other physiologic factors may affect SSEPs, including fluctuations in electrolytes and glucose, total blood volume, and central venous pressure [4].

Criteria for Intervention During Intraoperative SSEP Monitoring

Reproducible, recognizable baseline waveforms are the foundation of successful intraoperative SSEP monitoring. It is from these baselines that intraoperative changes are based. The dynamic intraoperative milieu,

including surgical and anesthetic influences, can make the process of SSEP monitoring challenging and complicate the interpretation of the significance of changes from baseline. Providing evidence-based alarm criteria for intraoperative changes in amplitude and latency is difficult. Intraoperative SSEP changes of 45–50 % amplitude reduction and 7–10 % latency increases can occur without changes in postoperative neurologic function [21, 73–75]. However, empirically, an amplitude reduction of 50 % or greater and/or a latency increase of 10 % or more, not attributable to anesthetic or physiologic causes, are considered significant changes warranting intervention [1, 21, 76, 77]. The validity of these alarm criteria has been studied [1, 78, 79].

Intraoperative Applications for SSEPs

Intraoperative SSEPs are employed for a wide range of surgeries. The common goal is to ensure maintenance of neurologic integrity throughout a procedure with resultant improved outcome and decreased morbidity. Nerve root function can be monitored with SSEPs intraoperatively, although SSEPs may be insensitive to changes in single nerve root function (see also Dermatomal-Evoked Potentials). Peripheral nerves and brachial plexus monitoring can be used for surgical guidance as well as for avoidance of position-related neuropraxia during surgeries such as total hip arthroplasty and shoulder arthroscopy. Spinal cord function can be monitored during spine fusions, spinal cord tumor removal, arteriovenous malformation repair, and abdominal and thoracic aortic aneurysm repair. The brain stem and cortical structures can be monitored during tumor resection, carotid endarterectomy, and cerebral aneurysm clipping. Also, SSEPs can be employed to localize the border of the motor cortex intraoperatively [2] (see Chap. 9, “Brain and Spinal Cord Mapping”).

Dermatomal-Evoked Potentials

Evoked potentials elicited by stimulating individual dermatomes are called dermatomal SSEPs (DSSEPs). Surface electrodes are used to stimulate a single dermatome mediated by a unique nerve root. Dermatome maps to guide optimal placement of surface electrodes exist [1, 80, 81]. In contrast to SSEPS where supramaximal stimulation intensities should be used to provide reproducible and reliable evoked responses, high stimulation intensities for

DSSEPs can cause current spread and elicit responses from adjacent dermatomes. Also, stimulus intensity can affect DSSEP latencies [1, 80]. Therefore, minimally effective stimulation intensities need to be used for DSSEPs. Recording parameters are the same for DSSEPs as SSEPs. Cortical responses are typically larger in amplitude than subcortical responses. Because DSSEPs are sensitive to nerve root compression and mechanical stimulation [1, 81], intraoperative employment of DSSEPs includes the following: pedicle screw placement, cauda equina tumor resection, tethered cord release, and surgical treatment of spina bifida. However, due to dermatomal overlap and variability, along with side-to-side relative stimulation intensity, usefulness of DSSEPs can be compromised [1, 80]. In addition, there are other limitations to the intraoperative employment that make DSSEPs controversial for assessing spinal nerve root function. Specifically, a misplaced pedicle screw is detected only when there is contact with the nerve root monitored [1, 80]. Use of DSSEPs is further limited by their exquisite sensitivity to anesthetics [81].

Questions

1. Which of the following statements regarding the dorsal column pathway is incorrect?

    a. The dorsal column pathway is also referred to as the dorsal column-lemniscal pathway.

    b. The dorsal column pathway mediates mechanoreception and proprioception.

    c. The dorsal column pathway does not decussate in the medulla.

    d. Perfusion of the dorsal column pathway is typically from the posterior spinal artery.

2. Which of the following is false regarding pharmacologic effects on SSEPs?

a. Nitrous oxide, when combined with volatile anesthetic, reduces SSEPs more than either agent by itself.

b. The effects of bolus narcotics on SSEPs are less pronounced than those of continuous infusions of narcotics.

c. Ketamine and etomidate are unique in that they may be beneficial to SSEPs.

d. In general, the effect of anesthetics on cortical SSEPs is more pronounced than effects on subcortical SSEPs.

3. What is the empirically accepted threshold of SSEP latency increase that warrants intervention?

   a. 25 %

   b. 35 %

   c. 10 %

   d. 50 %

4. What is the empirically accepted threshold of SSEP amplitude reduction that warrants intervention?

   a. 25 %

   b. 35 %

   c. 10 %

d. 50 %

Answers

1. c

2. b

3. c

4. d

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Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_2

2. Transcranial Motor-Evoked Potentials

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Keywords Basics – Motor-evoked potential monitoring – Operating room – Somatosenory-evoked potential – Intraoperative neurophysiologic monitoring – Central nervous system – Motor pathway blood supply – Technical aspects – Risk

Key Learning Points

- The motor-evoked potential response (MEP) is an indirect complex polyphasic muscle response that requires a coordinated response of the motor neuron pathway and the muscle.
- Due to the motor pathway's blood supply, the MEP is more vulnerable to and a better indicator of adequacy of perfusion, particularly spinal cord perfusion.
- In addition to age, the ability to obtain MEP responses is impaired by pre-existing medical conditions (e.g., diabetes, hypertension, chronic spinal cord compression, spinal stenosis, nerve root injury, chronic hypoperfusion, brain injury, and genetic neuromuscular disease).
- MEPs are vulnerable to hypoperfusion and drug effects. Thus, the

anesthesia caregiver is responsible for selecting an appropriate technique and maintaining adequate perfusion through maintenance of hemoglobin, blood pressure, and cardiac output.

- MEP change, loss or loss and recovery, has been shown to be a reliable predictor of immediate and long-term postoperative neurologic function.

Introduction

Motor-evoked potentials (MEPs) continue to be the most recent addition to routine intraoperative neurophysiologic monitoring (IOM) . The importance of MEPs continues to expand primarily due to the ability to isolate perfusion-related neurologic function in the spinal cord. Initial reports of improved patient outcomes obtained with the use of somatosensory-evoked potential (SSEP) monitoring, primarily during scoliosis procedures in children and young adults, were quickly followed by case reports of isolated postoperative motor injury without SSEP or postoperative sensory changes. This reflected the reality of the anatomy and physiology of motor/sensory pathways in the brain and spinal cord [1]. MEP and SSEP pathways are located in different topographic and vascular regions of the cerebral cortex, brainstem, and spinal cord. MEP pathways are very complex and include the standard voluntary pyramidal and extrapyramidal networks. The more complex extrapyramidal network establishes additional motor connections including those to the cerebellum [2]. This complex and multiple synaptic architecture makes motor pathways more sensitive to ischemic insults than SSEP pathways [3].

Rare isolated motor injury without sensory changes after idiopathic scoliosis procedures was not the only driving force behind the widespread adoption of MEP monitoring. Increasing surgical volume and operative complexity in the central nervous system (CNS, spinal cord) and spine also fueled the need to independently assess motor function.

MEPs facilitate better intraoperative decision-making in all patient groups. As surgical techniques (instrumentation, diagnostic imaging, and intraoperative imaging) advanced and perioperative anesthetic management options improved, many patients who were at high anesthetic, surgical, and medical risk underwent new extensive surgical procedures. This increased risk of permanent and devastating neurologic complications. MEP monitoring became a favored method to help prevent complex surgical intervention from exceeding safe limits where the risk of the potential surgical adverse event

exceeds possible functional gain [4]. New information suggests MEP monitoring, particularly in spine surgery, has a better correlation with good postoperative motor outcome than the use of SSEPs, and many experts advocate MEP monitoring for:

- Surgical correction of all axial skeletal deformities with instrumentation [5–8]
- Intramedullary spinal cord tumors [9–12]
- Intracranial tumors [13–15]
- CNS and spinal cord vascular lesions [16, 17]
- Seizure disorders [18]

MEP use continues to expand outside the area of neurosurgical and axial skeletal procedures to vascular procedures that put perfusion of the brain or spinal cord at risk like thoracoabdominal aneurysms, aortic arch procedures (both endovascular and open procedures) (see Chaps 39 and 40), and preemptive assessment of outcome in stroke [19–21].

Motor Pathway Blood Supply

To understand why MEPs provide essential information for surgical procedures where neural tissue perfusion is at risk, it is necessary to review the blood supply of the spinal cord and understand the relationship between ischemia, electrophysiology, and infarction. A detailed discussion is found in Chap. 40. The spinal cord is supplied by the anterior spinal artery (ASA) and the posterior spinal arteries (PSAs). Spinal cord motor tracts are primarily supplied by the ASA, a vascular network that supplies the metabolically active anterior two-thirds to four-fifths of the spinal cord including the gray matter and anterior horn cells, all of which are more sensitive to ischemia [3, 22].

Both ASA and PSAs arise as branches of the vertebral arteries in the brainstem and then descend along the spinal cord providing perforators into the spinal cord. The ASA receives blood radicular arteries, which originate in the aorta [23]. Typically, there are three cervical and two thoracic arteries located at T2, 3 and T7-L4, with the Artery of Adamkiewicz (AA) providing about 75 % of the blood supply to the anterior cord [3, 24]. The reduced

number of radicular arteries, the increased distance traversed, and increased metabolic demand make areas of the spinal cord perfused by the ASA more susceptible to hypoperfusion. While axons are quite resistant to ischemia, the anterior cord contains many more cells and synapses, which explains the rapid changes seen in MEPs when inadequate perfusion occurs. Disruption of blood flow through these vessels due to mechanical or pressure changes rapidly leads to deterioration of MEPs and is used to prompt a change in management (e.g., improvement in systemic perfusion, cerebrospinal fluid drainage) [24–26].

The intracranial blood supply to motor areas is also vulnerable. Perforator arteries and lenticulostriate arteries supply the motor cortex and internal capsule; they arise from the middle cerebral artery. These vessels transverse a significant distance and are vulnerable to hypoperfusion with a decrease in cerebral perfusion pressure (CPP) from an increase in intracranial pressure (ICP) or cerebrospinal fluid pressure (CSFP) (CPP = MAP−[ICP or CSFP]) or disruption of the source vessels (e.g., aneurysm or atrial-venous malformations (AVM)) or hypotension. The distance and caliber of these vessels creates a watershed area making motor function more vulnerable to hypoperfusion than the ascending sensory tracts [27, 28]. The normal spinal cord and brain will autoregulate blood flow to maintain normal perfusion. Autoregulation occurs with a CPP approximately between 50 and 150 mmHg; specific individuals with long-term high (systemic hypertension) or low (infant) BP can be outside these limits. If the perfusion pressure falls below this range, autoregulation is lost and spinal cord blood flow is directly dependent on perfusion pressure. Hypoperfusion, as evident by a change in evoked potential activity, can also be caused by reductions in oxygen delivery (e.g., anemia, hypovolemia). MEP monitoring provides unique information about the functional status of the anterior spinal cord and internal capsule (see Chap. 21).

Technical Aspects of MEP Monitoring

MEPs are elicited by transcranial stimulation of the motor cortex using an electrical or a magnetic technique. The stimulation creates motor neuron depolarization and a descending response that traverses the corticospinal tracts and eventually generates a measurable response either in the form of muscle activity (compound muscle action potential, CMAP) or a wave

propagation along the corticospinal tract (Direct wave or D wave) (Fig. 2.1). In humans, the exact structural connections that are activated by evoked potential stimulation have not been clearly defined. Structures involved in voluntary motor activity in animal models have been described. Recordings from deep brain (DB) electrodes used for stimulation and recording in patients being treated for epilepsy or movement disorders have led to better definition of motor transmission and its interaction with sensory function [29]. Use of magnetic stimulation , the only technique available for eliciting MEPs from awake humans, has allowed simulation to occur with simultaneous recordings of electroencephalography (EEG) and electromyography (EMG) as paired responses. These data suggest that the variability in MEP recordings is due to normal variations in inhibition and facilitation in the corticospinal and cortical pathways [30]. Much of the latency seen in MEPs is due to the slower conducting areas of the spinal pathway, which may explain the MEP sensitivity to hypoperfusion and anesthetic drugs (see Chap. 19) [31, 32]. Continued investigation using DB electrodes for therapy in movement and seizure disorders will lead to a clearer picture of the motor pathways activated by diagnostic transcranial MEPs during surgery and may lead to a better understanding of the difficulties in eliciting responses.

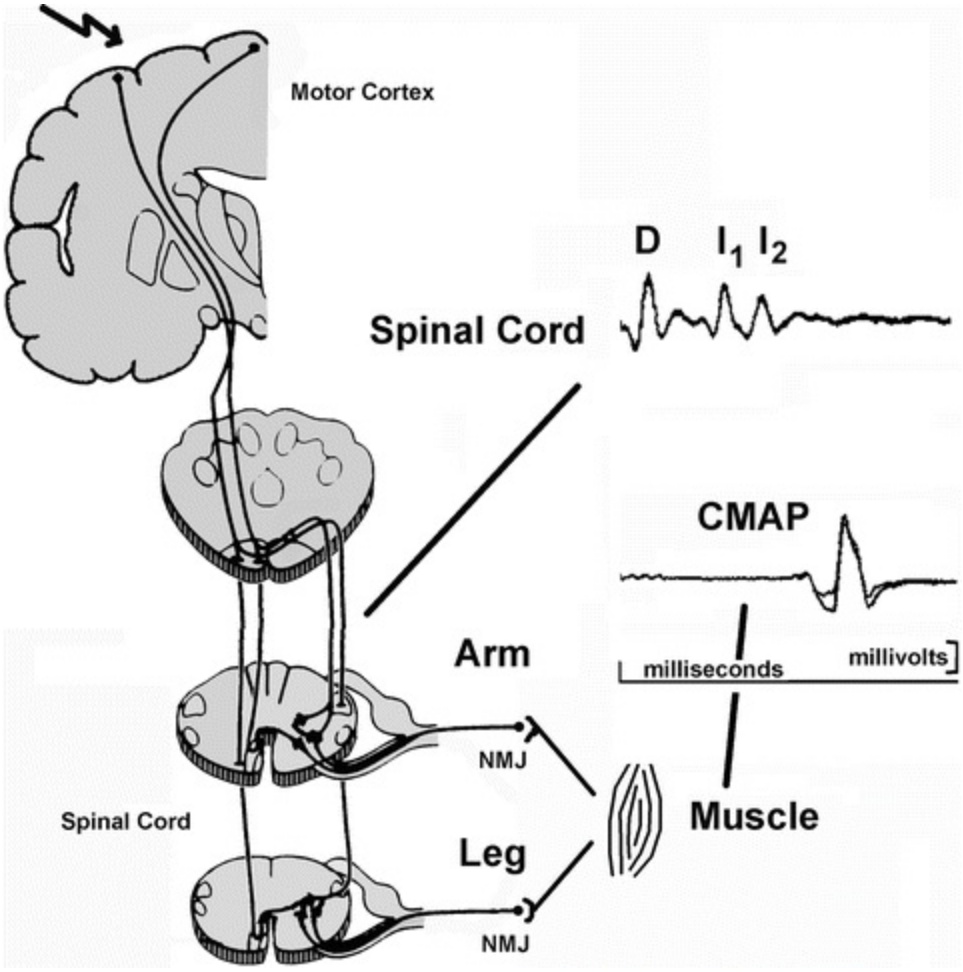

Fig. 2.1 Depiction of the neurologic response pathway with motor-evoked potentials. Stimulation of the motor cortex (*arrow*) results in a response that is propagated through the brain and spinal cord to cause a muscle contraction. The response typically is recorded near the muscle as a compound muscle action potential (CMAP) or EMG. The response can also be recorded over the spinal column as a D wave followed by a series of I waves (high frequency repetitive discharges fro the corticospinal fibers) (from Jameson and Sloan [33]; with permission)

All IOM MEP responses require continuity of the pathway since disruption of any component will change the measured response. Responses are affected by health of the neuron (e.g., peripheral neuropathy associated with diabetes), strength of the stimulus or number of neurons contributing to the response, propagation distance (height), sex, and temperature. Standard intraoperative transcranial electrical MEP monitoring in anesthetized patients uses a high-voltage electrical stimulus (measured in volts) to stimulate pyramidal cells of the motor cortex. This produces a wave of depolarization that is estimated to activate only 4–5 % of the corticospinal tract. The motor pathway descends through the motor cortex, crosses the midline in the

brainstem, and descends in the ipsilateral anterior funiculi of the spinal cord (Fig. 2.1) [2, 33].

Attempts to stimulate spinal cord motor tracts and then record neurogenic motor-evoked potentials (NMEPs) from peripheral nerves were done with stimulating electrodes placed into the epidural space (see Chap. 6) [8, 34]. An alternate, but less successful method was to use needle electrodes placed near the lamina of the appropriate spinal segment. Beginning in the 1990s, this technique for obtaining responses was instituted to eliminate the difficulties associated with the effects of anesthesia on the cerebral motor cortex when trying to elicit MEPs. NMEPs have largely been abandoned as a motor response since current evidence indicates that NMEPs are not mediated by the same motor pathways as MEP but instead by antidromic conduction in sensory pathways. Thus, NMEPs are not a motor response at all [32, 35]. Direct cortical or spinal cord stimulation using a strip electrode placed directly on the spinal cord or cerebral cortex to stimulate motor pathways continues to be used to map or identify neural tissue with motor functionality. A detailed treatment of spinal cord motor mapping techniques with grid electrodes is found in Chaps 9 and 36.

MEP stimulation utilizes a train of usually 3–7 electrical pulses of 100–500 V intensity (maximum 1000 V) applied through corkscrew electrodes most commonly placed a few centimeters anterior to the somatosensory recording electrodes at C3′–C4′ (International 10–20 system). Standard stimulus pulse durations are 0.2 ms with an interpulse or interstimulus interval (ISI) (period between stimuli) between 2 and 4 ms (Table 2.1). Corkscrew scalp electrodes increase the electrode surface area and reduce the risk of burns from the high-energy stimulus. Manipulation in the number of stimuli, ISI, pulse duration, pulse strength or intensity, and stimulating electrode locations allows for adequate cortical neuron depolarization. Parameter changes overcome some of the impediments to propagation such as the anesthetic effect on the anterior horn cell synapse, preexisting neuropathy and myelopathy, distance of the motor cortex from the stimuli, loss of motor neurons, comorbid conditions, and age. The time required to obtain a MEP is generally less than 10 s. Multiple organizations have published best practice algorithms that in their hands produce the best signals [36]. ISI manipulation is frequently cited as a critical stimulus parameter to adjust to optimize MEP acquisition (Table 2.1) [7, 36, 37].

Table 2.1 Effect of varying the interstimulus interval (ISI) and the stimulus pulse duration on the threshold stimulus Threshold stimulus, which can be in volts or mAmps (mA), is the energy required to produce a response in 50% of the patients

ISI (ms)	Pulse duration (ms)		
	0.1 ms	0.2 ms	0.5 ms
	Mean motor threshold (mA)		
2	158 ± 67	105 ± 33	76 ± 26
3	140 ± 55	97 ± 33	64 ± 20
4	126 ± 56	91 ± 35	61 ± 19
5	179 ± 74	120 ± 45	83 ± 31

Stimulus was applied at C3/C4. All combinations of ISI and pulse duration are significantly different from each other at the *P* value of <0.001. The lowest mean motor threshold occurred at an ISI of 4 ms and pulse duration of 0.5 ms (adapted from Szelényi et al. [36])

Once stimulation has occurred, a reliable and easily detected response is required for monitoring purposes. The response typically used is the CMAP recorded from muscle groups in the extremities, although percutaneous epidural D and I waves [38], can be used to confirm a response (Fig. 2.1). D waves, direct activation of the corticospinal neurons [38], have a variable success rate and following them as a sole source of monitoring is currently uncommon except in specific surgical procedures such as intramedullary spinal cord tumors [39, 40].

Standard muscle responses differentiate laterality and therefore localize neural tissue at risk. These CMAP or EMG responses are recorded using needle or skin electrodes that are placed in hand muscles of the thenar eminence (abductor or flexor pollicis brevis), in muscles of the lower extremities (gastrocnemius, tibialis anterior, and abductor hallucis brevis), and trunk muscles (intercostals, rectus abdominis). The “best” (largest and most reproducible) specific muscle response below the site of the surgical procedure is selected to be followed [36, 40–46]. In our organization, acceptable CMAP responses are polyphasic with a consistent latency and an amplitude greater than 150–200 μV. We will continue to follow lesser responses but inform the surgeon that the information is not reliable. Direct motor mapping in the spinal cord or cerebral cortex requires needle placement in the muscle groups that are innervated by the areas being stimulated (e.g., homunculus hand representation–abductor or flexor pollicis

brevis). This includes those muscles innervated by the cranial nerves (e.g., cranial nerve VII: orbicularis oculi or oris).

CMAPs can be difficult to obtain from patients at both extremes of age, elderly and young children. In addition to age, adults often have preexisting conditions such as diabetes, hypertension, chronic spinal cord compression, nerve root injury, chronic hypoperfusion, and axonal conduction changes that reduce CMAP responses [47]. Children, particularly those under 6 years, have an immature CNS that makes obtaining a motor response challenging [48]. CMAP responses can be difficult to obtain in procedures that are performed on patients with substantial neurologic deficits from preexisting brain injury (e.g., cerebral palsy) and genetic diseases that impair muscle function (e.g., Duchene muscular dystrophy, Charcot-Marie-Tooth). Recent comprehensive review articles address these issues and offer solutions to help the IOM team obtain signals [49]. Often the most critical decision in obtaining MEP responses, particularly in those with known neurologic, metabolic or muscular diseases, is the selection of the anesthetic management (see Chap. 19).

When spinal cord D and I wave responses are used, they do not differentiate laterality and D waves do not involve a synapse. The D wave correlates with the number of functioning fibers of the corticospinal tract responding to the stimulus. Thus, D wave amplitude changes have significance. D waves are more commonly used during intramedullary spinal cord surgery where recording electrodes are placed by the surgeon in the field [33, 50, 51]. Another alternate method of producing a motor response is the Hoffmans reflex (H-reflex). It is the electrical equivalent of the spinal cord reflex elicited by a tendon percussion knee jerk and monitors the sensory and motor efferent axons as well as the spinal gray matter and components of the reflex arc [50]. Discussion of this response is outside the scope of this chapter (see Chap. 8). CMAPs are by far the most common measure of the MEP response. The literature evaluating D, I, and H waves is very limited.

CMAPs can demonstrate considerable variability even in normal awake subjects [32, 52]. The variability is magnified during general anesthesia [31, 53]. Most organizations establish standardized criteria for a minimum baseline amplitude (difference between positive and negative peaks), complexity (number of positive and negative wavelets) but not latency (time from stimulus to response). This is necessary to prevent false-positive monitoring alert when the signal changes. Without these waveform

components, a reliable signal was never present. It assures the surgeon that the MEP responses will be a reliable measure of function throughout the procedure. MEP responses are presented in Fig. 2.2. What constitutes a CMAP change that must be acted upon has not been universally defined. Permanent loss, a straightforward event, is strongly correlated with permanent neurologic injury, whereas patients who experience temporary loss or alerts (a predetermined decrease in amplitude and/or latency) frequently have normal function at the end of the procedure and ultimately regain full motor function. Some IOM groups use the presence or absence of a CMAP response as their sole criteria for notifying the surgeon about a problem. This criterion allows the use of muscle relaxants as a component of the anesthetic, which is a common surgical request to eliminate patient movement at an inopportune time. Other suggested criteria include increases in stimulus strength greater than 50–100 V, changes in stimuli number or pattern required to elicit an MEP, or a significant decrease in CMAP amplitudes (usually >80 %) from the initial responses (without muscle relaxant). All are considered significant changes by some individuals (Fig. 2.3). Signal recovery after these changes is reassuring and usually predicts normal postoperative motor function. Loss of CMAP responses requires notification of the surgeon and anesthesiologist to correct, when possible, the physiologic issues contributing to the MEP change (see Chap. 20) [1, 54–59].

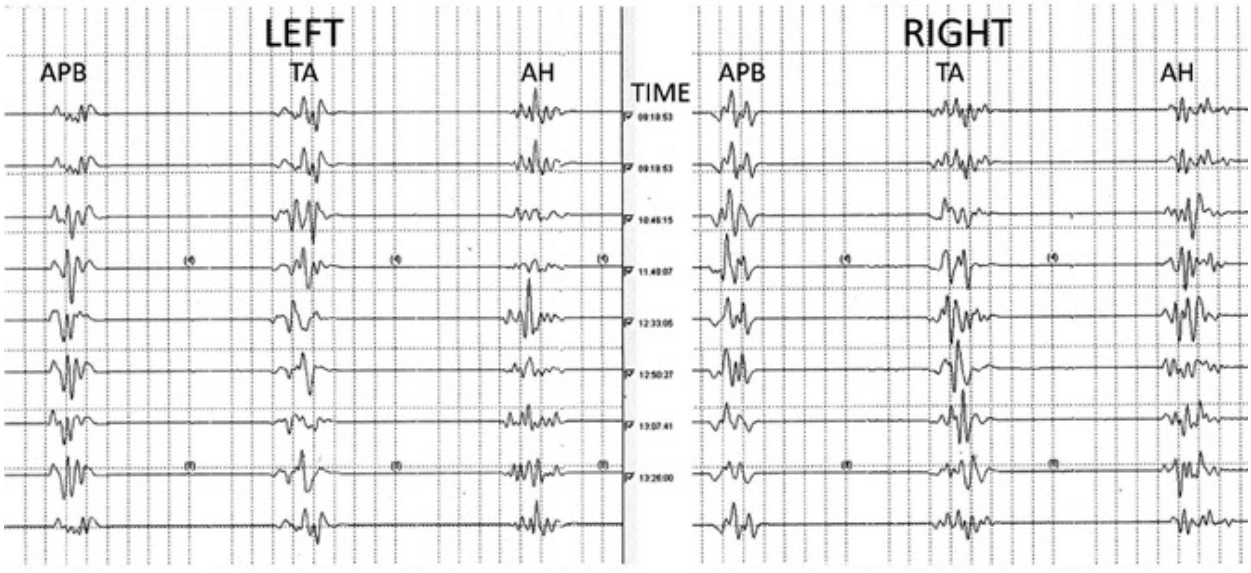

Fig. 2.2 Standard normal MEP responses. The CMAP response , a large polyphasic wave, is obtained from the upper extremity traditionally using the abductor pollicis brevis (APB) and from the lower extremity using tibialis anterior (TA) and abductor hallicus (AH) brevis. Two lower extremity muscle

groups are used due to the increased difficulty obtaining a consistent response particularly in adults. Other upper and lower extremity muscles can be used depending on the needs of the specific patient. Obtained from the author's archive

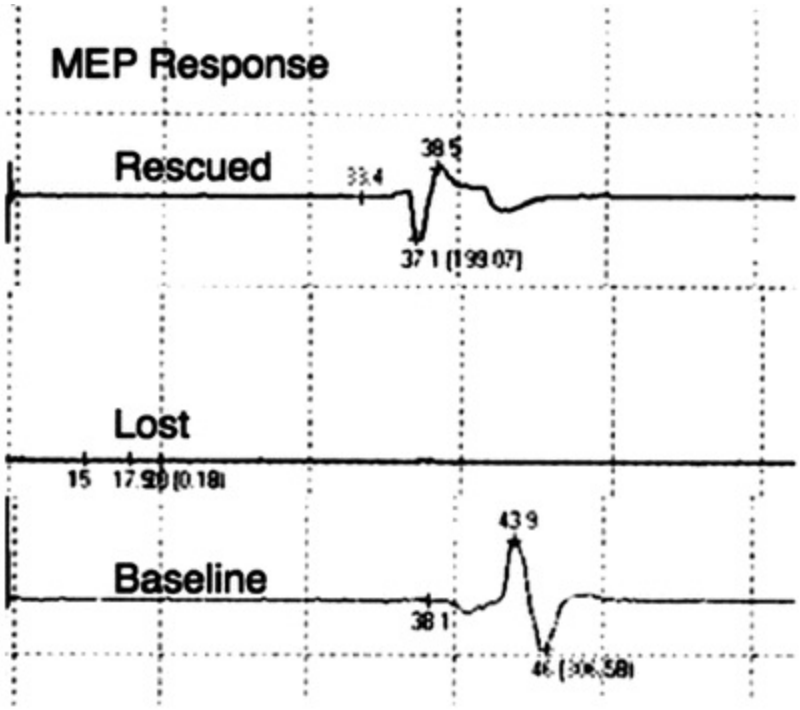

Fig. 2.3 Normal MEP baseline responses and acute injury . Placing the patient prone resulted in the loss of responses. There was a recovery of response to baseline configuration after adjusting the head position, increasing blood pressure and eliminating residual desflurane. Obtained from the author's archive

Application of MEP Monitoring

Monitoring during structural spine and spinal cord surgery is customarily multimodal and includes SSEPs, MEPs, and electromyography (EMG, free running, and stimulated). MEP monitoring is considered essential whenever spinal cord function is at risk. Thus, MEP monitoring is usually performed during structural spine surgery from C1 to cauda equina whenever the risk of cord injury due to stretch, compression, or vascular damage [56, 60] could occur. "At risk" situations also include any surgery where a compromise of spinal cord perfusion or direct injury to motor tracks or nerve roots could occur. Consensus opinion is that the evidence supports MEP monitoring in the following specific spine procedures:

- Spinal deformities with scoliosis greater than 45° rotation

- Congenital spine anomalies
- Resections of intramedullary and extramedullary tumors
- Extensive anterior and/or posterior decompressions in spinal stenosis with myelopathy
- Functional disturbance of the cauda equina and/or individual nerve roots

However, the evidence does not meet the level 1 standard (large randomized, placebo-controlled, double-blind studies). The evidence is based on a large case series and meta-analysis (level 2, 3 evidence) where MEP changes predicted immediate postsurgical neurologic findings [1, 40, 54–56, 58, 59, 61–63]. A recent evidence-based analysis by the American Academy of Neurology and American Clinical Neurophysiology Society is strongly supportive of IOM in spine surgery [46, 56].

Obtaining MEPs remains challenging in some patient populations. They often require an alteration in anesthetic management to obtain adequate waveforms—a point that necessitates negotiations between the anesthesiologist, surgeon, and IOM team. Many of the older prospective series used SSEPs and EMG but only rarely MEPs due to this issue. In one study of 1055 adult patients undergoing cervical spine surgery between 2000 and 2005, MEP studies were attempted and obtained in only 26 of 1055 patients due to the perceived difficulties [61]. These were the highest risk patients for spinal cord injury. With the current relatively routine availability of total intravenous anesthesia (TIVA) based on propofol, MEPs can be relatively easy to obtain (see Chap. 19). When used during spine procedures, MEPs had 100 % sensitivity, 96 % specificity, and a positive predictive value of 96 % for postoperative motor changes [61]. Adults with cervical myelopathy had about a 12 % incidence of only MEP alerts (no EMG or SSEP changes). These alerts were usually followed by resolution after alterations in anesthetic and surgical management occurred. Nonetheless, these authors believed that the MEP monitoring provided 100 % sensitivity and 90 % specificity [64].

MEP changes are relatively infrequent [7] in pediatric procedures. One group reported that in 172 pediatric spinal deformity corrective procedures, there were 15 intraoperative MEP alerts, all of which resolved with changes in management. None of the patients (MEP-alert and MEP-unchanged patients) had new neurologic deficits. This group concluded that MEP

monitoring alone was adequate for spinal deformity surgery with a sensitivity of 1.0 and a specificity of 0.97. Patients with persistent MEP changes had immediate postoperative motor deficits. SSEP changes, when present, lagged significantly behind the MEP changes and often did not predict outcome [65]. For adults with spinal cord myelopathy, one of the diagnostic criteria includes changes in MEPs prior to surgical intervention; consequently, baseline studies, post anesthesia, and prepositioning are strongly recommended [66, 67].

Consensus opinion supports and studies suggest that the use of intraoperative spinal cord motor mapping improves long-term motor function in intramedullary spinal cord tumor resection (see Chap. 36) [68, 69]. The MEP is the only reliable monitor of motor pathways and is an early predictor of impending damage to the cord due to the precarious blood supply. For an anterior approach to an intramedullary spinal cord tumor resection, focal injury to the anterior spinal vasculature or motor tracts is generally detected only minutes after a hypoperfusion event; this is considerably faster than with SSEP monitoring alone [11, 68, 69].

During intracranial procedures , direct cortical stimulation is likewise used to map motor function and to delineate the demarcation between tumor and functional tissue. This can be performed using electrode strips, direct hand-held device, or a Penfield motor stimulation technique. Although the Penfield technique is often preferred in awake patients, the pulse train technique used for MEP is associated with less stimulation-related seizures and is more effective in producing CMAP responses during general anesthesia. The motor stimulation may replace or augment awake craniotomy procedures in the supratentorial area when eloquent areas (e.g., speech) or motor pathways (e.g., internal capsule, motor cortex, and premotor cortex) are at risk [70–72]. In large clinical studies, sensitivity and specificity are reported to be between 90 % and 100 %, respectively; however, in some reports, Broca’s area had a reported specificity of only 64 % and Wernicke’s area of just 18 % [73].

Excess stimulation strength can cause direct activation of structures at a distance from the stimulus location. Focal stimulation often involves manually stimulating portions of the cortex or inserting a strip electrode under the dura. The usual pattern of transcranial stimulation is performed at about 1/10th the MEP stimulus strength. A pattern of gradually increasing stimulus is applied. Recent large case reports have documented that MEP

monitoring assists in delineating the edge between tumor cells and functioning neural tissue. In a study of 404 patients, all with a low-grade glioma, MEP mapping substantially reduced the number and severity of permanent motor deficits while increasing the number of total resections. One hundred of these 100 patients had temporary motor deficits and only 4 patients had deficits (1 %) remaining 3 months after surgery. Total or subtotal tumor resection was done in only 11 % of patients prior to motor mapping but 69.8 % after motor mapping was initiated [74]. A number of other groups have published similar reports and noted that the long-term outcome is significantly improved by more extensive tumor resection in both children and adults for all supratentorial tumors [72, 75, 76]. Neurologic injury to the posterior fossa can have devastating consequences. Motor mapping is an effective way to identify both tumor margins and safe resection zones, areas between cranial nerve nuclei, or entry zones into the floor of the fourth ventricle. Stimulation can be either transcranial or, more frequently, direct brainstem stimulation [77].

Intracranial aneurysms and arteriovenous malformations can result in areas of hypoperfusion during the endovascular embolization, resection, or temporary and permanent clipping. MEPs identify hypoperfusion in motor areas and adjacent areas perfused by vessels involved in the vascular lesion. Identification of MEP change followed by therapeutic intervention appears to substantially reduce permanent injury. Two large studies with 108 and 129 patients undergoing supratentorial aneurysm clippings found that in cases where MEPs were unchanged, none of the patients had deficits. One study confirmed adequate flow with MEPs and with microvascular Doppler ultrasonography. Both studies reported between 13 and 33 % of patients had reversible MEP changes; these patients had no neurologic changes immediately after the procedure or had only transient neurologic changes from which they fully recovered. Patients with permanent MEP change (about 20 %) had permanent neurologic deficits, some quite severe [16, 78, 79]. Small case series generally support these findings. The neurosurgical community has reported improved outcomes during aneurysm occlusion on basilar, vertebral, and middle cerebral artery aneurysms when using MEP monitoring. Publications report MEP changes occur rapidly and better reflect long-term outcomes when the involved vessels provide perfusion to motor pathways.

Contribution of Anesthesiology to Effective MEP Monitoring

Without the cooperation and support of the anesthesia care provider, producing MEP responses and detecting changes is not possible. Most treatment options, when MEP change occurs, are in the hands of the anesthesia caregiver. MEP change is not only initiated by surgical activity but by physiologic management and anesthetic drug choices. Any event that will impact neural function can impact MEP waveforms (see Chap. 19). This reality stresses the importance of the team effort, cooperation between the surgeon, anesthesiologist, and IOM technologist.

Hypotension is of particular interest since deliberate hypotension to reduce blood loss was once considered a management technique, particularly in the idiopathic scoliosis procedures in children and during aneurysm clipping. There is a growing appreciation that the presumed lower limit of autoregulation is not always adequate for tissues undergoing surgical stress [80]. Mean BP that is adequate for a young adult patient may not be adequate for an older adult with many coexisting diseases. Hence, increasing or maintaining systemic perfusion pressure effectively treats many impending hypoperfusion injuries (Fig. 2.4).

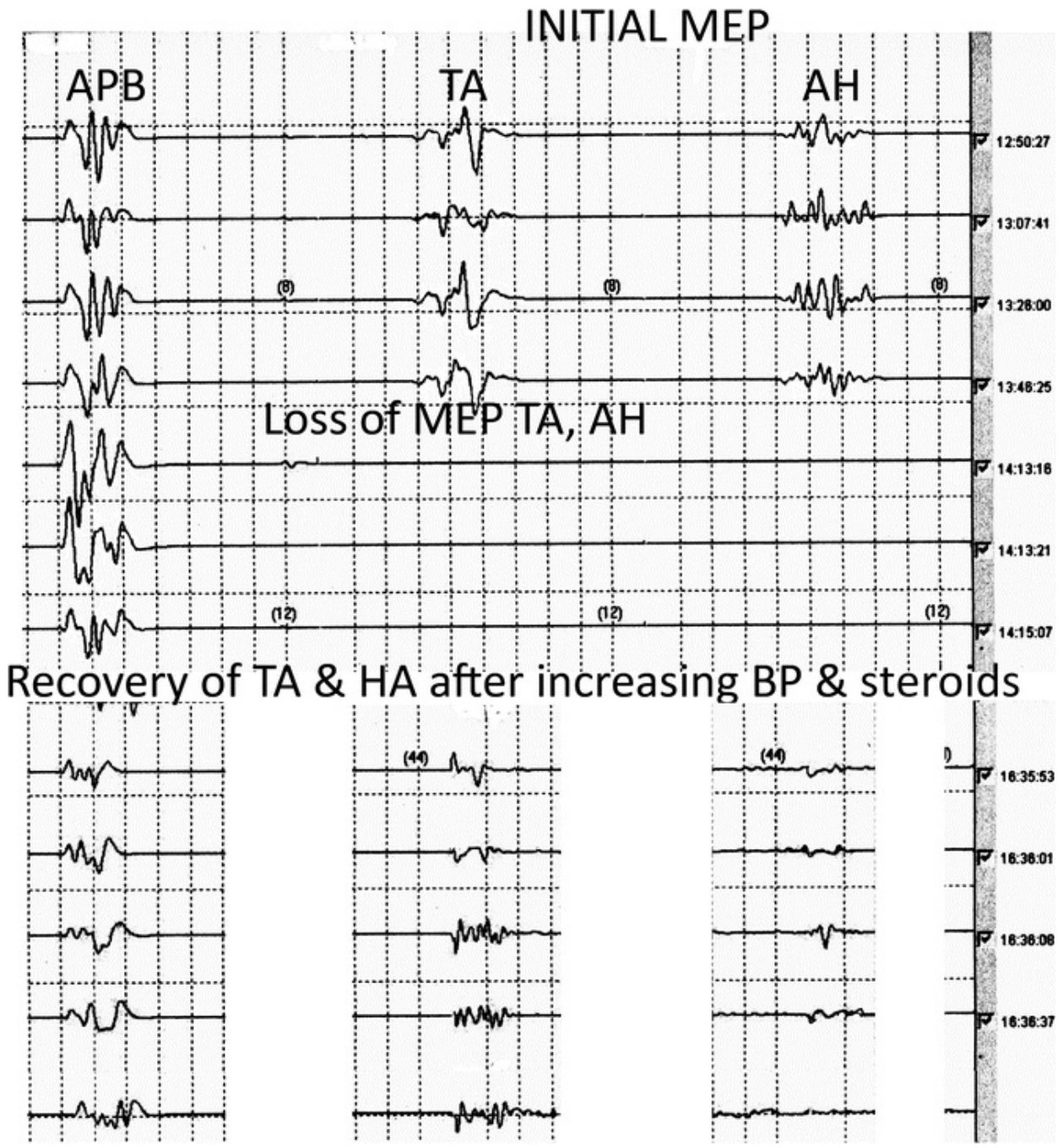

Fig. 2.4 Recovery of MEP responses after intraoperative loss. During a posterior cervical fusion of C5 to T4 the patient abruptly lost MEP responses in both lower extremities. After BP elevation and steroid administration, MEP responses returned only on the left. Patient had weakness on the left, which resolved over 2 weeks. On the right, the patient had a dense hemiparesis that had not changed 3 months after surgery. (Tibialis anterior–TA, Adductor hallucis–AH) Obtained from the author's archive

The acceptable lower limit for hemoglobin has come under question. Current recommendations by the blood banking community are to allow

hemoglobin to be as low as 7 g/dL during acute blood loss, particularly in healthy patients [81]. However, anemia can be compensated only within the limits of the patient's physiologic ability to increase cardiac output to maintain local tissue perfusion. Neurologic tissue has a high metabolic demand and may have compromised perfusion due to pre-existing systemic disease (hypertension, vascular disease, poor cardiac output, surgical stress, and inflammation) as well as regional compression (spinal cord stenosis, surgical activity, position, acute injury). Thus the acceptable lower limit of blood pressure and hemoglobin is unlikely to be the same for all situations and is poorly predictable. MEP monitoring allows a functional assessment of the combination of blood pressure and oxygen-carrying capacity. Consequently it assesses the adequacy of perfusion in specific patients under specific surgical conditions. When IOM signals deteriorate, increasing the systemic blood pressure to the patient's preoperative value or higher is the most common and most effective response the anesthesia care team can provide. Transfusion is also an effective therapeutic intervention when appropriate. Maintenance of "normal" physiologic conditions within the brain and spinal cord can be difficult but results in the ideal monitoring conditions and the best neurologic outcomes.

The impact of dexmedetomidine on MEP monitoring deserves special comment. Propofol infusion syndrome [82] is diagnosed primarily in pediatric patients and can prove fatal (see Chap. 19). Thus, substituting dexmedetomidine for propofol as the "recommended" TIVA hypnotic when IOM is required has been advocated. Early literature reports suggested that its use caused no negative physiologic effect or impairment in MEP monitoring [83–85]. Two recent carefully performed studies found a clinically and statistically significant attenuation in the amplitudes of MEPs when the targeted plasma concentrations of demedetomidine exceeded 0.6–0.8 ng/mL [83, 86, 87]. Another study in which dexmedetomidine was administered in combination with propofol was discontinued by the safety monitoring board. Reduction or loss of MEPs occurred in healthy pediatric spines when both drugs were used in any combination [83]. Dexmedetomidine also has a long context-sensitive half-life consequently wakeup times can be prolonged.

Risk of MEP Monitoring

MEP monitoring is not without risk. The US Food and Drug Administration

has specified relative MEP contraindications. The most common concern was direct cortical thermal injury (kindling), but over the last 18 years only two cases of cortical thermal injury have been reported. In a 2002 survey of the literature, published complications included tongue laceration (n = 29), cardiac arrhythmia (n = 5), scalp burn at the site of stimulating electrodes (n = 2), jaw fracture (n = 1), and awareness (n = 1) [88]. Placing a bite block between both molars can ameliorate tongue laceration. Notably no new-onset seizures, epidural hematomas, or infections from epidural electrodes or movement injuries (e.g., surgical, joint dislocation), neuropsychiatric disease, headaches, and endocrine abnormalities have been reported. Relative MEP contraindications include epilepsy, a cortex lesion, skull defects, high intracranial pressure, an intracranial apparatus (electrodes, vascular clips, and shunts), cardiac pacemakers, or other implanted pumps. The most common patient identified side effect is sore muscles [89, 90]. Needle placement will lead to bleeding and bruising at the insertion site. Infection is always possible. The prevalence of major and minor problems is astonishingly low.

Conclusion

Clearly the goal of intraoperative monitoring is to provide the greatest degree of assistance to the operative team for optimal intraoperative decision-making. The current literature suggests that MEP monitoring provides excellent specificity and sensitivity whenever motor tracts are involved. As such, the real question for consideration is which of the techniques available should be used to complement MEP monitoring in individual patients.

Questions

1. Which of the following does NOT decrease the likelihood that MEP can be acquired in the OR

    a. Very young age

    b. Diabetes

    c. Long-standing hypertension

d. Myelopathy

e. All of the above

2. During surgery, MEP change in the tibialis anterior that is NOT resolved by the conclusion of surgery correlates with

   a. Loss of proprioception in the feet

   b. Loss of vibration sense in the hands

   c. Loss of motor function in the leg

   d. Loss of speech discrimination

   e. Loss of visual acuity

3. Which of the following has been associated with EMG monitoring?

   a. Epidural D waves

   b. H reflex

   c. Stimulation of cranial nerve VII during an acoustic neuroma

   d. Stimulation of the posterior tibial nerve

   e. Neurogenic motor-evoked potentials

4. Which of the following are associated with deterioration of MEP muscle responses during surgery?

a. Inhalational anesthesia

b. Hypotension

c. Anemia

d. Administration of muscle relaxant

e. All of the above

5. Compared to SSEP

a. MEP has the same vascular supply in the spinal cord

b. MEP has more synapses in the spinal cord than SSEP

c. MEP is supplied by the posterior spinal artery while the SSEP is supplied by the anterior spinal artery

d. The MEP is less sensitive to ischemia in the spinal cord

e. All of the above

6. When MEP responses are lost during surgery, the most frequent rescue technique is

a. Change to volatile anesthesia

b. Decrease blood pressure

c. There is no effective therapy

d. Increase BP to preoperative values or higher

e. None of the above

Answers

1. c

2. c

3. c

4. e

5. b

6. d

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Footnotes

1 Asterisks indicate key references.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_3

3. Auditory-Evoked Potentials

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Electronic supplementary material:
The online version of this chapter (doi:10.1007/978-3-319-46542-5_3) contains supplementary material, which is available to authorized users.

Keywords Auditory brainstem-evoked potentials – Ear – Cochlea – Electrocochleogram – Auditory pathway – Techniques – Recording – Stimulation – Anesthetic considerations – Physiologic considerations

Key Learning Points

- Auditory-evoked potentials are most useful to monitor the integrity of the intracranial auditory nerve (cochlear portion of cranial nerve 8)
- The electrocochleogram (ECochG) can provide independent verification

of stimulus delivery

- Waves I and V are most robust on the AEP; wave I originates from the cochlea, which is typically not directly in harm's way. Wave V originates at the level of the inferior colliculus, medial geniculate body
- Brainstem pathways of the auditory system run predominantly contralateral to the stimulated ear
- Brainstem auditory potentials are very resistant to the effects of anesthetic agents

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Anatomy of the Auditory System

Sound signals are processed by the auditory system in a sequential manner. First, the acoustic energy of sound is conducted to the cochlea located within the inner ear, where conversion to a coded electrochemical signal takes place. This signal is then transmitted along the auditory pathway via the eighth cranial nerve, brainstem, and midbrain to the primary auditory cortex. Various auditory-evoked potentials can be recorded from all these elements (Fig. 3.1, see also supplemental electronic content (Video 3.1)). The tracings consist of waves with peaks and troughs that correspond to fluctuations in electrical potential. Each wave is described as being either a peak (P = positive deflection) or trough (N = negative deflection) and is further described in terms of both amplitude (peak-to-peak height) and latency (time from stimulus). The waves can be divided on the basis of the time between acoustic stimulus and evoked response into short-, mid-, and long-latency acoustic-evoked potentials. The long-latency acoustic-evoked potentials originate in the association cortex and require cooperation and attention. They are abolished under anesthesia and will, therefore, not be further considered. Another type of recording that will not be discussed is the recording of compound action potentials from the auditory nerve, which requires the surgeon to place an electrode intraoperatively on an anatomic structure of interest (for a recent review see Simon [1]).

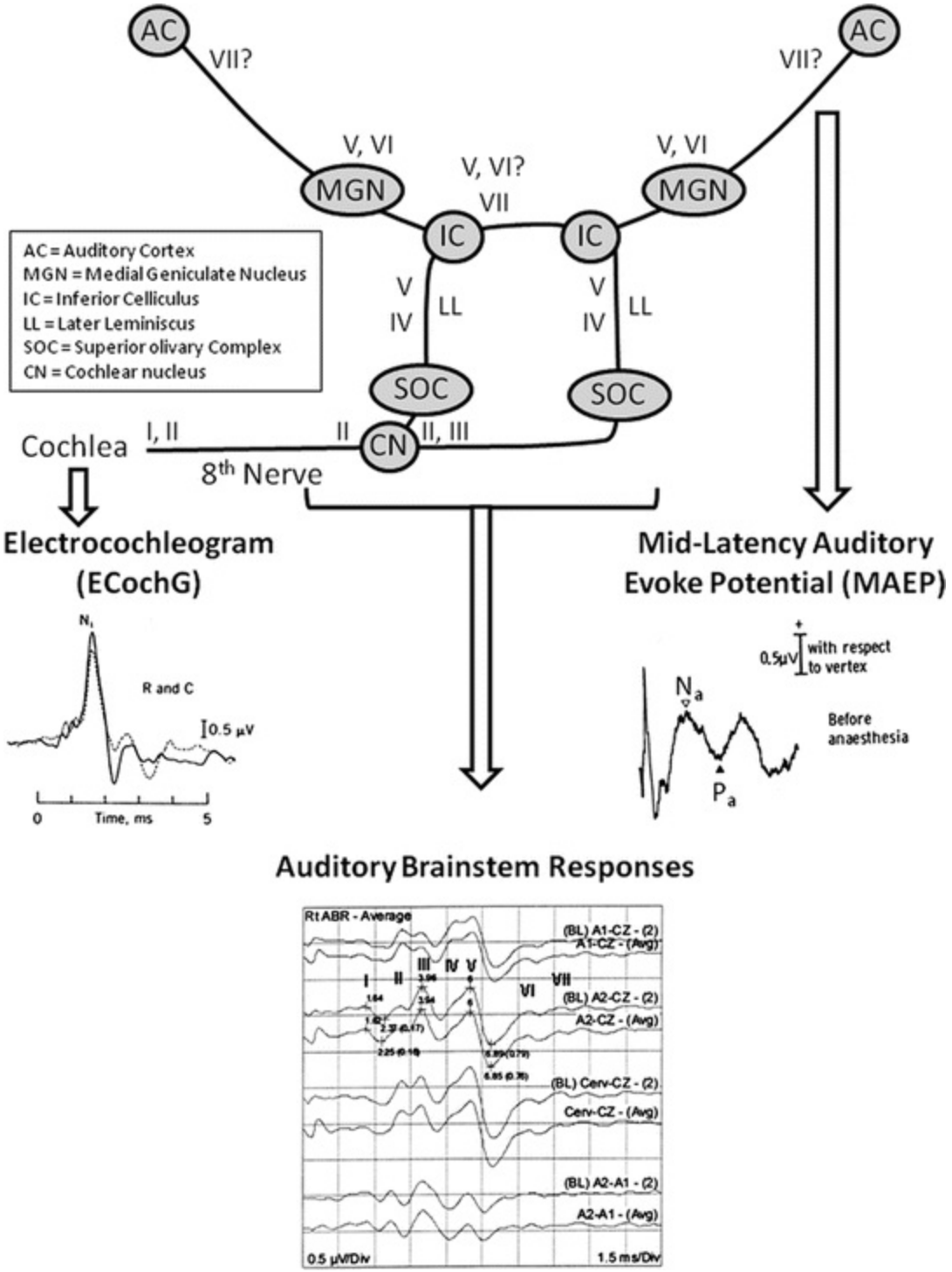


Fig. 3.1 Neural pathway of the auditory system and recordable potentials. Note that auditory input is transmitted to bilateral primary auditory cortices and ascends through brainstem and midbrain partially ipsilateral and partially contralateral to the side of stimulation (for details, see text). The electrocochleogram (ECochG) contains near-field signals from cochlea and distal auditory nerve (adapted from Coats [44]; with permission). The brainstem auditory-evoked potential (ABR) reflects activity in the entire neural pathway. Note how the morphology of individual waves projects differently

in the individual recording channels. In addition to Na and Pa waves reflecting activation of the primary auditory cortex, the mid-latency auditory-evoked potential (MLAEP) contains a distinctive wave V of the ABR within its first 10 ms (adapted from Thornton et al. [47]; with permission). Anatomic and radiographic representations of the auditory pathway can be found in the supplemental on-line materials

Conduction of Auditory Signals from Ear to Cochlea

The ear is subdivided into external, middle, and inner parts. The external ear is composed of the auricle that acts to collect and direct sound through the external auditory meatus toward the tympanic membrane. The tympanic membrane forms the boundary between the external and middle parts of the ear. The tympanic membrane is covered in a very thin squamous epithelial layer externally and by a mucous membrane internally. It moves in response to air vibrations that pass to it through the external auditory meatus. Movements of the tympanic membrane are transmitted by three auditory ossicles, the malleous, incus, and stapes, through the middle ear to the inner ear.

The middle ear lies within the petrous portion of the temporal bone. The tympanic cavity lies directly behind the tympanic membrane and shares important anatomical relationships to neighboring structures. Superiorly, the epitympanic recess is separated from the middle cranial fossa by a thin roof of bone, the tegmen tympani. The anterior (carotid) wall separates the carotid canal from the tympanic cavity. The eustachian tube projects through the anterior wall to connect the middle ear to the nasopharynx. The floor (jugular wall) is formed by a layer of bone that separates the tympanic cavity from the superior bulb of the internal jugular vein. The medial or labyrinthine wall separates the tympanic cavity from the inner ear. The middle ear also connects posterior and superior with the mastoid air cells through the mastoid antrum.

The auditory ossicles form a chain that extends across the tympanic cavity from the tympanic membrane to the oval window (fenestra vestibuli). The malleous (hammer) is attached to the tympanic membrane. Its superior head lies within the epitympanic recess, and its handle is embedded in the tympanic membrane. Movement of the tympanic membrane results in movement of the malleous. The head of the malleous articulates with the incus (anvil). The long process of the incus articulates with the stapes (stirrup). The base of the stapes is attached to the oval window. Typically, the majority of the sound energy travels via this ossicular chain to the cochlea. If movement of the tympanic membrane or ossicular chain is restricted by fluid

or a disease process, a conductive hearing deficit results and the far less effective conduction of sound via bone becomes an important input to the cochlea. Conversely, during bone drilling, bone-conducted noise may overwhelm the cochlea and lead to a temporary hearing deficit.

Two muscles lie within the middle ear and act to prevent excessive movement of the ossicles due to loud noises. The tensor tympani muscle arises from the superior surface of the cartilage forming the auditory tube, the greater wing of the sphenoid bone and the petrous part of the temporal bone. It is innervated by the mandibular division of the trigeminal nerve and inserts on the handle of the malleolus. The tensor tympani pulls on the handle of the malleolus , tenses the tympanic membrane, and thus dampens oscillations of the tympanic membrane. The stapedius muscle arises from the pyramidal eminence on the posterior wall of the tympanic cavity. It inserts on the neck of the stapes. It is innervated by a branch of the facial nerve. The stapedius pulls the stapes posteriorly and tilts the base of the stapes in the oval window. This acts to tighten the stapes and reduce excessive movement.

Neural Components of the Auditory System and Electrical Generators Along the Auditory Pathway

Cochlea : Electrocochleogram

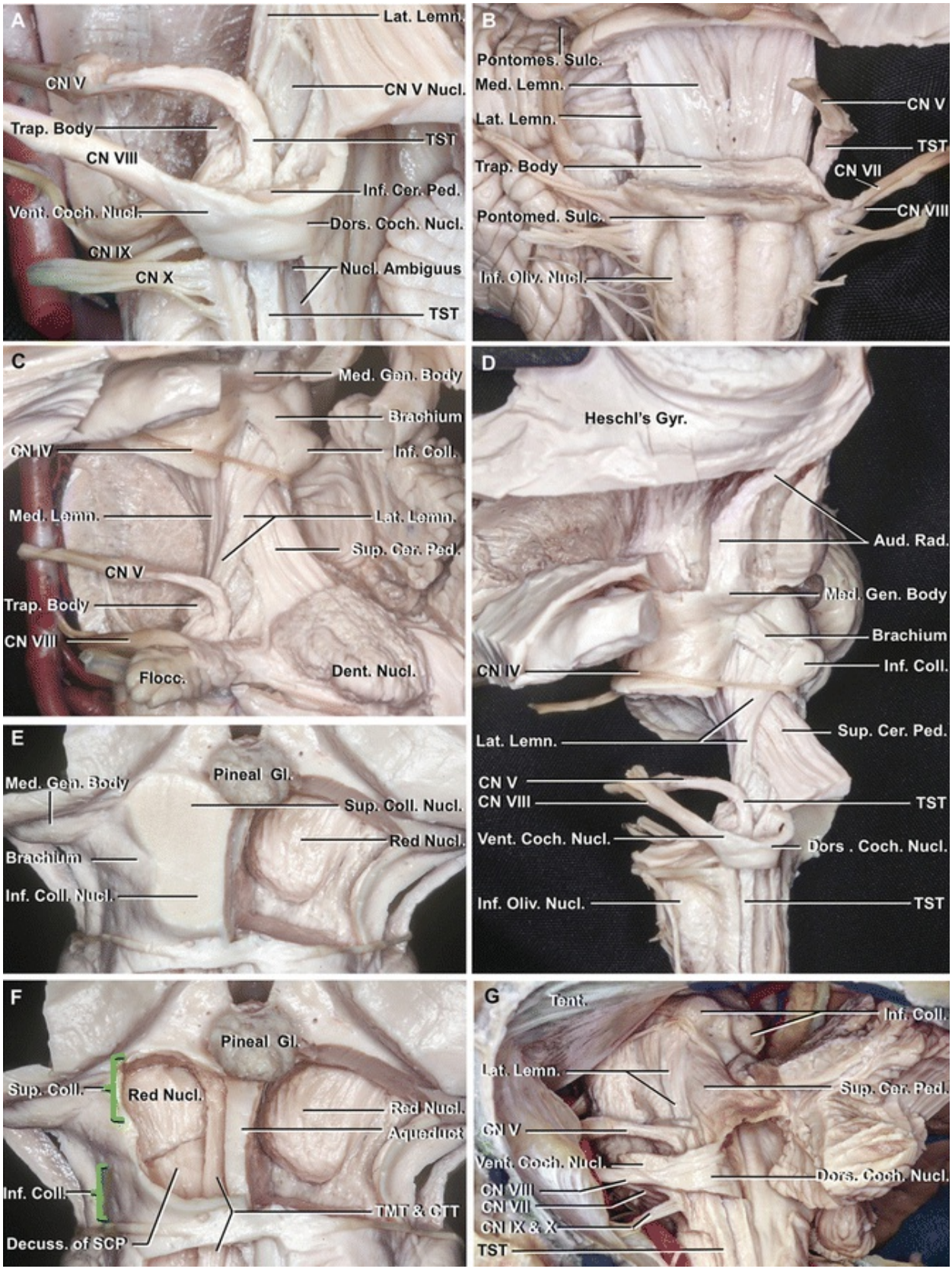
The cochlea converts sound waves into action potentials in the neurons of the cochlear nerve. Sound waves conducted to the oval window propagate in the perilymph of the cochlea. The action of these waves on the spiral organ of Corti generates excitatory synaptic input from the cochlear hair cells, which in turn depolarizes the cochlear end of the auditory nerve. This depolarization leads to the generation of the eighth nerve compound action potential.

The electrical activity within the cochlea can be recorded in the form of an electrocochleogram (ECochG; Fig. 3.1). The ECochG includes the cochlear microphonic, the summation potential, and the eighth nerve compound action potential. The hair cells generate the cochlear microphonic and summation potential within the cochlea (for details see section “Electrocochleogram” below). The eighth nerve compound action potential results from depolarization within the distal (cochlear) portion of the auditory nerve axons. It generates wave N1 of the ECochG. It is recorded as a phase negativity in the middle ear or extratympanic recording site. Sounds used to elicit ECochGs may produce more than one volley of action potentials within

the auditory nerve, thus producing N1 and N2 (and sometimes N3) components of an eighth nerve compound action potential. The N1 potential corresponds to wave I of the brain stem auditory response discussed below.

Auditory Pathway from Cochlear Nerve to Midbrain : Auditory Brainstem-Evoked Responses

Neural transmission of auditory signals starts with input from cochlear hair cells into the distal auditory nerve, whose anatomic course puts it at risk of injury during many procedures in the posterior cranial fossa. Once the signals reach the brainstem, they pass through a complex series of relay and processing stations to the midbrain. The signals travel partially ipsilateral to the side of stimulation, but mostly cross over to the contralateral side (see Figs. 3.1 and 3.2).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Aqueduct
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Tent.
Inf. Coll.
Lat. Lemn.
Sup. Cer. Ped.
CN V
Vent. Coch. Nucl.
Dors. Coch. Nucl.
CN VIII
CN VII
CN IX & X
TST

Fig. 3.2 Fiber dissection of the central auditory pathway . (**a**) Ventral and dorsal cochlear nuclei. Posterolateral view of the junction of the cranial nerve with the brainstem. The ventral cochlear nucleus is situated on the lateral and dorsal cochlear nucleus on the dorsal surface of the inferior cerebellar peduncle. They are positioned close to the trigeminal spinal tract, facial nucleus, and nucleus ambiguus, which are located ventromedial to the trigeminal spinal tract. The facial nucleus is hidden deep to the cochlear nuclei. (**b**) Anterior view. The ventral pons was removed to expose the medial and lateral lemnisci and the trapezoid body formed by crossing auditory fibers at the level of the lower pons. (**c**) Left lateral view. Fig. 3.2 (continued) The lateral lemniscus ascends medial to the intrapontine segment of the trigeminal nerve and lateral to the medial lemniscus and superior cerebellar peduncle to reach the inferior colliculus. (**d**) After reaching the inferior colliculus, auditory information is carried to the medial geniculate body by the brachium of the inferior colliculus, which ascends obliquely on the lateral surface of the midbrain. After reaching the medial geniculate body, the auditory pathway crosses beneath the lentiform nucleus in the sublentiform pathway to reach the auditory cortex on the most anterior transverse temporal gyrus, referred to as Heschl's gyrus. (**e**) Posterior view of the midbrain. The nuclei of the superior and inferior colliculi are located below the surface. The red nucleus is located at a deeper level. (**f**) Further dissection. Structures near the inferior collicular implant, in order from dorsal to ventral, are the oculomotor and trochlear nuclei located just ventral to the aqueduct in the midline, the trigeminal mesencephalic and central tegmental tracts near the midline, decussation of the superior cerebellar peduncle at the level of the inferior colliculus and the red nucleus located between the mid-level of the inferior colliculus, and the lateral wall of the third ventricle. (**g**) Left retrosigmoid view. The left cerebellar hemisphere was removed to expose the dorsolateral brainstem and the ventral and dorsal cochlear nuclei, lateral lemniscus, and inferior colliculus. *Aud.* auditory, *Cer.* cerebellar, *CN* cranial nerve, *Coch.* cochlear, *Coll.* colliculus, collicular; *CTT* central tegmental tract, *Decuss.* decussation, *Dent. dentate*, *Dors.* dorsal, *Flocc.* flocculus, *Gen.* geniculate, *Gl.* gland, *Gyr.* gyrus, *Inf.* inferior, *Lat.* lateral, *Lemn.* lemniscus, *Med.* medial, *Nucl.* nucleus, *Oliv.* olivary, *Ped.* peduncle, *Pontomed.* pontomedullary, *Pontomes.* pontomesencephalic, *Rad.* radiations, *Sulc.* sulcus, *Sup.* superior, *Tent.* tentorium, *TMT* trigeminal mesencephalic tract, *Trap.* trapezoid, *TST* trigeminal spinal tract, *Vent.* ventral

First-order auditory neurons run in the cochlear division of CN VIII from the spiral organ of Corti to the dorsal and ventral cochlear nuclei in the upper medulla. Myelinated dendrites of the auditory nerve pass into and through the spiral ganglia and form a nerve bundle in the internal auditory canal. Both the acoustic and vestibular portions of the auditory nerve pass through the temporal bone alongside the intracranial portion of the facial nerve. Together, they exit the internal auditory canal and travel to the brainstem. At the point of exit from the internal auditory canal, both facial and vestibulocochlear nerves make an acute turn from the anteromedial trajectory of the internal auditory canal within the petrous pyramid of the temporal bone posterolaterally toward the cerebellopontine angle of the brainstem. This acute turn "anchors" the vestibulocochlear nerve and puts it at risk of a stretch-induced neurapraxic injury during retraction of the brainstem, especially if the anatomy of the posterior fossa is already disrupted by pathology such as a cerebellopontine angle tumor.

Auditory nerve fibers synapse at either the posterior ventral cochlear

nucleus or the anterior ventral cochlear nucleus. Fibers that synapse at the posterior ventral cochlear nucleus also have connections with the dorsal cochlear nucleus. From the cochlear nuclei, second-order neurons may follow several pathways or combinations of pathways en route to the inferior colliculus. Most fibers decussate via the trapezoid body and pass up the lateral lemniscus to the contralateral inferior colliculus of the midbrain. Some fibers synapse in either the medial or lateral superior olivary nuclei. Others pass through the ipsilateral lateral lemniscus to the ipsilateral inferior colliculus. All ascending fibers synapse at the inferior colliculus. Third-order neurons from the inferior colliculus ascend to the medial geniculate body at the level of the thalamus on each side. Fourth-order neurons pass through the internal capsule and then form the auditory radiation to the primary auditory cortex. This complex pattern of tracts and relay stations is involved in elementary processing of auditory input, e.g., by extracting directional information about the source of sounds or as the afferent limb of auditory startle responses.

Activity in the neural pathways from the cochlea up to the midbrain can be recorded in the form of auditory brainstem responses (ABRs, sometimes also called brainstem auditory-evoked responses [BAERs] or brainstem auditory-evoked potentials [BAEPs]; see Fig. 3.1). Peaks in a recording of ABRs are labeled I through VII. As with other sensory-evoked potentials, the wave amplitude, absolute latencies, and interpeak latencies are evaluated to assess the integrity of the auditory system . The purported generators for these peaks are shown in Fig. 3.1 and are summarized in Table 3.1. Although some researchers have postulated that each peak corresponds to one generator, it appears that most ABRs are a result of the summation of inputs from multiple generators [2–4]. The pattern of connections in the auditory system contributes to this complexity, as ascending fibers both cross and bypass relay nuclei [4–6]. Nonetheless, the information in Figs. 3.1 and 3.2 and Table 3.1 can be used to help localize the site of an injury. While functional deficits can often be localized when injury or ischemia occurs, the complexity of the system may sometimes lead to changes in ABRs with no change in function [7, 8].

Table 3.1 Purported neural generators of ABR peaks[a]

Peak	Generator
I	Acoustic nerve (extracranial)

II	Acoustic nerve (intracranial), cochlear nuclei
III	Cochlear nuclei
IV	Lateral lemniscus, superior olivary complex
V	Inferior colliculus; contralateral lateral lemniscus
VI	Medial geniculate nuclei
VII	Thalamocortical radiations

[a]Peaks I, III, and V are considered the most useful for intraoperative neuromonitoring of ABRs. Most peaks are likely a result of the summation of inputs from multiple generators. While not all of these generators have been proven, the designations are clinically useful because they point out the approximate location of an injury. *ABR* brain-stem auditory-evoked potentials

Wave I of the ABR arises from action potentials in the most distal portion of the myelinated auditory nerve [9]. Wave I of the ABR is equivalent to N1 of the ECochG [10]. Wave I is a near field potential, recorded in the vicinity of the ipsilateral stimulated ear. It represents the peripheral potential of this sensory modality. Loss of wave I may indicate damage to the inner ear, but may also be caused by technical problems in the delivery of acoustic stimuli to the ipsilateral ear . When wave I is absent, ABRs cannot be used to make inferences about the integrity of the brainstem. Wave II of the ABR occurs at approximately the same latency as N1 of the compound action potential of the proximal auditory nerve to the cochlear nucleus. It occurs on the ipsilateral side. Wave III predominately originates in the caudal pontine tegmentum and region of the superior olivary complex. Near-field activity in the ipsilateral cochlear nucleus corresponds with wave III [11]. Ascending projections are bilateral, so wave III may receive input from both the ipsilateral and contralateral ear. Scalp-recorded wave III has been recorded at the same time as near-field activity in the cochlear nucleus [12]. Other recordings from the area of the cochlear nucleus in the lateral recess of the fourth ventricle indicate activity that coincides with wave IIIn (the negative peak between III and IV) [13, 14]. The auditory nerve may continue to be active during generation of the scalp-recorded waves III and IV [4]. Waves IV and V are often fused into a IV–V complex and their generators appear to be in close proximity of each other. Wave IV appears to reflect activity in ascending auditory fibers within the dorsal and rostral pons, caudal to the inferior colliculus with input from both ipsilateral and contralateral sides.

Wave V appears to predominantly reflect activity at the level of the inferior colliculus, perhaps including activity in the rostral portion of the lateral lemniscus as well as activity in the contralateral lateral lemniscus as it terminates on the inferior colliculus [4, 11]. Waves VI and VII are inconsistent and variable; therefore, they are not routinely monitored [15]. Most intraoperative neuromonitoring utilizes only waves I, III, and V to guide the intraoperative course [6, 16, 17].

Primary Auditory Cortex: Mid-Latency Auditory-Evoked Potentials

Tracts carrying auditory information project from the medial geniculate body to the cortex and other brain areas by multiple routes [18]. The medial geniculate body and cortex are linked by two main routes. The first pathway from the ventral medial geniculate body carries only auditory input and follows a sublenticular route through the internal capsule to Heschl's gyrus in the superior temporal lobe. The second pathway from the medial geniculate body projects into the inferior portion of the internal capsule and carries mixed auditory, somatic, and possibly visual sensory input. Auditory fibers from the medial geniculate body also project to the caudate nucleus, the putamen, and the globus pallidus.

Intrahemispheric and interhemispheric connections occur within the primary auditory cortex . Multisynaptic pathways likely exist in the middle and posterior areas of the superior temporal gyrus. Fibers also extend from the superior temporal gyrus to the insula and frontal operculum. The arcuate fasciculus provides auditory input from the auditory cortical areas in the temporal lobes to the frontal lobes. Wernicke's area in the temporal lobe and Broca's area in the frontal lobe receive auditory information via the arcuate fasciculus. Auditory input also passes to the hippocampus and occipital regions of the brain. Although these areas and pathways are not anatomically defined, they provide auditory input to memory and visual association areas. Auditory information passes between the two hemispheres through the corpus callosum, the primary connection between the left and right hemispheres. The transcollosal auditory pathway begins at the auditory cortex and passes posteriorly and superiorly around the lateral ventricles.

Electrical phenomena associated with activation of auditory cortex can be recorded in the form of mid-latency auditory-evoked potentials (MLAEPs,

see Fig. 3.1). MLAEPs are observed 10–60 ms after an auditory stimulus [19]. They appear to arise from the ventral portion of the medial geniculate body and primary auditory cortex in the primary pathway and also nonprimary pathways in the auditory thalamocortical projection [20, 21].

MLAEPs consist of four deflections, labeled Na, Pa, Nb, and Pb. Na and Pa latencies are between 10–25 and 22–40 ms, respectively [19]. Nb latency is at 40 ms and Pb is at 40–60 ms. Magnetoencephalographic and intracerebral recordings suggest that the Na/Pa complex is generated in the posteromedial part of the first transverse gyrus. MLAEPs correlate well with wakefulness during general anesthesia when using desflurane or propofol [22] and are associated with awakening from anesthesia following verbal command [23]. MLAEPs may be abnormal in neurologic diseases such as dementia, Parkinson's disease, multiple sclerosis, and myotonic dystrophy [24–32].

Vascular Supply of Auditory Pathway Structures

The cochlea receives its blood supply from the internal auditory artery, which is usually a branch of the anterior inferior cerebellar artery. The internal auditory artery is quite small in diameter and passes through the internal auditory canal along with the eighth nerve [33]. Damage to this artery will cause cochlear ischemia or infarction. Cochlear ischemia from obstruction or disruption of the internal auditory artery may affect the ECochG and wave I of the ABRs resulting in the loss of all subsequent components [34]. This may occur during tumor resection and lead to postoperative deafness [35]. These effects may be reversible if perfusion is restored within 15 min [35].

The brainstem (medulla, pons, and midbrain) receives the bulk of its blood supply from the vertebrobasilar system [36]. Except for the labyrinthine branch and early branches of the vertebral arteries, all other branches supply the brainstem and medulla. In principle, conducting vessels run along the brainstem surface, whereas the nuclei within the brainstem and the fiber tracts are supplied by perforating vessels. The vertebral arteries supply the medulla. The paramedian branches of the basilar artery supply medial pontine structures. Short circumferential arteries supply the anterolateral pons. Long circumferential branches of the basilar artery run laterally over the anterior surface of the pons and anastomose with branches of the anterior inferior cerebellar artery . The inferior colliculus receives blood from the anterior inferior cerebellar artery (caudally) with some

reinforcement rostrally from the superior cerebellar artery. Quadrageminal arteries arise from branches of the basilar artery and also supply the inferior colliculus.

The medial geniculate nucleus lies in the dorsal thalamus and receives its blood supply from posterolateral arteries (thalamogeniculate), which arise from the posterior cerebral artery. The primary auditory cortex, which lies in the superior temporal lobe, is supplied by branches of the middle cerebral artery and, therefore, by the anterior cerebral circulation. Interhemispheric fibers that connect the left and right auditory cortex pass through the posterior corpus callosum, which receives its blood supply from the pericallosal artery, a branch of the anterior cerebral artery [18, 37].

ABRs may change during posterior fossa surgery as a result of ischemia or infarction from clipping or compression of arteries that perfuse the brainstem auditory pathways [8]. Patients who experience major changes in ABRs that persist to the end of the operation almost always have new postoperative neurologic deficits [38, 39]. Changes in waveforms almost always reflect anatomical deficits. For example, damage below the mesencephalon will affect wave V, and wave III may or may not be spared depending on the location of the lesion. Wave III would be lost if the lesion is caudal to or at the superior olivary complex. However, wave I would remain intact. Interruption of the blood supply proximal to the internal auditory artery may affect wave I. For example, during posterior fossa vascular surgery, damage to the vertebrobasilar system, which supplies the anterior inferior cerebellar artery and the internal auditory artery, could cause ischemic cochlear damage and loss of all waveforms.

Techniques for Recording Auditory-Evoked Potentials

Auditory-evoked potentials can be recorded from all neuronal structures that contribute to the auditory system [40]. The first potentials generated in response to sound come from the cochlea. They can be recorded in the form of the ECochG . Because the cochlea lies well protected in the temporal bone, direct damage during surgery is typically either not a concern or planned as part of the surgical access, such as in the translabyrinthine approach to the posterior fossa. Therefore, monitoring of the ECochG is not widely used. From the cochlea, potentials are carried along the auditory nerve and the brainstem to the primary auditory cortex and further to association areas of

the cortex. MLAEPs reflect activation of the primary auditory cortex occurring 10–50 ms after acoustic stimulation. MLAEPs are also sensitive to the effects of general anesthetics and are therefore not used for intraoperative monitoring of the integrity of the auditory pathway. On the contrary, because of their sensitivity to anesthetics, they have been used to monitor cortical anesthetic drug effect in order to help assess “anesthetic depth.” Their performance as a monitor of anesthetic depth is comparable to that of other monitors relying on the processed electroencephalogram (EEG) [41]. Recording MLAEPs requires both stimulation and recording and is therefore technically more elaborate than the set-up for processed frontal EEG. This fact has hampered commercial exploitation and clinical acceptance of MLAEPs as a monitoring technique during anesthesia.

Short-latency potentials occur less than 10 ms after an acoustic stimulus and originate in the acoustic nerve and brainstem. They are typically referred to as auditory brainstem responses (ABRs); sometimes also described as BAERs or BAEPs. An anesthesiologist is most likely to encounter intraoperative use of auditory-evoked potentials in the form of ABRs.

The recording of auditory-evoked responses presents significant technical challenges because the signals originate from anatomical structures that are far removed from the site of electrode placement on the head’s surface. Because of this distance between purported anatomical generator and recording electrode, these types of responses are called far-field responses. Their amplitude is small, typically less than 0.5 μV, compared to the EEG and the electrocardiogram, which are a 100 and a 1000 times larger, respectively. Because of their small amplitude, auditory-evoked potentials cannot be seen on continuous recordings of electrical activity. Instead they require signal averaging of the responses to 500–2000 acoustic stimuli.

Stimulation

Acoustic stimuli are presented intraoperatively as “clicks” of 100-μs duration. The clicks comprise a broad spectrum of tone frequencies and thus activate much of the cochlea. This nearly simultaneous activation of the cochlea triggers a synchronized volley of action potentials in the acoustic nerve, which in turn can be recorded as well-defined peaks in the auditory-evoked response. Clicks can be delivered in three different “polarities”—rarefaction, condensation, or alternating (Fig. 3.3). The description of the click polarity refers to the initial movement of the tympanic membrane away from, toward

or alternating between away and toward the stimulator. In practice, either an alternating polarity is used in order to cancel out the stimulus artifact or the polarity that results in the clearest response. In rare instances bone conduction can be used to deliver the acoustic stimulus.

The intensity/volume of the click stimulus can be based on the results of preoperative determinations of hearing thresholds. A stimulus intensity of 70 dB above normal hearing level (70 dB nHL) normally yields maximal auditory responses. In the absence of a preoperative audiogram, 90–95 dB is frequently used, particularly in the presence of a preoperative hearing deficit. Note that a decrease in the stimulus intensity as it is delivered to the cochlea reduces the amplitude of the auditory-evoked potentials (see Fig. 3.3). Such a reduction can result from a dislodged stimulator, fluid in the middle ear (e.g., from breached mastoid air cells), accumulation of nitrous oxide in the face of a blocked eustachian tube, or damage to the auditory pathway.

Depending on the structures at risk during surgery, stimuli are typically presented unilaterally even though rostral parts of the auditory pathway proceed largely crossed over to the contralateral side, but also to a lesser extent uncrossed (see above). Unilateral presentation of stimuli allows diagnosis of lesions to the cochlea and distal auditory nerve ipsilateral to the side of stimulation. If unilateral stimulation is used, bone conduction to the contralateral ear is typically “blocked” by masking. Masking refers to the continuous administration of white noise to the nonstimulated ear typically at intensities 30 dB less than the click stimulus. An alternative way of stimulation is the use of interleaved stimuli alternating between right and left ear, but sorted into separate averaged recordings for left and right ear stimulation. Such interleaved stimulation does not allow for masking, but the small decrement in sensitivity is made up by the fact that both sides are monitored continuously. Bilateral stimulation is sometimes used to record MLAEPs.

Because auditory responses up to the level of the brainstem occur within 10 ms of stimulation, stimuli can be presented as frequently as 30–50 times per second (30–50 Hz). If there is a preexisting hearing deficit such as that caused by a large acoustic neuroma, slower stimulation at 10–15 Hz may be necessary. Stimulus rates should never be equal to or a divisor of the line frequency of 60 Hz, because signal averaging will then tend to augment the electromagnetic interference from the line frequency rather than canceling it out.

Physically, the stimuli can be presented either with earphones or with foam ear inserts connected by a tube to stimulators placed at a short distance (i.e., <10 cm) from the ear. Earphones are used less frequently, because they put a source of electromagnetic interference close to the generators of the auditory response. Ear inserts are less bulky and do not contribute to noise. The acoustic transmission of sound from the stimulator through the tube insert to the tympanic membrane delays auditory responses by less than 1 ms.

Electrocochleogram

Recordings of the ECochG require placement of a primary electrode close to the cochlea. During middle ear surgery, such an electrode can be placed on the promontory or the round window. A noninvasive recording is possible from the external ear canal, which is preferred over a more distal mastoid electrode [42]. The secondary or reference electrode can be at the contralateral ear or at Cz. The filter bandpass is set to 5000–3000 Hz. Stimulation parameters are typically the same as those described above, even though the two cochlear potentials depend on stimulus duration and are more pronounced, when longer stimuli are used [43]. Typical timebases used for ECochGs are less than 10 ms.

Three potentials characterize the ECochG (Fig. 3.3). In sequence of activation, they are the cochlear microphonic, the summating potential, and the N1 potential. Based on the sequence of steps that translate auditory input into nerve impulses, the cochlear microphonic and summating potential originate in the hair cells of the organ of Corti and the N1 potential originates in the distal auditory nerve. The cochlear microphonic is an AC voltage that mirrors the waveform of the acoustic stimulus. Therefore, it can be minimized by stimulating with alternating polarity and can be augmented by subtraction of traces recorded with alternating polarity (Fig. 3.3) [44]. In contrast, the summating potential is a DC current thought to reflect the fact that transduction of the stimulus by the hair cells does not occur uniformly and at the same time throughout the cochlea. Therefore, the summating potential is increased in patients with inner ear diseases such as Meniere's disease that further distort the transduction of acoustic stimuli in the inner ear [44]. With the short clicks typically used for stimulation, the summating potential is reflected as a "shoulder" on the much larger N1 potential. The final potential recorded in the ECochG is the N1 potential, which reflects activation of the distal auditory nerve and thus the same physiologic

phenomenon as wave I of the ABR. Because it is a near-field potential, it is large in amplitude and requires fewer averages than a full ABR. Those laboratories that use ECochG for intraoperative monitoring typically focus on the N1 potential to quickly ascertain successful stimulation of the auditory system similar to the more familiar Erb's point recording used with SSEPs.

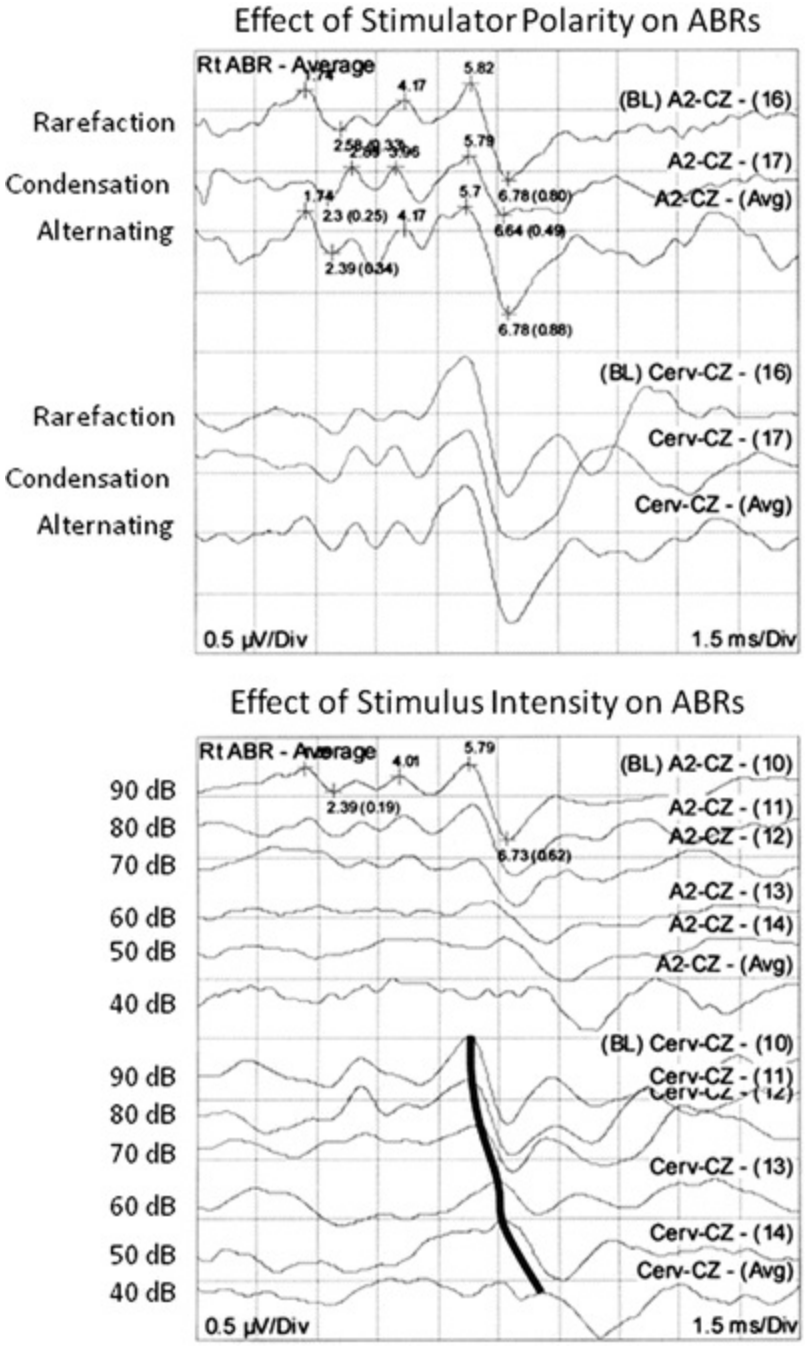

Fig. 3.3 Effect of click polarity and stimulus intensity on brainstem auditory-evoked potentials. The

top panel shows ABRs recorded in response to three different click polarities. Note that click polarity has notable effects on the early ABR in the A2-Cz channel, because it contains information from the ECochG. The *bottom* panel shows the effect of a stepwise decrease in stimulus intensity on the ABR. Note that wave I is lost at stimulus intensities less than 80 dB, suggesting a problem with sound delivery, whereas the desynchronization of waves III and V at low stimulus intensities are indistinguishable from changes caused by damage to the auditory system

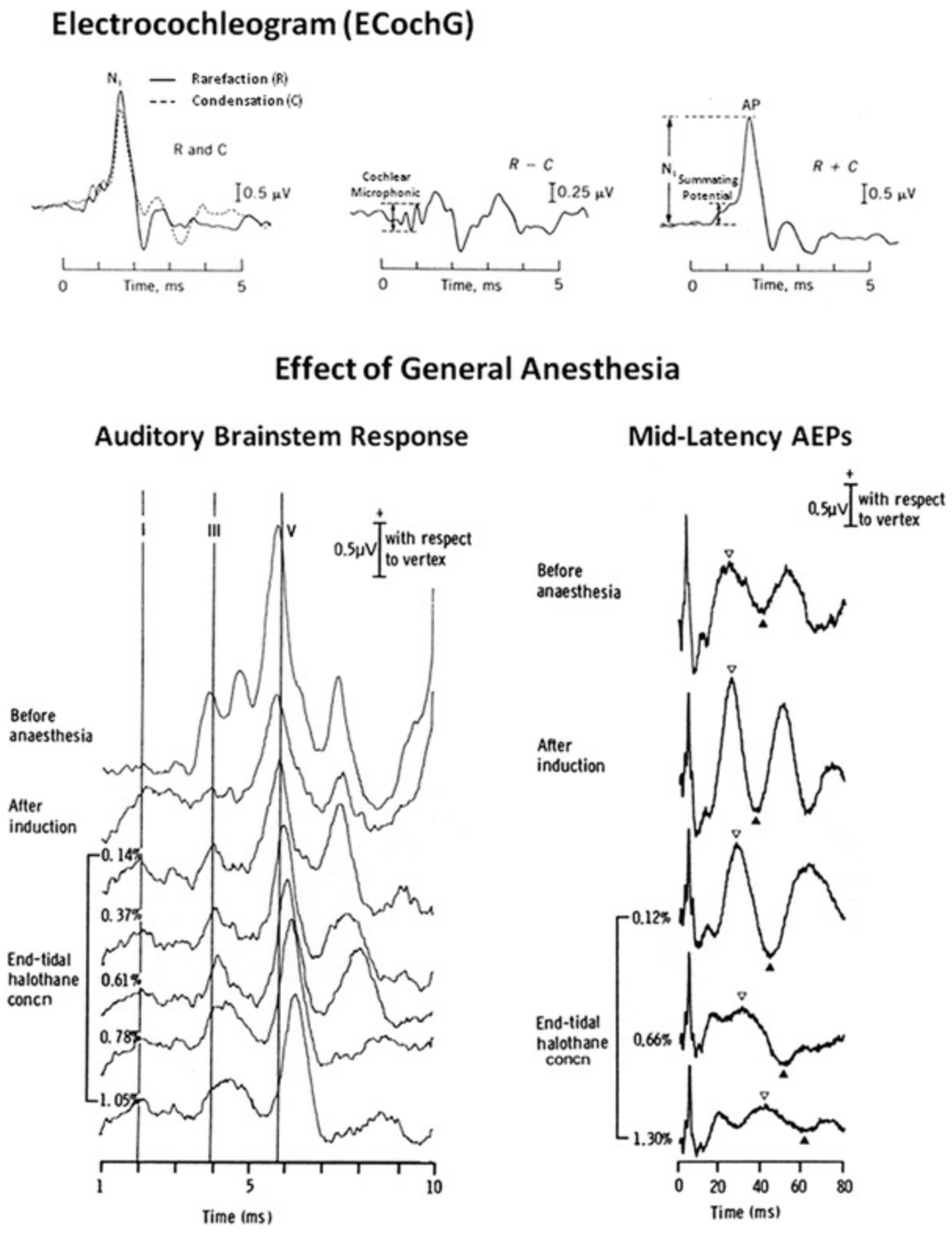

Fig. 3.4 ECochG and effects of anesthesia on brainstem and MLAEPs. The ECochG contains a prominent wave N1 that coincides with activation of the distal auditory nerve. N1 is larger than a typical ABR and therefore easier to record than wave I of the ABR. Electrical activity within the

cochlea is reflected in the cochlear microphonic and summating potential. Subtraction of ECochG traces in response to rarefaction and condensation clicks emphasizes the cochlear microphonic (middle panel), whereas addition emphasizes the summating potential. Anesthesia with halothane differentially affects ABRs and MLAEPs. Whereas the latency of wave V of the ABR increases by less than 1 ms and the amplitude is unaffected (left panel), the mid-latency response nearly vanishes at high concentrations of halothane. (Right panel adapted from Coats [44]; with permission. Right panel bottom adapted from Thornton et al. [47]; with permission.)

Brainstem Auditory-Evoked Potentials

A normal ABR recording should show at least three clearly identifiable waves/peaks. Although an ABR recording is classically described as containing seven waves (see Fig. 3.1), a minimum of waves I, III, and V should be present for the signal to be useful for intraoperative monitoring. A typical montage includes electrodes on the ipsilateral ear and one at the vertex, i.e., A1-Cz and A2-Cz for left and right sides, respectively. Additional channels can be used to aid in the identification of individual peaks (see Fig. 3.1). Specifically, a cervical midline electrode referenced to Cz sometimes aids in identification of wave V, whereas an A1-A2 or A2-A1 channel can aid in identification of wave I if the ECochG is not monitored separately. With the exception of wave I, all potentials recorded as ABRs originate from structures deep within the head and are considered far-field potentials. Therefore, wave I shows up best in channels that contain an electrode near the ipsilateral ear. Subsequent waves, in contrast, can be activated by stimulation from either side and contain limited information that allows assignment of changes to either the right or left side. In a baseline recording, it is important to clearly identify wave I and compare it with that from the contralateral ear. Clear identification of wave I guards against situations when the stimulators for the right and left sides have mistakenly been reversed. Furthermore, the presence of wave I assures delivery of an adequate stimulus and thus allows identification of unilateral damage to the ipsilateral auditory nerve.

The typical epoch for ABRs is 10 ms although the stimulus delay imposed by ear insert stimulators and the presence of hearing loss sometimes requires a longer epoch. The bandpass is set from 100 or 150 to 3000 Hz and a notch filter for the 60-Hz line frequency can be added.

MLAEPs

Auditory-evoked potentials beyond the brainstem are recorded either for

research purposes or to measure anesthetic drug effect [45, 46]. Examples of late potentials include the event-related potential P300, which occurs about 300 ms after an appropriate stimulus or the mismatch negativity that occurs late after an oddball sequence of stimuli. Both reflect elements of higher order processing and are absent under anesthesia. Latency and amplitude of early peaks of the MLAEP correlate with anesthetic drug effect (see Fig. 3.3) [47]. Two commercial monitors of anesthetic drug effect have been developed based on MLAEP technology, although neither is widely used [48]. Stimulation for MLAEPs can be done as described above, although stimulus durations up to 500 μs and simultaneous stimulation of both ears are described. The typical band pass is set to 15–250 Hz. The stimulation rate needs to be less than 10 Hz because the epoch is at least 50 ms. The montage can be mastoid—Cz, especially under anesthesia, but can also be a midline montage of a cervical electrode referenced to Cz or Fz. The benefit of using a midline montage is that it avoids recording the postauricular muscle response [45]. The postauricular muscle response is an involuntary muscle reflex in response to loud acoustic stimuli. Its amplitude may exceed that of the MLAEP and its latency of 15–20 ms coincides with the early peaks of the MLAEP. Furthermore, because it is triggered by the acoustic stimulus, signal averaging will not remove it.

Anesthetic and Physiologic Considerations for Monitoring of Auditory Brainstem Responses

Auditory brainstem responses are very resistant to the effects of general anesthetic agents (see Fig. 3.3) [47]. Therefore, no modification of the anesthetic approach to a patient is needed because of ABR monitoring. The small increases in latency caused by anesthetic agents are not clinically significant and are easily distinguished from changes in ABRs caused by technical and physiologic factors.

Sometimes technical problems cause gradual or abrupt changes in ABRs intraoperatively in the absence of physical damage to the auditory pathway (see also Chap. 29, “ENT and Anterior Neck Surgery”, Tables 29.2 and 29.3). Diminished input can occur abruptly, e.g., by kinking the tube of an ear insert on the down ear in a lateral or park bench position, or gradually, e.g., by fluid accumulation in the middle ear. Conduction in the middle ear diminishes when fluid enters the middle ear either in the form of irrigation

fluid, e.g., during drilling in the mastoid bone, or as blood from any of the anatomic structures in the vicinity. Accumulation of nitrous oxide in the face of a blocked eustachian tube can also decrease conduction in the middle ear. Note that the changes caused by diminishing acoustic input look very similar to progressive damage of the auditory pathway if changes to wave I are not assessed (see Fig. 3.2). Finally, drilling of bone causes noise of an intensity that overwhelms the cochlea, prevents recording of ABRs during drilling, and alters ABRs recorded shortly after the cessation of drilling.

Physiologic factors that affect the entire ABR are interruption or vasospasm of the cochlear artery or avulsion of fascicles of the distal auditory nerve within the inner auditory canal. Both diminish or abolish wave I and all subsequent waves of the ABR and result in diminished hearing or deafness, respectively.

The intracranial portion of the auditory nerve can be affected by traction on either nerve or brainstem resulting in an increase in the latency between waves I and III. This change occurs only ipsilateral to the side of the injury. The degree of desynchronization of wave III reflects the severity of the insult and frequently the rate of change of the potential is inversely related to reversibility, i.e., a signal that changes profoundly and rapidly is less likely to recover [49]. Similar changes can be caused by cold irrigation or heat from the cautery or drying of the auditory nerve [50, 51]. Application of papaverine to relieve vasospasm [52] or aggressive attempts to fill the subarachnoid space with irrigation fluid prior to dural closure may lead to ABR changes [53].

Damage to the brainstem either in the form of direct trauma or through compromise of blood supply or blood flow will be reflected in ABRs to the extent that the auditory pathway is involved. While persistent ABR changes nearly always predict brainstem dysfunction, damage to the brainstem may still occur even though ABRs remain unchanged. Many centers use ABRs together with other modalities such as somatosensory-evoked potentials (SSEPs) and motor-evoked potentials (MEPs) to monitor the integrity of the brainstem. Again persistent changes in monitored signals typically predict new postoperative deficits, but unchanged signals do not rule out the potential for injury to the brainstem. That is because the monitored pathways only cover a small part of the cross-sectional area of the brainstem. Thus, multimodality monitoring has good specificity, but limited sensitivity for assessing brainstem integrity.

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Footnotes

1 Asterisks indicate key references.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_4

4. Visual-Evoked Potentials

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Keywords Intraoperative monitoring – Visual pathways – Visual-evoked potentials – Visual pathway stimulation – Flash electrographic response – Flash VEP response – Monocular stimulation – Binocular stimulation – Light stimulation – Flash stimulation – Retinal stimulation

Introduction

One of the important goals of surgical procedures involving the visual pathways (retina, optic nerve (ON), optic chiasm, optic tracts, lateral geniculate nucleus in the thalamus, optic radiation, and occipital visual cortex) is the preservation of visual function and in cases of visual impairment, where possible, its improvement [1–4]. With these goals in mind, efforts to evaluate and enhance the usefulness of intraoperative monitoring (IOM) of the visual pathways that began in the early 1970s have continued. Wright et al. [5] are generally credited with the first report of a method for continuous monitoring of the visual pathways in 1973; utilizing brief flashes of light to evoke electroretinographic (F-ERGs) and visual-evoked potentials (F-VEPs) during orbital surgery. This triggered a number of other researchers to test their usefulness [2, 3, 6–21]. While some have reported favorable results and outcomes [5, 22–31], others have dismissed

their use, citing technical difficulties associated with the delivery of visual delivery in an operating room (OR) setting, large inter- and intra-individual variability, instability and unreliability of the visual responses [32–36], their susceptibility to anesthetics, particularly inhalational agents [32–37], and lastly and most damning, the poor correlation of IOM results to postoperative functional outcomes. All of these findings have led to a general disenchantment with their intraoperative use [7, 12, 18, 32–35, 37–45].

Still, on a *case-by-case basis*, monitoring of visual-evoked potentials (F-VEPs) has helped guide surgeries of the orbit [46–48], and anterior visual pathways during tumor or lesion removal where its use has helped identify encroachment of tumors on the optic chiasm, and has aided in the differentiation of normal ON tissue from tumor tissue; especially when the tumor encompasses the ON [2, 12–15, 19, 20]. Direct ON stimulation has helped navigate during surgical removal of tumors involving the anterior visual pathway and skull base tumors [13–15, 49, 50] with good outcomes. Though improved microsurgical techniques during procedures involving the sellar and parasellar regions [19] have significantly reduced the incidence of visual complications related to ON or chiasmal manipulation and/or devascularization, the potential remains for real-time, inadvertent, and potentially harmful maneuvers that may cause prolonged or intense indirect traction or compression of the ON to go unnoticed. Concern for preventing devastating outcomes to the visual pathway has encouraged a small but dedicated group of researchers to pursue refinement of the techniques for IOM of the visual pathways [2, 3, 13, 15, 19–25].

Other reports of beneficial use of IOM visual pathway monitoring have been contained in the literature. F-ERGs [51, 52] and F-VEPs [36, 37, 53, 54] have been reported to be helpful in assessing the depth of anesthesia. F-ERGs have been utilized in monitoring retinal function during eye surgery [46, 47, 54–56] and endovascular procedures involving orbital or periorbital vascular lesions [21] with good outcomes. They also have been used to monitor retinal perfusion during procedures employing extracorporeal circulation and hypothermic circulatory arrest [11, 57]. F-VEPs have reportedly been helpful for anatomic navigation of the optic radiations during surgical treatment of an occipital arteriovenous malformation [17], and by use of diffusion tensor imaging-based tractography for functional monitoring of the visual pathway [58]. Finally, visual-evoked responses obtained from direct stimulation of the optic tract have been used as a method for globus pallidus internus (GPi)

targeting during pallidotomy [59, 60] and deep brain stimulation (DBS) interventions for treatment of Parkinson's disease where such procedures are performed under general anesthesia or for patients who otherwise are unable to cooperate during the procedure [16]. Although many of the above reports involved case report(s) or series, their findings suggest that further examinations of these monitoring methodologies and applications are needed. A better understanding of visual stimuli, the portions of the visual pathways that are stimulated, the methods for recording neurophysiologic responses, the effects of surgical manipulation, anesthetic management, and other perioperative factors on responses, will hopefully lead to improved IOM results. This in turn may spark renewed interest in research to further enhance techniques and outcomes for IOM of the visual pathways.

Anatomy and Physiology of the Visual System

The optic structures of the eye project images onto the light-sensitive receptors of the retina, where a surprisingly high degree of neural processing is accomplished through the retina's complex pattern of interconnections between excitatory and inhibitory neurons . Some nerve fibers have small excitatory fields surrounded by inhibitory areas, and others have inhibitory center areas surrounded by excitatory ones. As a result, a good stimulus for exciting the visual pathway would be one that undergoes changes in contrast gradients (i.e., pattern-reversal). Because, in general, patient cooperation is not possible for the majority of surgical procedures, it is not feasible to utilize stimulation using high-contrast pattern reversing checkerboard stimuli that are used in diagnostic testing. Hence, the frequently employed stimulus for eliciting VEP responses for monitoring purposes has been flash stimuli [24, 61–63]. While the spatial distribution of the light over the visual field of each eye is transmitted to the brain through the optic nerves, very little information regarding the temporal variations in illumination is conveyed. Therefore it is key to note that when flash stimuli are employed for IOM monitoring purposes, what is actually being monitored is the visual pathways for light perception and not for visual acuity [64].

The neural information of flash stimuli travels from the optic chiasm onward, via the optic tracts to the lateral geniculate body in the thalamus, which then projects via connections to the visual cortex (Fig. 4.1) [64]. Though coding of the visual system has been intensively studied yielding a

wealth of information about the retina's complex neural network responses [65], information about the gross response from the ON and lateral geniculate body to flash stimuli remains relatively sparse, and in general, early cortical activation following flash visual stimulation is not well understood in humans [65]. It is important to note that the optic pathways cross at the chiasm such that monocular or binocular flash stimuli used in monitoring will produce bilateral pathway activation behind the chiasm unless a means of hemifield visual stimulation can be utilized (as can be done in awake subjects).

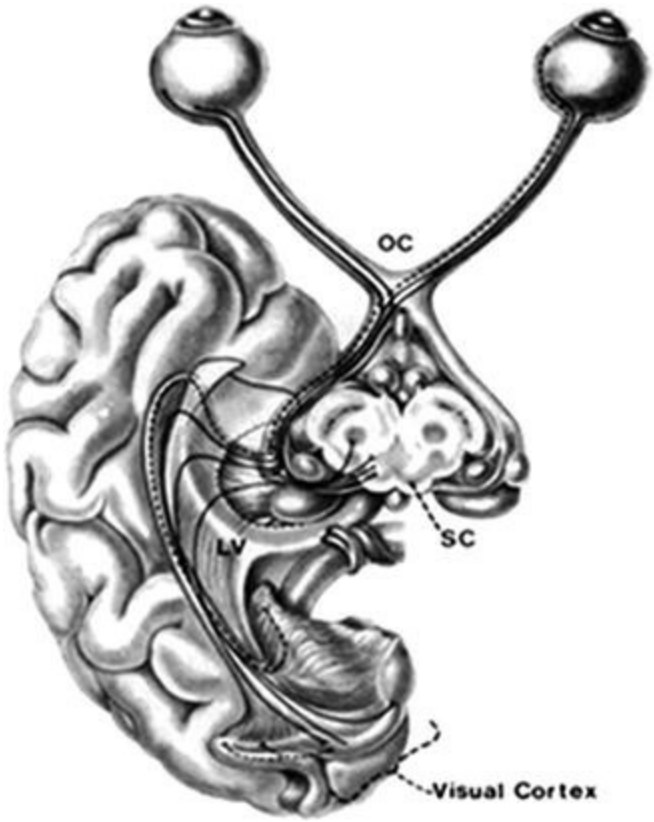

Fig. 4.1 Schematic drawing of the visual pathway. *OC* optic chiasm, *SC* superior colliculus, *LV* lateral ventricle (from Moller et al. [64]; with permission)

Eliciting and Recording Flash Visual-Evoked Potentials

Depending on the portion(s) of the visual pathways at risk during surgical procedures, a number of strategies for stimulation of those pathways have been explored.

Flash Electrographic Response

Responses generated by stimulation of the retina (F-ERG) have played a fundamental role in the diagnostic evaluation of retinal health [66]. For IOM purposes, they have been primarily used to ensure retinal and visual pathway stimulation . They also have been used to monitor surgeries of the orbit and as a measure of anesthetic depth [46, 47, 51, 52]. The main components of the F-ERG are a negative-going a-wave with latencies occurring between 24.2 ± 1.1 and 27.2 ± 3.7 ms and a positive-going b-wave with latencies of 45.0 ± 1.5–55.1 ± 7.4 ms. The a-wave, in response to a bright flash, largely reflects photoreceptor function but there may be a contribution from postreceptoral structures [67]. The b-wave, which is of higher amplitude than the a-wave in normal subjects, reflects postphototransduction activity. The origin of the ERGs' a- and b-waves is reportedly a combination of activities that include photoreceptor potentials, potassium-mediated current flow, and DC potentials within Müller cells [67]. The F-ERG to a flash stimulus is a mass response; thus F-ERG responses can appear normal when dysfunction is confined to small retinal areas (e.g., macular dysfunction). It has been reported that despite the macula's high photoreceptor density, an eye with purely macular disease has a normal bright single flash ERG response [67]. Typical ERG-VEP responses to flash stimuli delivered by light-emitting diode (LED) goggles are included in Fig. 4.2.

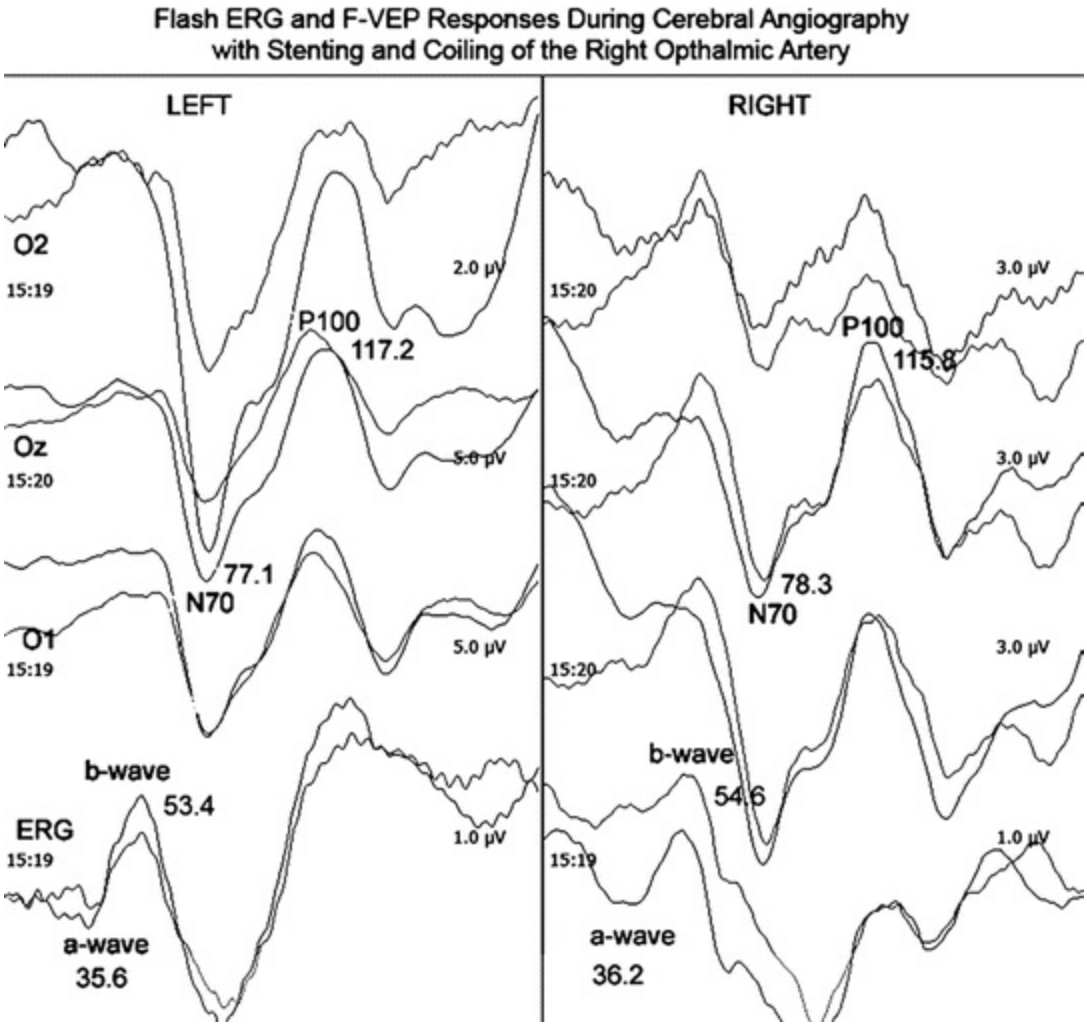

Fig. 4.2 An example of intraoperative flash electroretinograms (F-ERGs) recorded from surface electrodes placed in the orbital notches bilaterally and referenced 3 cm laterally and flash visual-evoked responses (F-VEPs) recorded from electrodes placed at left occipital (O1), mid-occipital (Oz), and right occipital (O2) scalp locations is shown. The responses were obtained at baseline for a patient undergoing endovascular cerebral angiography with stenting and coiling for treatment of a right ophthalmic artery aneurysm. The rate of flash stimulation was 1.1/s. An average of 100 responses was obtained. Anesthetic management included induction with thiopental, sufentanil and dexmedetomidine (1 μg/kg), and maintenance with sufentanil infusion, 0.5 MAC of isoflurane and continuous infusion of dexmedetomidine (0.7 μg/kg/h)

Flash VEP Response

The F-VEP is generated by postretinal areas of the central nervous system in response to visual light stimulation and is a reflection of activity in segments of the primary visual pathway that project through the lateral geniculate body to the cortical visual fields. The response is composed of a triphasic waveform with an initial small positive deflection (40–50 ms), followed by a

second negative deflection at 70–89 ms (often referred to as N70 or N1), followed by a positive wave at about 100 ms (P100 or P1) [68]. Though not unequivocally documented, the generator sites for the three waves of the F-VEP to LED stimulation are believed to originate from the lateral geniculate, striatum, and areas 17, 18, and 19 of the visual cortex [27, 68, 69].

Techniques for Eliciting F-ERG and F-VEP

The lack of suitable equipment for visual stimulation has been a severe handicap to the use of ERG-VEP for IOM. Pattern-reversal stimuli or multifocal electroretinographic stimuli (which are routinely utilized in diagnostic settings to evaluate retinal function related to acuity) cannot be utilized on unconscious patients in the OR setting given the requirement for their cooperation and visual fixation on the stimuli. Moreover, the shift in dark vs. light pattern/contrast of these stimuli, which is key to stimulating the retinal structures related to visual acuity, would certainly be diminished if not lost if one were to try to deliver these stimuli through closed eyelids. Because flash stimuli do not require patient fixation and cooperation and can be delivered through closed eyelids, they have been the most frequently used stimulus in the OR setting. Unfortunately, early research demonstrated that even when flash stimuli were employed for clinical diagnostic use (e.g., for assessment of ON pathology in multiple sclerosis patients), VEP responses to bright flashes were found to be normal while their responses to pattern-reversal stimulation were abnormal [68]. Moreover, the amplitude and latency of VEPs elicited by the above flash stimulation methods unfortunately demonstrate considerable patient inter- and intra-variability of amplitude both in diagnostic and intraoperative settings [70]; especially in neonates, where maturation of the cerebral cortex appears to play a factor [71]. So although flash stimulation has largely been the stimulus of choice for IOM, it is not the best stimulus for assessing the preservation of fine visual acuity and function. Rather it has been used to assess in a rudimentary fashion whether response to stimulation can be conveyed along various points of the visual pathways [71]. Even so, it is important to note that when there is preexisting visual dysfunction that may disrupt the ability to convey such stimulation, recording responses may be compromised, although that has not been entirely confirmed. Multiple studies [2, 3, 20, 23–25] reported that preexisting severe visual dysfunction (even for patients with preexisting visual acuities of <0.4 (20/50)) negatively impacted their ability to record F-

VEPs while others indicate that F-VEPs for IOM can be obtained successfully from some patients with severe visual deficits [3, 19], when onset of the dysfunction was acute.

Devices for Flash Stimulation

Researchers have worked to develop improvements in devices for the delivery of flash stimuli for IOM use, since the problems of delivering stimuli may be key to developing more effective activation of the pathways that correlate with functional vision. Initially a traditional strobe light was used to elicit responses but was found to be cumbersome in the OR and delivery of the flash could be ineffective since it might be partially obscured by the scalp flap and drapes if a bicoronal scalp incision is used, thus requiring a modification of the surgical approach.

Fiberoptic haptic lens [72] and scleral contact lens [26] connected to photostimulators were developed to provide flash stimuli in the 1970 and 1980s. Although some claim the resulting responses were more robust than those later obtained with LED stimulation (especially through dilated eyes) [72], use of contact lens for IOM has lost favor due to the invasive nature of the technique (e.g., lid sutures to keep the corneal lens recording/stimulating device in place) and the potential risk of corneal abrasions and ulcerations with their use. The American Electroencephalographic Society (AEEGS) Guidelines for IOM recommend that such hard lens stimulators be kept on the eyes for a maximum of 45 min (limiting their practical use for a majority of surgical procedures) and that users need to carefully examine the safety data from the stimulator's developer before employing such lenses in the OR [73].

Because most shy away from the use of contact lens stimulators, LEDs mounted in eye patches [23–25] or goggles [9, 27] have been used, but the latter are bulky, require a headband, and can interfere with surgery. Their use also carries some risks . Care needs to be taken to ensure that the goggles are well-supported by the bony ridge of the patient's orbit and that they remain in place during the surgery. Should they inadvertently slip down and put direct pressure on the globe of the eye, they can cause central retinal artery thrombosis [9].

Type of Light Stimulation

The AEEGS issued a recommendation that flash VEPs induced by white stroboscopic light (F-VEPs) be differentiated from those induced by red LEDs (LED-VEPs) [73] by utilizing the appropriate abbreviations. However, in general, in the IOM literature, the terms F-ERG and F-VEPs have been used to represent both. However, abbreviations aside, the two methods of stimulation may actually activate different retinal and cortical pathways [12]. Newer LED stimulating goggles and patches provide significantly increased luminosity [23–25]. Although safety data regarding their use is scant, authors reporting on their IOM use have not reported any postoperative sequelae, including cases involving lengthy neurosurgical procedures [2, 3, 20, 23–25].

Monocular vs. Binocular Stimulation

Although binocular stimulation has been used for some studies, when the goal is to evaluate individual retinal and anterior pathways, the visual stimulus should be delivered and recorded monocularly with responses from the contralateral eye, if clinically unaffected, used as a control [73].

Pupillary Size and Retinal Luminance

When employing flash stimuli to elicit F-ERGs and F-VEPs, efforts to maintain pupil size and retinal luminance throughout the surgical procedure are important because these parameters affect the response latency and amplitude. Kriss et al. [74] showed that F-VEP latency through closed eyes is increased when compared to those recorded through open eyes. Intraoperative use of narcotics often results in miotic pupils that reduce retinal luminance, and staged dosing of narcotics during the surgical procedure may induce changes in latency and amplitude that may be misinterpreted as a surgically related event. It has been recommended that maximal dilation of the pupils be done through use of conjunctival instillation of mydriatics at the start of the case [73], but that may be contraindicated when perioperative assessment of pupillary response is required or preferred. Of note, recent and notably successful reports of intraoperative recordings of F-ERG and F-VEPs did not employ pupil dilation as part of their total intravenous anesthetic and monitoring management: propofol [2], administration of opioids [23–25], or remifentanil [2]. It is important to note that those with successful IOM recordings of F-VEPs employed newer and brighter 16 LED arrays embedded in soft round silicone disks [2, 20, 23–25] or in goggles [3, 18] with luminosity adjustable from 500 to 20,000 Lumens

(Lx), which helped to ensure retinal illumination and stimulation.

Recording F-ERGs and F-VEPs

The recommended standards for IOM of VEPs were issued in 1987 by the American EEG Society [73]. To obtain consistent results, the guidelines advised that the following parameters be documented and remain constant throughout the IOM period. Though no such standards for IOM recording of ERG have been published, the following would likely apply to them as well. Given the expected high degree of F-VEP response variability even in *awake* subjects [73], each patient with a reproducible response should serve as his or her own control in the IOM setting. A simultaneous recording of F-ERG responses is useful for confirmation of retina stimulation.

Before the surgeon approaches the optic pathways, the monitoring team should have identified reproducible waves to be used as benchmarks for meaningful assessment during subsequent monitoring during critical stages of the surgery. Stacked plots of sequentially recorded averages are indispensable for assessing changes during surgery. Interpretation of intraoperative VEPs should be done in relation to pharmacologic, physiologic, and surgical factors. Change in response trends should be reported as soon as identified, and immediate steps should be taken to prevent the risk of lasting damage and to optimize normal function [73].

Stimulus Color

The color of the flash or LED (white vs. red) should be indicated on the record and kept constant throughout the case.

Stimulus Rate

For transient F-ERGs and F-VEPS , a stimulus rate of 1–2.5 Hz is suggested and for steady-state responses a rate of 8–30 Hz may be used. Steady-state stimulation has not gained wide use for monitoring purposes. In a study published in 2004, their use during surgery for monitoring purposes did not facilitate improved or more stable F-VEP recordings [42].

Recording Electrodes and Their Placement

Corneal or scleral lenses for IOM recording of ERG responses were supplanted in the 1980s with less invasive devices and methods. Corneal

recording devices using a Burian Allen electrode and other devices placed on or near the cornea yielded larger, robust responses but are rarely used due to the risks of corneal abrasion and ulceration with IOM use. F-ERGS can be recorded from skin with subcutaneous needles or skin disc electrodes placed at the center of the right lower lid proximal to the lid margin (infraorbital notch), and referenced to an electrode 2 cm lateral to the lateral canthus where the largest amplitudes of ERG responses from skin can be obtained [75, 76]. Esakowitz et al. [77] compared the relative amplitudes of F-ERG b-wave responses when recording with corneal versus other electrode types placed on the skin. The largest response amplitudes were obtained with the Burian Allen electrode (125 uV, 100 %), with other corneal electrodes yielding responses of less amplitude in proportion to those made with the Burien Allen electrode: JET (93 %), C-glide (78 %), gold foil (60 %), and DTL (60 %). Recordings from skin electrodes yielded the smallest response amplitudes (14 %). Obviously, one has to weigh the risks and benefits of the use of these devices for recording F-ERGs [77]. F-ERGs recorded with noncorneal versus corneal electrodes, except for amplitude differences, are nearly identical in both time (a- and b-wave latencies) and frequency domains (dominant power spectrum peaks), meaning noncorneal F-ERGs do not differ significantly from corneal ERGs aside from amplitude [78].

One intriguing way to record F-ERGs was recently reported by Houlden et al. [3]. In their small sample of study patients (N = 12), they were able to reliably record F-ERGs from EEG electrodes placed at Fz′ (2 cm behind Fz) and referenced to FPz (10–20 International EEG placement) to confirm retinal stimulation in the patients (N = 12) evaluated in their study. Though a novel and appealing recording methodology for F-ERGs, further studies are needed in larger patient populations to confirm its feasibility and utility for IOM.

For F-VEPs, standard subdural needle or surface EEG electrodes may be used to record scalp responses [73]. Ota et al. [29] reported that F-VEPs acquired with subdural electrodes better reflect cortical activity since they have considerably greater spatial resolution and amplitude when compared to responses acquired from surface EEG electrodes placed on the scalp. Single-channel response recordings are acquired using the 10–20 International nomenclature for the placement of EEG electrodes with electrodes typically placed at the midline occipital (5 cm above inion) to midline frontal (MQ-MF or Oz-Fz) positions. The AEEGS guidelines [73] recommend a second

channel be recorded for signal confirmation (however, few studies employ them). When used, the secondary set of electrodes would be placed at midline occipital and referenced to linked earlobes (MQ-Ipsilateral Earlobe (AI)/Contralateral Earlobe (A2) or Oz-AI/A2) locations. Typically the ground electrode is placed at CZ. Additional channels may be used to study the scalp distribution of VEPs [73].

Analysis Periods for F-ERGs and F-VEPs

The AEEGS guidelines recommend the use of analysis periods of 100–200 ms for F-ERG [79] and 250–500 ms for F-VEP [73]. A total of 50–200 responses are commonly recorded per average [73], with the caveat that the number per average should remain constant throughout the monitoring period. At least two consecutive ERG and VEP averages should be acquired to confirm the reproducibility of the ERG and VEP waveforms after setup and prior to surgical incision to establish a baseline (control) recording [23, 73].

Amplifier Settings for Recording F-ERG and F-VEP

For years the standard “clinical diagnostic settings” for system bandpass settings for F-VEPs have also been employed for IOM purposes, which are 1 to 200–300 Hz (−3 dB) with filter roll-off slopes not exceeding 12 dB/octave for low frequencies and 24 dB/octave for high frequencies. If irreducible artifacts occurred, filter settings could be adjusted to 5–100 Hz. Digital smoothing and filtering could also be employed to reduce artifact, and filter settings should remain constant throughout the monitoring session [73].

Houlden et al. [3] recently suggested that the difficulties in recording F-VEPs in IOM settings may be due to the high mean alpha EEG amplitudes (>50 μV) in patients, contributing “noise” that impedes recording the F-VEP “signal.” For 9 of 12 patients with low mean alpha EEG amplitudes (<30 μV), IOM F-VEPs were reproducible, including one whose vision was limited to finger counting. To improve the recording of responses in three patients with high mean alpha amplitudes (>50 μV), Houlden et al. [3] elected to see if raising the low pass settings had any effect. In these patients, they simultaneously recorded EEG from Oz–Fz and Fz–Fpz′ using 3-, 10-, and 30-Hz low cut filters (six independent recording channels) and two channels of F-VEP using low cut filters settings of 10 and 30 Hz. They found

that F-VEP amplitude reductions were minimal for low pass filter settings of 3–10 Hz but at 30 Hz, the F-VEP's N1–P1 amplitude decreased by about 40 % and its morphology was significantly altered. They also found that as the low pass filter setting increased, the "noise" contribution to the averaged F-VEP associated with electrocautery blocking time was also reduced. Based on those findings, Houlden et al. recommended using 15–20 Hz as a low pass filter setting for F-VEP responses. Houlden et al. points out that over 30 years ago, Nuwer and Dawson [80] recommended increasing the low cut filter settings from 1 to 30 Hz to improve intraoperative somatosensory-evoked potential (SSEP) reproducibility, but at the time, did not offer any reasons why the change improved the SSEP response. Houlden et al. [3] suggested that the improvement was due to reduction from the averaged response of the patient's alpha EEG and artifact due to electrocautery amplifier blocking . Though it seems a simple enough change to implement, only one recent study, by Kamio et al. [20], has employed a higher low bandpass setting (20 Hz) during recordings of F-VEP. Hopefully others will take the opportunity to test Houlden et al.'s hypotheses and determine whether indeed raising the low pass filter setting improves the reproducibility of F-VEP responses in IOM settings.

Monitoring Criteria

Given the documented variability of flash VEPs, responses recorded from patients in operative settings cannot be universally characterized [73]. That and perhaps the technical difficulties associated with obtaining reproducible F-VEPs in operative settings have contributed a lack of clear guidelines for warning criteria to be used during surgery to preserve the visual pathway. For recent neurosurgical procedures involving removal of intraorbital, parasellar, and cortical lesions, Kodama et al. [23] and Sasaki et al. [24, 25] have used a warning criterion whereby a F-VEP amplitude decrease >50 % from baseline control levels prompted cessation of the surgical procedure until recovery of the F-VEP occurred and provided that other factors (e.g., anesthesia, use of bipolar cautery) could not be used to explain the amplitude changes. Martinez Piñeiro et al. [81] reported on monitoring patients undergoing endovascular treatment of their occipital arteriovenous malformations (AVM) with F-VEPs. He reported successful intraoperative recordings and postoperative outcomes employing the same stimulation methods and parameters that Kodama et al. [23] and Sasaki et al. [24, 25] used as well as their warning

criteria. On the other hand, Kamio et al. [20], who examined the use of F-VEPs for patients undergoing transphenoidal surgery for tumor removal, employed a warning criterion of either an increased or decreased amplitude of greater than 50 % compared to control levels. In a study utilizing a similar study population, Chacko et al. [40] used a complete loss of visual responses as the warning criteria to halt surgery until responses returned to baseline. Hussain et al. [44], reporting on the use of monitoring F-VEPs from five patients undergoing functional endoscopic sinus surgery, was the only study involving the anterior visual pathway to employ an increase in F-VEP P100 latency as an indicator of optic nerve compression. They noted that for this criterion to be useful for IOM, the patient's intraoperative diastolic blood pressure had to remain higher than 50 mmHg, oxygen saturations 98 % or higher, and bleeding to be minimized. Given the notable disparity of F-VEP IOM warning criteria in the previously discussed studies, it is clear that more research is needed to better define IOM F-VEP warning criteria that better correlate with patient outcomes.

Regarding warning criteria for studies utilizing F-ERGs for monitoring, Padalino et al. [21] used them to monitor retinal perfusion during a single case involving endovascular treatment of a dural AVM supplied by the bilateral superficial temporal, ophthalmic, and the right middle meningeal arteries. The intraoperative monitoring warning criteria that they employed was a 10-ms increase in the F-ERG latency and a 30 % decrease in its amplitude compared with baseline and control responses from the other eye. As with the warning criteria for F-VEPs during IOM, further study is needed to define and confirm warning criteria for use of F-ERGs for IOM.

Other IOM Applications with F-ERG and F-VEP

Keenan et al., Burrows et al., and Reilly et al. [11, 82, 83] have explored the F-VEP as an objective measure of the short-term effects of various cardiopulmonary procedures on neurophysiological function given the cortex's sensitivity to small changes in cerebral perfusion due to its proximity to the watershed area of the posterior and middle cerebral arteries. Reilly et al. [83] showed that F-VEPs are a more sensitive indicator of central nervous system (CNS) stress provoked by combined hypothermia and hypoxia than EEG. Burrows et al. [11] found F-VEPs to be an objective measure of neurophysiologic function in the visual pathway during profound hypothermic circulatory arrest (PHCA) in neonates and infants undergoing

surgical correction of congenital heart defects . Although their findings seemed promising as an IOM tool for such cases, Markand et al. [84] found VEPs to be too inconsistent during the surgical course of hypothermia and recovery; and that their disappearance at temperatures below 25 °C made them less than ideal for monitoring brain function during hypothermia. Even Burrows and Bissonnette [85] appear to have abandoned the use of F-VEPs for this application, opting instead to use other measures of cerebral blood flow (transcranial Doppler sonography) for monitoring perfusion during CPB surgery in their subsequent study.

However, the use of F-ERGs to monitor *cardiac surgery and extracorpeal circulation* may serve as a new area to consider for IOM purposes. Indeed, monitoring the retina as an extension of the brain for such cases has been encouraged by Nenekidis et al. [86]. They believed that better quantification of the hemodynamic state of retina–optic nerve head (ONH) during on-pump CPB, is needed, stating that, “The retina provides a ‘window’ for the study of cerebral microcirculation; it lies in the territory of the internal carotid artery and has a blood barrier analogous to the blood–brain barrier. It would seem reasonable to assume that the changes observed in the retinal microcirculation also occur in brain. The central nervous system can suffer from the same pathophysiological entities that affect the retina and the ONH during hypothermic CPB procedures.” During CPB procedures , retinal ischemia and infarction due to emboli, anterior ischemic optic neuropathy (AION) , posterior ischemic optic neuropathy (PION) , damage of nerve fibers, chorioretinal hypoperfusion and hypoxia secondary to hemodynamic and hematologic changes have resulted in profound visual deficits and other neuro-ophthalmological complications [86]. Because F-ERG responses are sensitive to (1) alteration of blood flow as a consequence of the reduction of perfusion pressure and (2) to body hypothermia, associated with hemodilution, which helps to depress neural function and neural tissue oxygen requirements, but may also bring on tissue hypoxia, it stands to reason that focus be given to the use of F-ERGs as a tool to monitor patients undergoing cardiosurgical procedures with CPB. A recent, intriguing recent paper by Brandli and Stone [87], while not directly related to intraoperative monitoring and performed in rats, suggests that F-ERGs are indeed sensitive to ischemia, even when the induced ischemia is remote to the retina. A pilot study done by Nebbioso et al. [57] examined the use of F-ERGs for monitoring patients during extracorporeal circulation (ECC) , both

hypothermic and normothermic with some promising results. Under hypothermic ECC, they reported that the amplitude of the F-ERG response decreased by 50 % while those under normothermic ECC only decreased 10 %. Recovery of response amplitudes to baseline levels occurred upon the end of ECC and with the rewarming of the patient, with the exception of one individual whose F-ERG response recovery was very prolonged. That patient required postoperative ventilatory support and a long stay in the intensive care unit [57]. Time and further studies will tell whether use of F-ERGs will become a useful tool for monitoring and maintaining adequate retinal as well as cerebral microcirculation and perfusion during surgical procedures.

Retinal Stimulation and Intracranial Recording of Responses

Recording directly from cortical structures for lesions of the visual pathways, though feasible (albeit in studies with relatively small sample sizes), has limited utility but has yielded responses with greater amplitudes and better signal-to-noise ratio [45]. Møller et al. [88] recorded compound action potentials directly from optic nerve (ONEP) elicited by short light flashes via LEDs during tumor resection in two patients and was able to record responses that had an initial small positive deflection, with a latency of about 45 ms, followed by a negative wave with a latency of 60–70 ms, although considerable individual variation in the shape and size of those responses was observed [88].

In another application of this type of recording, Curatolo et al. [89] found that monitoring the responses recorded from the visual cortex during photic stimulation proved to be a reliable technique for preserving central vision during occipital lobe surgery [89]. Ota et al. also evaluated the usefulness of cortically recorded VEPs as an IOM tool of the posterior visual pathway in 17 patients who underwent posterior craniotomy for lesions or epileptic foci in the parietal, posterior temporal, and/or occipital lobes; reporting detection of VEPs in over 90 % of cases with preserved vision that was independent of the type of anesthesia employed for those procedures [29].

In still another application of this type of recording, photic stimulation while recording averaged visual responses in the optic tract during pallidotomy and deep brain stereotaxic surgery has been reported to be useful in guiding those surgeries [16, 59]. Such recordings have also been useful in

determining the generators for scalp-derived VEP responses. Tobimatsu et al. [90] was able to record VEPs using pattern-reversal stimuli in eight awake patients with Parkinson's disease undergoing stereotactic pallidotomy using a depth recording electrode located at or below the stereotactic target in the ventral part of the GPi and dorsal to the optic tract. They simultaneously recorded VEPs from the scalp to provide information for differentiation of the generators of the scalp VEP components. In such cases where little or no anesthesia is used during surgery, the option to use pattern reversal and other visual stimuli that provide more information in visual pathway function (e.g., visual acuity), may open up a new era for using VEPs for monitoring purposes. Indeed, their use during other "awake" procedures (e.g., endovascular stenting and coiling procedures) when visual function is at risk, has yet to be fully explored.

Direct Electrical Stimulation of Optic Nerve

Bošnjak and Benedičič [14, 15, 50] evaluated the feasibility and utility of recording scalp VEP responses to direct electrical stimulation (eVEP) of the ON during tumor removal surgery involving the anterior visual optic pathways [14], skull base [15], and during orbital enucleation due to malignant melanoma of the choroid or the ciliary body [91]. To acquire cortical potentials elicited by electrical epidural stimulation of the optic nerve (ON), insulated platinum needle-stimulating electrodes with a noninsulated ball tip were attached epidurally to both sides of the ON. Bošnjak et al. [50] used the following procedure for placement of these electrodes, noting that "When the exit of the optic nerve (ON) from the periorbit is fully visualized through a small fenestration of the orbital apex, needle electrodes are placed in contact on each side of the ON into the cleft between the nerve itself and the basal remnants of the lateral walls of the optic canal. The needles are manipulated during positioning with bipolar forceps through grip connectors. After placing the epidural stimulating electrodes , their position is secured with wet cotton patties laid over the orbital apex and leads." Monopolar optic nerve potentials after retinal flash or electrical epidural stimulation of the ON were then recorded with insulated platinum ball-tipped wire electrodes placed on the surface of the ON using an extracephalic reference electrode. The distance between the stimulating and recording electrodes was approximately 25 mm. The same recording electrodes were used for monopolar recordings from structures outside of the visual pathway to collect control data. The

electrical stimulus consisted of a rectangular current pulse of varying intensity (0.2–5.0 mA) and duration (0.1–0.3 ms) using a stimulation rate of 2 Hz [14, 15]. The bandpass filter settings utilized in previous studies were 1–1000 Hz when recording these cortical potentials after electrical epidural stimulation of the ON. The analysis time used was between 10 and 300 ms. Each trace was generated from the average of 100 responses. Of note, considerable stimulus-related artifact from direct ON stimulation does present a technical hurdle to recording these potentials [14, 15]. Using this stimulation and recording technique, Benedičič and Bošnjak [14, 15] concluded that it was beneficial in preventing ON damage and improving outcomes. They did not report any warning criteria used in the studies and their sample sizes were small [4]. The typical eVEP they recorded consisted of N20 and N40 waves (Fig. 4.3) [50]. Considerable variability in the amplitude of the responses was observed (e.g., N40 wave amplitudes prior to tumor removal varied as much as 25 %). Not surprisingly, artifact was observed with use of bipolar coagulation, ultrasonic aspirator, laser, and craniotome-hampered IOM [15]. In one patient with an ON sheath meningioma and vision limited to light sensation, only the N20 wave was observed (*see* Fig. 4.3) [50]. In their subsequent report of IOM monitoring for a very small sample ($N = 3$) of patients undergoing orbital enucleation due to malignant melanoma of the choroid or the ciliary body, both F-VEPS and cortical potentials from direct stimulation of the optic nerve were inconsistent or absent in patients with a history (>3 months) of severe visual deterioration, but obtainable from a single patient with a short history of mild visual impairment [91]. Clearly, more studies are needed to confirm the utility of direct electrical stimulation of the optic nerve for visual pathway IOM use and for the development of effective preoperative criteria for patients in whom these techniques may be useful, as well as warning criteria that correlates with and improves patient outcomes.

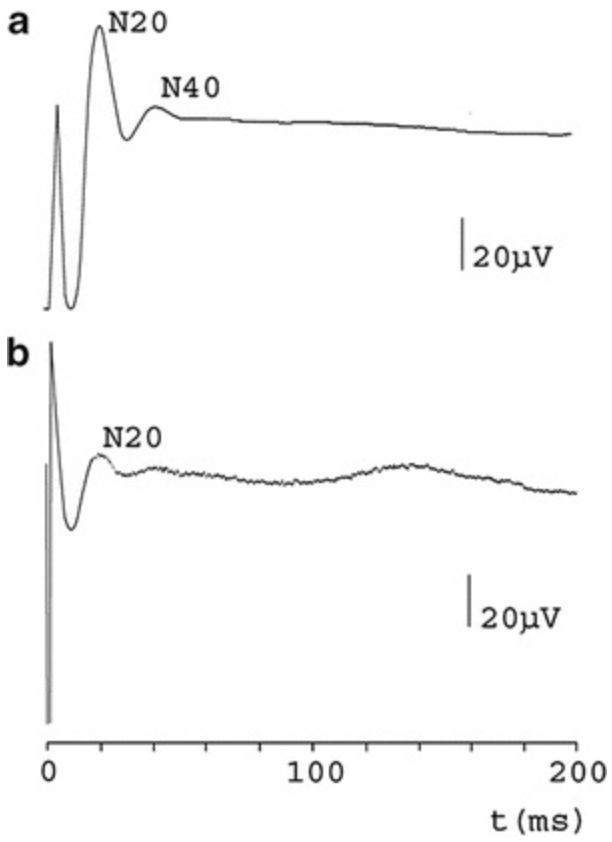

Fig. 4.3 (**a**) An example of a typical electrically elicited visual-evoked potential (eVEP) response is depicted. The response consists of a larger N20 wave and a smaller N40 wave. The stimulus duration was 0.5 ms, and its frequency 2 Hz. An average of 100 responses was obtained. (**b**) The eVEP responses recorded from a patient with an optic nerve sheath meningioma and visual perception of light only is shown for which a decreased N20 wave and absent N40 wave are observed (from Bošnjak and Benedičič [50]; with permission)

Duffau et al. [13] described the use of intraoperative electrical stimulations (IES) during surgery to help identify and preserve afferent visual fibers during removal of a low-grade glioma invading the whole temporal lobe and temporo-occipital junction. They used a 5-mm spaced bipolar electrode to deliver biphasic current stimuli (pulse frequency of 60 Hz, single-pulse duration of 1 ms, and amplitude of 5 mA) to cortex involving the optic tracts, in a nonsedated patient, to guide tumor removal. By mapping the optic radiations using this electrical stimulation and obtaining the patient's report of visual effects related to that stimulation, they were able to detect the posterior and deep functional boundary of the tumor resection, and to avoid production of a postoperative symptomatic homonymous hemianopsia. Given the incidence of visual field defects following surgeries involving the posterior temporal lobe and temporo-parieto-occipital junction (TPOJ) with

considerable risk for the occurrence of permanent homonymous hemianopsia, it may be of great interest for surgeons and IOM practitioners to consider conducting further research in the application of this direct electrical stimulation technique to help preserve visual function and improve patient outcomes for those undergoing such procedures [13].

Effects of Temperature

In conscious humans, F-VEP latency is 10–20 % longer at 33 °C than at 37 °C. With increasing hypothermia, progressive increases in F-VEP latency and decreases in F-VEP amplitude occur with complete loss of the components of the responses at 25–27 °C. When cooling occurred more swiftly, F-VEP responses disappeared at higher temperatures than when a slower cooling process was utilized [92].

Effects of Anesthesia on F-ERGs

Although for IOM purposes, F-ERG responses are most frequently being employed for confirmation of stimulation of the retina, gaining an understanding of the reported effects of anesthetic and sedative agents on retinal responses, and conducting additional studies to further elucidate the effects of these agents on retina physiology, is of interest.

Wongpichedchai et al. [93] evaluated the effects of halothane in a pediatric population, on dark-adapted (scotopic) and light-adapted (photopic) F-ERGs and found it had little effect on the a-wave and b-wave latency and amplitude of the scotopic F-ERG and amplitudes and latencies of the F-ERG photopic responses to red flashes and 30 Hz flickering white light. In another study, Tremblay et al. [66] retrospectively compared the effects of sedatives and inhalational agents on scotopic and photopic F-ERGs in a small sample of pediatric patients diagnosed free of retinal disease. In that study, F-ERGs were recorded in subjects who either were (1) conscious (no anesthetic or sedative medications) [n = 9]; (2) under sedation (chloral hydrate [75–125 mg/kg] and pentobarbital sodium sedation [5–6 mg/kg]) (n = 9); or (3) under general anesthesia (intravenous injection of propofol [2 mg/kg] with or without fentanyl 4 μg/kg, and maintained with isoflurane 2–3 % or halothane 1–2.4 % with 50 % O_2 and 50 % N_2O [n = 9]). They found that sedation appeared to decrease a- and b-wave amplitudes of the scotopic bright-flash F-

ERG responses, without affecting the responses' latencies. Though Tremblay et al. [66] reported that F-ERG responses recorded under photopic conditions showed minimal changes in latencies and amplitudes, if one examines the table provided in the paper [66] (Table 4.1), it appears that while the amplitude of the responses are not affected, the latencies of the photopic responses recorded under anesthesia versus consciousness are significantly and statistically increased and that the same holds true for F-ERG responses recorded under sedation versus under anesthesia [66].

Table 4.1 Summary of statistical analysis performed on ERG parameters obtained after 5 min in photopic conditions in the conscious (C), sedated (S), and anesthetized (A) patients

ERG parameter	Conscious	Sedated	Anesthetized	C-S	C-A	S-A
Amplitude (μV ± 1 SD)						
a-wave	76 ± 20	63 ± 9	54 ± 20	−	+	−
b-waveparameters	216 ± 49	186 ± 35	163 ± 47	−	−	−
OP2	19.1 ± 0.9	15.2 ± 4.0	17.1 ± 4.6	−	−	−
OP3	21.1 ± 2.7	17.3 ± 7.2	18.5 ± 11.7	−	−	−
OP4	35.5 ± 14.5	22.6 ± 11.6	9.6 ± 4.7	−	+	−
OP5 2	9.2 ± 10.7	20.1 ± 8.6	8.8 ± 2.0	−	+	−
Implicit time (ms ± 1 SD)						
a-wave	13.7 ± 0.4	14.1 ± 0.5	16.2 ± 1.0	−	+	+
b-wave	33.1 ± 0.8	34.4 ± 1.5	46.8 ± 4.9	−	+	+
OP2	16.4 ± 0.3	17.2 ± 0.4	20.0 ± 0.8	+	+	+
OP3	24.3 ± 1.1	25.4 ± 1.6	29.3 ± 1.6	−	+	+
OP4	32.0 ± 1.1	32.6 ± 1.5	44.3 ± 5.2	−	+	+
OP5	40.8 ± 1.5	41.1 ± 1.7	52.6 ± 4.8	−	+	+

Stars in the three rightmost columns indicate statistical difference between paired-wise groups after post hoc Bonferonni/Dunn correction (P>0.016) (from Tremblay et al. [66]; with permission)

Early studies by Raitta et al. [94] evaluated F-ERG responses recorded in ten adults before and 15–20 min after induction of anesthesia with a combination of thiopentone sodium, halothane, and nitrous oxide (N_2O) and found that the amplitudes of F-ERG a- and b-waves were significantly decreased when compared with preoperative levels, but that latencies were unchanged. The findings of a study by Yagi et al. [52] evaluated the effects

of enflurane on F-ERG in a small sample of patients undergoing surgical procedures and found that use of enflurane significantly increased latencies of F-ERG a-waves and b-waves and decreased their amplitudes but did not have any significant effects on F-ERG b-wave responses, with increasing concentrations of enflurane (0, 0.8, and 1.7 %) [52]. Interestingly, a study conducted by Ioholm et al. [95] in adult populations examined photopic F-ERGs before and after surgery under general anesthesia induced with sevoflurane (8 %) in 100 % oxygen (O_2) and maintained with sevoflurane (range, 0.05–0.31 %, mean 0.22 ± 0.07 %) and nitrous oxide (mixture of 33 % O_2 and 66 % N_2O). The F-ERG responses were recorded preoperatively from unpremedicated American Society of Anesthesiologist (ASA) classification I and II patients, and again immediately following discharge from the recovery room, and 24 h following sevoflurane/N_2O anesthesia. Ioholm et al. [95] found that the F-ERG b-wave latency in these subjects was increased at both postoperative time points compared with preoperative responses and that b-wave amplitudes were also decreased postoperatively compared with their preoperative levels. Similar findings were obtained in a subsequent study conducted by Ioholm [96]. Of interest, Sasaki et al. [24] reported that “after induction of inhalation anesthesia with sevoflurane, ERG data were not reproducible” [24]. An example of the comparison of the F-ERG responses obtained by Sasaki et al. [24] with anesthesia employing sevoflurane versus total intravenous infusion of propofol with fentanyl is shown in Fig. 4.4. Given the variance in the reports regarding the effects on F-ERG responses to different combinations of sedative and halogenated agents, one would have to agree with Tremblay’s conclusion that normal retinal physiology is affected by sedation and anesthesia through different mechanisms that remain to be fully elucidated by future research [66].

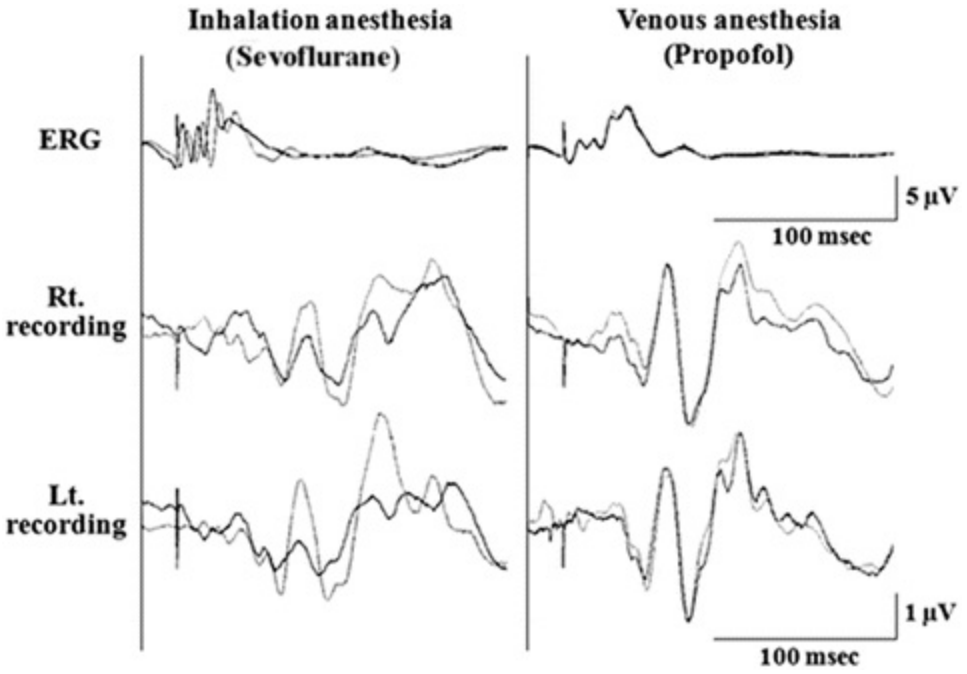

Fig. 4.4 Illustrates the reproducibility of ERG and VEP following induction of inhalation and venous anesthesia in the same patient, same eye (without visual dysfunction). F-ERG and VEPs were obtained twice to confirm the reproducibility of the data in the absence of surgical procedures. Following induction with inhalation anesthesia (*left*), F-ERG responses were not reproducible and the VEP amplitude was also affected. Conversely, following induction of propofol-based infusion anesthesia, reproducibility of ERG and VEPs were both good (from Sasaki et al. [24] with spelling modifications: revised "Seboflurene" to "Sevoflurane"; with permission)

Total intravenous anesthesia (TIVA) utilizing propofol and opioid medication is touted as F-ERG friendly. Indeed F-ERGs obtained from 20 normal children undergoing evaluations of their visual function under anesthesia with propofol and fentanyl versus topical anesthesia showed that F-ERG b-wave response latencies were only slightly increased and b-wave amplitudes decreased when propofol and fentanyl versus topical anesthesia were employed and were not statistically different [97]. This finding was further supported by an animal study conducted in pigs [98]. Although no specific reports have been published on the effects of bolus administrations of fentanyl or other opioids on F-ERGs in humans during surgery, bolus administrations (additional injections of fentanyl every 60 min) were used in Sasaki's et al. study [24], with what can presumed to be little detriment to their use of F-ERG responses (chiefly to ensure retinal stimulation) for IOM purposes.

Effects of Anesthesia on VEPs

A summary of the effects of anesthesia on F-VEPS prepared by Banoub et al. is shown in Table 4.2 [1]. F-VEPs are very sensitive to the effects of anesthetics and physiologic factors because they represent polysynaptic cortical activity. Because flash stimulation activates both temporal and nasal parts of the retina and the nasal fibers cross to the contralateral side at the level of the optic chiasma, retrochiasmatic lesions cannot be monitored [33]. In addition, VEPs are highly dependent on appropriate stimulation of the retina and may be unduly affected by narcotic-induced pupillary constriction [99].

Table 4.2 Summary of the effects of anesthetics on visual-evoked potentials responses

Anesthetic drug	Dose/concentration	Latency of P-100	Amplitude
Halothane [102]	1 MAC	≈10 % ↑	Inconsistent
Isoflurane [41, 103]	0.5 MAC	10 % ↑	40 % ↓
	1.0 MAC	20 % ↑	66 % ↓
	1.5 MAC[a]	30 % ↑	80 % ↓
	1.0 MAC + 70 % N_2O	Abolished	Abolished
	1.5 MAC + 70 % N_2O	Abolished	Abolished
Sevoflurane [104]	0.5 MAC + 66 % N_2O	5–10 % ↑	20 % ↓
	1 MAC + 66 % N_2O	Abolished	Abolished
	1.5 MAC + 66 % N_2O	Abolished	Abolished
	1.4–1.7 MAC	Abolished	Abolished[b]
Nitrous oxide [105–107]	10–50 %	No effect	25–80 % ↓[c]
Propofol [108]	2 mg/kg + 10 mg kg^{-1} h^{-1}	Negligible	≈20 % ↓
Thiopental [109]	3 mg/kg	<10 % ↑	No change
	6 mg/kg	Abolished	Abolished
Etomidate [109]	0.3 mg/kg	<10 % ↑	No change
Fentanyl [99]	10–60 μg/kg	<10 % ↑	30 % ↓
Ketamine [108]	1 mg/kg + 2 mg kg^{-1} h^{-1}	Negligible	≈60 % ↓
Morphine scopolamine (premedication) [99]	0.2 mg/kg morphine + 0.4 mg scopolamine	No change	≈20 % ↓
Neuroleptanalgesia [110]		10 % ↑	No change

Fentanyl, droperidol nitrous oxide			

From Banoub et al. [1]; with permission. All data are from humans
MAC minimum alveolar concentration, N_2O nitrous oxide, ↑ increase, ↓ decrease

[a]In a substantial fraction of patients, waveforms were not recordable at this concentration

[b]During electroencephalogram suppression; visual-evoked potentials reappeared during electroencephalogram bursts [111]

[c]Some report a 40 % increase in N-70–P-100 amplitude [108] (Fig. 4.10)

The findings included in Table 4.1 suggest volatile anesthetics prolong VEP latency and decrease F-VEP amplitudes in a dose-dependent fashion. Nakagawa et al. [37] found that even at a 1 % (0.5 minimum alveolar concentration [MAC]) concentration of sevoflurane, responses were significantly decreased. At 1.5 MAC, responses could not be interpreted [37]. However, as mentioned previously, conflicting information about the effect of low-dose sevoflurane on F-VEP responses have been reported, with one researcher finding amplitude decreases with its use [37] while another did not find any such decrease [29], although the latter recorded responses directly from cortex and those responses are reportedly not as susceptible to the effects of inhalational agents as those recorded from scalp [45, 88]. Nitrous oxide (N_2O) alone considerably reduces VEP amplitude. Its use in addition to volatile anesthetics can make VEP responses unrecordable. Increased concentrations of nitrous oxide significantly increase VEP latencies.

In general, it appears that opioid and ketamine or propofol-based anesthetic techniques (TIVA), along with those employing low-dose volatile anesthetics without nitrous oxide, seem to facilitate intraoperative recording of VEPs but do not ensure it. In some cases, the use of these anesthetic protocols may involve a high incidence of false-positive and false-negative results [33].

Opioids (e.g., fentanyl, alfentanil, sufentanil, and remifentanil) reportedly have a very mild effect on other evoked responses [100], which presumably extend to VEP responses. However, it is important to keep in mind that bolus administration of opioids has been reported to significantly reduce the amplitude of scalp-recorded responses [101]. Chi et al. [99] studied the effects of incremental doses of fentanyl (10 μg/kg) given every 10 min for a

total dose of 60–90 μg/kg for patients undergoing coronary artery bypass graft procedures and observed that while fentanyl administration did not affect latency, amplitude was decreased. They posited that those decreases may be due to changes to retinal luminance related to pupillary-induced constriction associated with fentanyl bolus administration [99]. Accordingly, bolus administraton of fentanyl, while not precluded during such surgeries, may indirectly affect F-VEP responses induced by retinal flash stimulation, and therefore should be taken into account if responses change post-administration. Loughnan et al. [100] showed that neither fentanyl, 200 μg, nor diazepam, 20 mg administered intravenously, significantly changed F-VEP latency or amplitude, suggesting that an anesthetic technique based on these two drugs might be suitable when intraoperative evoked potential monitoring is required to assess ischemia and preservation of visual-evoked responses [100].

With respect to anesthetic techniques that employ infusion of propofol , although most of the new studies for visual pathway IOM espouse the use of propofol, Neuloh [45] points out that TIVA alone cannot ensure success, as one recent study found that “a satisfactory rate of successful VEPs could not be achieved despite use of TIVA for anesthetic management” [41]. Moreover, a couple of studies have found that the amplitude of VEP is strongly affected by the concentration of propofol and that caution and perhaps further studies are needed in evaluating VEP in patients undergoing propofol anesthesia. Nakagawa et al. [37] found that at a propofol concentration of 3.0 μg/mL (80–100 μg/kg/min), VEP amplitudes were decreased significantly compared with the amplitude at 1.5 μg/mL concentration (40–50 μg/kg/min). It led him to conclude that a propofol-based TIVA technique appears to induce less change in evoked potentials, including VEP, than halogenated agents [37]. Hamaguchi et al. [36] further investigated the influence of propofol concentration on F-VEP components in three patients with cranial aneurysm and four with brain tumor. Anesthesia was maintained with intravenous propofol using target controlled infusion. Changes in F-VEP amplitude and latency were measured during three propofol concentrations (effect site concentrations of 1.5, 2.0, and 3.0 μg × mL^{-1}, and correlated with bispectral index (BIS) readings at each concentration. At 3.0 μg × mL−1 propofol concentration, F-VEP amplitude was decreased significantly compared with the amplitude at 1.5 μg × mL−1 concentration. No significant change was observed with the latency of F-VEP. The value of BIS at 3.0 μg × mL−1

propofol concentration also decreased significantly compared with 2.0 μg × mL−1 concentration.

Thankfully, neuromuscular blocking drugs do not directly influence F-VEP responses. In fact, their use may contribute to an improved signal-to-noise ratio by eliminating electromyographic artifact [12].

Conclusion

A number of researchers [2, 3, 13–15, 19–21, 23, 25, 78, 79] have continued their efforts to overcome the poor reputation that IOM of the visual pathways has had for several decades. By employing new and brighter stimuli, direct cortical stimulation methods, and monitoring new types of cases, these researchers hope to spawn revitalization of research that will help evaluate, establish, and improve the usefulness of visual pathway intraoperative monitoring. Certainly, the success of Sasaki et al. [24, 25] (93.5 %), Kodama et al. [23] (97 %), and subsequent research [19, 20] for acquisition of stable scalp F-VEPs recordings during surgeries involving the anterior pathways, with good correlation of monitoring results and visual outcomes, have been encouraging. Their ability to achieve those goals has largely been attributed to the combined use of (1) a brighter reusable (sterilizable); (2) flexible LED stimulating devices that guarantee supramaximal retinal stimulation, even when VEPs cannot be recorded; and (3) use of TIVA with propofol to minimize the effects of anesthetics on the responses. However, monitoring of patients with preoperative visual deficits remains controversial. Indeed, Kodama et al. limited their monitoring to patients with preoperative acuities of less than 0.4 (20/50) [23]. Because impaired preoperative vision is a major predictor of postoperative deterioration [45], eliminating such patients from monitoring limits the broad usefulness of VEPs for IOM of these surgical procedures. Regarding enhancements in anesthetic management, it is still not clear that the use of TIVA with propofol ensures F-VEP recording in all patients [41]. Still, there clearly is a need for continuous monitoring during cases involving the visual pathways, and indeed studies indicating that they were able to detect ischemic response changes in the F-VEP that would have been missed by imaging data [58] make a compelling argument to encourage those who would continue efforts to optimize the methodologies for use of VEPs for IOM purposes. Certainly, replication of their protocols and confirmation of their results will help solidify their methods. Only time will

tell if others take up that cause [5, 45]. The development of visual stimulation methodologies that can better assess visual acuity during surgical procedures, coupled with improved anesthetic management techniques may serve to revitalize the efforts to confirm the usefulness of IOM of the visual pathways: a plea that was issued years ago and still remains true [73].

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Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_5

5. Deep Brain Stimulation

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Keywords Deep brain surgery – Microelectrode recording – Dystonia – Parkinson's disease – Movement – Disorders – Surgery – MER procedure

Key Learning Points

- The role of the anesthesiologist in the DBS case is critical to maintain patient comfort and cardiovascular support in an awake patient without the use of common sedative medications.
- In complex movement disorder procedures, the use of sedation is almost always necessary and the fine balance between these medications and the consciousness of the patient is critical to allowing the physiologists

to obtain the data necessary for optimal electrode placement.

Introduction

Intraoperative monitoring (IOM) may generally be separated into two categories: (1) evaluating real-time data to detect adverse changes in the nervous system, giving the surgical team a chance either to reverse or to stop what is causing the change; (2) evaluating real-time data to help determine related physiologic localization or guidance for the surgical team through specific procedural steps of a particular surgery. In both categories, the surgical, anesthetic, and neuromonitoring personnel play a role in how the data are interpreted and incorporated during the procedure. Deep brain stimulation is challenging in that the patient needs to be comfortable enough to be alert through the complete procedure, yet not affect the properties of the single unit recordings.

Deep brain stimulation (DBS) surgery, with the use of microelectrode recording , for movement disorders falls into the second category. For the anesthesiologist, the challenge is that most anesthetics used to minimize pain and sedate a patient affect the firing patterns of the neurophysiologic data necessary to locate functional targets during the surgery, which in turn makes localization based on the firing patterns more difficult. In addition, the patient is likely to be fully awake and in their “worst” clinical state, which further complicates the situation. These issues make the communication between the anesthesiologist, surgeon, and neurophysiologist critical, and not something that should occur only in the morning before the procedure starts. A dedicated member of each of those three disciplines, who is always present, is preferable in making this procedure successful in every case.

The most common movement disorders that are treated with DBS are ones that are associated with some abnormality of the basal ganglia (BG) . The BG are a group of six nuclei in the brain with two principal input structures: the corpus striatum (Striatum) and the subthalamic nucleus (STN), two output structures (internal segment of the globus pallidus [GPi] and substantia nigra pars reticulata [SNr]), and two intrinsic nuclei (external segment of the globus pallidus [GPe] and substantia nigra pars compacta [SNc]). The striatum receives excitatory (glutamatergic) input from multiple areas of the cerebral cortex as well as feedback inhibitory and excitatory input from the dopaminergic cells of the SNc. One subset of these cells

projects directly to the GPi, forming the “direct pathway,” while another subset projects to the GPe, the first relay station of a complementary “indirect pathway,” which passes through the STN before terminating at GPi. The antagonistic actions of the direct and indirect pathways regulate the neuronal activity of GPi, which in turn provides inhibitory input to the pedunculopontine nucleus (PPN) and the ventrolateral (VL) nucleus of the thalamus, which contains the sensory receiving area (ventral caudal nucleus [VC]) and the cerebellar receiving area (ventralis intermedius nucleus [VIM]). The VL nucleus projects back to the primary and supplementary motor areas, completing the cortico-ganglio-thalamo-cortical loop. The direct pathway inhibits GPi, resulting in a net disinhibition of the motor thalamus and facilitation of the thalamocortical projections. The indirect pathway, via its serial connections, provides excitatory input to the GPi, inhibiting the thalamocortical motor pathway.

In various movement disorders, the signaling between the complementary balance between the direct and indirect pathways is disrupted, which results in clinical symptoms . In Parkinson’s disease (PD) , the disruption results in a hypokinetic clinical picture, whereas for dystonia the disruption results in a hyperkinetic clinical picture. DBS is thought to act by *renormalizing* the aberrant firing patterns caused by the disbalance of the direct and indirect BG pathways. The exact mechanism by which DBS affects this *renormalization* is unknown.

We present three different scenarios to help illustrate important points. The first will involve a classic parkinsonian patient undergoing a *straightforward* placement of a DBS electrode in the STN with minimal anesthetic intervention. The second involves a complex dystonic patient who required continuous changes in anesthetic management throughout the procedure. The third involves a patient with a medication-induced movement disorder that was on a continuous infusion of propofol prior to surgery to reduce the adverse effects of the movement disorder. In addition to these three examples, we also include a basic surgical methodology common to all DBS procedures for movement disorders.

Surgery

Movement disorders surgery is performed stereotactically. This means the brain is placed in a three-dimensional (3D)-coordinate space that allows

accurate and reliable targeting of specific anatomic areas. Historically, the most common stereotactic systems consist of a frame that is attached to the outer table of the patient's skull followed by either a computed tomography (CT) scan or magnetic resonance imaging (MRI) scan. A more recent technique uses a smaller stereotactic platform (FHC Starfix system, Bodenheim, ME; or Medtronic Nexframe, Minneapolis, MN) where trajectory guidance is done using "frameless" stereotactic techniques. These new "frameless" techniques offer anesthesiology advantages of easy access to the patient's airway. The standard frames make access to the patient's airway more difficult due to frame components making emergent mask access difficult, so the use of a laryngeal mask airway (LMA) should be considered. Once the imaging has been performed, the surgeon calculates the target location in the 3D space. Due to anatomical variations, imaging distortions, and functional neurophysiologic differences among patients, this initial targeting acts only as a guide to reach the target structure. Once targeting is complete, the surgeon creates a 14-mm burr hole in the skull to accommodate the electrode trajectory and readies the neurophysiology recording equipment attached to the stereotactic frame.

Microelectrode recording (MER) is best performed with the patient's full, nonmedicated attention. After MER is performed and the appropriate functional target is located, the permanent DBS electrode is placed and a second neurophysiologic test using stimulation, which mimics the DBS therapy, takes place. The wound is then closed and the controlling implantable pulse generator (IPG) is implanted.

The most serious complication during a DBS procedure is a fatal hemorrhage [1]. During a *standard* DBS procedure, blood pressure (BP) control is a critical anesthetic concern during both microrecording and permanent lead placement. While symptomatic hemorrhages may be readily detected, asymptomatic hemorrhages may yet presage clinical demise, so postoperative imaging is highly recommended [2]. To minimize the chance of intraoperative hemorrhage, systolic BP should be kept below 150 mmHg. If systolic pressure rises above this level, the procedure is halted until the systolic BP returns below 150 mmHg. For patients with PD there may be rebound hypertension when dopaminergic agonists have been halted prior to the procedure, often making BP control more challenging. Several standard BP control medications have been demonstrated to cause no hindering effects on single-unit recordings. These include most notably hydralazine,

nimodipine, nitroglycerine, and sodium nitroprusside (authors' experience and Venkatraghavan [3]), although there are no specific references in the literature describing the effects in detail. The one report that discusses the effect of the β-blocker metoprolol demonstrated a significant reduction in STN spiking activity with a transient reduction in rigidity after intravenous administration to reduce BP in three patients [4]. Some clinicians recommend avoiding the use of β-blockers because these may reduce the ability to assess the movement disorder during the electrode placement.

Dehydration may be a concern in longer DBS procedures. Intravenous (IV) fluids at maintenance levels should be given throughout the surgery. Bladder catheters are placed in all patients to save patients from worrying about voiding during the procedure and because many movement disorder patients can have difficulty moving after surgery. Because the patient is in a modified sitting position with the head above the chest, the occurrence of a venous air embolism should always be considered a possibility; particularly with the burr hole allowing for surface vein exposure. Standard pulse oximetry and end-tidal CO_2 monitoring are helpful in this regard. Pulse oximetry monitoring, IV access, and an arterial line (if used) should be placed on the hand or foot that is on the same side as the surgery, so as to allow unhindered examination of the tremor, rigidity, and movement speed in the contralateral limb. If a venous air embolism is suspected or detected, the subdural space should be continually flushed with saline to avoid further air entering the venous system. All stereotactic frames allow for the placement of endotracheal tubes or laryngeal mask airways without removing the frame. Specific wrenches for frame removal and adjustment should be kept handy for potential emergency use.

Although sedatives and systemic analgesic anesthetics are categorically contraindicated prior to and during the parts of the procedure when neurophysiologic data are being acquired, there are times when both are beneficial and even necessary. When the stereotactic frame is being placed on the patient's head, a local anesthetic (e.g., lidocaine/bupivacaine) is injected subcutaneously at the sites where the pins will be placed. At our center, we also use sedation (propofol boluses of 20–50 mg/kg or constant infusions of ~ 100 μg/kg/min) during frame placement, incision, burr hole, and opening of the dura. Due to varying degrees of tolerance in some patients, higher doses (as much as 250 μg/kg/min) may be needed (see example 3). A second anesthetic that has been shown to be acceptable during such procedures is

dexmedetomidine (Dex). For these procedures, ideally it is important to use an anesthetic that is metabolized rapidly (propofol) and has minimal effects on single unit recordings. Anesthetics may be used without restrictions during wound closure. On occasion, it may also be necessary to use small doses of anesthetics for brief periods to sedate patients between recording tracts. As described in the second case below, there are also special circumstances in which anesthetics are needed even while performing MER.

Because anesthetics can alter neuronal firing frequency [5] and impair patient assessment, the use of gabaminergic sedative medications, even in small doses, has been shown to affect the quality of MER adversely [6]. Temporary modification and suppression of parkinsonian tremor [7, 8] and increase in dyskinesias [9] have been reported with the use of propofol and remifentanil and thus, at our center, we require at least 10 min for the propofol to wear off prior to tremor testing. It is unclear which general anesthetic agents allow the most effective MER because all of them affect recordings to some extent [6, 10] and no studies comparing their effects on data acquisition have been performed intraoperatively. An “awake” technique has obvious advantages and most centers avoid anesthesia at least during the recording and mapping phase of DBS electrode placement in order to detect cellular activity and movement-related responses to neurostimulation. Another common technique used to improve intraoperative recordings and patient assessment is the withholding of antiparkinsonian medications beginning the night before surgery; this can be unpleasant for the patient but is necessary to assure optimal DBS electrode placement. On the other end of the movement disorder spectrum are dystonic patients who usually do need sedation during the initial phase of surgery before neurophysiologic testing, and potentially even during the testing phases. Ideally, any sedative effects should be readily reversible. Benzodiazepines and opioids with longer half-lives should be avoided. Opioids can also cause agitation, muscular rigidity, sweating, and hyperpyrexia in combination with some PD medications (e.g., selegiline) [8].

In PD patients , propofol has been used extensively, but its use requires vigilance to ensure patient alertness. Erring on the side of less medication ensures that its effects wear off more quickly and decreases the risk of airway loss. The surgeon may use extra local anesthetic with the scalp incision to reduce surgical pain. Also, as stated earlier, Dex is a good choice for dystonic patients and has been successfully used in pediatric patients [11]. A critical

reason for choosing Dex is its minimal effect on single-unit MER recording data, as one can appreciate that neuronal activity is still readily obtainable (Fig. 5.1). Dex reliably produces conscious sedation while the patient remains responsive and cooperative to verbal commands [2, 12]. One reason that Dex most likely does not affect BG recordings is that its effect is on the α_2-adrenoreceptors in the locus coeruleus, a major site of noradrenergic innervation in the central nervous system, and not on the gabaminergic receptors of the BG. The locus coeruleus has been implicated as a key modulator for a variety of critical brain functions, including arousal, sleep, and anxiety [13]. This, together with minimal respiratory depression, makes it an attractive agent to use in "awake" functional craniotomies. Low-dose infusion of this drug provides sedation from which patients are easily arousable and cooperative to verbal stimulation. Consequently, there are several reports on the successful use of the drug, both alone [3, 14, 15] and in combination with intermittent propofol [16]. Dex has also been shown to attenuate the hemodynamic and neuroendocrine responses to headpin insertion (the method for attaching the frame to the patient's head) in patients undergoing craniotomy and to significantly reduce the concomitant use of antihypertensive medication [17, 18]. It can theoretically decrease cerebral blood flow via direct α_2-mediated vascular smooth muscle constriction and, indirectly, via effects on the intrinsic neural pathways modulating vascular effects. α_2-Agonists have a more potent vasoconstrictor effect on the venous rather than on the arteriolar side of the cerebral vasculature and can, therefore, decrease ICP. There is, so far, no evidence of adverse effects on cerebral hemodynamics associated with its use, even in the setting of a compromised cerebral circulation; nor does Dex ameliorate the clinical signs of Parkinson's disease, such as tremor, rigidity, and bradykinesia. The pharmacologic profile of Dex suggests that it may be an ideal sedative drug for DBS implantation [19]. General anesthesia (GA) is an option reserved for patients with severe disorders for whom awake surgery would compromise their safety. These include patients with dystonia and related disorders who are on multiple medications to prevent contractions and spasms. Another group of patients are those that may not be able to tolerate the procedure, have severe respiratory conditions, or bad tics (such as patients with Tourette syndrome) that preclude them from remaining relatively motionless.

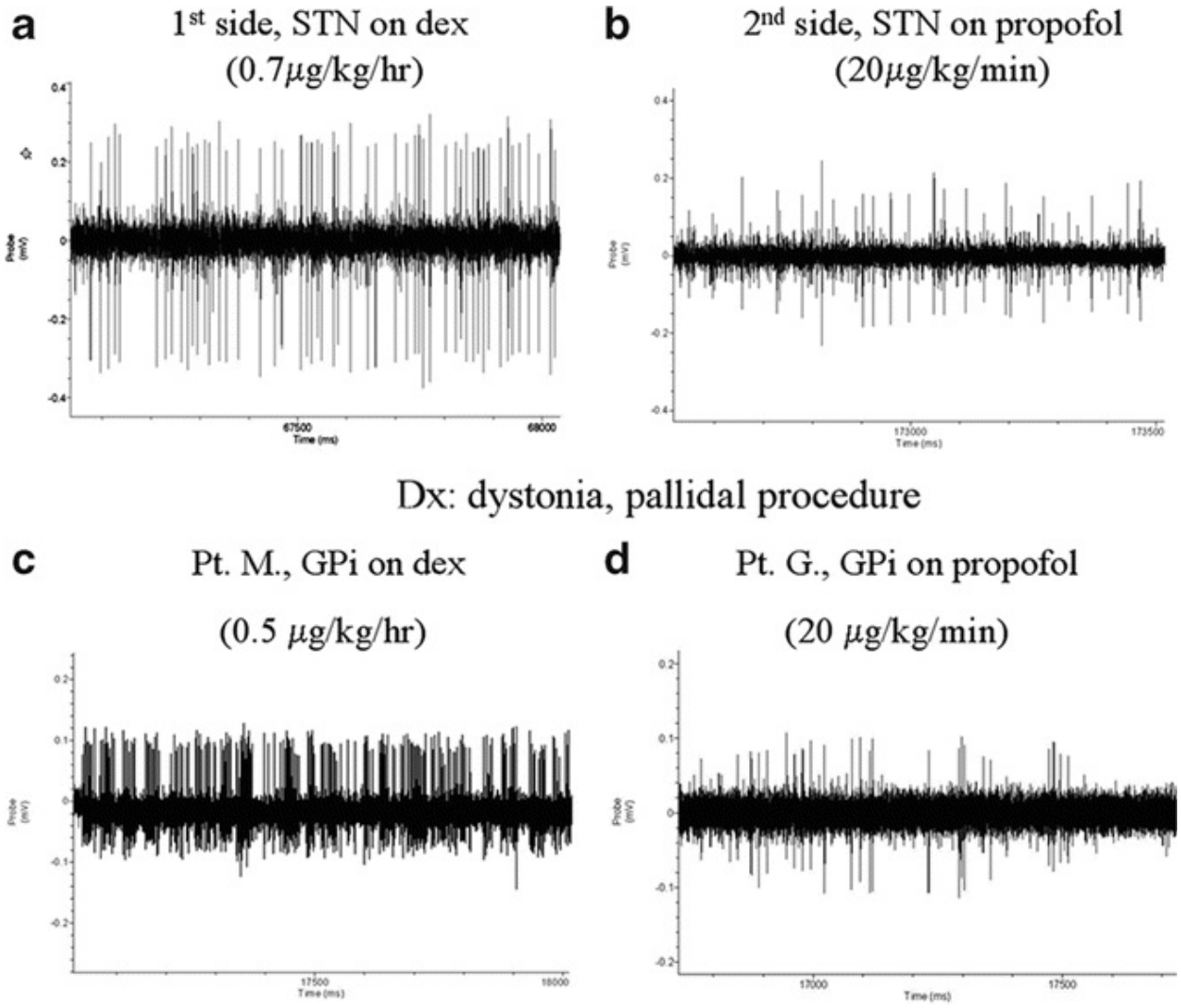

Fig. 5.1 Single-unit recordings under two different anesthetics . Each tracing shows 1 s of data. Tracings recorded from the same patient during a bilateral DBS STN procedure (**a** and **b**). Tracings recorded during a GPi DBS in two different patients (**c** and **d**). **a** and **c** were recorded using low-dose Dex (~0.1 μg/kg/h); **b** and **d** were recorded using low-dose continuous infusions of propofol (<20 μg/kg/min). The recordings with propofol are much less robust than the ones during Dex infusions

After the DBS electrodes are inserted, sedation can be increased and the frame removed. Implantation of the pulse generator and internalization of electrodes can be performed either immediately or as second-stage surgery under GA. Patients should receive their usual antiparkinsonian medication as soon as possible after the procedure to avoid possible deterioration in neurologic function and respiratory muscle impairment.

There is limited information on the incidence of intraoperative anesthetic complications during these procedures. A review of intraoperative anesthetic-

related complications in a series of 158 cases of deep brain ablation or stimulation under sedation with propofol or Dex [20] found that intraoperative events occurred in 6.96 % of cases. These events included coughing, sneezing, aspiration, pulmonary edema, combative behavior and agitation/confusion, bronchospasm, angina, and intracranial hemorrhage. All of these have the potential of moving the electrodes and cannula in the brain and causing an intraparenchymal hemorrhage. Yet, with an anesthesiologist who understands the specific movement disorder of the patient, the surgical procedure, the need for quality, and who pays constant attention to the alertness of the patient, these effects can be minimized. In our experience, the only case of a complication was when the anesthesiologist was concentrating on the infusion numbers and not the patient.

The MER Procedure

Due to accuracy problems with direct CT or MRI targeting, visualization is generally only a first step in locating the target, whereas MER gives a much more detailed spatial and functional map. Several excellent descriptions of the MER technique exist [21–32]. Understanding the type of neuronal activity from regions immediately adjacent to the intended target is critical to the success of the procedure. Following are two case examples (one fairly typical and the other unusual and complex) illustrating the integration of diagnosis, technique, and anesthetic management. During a MER recording session, not only are recordings acquired from the target location but also from structures located above and below that location. These recordings from other structures are useful in helping to determine the correct sagittal, coronal, and axial positions of the target. At the time of the writing of this chapter, both patients are significantly improved and are still benefiting from the procedure. In addition to looking for spontaneous single cell firings, it is important to look for cells that respond to specific types of evoked activity given that the basal ganglia is composed of segments that are nonsensory motor. Finding cells that respond to voluntary patient movement and cells that respond to limb joint position (kinesthetic) are key in making sure the electrode will be placed in the sensory motor region of the specific target. Both voluntary and kinesthetic cells will either increase or decrease their firing rate during the activity and are only found in the sensory motor region of the specific nuclei. Voluntary testing is performed by asking the patient to

move a particular body part while looking for changes in the firing pattern of the single unit under study. Kinesthetic testing is performed by moving an isolated joint and looking for changes in the single unit's firing rate.

Target Structures for the Case Examples

For movement disorders surgery, there are three common targets : (1) the ventral intermediate nucleus (VIM) of the thalamus, (2) the internal globus pallidum (GPi) , and (3) the STN. Each of these targets is thought to best treat a specific symptom of a movement disorder of a specific disease, although research is still underway to prove these hypotheses. Two of the three cases that will be presented in this chapter involve placing DBS electrodes in the GPi and, for the other case, in the STN. These cases were chosen because they demonstrate the extremes of movement disorder surgery. VIM is the primary target for tremor-related diseases such as essential tremor and one can still use the lessons from the cases below in a VIM case because it is the patient that dictates the anesthetic intervention and not the disease. To get a better feel for the procedures, we have included a short description of what type of physiology is encountered to show what can be lost if the anesthetic technique is not appropriately applied.

Although the complete GPi may be visualized on an MRI, the functional target location in the GPi is in the posterior and ventral region of the nucleus [33–39]. As the microelectrode is lowered into the brain along its recording trajectory toward the target location, the firing patterns from three anatomical structures must be recognized to confirm optimal placement: the striatum, the external globus pallidum (GPe), and the internal GPi. Figure 5.2 shows the anatomy of the GPi and the surrounding structures. The recordings on the right show representative firing patterns from each area. These are the critical physiologic markers in differentiating the structures. During placement of the DBS electrode, proximity to certain structures must be avoided such as the optic tract and internal capsule, which can render the therapy useless.

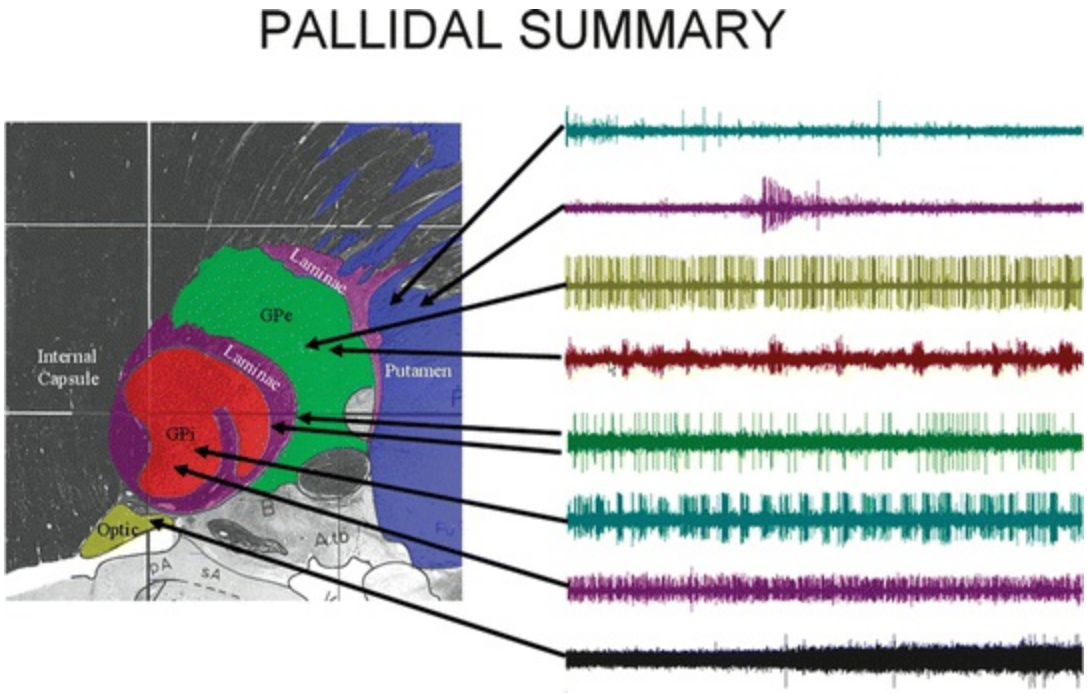

Fig. 5.2 A sagittal image , ~21.5 mm from midline, through the GPi and associated anatomy. Traces to the *right* are representative firing patterns from each area. Each trace represents single-unit activity as recorded from a representative cell in that structure [68]

After the microelectrode mapping is performed, micro- or macroelectrode stimulation is performed prior to permanent DBS placement to ensure that the electrode is at a safe distance from the internal capsule and the optic tract. If the patient is awake and alert, they can easily respond by indicating when they see *flashing lights* or experience muscle contractions. If the patient cannot respond, they cannot indicate when the optic tract is being activated or if they are having muscle tightness. In these cases, EMG recordings are used to indicate if muscles are being activated by either direct stimulation of the motor fibers in the internal capsule, which is an adverse effect, or the contractions are not a direct result of the stimulation but an indirect effect of stimulation at the appropriate location in the GPi. Thus, it is critical that no muscle relaxant be used.

The functional target in the STN is in the middle of the structure between 10.5 and 13.0 mm lateral from midline [28, 32, 40–42]. Once again, as the microelectrode is slowly lowered toward its target location, the neuronal firing patterns from three anatomical structures must be recognized to confirm optimal placement: the thalamus, the STN , and the substantia nigra pars reticulata (SNr). Figure 5.3 shows the anatomy of the STN and the

surrounding structures. The waves on the right show representative firing patterns from each area, which are the critical physiologic markers in differentiating the structures. If the DBS electrode is placed too medial and posterior within the STN, it can activate the sensory thalamus and/or medial lemniscus; if it is placed too lateral and anterior, it can adversely affect the internal capsule and render the therapy useless.

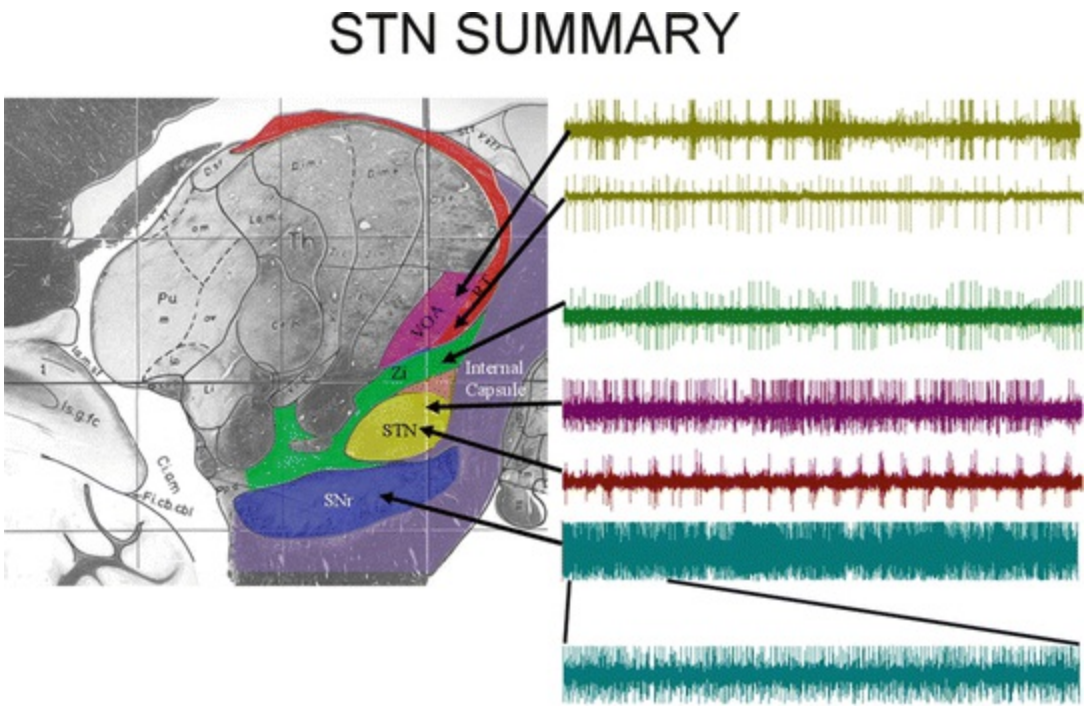

Fig. 5.3 A sagittal image, ~12.5 mm from midline , through the STN and associated anatomy. Traces to the *right* are representative firing patterns from each area. Each trace represents single-unit activity as recorded from a representative cell in that structure. For the SNr, the recording is from multiple units [68]

Cases and Disorders

Case 1: Noncomplex (PD-STN): A 60-year-old male with a 10-year history of PD, well controlled on Sinemet until age 59.

Clinical symptoms of PD began on the patient's right side starting with tremors in the upper extremity and rigidity in both the upper and lower extremities. As the disease progressed, symptoms became as problematic on the left side and started to affect the patient's ability to ambulate. One year prior to surgery, levodopa-induced dyskinesias began in the head and face, followed by a progressive difficulty swallowing. At the time of the surgery,

the patient was on Stalevo (a mixture of carbidopa, levodopa, and entacapone) 37/5/150/200 q.i.d., Requip 4 mg t.i.d., Amantadine 100 mg t.i.d., and Neurontin,300 mg t.i.d. Due to the medication-induced symptom of dyskinesia and the minimal amount of benefit, surgical implantation of a DBS electrode in the STN was then planned.

Parkinson's Disease

PD is a slowly progressive degenerative disorder of the BG. Nerve cells in SNc produce dopamine, which is transported to the input of the BG (striatum). In PD, for reasons not yet understood, the dopamine-producing nerve cells of the substantia nigra die off. The clinical signs of tremor, bradykinesia, and rigidity do not fully become apparent until significant dopaminergic neuronal cells are lost [43–45]. Medications are the first line of treatment to alleviate symptoms of PD, yet in many patients who have been responding to medications, their symptoms usually begin to gradually worsen with time. As they become more pronounced, patients may start to have difficulty walking, talking, or completing other simple tasks. Surgery should be considered when the patient develops moderate to severe motor fluctuation, medication-induced dyskinesia, medication refractory tremor, or intolerance to medication. Levodopa-sensitive symptoms may be more likely to respond to surgery [46], although in our experience, surgery in the STN and the GPi for PD has demonstrated a benefit to dopa-induced symptoms [41, 42]. Continued refinement of the knowledge of BG circuitry and PD pathophysiology has narrowed the focus of movement disorder surgery to three nuclei: (1) the thalamus, (2) GPi, and (3) the STN. The STN is the preferred surgical target for DBS electrode placement in PD [41, 47–50]. Serious complications such as hemorrhagic bleeding associated with STN-DBS electrode placement is relatively uncommon [51]. Hypertension must be treated prior to surgery because of the risk of hemorrhage [52, 53]. PD patients commonly suffer from orthostatic hypotension, contributed to by the use of levodopa and dopamine agonists, as well as other autonomic disturbances [54–56]. Respiratory dysfunction is well known in PD [55]. This includes an obstructive ventilation pattern, dysfunction of upper airway musculature, rigidity, bradykinesia , and dystonia of respiratory muscles [57]. These problems are exacerbated by withdrawal from antiparkinsonian medications.

Procedure and Decisions

The patient arrived at the hospital on the morning of surgery “off” of all PD medications from 7:00 p.m. of the night before. During frame placement, propofol was given in 20 mg boluses for sedation and monitored by the anesthesiologist. A foley catheter was also placed while the patient was sedated. The patient was then taken to the CT scanner (an MRI was performed at an earlier visit) with propofol given as needed to keep the patient relaxed. After the CT, the patient was brought to the OR, transferred to the bed and positioned with the frame also locked to the bed. It is important that the patient feel comfortable with both their ability to breath as well as with the position of their neck and back because they will be locked in that position for the duration of the surgical procedure, which can be several hours. When the patient is comfortable, either a propofol infusion or bolus doses are given until the dura is opened. Once the dura is incised (about 10–15 min before the MER is to start), the propofol is stopped to allow the patient to be awake for testing. Recording tracts in this patient included one on the left side and three on the right side. This difference in the number of recording tracts can be caused by potential asymmetries in anatomy, effects of nonlinear errors in imaging, or brain shift during the procedure. It is hard to pinpoint the exact reason, but in about 15 % of our cases we find this discrepancy. Each move requires the surgeon to remove the recording system and electrode from the head and place a new tract in the brain. Any time an electrode or cannula is placed in the brain, the chance for hemorrhage increases. Thus, it is critical to keep the BP below 150 mmHg systolic. On the left side, 4.9 mm of STN were encountered with four kinesthetic cells. On the right side, the first tract had 4.6 mm of questionable STN and no kinesthetic cells. The second tract had 5.7 mm of STN with three kinesthetic cells, and the third tract had 1.3 mm of STN with no kinesthetic cells. At the start of the second tract on the right side, the systolic BP increased above 150–165 mmHg. Recordings were halted and 10 mg of labetolol were given until the systolic BP dropped to 135 mmHg. Subsequent stimulation and recording required no changes or additions to the anesthesia. All of our PD patients have nasal cannula O_2 administered throughout the procedure and SpO_2 monitoring.

The DBS electrode was placed in the first recording tract on the left side and the second recording tract on the right side. These placements were

chosen due to the number of kinesthetic cells and length of STN encountered. Once the DBS electrodes were placed, they were tested with an externalized stimulator (Medtronic Dual 7240 stimulator, Minneapolis, MN). Testing is performed in a sequential bipolar fashion (−0,+1: −1,+2; −2,+3) using a pulse width of 60 μs and a frequency of 180 Hz. Voltage is slowly raised to 4 V. For this patient, no continuous adverse effects were noted with stimulation up to 4 V. There were some transient sensory paresthesias in the arm that lasted for about 5–15 s. Transient adverse effects are acceptable since the device is never supposed to be turned off. We were able to get improvements in bradykinesia and rigidity at the −1,+2 for the left side and both −0,+1 and −1,+2 on the right side. Postoperatively the patient was improved by 72 % based on the unified Parkinson's disease rating scale part III (a common motor classification system for PD patients).

Case 2: Complex: A 14-year-old boy with methylmalonic acidemia (MMA) was diagnosed at age 3 months. His condition was well controlled and in good health until acquiring H1N1, when he subsequently developed pancreatitis, sepsis, and in turn bilateral BG strokes.

As a consequence of the strokes, he developed spastic quadriparesis for which a baclofen pump (a common treatment for spasticity) was placed without benefit. He was admitted for worsening dystonia, and resistance to multiple medical therapies. Due to the severity and worsening dystonia, including fixed posturing and dynamic spasms, it was decided to move forward with bilateral GPi stimulation. During the time between the baclofen trial and the decision to move forward with DBS electrode implantation, the patient's respiratory status deteriorated somewhat as well.

Dystonia

Dystonia refers to a syndrome of involuntary sustained or spasmodic muscle contractions involving cocontraction of the agonist and the antagonist muscles [58–60]. The movements are usually slow and sustained, and they often occur in a repetitive and patterned manner. However, they can be unpredictable and fluctuate. The frequent abnormal posturing and twisting can be painful and functionally disabling. Regardless of the causes, the dystonic contractions can have a chronic course and can lead to severe persistent pain and disability. Because each type of dystonia is treated in a different manner, the distinction between the various types is therapeutically important [61–66]. On the basis of its clinical distribution, dystonia is

classified as focal dystonia, segmental dystonia, multifocal dystonia, generalized dystonia, and hemidystonia.

Systemic medications benefit about one-third of patients and consist of a wide variety of options, including cholinergics, benzodiazepines, antiparkinsonism drugs, anticonvulsants, baclofen pump, carbamazepine, and lithium [67]. Many patients with dystonia realize an inadequate response to those treatments [68]. For such patients whose symptoms are sufficiently troublesome, surgical treatment can be used to reduce symptoms and improve function. For dystonia, stimulation is primarily directed at the GPi, which has been the most thoroughly studied stimulation site to date.

Procedure and Decisions

This particular case was one of the most complex of all that we have experienced for DBS electrode implantation. The patient was extremely tenuous metabolically due to the MMA and required anesthesia for the procedure due to excessive movement. The anesthetics themselves can cause not only poor recordings but also adverse metabolic effects. In this case, the surgeon, neurophysiologist, anesthesiologist, critical care physicians, neurologists, and social workers all met to plan the pre-, intra-, and postsurgical management of the patient. Each group discussed their particular needs for the case and the effects each would have on the patient. As discussed previously, the most common issue facing the anesthesiologist in most DBS cases is BP control. A plan was made to use Dex initially and if that proved unacceptable, then propofol would be used if the patient could tolerate it. Due to the underlying metabolic issues, it was questioned whether a controlled amount of Dex could be given to allow for patient comfort and also the ability to record. Also, one of the main problems with Dex is the potential for causing hypotension in a patient. This is not a major issue in PD patients, where this effect is usually helpful, but in children, it needs to be a consideration. Three days prior to the procedure, the plan was to try and wean the patient off of some medications, including high doses of benzodiazepines, which proved unsuccessful.

On the morning of surgery the patient was taken directly to the CT scanner and intubated. Anesthesia included 3 mg of midazolam, 10 mg of etomidate initially followed by another 5 mg, 12 mg of cisatracurium, and 100 μg of fentanyl. The patient was maintained on sevoflurane (1.5 %) for the placement of the frame, and also while they were in the CT area. Prior to

moving the patient to the CT area, Dex was started at 0.7 μg/kg/h with remifentanil at 0.1 μg/kg/min. Five minutes after this the sevoflurane was stopped. This infusion continued up to the creation of the first burr hole in the operating room. At this point the Dex was reduced to 0.1 μg/kg/h and the remifentanil was stopped. The purpose of reducing the Dex at this time was to allow about 10–15 min to slightly awaken the patient for the recordings. Once the burr hole was created and the dura incised, the BP was confirmed to be 127/77 and the initial cannuli were inserted into the brain, followed by the microelectrode. At this point (with the patient still intubated yet alert and able to follow simple commands) the patient exhibited no spasms and even had his eyes open. Once the electrode entered the brain, "burster" cells were recorded indicating: (a) that the tip was in the GPe, and (b) that the sedation level (Dex at 0.1 μg/kg/h) permitted the ability to record single units while still preventing excessive movements. Recordings continued, moving through GPe, through the laminae separating the two structures and into GPi. Because the firing rates of the GPe and the GPi are similar, the ability to record kinesthetic cells is critical to distinguish between the two. Keeping all anesthetics constant, kinesthetic testing was done on all cells encountered. Eight distinct single units were located on the first side with kinesthetic activity noted on three of them. Recording was stopped near the base of the GPi due to an increase in BP to 168/120 mmHg, which was most likely due to a continued wearing off of the Dex and the patient becoming more alert to his surroundings. Advancing of the electrode stopped and two 6-mg doses of hydralazine and a 1.5-μg/kg/min infusion of sodium nitroprusside was needed to bring the pressure down. The pressure eventually stabilized to 114/50 mmHg. The Dex was increased to 1 μg/kg/h and the remifentanil was increased to 0.1 μg/kg/min. Upon exiting GPi, a border cell was noted and then the optic tract 2 mm below. Because it was impossible for the patient to describe muscle activity to the team during macrostimulation (stimulation testing through the permanent DBS lead after it is placed to assure there are no significant adverse events), we used EMG recordings to assess muscle activation. No direct driving activity was noted at 5 Hz, while a minor thumb contraction was noted at 130 Hz and 7.0 V. 5 Hz is used because it is the lowest output of the test stimulator and will give muscle contractions that follow the stimulus train. If this occurs, the muscle activity is related to direct activation of the internal capsule and demonstrates that the electrode is too medial and posterior. If no muscle activity is noted, then the contracture

noted previously is most likely due to stimulation of the GPi. In our experience, this has been shown to be a positive indicator of electrode placement, as is a contraction of the nasal labial fold, when stimulation is above 5.0 V. With this information the electrode was then placed. The Dex was then increased to 1.4 μg/kg/h and the remifentanil was adjusted to 0.07 μg/kg/min for the closure of the first burr hole and the creation of the second burr hole. Once the second burr hole was created, the Dex was reduced to 0.7 μg/kg/h and the remifentanil was stopped. Nitroprusside was continued at 0.5 μg/kg/min. No further changes in anesthetic were needed during the recording or stimulation on this side. The patient was able to open his eyes during the procedure. On this second side, 12 distinct GPi cells were recorded, and a small area of the internal laminae that separates the external and internal segments of the internal GPi was detected. Kinesthetic activity was noted on five of those 12 cells. The optic tract was also noted about 1.7 mm from the base of the GPi. Stimulation testing, similar to the first side, was performed with no adverse events. At this point, sevoflurane was added at 0.7 % for the remainder of the procedure, which included the implantation and tunneling of the connecting wires and IPG.

Case 3: Complex: A 29-year-old male with mild cerebral palsy and severe status dystonicus, which developed after a surgical lysis of omental adhesions and a partial omentectomy.

There were no complications during the omentectomy yet upon awakening from surgery, the patient presented with intractable *spasms and jerky movements*, which were thought to be related to the opiate (fentanyl) or the scopolamine the patient received during the procedure. The patient had a similar reaction after an earlier surgery. At this time the patient was placed on Ativan (2 mg IV) and Benadryl (50 IV every 6 h) with no change over the next couple of days. At this time a diagnosis of myoclonic dystonia was made. Due to the excessive and painful dystonia and dystonic posturing, the patient was intubated and placed on a propofol drip (95 mg/h [25.13 μg/kg/min]; the patient weighed 63.1 kg), valproic acid (250 mg t.i.d.) and put back on Ativan and Benadryl on postoperative day 5. Attempts were made to reduce both the propofol (40 mg/h (10.57 μg/kg/min)) and Ativan to levels to that which the patient could communicate; yet the painful dystonic cramping would return. At 4 weeks postsurgery, Dex was started and the propofol was decreased with the hope of reducing the spastic movements. At this point, the patient was extubated but continued to have the spastic

movements, which eventually led to reintubation, being placed back on a propofol drip (95 mg/h), and started on tetrabenazine (50 mg IV q.6 h). The patient was transferred to our institution for GPi DBS to treat the status dystonicus [69].

Status Dystonicus

Status dystonicus (SD) was first recognized by Jankovic and Penn in 1982 and had been defined as “increasingly frequent and severe episodes of generalized dystonia and rigidity, which may be refractory to standard drug therapy” [70]. This condition had been labeled as “status dystonicus” or “dystonic storm.” The condition is quite rare, with less than 40 episodes reported in the literature [71]. Patients with SD usually develop life-threatening complications such as bulbar weakness, compromising upper airway patency with the risk of pulmonary aspiration , progressive impairment of respiratory function leading to the development of respiratory compromise, exhaustion and pain and metabolic derangements.

Several drugs and surgical procedures have been tried for SD with no consistent outcome. Orally active medications have been tried [72], once again with no consistent outcome, and in many cases the current literature favors using intravenous agents for deep sedation [73]. Patients with SD often develop metabolic complications such as rhabdomyolysis, which can lead to renal failure, and bulbar and respiratory complications, which require tracheal intubation. Other complications often seen include hyperpyrexia, muscle exhaustion, pain, and dehydration. For all the above reasons, patients need to be treated in the intensive care unit (ICU) setting. Patients commonly require deep sedation under muscle paralysis and assisted ventilation [71]. Intravenous infusion of midazolam and propofol may be used in the management of SD. Second-line strategies, especially in those with progressive disorders, involve deep brain stimulation surgery.

Procedure and Decisions

Given the lack of a “best medical therapy ” benefit, bilateral GPi DBS surgery was performed 2 months after the onset of the intractable *spasms and jerky movements*, which led to an improvement in symptoms. During the procedure, three MER tracts were performed (two on the right side and one on the left side). An average of 3.3 GPi cells were recorded per stereotactic

pass. This is somewhat less than the normal 10+ cells that we find in the GPi in PD and a DBS dystonia patient. The average GPi firing rate of this patient was also significantly less: 34.3 +/− 16.5 Hz as compared to PD patients, which are in the range of 60–80 Hz. While for GPe, in this patient, it was 44.5 +/− 16.6 Hz, which is lower than found in PD, yet not as significant as was found in the GPi firing rate. Figure 5.4a shows the spike activity in both the GPe and the GPi of this patient at different propofol concentration levels. This reduced activity is similar to what is observed during surgery in patients for dystonia when on propofol as compared with no propofol (Fig. 5.4b). The change in firing rate appears to be related to the level of propofol, as seen in Fig. 5.4a. It is interesting to note that given the continuous propofol infusions over 2 months prior to surgery, the intraoperative dose needed to be much higher for sedation when compared to other patients undergoing a variety of surgical procedures, and even at these high propofol concentrations the patient was still interacting in a meaningful way. Even with the ability of the patient to interact with the surgical team, there was still a reduction in basal ganglia activity (as measured by the GPi firing rate), which clinically manifests as a reduction in abnormal movements. In a review article, Wilson et al. [74] found multiple instances of patients demonstrating a propofol tolerance with continuous infusion, thus requiring greater and greater doses for sedation and reduction of pain over time. Propofol directly activates $GABA_A$ receptors, which have the effect of reducing the overall activity in the BG due to the receptors' inhibitory nature. Additionally, propofol has been shown to affect other neuotranmitters and neuromodulators, specifically cannabinoid receptors, which are thought to be sedative sites of action of anesthetics [75]. The variation in accommodation between these two receptors may account for the clinical differences (communication versus BG activity reduction) noted in this patient.

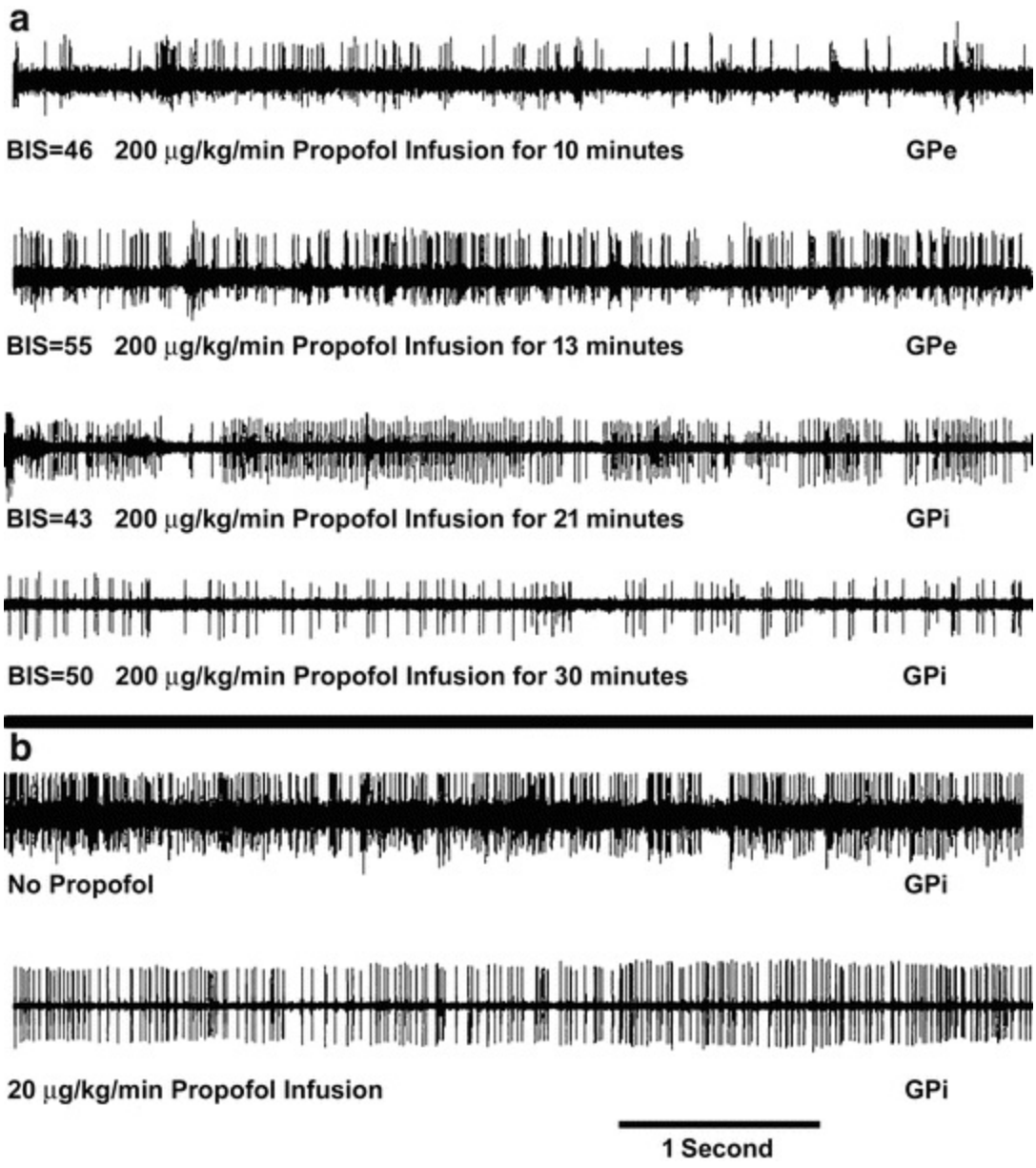

Fig. 5.4 Single-unit recordings from both the GPe and GPi during different infusion concentrations of propofol in a patient with status dystonicus (**a**). Single-unit recordings from the GPi in a patient with dystonia during a propofol infusion and with no infusion (**b**)

Conclusion

As in most other areas of intraoperative neurophysiology, the trade-offs between anesthetics and the collection of neurophysiology data are a challenge. One advantage in most movement disorder procedures is that very little sedative or global pain medication is needed, but because of the highly

sensitive nature of the tissue, BP control is critical as is O_2 saturation. Finally, due to the diversity of movement disorders, there may be times where sedative anesthesia or even GA is needed, and the procedures can only be performed by a close collaboration between the surgeon, the anesthesiologist, and the neurophysiologist.

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Footnotes

1 Asterisks indicate key references.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_6

6. Monitoring of Spinal Cord Functions

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Keywords Monitoring – Spinal cord function – Spinal cord – Surgery – Spinal cord potentials (SCPs) – Spinal cord stimulation (SCS) – Transcranial motor-evoked potentials (tc-MEPs)

Key Learning Points

- The methods to record the spinal cord potentials

- Segmental nerve stimulation
- Transcranial electric or magnetic stimulation
- Spinal cord stimulation
- Heterosegmental nerve stimulation
- The techniques to introduce the catheter electrodes into the epidural space
- To identify the components of segmental spinal cord potentials—initial spikes, negative waves, slow positive waves
- Conducting (conductive) spinal cord potentials
- Heterosegmental spinal cord potentials—slow positive waves

Introduction

Spinal and cardiovascular surgeries impart mechanical [1] or ischemic [2] stress to the spinal cord. To prevent spinal cord injury due to such surgical stresses , the intraoperative monitoring of spinal cord function is important. Until the 1960s, there were no available methods of spinal cord function monitoring. In the late 1960s, a novel tool for monitoring spinal cord function became available; it recorded somatosensory-evoked potentials (SSEPs) from the scalp. In this technique, the electrical potentials evoked by peripheral nerve stimulation are recorded on an electroencephalogram (EEG). The short-latency component of SEPs may indicate cervical spinal cord function in waveforms (latencies and amplitudes) [3].

Since their introduction, SEPs have been used in clinical monitoring, diagnosis and investigations, as well as in animal experiments [4]. In the 1980s, SSEPs were also adopted for the monitoring of spinal cord function during spinal [5] or cardiovascular [6] surgery. The recording of small electrical changes, such as SSEPs, requires the close attachment of electrodes to spinal cord tissues. Commonly, electrodes are placed on the scalp close to the sensory cortex. These potentials recorded from the scalp or even the cervical skin surface may not reflect the spinal cord function because they interact with brainstem potentials or far-field potentials. Thus, segmental or regional electric changes in the spinal cord cannot be recorded from the body surface, because the spinal cord is situated deep in the body, and its activities

are obscured by other electrical activities such as electroencephalogram (EEG), electromyogram (EMG), and electrocardiogram (ECG) [7].

During the same time, another novel technique of recording SCPs directly from the spinal cord by inserting electrodes into the dorsal epidural space was developed by Shimoji et al. [8]. A catheter electrode was placed percutaneously in the same manner as for a continuous epidural block. From the epidural electrodes, spinal cord field potentials were recorded [9]. In addition, the spinal cord was stimulated electrically using the same epidural electrodes utilized for pain management (spinal cord stimulation [SCS]) [10, 11].

Intrathecal electrodes were utilized by Magladery et al. [12] initially, but the risks associated with electrode insertion raised great concern. As a result, intrathecal electrodes were not used clinically except in those cases in which surgical manipulations were carried out directly on the cord [13]. With the idea that epidural recording can minimize the risks compared with those of intrathecal recording, Shimoji et al. [9, 14] further developed techniques to exclude contamination by ECG activity when recording evoked SCPs (discussed later). Following these developments, recording and stimulation with epidural electrodes have been used in routine clinical monitoring, therapeutics, and investigations, as well as in animal experiments at various institutes [15].

The acquisition of SSEPs requires a somewhat lengthy period of time from a few to several minutes, because the repetitive recording (50–200 times) of waveforms is needed for amplification by computed averaging [3–6]. Both SSEP and SCP recordings are easily interfered with by the noise from electrocoagulation or other electrical sources of noise during surgery. SSEPs are cerebral electrical changes evoked by sensory nerve stimulation, and evoked SCPs are spinal electrical changes evoked by sensory nerve or spinal cord stimulation (SCP). Therefore, it is advantageous to acquire simultaneous records of both electrical activities (SSEPs and SCPs) when monitoring spinal cord function, particularly when surgical manipulations involve the sensory spinal tracts (see Appendix).

Thoracic and lumbar aortic occlusion has frequently been demonstrated to result in ischemia of the ventral two-thirds of the spinal cord [16]. As such, there was also a great demand from surgeons and anesthesiologists for the monitoring of spinal motor function. In the late 1990s, transcranial motor-evoked potentials (tc-MEPs) were utilized to monitor spinal motor function.

Using this monitoring technique, impulses generated by transcranial stimulation of giant pyramidal cells descend the pyramidal tract to the spinal motoneurons, producing skeletal muscle contractions. In this way, the stimulation technique and the recording of tc-MEPs are simple. Both electric and magnetic stimulation are currently used in clinical practice (electric tc-MEPs [17] and magnetic tc-MEPs [18, 19]). The motor responses resulting from transcranial stimulation are recorded as EMG responses.

Following the development of tc-MEPs, transcranial stimulation was used to evoke SCPs (transcranially evoked SCP [tc-SCP]) in the early 2000s. Either transcranial electric (electric tc-SCP) [17] or magnetic (magnetic tc-SCP) [18, 19] stimulation is applied to giant pyramidal cells and the responses can be recorded directly from the spinal cord epidurally [15]. The tc-SCPs provide highly precise data, because spinal motor function can be directly monitored.

Recording Evoked SCPS for Intraoperative Monitoring

A catheter equipped with several Ag-AgCl electrodes , designed by Shimoji et al. [8], is inserted into the epidural space, using the same technique as that for the continuous epidural block, at a level corresponding to the spinal segment to be monitored. The catheter with platinum–iridium electrodes (Medtronic™ Inc., Minneapolis, MN), which was developed for SCS, is also available for SCP recording. Because evoked SCPs are easily affected by ECG artifacts, the exclusion of ECG contamination is very important. To exclude such contamination, a peripheral nerve is stimulated by square pulses triggered by a QRS component of ECG with a delay of 0.3–0.5 s, when the triggered pulses coincide with the end of a T wave. Thus, evoked SCPs are recorded on the electrically silent phase (0.5–0.7 s) between T and P waves (Fig. 6.1) [8, 20–23].

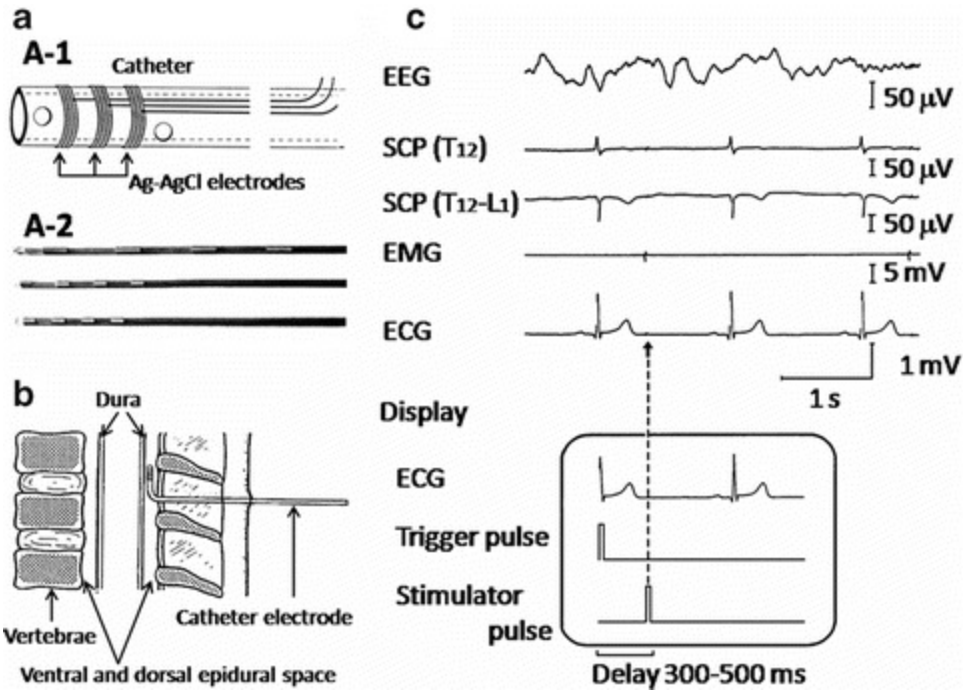

Fig. 6.1 Recording methods of spinal cord potentials (SCPs). A catheter electrode is inserted into the dorsal epidural space using the same technique as that for the continuous epidural block at a level corresponding to the spinal segment to be monitored [8]. To exclude ECG contamination, stimulation pulses are triggered by a QRS component of ECG with a delay of 0.3–0.5 s, when the triggered pulses coincide with the end of a T wave. In this manner, evoked SCPs are recorded in the electrically silent phase (0.5–0.7 s) between T and P waves [9]. (**a**) A catheter (1 m diameter) equipped with several Ag-AgCl electrodes (A-1), and platinum–iridium electrodes (A-2), which are designed for spinal cord stimulation, are also available. (**b**) An illustration of a catheter electrode inserted into the epidural space. (**c**) The relation between ECG and electrical stimulation [14, 15]

The peripheral nerve trunk is electrically stimulated to evoke SCP responses. For monitoring of cervical spinal cord activity, epidural catheter electrodes are inserted into the cervical epidural space close to the cervical enlargement. Next, the brachial plexus or the radial, ulnar, or median nerve is stimulated (segmentally evoked SCPs, Fig. 6.2a). To monitor lumbar spinal cord function, the recording electrodes are placed close to the lumbar enlargement, and the common tibial or peroneal nerve is stimulated (segmentally evoked SCPs, Fig. 6.2a, c) [7, 9, 12].

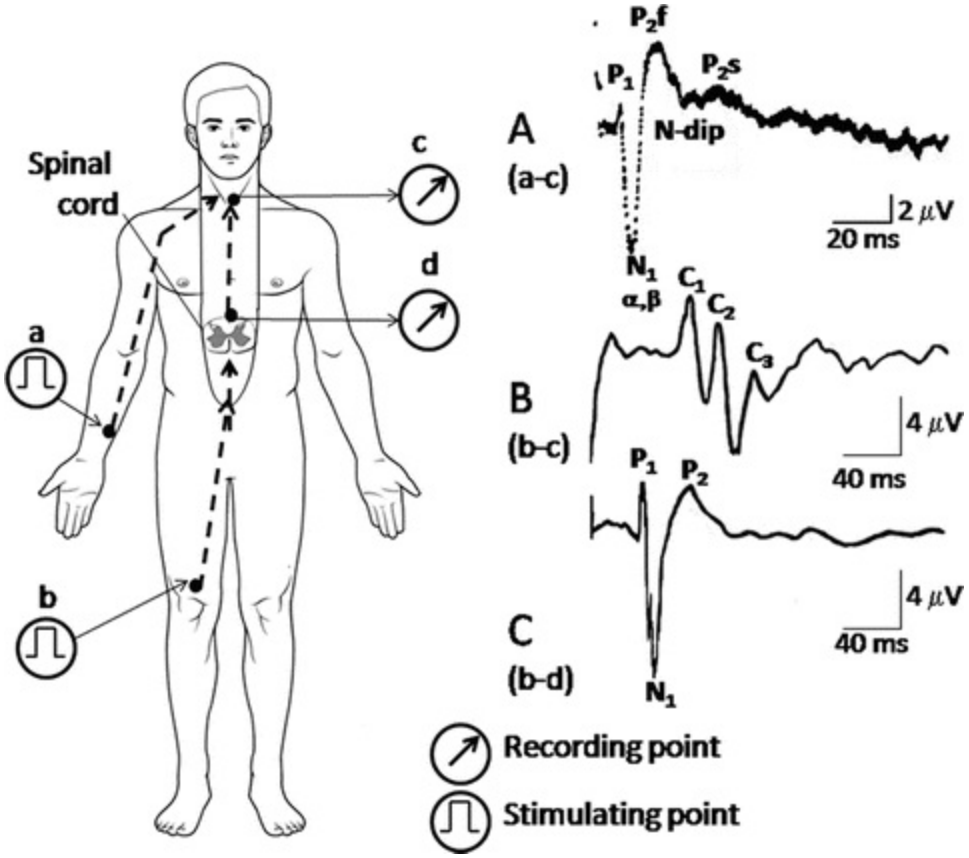

Fig. 6.2 Recording of spinal cord potentials (SCPs). A peripheral nerve trunk is electrically stimulated (see Fig. 6.1). Recording electrodes are inserted into the epidural space to monitor the dorsal spinal activity. Dysfunction of the spinal cord is reflected as abnormalities in the waveforms, such as prolongation of peak latencies and depression or augmentation of amplitudes. The waveforms of the segmental SCPs recorded in the cervical and lumbosacral enlargements are very similar to each other. In the ascending evoked SCPs, complex positive waves (C1, C2, and C3) are recorded, but N1 and P2 waves are hardly noticed. (**a**) The waveforms of segmental evoked SCPs recorded from the cervical enlargement (c) by stimulation of the ulnar nerve (a). (**b**) Ascending evoked SCPs recorded from the cervical enlargement (c) by stimulation to the common tibial nerve (b). (**c**) Segmental evoked SCPs recorded from the lumbar enlargement (d) by stimulation at the common tibial nerve (b). P_1: action potential of spinal nerve roots. N1: synchronized activities of interneurons. P_2: primary afferent depolarization (PAD). Sometimes, P_2 splits into two components, first (P_2f) and second (P_2s) components. N-dip: negative dip driving P_2f and P_2s [8, 22, 23]

The waveforms of the segmental SCPs recorded in the cervical and lumbosacral enlargements are very similar. Evoked SCPs can be recorded at the level of the cervical enlargement by the stimulation of a nerve trunk in the lower limb (ascending evoked SCPs; see Fig. 6.2b). The waveforms of SCPs recorded at the lumbar enlargement by epidural stimulation of the cervical spinal cord are similar to those of the segmentally evoked SCPs (descending

evoked SCPs; see Fig. 6.2a, c) [8, 9, 10, 14, 15, 22, 23].

The summated electrical potentials travel along the spinal cord in response to SCS in the epidural space of the upper or lower spinal segments, cauda equina, or from peripheral nerve stimulation. Thus, the human SCPs can be recorded from the cervical epidural space in response to cauda equina stimulation at the L3–4 vertebral level or SCS by an electrode situated in the epidural space close to the lumbar enlargement (ascending SCPs; see Fig. 6.2b, c) and vice versa (SCS from cervical epidural space and recording at the lumbar enlargement level) (descending SCPs) [8, 10, 15].

Recording Electric tc-MEPS and Magnetic tc-MEPS for Intraoperative Monitoring

In transcranial electrical stimulation , electrodes are placed at C3 or C4 on the scalp, and a train of square wave stimulation pulses (with a pulse duration of 0.02–0.2 ms and an interpulse interval of 0.2 ms) are applied at an intensity of 250–1000 V [24–26]. Because of the use of high-voltage stimulation to obtain electric tc-MEPs, durable electrodes such as corkscrew-shaped electrodes are used for stimulation so as to avoid scalp burns. For magnetic tc-MEPs, a magnetic coil is used for stimulation. For both forms of stimulation, EMG (CMAP) responses are usually recorded from the abductor pollicis brevis muscle (upper limb) or the tibialis anterior muscle (lower limb) using needle or surface electrodes [24–26].

In response to pulse train stimulations, giant pyramidal cells are directly depolarized generating D waves [27–29]. However, during magnetic stimulation, interneurons are depolarized first and the firing of giant pyramidal cells follows sequentially generating several I waves at 1.5- to 2.0-ms intervals [28, 29]. Both D and I waves descend the pyramidal tract as a group of several spiky waves (multiple descending volleys), and the spinal motor neurons are stimulated by these piston-like multiple descending volleys, resulting in summation of excitatory postsynaptic potentials (EPSP) [18, 29–31]. Thus, the spinal motor neurons are excited with a few milliseconds of delay (Fig. 6.3) [18, 19, 28–33].

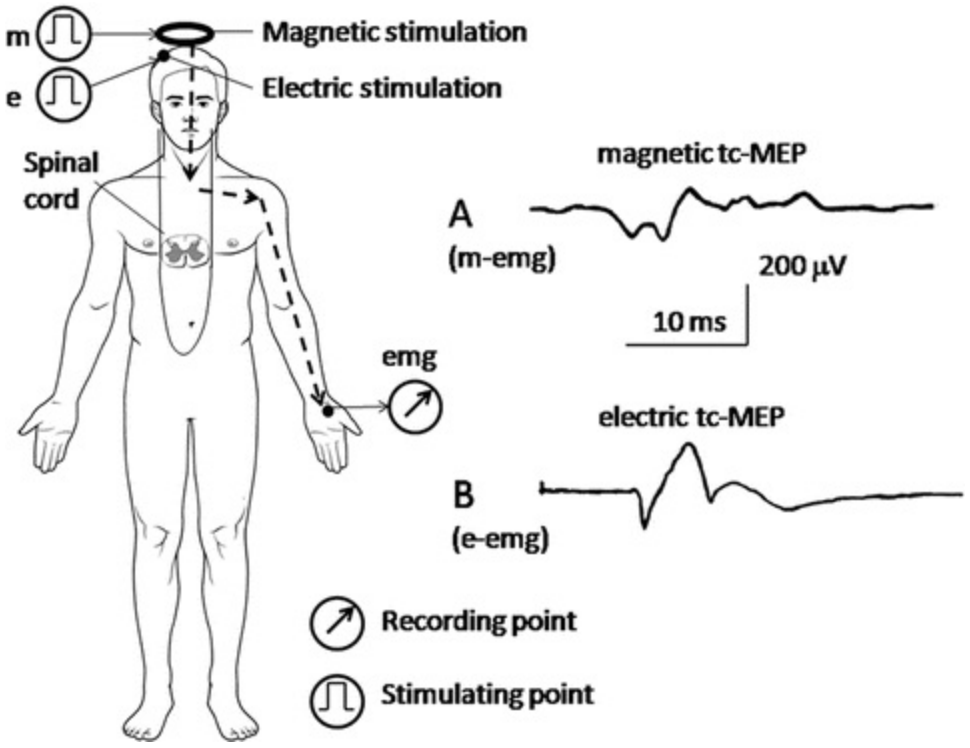

Fig. 6.3 Recording of transcranially stimulated motor-evoked potentials (tc-MEPs) . The brain is stimulated electrically or magnetically, and the evoked EMG (motor-evoked potential [MEP]) is recorded from the abductor pollicis brevis muscle (upper limb) or the tibialis anterior muscle (lower limb). (**a**) Magnetic tc-MEP, which is stimulated magnetically at the parietal cranium (m) and recorded from the abductor pollicis brevis muscle (m-emg). (**b**) Electric tc-MEP, which is stimulated electrically at the contralateral scalp, C3 or C4 (e), and recorded from the abductor pollicis brevis muscle (e-emg)

Convulsions are occasionally induced during brain stimulation for a clinical examination in the arousal state [32], but they are rare during stimulation for intraoperative monitoring under general anesthesia [33, 34]. Surgical procedures on the spine or spinal cord should be performed under general anesthesia with adequate monitoring of spinal cord function [35].

Recording tc-SCPS for Intraoperative Monitoring

Transcranial stimulation also results in electrical changes in the SCP recordings, which appear to provide better evidence of spinal motor function than tc-MEPs [18, 19, 27–29]. The methods of electric and magnetic stimulation are described for the respective tc-MEPs. However, the methods of recording the tc-SCP responses are the same as those described for the segmental SCPs [8–10, 17, 18].

When acquiring magnetic tc-SCP responses, the generation of multiple

descending volleys in the pyramidal tract as well as the process of electric summation in the dorsal horn are clearly depicted [18, 19, 27, 29]. These phenomena are never evident when acquiring magnetic tc-MEP responses because only evoked EMG activity can be observed [14, 18, 19]. Therefore, magnetic tc-SCPs may provide fine data quality when monitoring spinal motor function (Fig. 6.4).

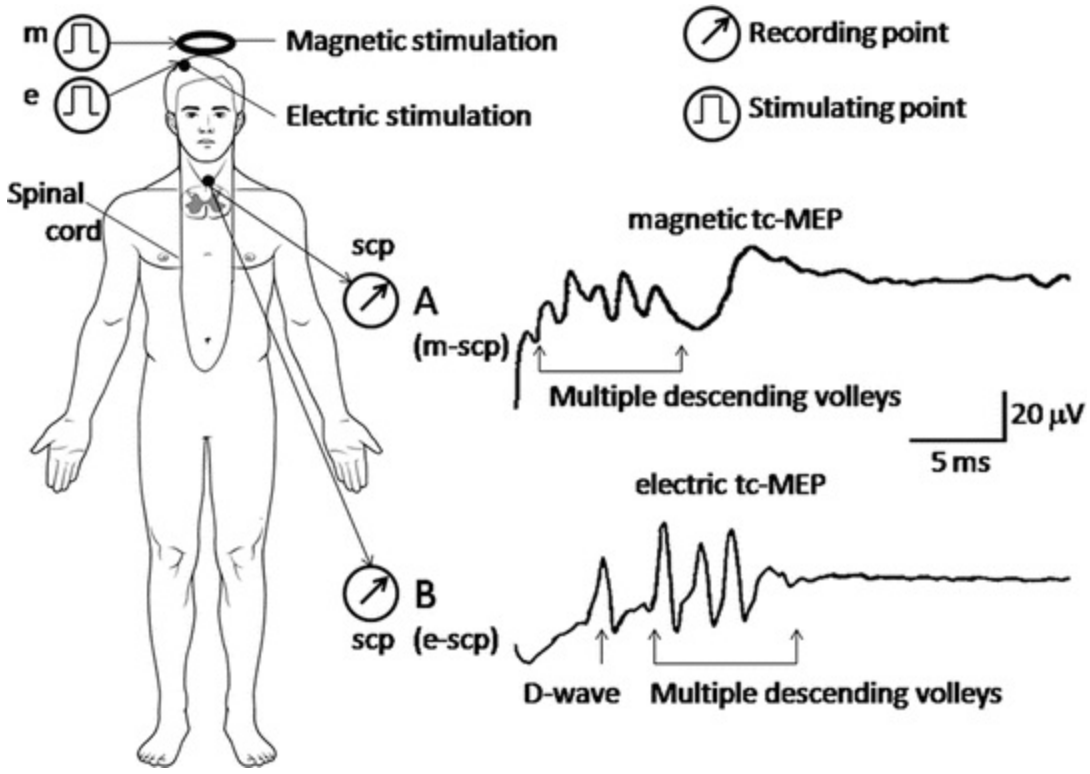

Fig. 6.4 Recording of transcranially stimulated evoked spinal cord potentials (tc-SCPs). The brain is stimulated magnetically or electrically, and the resulting spinal cord potentials (SCPs) are recorded with epidural electrodes. Both forms of stimulation evoke a group of several spiky waves (multiple descending volleys) descending the pyramidal tract. The volleys result in the summation of excitatory postsynaptic potentials (EPSPs). (**a**) Magnetic tc-SCP, which is stimulated magnetically at the parietal cranium (m) and recorded from the spinal cord (scp). (**b**) Electric tc-SCP, which is stimulated electrically at the contralateral scalp, C3 or C4 (e), and recorded from the spinal cord (scp)

Anesthetics Used in Spinal Cord Monitoring

Many general anesthetics , especially inhalation anesthetics, suppress spinal electrical activity, thereby reducing the amplitudes and prolonging the latencies of SSEPs, SCPs [36–39], and tc-MEPs. Therefore, the use of intravenous anesthetics, including low-dose propofol, ketamine, fentanyl, and

remifentanil, are usually recommended for surgeries that use spinal cord monitoring. Also, anesthesia can suppress spinal electrical activity, leading to incorrect judgments [19, 23, 24, 40, 41]. In light of this, simultaneous monitoring of the bispectral index (BIS) is recommended for maintenance of adequate anesthesia depth (40–60 % in BIS) [42]. Administration of a muscle relaxant is desirable when recording SSEPs and SCPs because the use of relaxants diminishes the presence of muscle contractions and noise due to EMG artifact. Muscle relaxants, however, interfere with MEP monitoring.

Intravenously administered anesthetics, which are mixed with venous blood, stream into the heart (right atrium). After circulating through the lungs, the anesthetics return to the heart (left atrium) with minimal loss or consumption. Thus, most of the anesthetics enter the aorta. When the aorta is occluded during a surgical procedure, blood flow in the distal region of the occlusion becomes very small, and blood is pooled in the proximal region, where 30 % of the circulating blood volume is distributed [43]. Therefore, when intravenous anesthetics are continuously infused using a syringe pump, the concentration of an anesthetic in the proximal region of the aortic occlusion elevates two- to fourfold [44]. This elevation results in a deeper anesthetic state than was assumed before the aorta occlusion, leading to misjudgments. The monitoring of BIS is therefore helpful in realizing correct judgments in such cases [45].

Case Studies (Clinical Applications)

Spinal cord monitoring by SCP, tc-MEP, or tc-SCP is utilized during spinal surgery to assess the force on spinal neurons caused by traction, the stress or injury caused by surgical manipulation, the stress or damage due to ischemia, and hypofunction under conditions of hypothermia. Representative cases of each clinical application are presented below.

Traction force on the spine and spinal cord produces immediate spinal cord ischemia as a result of blood vessels being stretched. The force can reduce the amplitudes of SCPs by over 50 %. Amplitude reduction in the SCP due to ischemia can occur with or without prolongation of latency. Based on findings obtained from SCP monitoring, a nonharmful traction force on the spine can be determined. Consequently, a spinal cord injury was able to be prevented in the following case involving open traction and fixation of the spine to correct idiopathic scoliosis (Fig. 6.5) [46].

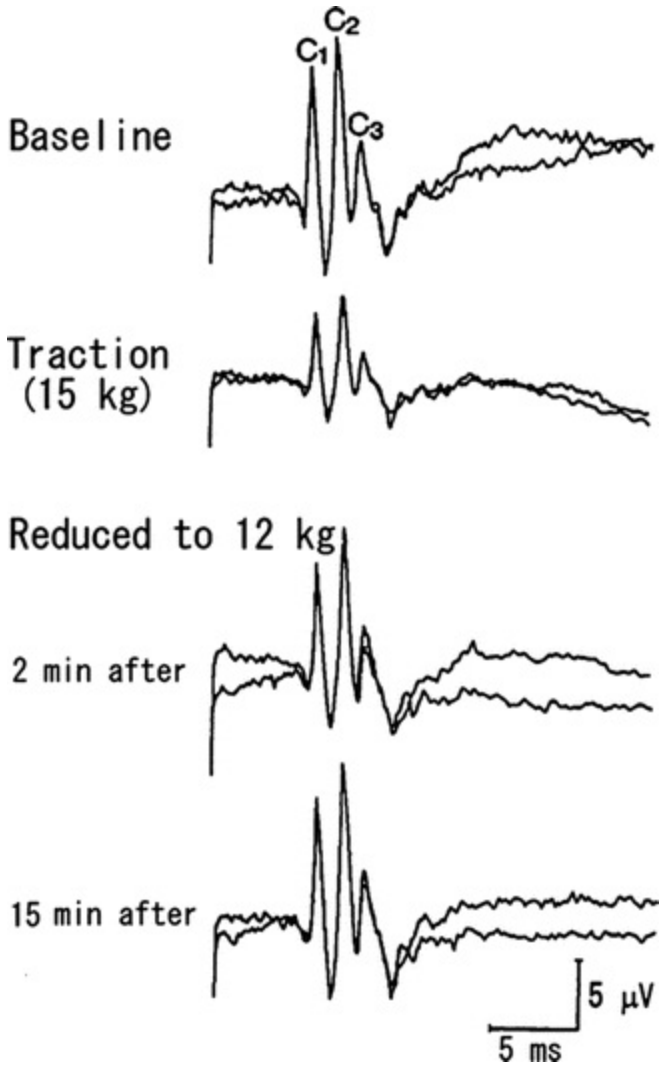

Fig. 6.5 Clinical application of SCP for spine traction . Open traction and fixation of the thoracic spine to correct idiopathic scoliosis in a 26-year-old female. Anesthesia was maintained with fentanyl and ketamine. The cauda equina (L4) was supramaximally stimulated by electric pulses. Ascending SCPs were recorded from the posterior epidural space at the C7 spinal cord level. Immediately after traction of the spine at 15 kg, the amplitudes of C1, C2, and C3 were reduced to 47.0, 47.5, and 49 %, respectively. These reductions in amplitude recovered within 15 min after the traction force was reduced to 12 kg. In this case, the latency did not change. Reprinted with permission from Fujioka et al. [46]

The surgical manipulation during resection of spinal cord tumors causes direct and/or indirect mechanical stress or injury to spinal neurons, which can be determined by using tc-MEP monitoring. When spinal cord damage occurs, the amplitudes of the tc-MEP responses drop and the stimulation thresholds elevate. Based on observations of the tc-MEPs, alterations to the tumor resection can be recommended so as to avoid postsurgical motor

dysfunction (Fig. 6.6). When amplitude reductions exceed 50 % during the resection, the surgical approach or the resection size needs to be reconsidered: should the resection be continued, should a smaller resection be performed, should the angle or direction of the section be changed, or should the resection be discontinued altogether? Also, based on the final findings from the tc-MEP monitoring, the level of postsurgical motor dysfunction can be predicted [15].

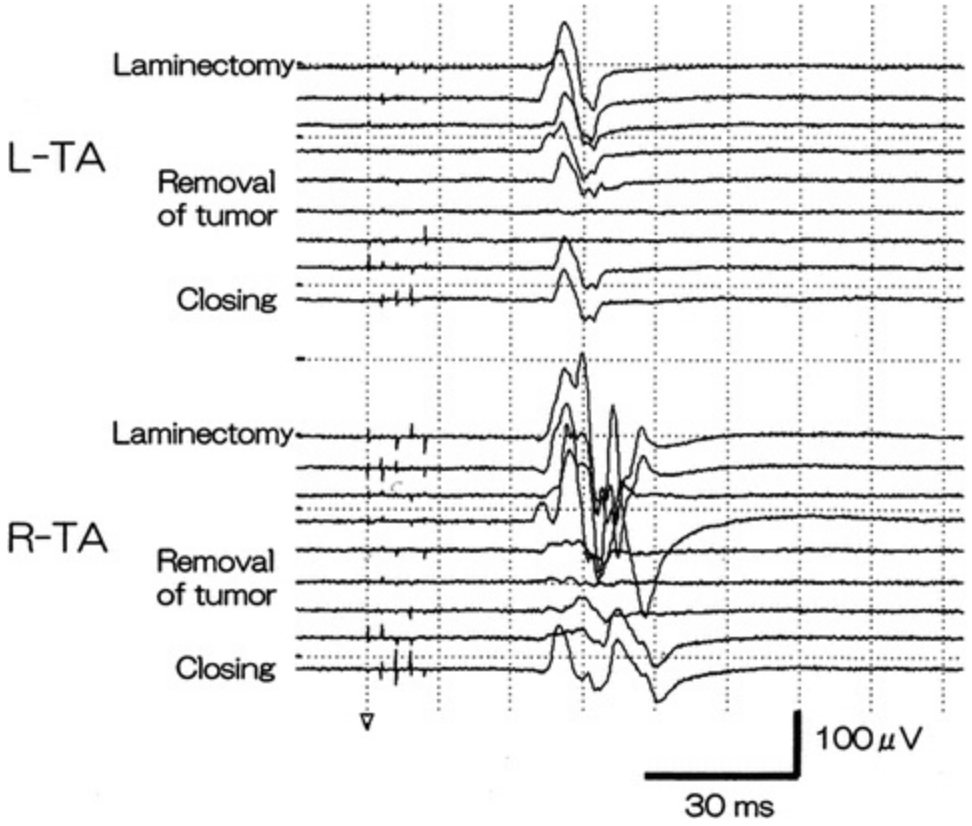

Fig. 6.6 Changes in tc-MEPs during spinal cord tumor resection. A 38-year-old male patient with a spinal cord tumor in the T5–6 area underwent tumor resection. Anesthesia was maintained by TIVA. While monitoring tc-MEPs, electric stimulation was performed with a five-pulse train (50–100 μs of duration, 2-ms intervals, 600 V) on the scalp (C3 and C4), and an EMG of the tibialis anterior (TA) muscles was recorded. During tumor resection, the amplitudes decreased, but they recovered immediately after the surgical approach was altered. The tumor resection was continued from the other direction. Thus, postsurgical motor weakness was not evident. Reprinted with permission from Fukaya et al. [15]

Aortic surgery usually requires aortic cross-clamping , which often results in spinal cord ischemia [47, 48]. Because of the prompt response to ischemia, SCPs are monitored during aortic surgery to assess the severity of ischemic stress to the spinal cord. Sequential changes in segmental SCPs during

surgery for aortic aneurysm are shown in Fig. 6.7. Ischemia due to aortic cross-clamping caused a rapid decrease in the amplitude and an increase in the latency of the responses. The waveforms recovered quickly after declamping. However, the duration of ischemia that is tolerable or reversible when a reduction/abolition of the SCP occurs without any resulting postsurgical neurological symptoms is still not clear (see Fig. 6.7).

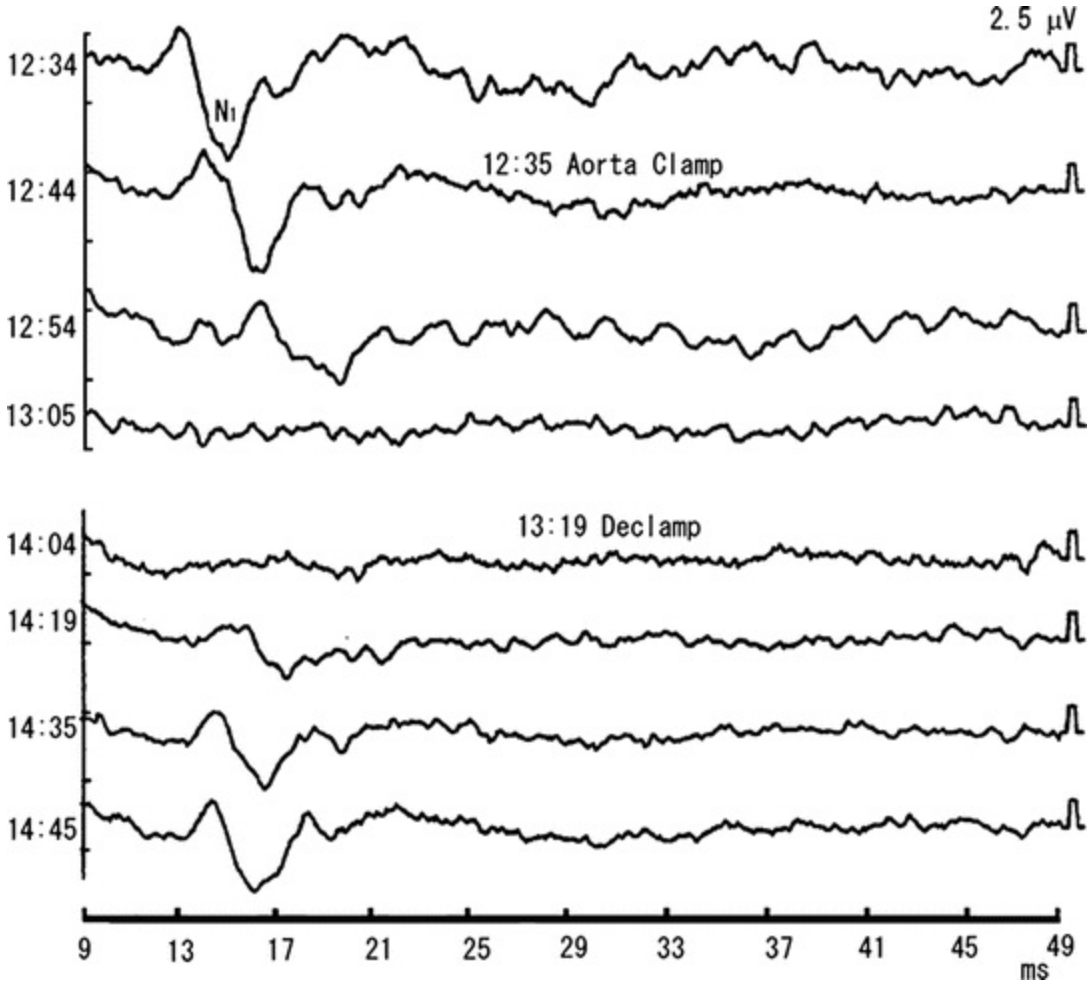

Fig. 6.7 Effects of aortic cross clamping on segmental SCPs. A 71-year-old man underwent abdominal aortic surgery. Segmental SCPs were recorded from the epidural space at the T12/L1 vertebral level, and the common tibial nerve was stimulated supramaximally at the popliteal fossa. Anesthesia was maintained mainly with fentanyl and midazolam, and blood cooling was initiated by cardio pulmonary bypass. The N1 wave disappeared 30 min (13:05) after cross-clamping (12:35) and reappeared (14:12) after the declamping (13:19), with the time lag between its reappearance and the declamping being 53 min. The durations of aortic cross-clamping and that of the disappearance of SCP were 44 and 67 min, respectively. There were no neurological sequelae after surgery. Reprinted with permission from Kondo et al. [49], with modification

Thus, test cross-clamping before dividing an aneurysm is recommended (i.e., SCP is closely observed for 15 min after aortic cross-clamping). If a greater than 50 % reduction of the amplitude is observed, the surgeons should make repeated short-term releases of the clamp during the surgery so as to avoid long-term ischemia or should change to another bypass route [49]. This test can also be modified when monitoring via tc-MEPs or tc-SCPs. On the other hand, when no or only minimal recovery in the SCP is noted during the final observation, motor dysfunction corresponding to the amplitude decrease can be predicted. Because there are concerns that heparinization during aortic surgery causes an epidural hematoma, an epidural catheter electrode should be inserted at least 1 h before the surgery and extracted 1 day later when the effect of the heparin has dissipated.

Cardiovascular surgery is usually performed under moderate or deep hypothermia , which makes interpretation of waveform changes more complicated. The waveform of the SCP under moderate hypothermia responds very sensitively to a drop in body temperature with characteristic responses in the waveform under such conditions being prolongation of the latency, widening of the duration, and augmentation of the amplitude (Fig. 6.8) [49].

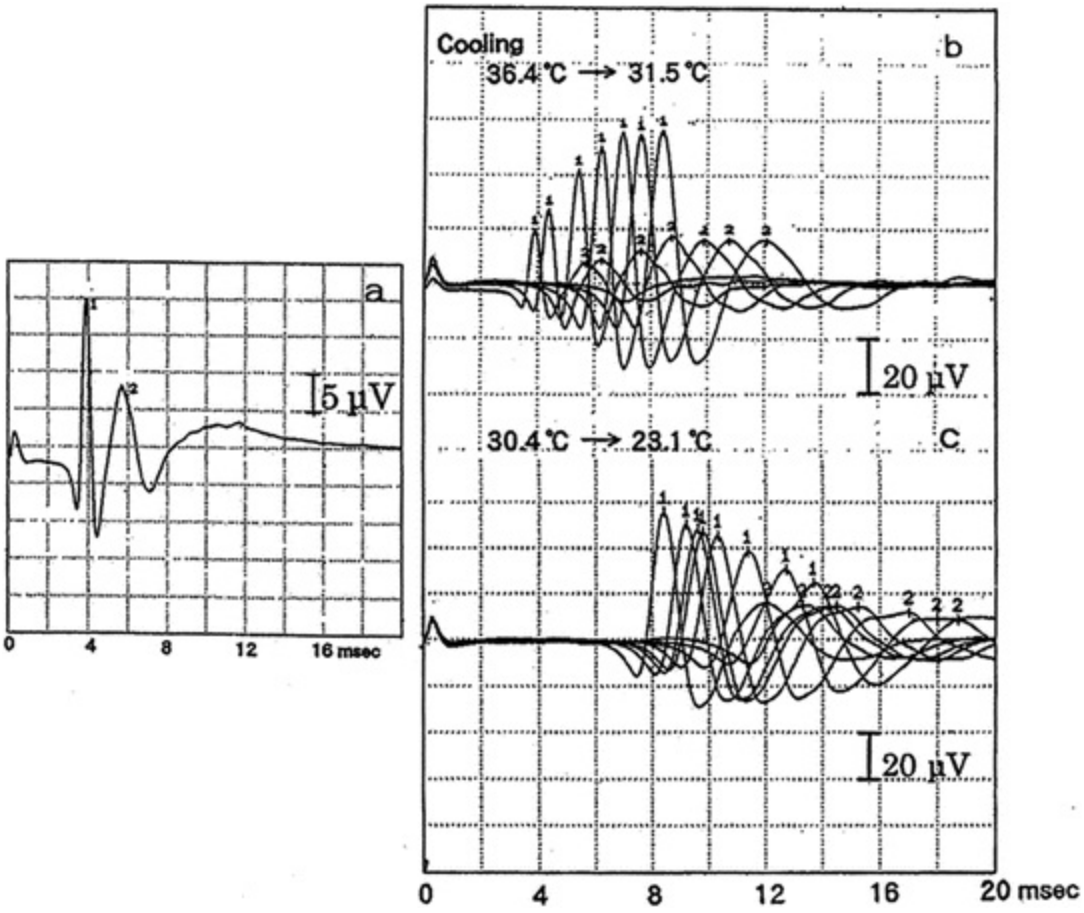

Fig. 6.8 Waveform changes of descending SCPs under moderate hypothermia . A 56-year-old patient underwent thoracoabdominal aortic surgery under hypothermic cardiopulmonary bypass. Descending SCPs were recorded from the epidural space at the T12/L1 vertebral level, and the spinal cord was supramaximally stimulated at the C6/7 vertebral level with epidurally inserted electrodes. Anesthesia was maintained with fentanyl and midazolam, and rectal body temperature was measured. Subsequent serial changes of N1 and N2 waves were superimposed: (**a**) before cooling; (**b**) SCPs during cooling process; (**c**) SCPs during rewarming process. Prolongation of the latency, widening of the duration, and augmentation of the amplitude are noted under moderate hypothermia. Reprinted with permission from Kondo et al. [49]

Interestingly, the change in the amplitude was biphasic when the body temperature was lowered even further: the amplitude gradually increased until around 30 °C, and then began to decrease under deeper hypothermia . The precise mechanisms of the biphasic response are still not clear. Under profound hypothermia (below 20 °C), the amplitude decreases or disappears. Under even lower body temperature of approximately 10 °C, the N1 wave is split into two peaks (not illustrated in Fig. 6.7) [49]. These changes recover to the baseline level immediately upon rewarming. Thus, body temperature measurements are indispensable for the interpretation of the waveform

changes in the SCP monitoring.

Conclusion

In conclusion, besides basic routine monitoring of SSEPs and tc-MEPs [47], combined monitoring of other parameters such as tc-MEP or tc-SCP and MEPs may provide an accurate monitoring of spinal cord function during surgical manipulations of the spine or nearby structures depending on individual surgeries [50–52].

Recording of the spinal cord potentials recorded from the epidural space may add more precise monitoring of spinal cord functions in certain cases.

Appendix: Techniques and Physiology

Introduction

The development of the catheter electrode has made it possible to stimulate the spinal cord from the epidural space for pain management [53] and to record epidurally human spinal cord potentials for monitoring spinal cord function during an operation [8].

The Catheter Electrodes

Human spinal cord potentials (SCPs) can be recorded from the epidural space using the same catheter used for continuous epidural block. The epidural catheter electrode can be made simply by insertion of a stainless steel wire through the epidural catheter approximately 5 mm beyond its tip (Fig. A6.1a). This simple catheter has been used for the recording of spinal cord potentials in patients during surgical operations or for the stimulation of the spinal cord in patients with various spinal cord diseases [54]. An epidural catheter with three orifices on the side and three platinum wire electrodes was developed in our laboratory for multiple applications (Fig. A6.1b, c), including monitoring of spinal cord potentials, measurement of epidural pressure and epidural tissue blood flow, epidural spinal cord stimulation, and epidural injection of drugs [55].

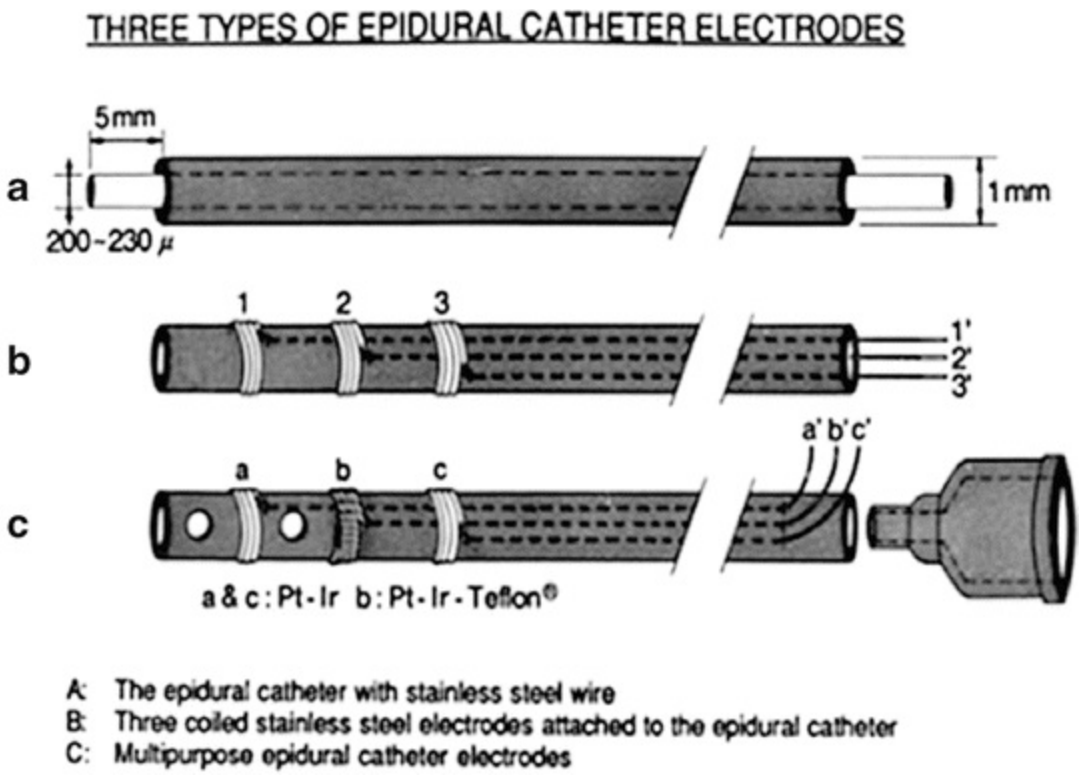

Fig. A6.1 Three types of epidural catheter electrodes are shown. A stainless steel wire can be placed through an epidural catheter approximately 5 mm beyond its tip (**a**). Three platinum wire electrodes can be placed on the catheter (**b**) that may also have three orifices on the side to measure epidural pressure and epidural tissue blood flow, epidural spinal cord stimulation, and epidural injection of drugs (**c**)

Accurate insertion of the catheter electrode at the required site in the epidural space is critical for these applications. We have been using three methods to determine the proper placement of the catheter electrodes in the posterior epidural space: (1) epidural electrical stimulation test, (2) recording of the spinal cord potentials evoked by stimulation of the segmental, heterosegmental nerves, or dorsal cord [14, 56, 57], and (3) image examination such as X-ray, MRI, or CT scan.

When the catheter electrodes are situated in the posterior epidural space on the mid-line, stimulation through the catheter electrodes produces the bilateral twitches of the segmental muscles. When it produces unilateral muscle twitches in the same spinal segment, the electrodes might be situated laterally in the epidural space. By this stimulation test, you can verify the spinal segment position and the laterality of the catheter electrode in the epidural space. When the catheter electrode is situated in the anterior epidural space, the polarity of the segmental SCPs is reversed as expected. Laterality of the catheter electrodes in the epidural space can also be determined by the

waveform characteristics of the SCPs. When the catheter electrodes are situated ipsilateral to the stimulated peripheral nerves and close to the roots, the recorded initial positive spikes and P_2 wave are larger than those recorded contralateral to the nerves.

The procedure used to introduce the catheter electrodes into the epidural space is the same as that used to place catheters for continuous epidural anesthesia [53]. The patients are placed in the lateral position and flexed to open the interspaces of the vertebral column. After making a skin wheal aseptically and injecting 0.5–1.0 % lidocaine (5 mL), a 16- to 18-gauge Tuohy needle is inserted into the epidural space using the paramedian approach, with the bevel parallel to the sagittal plane and targeting the predicted segment. When the tip of the Tuohy needle is located in the epidural space, the direction of the bevel is adjusted, and the catheter electrode is inserted approximately 5 cm into the epidural space. The tip of the catheter electrode and the skin surface electrode are connected, respectively, to the negative and positive outlets of an electrical nerve stimulator [57]. Using these electrodes, recordings can be made at several spinal levels (Fig. A6.2).

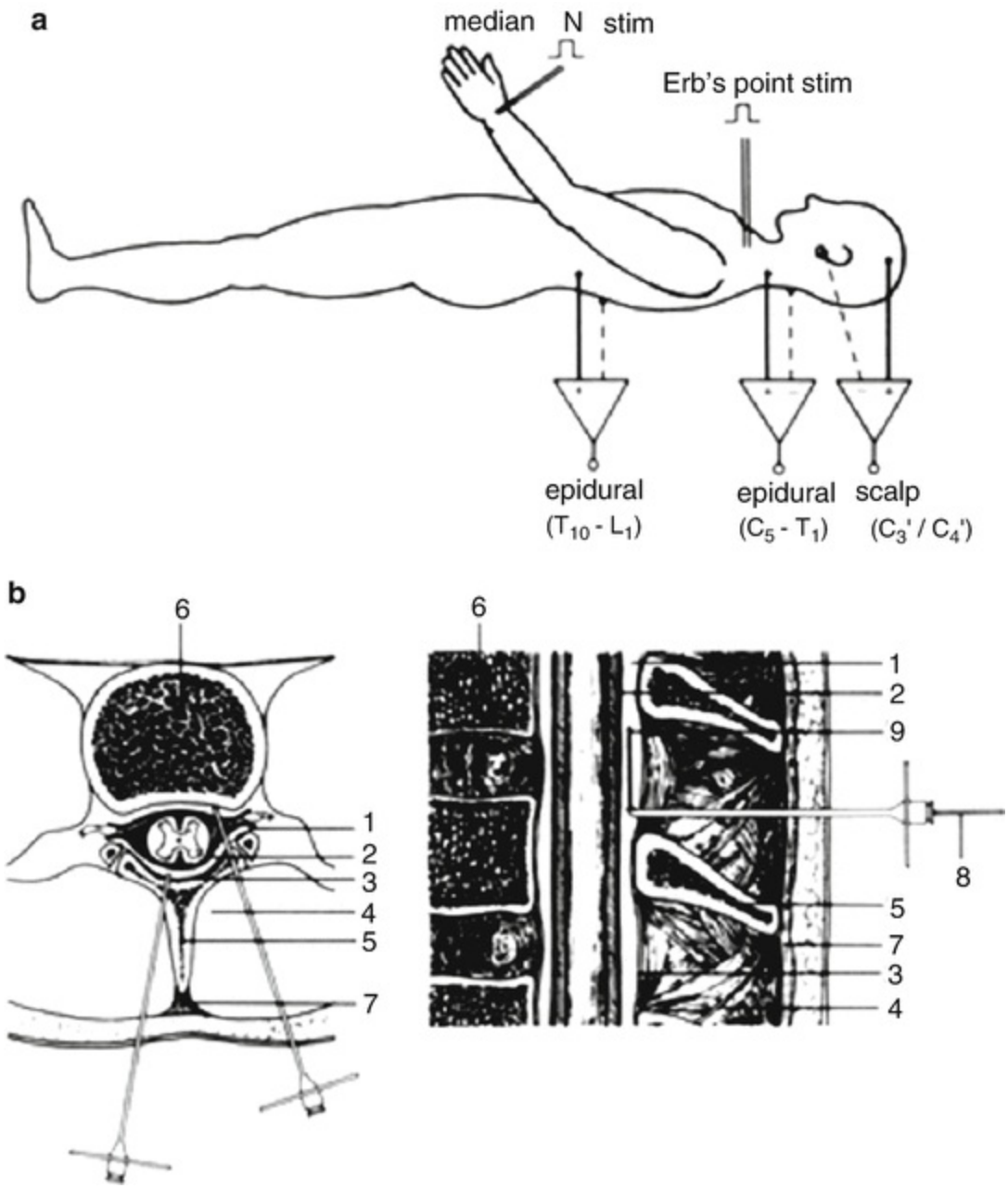

Fig. A6.2 Recording of the human SCPs. The recording electrodes are placed at various levels of the spine (**a**) into the epidural space (**b**)

Origins of Each Component of the Segmental SCPs

The initially positive spike, P1, of the segmental SCPs is believed to be a reflection of the extracellular events associated with the action potential propagation through the roots into the spinal cord [14, 58–62]. The generation of an action potential at a node of Ranvier creates a positive

capacitive current, which is conducted electronically down the axon and the nearby tissues. This current is responsible for the initial positivity of the triphasic spikes (Fig. A6.3a). The capacitative current is also responsible for depolarizing the cell membrane at the next node to threshold, thereby initiating the production of an action potential here. The rising phase of the action potential is generated by an influx of Na + into the axon from the extracellular space. The loss of Na + causes the extracellular space to become negatively charged; this event is recorded as the negative component of the triphasic spikes (Fig. A6.3b). The falling phase of an action potential is caused by a K+ efflux from the axon into the extracellular space. The additional positivity in the extracellular space is recorded from the cord dorsum as the second positive component of the triphasic spikes (Fig. A6.3b) [63].

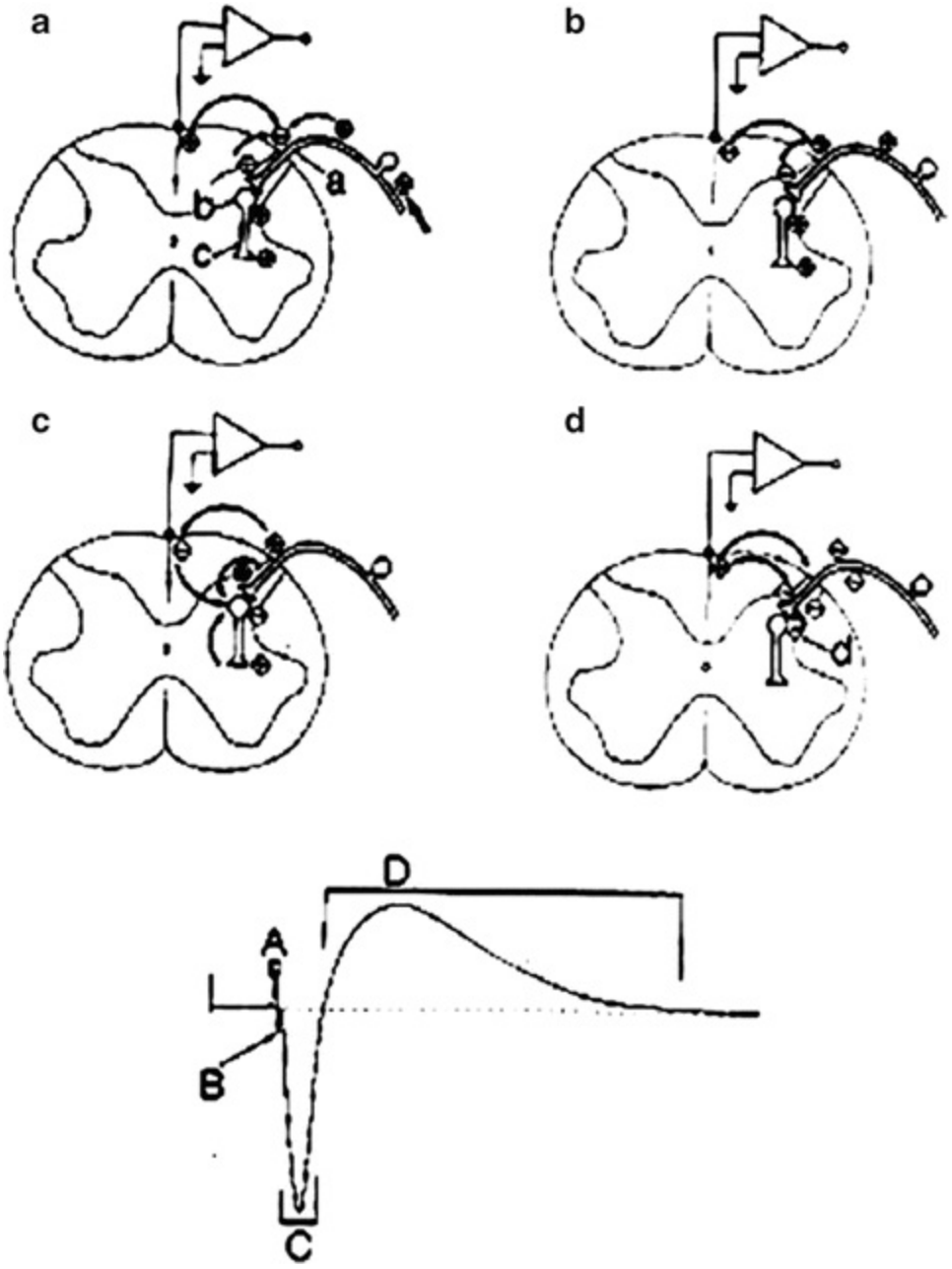

Fig. A6.3 Origins of each component of the segmental SCPs. The initial positivity of the triphasic spike is believed to be a reflection of the extracellular events associated with the propagation of action potentials through the roots down the axon into the spinal cord (**a**). The rising phase of the action potential is generated by an influx of Na + into the axon from the extracellular space resulting in the extracellular space becoming negatively charged; this event is recorded as the negative component of the triphasic spike (**b**). The falling phase of an action potential is due to a K^+ efflux from the axon into the extracellular space, which is recorded from the cord dorsum as the second positive component of the triphasic spike (**b**). The negative waves, N1 (**c**), are thought to be reflections of changes in the extracellular environment produced by activity of dorsal horn interneurons. The slow positive wave, P_2, of the segmental SCPs (**d**) has been demonstrated as the extracellular manifestation of the process of primary afferent depolarization. Positive ionic current leaves the extracellular space at excited axon-

axonal synapses (sinks) resulting in the dorsal most portion of the spinal cord becoming positively charged (**d**)

In addition, heterosegmental nerve stimulations also produce a slow positive potential (heterosegmental slow positive [HSP] wave) in cervical and lumbar enlargements in animal [58, 60, 61, 64] and man during wakeful state [61].

The negative waves, N1, of the segmental SCPs (Fig. A6.3c) are thought to be reflections of changes in the extracellular environment produced by activity of dorsal horn interneurons (see also Fig. A6.4). When the interneurons are synaptically activated, positive ionic current leaves the extracellular space at the synapses (sinks) and reappears along the ventrally projecting axons of the cells (sources). Thus, the dorsal horn takes on a negative charge and the ventral horn takes on a positive charge [62, 65, 66].

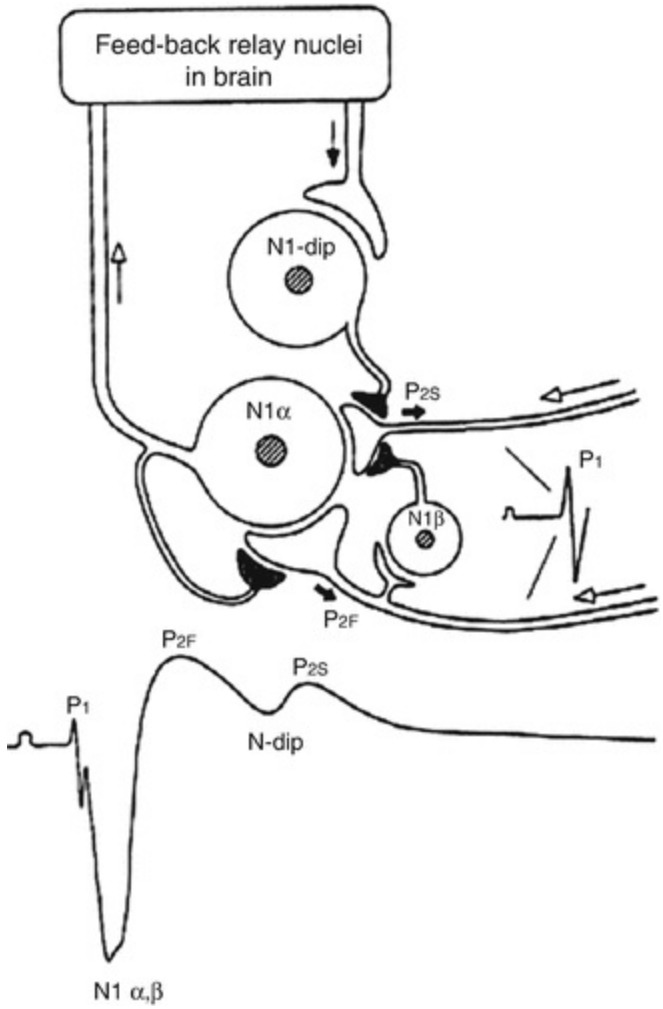

Fig. A6.4 Proposed origins of each component of the segmental SCPs. The negative waves, N1, are thought to be reflections of changes in the extracellular environment produced by activity of dorsal horn interneurons. The positive wave, P_2, of the segmental SCPs has been demonstrated as the extracellular manifestation of the process of primary afferent depolarization and/or intracellular hyperpolarization [68]

The slow positive wave, P_2, of the segmental SCPs (Fig. A6.4d) has been demonstrated as the extracellular manifestation of the process of primary afferent depolarization (PAD) just as observed in the spinal animals (Fig. A6.4) [14, 65, 66]. Positive ionic current leaves the extracellular space at excited axo-axonal synapses (sinks) and reappears along the primary afferents (sources). Thus, the dorsal most portion of the spinal cord becomes positively charged (Fig. A6.3d) [21, 23, 67–72]. Another component, inhibitory postsynaptic potential (IPSP), might be involved in the P2 wave [68, 69].

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Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_7

7. Electromyography

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Keywords EMG monitoring – Intraoperative neurophysiologic monitoring – Electromyographic – H-reflex testing – Cranial nerve monitoring technique – Brain stem mapping – Motor strip mapping

Introduction

Intraoperative neurophysiologic monitoring (IOM) using either electrically elicited triggered or mechanically elicited spontaneous electromyographic (EMG) activity has become widely used for the preservation of neurologic function during various surgical procedures. Its use has a long history dating back to the 1960s when it was first used for the preservation of facial nerve function [1, 2]. Its use at that time was prompted by the high incidence of loss of such function during surgical procedures involving tumors of the acoustic nerve. As techniques evolved for performing surgery in the cerebellopontine angle, on large skull base tumors, and for other intra- and extra-cranial procedures, monitoring techniques for assessing and preserving the function of the auditory nerve and other cranial nerves also evolved [3–23]. Much the same can be said regarding the advent of the revolutionary use of metallic, internal fixation devices for the treatment of spinal deformity. In the

lumbosacral and increasingly in the thoracolumbar and cervical regions of the spine, it has become the standard of care for the surgical management of spinal deformity, degenerative spinal disease, and traumatic insults to use pedicle screws to hold rods in place for the purpose of segmental transpedicular fixation. Although the scope of their usage is increasing, these screws are most commonly utilized in the most caudal aspects of the spine from L2 to S1, where their usage has resulted in primarily placing nerve root rather than spinal cord (which ends in the conus medullaris at about L1–L2) [24] function at risk.

It is now widely recognized that the use of monitoring can improve surgical outcomes by several means. It can help to reduce the risk of surgically induced injuries and can help to properly identify specific neural structures. As a result, the scope of its use during various neurosurgical and orthopedic surgical procedures has significantly expanded. The EMG monitoring techniques that are used for this purpose provide an inexpensive and effective means for assessing functional integrity such that, if needed, surgical intervention and correction can occur in a timely fashion so as to preserve function. These techniques that utilize EMG responses to protect neurologic function when brain, spinal cord, cranial nerve, cauda equina, and nerve root function are at risk, include cranial nerve monitoring, brainstem and cortical motor strip mapping, nerve root monitoring for surgeries in the region of the cauda equina, nerve root monitoring during pedicle screw placements, H-reflex testing, and transcranial motor-evoked responses. The latter technique is only mentioned here and will be further discussed in Chap. 2 (“Transcranial Motor-Evoked Potentials”) and elsewhere.

General Principle of EMG Monitoring

The methodology for protecting neurologic function during various neuro- and orthopedic surgical procedures using EMG techniques is relatively simple and straightforward. The brain, spinal cord, cranial nerves, and spinal nerve roots contain motor pathways that innervate various muscle groups. By placing recording electrodes in these muscles and with controlled usage of neuromuscular junction blocking agents, EMG activity can be acquired when these pathways are irritated or stimulated due to surgical manipulation or activated by means of an external electrical stimulus.

The monitoring of cranial nerve function is dependent on being able to

record EMG activity. Such activity cannot be recorded if the patient is pharmacologically relaxed. Hence, if muscle relaxants are given, they should be short acting and should be allowed to wear off or reversed before monitoring is attempted. To avoid extended paralysis as a result of the use of neuromuscular blocking agents, there should be good communication between all members of the surgical and monitoring teams regarding the use of relaxants and when the use of monitoring will be needed. In addition, a means of accurately assessing the degree of muscle relaxation should be used in order to validate the monitoring findings when relaxants are utilized.

Cranial Nerve Monitoring Technique

The technique that was initially used for monitoring cranial nerve function in the 1960s involved a handheld stimulation electrode to elicit muscle contractions. The methodology for eliciting these contractions has not changed to any great extent. However, the way in which these contractions are detected has changed. Initially, an observer detected the muscular contractions of the facial musculature [1, 2]. Later, mechanotransducers [25, 26] were used for this purpose but it was soon found that these contractions could be detected by simply recording the EMG activity from facial muscles [8, 9, 27]. As a result, during a surgical procedure, the general principle for monitoring cranial nerve function involves the use of a handheld monopolar electrical stimulating electrode to probe the surgical field and single or pairs of needle electrodes that are used to record EMG activity from muscle groups innervated by cranial nerves at risk [28] (Fig. 7.1, Table 7.1). During procedures involving tumor removal, short constant-voltage [28] or constant-current pulses are typically used intermittently for stimulation and recordings of spontaneous or free-running EMG activity are continuously monitored. Stimulus pulse durations are usually 50–100 μs, with a rate of stimulation of 3–5 pulses per second [10]. The intensity of the stimulus is an important consideration. When using monopolar stimulation , nerves that are located within its sphere of influence will be activated; the more intense the stimulus, the larger the diameter of its sphere of influence. In this way, it is possible to identify regions of a tumor where there is no motor component of a cranial nerve present so that large portions of the tumor can be quickly resected with a low risk of causing any permanent neurologic injury. A stimulus intensity that is too low can result in unintended surgical nerve injury because the

nerve may not react to the stimulus intensity and may be part of tissue that is resected. A stimulus intensity that is too high may give a false indication that the nerve is located close to the stimulator and may slow down and lead to incomplete tumor removal. At the same time, the same methodology can be used to identify the anatomic location of cranial nerves in order to avoid surgical manipulation and preserve functional integrity. Initially keeping the stimulus intensity high will protect the nerve from damage, and once a response is obtained, the intensity should be reduced in order to determine its exact location. Therefore, when using constant-current stimulation, initially the stimulus may be as high as a few milliamps, but once a response has been obtained, 0.1–0.2 mA may be sufficient to elicit a robust EMG response when cranial nerves are directly stimulated [10].

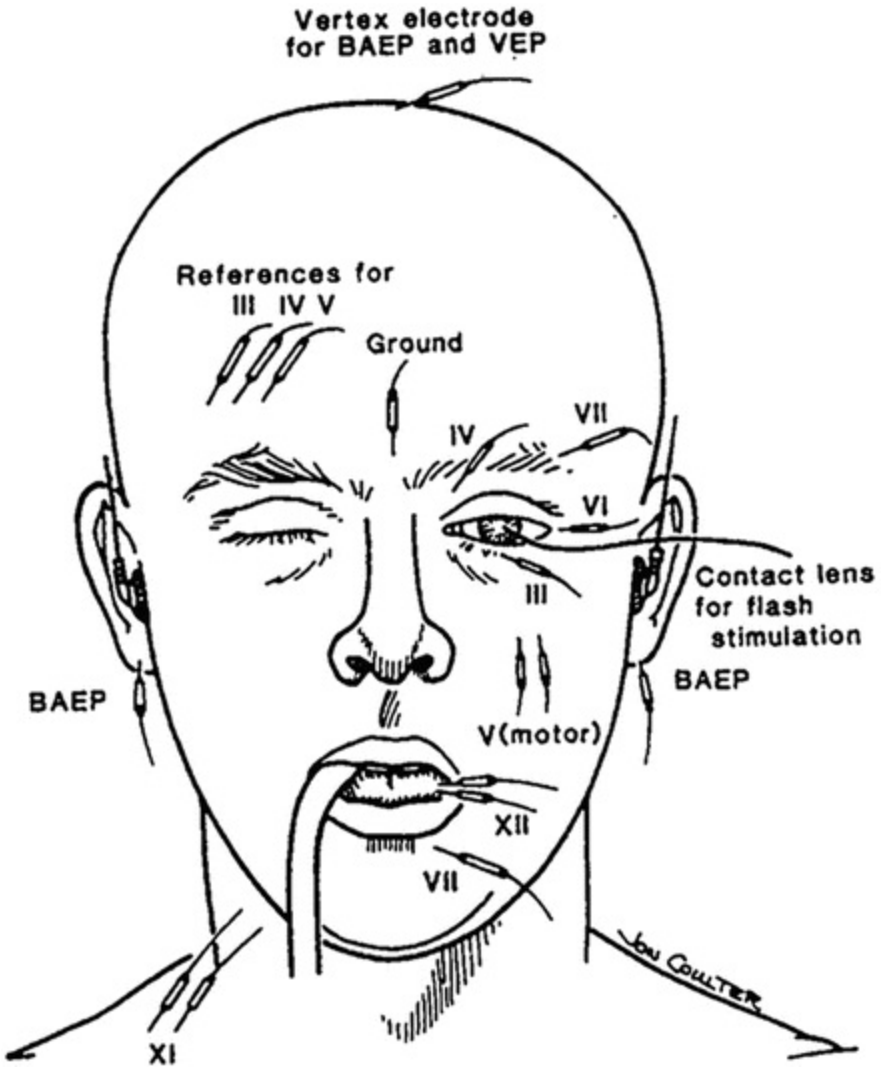

Fig. 7.1 Placement of electrodes for recording EMG responses from the extraocular muscles (CNs III, IV, VI), facial muscles (CN VII), masseter muscle (CN V), trapezius muscle (CN XI), and the tongue (CN XII). Cranial nerve IX is monitored by either placing needles or an adhesive surface electrode in or on the soft palate. Cranial nerve X can be monitored by placing needle electrodes in the vocal folds, percutaneous needle electrodes in the larynx muscles, or by using a tracheal tube with built-in surface electrodes. Also included are electrodes for recording auditory brainstem responses (ABRs) or brainstem auditory evoked potentials (BAEPs) and visual evoked potentials (VEPs). Also shown are insert earphones for presenting a click stimulus to the inner ear and eliciting the ABRs and a contact lens with light-emitting diodes for stimulating the eye and eliciting the VEPs. As a result, the function of cranial nerves VIII and II can be assessed as well. Reprinted from Moller et al. [28]

Table 7.1 Muscle groups commonly used to assess cranial nerve function based on their innervations

Cranial nerve	Muscle group
III	Medial rectus
IV	Superior oblique
V	Masseter, temporalis
VI	Lateral rectus
VII	Orbicularis oris, orbicularis oculi
IX	Soft palate
X	Vocal cords
XI	Trapezius
XII	Tongue

As below, continuous monitoring of spontaneous or free-running EMG activity provides a means for assessing if an injury may occur to a cranial nerve. Normally, the activity should remain flat or quiet, indicating that the nerve has not become activated as a result of mechanical stimulation. Manipulation of a nerve may result in periods of activation. The length of time a nerve is activated depends on the degree of nerve irritation [4, 29]. Short periods of activation generally correlate with no permanent injury. Frequent or sustained periods of activation have a greater likelihood of being associated with a postoperative neurologic deficit [30]. This type of sustained activation has been given the name “A-train” activity , the occurrence of which has been associated with postoperative paresis in patients operated on for vestibular schwannoma [11, 13, 31] and microvascular decompression for trigeminal neuralgia [12, 27, 28]. The condition of a nerve prior to manipulation also plays a role in determining how it will react to mechanical stimulation. Manipulation of normal healthy nerves will generally produce little or no activation, whereas nerves that are already slightly injured will tend to react more strongly when manipulated and may act as impulse

generators of spontaneous EMG activity even when no manipulation is taking place [4, 30]. However, severely injured nerves may not react to mechanical stimulation at all and therefore the absence of EMG activity does not guarantee that a nerve has not sustained an injury. As a result, it is important to use electrical stimulation to validate that an injury has not occurred. If the responses that result have latencies or amplitudes that are prolonged or diminished relative to baseline responses, these are indications that an injury has occurred.

Monitoring Specific Cranial Nerve Function

Cranial Nerves V and VII

Historically, monitoring cranial nerve function began with attempts to assess and preserve the motor function of the facial (VIIth cranial nerve) and trigeminal (Vth cranial nerve) nerves during operations for removal of large acoustic or other skull base tumors [1, 2]. The facial nerve provides innervation to the orbicularis oculi and orbicularis oris muscles, whereas the trigeminal nerve innervates the muscles of mastication (masseter and temporalis muscles). Therefore, if pairs of needle electrodes are placed in these muscles, they provide a means for recording EMG activity during tumor removal and other surgical procedures [12–15, 19, 20, 32]. If each pair is connected to a different recording channel, the recordings provide a means for differentiating between which muscle group is being activated and hence which cranial nerve is being irritated or stimulated. Electrical stimulation of the trigeminal nerve will result in responses with a peak latency less than 6 ms, whereas the responses elicited by facial nerve stimulation will have peak latencies greater than 8 ms [30]. This provides another means for differentiating which cranial nerve is being activated.

During operations for removal of large acoustic tumors or during operations in the cerebellopontine angle, the function of the component branches (acoustic and vestibular) of the VIIIth cranial or auditory nerve is clearly at risk. Unlike the other cranial nerves where the monitoring is dependent upon recording EMG activity, the auditory nerve consists of sensory pathways and, as a result, monitoring of auditory nerve function is dependent on assessing sensory pathway function using brainstem ABRs. This monitoring technique is thoroughly discussed in Chap. 3 (“Auditory

Evoked Potentials").

Cranial Nerves III, IV, and VI

Cranial nerves III, IV, and VI innervate the extraocular muscles. Hence, as is the case when monitoring facial and trigeminal nerve function, if needle electrodes are placed in or in close proximity to these muscles, cranial nerve function can be monitored by recording the EMG activity from the muscles that these nerves innervate [27, 28]. Cranial nerve III function can be monitored by recording from the medial rectus muscle. Similarly, cranial nerve IV function is monitored by recording from the superior oblique muscle. Recordings from the lateral rectus muscle are used to monitor cranial nerve VI function [21]. Because of space limitations, only single electrodes are placed in each of these muscles with a reference electrode placed contralateral to the side of surgery.

Cranial Nerves IX, X, XI, and XII

As was the case with monitoring cranial nerve III, IV, and VI function using the EMG activity from extraocular muscles, the function of the IX, X, XI, and XII cranial nerves is assessed by monitoring the EMG activity from muscles innervated by the motor components of these cranial nerves [15–20, 33]. Although these cranial nerves also contain sensory and autonomic components, it is assumed that the EMG activity associated with these nerves represents the condition of the entire nerve and not just the motor component. The motor component of the IXth cranial nerve is monitored by recording the EMG activity from the soft palate using needle electrodes [9, 27]. Although it is possible to monitor the motor function of the Xth cranial nerve (the vagus nerve) using needle electrodes placed in the vocal folds, it is difficult to place these electrodes [9]. As a result, recording of vagal nerve EMG activity is typically done using a tracheal tube with attached electrodes that are able to make contact with the vocal cords. Monitoring of recurrent laryngeal nerve (a branch of the vagus nerve) function during surgery is a common application of this technique [16, 17]. Monitoring the motor function of the spinal accessory or XIth cranial nerve is relatively easy. This is done by placing needle electrodes in the trapezius muscle and recording the ongoing EMG activity. Finally, monitoring of the XIIth cranial or hypoglossal nerve is done by placing needle electrodes in the tongue [9, 28], although other techniques

have been shown to be effective as well [34]. The hypoglossal nerve is very small but very important. Therefore, if there is any question regarding its location or identity, electrical stimulation can elicit EMG responses from the tongue or other appropriate muscles. When monitoring the function of all of these cranial nerves, caution must be taken with regard to the stimulation intensity that is used for eliciting EMG responses from the muscles that they innervate. If the intensity is too high, the resulting responses may be excessive and possibly injurious.

Although the amplitude of the EMG responses resulting from electrical stimulation of the various cranial nerves may vary, the responses are typically monitored by viewing their traces on an oscilloscope-type display with each trace dedicated to a particular cranial nerve. In addition, the surgeon may want to receive auditory feedback of the stimulus and any elicited EMG activity each time they stimulate. Therefore, most monitoring equipment comes equipped with a speaker system for this purpose.

However, the use of electrical stimulation to test cranial nerve function is necessarily only intermittent and, in addition, sometimes a nerve will be inaccessible to test because of the size of a tumor. Hence, even when a nerve is available for testing, this method cannot provide the desired ongoing functional assessment. In such cases, the use of multipulse transcranial electrical stimulation provides a means for continuous monitoring of cortibulbar pathway function. The technique involves the use of the same standard scalp stimulation sites and parameters that are routinely utilized to elicit transcranial motor-evoked potentials (tcMEPs) (see Chap. 2, “Transcranial Motor-Evoked Potentials”). However, rather than recording these MEP responses from muscles in the extremities, the recordings are acquired from the same muscles in the face and head that are routinely used to monitor triggered and spontaneous EMG activity when assessing cranial nerve function in the traditional manner as discussed earlier. These responses are known as corticobulbar tract motor-evoked potentials (CBT-MEPs) . The successful use of this corticobulbar technique during cerebellopontine angle (CPA) tumor removal when facial nerve function is at risk or for other skull base surgeries when the function of other cranial nerves is at risk, including the vagal nerve pathways, has been reported [35–38].

Brainstem Mapping

Brainstem mapping is a neurophysiologic technique for locating the cranial nerve motor nuclei (CMN) on the floor of the fourth ventricle. This technique has proven to be valuable for preventing damage to the CMN during surgery for the removal of tumors and other pathologies located in and around the brainstem [20, 39–43]. Occasionally, the surgeon is confronted with having to make a decision regarding the safest approach to reach structures below the brainstem surface. When this approach involves the floor of the fourth ventricle, stimulation of the floor at various locations using a handheld stimulation probe can result in EMG responses from various muscle groups that are innervated by cranial motor nerves of the head. These muscle responses can provide information regarding the location of various CMN and also safe entry points to the brainstem. The motor nuclei are generally located near specific anatomic landmarks such as the facial colliculus and striae medullares. However, even in normal patients, visualization of these landmarks is not always apparent; when these landmarks become distorted due to the presence of a tumor, the locations of these nuclei become even more problematic. This is when this technique is of particular value. However, because it is only used intermittently during tumor resection to localize and confirm the location of CMN, it is only a mapping and not a monitoring technique. Unlike monitoring techniques, it is not used continuously to assess function and validate the integrity of neural pathways. Therefore, any neural damage that might occur during brainstem tumor resection would not be preventable using this technique.

Mapping Technique

Stimulation of the floor of the fourth ventricle is performed using a handheld monopolar stimulation probe with a tip that allows for very focal stimulation. The anode or return electrode is generally placed at Fz, near the front of the scalp. Stimulation consists of 0.2-ms pulses presented at a frequency of 4 Hz. The stimulation intensity is kept low and generally begins at 1.5–2.0 mA. Once muscle responses are obtained, the intensity is gradually reduced in order to establish stimulation thresholds. This is generally between 0.3 and 2.0 mA [43].

As is the case with cranial nerve monitoring, recording electrodes are inserted into the appropriate muscle groups. These are placed in the extraocular muscles for mapping the cranial nerve III, IV, and VI motor nuclei. For the CMN VII, they are placed into the orbicularis oris and oculi

muscles. For mapping the cranial nerve IX and X motor nuclei, the electrodes are inserted into the soft palate and posterior pharyngeal wall using direct laryngoscopy. Alternatively, a tracheal tube with attached electrodes can be used. For the CMN XI, electrodes are placed in the trapezius muscle, and for the CMN XII, electrodes are inserted into the lateral aspect of the tongue. The EMG responses that result from stimulation of these nuclei are typically several hundred microvolts in amplitude and can be recorded using a time base of 20 ms and a filter bandwidth between 50 and 2000 Hz.

Anesthetic Management

Because the EMG responses used for mapping purposes result from the activation of lower motor neurons, the anesthetics used for general anesthesia have little or no effect on these responses. Because lower motor neurons are being stimulated via the motor nuclei of cranial nerves or their intramedullary roots, as long as muscle relaxants are not utilized during the mapping and monitoring period, any type of anesthetic management is compatible with brain stem mapping.

Motor Strip Mapping

Identification of the motor cortex is typically performed by placing a recording grid of electrodes directly on the cortical surface of the pre- and post-central gyri. The contralateral median or ulnar nerves are then stimulated and the resulting somatosensory-evoked potentials (SSEPs) can be recorded from each of the grid electrodes. At the transition between the sensory and motor cortex, the elicited responses reverse polarity or undergo a phase reversal. In this way, in most instances, the location of the motor cortex can easily be identified. However, with distortion of the cortical anatomy that can occur as a result of the presence of a brain tumor, these results can become unreliable. Phase reversal may not be obtained and other techniques may have to be used. One of these techniques utilizes direct electrical stimulation of the cortical surface to elicit motor responses that can be visualized or to elicit EMG responses that can be recorded from various muscle groups of the limbs, face, or trunk [44]. Location of the lesion within or adjacent to the motor cortex will dictate what muscle groups to focus on. Subdermal needle electrodes are then placed within the appropriate muscles.

The surgeon uses a handheld stimulator to excite the cortex. The electrical stimulation technique relies on the activation of the cortical circuitry by means of a train of bipolar, biphasic short-duration (1 ms) rectangular electrical pulses. These pulses are applied at a rate of 50–60 Hz. The intensity of the stimulus is normally kept low (3–5 mA) and is gradually increased in 1- to 2-mA steps until motor responses are elicited. The duration of the stimulus train is typically applied for a few seconds in order to detect any elicited motor responses in the spontaneous EMG activity that is being observed. The surgeon notes the location of these occurrences and in this way is able to determine what tissue can be removed while still preserving function. Chapter 9 (“Cortical Mapping”) provides a more comprehensive discussion of this topic.

Techniques for Assessing Nerve Root Function and Pedicle Screw Placement

The use of pedicle screws for spinal stabilization is becoming increasingly more common. However, proper placement of pedicle screws such that they do not irritate or injure nerve roots requires that the surgeon doing the screw placement be very experienced and knowledgeable about the anatomic characteristics of all aspects of the spine. Although a surgeon will rely on anatomic landmarks and fluoroscopy for accurate placement, the placement is still largely done blindly. Ideally, screw placement should result in the screws being placed within the pedicles with about 1 mm of bone between the lateral and medial walls of the pedicle and with no breaches of the pedicle walls. However, when significant deformity is present, even a skilled surgeon can misplace screws. Nerve roots tend to position themselves near the medial and inferior aspects of the pedicles as they exit the spinal canal through the spinal foramen. If screws are misplaced such that they protrude from the pedicle wall in either of these areas, they can cause nerve root irritation or injury. The current literature indicates that the incidence of screw placements that result in cortical perforations of the pedicle wall ranges between 5.4 and 40 % [45]. Such events might go undetected because most surgeons are reluctant to visualize and validate screw placements unless such actions are warranted. To do so would require multiple laminotomies, which is time-consuming; in addition, these actions by themselves could affect postoperative outcomes. As a result, fluoroscopy has largely been relied on to detect misplaced screws.

The incidence of screws associated with neurologic functional impairment has been reported to range from 1 % to more than 11 % [46–49]. Improved imaging technology, including intraoperative computed axial tomography (CAT) scans and stereotactic imaging technology may help to reduce the incidence of misplaced screws. However, in the meantime, electrophysiologic techniques have evolved for monitoring and assessing screw placements that rely on the use of both spontaneous and triggered EMG activity.

Methodology

As indicated earlier, the purpose of monitoring during surgical procedures involving pedicle screw placements is to protect and preserve nerve root function. Because all nerve roots consist of both sensory and motor fibers, the monitoring techniques that can be used to assess nerve root function can involve the acquisition of either sensory or motor responses. The sensory responses that are mediated by a single nerve root are known as dermatomal evoked responses and can be elicited by electrically stimulating a specific body surface area known as a dermatome. These responses are mediated by the dorsal column pathways and can be recorded from the scalp, much like SSEPs [50]. Conversely, the responses that are mediated by the motor components of a single nerve root result from either direct or indirect mechanical or electrical stimulation of these motor components and consist of EMG activity from a group of muscles known as a myotome. Myotomes are the motor complement to dermatomes and myotomal distributions as with dermatomal distributions can be quite variable between individuals. Whereas a myotome is a group of muscles that receives innervation from a specific spinal nerve root, most muscles receive their efferent innervation from several nerve roots. Like the afferent innervation for dermatomes, the amount and type of efferent innervation to a muscle will vary between individuals. Typically, during pedicle screw placements, EMG activity is recorded from several muscle groups using either surface or subdermal needle electrodes placed over or into these muscles. The selection of what muscle groups to monitor is dictated by which spinal nerve roots are at risk for irritation or injury. Although muscles typically receive their innervation from nerve roots associated with more than one spinal level, one spinal level generally predominates. The selection of what muscles to use for monitoring purposes is based on knowledge of this innervation. In most cases, recordings are made from muscles of the lower extremities because screw placement is generally

done in the lumbosacral area of the spine where lumbar or sacral nerve roots are at risk. However, the mechanical advantages of pedicle fixation are not restricted to the lumbosacral spine. As a result, the use of pedicle screw placement in both the thoracic [51–60] and cervical [18, 61] regions of the spine has gained popularity. This has occurred despite the known risks to the spinal cord, nerve roots, and major blood vessels in these regions. In such cases, myogenic activity can be recorded from muscles innervated by cervical and/or thoracic nerve roots. Using this approach, monitoring of thoracic screw placement was first reported in 2001 [62]. However, this type of monitoring has had mixed success for thoracic screw placements [51, 54, 55, 57–59, 62]. In particular, the ability to detect medially misplaced thoracic screws has been very variable. As with the placement of lumbosacral instrumentation, nerve root injury can occur as a result of inferior, superior, or lateral pedicle screw placement. However, a thoracic screw that is misplaced too medially can result in a spinal cord injury. To avoid such occurrences, a technique has been developed that utilizes multipulse stimulation of the spinal cord, in particular the corticospinal tract, to elicit EMG responses from lower extremity musculature when a medial breach occurs [63]. This technique has been shown to successfully detect such occurrences [64, 65].

Because a single nerve root typically innervates more than one muscle, a choice between several muscles is possible when selecting a muscle for monitoring purposes. A list of those muscles that are commonly used for recording purposes and their innervation appears in Table 7.2. As with monitoring cranial nerve function, EMG monitoring for pedicle screw placement and for surgical procedures in the region of the cauda equina consists of detecting two types of activity: spontaneous or free-running activity and triggered EMG activity. The activity of interest in both cases will consist of compound muscle action potentials (CMAPs) , which are elicited either as a result of mechanical or electrical stimulation and are recorded from appropriate muscle groups (muscles that are innervated by nerve roots at risk for injury) using pairs of needle or surface electrodes. However, it has been reported that intramuscular electrodes are preferred over surface electrodes for obtaining these recordings [66]. When monitoring both types of activity, it is assumed that the muscles are sufficiently recovered from any muscle relaxants used so that activity can be elicited when stimulation occurs. For spontaneous activity, CMAP activity can generally be detected when

train-of-four (TOF) testing produces only one twitch but having more than one twitch is desirable, because the amplitude of the CMAPS is reduced by muscle relaxants and small CMAPs may be missed if a patient is too relaxed. In most cases, nerve root irritation is an infrequent occurrence. As a result, the tracings of spontaneous EMG activity are generally flat and consist of little or no CMAP activity. When activity is present, it is generally associated with nerve root decompression (Fig. 7.2). Depending on the activated nerve root, the muscle groups being monitored, and the placement of the recording electrodes on or in these muscle groups will determine how many muscle groups are activated when stimulation occurs. This is true for triggered EMG activity as well.

Table 7.2 Muscle groups commonly used to assess pedicle screw placements based on their innervation

Spinal region	Nerve root innervation	Muscle groups
Cervical	C2, C3, C4	Trapezius, sternocleidomastoid
	C5, C6	Biceps, deltoid
	C6, C7	Triceps, flexor carpi radialis
	C8, T1	Abductor pollicis brevis, Abductor digiti minimi
Thoracic	T1, T2, T3, T4	Intercostals
	T5, T6	Upper rectus abdominis, Intercostals
	T7, T8	Middle rectus abdominis, Intercostals
	T9, T10, T11	Lower rectus abdominis, Intercostals
	T12	Inferior rectus abdominis, Intercostals
Lumbar	L1	Psoas
	L2, L3	Adductor magnus
	L3, L4	Vastus medialis
	L4, L5	Anterior tibialis
	L5, S1	Peroneus longus
Sacral	S1, S2	Medial gastrocnemius
	S2, S3, S4	External anal sphincter

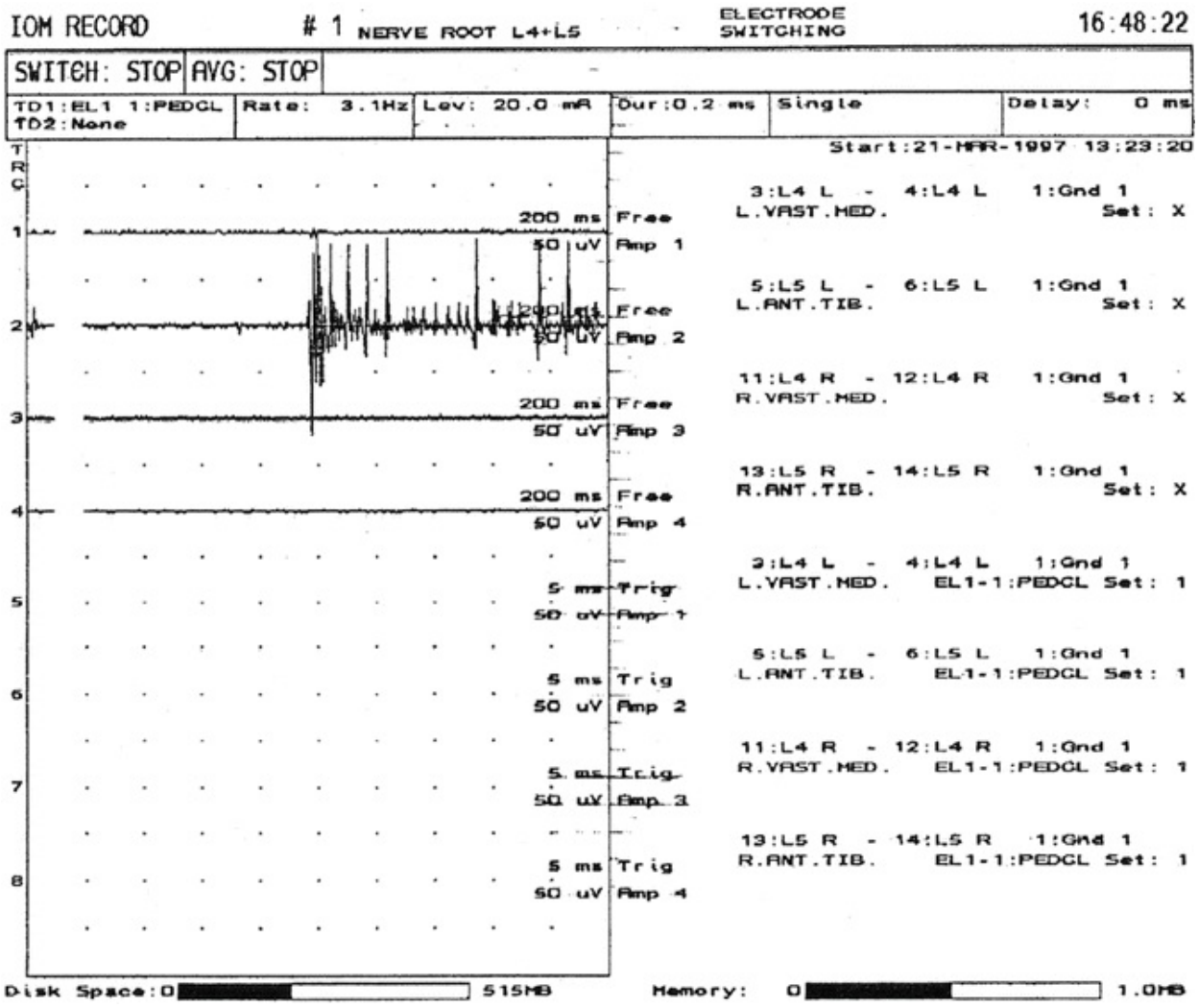

Fig. 7.2 Spontaneous EMG activity elicited from the left anterior tibialis muscle as a result of mechanical irritation of the left L5 nerve root. If the activity is of short duration (<1 s), it is generally considered not to be significant and rarely results in postoperative sequelae. However, if the activity is of a longer duration, it may be caused either by mechanical irritation of a nerve root that is already irritated, or a nerve root injury. Such activity warrants notification of the surgeon and should be avoided in order to minimize any chance of a postoperative deficit. Reprinted from Toleikis et al. [67]; with permission

Not all nerve roots react in the same manner when irritation occurs. Normal nerve roots and irritated or regenerating nerves in continuity react differently to mechanical forces. When such forces are statically or rapidly applied to normal nerve roots, they result in no elicited activity or only short-duration trains of CMAP activity [68]. However, when similar forces are applied to nerve roots that are already irritated or injured, they result in periods of firing of long duration. In cases of preexisting nerve root irritation,

recordings of the activity will often consist of low-amplitude low-frequency activity even prior to mechanical irritation. Short aperiodic bursts of activity are common. Although attention should be paid to these, they are rarely indicative of neural injury. As indicated earlier, they are often associated with nerve root decompression and result from tugging and displacement, irrigation, electrocautery, metal-to-metal contact, or application of soaked pledgets. However, long trains of activity may be indicative of neural injury and are causes for concern and alarm. They are commonly related to sustained traction and compression and the more sustained the activity, the greater the likelihood of nerve root damage. When such activity occurs, it is imperative that the surgeon be notified so that corrective measures can immediately be taken. The presence of sustained spontaneous activity during both spinal and intracranial tumor removal surgeries has been reported to correlate with postoperative motor deficits [69, 70]. The presence of continuous activity has been used as a means for determining where spinal decompression is needed [71] and even the adequacy of decompression [72]. However, the presence of continuous EMG activity in patients undergoing surgery for tethered cord syndrome has been reported to be a poor predictor of postoperative outcome, with a sensitivity of 100 % but only a specificity of 19 %, and suggests that continuous EMG monitoring and the understanding of its significance remains an evolving technique [73]. When the significance of EMG activity is questionable, the combined acquisition of MEPs and spontaneous EMG activity has been reported to provide a means for corroborating the significance of the EMG activity. The presence of sustained or the sudden loss of EMG activity is an indication for acquiring an MEP [74]. The complementary use of both of these monitoring modalities has been shown to be a means for detecting and minimizing both nerve root and spinal cord injuries [74–80].

During spinal fusion procedures involving pedicle screws, triggered as well as spontaneous EMG activity are utilized for monitoring purposes. Triggered activity is elicited in two ways: either through direct stimulation of nerve roots at risk for threshold determination purposes [45] or via indirect nerve root stimulation when pedicle screws are stimulated in order to assess their placement [47, 49, 52, 53]. Ideally, these two stimulation techniques should be used in conjunction with one another. Direct stimulation is used to determine if a nerve root has an elevated stimulation threshold; generally, the result of chronic nerve root compression as is the case when a radiculopathy

is present. The indirect stimulation technique relies on data obtained from the stimulation of healthy, normal functioning nerve roots and is used for assessing the placement of pedicle screws [47]. These data indicate that normal nerve roots have an average stimulation threshold of about 2 mA and that under these circumstances, an indirect stimulation warning threshold of about 10 mA is adequate for detecting misplaced pedicle screws [47]. However, if a direct stimulation threshold is elevated (above 2 mA), the indirect stimulation detection threshold needs to be elevated as well in order to compensate. It has been reported that the direct stimulation thresholds for some chronically compressed nerve roots are as high as 20 mA [81]. If such elevated thresholds are not taken into account, they can lead to false-negative findings, e.g., a screw that is reported to be adequately placed when in fact it is not. The physiologic factors that can contribute to false-negative findings largely pertain to the health status of the nerve roots that are involved because the criteria for assessing pedicle screw placements are based on results involving healthy nerve roots. In addition, stimulation thresholds may be elevated when assessing patients with metabolic disorders such as diabetes. The obvious way to avoid such findings is to directly stimulate each nerve root at risk in order to ensure that it is functioning normally before pedicle screw stimulation. If decompression is already being performed, this may seem like a reasonable thing to do. However, if this is not the case, routine laminotomies to explore each nerve root are time-consuming and not without some degree of risk. Therefore, most surgeons choose not to directly stimulate each nerve root at risk prior to pedicle screw stimulation testing. In cases when patients do exhibit signs of nerve root malfunction, it is strongly recommended that direct nerve root stimulation be utilized in order to establish stimulation thresholds.

Although most surgeons prefer to use indirect stimulation for testing the placements of pedicle screws, the technique can also be used to test for breaches in the pedicle wall by stimulating the markers that are placed in the spinal pedicles. Fluoroscopy is generally used by surgeons to identify the potential trajectory of pedicle screws, the taps, and/or the pedicle screw holes prior to screw placements. Stimulation is typically performed using a ball-tipped probe with a needle electrode used as an anode to complete the return current path (Fig. 7.3). The same assessment criteria are used to determine if the pedicle wall has been breached regardless of whether a marker, tap, screw, or hole is stimulated. Although the technique is generally the same

regardless of who is providing monitoring services, there is some variability in the stimulation parameters used [47–49, 51–53, 67, 81–86]. Stimulation rates have ranged from 1 to 5 Hz with pulse durations of 50–300 μs. Typically, the stimulation intensity is gradually increased starting at or near zero until either CMAPs are elicited from one or more monitored muscle groups or a preset intensity limit is reached. The lack of elicited CMAP responses at intensities of 20–30 mA is probably a sufficient indication that a breach has not occurred even if nerve roots have elevated stimulation thresholds due to factors such as chronic nerve root compression. If EMG responses are elicited at stimulation intensities lower than a predetermined "warning threshold," the course of action is to advise the surgeon to examine the pedicle hole or the pedicle screw placement. Just as the stimulation parameters may vary among groups, so too do the "warning thresholds." Some have used stimulus intensities of 10 mA or greater, whereas others have used intensities of 8 mA or less as "warning thresholds" [84, 87–90]. As indicated earlier, normal nerve roots have a stimulation threshold of about 2 mA [47]. This threshold depends on both the amplitude of the pulsatile stimulus as well as the stimulus pulse width. Therefore, different "warning thresholds " may result from different stimulus parameters. As indicated in Fig. 7.3, stimulation current can take many pathways but ultimately it will follow those that provide the least resistance. When a pedicle is intact, the pathway through bone is generally one of high resistance depending on bone density. However, when there is a breach of a medial or inferior pedicle wall, the fluid and tissue outside of the wall is likely to provide a path of least resistance. Now the distance from a stimulation probe or a screw becomes a factor. The intensity of the current that is present to excite a proximal nerve root will obey Coulomb's Law ($E = K[Q/r^2]$), where E = stimulating current present at a nerve root, K = a constant, Q = applied stimulating current, and r = pedicle screw to nerve root distance, and will depend on the inverse square of the distance between the nerve root and the pedicle screw [91]. When testing a screw placement, the current intensity that is needed to elicit a CMAP response simply provides an indication of whether a breach is likely to have occurred and if it has, whether the position of the screw could potentially cause nerve root injury. A "warning threshold" of 10 mA is often used to assess whether such a breach has occurred; it is then verified either visually, or via palpation or fluoroscopy [47, 67]. In one study [67], it was found that on visual inspection by the operating surgeon, screws that require

more than 7 mA of stimulation to elicit a CMAP response were associated with no breach, a cracked pedicle, or a slight medial exposure of one or two threads of the pedicle screw. In the surgeons' judgment, in most cases, such findings posed no threat to nerve root functional integrity or of neural injury and the screws were generally left in place. It was only those screws with stimulation thresholds of 5 mA or less that were typically removed or redirected. Those screws with stimulation thresholds in the 5–7 mA range were equally likely to be left in place or removed. It is noteworthy that none of the screws that were left in place (except one) resulted in new postoperative deficits, including two screws with thresholds of 4 and 5 mA—an indication that low stimulation thresholds, unless they are far below a "warning threshold," are unlikely to be associated with new postoperative neurologic findings. Therefore, a "warning threshold " is only that and is meant to indicate when a screw has breached a pedicle wall such that its placement should not be ignored. The lower this "warning threshold" is set, the greater the likelihood that a screw with a lower stimulation threshold is misplaced and consideration should be given to having it removed. The results of other studies have suggested that a "warning threshold" should be set to at least 8 mA. However, it is more likely that only screws with stimulus threshold intensities less than 5 mA pose a real danger for nerve root injury [67, 88, 90, 92, 93]. Even in cases when radiographs are suggestive of adequate screw placement, low stimulation thresholds with resulting visual inspection or a postoperative CT have revealed that screw placements needed to be revised (Fig. 7.4).

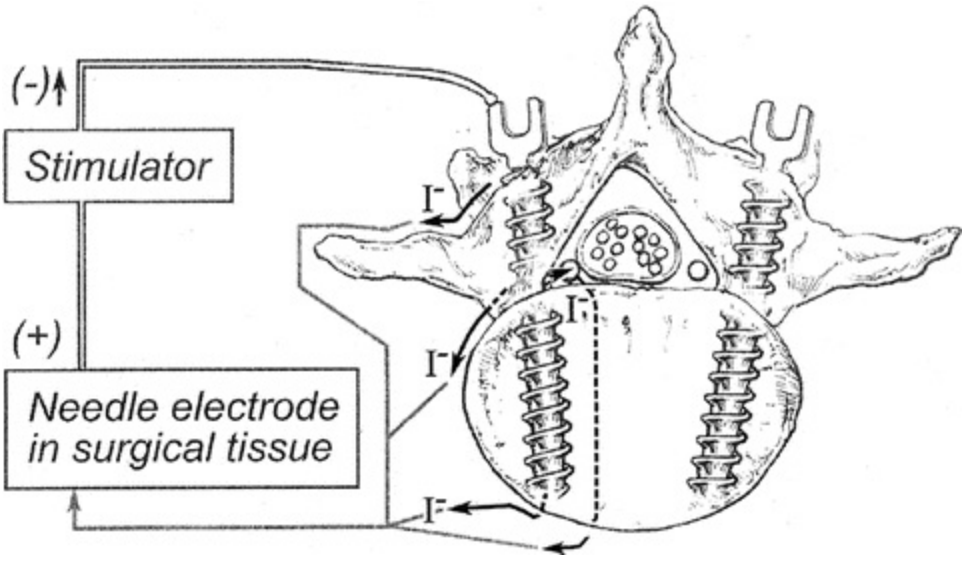

Fig. 7.3 The stimulation technique used to assess pedicle screw placements that can also be used to test markers, the tap, and pedicle screw holes. The stimulation current can take many pathways as it returns to the anodal electrode that is placed in muscle tissue. The current will follow those pathways that provide the least resistance. In this case, the pedicle screw has broken through the wall of the pedicle and is situated very close to an emerging nerve root. The electrical current, following the path of least resistance through the pedicle screw and the breach in the pedicle wall, is expected to excite the nerve root resulting in triggered EMG responses at a low stimulus intensity from those muscles that receive innervation from that nerve root. However, if the screw is in contact with fluid or tissue, current shunting can occur and only a fraction of the applied stimulus current will pass through the screw, resulting in elevated stimulation thresholds and possible false-negative findings. Reprinted from Toleikis [94]; with permission

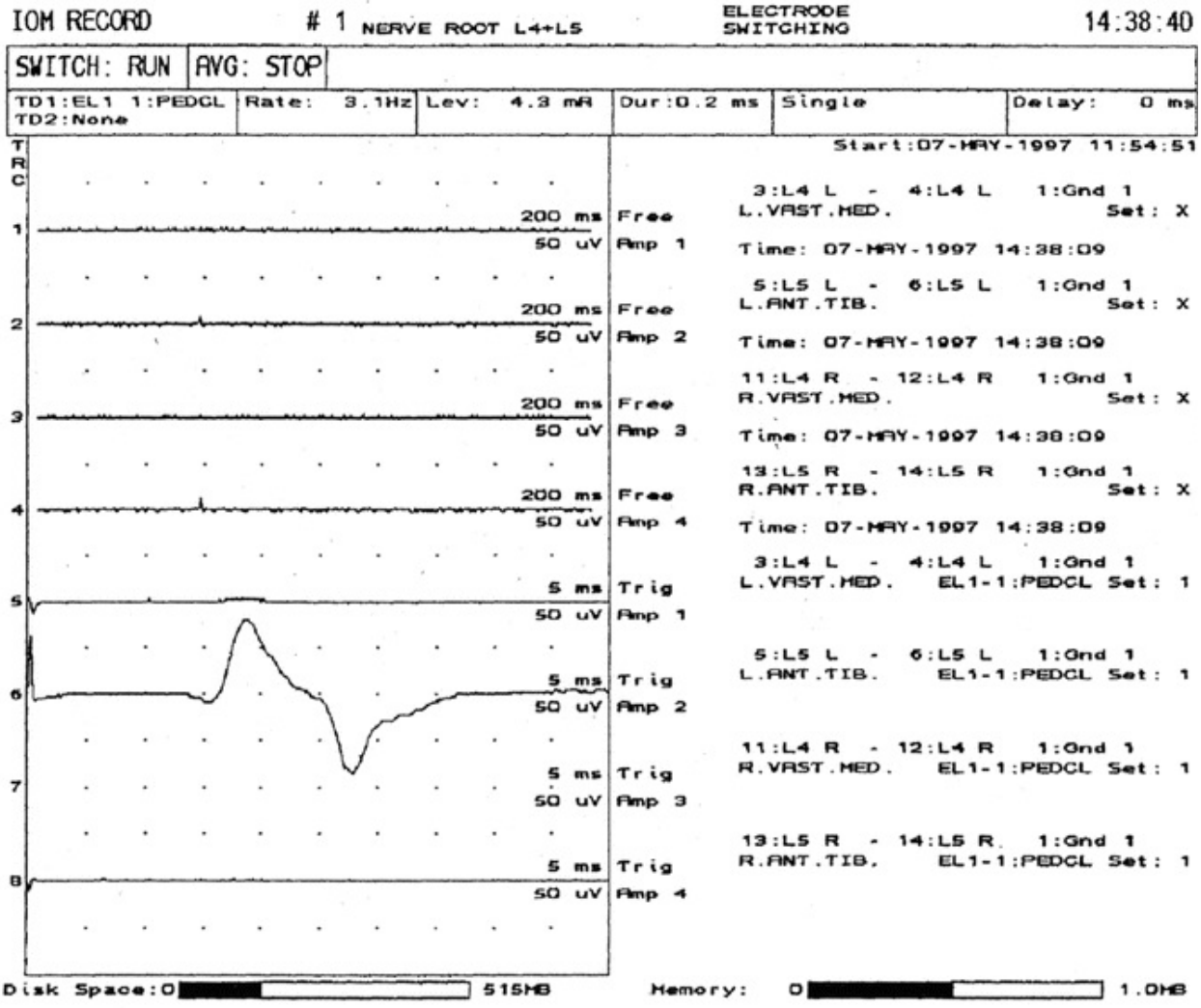

Fig. 7.4 Triggered EMG response elicited from the left anterior tibialis muscle as a result of stimulation of the left L5 screw at a stimulus intensity of 4.3 mA. The stimulus intensity was below the 10-mA warning threshold that is suggestive of a possible breach of the pedicle wall. On visual inspection of the screw placement, it was found to be located in the spinal canal and thus removed. No postoperative deficits resulted. Reprinted from Toleikis [94]; with permission

Another factor that can contribute to stimulation thresholds being artificially elevated is current shunting, which results from fluid or tissue being in contact with the screws, thus allowing current to take an alternate additional pathway when screws are stimulated [94]. In such cases, only a fraction of the current that is being applied actually passes down the screw and is available to excite a nerve root if the screw placement has resulted in a breach of the pedicle wall (see Fig. 7.3). This is another way in which false-negative findings can occur. In addition, some screws are made from a material such as titanium alloy, which is not a good current conductor, or are coated with a material such as hydroxyapatite, which is also not a good conductor and, as a result, stimulation testing can result in false-negative findings [95, 96]. Some screws are constructed in such a fashion that they do not allow current flow. It has been reported that if the top of polyaxial pedicle screws are stimulated rather than the stem of the screw, this can result in elevated stimulation thresholds [97]. In both instances, stimulation will result in current taking an alternate pathway to the anode rather than through the screw and can result in false-negative findings.

More recently, surgical procedures involving a lateral transpsoas approach to achieve interbody fusion in the lumbar spine using either the extreme lateral interbody fusion (XLIF) (Nuvasive) or direct lateral interbody fusion (DLIF) (Medtronic Sofamor-Danek) minimally invasive techniques have become an increasingly popular method to treat spinal disease. However, both techniques require dissection and dilation through the iliopsoas muscle, which places the lumbosacral plexus at risk for injury. While this is occurring, the visibility of the neural structures at risk is minimal. As a result, emphasis has been placed on the importance of performing these procedures with the aid of intraoperative monitoring so as to identify the proximity of nerves to the muscle dissection plane. To do so, spontaneous and triggered EMG monitoring are used often in conjunction with other monitoring modalities such as MEPs and SSEPs . EMG activity is recorded from muscle groups that receive their innervations from neural structures at risk. As dilation and dissection occur, the instrumentation for doing so is electrified such that proximity to neural structures is identified via triggered EMG responses that result from the application of Coulomb’s law. The closeness of instrumentation to neural structures is determined by the intensity of the stimulation current that is required to elicit triggered EMG responses. As instrumentation approaches these structures, decreasing

amounts of current are required to elicit CMAP responses. The use of this technique provides a means for avoiding neural structures as the instrumentation passes through the iliopsoas muscle on its way to the spine. However, use of the technique has had mixed results [98–100], with reports of new postoperative motor neuropraxia despite its use [98, 100]. These results appear to be associated with prolonged retraction time and suggest that this is a predictor of declining nerve integrity [100].

Anesthetic Management

The degree of muscle relaxation is the only anesthetic factor of concern when myogenic activity is used for monitoring purposes, and it cannot be overstated how important it is to have the patient adequately un-relaxed when pedicle screw testing is being performed. When monitoring nerve root function using spontaneous and/or triggered myogenic activity from appropriate muscle groups, it is imperative that these muscle groups be reactive to changes in nerve root function that result from a mechanical insult such as traction or compression of the nerve roots. The myogenic responses that result from such an insult are significantly affected by the degree of muscle relaxation. In addition, when electrical stimulation is used to either directly or indirectly stimulate nerve roots, the degree of muscle relaxation can significantly influence the stimulation thresholds at which responses are elicited. Therefore, it would be ideal if no muscle relaxants were used when monitoring myogenic activity and, in fact, some neurophysiologists insist on patients being totally un-relaxed when monitoring. However, in many clinical settings, this degree of relaxation may be difficult if not impossible to achieve because some surgeons may feel that it compromises their ability to adequately perform surgery. What generally occurs in these situations is that muscle relaxation is used during the exposure period when there is frequent use of the Bovie knife, which makes continuous monitoring difficult. In addition, there is a low risk of neurologic injury during this time. The muscle relaxation is then allowed to wear off so that the patient is sufficiently un-relaxed, permitting monitoring during the periods of surgery that are associated with a higher risk of injury.

An accurate assessment of the degree of muscle relaxation is essential. An effective means for making the assessment is to use the TOF technique. For the hands, the ulnar nerve can be stimulated at the wrist and CMAPs can be elicited and recorded from the adductor digiti minimi or thenar muscles.

For the legs, the peroneal nerve can be stimulated at the fibular head and CMAPs can be recorded from the anterior tibialis muscle. Although the anesthesiologist often has access to the hands and can make an assessment of the degree of relaxation, TOF testing for monitoring purposes should be done by the person providing the monitoring rather than the anesthesiologist for several reasons. First, the anesthesiologist typically uses a small portable battery-driven device to perform a TOF assessment. Depending on how these devices are used, findings can sometimes be erroneous. Second, the anesthesiologist's assessment of TOF testing is a subjective one. It is based on visible twitches from muscle groups that the anesthesiologist has access to, e.g., either the hand or facial muscles. However, it is unlikely that these muscles will be relaxed to the same degree as leg muscles, which are the muscles of interest when pedicle screw stimulation is performed. In addition, the device that the anesthesiologist uses has an output stimulation intensity of 80 mA—greater than that typically used by monitoring personnel with their devices. As a result, the perception that a patient is sufficiently un-relaxed for testing purposes based on the responses from face or hand muscles may be false and may lead to false-negative findings. Finally, it is appropriate that the person providing the monitoring be responsible for guaranteeing that the test results are accurate by doing their own TOF testing of leg musculature. Their machine may provide more accurate results than that of the anesthesiologist. However, their findings can also be erroneous due to technical and other factors. Therefore, it is useful for the person providing the monitoring and the anesthesiologist to periodically compare relaxant findings.

The issue of how relaxed a patient must be in order to accurately assess both spontaneous and triggered myogenic activity remains controversial [101]. Chapter 19 ("Anesthesia Management and Intraoperative Electrophysiological Monitoring") provides a much fuller discussion of muscle relaxants. Clearly, 100 % blockade is not suitable for making these assessments. On the other hand, although it may be ideal from a monitoring perspective to insist on no blockade for making these assessments, it may not be necessary or even feasible. A surgeon may feel that at least partial muscle relaxation is essential for adequate exposure and accurate screw placement. From personal experience, as indicated earlier, spontaneous EMG activity can be elicited and observed when one twitch out of a TOF or 90 % neuromuscular blockade is present but, for accuracy purposes, it is preferable that patients be less relaxed. However, relaxant levels become a lot more

stringent when triggered EMG is used for assessment purposes. If a patient is too relaxed when testing is performed, the stimulation thresholds are likely to be artificially elevated, which can lead to false-negative findings. It has been reported that the minimal criterion for making such assessments is the presence of a fourth twitch when TOF testing is performed [67, 102]. Using an amplitude ratio of the fourth to the first twitch to determine adequacy of relaxation criteria for accurately assessing pedicle screw placements, our findings suggest that this ratio must be 0.1 or higher [94] (Fig. 7.5). Direct electrical stimulation of nerve roots is another means for determining whether the degree of muscle relaxation is sufficient for accurate assessments. If a healthy nerve root is stimulated using a constant current stimulation intensity between 2 and 4 mA and no myogenic responses are elicited, it is likely that the degree of muscle relaxant is contributing to elevated stimulation thresholds and potentially incorrect monitoring findings.

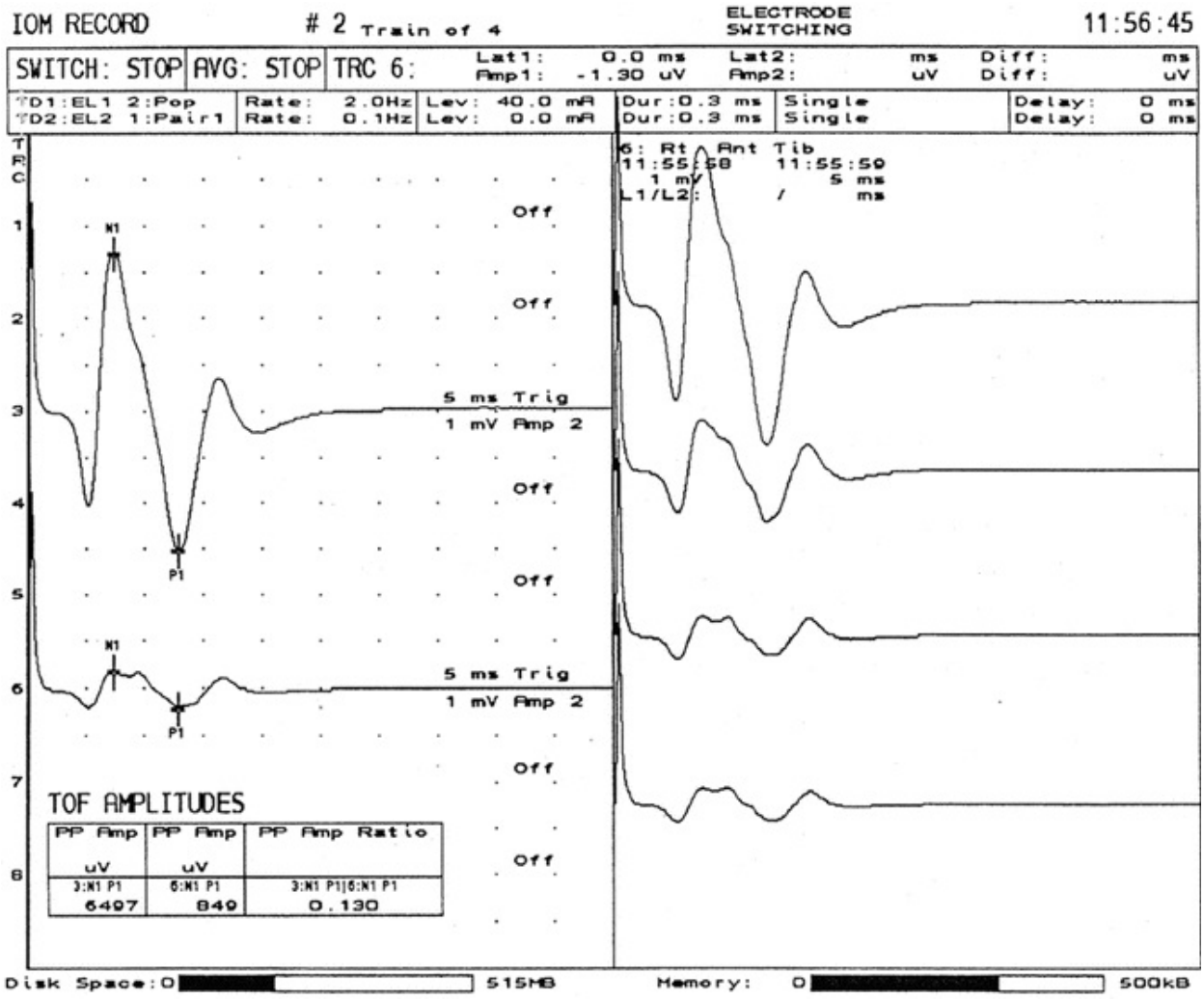

Fig. 7.5 Train-of-four testing . The right side of the figure indicates four EMG responses from the right anterior tibialis muscle that resulted from four 2 Hz 0.3-ms pulse stimuli being presented to the right peroneal nerve at the head of the fibula at an intensity of 40 mA. Excessive relaxation levels can result in elevated stimulation thresholds and false-negative findings during screw testing. For accurate results, the patient should have at least four twitches present, with a twitch four to twitch one amplitude ratio of at least 0.1–0.2. Reprinted from Toleikis et al. [67]; with permission

H-Reflex Testing

Two techniques have been traditionally used to monitor spinal cord function: SSEPs and TcMEPs. These techniques are a means for assessing long tract sensory and motor function. Although preservation of this function is necessary in order to interact with our environment in a normal fashion, the monitoring techniques that are used to preserve this function are not sufficient to ensure that complex coordinated motor function remains intact [103]. Simply preserving the ability to walk does not guarantee that the ability to dance or to perform other complex motor functions has been preserved. Such functions rely on and are controlled by groups of electrically coupled spinal cord central pattern generators (CPGs) . The components that contribute to these generators consist of descending and propriospinal pathways in addition to peripheral input and segmental interneurons . It is the interneurons that integrate and summate the excitatory and inhibitory effects of the other components and determine their level of excitation. This level of excitation is reflected in the activity that can be elicited and recorded from muscle groups that they innervate. If there is a disruption in the input to the interneurons, it will be reflected in the activity of the muscles that rely on the descending influences of these interneurons.

H-reflex muscle responses are monosynaptic and result from processing at a single segment of the spinal cord. They are of short latency, short duration, simple configuration, and high amplitude. If an acute transection of the spinal cord were to occur, the result would be spinal shock, which is characterized by complete paralysis, hyporeflexia, loss of sensation, and muscle hypotonia distal to the lesion. The hyporeflexia may be due to an increase in the efficacy of presynaptic inhibition because this type of spinal cord insult disrupts the suprasegmental influences that mediate presynaptic inhibition. This hyperpolarization of motor neurons is thought to be caused by decreased suprasegmental facilitation of motor neurons, which normally keeps them slightly hypopolarized. Over time, the presynaptic inhibition subsides, resulting in enhanced spinal reflexes.

H-reflex responses reflect the level of excitation of a large percentage of the motor neuron pool in the spinal gray matter [104, 105]. As a result, these responses may be more helpful than SSEPs in detecting intraoperative spinal cord ischemic insults because gray matter excitability is depressed more than white matter excitability when such an insult occurs. In animals, the dorsal horn potentials that result from postsynaptic gray matter activity disappear within 3–5 min when cessation of spinal cord perfusion occurs, whereas SSEPs mediated by the posterior column white matter tracts remain for 12–15 min [106]. A thorough discussion of this monitoring modality appears in Chap. 8, “The Use of Reflex Responses for IOM.”

H-Reflex Response Acquisition

The H-reflex response is a CMAP recorded from muscle, which results from what is believed to be electrical activation of a monosynaptic reflex . The first part of the reflex pathway is the afferent or sensory portion and involves activation of large 1a nerve fibers which originate in muscle. This activation typically results from stimulation of the posterior tibial nerve at the popliteal fossa. Because the nerve is made up of both sensory and motor components, stimulation results in both orthodromic and antidromic sensory and motor activity, respectively. With supramaximal stimulation, the antidromic motor activity ascends to the spinal cord and invades motor neurons in the ventral gray matter, which are activated. This results in orthodromic motor conduction down the same motor fibers to muscle, which produces an F response. The orthodromic sensory activity is mediated by the 1a nerve fibers and ascends to the spinal cord where it enters the dorsal horn via the dorsal roots and then synapses with motor neurons. Activation of these motor neurons then results in efferent orthodromic conduction through motor fibers that are located in the same homologous spinal segment as the 1a afferent fibers, which then activates muscles in the legs. H-reflex responses can be recorded from several muscles in the adult. However, the reflex is most often acquired from the gastrocnemius muscle following stimulation of the tibial nerve at the popliteal fossa. In order to excite the fast-conducting, low-threshold 1a fibers, long duration 1000-μs low-intensity pulses are presented at a low stimulation rate (0.1–0.5 Hz) to the peripheral nerve which, as indicated earlier, consists of both sensory and motor fibers. The intensity of the stimulation is gradually increased from 0 mA and because 1a sensory fibers are activated before motor fibers, the H-reflex appears before what is

known as the M-wave. When the M-wave does occur, it is the result of orthodromic conduction from the stimulation site to the muscle. Hence, it will have a very short latency compared to the H-reflex response (Fig. 7.6). The H-reflex response usually reaches its peak amplitude at or just before the M-wave appears. Further increases in stimulation intensity result in larger amplitude M responses and smaller amplitude H responses until no further increases in the amplitude of the M responses occur and the H responses have largely disappeared only to be replaced by the F response. Once an H-reflex response has been acquired and the stimulus intensity is kept constant for each subsequent stimulus, the responses will be short latency, short duration responses with a simple configuration and constant amplitudes. In order to determine if the CMAP response is an H-reflex response, the amplitude of the response should exceed the amplitude of the M-wave, and the waveform configuration and latency should remain constant each time a stimulation pulse is presented. Intraoperative normal parameters have not been established for the latency of these responses, which are age and height dependent. However, in a clinical setting, the mean latency has been found to be 28.9 ± 2.7 ms in awake human [103]. In the operating room, these onset latencies are likely to be greater due to decreased limb temperatures.

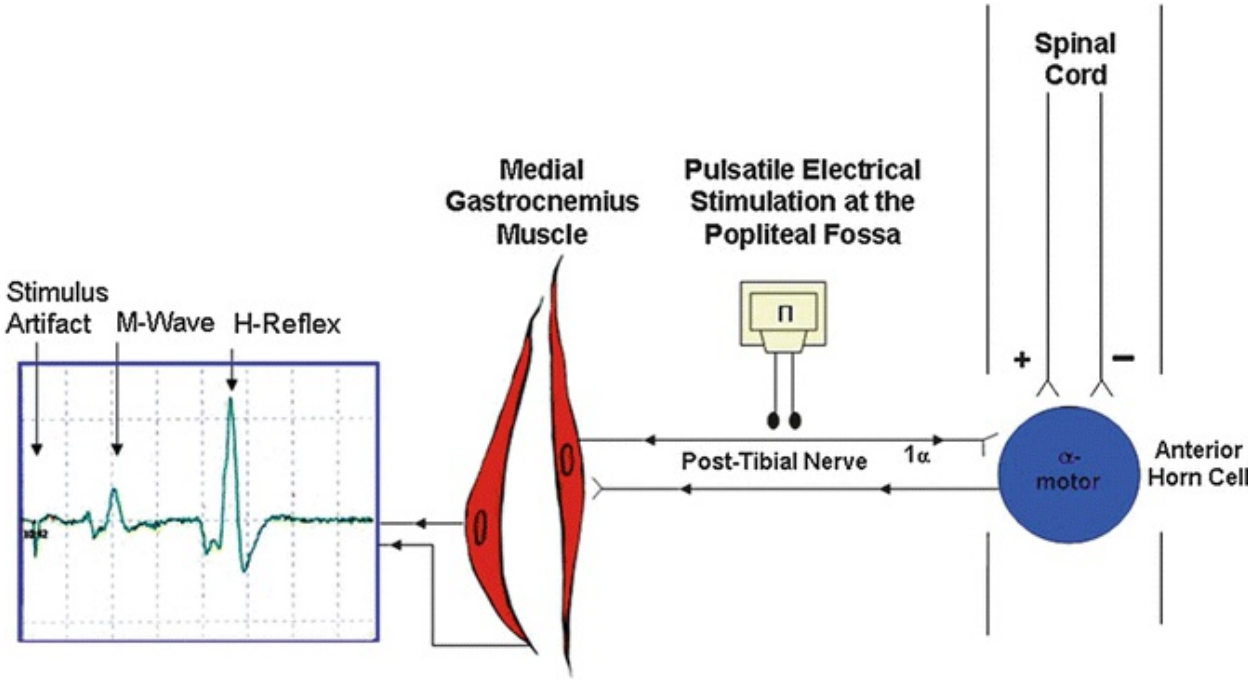

Fig. 7.6 Monitoring with H-reflex responses . H-reflex responses were elicited continuously using 0.1-Hz single-pulse stimulation (1000 μs duration, 2–35 mA) of the posterior tibial nerves at the popliteal

fossae and recorded bilaterally from the medial gastrocnemius muscles. Use of SSEPs and MEPs represents the gold standard for monitoring neural function during spinal surgery. However, the ability to reliably acquire H-reflex responses when SSEPs and MEPs could not be obtained makes them a potentially useful complement to or substitute for these latter modalities

Anesthetic Management

The amplitudes of both the H-reflex and M-wave responses may be reduced because of the use of neuromuscular junction blocking agents. Like any of the other monitoring modalities that rely on the presence of either mechanically elicited spontaneous or electrically elicited triggered myogenic activity to make assessments of neurologic function, controlled usage of these agents is essential in order to avoid false-negative monitoring findings. The H-reflex can be monitored using maintenance anesthetic management consisting of less than a 0.5 MAC of any inhalational agent and a continuous infusion of any narcotic. This anesthetic management will also usually allow for other monitoring modalities such as SSEPs, MEPs, and spontaneous and triggered EMG to be used in conjunction with H-reflex monitoring.

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Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_8

8. The Use of Reflex Responses for IOM

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Keywords Anatomy and neurophysiology – Pathophysiology – Late responses – H-reflexes – Anesthesia – Bulbocavernosus reflex – Selective dorsal root rhizotomy – Blink reflex – Intralimb and interlimb reflexes

Introduction

There are three goals for intraoperative neurophysiologic monitoring. The first is to reduce the risk of neurologic complications by detecting insult to neuronal structures. The second is to provide guidance that may affect a surgeon's approach or actions, such as mapping the location of sensory and motor tracts within the spinal cord. The third is to perform studies detailed enough to help understand normal and pathophysiologic function. Intraoperative reflex techniques are used to help accomplish these three goals. They are used to monitor the function of peripheral nerve, plexus, nerve root, and segmental and suprasegmental function. These reflex techniques will be reviewed in this chapter.

At the spinal cord level, orthodromic ascending somatosensory-evoked potentials (SSEPs) monitor spinal cord sensory function. Motor-evoked potentials (MEPs) recorded with transcranial electrical motor stimulation (tcMEPs) monitors spinal cord motor function but only 4–5 % of the motor

units innervating a muscle are activated. Therefore, 95–96 % of the motor spinal cord systems activating the motor units are not monitored [1]. Our ability to interact with the environment involves not only intact sensation and strength but also complex coordinated motor behavior. SSEPs and MEPs monitor those systems that are responsible for sensation and strength. Reflexes can be used to monitor complex integrated motor behavior. When used in conjunction with SSEPs, tcMEPs, free-run and electrically stimulated electromyography reflexes provide a multisystems approach to monitoring. The advantage of the use of intraoperative reflexes to detect neuronal compromise is that the recordings are single sweep. They are real time with no delay after the onset of compromise that is present when using averaged SEPs. They provide the surgeon with immediate feedback and can be acquired continuously throughout surgery with little or no noticeable patient movement. Reflexes may be monitored in patients in whom SSEPs and tcMEPs cannot be recorded because of a pre-existing neurologic deficit [1–4].

Anatomy and Neurophysiology

Reflex processing can be considered relatively simple. An example is the monosynaptic or oligosynaptic H-reflex that involves simple spinal cord processing. It can also be considered complex, with polysynaptic reflexes involving processing at multiple spinal cord levels. Monosynaptic reflex muscle recordings are of short latency, short duration, simple configuration, and high amplitude. These parameters are stable and vary little from one stimulus to the next. Polysynaptic recordings are of longer latency, longer duration, complex configuration, and low amplitude. Polysynaptic recordings are not stable and vary from one stimulus to the next [5].

At the spinal cord level, one approach to understanding complex motor behavior is to consider spinal cord integrating function to be controlled by a system of tightly electrically coupled central pattern generators (CPGs) . The integrated activity of these spinal cord CPGs is responsible for controlling the stepping mechanism of gait and the coordination of upper and lower extremity function [6–10].

Spinal cord CPGs may be thought of as having four components: the segmental interneurons, the descending suprasegmental systems, the propriospinal systems, and the peripheral afferent input. The point of control

is the level of excitation of interneurons, which is determined by the integrated summated synaptic excitatory and inhibitory effect of the other components on the interneurons and motor neurons. The level of excitation of interneurons determines the level of reflex gain. Sensory afferent and antidromic motor response signals following peripheral nerve stimulation provide the time-locked synchronization of the system. Summated activity from descending spinal cord systems, especially the corticospinal, rubrospinal, vestibulospinal, and reticulospinal systems, contribute to controlling the gain set by the interneurons. Vestibulospinal and reticulospinal tracts control proximal function, and rubrospinal and corticospinal tracts control distal lower extremity function [11]. The gain is also controlled by short, intermediate, and long propriospinal systems that control processing at multiple spinal cord levels ipsilaterally and contralaterally. Interaction between the cervical and lumbosacral networks is mediated by propriospinal neurons [8]. The output from the system is through the motor neurons , which is measured by reflex recordings from muscle. Intraoperative reflex recordings provide information about the degree of coupling between CPGs. Acute or chronic damage to the peripheral afferent input, the descending suprasegmental systems, the propriospinal systems, or the segmental interneurons results in the uncoupling of these components. This changes the level of excitability of the segmental interneurons, which results in a change in the segmental reflex gain. The change in the reflex gain can be detected by changes in reflex processing recorded from muscles. Changes in reflex processing can be used as a monitoring technique to detect acute and chronic compromise of the spinal cord suprasegmentally and segmentally, and of the nerve roots and peripheral nerve (Fig. 8.1).

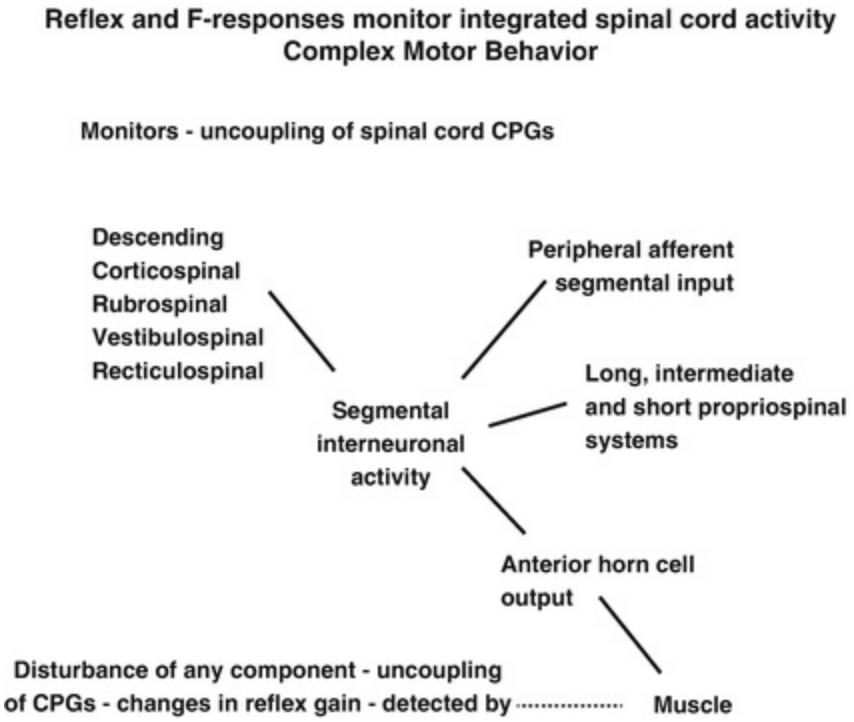

Fig. 8.1 Spinal cord central pattern generator (CPG) components. The point of control is the level of excitability of segmental interneurons, which is determined by the integrated activity of the other components. Disturbance of any component results in CPG uncoupling which is detected by reflexes and F-responses from the output through anterior horn cells

Spinal Cord Pathophysiology

Acute spinal cord transection causes spinal shock that is characterized by complete paralysis, hyporeflexia, loss of sensation, and muscle hypotonia caudal to the lesion. Spinal cord injury (SCI) disrupts or disinhibits the suprasegmental influence over segmental interneurons mediating presynaptic inhibition. The hyporeflexia associated with spinal shock may be due to an increase in the efficacy of presynaptic inhibition [12]. Over time, presynaptic activity decreases, resulting in enhanced spinal reflexes [13]. Observations in cats indicate that rostral acute SCI causes postsynaptic caudal lumbar motor neuron changes. In cats, rostral acute SCI causes hyperpolarization of caudal lumbar segment motor neurons [14–17]. Immediately following rostral spinal cord transection, the monosynaptic reflexes from the medial and lateral gastrocnemius, soleus, posterior biceps, and semitendinous muscles are reduced in amplitude or completely absent. During the 6 h following transection there is some recovery of reflex activity [18]. When using cold as

a model for acute reversible spinal cord transection, hyperpolarization of caudal motor neurons occurs within 30 s and monosynaptic reflex amplitudes are gradually decreased. These changes persist during the application of cold. Rewarming restores reflex amplitudes to original values in 30 s, and the resting motor neuron membrane potential back to the original value in 1 min [14–16].

The hyperpolarization of motor neurons following spinal cord transection or cooling is thought to be secondary to decreased suprasegmental facilitation of motor neurons, which usually keeps them in a slightly hypopolarized state [14–17]. Fusimotor drive is also depressed early after acute spinal cord injury, for gamma motor neurons are also hyperpolarized [19]. H-reflexes and F-responses reflect the level of excitation of a large percentage of the motor neuron pool in the spinal cord gray matter [20, 21]. These recordings may be very helpful in detecting intraoperative spinal cord ischemic insults, since the level of gray matter excitability is depressed more with ischemia than is posterior column function. In animals the dorsal horn potential that is generated by postsynaptic gray matter activity disappears within 3–5 min after cessation of spinal cord perfusion. Posterior column potentials persist for 12–15 min [22].

Changes in spinal cord electrophysiologic signal processing can be used to help understand the electrophysiologic mechanisms occurring during acute SCI [23]. Changes in serial, parallel, and oscillatory processing, hyperpolarization, inhibition, and disinhibition may be observed.

Spinal Nerve Root Pathophysiology

Spinal nerve roots are more susceptible to injury than are peripheral nerves [24]. Spinal nerve roots are susceptible to injury by two mechanisms. The first is that proximally the dorsal and ventral roots split into rootlets and minirootlets [25]. The area where this split occurs is the central-peripheral transitional region, which is the point where the nerve root is more susceptible to mechanical injury. The axons at this point are enclosed by a thin root sheath, cerebrospinal fluid and meninges, and lack the protective covering of epineurium and perineurium that is present in peripheral nerve [26]. The second mechanism of injury is that there is an area of hypovascularity at the junction of the proximal and middle one-third of the dorsal and ventral roots. This is the point of anastomosis between the central

vasa corona and peripheral segmental vessels. At this point, the nerve roots are more susceptible to mechanical injury [25].

The relationship between compression and traction forces on nerve conduction is well described in peripheral nerves and nerve roots [24, 27, 28]. The conduction abnormalities are coupled to the perfusion of the nerve root [24, 28]. A 3-mm retraction distance (pressure around 70 g/cm^2) caused the intraneural blood flow to decrease to 20 % of initial value [28]. If nerve root dysfunction is recognized in the reversible phase, permanent injury can be avoided. Compression and traction may produce a mechanical effect on the nerve tissue in addition to compromising the blood supply to the nerve. Physiologic block is the first sign of nerve dysfunction and can be reversed in seconds.

When more axons in the nerve are blocked, the latency of the averaged nerve action potentials may increase and the amplitude may decrease. A more intense or prolonged compression or traction may produce myelin deformation at the edges of compression and prolongation of the nerve action potential latencies [28]. Further mechanical loading may produce a conduction block from segmental demyelination with reductions in action potential amplitudes. With injury, reversible functional changes precede more severe morphologic nerve changes such as neurapraxia (segmental demyelination) and axonotmesis (Wallerian degeneration). Although both these morphologic changes may be reversible in weeks to months, perineural and intraneural scarring may result and propagate further nerve damage [26, 27, 29, 30].

The mechanosensitivity of normal and abnormal dorsal root ganglia and axons has been defined in human and animal models [24]. In a cat model, rapidly applied mechanical forces induce short-duration (200 ms) impulses in normal nerve root. Static mechanical forces do not induce impulses in normal nerve root. Rapidly and statically applied mechanical forces induce long periods (15–30 s) of repetitive impulses in irritated or in regenerating nerves in continuity. Minimal acute compression of normal dorsal root ganglion induces prolonged (5–25 min) repetitive firing of nerve [31]. Mechanically induced trains of nerve action potentials can desynchronize afferent 1a nerve action potentials during H-reflex recordings and decrease the H-reflex amplitude. When interpreting intraoperative motor nerve root studies, it is important to understand the pathophysiologic mechanisms of nerve root injury and to understand the response of normal and pathologic nerve to not

only different types of mechanical force, but also to electrical stimulation.

Late Responses

Following electrical stimulation of a mixed sensory–motor peripheral nerve, the compound motor action potential (CMAP) or M-wave is recorded from the peripherally innervated muscle. The M-wave is the result of orthodromic motor conduction from the point of stimulation to the muscle. In addition to the short latency M-wave, three late responses can be recorded: H-reflex, F-response, and A-wave (axon reflex). The mechanisms responsible for generating F-responses and A-waves are different from H-reflexes [32]. When recording intraoperative H-reflexes, the F-response and A-wave should not be confused with H-reflexes.

The F-response is not a reflex. After supramaximal stimulation of a mixed peripheral nerve, antidromic motor nerve impulses are conducted proximally to the ventral horn where they activate from 1 to 5 % of the motor neurons. This is followed by orthodromic conduction through motor fibers, and the F-response is recorded from muscle. The F-response is of low amplitude, and the latency, configuration, and duration vary from one stimulus to the next. This variability occurs because each time the motor neuron pool is activated, a different population of 1–5 % of the motor neuron pool is activated that have different conduction characteristics [33]. Both afferent and efferent components of the F-response follow the same motor neurons. The subpopulation of the motor neuron pool activated by the F-response and H-reflex are not the same [34]. F-response persistence is a measure of the excitability of the motor neuron pool. Persistence is the number of recorded F-responses divided by the number of stimuli. Clinically, a persistence less than 50 % is considered to be abnormal [35] (Fig. 8.2).

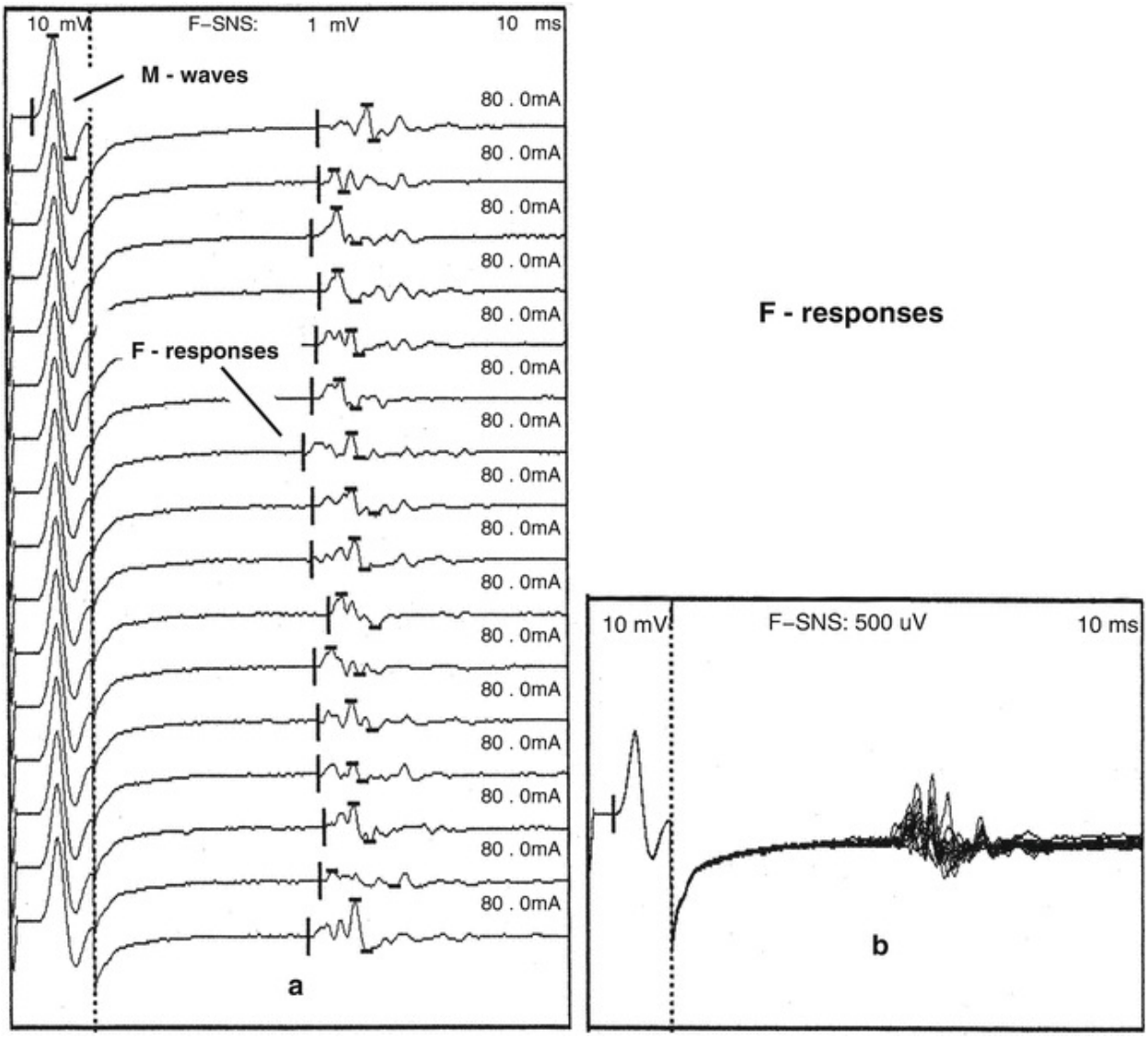

Fig. 8.2 F-responses are generated by antidromic motor impulses that activate 1–5 % of the motor neuron pool. The amplitude, latency, duration, and configuration change with each stimulus. Sequentially, recorded abductor hallucis F-responses (**a**) following tibial nerve stimulation at the ankle that are superimposed in (**b**)

The A-wave is a late motor response that is present with constant latency, configuration, and amplitude. Low-intensity stimulation elicits the A-wave, and it is usually blocked by higher intensity of stimulation. A-wave latency is between the CMAP and the F-response latency or exceeds the F-response latency. It may also appear with a latency between the M-wave and H-reflex latency or the latency may exceed the H-reflex latency. A-wave amplitude is less than the H-reflex amplitude. The A-wave should not be confused with the H-reflex or F-response. The A-wave is generated by peripheral nerve

changes rather than changes in the central nervous system signal processing. The physiology of the A-wave is that there is peripheral neural damage with the presence of a collateral sprout from a proximal point of damaged motor nerve. The collateral sprout innervates muscle. When the antidromic impulse reaches the point of damage, a portion of the electrical impulse proceeds distally along the collateral sprout, and a small portion of the muscle is activated. Depending on the nerve stimulated, A-waves may be normal or abnormal (Fig. 8.3) [32].

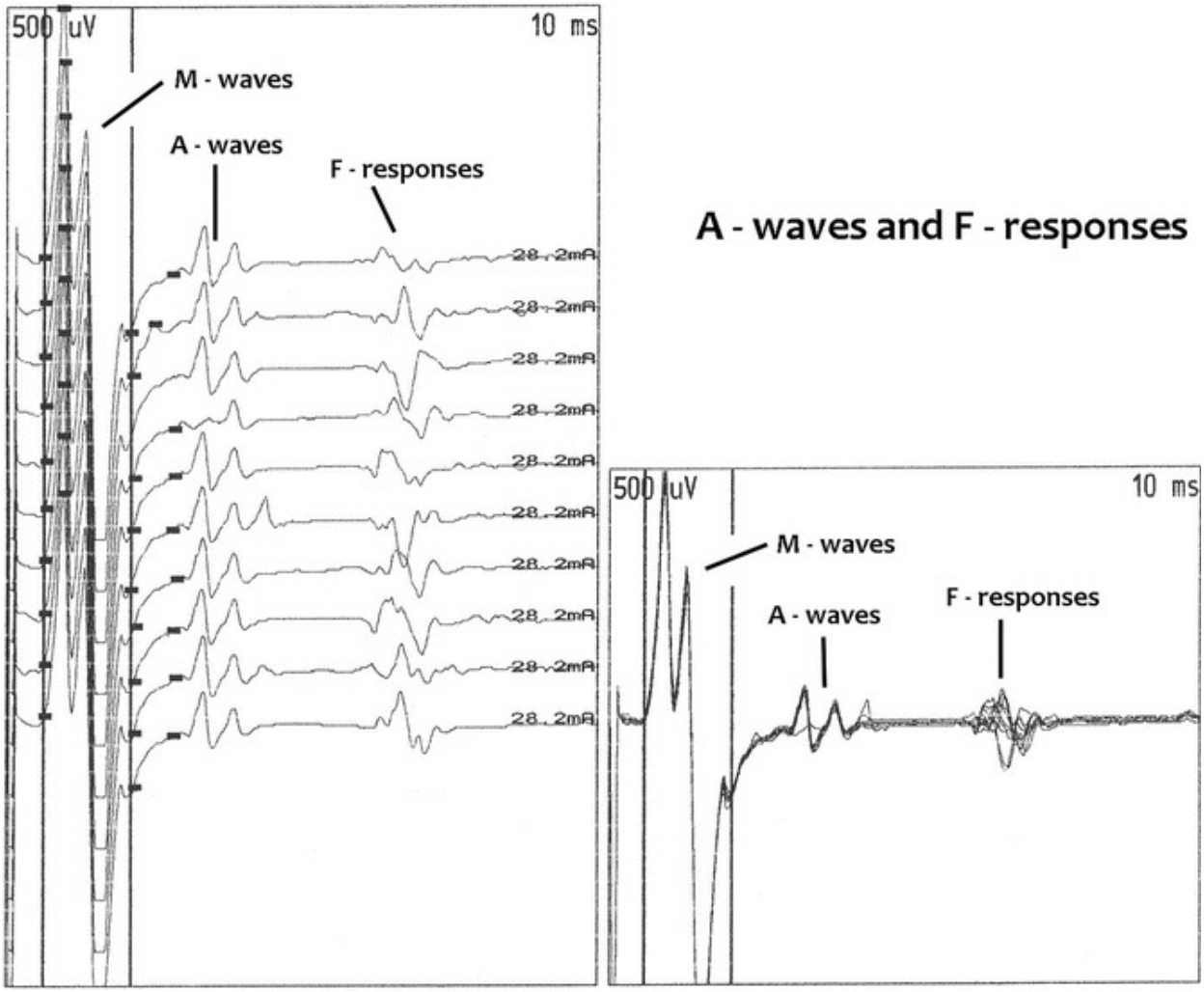

Fig. 8.3 A-wave amplitude, duration, latency, and configuration do not change from one stimulus to the next, but F-responses do. These are ten abductor hallucis recordings following tibial nerve stimulation at the ankle

H-Reflexes: Monosynaptic, Oligosynaptic

See Chap. 7 for a discussion of H-reflex testing.

Neurophysiologic Basis of H-Reflexes

The H-reflex is a CMAP recorded from muscle after electrical afferent activation of a monosynaptic reflex. The afferent pathway involves electrical activation of the large 1a nerve fibers originating from muscle. After entering the dorsal horn of the spinal cord, the 1a fibers synapse with the motor neurons. The efferent pathway involves orthodromic motor conduction through motor fibers in the same homologous spinal segment as the afferent pathway [32]. In normal newborns, H-reflexes may be recorded from many widely distributed muscles. After 2 years of age, they are primarily present in the gastrocnemius, soleus, and flexor carpi radialis muscles. The more restricted distribution of H-reflexes in adults reflects the refinement of motor neuron pool activation with central nervous system maturation. In adults, they are also frequently found in the quadriceps and plantar foot muscles [36–38].

The H-reflex was first described by Hoffman in 1918 [39] and characterized more in the 1950s [40]. The reflex is most easily recorded from the gastrocnemius muscle after stimulation of the tibial nerve in the popliteal fossa. The fast-conducting low-threshold 1a fibers are activated with long-duration (1 ms) low-intensity stimulation. The stimulation rate is 0.5 Hz. The intensity of stimulation is slowly increased. Low-intensity stimulation activates the 1a fibers before the motor fibers, so at low intensity of stimulation, the H-reflex appears before the M-wave. The H-reflex CMAP is usually of a biphasic or triphasic configuration. The 1a fibers are activated first either because they have a lower threshold than motor fibers to long-duration stimulation or because they are located anatomically more superficial than the motor fibers in the popliteal fossa [41].

As the intensity of stimulation is increased, a greater percentage of the motor neuron pool is activated and the H-reflex amplitude increases [32]. In an awake human, when recording the gastrocnemius H-reflex, the percentage of the motor neuron pool activated averaged 50 % (range, 24.0–100 %) [20]. The motor neurons recruited with an increasing intensity of stimulation obey the Henneman size principle . Low-force motor neurons are recruited with low intensity of stimulation, and high-force motor neurons are recruited with higher intensity of stimulation [42].

The H-reflex amplitude usually peaks at or just before the M wave

becomes present. Further increases in stimulation intensity result in a steady increase in the M-wave amplitude. When the M wave no longer increases in amplitude, the H-reflex is usually replaced by the F-response (Fig. 8.4). When the stimulus intensity is held constant from one stimulus to the next, the H-reflex is of short latency, short duration, simple configuration, and constant amplitude [32]. To determine if a CMAP is a H-reflex, the amplitude should exceed the M-wave amplitude, and the configuration and latency should be the same from one stimulus to the next [32]. Changes in the effect of the central facilitation and inhibition on the spinal interneurons and motor neurons may change the pattern of how the H-reflex is activated. With an increased presynaptic inhibition and hyperpolarization of motor neurons, the M-wave may be present before the H-reflex, and the H-reflex amplitude may be smaller than the M-wave amplitude. With a decreased presynaptic inhibition, the H-reflex may be robust, and it may not be possible to suppress and replace it with the F-response.

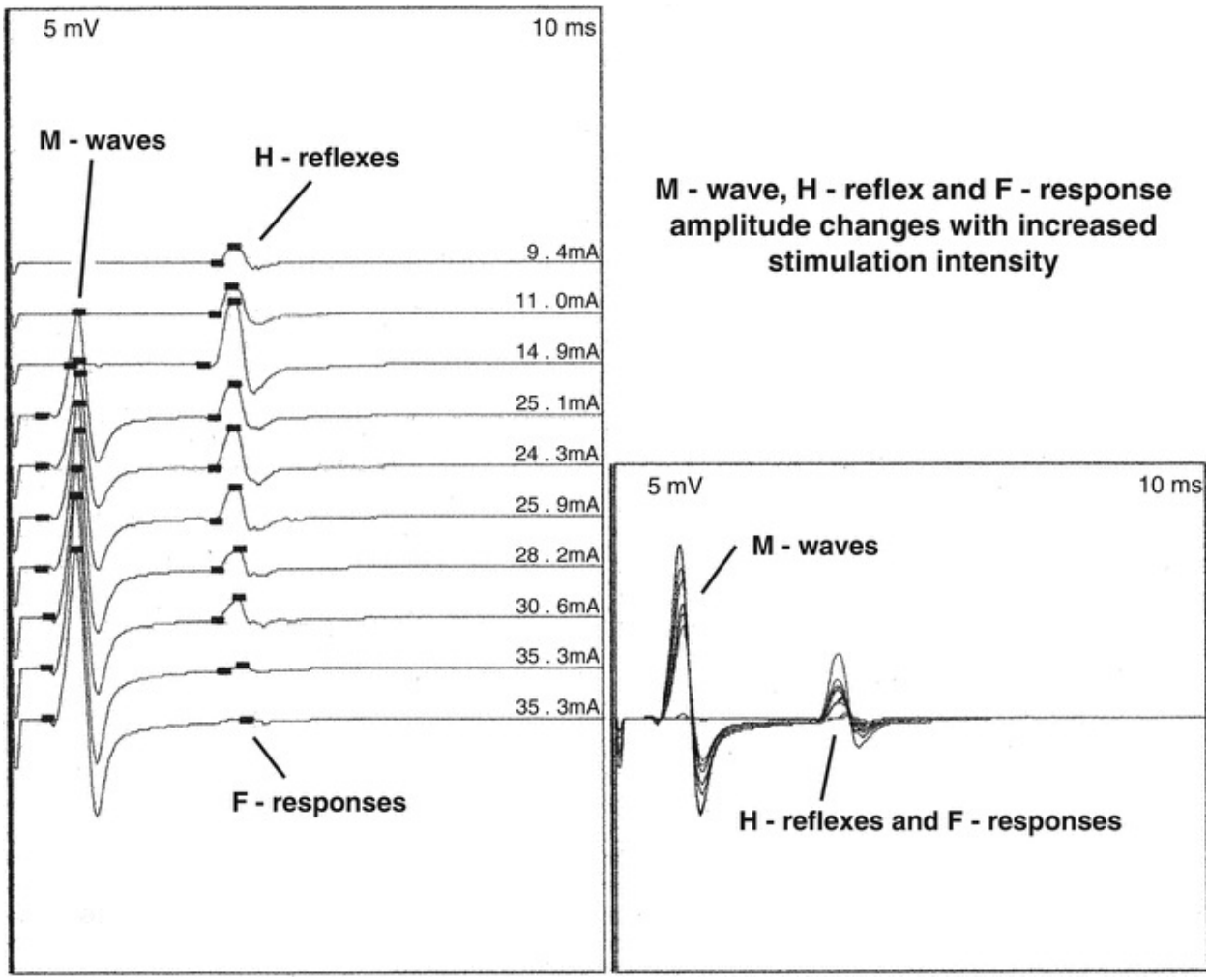

Fig. 8.4 The H-reflex is the first component elicited from the gastrocnemius muscle with increasing stimulus intensity of the tibial nerve in the popliteal fossa. The second is the M-wave and the third is the F-response

The H-reflex has been thought of as a monosynaptic reflex . The central conduction time between dorsal and ventral roots reveals only enough time for one synapse, that is, between 0.5 and 1.0 ms [32]. There is also evidence to indicate that the H-reflex is an oligosynaptic reflex. Low-threshold motor neurons may be activated by a single (monosynaptic) synapse through the fastest 1a afferents. Higher threshold motor neurons may be activated through several (oligosynaptic) synapses by the fastest 1a afferents and through single synapses by slower 1a afferents [32].

In the lower extremity of man, there are two types of prewired monosynaptic 1a H-reflex connections: homonymous (homosynaptic) and heteronymous (heterosynaptic). They are both part of the functional

synergistic spinal cord CPGs. Both types may be recorded in the operating room. Homonymous monosynaptic H-reflexes are H-reflexes that are recorded from muscles that are innervated by the same nerve root as the 1a-activated sensory fibers. The gastrocnemius H-reflex is an example of a homonymous monosynaptic H-reflex (Fig. 8.5). 1a sensory action potentials may also make monosynaptic connections with motor neurons at spinal cord levels other than the 1a sensory segmental level. As a result of this activation, H-reflexes may be recorded from muscles having segmental innervation other than the 1a segmental afferent activation. These H-reflexes are called heteronymous monosynaptic H-reflexes (Fig. 8.6).

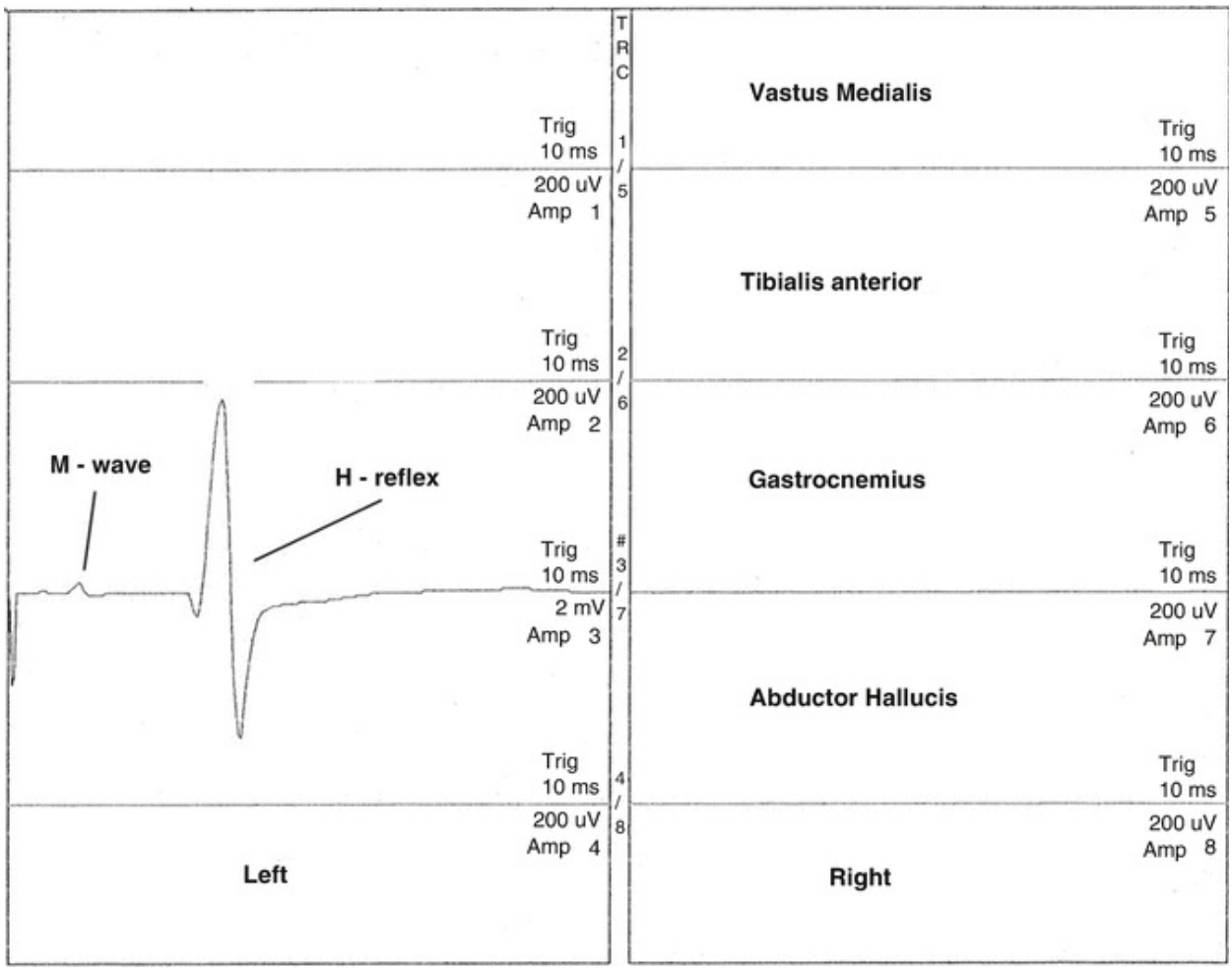

Fig. 8.5 Homonymous monosynaptic left intraoperative gastrocnemius H-reflex recorded following electrical stimulation of the left tibial nerve in the popliteal fossa

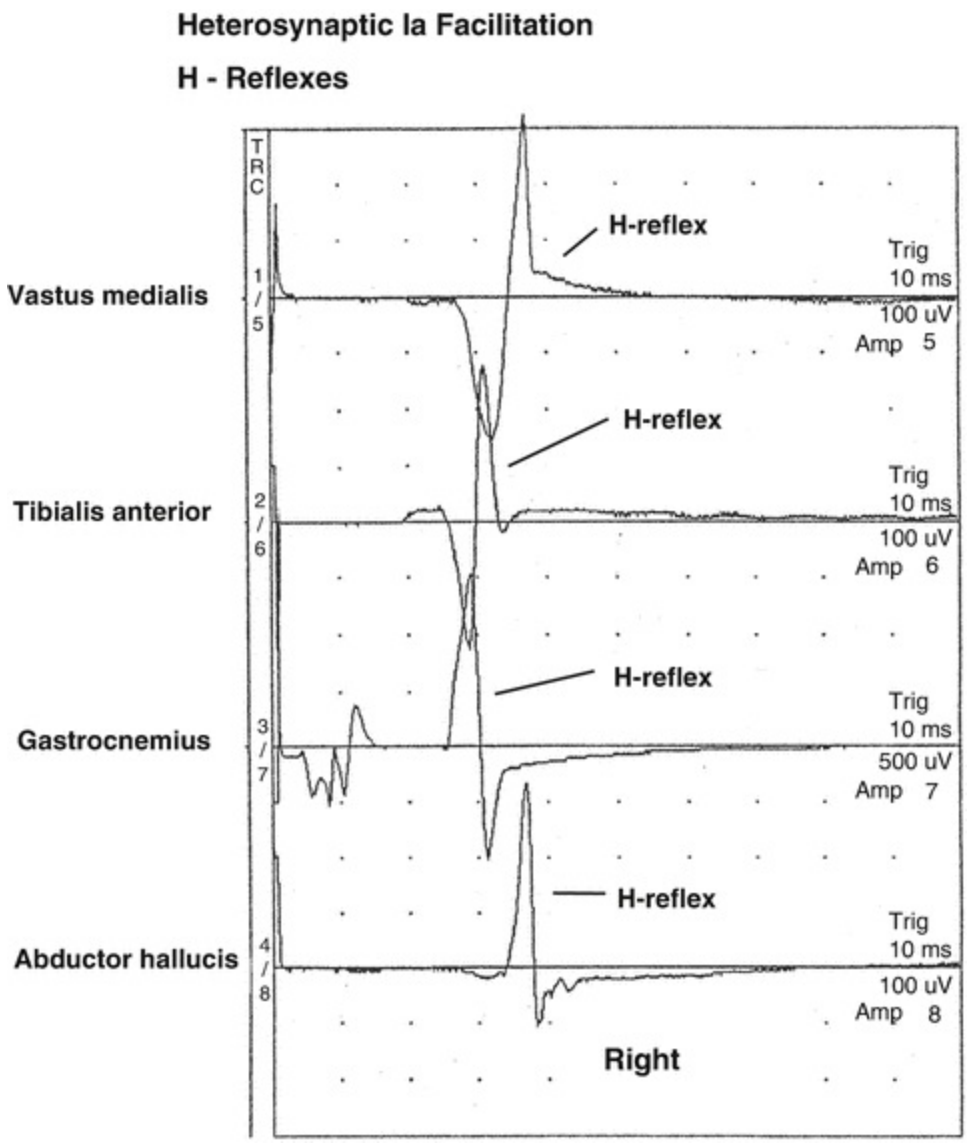

Fig. 8.6 Following intraoperative low-intensity electrical stimulation in the right popliteal fossa, decreased spinal cord presynaptic inhibition may allow not only the homonymous H-reflex to be recorded from the gastrocnemius muscle but also heteronymous H-reflexes may be recorded from the vastus medialis, tibialis anterior, and abductor halluces muscles

In humans, heteronymous connections normally exist between ankle and knee muscles. Functionally heteronymous connections provide coupling between muscles operating at different joints. These transjoint monosynaptic connections are important for maintaining equilibrium during bipedal stance and during gait. Intraoperatively, heteronymous H-reflexes are inhibited by presynaptic inhibition. When presynaptic inhibition is decreased, heteronymous H-reflexes may become present [43].

The presence of H-reflexes in muscles where they are not usually

recorded can be an indication of a lesion of the suprasegmental central nervous system that results in a decreased effect of presynaptic inhibition on motor neurons. The abnormal distribution of H-reflexes in adults, such as in the tibialis anterior and intrinsic hand muscles, may indicate a disordered central motor system state. These changes occur because of uncoupling of the different components of CPGs [44–47].

Gastrocnemius H-Reflex

Gastrocnemius H-Reflex Normal Parameters

In the lower extremity , the H-reflex can be recorded from the gastrocnemius and soleus muscle after electrical stimulation of the posterior tibial nerve in the popliteal fossa [48]. This reflex is mediated by segmental S1 afferent and efferent activity [45]. Intraoperative normal parameters have not been established. Normal parameters established for clinical studies may serve as a guide for intraoperative studies. Clinically, the gastrocnemius H-reflex latency varies with age and leg length and has a mean latency of 28.9 ± 2.7 ms in an awake human. A regression equation may be used to calculate the expected latency for each individual: H-reflex (in ms) = 9.14 + 0.46 (leg length in centimeters) + 0.1 (age in years). A normogram based on this equation is available as a reference [49]. Clinically, the normal side-to-side amplitude difference between 21 and 67 years of age may reach 60 % [50]. The upper limit of normal clinical side-to-side latency difference is 1.5 ms [37]. When measuring latency, the most concise departure from the baseline occurs when the active recording electrode is over the motor point. It is therefore necessary to know the location of the motor point of the gastrocnemius muscle [51]. The H:M ratio is a measure of H-reflex motor neuron pool activation or excitation. It is calculated by dividing the maximum H-reflex amplitude by the maximum M-wave amplitude. It is normally less than 0.7 [37]. Intraoperatively, onset latencies may be greater because of the decreased limb temperature. In the operating room, H-reflex and M-wave amplitudes that are recorded in the clinical setting may be reduced by the use of neuromuscular junction (NMJ) blocking agents. Intraoperatively, the gastrocnemius H-reflex parameters that have been monitored are H-reflex amplitude, latency, and the H:M ratio. Right–left amplitude and latency differences are also used.

Gastrocnemius H-Reflex Stimulation and Recording Techniques

Stimulation is with needle or surface electrodes . The cathode is placed proximally in the popliteal fossa between the tendons of the medial and lateral hamstring muscles. The anode is placed 2–4 cm distal to the cathode. The stimulation rate is 0.5 Hz and the stimulus duration is 1.0 ms. The stimulus intensity is adjusted so that the H-reflex amplitude is maximal. The most effective stimulus intensity is chosen such that any increase or decrease in stimulus intensity results in a decrease in the H-reflex amplitude. Baseline recordings are made with the patient anesthetized before the start of the surgical procedure. Any variability in latency and amplitude should be noted in the baseline recordings.

For subdermal electroencephalographic (EEG) recording, needle electrodes are inserted in the medial head of the gastrocnemius muscle. The H-reflex may also be recorded in the calf from the soleus muscle. The technique for recording the H-reflex from the soleus muscle is the same as that for recording from the gastrocnemius muscle, only that the recording electrodes are placed over the mid-dorsal line of the leg with the active electrode 4 cm above the point where the two heads of the gastrocnemius muscle join the Achilles tendon. The reference electrode is placed 3 cm distal to the active electrode [48]. Monopolar electromyographic (EMG) needle electrodes and longer uncoated stainless steel needle electrodes may also be used.

Fine Teflon-coated silver wires with the wire exposed at the end and that are inserted with a spinal tap needle may also be used for recordings when the subcutaneous tissue is thick. The active electrode is inserted at the motor point of the gastrocnemius muscle and the reference electrode is inserted over tendon or bone. The needles are secured with tape. A range of different high- and low-frequency filters are used. A high-frequency filter of 10 KHz and a low-frequency filter of 20 Hz are most often used [32]. The time base is 100 ms. Recordings are single sweep.

In addition to recording H-reflexes from the gastrocnemius muscle , recordings may also be made bilaterally and simultaneously from the vastus medialis, tibialis anterior, and abductor hallucis muscles. Recording from these muscles will allow for the detection of heteronymous H-reflexes. This also allows for the monitoring of proximal vestibulospinal and reticulospinal

controlled motor neurons and distal rubrospinal and corticospinal controlled motor neurons [11]. The gastrocnemius H-reflex may be used to monitor peripheral tibial nerve, proximal sciatic nerve, sensory and motor S1 nerve root, and S1 segmental spinal cord function. These reflexes can also be used to monitor the function of a variety of suprasegmental descending spinal cord systems that control the S1 segmental interneurons [52]. When present, heterosynaptic H-reflexes may be used to monitor other nerve roots. The ability to record lower extremity H-reflexes may be affected by pre-existing abnormalities, such as a generalized polyneuropathy, plexopathy, or radiculopathy. H-reflexes may be absent, latencies may be prolonged, amplitudes may be decreased, and the CMAP configuration may change. Amplitudes may also be decreased with the presence of a myopathy [1, 2].

Flexor Carpi Radialis H-Reflex

Flexor Carpi Radialis H-Reflex Background and Normal Parameters

In the upper extremity, the flexor carpi radialis H-reflex can be recorded after electrical stimulation of the median nerve over the distal medial upper arm or over the anterior medial elbow. This reflex is mediated by segmental C6/C7 afferent and efferent activity (Fig. 8.7). Intraoperative normal parameters have not been established. Normal parameters established for clinical studies may serve as a guide for intraoperative studies. Clinically, the flexor carpi radialis H-reflex latency varies with the arm length. When measuring latency, the most concise departure from the baseline occurs when the active recording electrode is over the motor point. It is therefore necessary to know the location of the motor point of the flexor carpi radialis muscle [51]. In awake humans, the mean latency is 17.07 ± 1.77 ms. The interlatency time is calculated by subtracting the M wave from the H-reflex latency. The interlatency time mean latency is 14.5 ± 1.8 ms. The maximum side-to-side H-reflex latency difference is 0.002 ± 0.42 ms. The maximum side-to-side interlatency time latency is 0.11 ± 0.44 ms. A regression equation is used to calculate the expected H-reflex latency: H-reflex (in ms) = 0.29 ± 0.195 × arm-length in centimeters. The equation for the interlatency time is −2.08 + 0.1878 × arm-length in centimeters. A normogram based on these equations is available as a reference. The arm length is measured from the tip of the third finger to the C6 spinous process with the arm pronated and the shoulder

abducted to 90° [53, 54]. Intraoperatively, onset latencies may be greater because of the decreased limb temperature. Flexor carpi radialis H-reflex parameters that have been monitored are H-reflex amplitude, latency, and the H:M ratio. Right–left latency and amplitude differences are also used.

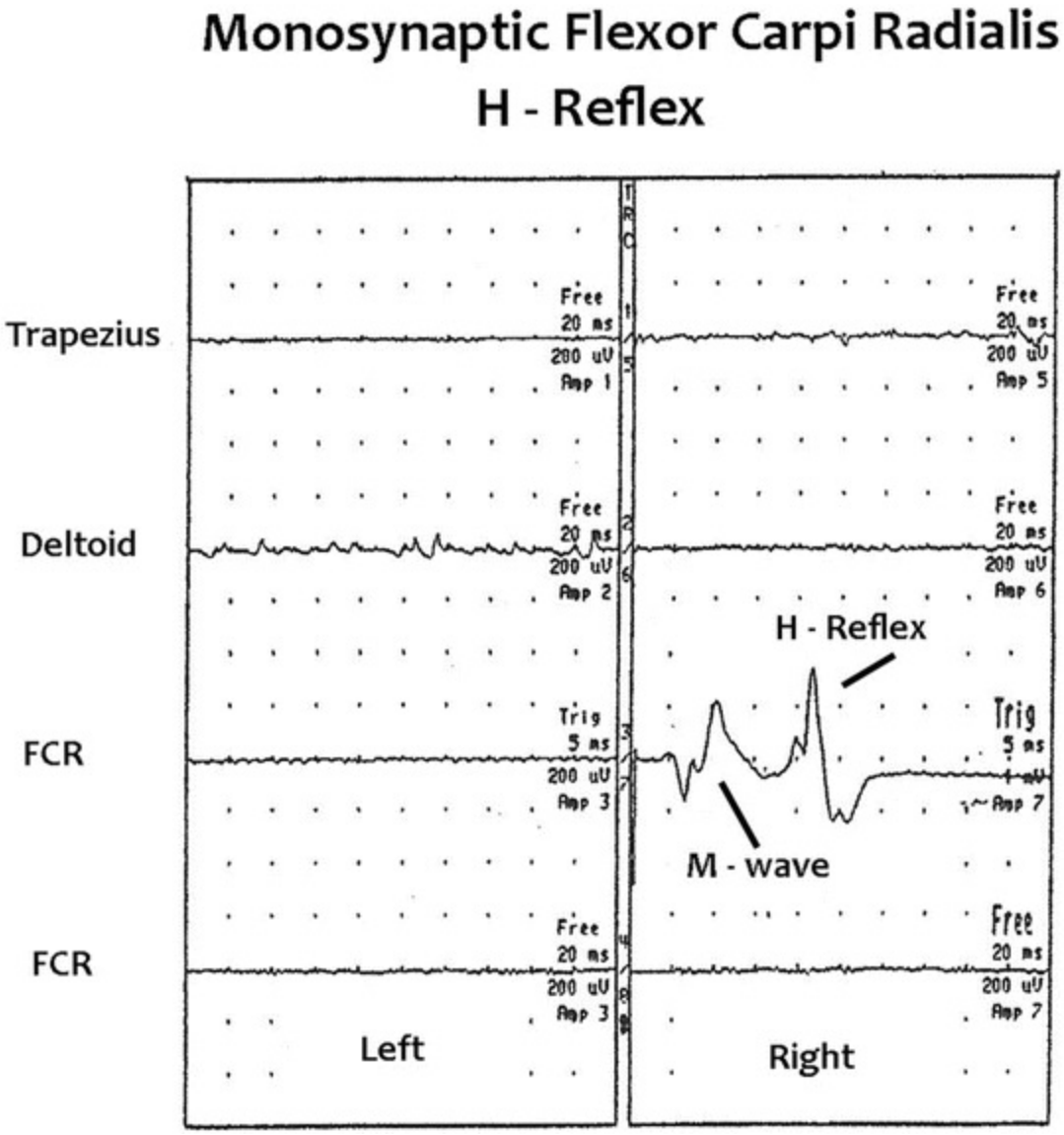

Fig. 8.7 Baseline intraoperative right flexor carpi radialis M-wave and H-reflex recordings. Free-run EMG activity is also recorded bilaterally from the trapezius, deltoid, and flexor carpi radialis muscles. Baseline free-run EMG activity is present in the left deltoid muscle secondary to left C5 and/or C6 nerve root irritation

Flexor Carpi Radialis H-Reflex Stimulation and

Recording Techniques

Stimulation is with needle electrodes spaced 2 cm apart unilaterally over the distal medial upper arm or over the anterior medial elbow at 0.5 Hz and 1.0 ms duration. The cathode is proximal. The stimulus intensity is adjusted so that the H-reflex amplitude is maximal. The most effective stimulus intensity is chosen such that any increase or decrease in stimulus intensity results in a decrease in the H-reflex amplitude. Baseline recordings are made with the patient anesthetized before the start of the surgical procedure. In the operating room, H-reflex amplitudes that are recorded in the clinical setting may be reduced by the use of NMJ-blocking agents. Any variability in latency and amplitude should be noted in the baseline recordings.

For recording subdermal EEG , needle electrodes are inserted in the flexor carpi radialis muscles. Monopolar EMG needle electrodes and longer uncoated stainless steel needle electrodes may also be used. Fine Teflon-coated silver wires with the wire exposed at the end that are inserted with a spinal tap needle may also be used for recordings when the subcutaneous tissue is thick. The active electrode is inserted at the motor point and the reference electrode is inserted distally over tendon or bone. The needles are secured with tape. A range of different high- and low-frequency filters are used. A high-frequency filter of 10 KHz and a low frequency filter of 20 Hz are most often used. Flexor carpi radialis H-reflexes may be used to monitor median peripheral nerve, brachial plexus, and segmental sensory and motor spinal nerve root and spinal cord function. These reflexes can also be used to monitor the function of a variety of suprasegmental descending spinal cord systems that control the C6/C7 segmental interneurons. The ability to record flexor carpi radialis H-reflexes may be affected by pre-existing abnormalities, such as a generalized polyneuropathy, plexopathy, or radiculopathy. H-reflexes may be absent, latencies may be prolonged, amplitudes may be decreased, and the CMAP configuration may change. Amplitudes may also be decreased with the presence of a myopathy process [1, 2].

Anesthetic Technique

To record reflexes intraoperatively, it is critical that the anesthetic technique does not significantly inhibit the activity of suprasegmental spinal cord function, spinal interneurons, and segmental motor neurons. Also, adequate

neuromuscular junction (NMJ) transmission must be present. Reflexes and F-responses are usually monitored during the recording of SSEPs, tcMEPs, EEG, and free-run EMG. The anesthetic technique used must allow for the recording of all these signals with maximum sensitivity (see Chap. 19 for a discussion of general anesthesia monitoring) [2, 55–60].

The technique used varies depending on the surgical procedure, patient's age, medical history, and the presence of a pre-existing neurologic deficit. Frequently, total intravenous anesthesia (TIVA) with constant infusion of propofol and fentanyl and other opioids are used. Bolus injections of these agents should be avoided to prevent suppression of recordings and if nitrous oxide is used it should not exceed 50 vol.% [61]. Ketamine may serve an adjunctive role to reduce propofol utilization. High dose of ketamine may suppress tcMEP amplitudes [58]. Ketamine is an excitatory agent and increases SSEP, tcMEP, and H-reflex amplitudes [62].

Dexmedetomidine can be used to supplement propofol during TIVA. Suggested therapeutic levels (0.5–0.7 μg/kg/h) suppress MEP amplitudes but not SSEP amplitudes [63, 64]. One study found that 0.6 μg/kg/h did not suppress SSEP, tcMEPs, and visual evoked potentials [65]. Subtherapeutic doses of less than 0.5 μg/kg/h combined with propofol do not suppress tcMEPs [66, 67].

The author studied the effect of dexmedetomidine on intraoperative SSEPs, tcMEPs, EEG, H-reflexes, and F-responses in 17 patients during correction of scoliosis. After completion of distraction and fixation, a loading dose of 1 μg/kg of dexmedetomidine was added to the fentanyl and propofol technique and this was followed by an infusion of 0.5 μg/kg/h to the end of surgery. No muscle relaxants were used. The addition of dexmedetomidine had no effect on SSEPs or EEG but the effect on motor signals was variable. Lower extremity tcMEP amplitudes decreased from 0 to 100 % (mean, 86 ± 16.6 %), F-response amplitudes decreased from 0 to 100 % (mean, 58 ± 12.5 %), and H-reflex amplitudes decreased from 0 to 100 % (mean, 71 ± 13.9 %). Because of the variable and at times pronounced effects on motor signals, it was recommended that dexmedetomidine not be used to monitor tcMEPs, H-reflexes, or F-responses [68].

NMJ-blocking agents should be avoided other than using short-acting agents for intubation. NMJ function needs to be carefully monitored. The most common technique is the train-of-four (TOF) response . Another technique is the T1 % response. T1 % = first unblocked response/control

response × 100. NMJ monitoring should be conducted on muscles that may be affected by the surgical procedure.

The effects of propofol on the soleus H-reflex were studied in 33 patients. No NMJ-blocking agents were used. H-reflexes were recorded before administration of anesthetics and after an initial dose of 2 mg/kg over 1 min followed by a continuous infusion at a rate of 167 μg/kg/min for 10 min. Measurements were also made after infusing propofol to a blood level of 6 and 9 μg/mL. The initial dose of 2 mg/kg decreased the H-reflex amplitude and H:M ratio. The following 10-min infusion did not further decrease these values. The 6-μg/mL injection did not change the H-reflex amplitude and H:M ratio. The 9-μg/mL injection decreased the amplitude and H:M ratio. They recommended that the propofol induction dose be 1.0–2.5 mg/kg and this should be followed by an infusion from 100 to 200 μg/kg/min. They concluded that the immobility during propofol anesthesia is not caused by a depression of spinal motor neuron circuit excitability. Propofol does not decrease axon conduction peripherally nor transmission at the neuromuscular junction [69].

Soleus H-reflexes were used to determine the level of motor neuron excitability intraoperatively. In ten normal human volunteers, 1.0–1.5 % enflurane was found to decrease H-reflex amplitudes from 35 to 100 % of baseline values [70].

The effect of isoflurane alone and isoflurane with N_20 on the soleus H-reflex was studied under general anesthesia in 25 patients. No NJM-blocking agents were used. Twenty-three of these patients had consistently measurable stable H-reflexes with baseline amplitudes varying from 3.43 to 11.97 mV. The addition of 0.68 % isoflurane decreased the amplitude to 48 % of the baseline. Increasing the isoflurane to 1.37 % decreased the amplitude to 33.8 % of baseline. The combination of 0.81 % isoflurane with 30 % N_20 decreased the amplitude to 66.2 % of baseline. The combination of 0.37 % isoflurane with 70 % N_20 decreased the amplitude to 30.4 % of the baseline. They reported that increasing isoflurane concentration results in decreased H-reflex amplitude. Increasing the N_20 concentration results in decreased H-reflex amplitude. They concluded that the H-reflexes may be recorded with a combination of isoflurane and N_20. The H-reflex is maximally stable within the range of anesthetic concentrations used to achieve surgical immobility [55].

The effect of isoflurane and N_20 on spinal motor neuron excitability was studied in eight adult patients by monitoring soleus H-reflexes and abductor hallucis F-responses. No NMJ-blocking agents were used. H-reflex amplitude was decreased to 48.4 ± 18.6 % of the baseline with 0.6 minimum alveolar concentration (MAC) isoflurane and to 33.8 ± 19.1 % with 1.2 MAC isoflurane. MAC is defined as the alveolar concentration of an anesthetic agent that prevents movement in 50 % of patients in response to a painful stimulus. F-response amplitude and persistence decreased to 52.2 ± 22.8 % and 44.4 ± 26.0 % of the baseline at 0.6 MAC isoflurane and to 33.8 ± 26.0 % and 21.7 ± 22.8 % at 1.2 MAC. With 1.0 MAC isoflurane, the H-reflex amplitude was decreased by 32.5 ± 19.2 %, 33.3 ± 20.8 %, and 30.4 ± 23.5 % of baseline levels at 30, 50 and 70 % nitrous oxide, respectively [71].

In 12 adult patients, a comparison of the effects of isoflurane on tcMEPs and F-responses were studied. Anesthesia was maintained with 60 % N_20, 100 μg/kg/min of propofol and supplementary fentanyl, 0.5–1.0 μg/kg. Recordings were made before and after adding 0.5 % isoflurane. Baseline tcMEP amplitudes (median, 205 μV, 25th–75th percentiles, 120–338 μV), F-response amplitudes (median, 100 μV, 25th–75th percentiles, 64.2–137.5 μV) and F-response persistence (59 ± 29 %) were decreased to 0.0 μV (0–15 μV), 49 μV (12.4–99.6 μV), and 30 ± 31 %, respectively, by 0.5 % isoflurane. The tcMEPs were suppressed more than the F-responses. No NMJ-blocking agents were used [72].

Soleus H-reflexes and abductor hallucis F-responses were monitored to determine the effect of hyperventilation and hypoventilation on motor neuron excitability during isoflurane anesthesia. H-reflex and F-responses were recorded before and after changing the end-tidal CO_2 ($ETCO_2$) concentration. Anesthesia was maintained with 0.8 % isoflurane and no muscle relaxants were used. An $ETCO_2$ of 25 mmHg decreased the preanesthetic H-reflex amplitude from 6.8 ± 2.7 mV to 4.0 ± 2.0 mV and to 2.0 ± 2.2 mV at an $ETCO_2$ of 45 mmHg. F-response persistence decreased from the preanesthetic value of 100 % to 77 % ± 24 % at an $ETCO_2$ of 25 mmHg and to 61 ± 19 % at an $ETCO_2$ of 45 mmHg. They concluded that hyperventilation and hypoventilation effects motor neuron excitability and may affect the probability of patient movement during surgery [73].

Volunteers were sedated with a constant level of propofol (2 mg/L) and to a constant level of sevoflurane (0.8 vol.%). Soleus H-reflexes were used to

study the depressive effects of these agents individually. The amount of depression was found to be dependent on the size of the H-reflex and is different at different stimulus intensities, indicating a varying effect of propofol and sevoflurane on motor neurons of different size. H-reflex depression is more for both agents at a lower intensity of stimulation than at a higher intensity of stimulation, indicating that smaller motor neurons are depressed more than larger motor neurons. In contrast, excitability of motor neurons by supraspinal effects affects the larger before smaller motor neurons [74]. From a practical standpoint, if H-reflexes are being recorded with a low stimulus intensity and injury occurs that effects the larger motor neurons, this injury could be missed because only the function of the smaller motor neurons would be monitored. The smaller motor neuron population would already be suppressed by the anesthesia, further decreasing the sensitivity for detecting injury. A higher intensity of stimulation would activate small and large motor neurons, allowing the monitoring of a greater percentage of the motor neuron pool.

Clinical Correlation of H-Reflexes and F-Responses

Studies of the normal and abnormal electrophysiology of the spinal cord CPG components in humans and animals have resulted in the understanding of the mechanisms involved in acute complete and partial SCI in humans. How H-reflex and F-response changes correlate with the patient's postoperative status is derived from the publications discussed as follows.

Soleus H-reflexes and abductor hallucis F-responses were recorded in 32 patients during spinal cord surgery. In six patients, an abrupt fall in H-reflex amplitude beyond 3 SD from the baseline or significant drop in F-response persistence coincided to perturbation or injury to the spinal cord. Transient suppression occurred in four patients with less than a 50 % drop in H-reflex amplitude or abductor hallucis F-response persistence. These patients did not develop a new postoperative neurologic deficit. Suppression exceeded 90 % of the baseline values and persisted through surgery in two patients. Both patients had profound postoperative neurologic deficits. The author concluded that rostral SCI suppresses H-reflexes and F-responses and the degree of suppression reflects the severity of injury. The mechanism responsible for these changes is thought to be hyperpolarization of caudal motor neurons, which occurs within seconds of injury [75].

H-reflexes were recorded in the lower extremities in 31 patients during spinal surgery. A significant change in amplitude was considered significant if it exceeded 3 SD of the mean postanesthetic baseline. In six patients, a significant decrease in H-reflex amplitude occurred. The onset of H-reflex suppression coincided with a potentially injurious event in each case. In one case involving a cervical myelotomy, a large syrinx collapsed during decompression, producing immediate fluctuation in the H-reflex amplitude. The amplitude recovered to the baseline level 9 min later. Postoperatively, no neurologic deficit was noted. Another case involved mechanical reduction of a T-8 spinal fracture. Increased variability in H-reflexes developed with manipulation of the spine before reduction. The first attempt to reduce the fracture produced a transient fall in H-reflex amplitude . The second attempt at reduction produced a pronounced reduction in amplitude to less than 10 % of baseline. H-reflexes remained suppressed until the end of surgery and postoperatively the patient had severe motor and sensory deficits in both legs that were not present preoperatively. A third case involved a cervical myelotomy for decompression of a posttraumatic syrinx.

During surgery, cervical cord hemorrhage occurred and was followed by reduction H-reflex amplitude. The amplitude steadily declined and the H-reflexes disappeared and remained absent. Postoperatively, the patient had profound weakness in both lower extremities. The changes in these patients demonstrated that H-reflex changes occur immediately at the time of spinal injury. H-reflex changes may be reversible and reflect the severity of SCI [4].

H-reflexes may indicate intact spinal cord function with changes in SSEPs. Soleus H-reflexes and tibial SSEPs were monitored in a patient during T7–T12 laminectomy for spinal stenosis. During laminectomy, the left SSEP became absent and the right amplitude was significantly transiently reduced. No H-reflex changes occurred. Postoperatively, no lower extremity motor deficits were present and no new sensory deficits [76].

Spinal cord function was monitored in 278 pediatric spine with gastrocnemius H-reflexes and SSEPs. Combined H-reflex and SSEP monitoring improved the reliability for detecting spinal cord compromise compared with either procedure alone. H-reflexes changed more than SSEPs. The changes reflected changes in spinal cord gray matter function related to acidosis and changes in hematocrit and blood pressure [77].

In a clinical setting, soleus H-reflexes and abductor halluces F-responses were recorded in 14 patients following SCI that resulted in either partial

injury without spinal shock or injury with spinal shock. Deep tendon reflexes following tap of the Achilles tendon and patellar tendons were also evaluated. Patients were evaluated within 24 h of injury and on day 10, 20, and 30 after injury. F-responses were absent in patients with spinal shock, reduced in persistence in patients with acute injury without spinal shock, and normal in persistence in patients with chronic injury. F-response changes persisted up to 2 weeks following SCI. H-reflexes were absent or markedly suppressed in patients with spinal shock within 24 h of injury but recovered to normal amplitude within several days of the injury. Deep tendon reflexes were proportionally more depressed in spinal shock than H-reflexes. This demonstrated dissociation between electrically and mechanically induced reflexes during spinal shock . The observation that the stretch reflex is more depressed than the H-reflex is consistent with depressed fusimotor drive with SCI [19].

A 63-year-old woman with a large T8–9 herniated disk that was causing spinal stenosis with cord compression was treated with a bilateral T8–9 laminectomy with left far lateral costovertebral exposure for disk removal. She presented clinically with right T8 dermatomal and bilateral lower extremity pain. Baseline intraoperative tibial SSEPs were bilaterally normal. Baseline lower extremity tcMEPs were present. Baseline lower extremity H-reflexes and F-responses were present bilaterally. During removal of the calcified disk, the lower extremity tcMEPs became absent. The left vastus medialis H-reflex became absent and the left tibialis anterior, gastrocnemius, and abductor hallucis H-reflex amplitudes were decreased 47, 61, and 97 %, respectively. The right tibialis anterior, gastrocnemius, and abductor hallucis H-reflex amplitudes were decreased 75, 88, and 97 %, respectively. The F-responses were present with 35 % of the stimuli on the left and with 30 % of the stimuli on the right. Baseline F-responses were present bilaterally with each stimulus. There were no changes in the tibial SSEPs. Postoperatively, the patient’s lower extremity sensory function was normal. The lower extremity pain was gone but pain was still present in the right T8 distribution. The lower extremities were weak; she could not stand and could not perform coordinated lower extremity functions. Her strength improved and she was able to walk with assistance on discharge 12 days after surgery. The 1.9 to 8.4 % [78, 79] of the motor neuron pool activated by transcranial electrical stimulation was lost. The 24–100 % [20] of the motor neuron pool activated by the H-reflexes was decreased from 47 to 100 %. The 1.0–5.0 % [21] of the

motor neuron pool activated by the F-responses was deceased by 65 and 70 %. The pattern of change in these motor systems in this patient indicates that these techniques may activate the same, different, or overlapping populations of the motor neuron pool. Since the tcMEPs became absent and there was preservation of some H-reflex and F-response function, perhaps H-reflex and F-response changes are better predictors of postoperative motor function than are tcMEPs. The H-reflex and F-response changes correlated with the patient's postoperative motor function while the tcMEPs did not [80].

The soleus H-reflex and simultaneously recorded nerve root action potentials were used to detect conduction abnormalities caused by nerve root manipulation during discectomy for mild S1 radiculopathy. Direct nerve root action potentials were recorded above and below the disc compression site. Changes in the nerve root action potentials from a biphasic to a polyphasic configuration and a decrease in the amplitude or absence of the H-reflex were used as a sign of compromise of nerve root conductivity. A good surgical outcome measured by the postoperative preservation of the Achilles and H-reflex was related to the immediate return of the H-reflex and nerve root action potentials with stopping of the harmful manipulation and the preservation of these signals at the end of surgery [81].

Bilateral soleus H-reflexes were recorded in three patients with cerebral palsy to detect S1 nerve root conduction block during selective dorsal root rhizotomy for relief of intractable spasticity. During retraction and gentle dissection of the S1 nerve roots, there was a sudden drop of all ipsilateral H-reflex amplitudes from 60 to 100 % of baseline without a change in the contralateral H-reflex. This reflected the development of a conduction block of the reflex afferents. When manipulation was discontinued, amplitudes returned to baseline in 1.5–2 min in three roots and remained suppressed in the remaining three roots. The transient changes were thought to be secondary to reversible ischemia and the persistent changes to compressive paranodal demyelination of dorsal rootlet reflex afferents. These recordings helped to identify the cause of the development of areflexia with nerve root stimulation in these types of patients. H-reflexes may be used to determine the safe nerve root retraction pressure [82].

H-reflexes were used to monitor peripheral spinal nerve root function during surgery to reduce and stabilize dislocation of the sacroiliac joint, separation of the symphysis pubis and pubic ramus fractures, and in patients with cauda equina pathology. A multiple systems approach with SSEPs,

tcMEPs, free-run EMG, and F-responses in addition to H-reflexes was used [56].

Scoliosis, vertebral fractures, and vertebral neoplasm surgeries were monitored with H-reflexes, single-sweep SSEPs, and free-run EMG. H-reflexes and single-sweep SSEPs were recorded simultaneously from the same stimulus of the tibial nerve in the popliteal fossa. H-reflexes (1.0-ms rectangular pulse stimulation up to 150 V at 0.1 Hz) were recorded from the soleus muscle (62.5 ms window, 30 Hz–3 KHz). Single-sweep SSEPs were recorded from Cz′ with an auricular reference (125 ms window, 1–300 Hz). Single-trial SSEP extraction from background EEG was performed with a AutoRegressive filter with eXogenous input (ARX). The reference baseline SSEP requires less than 2 min to compute and requires 50 trials. The time needed to complete a single-trial SSEP extraction is less than 1 s. During monitoring, the single-trial SSEPs take less than 1 s to extract and are compared to the baseline.

Monitoring was carried out continuously from the induction of anesthesia until complete return to consciousness. The investigators made the following conclusions:

1. The H-reflex seems to be a sensitive means of detecting spinal cord impairment when it is still in a reversible stage.

2. When signal changes occurred and a normal wake-up test was performed and since patients presented with a postoperative deficit, waking patients after vertebral distraction and fusion does not provide any guarantee against spinal cord impairment soon afterward.

3. The deep depression of H-reflexes in spinal cord injury patients is probably attributed to a reversible vascular impairment directly involving the spinal reflex center or a higher cord segment.

4. Hammering with the osteotome chisel on vertebra should be limited or avoided since there are signs of spinal cord concussion associated with it. Bone graft retrieval from the ileum should be carried out after vertebral distraction because of the facilitating effect on the H-reflex caused by surgical hip stimulation. This facilitation seems to be caused by a long-

loop circuit involving a supraspinal reflex center.

5. The single-sweep SSEPs and H-reflex recordings were very sensitive to detecting changes in spinal cord function related to surgical procedures. The two signals are anatomically and functionally independent, generated by a single transcutaneous stimulus and are both related to the functioning of the spinal cord and are both affected by spinal cord injury. The two signals show different behavior.

6. When surgery is interrupted due to significant signal changes, the amplitude of the H-reflex returns quickly to initial values, while the SSEP amplitude requires a longer recovery time and does not restore completely, showing a global decreasing trend [83–85].

H-reflexes and SSEPs were simultaneously recorded in 19 patients during surgery for metastatic thoracic spinal cord tumors. Bilateral H-reflexes and SSEPs were stable throughout the monitoring in ten of 19 patients. Five of 19 patients had a less than 50 % transient reduction in H-reflex amplitude that later returned to baseline. SSEPs were absent from baseline throughout surgery in two of 19 patients. At 3- and 6-month follow-ups, none of the patients exhibited new postoperative neurologic deficits. Stable intraoperative H-waves are suggestive of preserved postoperative neurologic function. Intraoperative H-reflex monitoring is a reasonable alternative, especially when motor-evoked potentials are unattainable. Since H-reflexes have a greater sensitivity to spinal cord ischemia, are cost-effective and easy to record, H-reflex monitoring can be a useful adjunct during thoracic spine surgery [86].

SSEPs, tcMEPs, and H-reflexes were monitored in 92 pediatric patients during corrective scoliosis surgery. Baseline tcMEPs, SSEPs, and H-reflexes were obtainable in all idiopathic patients. In congenital patients, recordings were obtained in 100 % of tcMEPs , 87 % of H-reflexes, and 91 % of SSEPs. In neuromuscular patients, recordings were obtained in 91 % of tcMEPs, 54 % of H-reflexes, and 77 % of SSEPs. In 18 patients, tcMEP alerts occurred. In 17 of these, amplitudes returned to baseline levels with intervention. The H-reflex was lost in six patients. It did not improve in five with intervention and none had a postoperative neurologic deficit. One patient had a unilateral loss of tcMEPs without SSEP or H-reflex changes and had postoperative

hemiparesis. SSEP changes occurred in one patient with a tcMEP alert. No baseline H-reflexes were obtained. The results did not support the use of the H-reflex as a substitute for tcMEPs [87].

Spinal cord ischemia was detected using SSEPs, tcMEPs, and H-reflexes in 60 patients during thoracoabdominal aortic aneurysm repair. Following cross-clamping, H-reflexes were lost in 12 min in the SCI group and 25 min in the non-SCI group. In SCI, tcMEPs became absent in 10 and 31 min in the non-SCI group. SEPs became absent in 27 min in the SCI group and 44 min in the non-SCI group. A longer absence of H-reflexes, tcMEPs, and SSEPs seemed to be at a higher risk for paralysis. Ten minutes after aortic cross-clamp release, 100 % of H-reflexes, tcMEPs, and SSEPs were absent in the SCI patients compared with 65 % in the non-SCI patients. H-reflexes and tcMEPs followed a similar pattern for detecting spinal cord ischemia. H-reflexes detected milder ischemia than SSEPs [88].

Clinical Correlation Summary

1. If H-reflex amplitude and F-response persistence decrease less than 50 % of baseline, no postoperative deficit has been observed [75].

2. Persistent H-reflex and F-response suppression greater than 90 % correlates with the presence of a postoperative neurologic deficit [75].

3. Transient H-reflex changes are not associated with a postoperative deficit [4].

4. Slow suppression of H-reflexes may be secondary to ischemic spinal cord compromise [4].

5. An abrupt suppression of H-reflexes and F-responses may be associated with mechanical injury to the spinal cord [4, 75, 80].

6. The degree of suppression of H-reflexes and F-responses reflects the severity of SCI [4, 75].

7. Combined H-reflex and SSEP monitoring improves the reliability of detecting spinal cord compromise compared with either procedure alone [77].

8. Intact H-reflexes may indicate intact spinal cord function with changes in SSEPs [76].

9. Perhaps H-reflex and F-response changes are better predictors of postoperative motor function than are tcMEPs [80].

10. H-reflexes can be used to detect spinal nerve root and plexus injury during surgery to reduce and stabilize dislocation of the sacroiliac joint, separation of the symphysis pubis, and pubic ramus fractures and in patients with cauda equina pathology [56].

11. Because H-reflexes have a greater sensitivity to spinal cord ischemia, are cost-effective and easy to record, H-reflex monitoring can be a useful adjunct during thoracic spine surgery [86].

12. The single-sweep SSEPs and H-reflex recordings are very sensitive to detecting changes in spinal cord function during surgery [83–85].

Polysynaptic Reflexes

Sacral Reflex

Three polysynaptic sacral reflexes (bulbocavernosus [BCR] , vesicourethral, and vesicoanal) can be recorded. Clinically, the BCR can be elicited by gently squeezing the glans penis or clitoris and palpating the contraction of the bulbocavernosus or external anal sphincter (EAS) muscles by the index finger inserted into the anal canal. The BCR demonstrates the reflex integrity of the S2, S3, and S4 segmental afferent and efferent pudendal and interneuronal activity [33]. After electrical stimulation of the dorsal nerve of the penis, the latency to contraction of the bulbocavernosus muscle with needle electrode was recorded clinically in 1967. Clinically, this has become

important in the evaluation of patients with micturition, defecation, erectile impotence, and perineal pain disorders [89]. Intraoperatively, the BCR refers to stimulating the dorsal nerve of the penis/clitoris and recording EAS reflex activity [90] (see Chap. 34 in the discussion of surgery for tethered cord).

Intraoperatively, BCR practical recordings were first reported in 1997. The dorsal penile or clitoral nerves were electrically stimulated and reflex activity from the EAS muscles was recorded bilaterally. The BCR was recorded in 119 patients (38, surgery without risk to sacral nerves; 81, surgery with risk to damage of the conus or nerve roots in the cauda equina). In males, the cathode was proximally at the base of the penis and anode over the ventral aspect of the penis. In females, the cathode was placed over the clitoris and the anode over the adjacent labia. Recordings were made with Teflon-coated bare-tip hooked electrodes with two electrodes inserted into the right and left hemisphincter muscles. The best stimulation parameter was double-pulse stimulation (0.5 ms duration, interstimulus interval of 3.0 ms, 2.3 Hz) and 20 mA. Recordings were stable with propofol, fentanyl, and nitrous oxide anesthesia. Nitrous oxide (60 % inspired concentration) plus isoflurane (1.5 %) suppressed the BCR and muscle relaxants abolished it. This monitors the somatic sensory and motor pudendal nerve, S2, 3, and 4 nerve roots , cauda equina, and the excitability of conus medullaris (Onuf's nucleus) segmental activity. In awake nonanesthetized normal subjects, the BCR has two components: an early component having a latency of 30 ms and a longer latency component having a latency of 50 ms. The early component is thought to be oligosynaptic since it does not habituate. The longer latency component is obtainable with stronger electrical stimulation and habituates. Intraoperatively, it is possible to record both components but the early component is more suitable for monitoring because it is more stable (Fig. 8.8). Patients with chronic upper motor neuron abnormalities had more active responses [91].

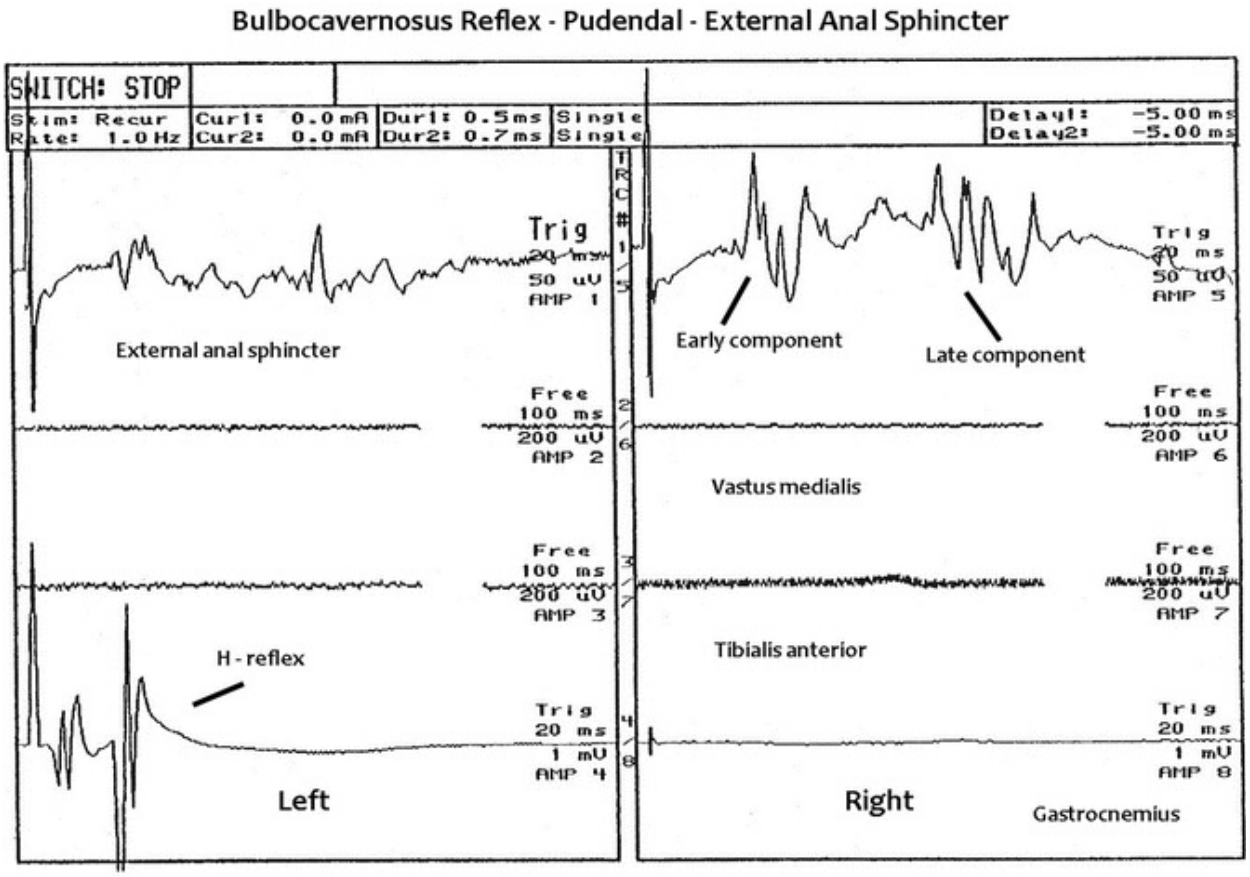

Fig. 8.8 Bilateral baseline intraoperative BCR recordings in a 17-year-old male patient with a L1 compression fracture following electrical stimulation of the right pudendal nerve. The left tibial nerve is simultaneously stimulated in the popliteal fossa eliciting the left gastrocnemius H-reflex. The left S1 and bilaterally the S2–S4 nerve roots are being simultaneously examined

In 2007, a double-train electrical stimulation technique was described using intertrain delays from 75 to 250 ms. Stimulating with two consecutive pulse trains was found to result in at least a 30 % increase in the amplitude, turn count (number of times the BCR potential changed direction and maintained this for at least 50 % of the previous turn amplitude), and duration of the second train response. Anesthesia was maintained with propofol, opiate infusion, and low inhalant without muscle relaxant [92]. Because of difficulty activating pudendal sensory fibers, the BCR is difficult to elicit in females [93].

The pudendal nerve in the male can be unilaterally stimulated with a subdermal EEG needle electrode as the cathode at the base of the penis lateral to the midline at the 2 and 10 o'clock positions. The reference anode surface electrode can be placed over the lateral aspect of the penis. Ring electrodes

should not be used. With female stimulation, the needle cathode is lateral to the clitoris and needle anode posterior between the major and minor labial folds. Stimulating electrodes are applied with the patient in the supine position and recording electrodes once the patient is positioned prone on the surgical table [1].

In normal awake volunteers, unilateral electrical stimulation of the pudendal nerve resulted in bilateral early and late bulbocavernosus reflex activity. This demonstrated that the early component recorded bilaterally is mediated by crossed spinal cord pathways [94]. Patients with pre-existing peripheral pudendal nerve neuropathy or neuropathy of caudal equina nerves may require a higher stimulation intensity to elicit the BCR. This may result in current spread and activation of both pudendal nerves. Because of this, it may be difficult to stimulate unilaterally in the operating room.

The pudendal innervation of the EAS is mostly uncrossed. The subcutaneous EAS muscle activity may be tonically active in some patients during the entire surgery. This does interfere with the identification of abnormal activity. The EAS muscle is thin and subdermal EEG electrodes are good for making contact with muscle. Two electrodes are inserted over each hemispincter at the anal verge. Surface electrodes should not be used [90].

In 110 patients with thoracolumbar and sacral extradural (degenerative, traumatic, and deformity) and sacral intradural cord untethering, bilateral baseline BCRs were recorded in 86 % of the patients. Responses were present only on one side in 8 % and no responses were elicited in 6 % [90]. Reliable BCRs have been recorded in patients as young as 10 months [95].

There is some variability of the sacral nerve roots involved in the afferent component of this reflex. Most pudendal afferent activity is carried bilaterally in the S1 (4.0 %), S2 (60.5 %), and S3 (35.5 %) roots, although a single bilateral (18.0 %) sacral root or single unilateral root (7.6 %) may be responsible for most pudendal afferent activity [96, 97]. The efferent component of this reflex is through the pudendal nerve supply of the external anal sphincter muscle. The majority of pudendal efferent activity is derived mainly from the second sacral nerve root [98]. These afferent and efferent anatomic variations need to be taken into consideration when interpreting intraoperative BCR recordings.

Intraoperative Application of BCRs

BCR reflexes can be used for real-time monitoring during surgeries such as

reduction of spinal fractures [52], removal of tumors, release of tethered spinal cord [91], etc., where the conus medullaris, sacral nerve roots in the cauda equina and peripheral pudendal nerve are at risk of injury [1]. Little data exist to support the use of the BCR in surgery for spinal cord tethering syndromes [93]. The BCR has been used to monitor the function of a variety of suprasegmental descending spinal cord systems that control the S2, S3, and S4 segmental interneurons [90, 99].

The BCR was recorded as a multiple modality approach including not only the BCR but also F-responses, free-run EMG, tibial SSEPs, and tcMEPs in 184 patients during cervical and thoracic decompression. Ulnar F-responses were also recorded in cervical cases. F-responses and BCRs were used to detect spinal shock secondary to corticospinal tract conduction block [99].

Simultaneously, recorded H-reflexes and the BCR were used to monitor S1–S4 sensory and motor nerve roots, conus medullaris, and suprasegmental function during reduction and stabilization of a L1 burst fracture. Pudendal and tibial SSEPs were also recorded [52].

There are no standard alert criteria for intraoperative BCR recordings. Disappearance of responses that have been stable is a sign of neuronal compromise, especially when associated with a surgical event. This change may be preceded by changes in waveform morphology and may be a warning of impending signal loss [90]. In disorders of the cauda equina, prolonged latency or absence of the BCR response has correlated with neurogenic bladder and erectile dysfunction. Low-threshold changes needed for eliciting the BCR have been observed in upper motor neuron lesions [91]. During surgery, presence of the BCR correlates with intact sphincter control. Loss of the BCR indicates at least transient loss of sphincter function. Long-term follow-up studies still need to be performed to determine the long-term correlation of BCR changes with function [100].

Monosynaptic and Polysynaptic Reflexes: Selective Dorsal Root Rhizotomy

Background

In 1978 and 1979, selective dorsal rhizotomy (SDR) was described. It is a neurosurgical technique designed to reduce spasticity and improve function

in patients with spastic cerebral palsy. At that time at the level of the conus medularis (T12–L1), a laminectomy was performed and to reduce spasticity the facilitatory input into the spinal motor neurons was decreased by selectively cutting 25–50 % of the dorsal spinal rootlets in the cauda equina. Hyperactive sensory rootlets, which contribute the most to spinal cord disinhibition and spasticity, were identified intraoperatively by electrical stimulation and monitoring monosynaptic and polysynaptic reflexes [101, 102].

In the 1980s, the operative site was changed to the cauda equina (L2/L5 or S1, L1/S2) for a clearer anatomic and electrical identification of the dorsal roots in relation to ventral roots [103, 104]. The goal was to decrease spasticity and improve function without disturbing bowel and bladder and sensory and motor function. Initial reports indicated that SDR was found to improve postoperative function, with 80 % of patients showing improved walking and 90 % a reduction of muscle tone. Improved muscle tone in the upper extremities and improved speech occurred in from 60 to 70 % of the patients following lumbosacral dorsal root rhizotomy [105]. SDR demonstrated improved ambulatory function at 1-year follow-up in 81 % of patients with cerebral palsy [106].

There is evidence that the functional results of dorsal root rhizotomy with and without selective electrophysiologic guidance may not be different [107]. Dorsal root rhizotomy was performed on 22 patients with selective electrophysiologic guidance and 22 without electrophysiology using clinical guidance. At 1 year after dorsal root rhizotomy, there were no differences in complications or functional outcome measures between the two groups [108].

Recent reviews with long-term outcomes have indicated that in properly selected patients, SDR remains a safe and clinically useful procedure for the surgical treatment of spasticity in cerebral palsy. Studies indicate that SDR can result in long-lasting benefits [108].

Technical Summary

There is no universally accepted technique but the basic components presented here are included in most protocols:

1. Anesthesia has consisted of isoflurane, nitrous oxide, and fentanyl and short-acting muscle relaxants used only at induction [109]. Total

intravenous anesthesia with no muscle relaxants after intubation can be used. The depth of anesthesia should be carefully adjusted to maintain little or no EMG background but preserve spinal reflexes.

2. Reflex activity can be recorded from the lower and upper extremities, the face and neck. Recording electrodes are inserted into the lumbosacral innervated muscles. All myotome levels from L2 to S4 are represented: adductor longus (L2–L4), vastus medialis (L2–L4), tibialis anterior (L4–S1), gastrocnemius (S1–S2), abductor hallucis (S2–S3), and external anal sphincter (S2–S4) [104].

3. Bowel and bladder function is protected by monitoring external anal sphincter EMG and averaged pudendal nerve action potentials in the cauda equine. The BCR has been recorded [97].

4. The suprasegmental upper extremity (deltoid, biceps, flexor carpi radialis, extensor digitorum communis, abductor pollicis brevis), facial (orbicularis oris, orbicularis oculi), and neck (sternocleidomastoid and trapezius) muscles that are most problematic clinically should be monitored when clinically needed.

   EMG recordings should be made in a bipolar fashion with subdermal EEG needle electrodes. Monopolar EMG needle electrodes and longer uncoated stainless steel needle electrodes may also be used. Fine Teflon-coated silver wires that have the tip bare, which are inserted with a spinal tap needle, can be used for recordings from deep muscles. The active needle is inserted at the motor point of each muscle and the reference needle is inserted distally 4.0 cm from the active needle. The needles are secured with tape. Surface electrodes should not be used because of far-field suppression of EMG signals. A high-frequency filter of 10 KHz and a low-frequency filter of 20 Hz are most often used [32]. At times at least 16 channels of single-sweep recordings are needed to detect all levels of suprasegmental reflex spread. Those muscles that have the greatest spasticity and that limit clinical function the most should be used for recording.

5. A L2/L5 or S1, L1/S2 laminectomy is performed and the nerve roots in

the cauda equina are exposed. During exposure, free-run EMG activity may be recorded during the laminectomy and during manipulation of the nerve roots to help prevent damage to the roots secondary to tension. The S1 nerve root is identified anatomically. The dorsal and ventral roots are separated and the ventral root is electrically stimulated to identify that it is S1. Counting upward the L2 nerve root is anatomically identified and separated into dorsal and ventral components. The remainder of the ventral and dorsal roots are identified.

6. Technique: Identification of sensory and motor roots . In addition to anatomic identification in the surgical field, sensory and motor roots can be identified by electrical stimulation parameters. The dorsal and ventral roots are identified by the difference in electrical single pulse (0.1-ms square wave) threshold needed to cause muscular contraction. Constant current and constant voltage stimulation has been used. With constant current stimulation, the duration is 0.1 ms and the rate of stimulation is 1 Hz (timebase: 100 ms). The sensory and motor root bundles at each spinal level are stimulated and are identified by threshold differences. When using a handheld bipolar hooked electrode, the motor roots have a constant current threshold of less than 1.0 mA and the sensory root threshold is from 2 to 10 mA [67] or 5 to 20 mA (20 V). Bipolar stimulation is used with an interelectrode distance of 0.5–1.0 cm [97]. The ventral root threshold with constant voltage stimulation is 200 mV and the dorsal root 20 V [104]. The S1 root is usually the first identified and is usually the first to be tested. During stimulation, the root is held by the surgeon clear of cerebrospinal fluid and the root is held without tension [105]. The cathode is distal and the intensity is increased until the threshold is reached. The CMAPs recorded help to determine which root has been stimulated. It is important to identify the S2 dorsal root to prevent damage to those sensory fibers subserving bladder reflexes [97]. The sacral sensory nerve roots that contribute to the pudendal nerve may be identified in the cauda equina by stimulation of the pudendal nerves distally and recording in a bipolar fashion from the sacral sensory roots in the surgical field [109]. The electrophysiologic technique used for the identification of sensory and motor nerve roots may block true reflex responses. Gentle retraction of the dorsal rootlets during electrical evaluation should be used to prevent a conduction block of the reflex

afferents. If too much retraction force is used, a conduction block may occur. This may cause confusion regarding identification of sensory and motor roots since electrical stimulation distal to the conduction block may stimulate adjacent ventral roots with the recording of non-reflex motor responses [82].

7. Technique: Identification of hyperactive sensory rootlets.

After the innervation pattern and threshold of the dorsal root has been determined, the root is carefully subdivided into from 2 to 7 smaller rootlets [110]. The threshold for each sensory rootlet may once again be determined. Each rootlet is next stimulated at 50 Hz for 1 s (timebase 2.0 s) to determine which sensory rootlets are hyperactive and need to be sectioned. The duration of each pulse in the 50 Hz train is 0.1 ms. This stimulation intensity is either at the single-pulse threshold or is reduced by 25–30 %. The type and distribution of the reflex EMG pattern is noted for each sensory rootlet stimulated. Bilaterally, the rootlets of the dorsal roots from L2 to S2 are stimulated. In addition to recording CMAPs, the pattern of contraction is observed and palpated by the neurophysiologist. Rootlets controlling the external sphincter muscle and producing pudendal nerve action potentials are spared at the S2 level and usually spared at the S1 level.

The response of each rootlet is graded as: 0—single discharge; 1—sustained, ipsilateral same myotome; 2—sustained, ipsilateral same and ipsilateral adjacent myotome; 3—sustained, many levels ipsilaterally; and 4—sustained, ipsilateral and contralateral and suprasegmental spread. The type of EMG discharge is noted as decremental, squared, decremental-squared, incremental, multiphasic, clonic, and sustained. Clonic, incremental, multiphasic, and sustained discharges are considered criteria for rootlet sectioning and rootlets with a grade of 3 or 4 are usually sectioned. From 25 to 80 % of the rootlets at each level are sectioned. Criteria for sectioning rootlets are based on clinical and electrical observations and the movement observed during electrical stimulation [110, 111].

Blink Reflex

The electrically elicited blink reflex (BR) is analogous to the corneal reflex tested in clinical practice. It was first reported in 1952 [112]. Unilateral

stimulation of the supraorbital nerve enters the pons and elicits two responses recorded bilaterally from the orbicularis oculi muscles. An earlier latency R1 direct response is recorded on the side of stimulation and a longer latency R2 indirect response is recorded bilaterally. Sensory fibers originating in the supraorbital nerve travel to their cell bodies in the trigeminal ganglion. From this ganglion, the action potentials diverge into two separate pathways. The first pathway is a disynaptic or oligosynaptic pathway that travels rostrally to synapse in the principal sensory nucleus. A second-order pathway travels from here to synapse and depolarize the facial nucleus and the R1 component is recorded. Those fibers not connecting in the principal nucleus form the second pathway that diverges caudally in the lateral medullary plate. After several synapses two separate tracts course rostrally both unilaterally and contralaterally to the side of stimulation. They synapse and depolarize the facial nuclei and induce contraction of both orbicularis oculi muscles. The ipsilateral and contralateral polysynaptic R2 components are recorded, which is the BR (Fig. 8.9).

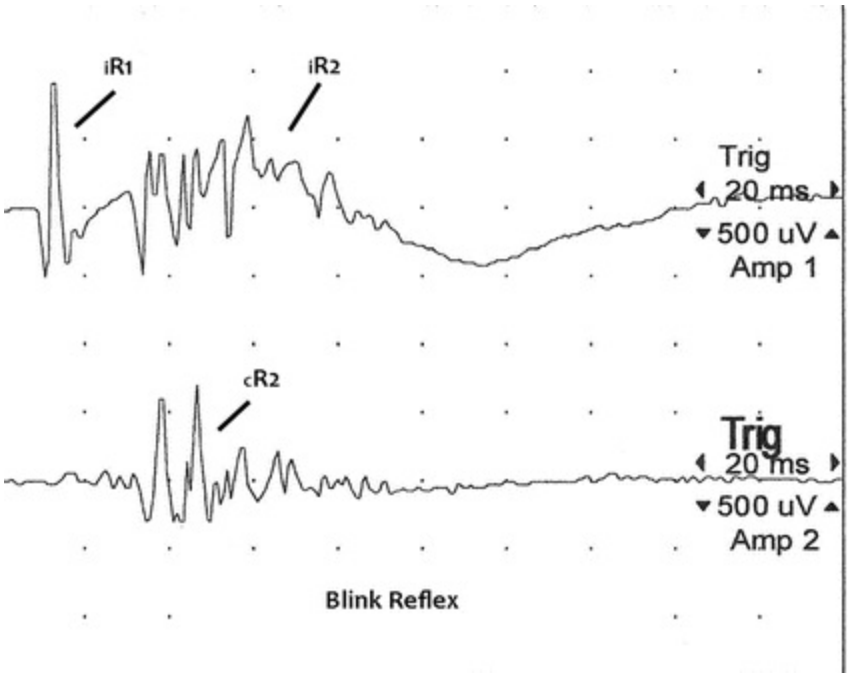

Fig. 8.9 Electrically stimulated blink reflexes recorded in a 20-year-old awake woman. The right supraorbital nerve is stimulated with the ipsilateral R1 (8.0 ms) and R2 (30.0 ms) and the contralateral R2 (30.0 ms) components recorded from the orbicularis oculi muscles

The BR examines the supraorbital and facial nerves and brainstem pathways. The BR can be elicited following infraorbital and mentalis nerve

stimulation but with less consistency than the supraorbital nerve. Clinically, the BR has been used to study lesions of the trigeminal nerve, Bell's palsy, hemifacial spasm, acoustic neuroma, polyneuropathy, multiple sclerosis, etc. [113–115].

Intraoperatively, a single stimulus or a short train of four to seven stimuli (interstimulus interval: 2 ms, intensity: 20–40 mA, train repetition rate: 0.4 Hz) applied over the supraorbital nerve were used to elicit the R1 component of the BR. Anesthesia was either propofol and fentanyl or low-dose inhalation agents (sevoflurane or desflurane). Supraorbital nerve stimulation in the first five patients was with a pair of subdermal EEG needle electrodes and the remainder with a pair of surface electrodes. Recording was from the ipsilateral orbicularis oculi muscle with subdermal EEG electrodes. Two single responses were averaged and after the first response the stimulation polarity was reversed to reduce the large stimulus artifact. Recordings were attempted in 27 patients without involvement of the facial and trigeminal nerves or brainstem. The BR was recorded in 23 patients. Boluses of propofol and muscle relaxation should be avoided with these recordings [116].

This BR technique , in addition to the ABR, lateral spread, F-response, and corticobulbar motor-evoked potentials were used to determine adequacy of decompression during microvascular decompression for hemifacial spasm. Before decompression, larger BR responses on the symptomatic side are the result of facial motor nucleus hyperexcitability. BR amplitudes are decreased with adequate decompression and may require an increase in the number stimuli in the train to elicit the response. This is because of decreased facial motor nucleus excitability [117].

In 17 cases of cerebellopontine angle operations, the BR in addition to free-run EMG were monitored. The BR was helpful to monitor facial nerve function during periods when the facial nerve could not be visualized before debulking of the tumor. Bilateral BRs were elicited by bilateral percutaneous supraorbital nerve electrical stimulation (0.1 ms duration, 5–20 mA) every 10–20 s. Orbicularis oculi BR R1 and R2 responses were recorded with surface electrodes. Preoperatively, R1 ipsilateral amplitudes were lower than contralateral R1 amplitudes. In two patients with 39- and 43-mm tumors, ipsilateral R1 was absent and contralateral R1 amplitude was deceased. R1 was considered to be abnormal when the response was lost or when the latency was longer than 15.0 ms or a side difference greater than 3.0 ms. R2 was considered to be abnormal when the response was lost or the latency was

longer than 55.0 ms or a side-to-side difference greater than 10.0 ms. Fifteen patients had preoperative changes present in the R1 and R2 responses. Postoperative recordings showed improved amplitudes and decreased latencies in all patients. Anesthesia was maintained with propofol or propofol/ketamine mixture plus narcotic. Muscle relaxants were avoided prior to EMG recordings [118].

The change in the R1 BR response latency was studied to determine if the change from before to after surgery could predict postoperative facial nerve outcome in 91 patients who had a translabyrinthine surgical approach for a vestibular schwannoma that filled the internal auditory meatus. If there was no change in the latency, normal facial function was present at 1 year. Outcome was not favorable with an increased latency unless the tumor was small. The value of R1 change is indicative of facial nerve function in patients with immediate complete facial paralysis. Change in R1 blink reflex has an excellent prognostic value for anticipating difficulties with facial nerve dissection and postoperative facial function after 1 year [119].

Bispectral index (BIS) and the R1 BR response were used to study the relative roles of forebrain and brainstem in producing adequate anesthesia using sevoflurane or propofol in humans. The blink reflex as a measure of brainstem function was more sensitive to sevoflurane or propofol than BIS as a measure of forebrain function. High-concentration sevoflurane suppressed the BR more than propofol. The results indicated that there are different effect sites for the BR and BIS [120].

Lower Extremity Intralimb and Interlimb Polysynaptic Reflexes

Another late response that can be recorded are intralimb (ipsilateral) and interlimb (contralateral) lower extremity reflexes , which are abnormal reflexes that are recorded simultaneously from four muscle groups in each lower extremity following unilateral simultaneous stimulation of the tibial and common peroneal nerves in the popliteal fossa. The onset latency is from 20.8 to 243 ms and the duration from 421 to 4095 ms [121, 122]. This technique not only monitors segmental afferent and efferent activity at the L4, L5, and S1, S2 levels and L4, L5, and S1, S2 interneuronal function, but also monitors complex spinal cord polysynaptic processing, which can involve multiple suprasegmental levels. The anesthesia was maintained with

50 % nitrous oxide, a continuous infusion of afentanil (2 μg/kg/min), 0.2–0.5 % isoflurane, and 50 % or less NMJ blockade.

These reflexes can be recorded from not only ipsilateral (intralimb) and contralateral (interlimb) lower extremity muscles but the distribution of the reflex activity also affects proximal and distal muscles differently. The explanation for this proximal-distal distribution is that vestibulospinal and reticulospinal pathways control proximal lower extremity muscles, and proximal lower extremity changes may represent a suprasegmental compromise of these descending vestibulospinal and reticulospinal pathways. Rubrospinal and corticospinal pathways control distal lower extremity function [11], and distal lower extremity reflex changes may represent a suprasegmental compromise of these descending rubrospinal and corticospinal pathways.

Baseline lower extremity intralimb and interlimb polysynaptic reflexes are present in the intraoperative recordings because of pre-existing neurologic deficits. Chronic spinal cord or nerve root compromise uncouples the spinal cord CPGs due to disinhibition, and polysynaptic reflexes may be present during the baseline intraoperative recordings. Baseline lower extremity intralimb and interlimb reflex activity was first observed in patients with idiopathic scoliosis. Since these reflexes were not present in baseline recordings in neurologically normal nonscoliosis patients, it was felt that the presence in idiopathic scoliosis patients was either because of congenital abnormal spinal cord signal processing or because of the effect of the spinal curvature on the spinal cord. These baseline reflexes in idiopathic scoliosis patients may contribute to the development of the spinal curve [123]. With intraoperative acute spinal cord or nerve root compromise, previously absent reflexes may become present with the abnormal uncoupling of the spinal cord CPGs.

During the monitoring of cervical spine surgery patients with cervical myelopathy and lower extremity symptoms, intraoperative baseline lower extremity intralimb and interlimb reflex activity was present while those without myelopathy did not have baseline lower extremity polysynaptic activity present. In both groups, transient intraoperative lower extremity intralimb and interlimb reflex changes were present with manipulation of the cervical spine without changes in SSEP components [122]. Transient asynchronous polysynaptic reflex changes have not been associated with a postoperative neurologic deficit, whereas persistent high-amplitude

synchronous reflex changes have been associated with a postoperative lower extremity deficit [1, 122, 124].

Before tcMEP became available for motor system monitoring, the author monitored spinal surgery with SSEPs, H-reflexes, F-responses, free-run EMG, and intralimb and interlimb reflexes using three monitoring instruments. With the addition of tcMEP monitoring, the intralimb and interlimb recordings were eliminated because of limited instrumentation. For suprasegmental spinal motor tract injury, monitoring these reflexes may provide similar information as the mechanically induced peripheral free-run EMG recordings that were described in 2009 [99].

Conclusion

Intraoperative reflex techniques help accomplish the three main goals of intraoperative neurophysiologic monitoring. Recordings are single sweep and in real time with no delay after the onset of compromise. They provide the surgeon with immediate feedback and can be acquired continuously throughout surgery with little or no noticeable patient movement. Reflexes may be monitored in patients in whom SSEPs and tcMEPs cannot be recorded because of a pre-existing neurologic deficit. When used in conjunction with SSEPs, tcMEPs, free-run, and electrically stimulated EMG, reflexes enhance a multisystems approach to monitoring [1, 2, 55, 91, 125].

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Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_9

9. Brain and Spinal Cord Mapping

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Keywords Cortical mapping – Presurgical mapping – Craniotomies – Central sulcus – SSEP polarity reversal – Motor-evoked potentials – Primary motor cortex – Electrical stimulation – Subcortical mapping – Spinal cord mapping

Key Learning Points

- Cantral sulcus can be identified by SEP polarity reversal.
- Brief high-frequency train stimuli are less likely to induce seizures than long lower frequency trains.
- Direct cortical stimulation of motor cortex after it is located can be continuously employed for monitoring corticospinal tract function.
- Subcortical stimulation can determine rough distance to CST using

calibration 1 mA = 1 mm.

Introduction

Surgery for resection of cerebral tumors or epileptic foci carries risks of damage to cortical areas involved in sensory, motor, language, and memory function. Even with modern anatomic and functional imaging techniques, preoperative studies are not sufficient if the surgeon wishes to obtain maximal resection of abnormal tissue while preserving neural function. Thus, intraoperative mapping techniques have been utilized for over 80 years to provide detailed delineation of functional areas during surgery. This chapter reviews the current state-of-the-art techniques and also briefly considers new techniques now being developed. While language and memory mapping during awake craniotomies will be discussed, the primary emphasis will be on techniques for mapping sensory and motor cortical regions during craniotomies performed under general anesthesia. Additionally, recent techniques for mapping the corticospinal tracts within subcortical and spinal regions as well as mapping of the dorsal columns will be highlighted.

Beginning in the 1930s, the pioneering neurosurgeon, Wilder Penfield, began the systematic mapping of sensory, motor, and language cortex. Working with the neurophysiologist Herbert Jasper, Penfield confirmed the topographic organization of the human cortex, and obtained the first detailed maps of the human sensory and motor homunculi. Using low-voltage stimulation at 60 Hz, the powerline frequency, and working during awake craniotomies, they also mapped the cortical regions subserving language and memory functions. Their observations were described in a landmark publication [1] and in a subsequent book [2]. This method remained the state of the art for almost 50 years.

In the 1970s, George Ojemann began the modern era of intraoperative mapping with a series of elegant studies, carried out in collaboration with neuropsychologists including Harry Whitaker [3]. These studies dramatically enhanced our understanding of cortical organization for language and memory functions, and also led to the development of a specialized battery-powered stimulator specifically designed for cortical stimulation . This stimulator, marketed by Radionics as the OCS-2, is still commonly used, although new developments to be described below may soon render the Penfield–Ojemann method obsolete. Other stimulators designed for a similar

purpose are the Grass S12X (Natus Neurology Incorporated–Grass Products, Warwick, RI) and the Nicolet Cortical Stimulator (Natus Neurology Incorporated, Middleton, WI). These devices, primarily designed for stimulation mapping with simultaneous electrocorticography, incorporate a switching matrix that allows the current to be delivered to any combination of electrodes in a multi-electrode grid. However, none of these devices can be externally triggered, a feature that would allow them to deliver brief high-frequency trains analogous to those used in direct cortical and transcranial motor-evoked potentials (tcMEPs).

Recent studies have shown a positive correlation between maximal resection for both low- and high-grade gliomas and patient outcomes, including long-term survival and quality of life [4, 5]. While gross total resection is always the goal, it has to be balanced with the risk of developing neurologic deficits by mechanical or vascular injury. To this end, the latest intraoperative techniques focus on precisely identifying eloquent cortical regions, monitoring their functional integrity, as well as providing continuous feedback on the distance to corticospinal tract fibers (see below).

Presurgical Mapping

The development of functional imaging technologies, particularly functional magnetic resonance imaging (fMRI) , magnetoencephalography (MEG) , and transcranial magnetic stimulation (TMS) , has made it possible to visualize cortical areas activated during sensory, motor, or language tasks. When superimposed on high-resolution anatomical images, and integrated with image-guided navigational systems, it is in principle possible to plan a craniotomy for optimal exposure of areas to be resected in relation to functional or “eloquent” cortex. Another potentially valuable technique is MRI diffusion tensor imaging (DTI) of white matter tracts involved in language and motor function. However, these techniques have not yet been standardized, and given the potentially devastating consequences of inadvertent damage to important functional regions, intraoperative mapping techniques utilizing electrical stimulation and recording are still the “gold standard.” Because presurgical mapping techniques have not yet been incorporated into routine clinical practice, they will not be further considered in this chapter.

Mapping During Awake Craniotomies

While it is now possible to localize cortical regions involved in sensory and motor function under general anesthesia, mapping of cortical areas subserving language still requires the participation of the patient during craniotomies conducted under local anesthesia (for a detailed description of the anesthesia, see Chap. 22, “Intracranial AVM Surgery”). Assessment of spontaneous speech, fluency, visual naming, and sometimes memory functions are then carried out, often with the collaboration of a neuropsychologist.

Mapping is based on the presumption that electrical stimulation disrupts the normal function of the cortical area being stimulated. Continuous stimulation, typically at 60 Hz, is briefly applied to exposed cortical areas during task performance. Areas with a positive response to stimulation (disruption of task performance) are tagged with sterile markers and the mapping proceeds until the entire region surrounding the desired resection zone has been mapped. Typically, a margin of 1 cm surrounding positive sites is left intact to minimize disruption of language function.

This method of mapping, termed “positive mapping ,” requires an extensive craniotomy to expose intact cortex adjacent to the zone of planned resection. Sinai et al. [6] proposed a different paradigm, based on negative mapping results within a more limited craniotomy restricted to the zone of planned resection. The presumption is that negative sites, those not producing disruption of language function with stimulation, can be safely resected even in the absence of positive mapping. This procedure is still controversial, and in fact contradicts recommendations previously made by one of the same authors but, if further validated, offers the promise of smaller, tailored craniotomies with minimal cortical exposure, less extensive intraoperative mapping, and a more rapid neurosurgical procedure.

Hamberger et al. [7] noted that surgery including hippocampal resection was associated with deficits in visual naming, where the patient speaks the name of familiar objects presented by pictures (e.g., house, car, dog) even with preservation of all cortical sites in which visual naming was affected by stimulation. This interesting finding suggests a role for the hippocampus in visual naming, as well as underlying the importance of memory testing as well as fluency and visual naming during resection of dominant hemisphere tumors during awake craniotomies.

Recent papers validate the safety and efficacy of performing awake

craniotomies. The perioperative complication rate is 10 %, including a 3 % risk of stimulus-induced seizures that typically can be successfully aborted with cold saline. Safety was found to be unrelated to the American Society of Anesthesiologists classification, body mass index, smoking status, mental illness history, seizure history, or type and size of tumor [8]. Moreover, in a meta-analysis study, awake craniotomy was associated with a decreased likelihood of developing postoperative deficits, shorter hospital stay, and even slightly decreased surgery time compared to surgery under general anesthesia [9].

Location of the Central Sulcus by SSEP Polarity Reversal

As is well known, the central sulcus is one of the most important landmarks in the human brain, with primary somatosensory cortex located in the postcentral gyrus and primary motor cortex in the precentral gyrus. Both sensory and motor cortical areas are organized according to the well-known "functional homunculus ," in which the face area occupies approximately the most lateral one-third of the homunculus, the hand area occupies the next one-third, and the representation of the rest of the body occupies the remaining one-third, with the foot representation located on the medial surface of each hemisphere. This functional distortion reflects the relative importance of direct cortical control of muscles involved in speech, facial expression, and manipulation of objects with the hands. In the original Penfield studies performed during awake craniotomies, patients would report sensations referred to appropriate parts of the body when the corresponding sensory cortical region was stimulated, and movements when the corresponding areas of primary motor cortex were activated.

Today, however, the sensory and motor cortical areas can be located and mapped under general anesthesia with the use of appropriate electrical stimulation and recording . We will first describe the localization of the central sulcus by mapping the polarity reversal of the initial cortical components of the somatosensory-evoked potential (SSEP). While there are many parallel pathways mediating the various modalities of somatic sensation (e.g., touch, joint position sense, pain, temperature), the SSEP is exclusively generated by activity in the dorsal column/medial lemniscus system (see Chap. 1, "Somatosensory-Evoked Potentials"). Information

travels in the dorsal columns of the spinal cord, synapsing in the dorsal column nuclei (gracilis and cuneatus) in the lower medulla, crossing the midline in the medial lemniscus, with a final synapse in the ventral posterior lateral nucleus of the thalamus (VPL) before projecting to the primary somatosensory cortex in the postcentral gyrus.

Whereas many neuronal cell types are activated by somatic stimulation , only the pyramidal cells have an extended geometry that can produce extracellular currents sufficient to be recorded with electrodes on the scalp or the surface of the exposed cortex. In the case of the SSEP resulting from median or ulnar nerve stimulation, the initial cortical response, typically recorded with scalp electrodes over the arrival region, is a negativity occurring at about 20 ms poststimulus, commonly termed N20. In fact, this response could equally be termed P20 because it is generated by a cortical dipole oriented parallel to the cortical surface, with its negative pole posterior and a corresponding positive pole anterior [10, 11] (Fig. 9.1a).

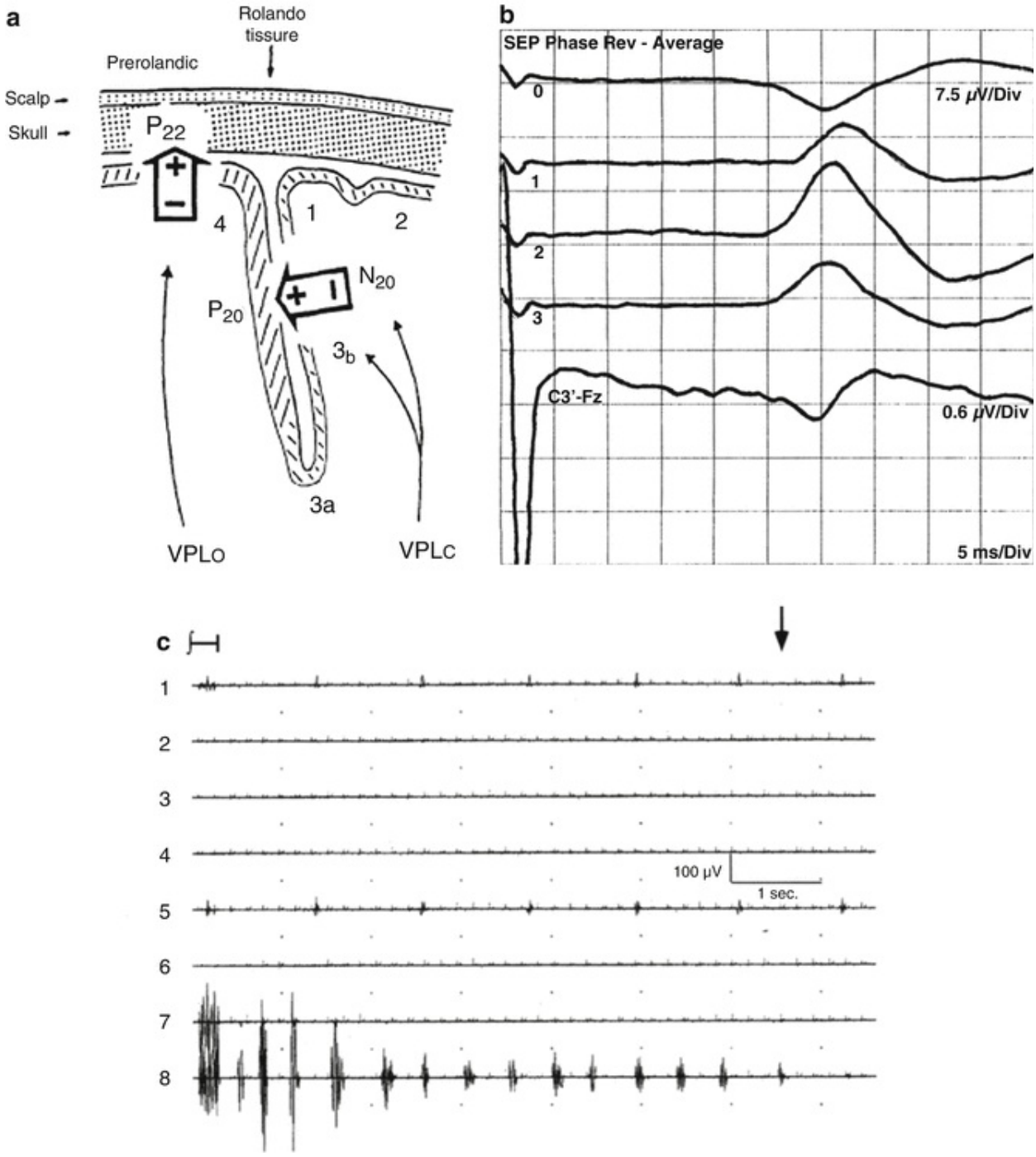

Fig. 9.1 (**a**) Diagrammatic axial section through the central sulcus at the level of the hand area of sensorimotor cortex, showing the earliest cortical dipoles activated after finger stimulation. Note the generator of the N/P20 in the postcentral gyrus , which is oriented parallel to the scalp so that the primary response reverses polarity from posterior–anterior, while the generator of P22 in the precentral gyrus is oriented perpendicular to the scalp so a surface electrode only sees the positive end of this dipole, which is activated slightly later. Responses seen at the scalp or cortical surface are a spatiotemporal summation of these two sources. (Adapted from Desmedt et al. [10]). (**b**) Photography of six contact strip electrode spanning the presumed central sulcus. (**c**) Responses to right (R) ulnar

nerve stimulation recorded from cortical surface with four contract strip (traces 0–3) and scalp (C3′—Fz). Positivity is up; note N20 (at latency of ~ 30 ms in this tall patient) in scalp recording and postcentral contact 0 with positivity at precentral contacts 1–3. Positivity shows longer latency in contact 1 due to contribution from second (P22) dipole in precentral gyrus

The polarity reversal of N/P20 is easy to visualize. Imagine a monopolar electrode, referenced to an inactive site, which is moved along the surface of the cortex perpendicular to the central sulcus at the time of the peak of N/P20. When the electrode is posterior to the generator (in the postcentral sulcus), a negativity will be recorded. As the electrode moves anteriorly, the negativity will reach a maximum and then drop to zero when the electrode is equidistant from the positive and negative ends of the dipole. As the electrode continues to move anteriorly, it will record the positivity, which will gradually decrease as the electrode is moved further forward away from the dipole area. If instead of a single electrode being moved, we now imagine a strip of electrodes with some contacts posterior and some anterior to the central sulcus, we see that the posterior electrodes will record a negativity at the same time as the anterior electrodes record a positivity. Paradoxically, an electrode contact directly over the dipole generator will record zero, even though it is closest to the active generator, because the contributions from the negative and positive poles of the dipole will cancel one another out.

The situation is slightly complicated by the fact that a second dipole, which is activated a few milliseconds later, is located in the precentral gyrus . This dipole, however, is oriented perpendicular to the cortical surface, and when activated causes a surface positivity and negativity that could only be recorded by a depth electrode underneath the pyramidal cell layer. This component is termed P22 and is recorded at the cortical surface only as positivity at a slightly longer latency than N20. Because an electrode at the cortical surface will record the sum of the activity of these two generators, the positivity over the precentral gyrus may appear to be at a slightly longer latency than the negativity seen posteriorly, depending on the exact orientation of the generators in relation to the location of the recording electrodes. With this minor caveat, the polarity reversal of the SSEP resulting from median nerve stimulation is easy to interpret, and will accurately define the location of the central sulcus. The polarity reversal can be easily recorded with a strip electrode, typically with four to eight contacts aligned at 1-cm intervals, or with a two-dimensional array or grid electrode (see Fig. 9.1b, c).

To record the polarity reversal , the electrode must be positioned so that it

is over the hand area of the somatosensory cortex, with some contacts anterior and some posterior to the central sulcus. This may require adjustment of the electrode position to obtain optimal recordings. For example, if a negativity is recorded at all contacts, the entire electrode is probably posterior to the central sulcus and needs to be moved anteriorly. This happens more often than might be expected, particularly if preoperative functional imaging is not available. This is because the location of the central sulcus, which divides primary sensory from primary motor cortex, may vary by several centimeters from individual to individual with respect to external skull landmarks. This variability is why functional mapping is vitally important to avoid inadvertent resection of primary sensory and motor areas.

With a one-dimensional strip electrode, the waveforms can be simply displayed, one above the other, in the same order as the electrode contacts. This makes identification of the polarity reversal quite easy. With a grid electrode, the situation is more complicated, and ideally the waveforms should be displayed in a two-dimensional pattern corresponding to the arrangement of the contacts on the electrode. Alternatively, the distribution of electrical potentials at each time point can be displayed as a color map, in much the same fashion that temperature gradients are displayed in weather maps. For example, if negative potentials are displayed in different shades of blue and positive potentials in different shades of red, then the border between red and blue areas will define the central sulcus [12].

Finally, note that the SSEP polarity reversal can be recorded either from the surface of the cortex, as would be done prior to resection of a tumor in this region, or epidurally, for example during implantation of a motor cortex-stimulating electrode for control of chronic pain. In all cases, it is important to record at least one scalp channel of SSEP, in order to confirm the precise latency of N20, which may vary during a procedure, as it is significantly affected by peripheral temperature changes.

Because the SSEP signals recorded directly from the cortical surface are much larger than those recorded at the scalp, any anesthetic technique that is compatible with recording scalp SSEP will be suitable for cortical recordings. In fact, if SSEP recordings are the only mapping technique that will be utilized, neuromuscular blockade can be used, and will often improve the signal-to-noise ratio by eliminating the possibility of scalp EMG contamination. However, because motor mapping is usually done in the same context, neuromuscular blockade is generally contraindicated.

Location of the Primary Motor Cortex with Electrical Stimulation

The SSEP polarity reversal is often recorded first, as this provides a quick indication of the location of the central sulcus. Once the central sulcus is defined, and the presumed location of primary motor cortex is thus established, then the motor cortex is typically mapped with electrical stimulation. This complementary method confirms the results obtained with SSEP mapping and allows further delineation of the topographic organization of the motor cortex.

Until recently, motor mapping has been performed using essentially the same techniques pioneered by Penfield in the 1930s. The Ojemann OCS-2 Cortical Stimulator (Integra Life Sciences, Plainsboro, NJ) is used with a handheld electrode. Using bipolar electrical pulses of 1-ms duration at 60 Hz, and beginning at approximately 3-mA intensity, the electrode is placed on the cortical surface for about 1 s, and any movements on the contralateral side are noted. Yingling et al. [13] showed that the sensitivity of this mapping technique could be enhanced by simultaneous EMG recordings from multiple muscle groups contralateral to the side of stimulation (Fig. 9.2a). This method has several advantages; EMG activity can often be seen at much lower stimulation intensities than are necessary to produce overt movements, and the requirement to expose and observe the entire contralateral body is eliminated as it is relatively easy to scan multiple EMG channels for activity occurring at any location. Patients who are awake (i.e., with local anesthesia) may note “tugging” or other motor changes before visible motor activity occurs.

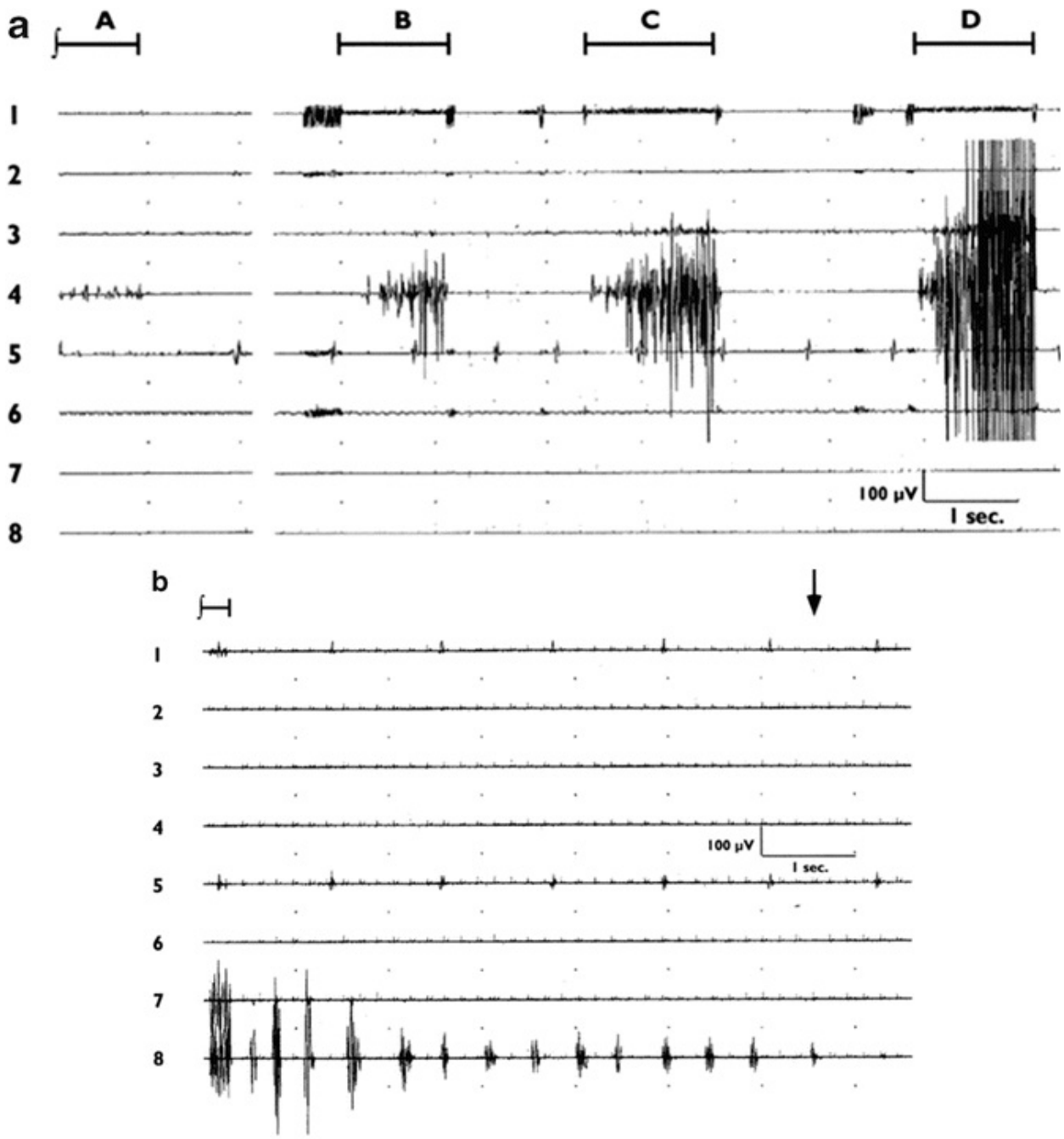

Fig. 9.2 (**a**) EMG responses to stimulation of the forearm area of cerebral cortex (time indicated by *bars* above traces) at 3.6 mA (*A*, *B*), 5 mA (*C*), and 6.2 mA (*D*). Traces (*top* to *bottom*) represent face, shoulder, upper arm, forearm, hand, upper leg, lower leg, and foot muscles. Overt movement was not evident except with the highest level of stimulation in trace *D*. (Reprinted with permission from Yingling et al. [13]). (**b**) Clonic seizure activity manifesting as rhythmic EMG activity in foot muscles after stimulation of the medial area of the sensorimotor cortex. (Stimulation began before the trace, as indicated by the *bar* at the *top left*). Activity was terminated by application of cold lactated Ringer's solution to the cortical surface (time indicated by an *arrow* at the *top right*). (Reprinted with permission from Yingling et al. [13])

If no motor responses are obtained at an initial current setting of 3 mA, the current is increased, typically 1 mA at a time, and the mapping process is repeated until consistent responses are obtained and the organization of the cortical homunculus is confirmed. However, this method is not without its faults. In the Yingling et al. [13] study, 1-s stimulus trains elicited motor seizures in 24 % of the patients (Fig. 9.2b). While many of these were minor and self-terminating, they occasionally persisted or even increased in intensity or spread to other regions of the body, and had to be terminated by application of cold Ringer's solution to the cortical surface [14]. A second problem with this technique is that it requires the active participation of the surgeon, and thus is a method for mapping, but does not permit continuous monitoring of corticospinal tract function during tumor resection. Transcranial MEPs (see Chap. 2, "Transcranial Motor-Evoked Potentials") are often used for monitoring motor tract function, but transcranial stimulation may activate white matter tracts at a considerable depth below the surface of the cortex, and thus fail to detect motor pathway compromise at more superficial locations [15].

Years of experience with transcranial MEP recordings have demonstrated that this technique has an extremely low incidence of induced seizures [16]. This is presumably due to the brief duration of the stimulus trains employed, typically on the order of 10 ms, compared to the 1-s simulation used in the Penfield/Ojemann technique . This has led to the development of a new technique for cortical mapping under general anesthesia, using brief pulse trains similar to those employed with transcranial MEPs , but at a much lower intensity and applied directly to the cortical surface. While this technique had first been described by Taniguchi et al. [17], the first clinical series were published by Cedzich et al. [18] and Kombos et al. [19]. The combined data from these two studies show a success rate of 96 % in obtaining direct cortical MEP, with no seizures reported in either study.

We have had extensive experience using this technique in the San Francisco area during the past 8 years (Fig. 9.3). Typically, trains of 3–5 pulses, with 2-ms interstimulus intervals, are sufficient. Using 50-μs duration pulses, we typically obtain thresholds ranging from roughly 20–150 mA. Although this seems high when compared with thresholds obtained using the Ojemann or comparable stimulators , the total charge per pulse delivered to the brain is roughly equivalent. This is because the 50-μs duration pulses used in our train technique (due to limitations of the stimulator) are each 1/20

of the duration of the 1-ms pulses commonly employed in the 60-Hz technique. Because the total charge delivered to the brain is the product of current × time, the thresholds obtained with such brief pulses should be divided by 20 to compare them with the thresholds obtained using the traditional technique. Thus, these thresholds would be equivalent to 1–7.5 mA using a 1-ms pulse width.

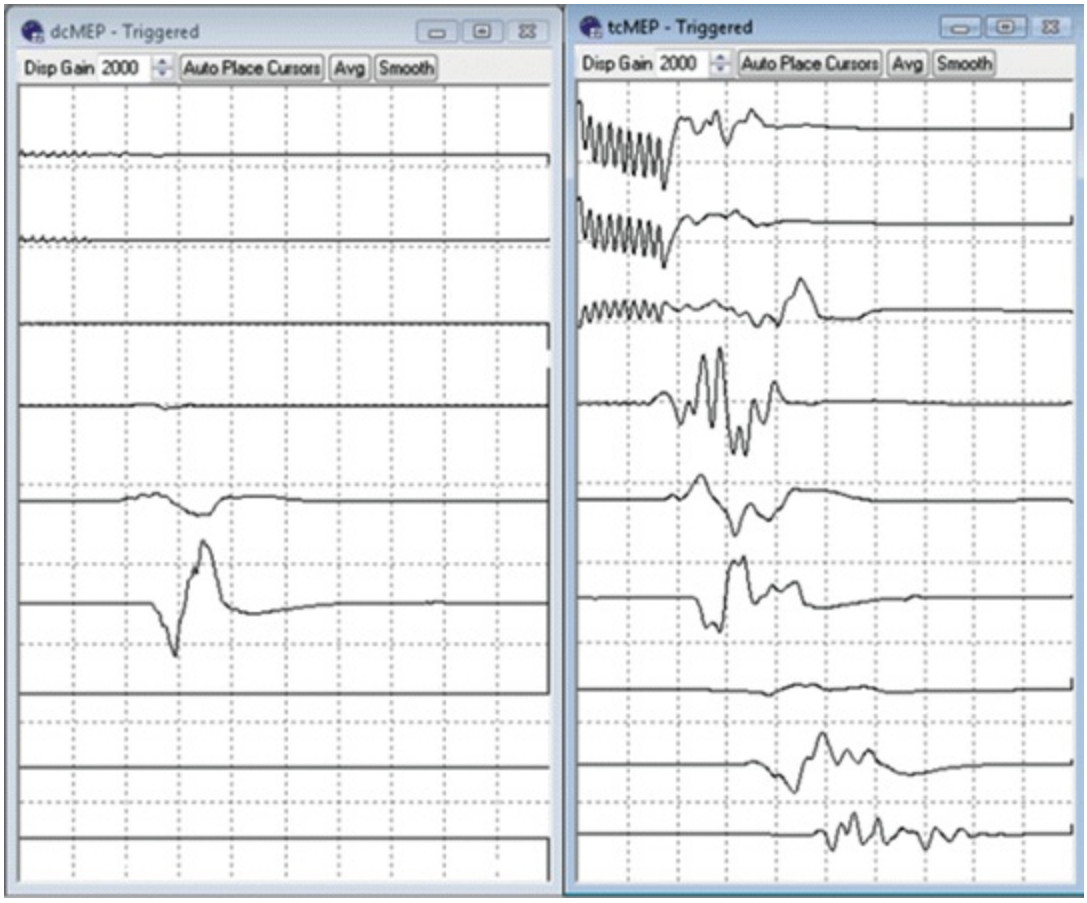

Fig. 9.3 MEP responses to direct cortical stimulation (*left*) and transcranial stimulation (*right*). Traces (*top* to *bottom*) orbicularis oris, trapezius, deltoid, biceps, flexor carpi ulnaris, abductor pollicis brevis, rectus femoris, gastrocnemius, and abductor hallucis. Note the focal nature of the responses to direct cortical stimulation (40 V), in contrast to responses seen in all channels following transcranial stimulation (300 V) due to spread of current through the scalp/skull and/or subcortical activation of the corticospinal tract

Note that the above comparisons are per pulse. With the traditional method, a 60-Hz pulse train is typically applied to the cortical surface for approximately 1 s, or 60 pulses total. (Even longer trains of 3–4 s duration are typically employed for language mapping.) In contrast, the direct cortical

stimulation technique (dcMEP) delivers a total of 5 pulses or less, a full order of magnitude fewer than with the traditional technique. This is a probable reason why the dcMEP technique does not appear to induce seizure activity. In our recent series, of 118 patients in whom the dcMEP technique was used, 12 were also stimulated at 60 Hz with the Ojemann stimulator. Five of these 12 exhibited overt seizures or after discharges with 60-Hz stimulation, whereas none of the 118 patients had seizures following brief train stimulation (Yingling et al., unpublished data).

The lack of induced seizures and the minimal movement produced are the foundation for the second great advantage of the train technique over the traditional 60-Hz technique. Once the precentral gyrus has been mapped, a strip electrode can be left over the motor cortex and regularly stimulated while tumor resection proceeds. Unlike transcranial MEPs, which may produce overt movement requiring the surgeon to temporarily halt resection during MEP stimulation, the strip electrode can be repeatedly activated to provide continuous monitoring of corticospinal tract function during tumor resection. Thus, the dcMEP technique for motor *mapping* can also be used to provide continuous *monitoring*.

Recent studies have used neuromonitoring equipment with stimulators capable of delivering rapid pulse trains with wider pulse durations (200–500 μs). These settings allowed for lower intensity thresholds (≤20 mA) to activate the motor cortex and frequent stimulation to provide early detection of changes during tumor resections [20–23]. (Note that as of July 2015, there are no FDA-approved cortical stimulators capable of delivering rapid pulse trains with any stimulus duration; therefore, all the techniques discussed in this section require the off-label use of FDA-approved products, with appropriate informed consent.) Whereas most authors noted the motor threshold (minimum stimulation intensity to elicit a response) and used increases in the threshold as a warning sign, there is no consensus on what amount of intensity increase constitutes a significant change.

Subcortical Mapping

While continuous dcMEP monitoring during tumor resection can detect damage to the corticospinal tract at the subcortical level, it is preferable to avoid such damage by utilizing subcortical mapping techniques. Again, stimulation of subcortical white matter can be performed using the Ojemann

stimulator with a bipolar probe or with the brief train technique using either bipolar or monopolar stimulation. While subcortical stimulation does not seem likely to induce seizure activity, presumably because of the lack of direct activation of cortical networks, the brief train technique is nevertheless emerging as the preferred method for subcortical mapping. Monopolar stimulation appears to be preferable to bipolar stimulation in this context [24]. More recently, monopolar cathodal stimulation is favored over monopolar anodal stimulation. The argument is that the former allows for better tissue penetration and activates the corticospinal tract at lower stimulation intensities [25].

The key issue for subcortical mapping is whether or not there is a consistent relationship between stimulation parameters and distance to the corticospinal tract. Fortunately, several recent studies have produced strikingly similar findings. Using similar stimulation settings as for direct cortical MEPs (pulse widths of 200–500 μs and trains of 5 pulses at 2–4 ms interstimulus intervals), a consistent relationship of approximately 1 mm/mA has been found [20–22]. In other words, a stimulation threshold of 10 mA indicates that the tip of the stimulating probe is 1 cm from the corticospinal tract.

The combination of subcortical mapping and continuous MEPs evoked by direct cortical stimulation has been shown to be an effective tool for optimizing tumor resection while avoiding inadvertent damage to motor tracts. Furthermore, recent papers have proposed methods that integrate monopolar stimulation with commonly used surgical instruments so that the distance to the corticospinal tract can be assessed at the same time tumor removal is taking place. Raabe et al. [23] connected the cable for the standard monopolar probe directly to the suction device, transforming it into a “continuous dynamic mapping device.” The tip of the suction-monopolar device held in one hand moves to the same areas within the tumor cavity as the bipolar forceps or the ultrasonic aspirator held in the other hand (Fig. 9.4). As tumor removal proceeds closer to the corticospinal tract, the stimulation intensity needed to elicit an MEP decreases. Resection was usually halted when the motor threshold was 3 mA. However, in cases in which the surgeon predetermined that a gross total resection could be safely achieved, resection continued until the motor threshold was as low as 1 mA. Likewise, Shiban et al. [26] connected an ultrasonic surgical aspirator to a neuromonitoring stimulator via an adapter cable in order for it to be used

simultaneously as a tumor removal device and a monopolar probe. In this study, a motor threshold of 3 mA or less was also defined as the tumor resection stopping point. Both methods enable the surgeon to work uninterrupted compared to having to test with the handheld monopolar probe, and thus rely less on the surgeon deciding to take a pause from resecting to evaluate the distance to the corticospinal tract. Thus, they hold the promise of enabling the surgeon to efficiently obtain maximal tumor resection with reduced risk of a patient developing post op weakness.

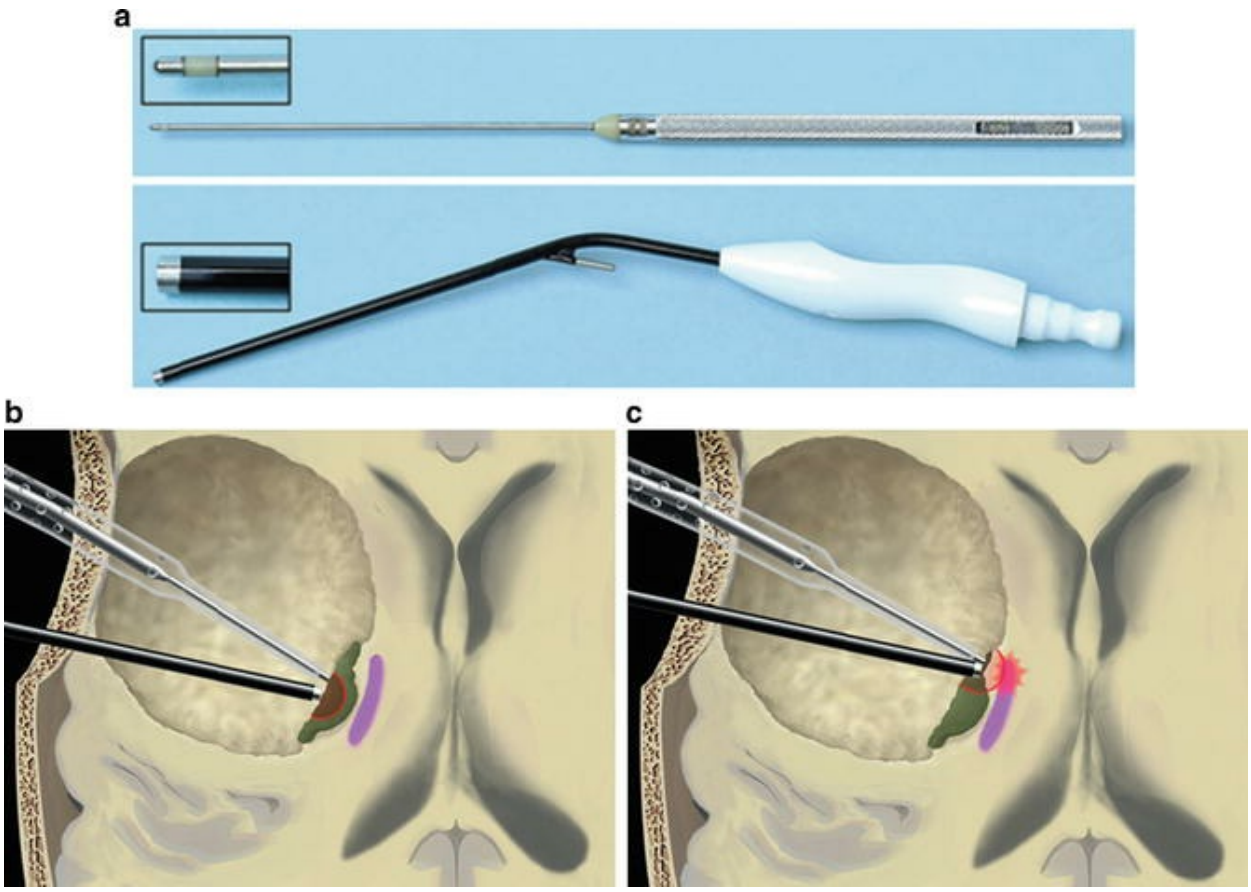

Fig. 9.4 (**a**) Photograph of combined suction-monopolar stimulator device . (**b**) Illustration of the device within the tumor cavity. Continuous stimulation is applied until the set current triggers an MEP response, indicating that the corticospinal tract is in close proximity (1 mA has been shown to be roughly equal to a 1-mm distance to the corticospinal tract). After an alert, the current is reduced to allow more precise determination of the distance to the corticospinal tract (**c**). (Reprinted with permission from Raabe et al. [23])

The same mapping techniques can be used to identify the corticospinal tract at more caudal locations, for example, at the level of the cerebral peduncles in the brainstem. Of course, access to neoplasms or vascular

abnormalities in these regions may involve risk to other structures, such as cranial nerves or the dorsal column–medial lemniscus pathway. Techniques for mapping cranial nerves have long been established, and are covered elsewhere in this volume (see Chap. 7, “Electromyography.”).

Spinal Cord Mapping

Access to the interior of the spinal cord itself, for resection of intramedullary tumors, requires the surgeon to perform a midline myelotomy. In the normal spinal cord, this midline is relatively easy to determine. However, when the anatomy is distorted by an intramedullary lesion, the physiological midline, i.e., the septum between the left and right dorsal columns, may not be evident, even under the operating microscope. Furthermore, the physiologic midline may not be in the anatomic midline and thus may not be straight (Fig. 9.5).

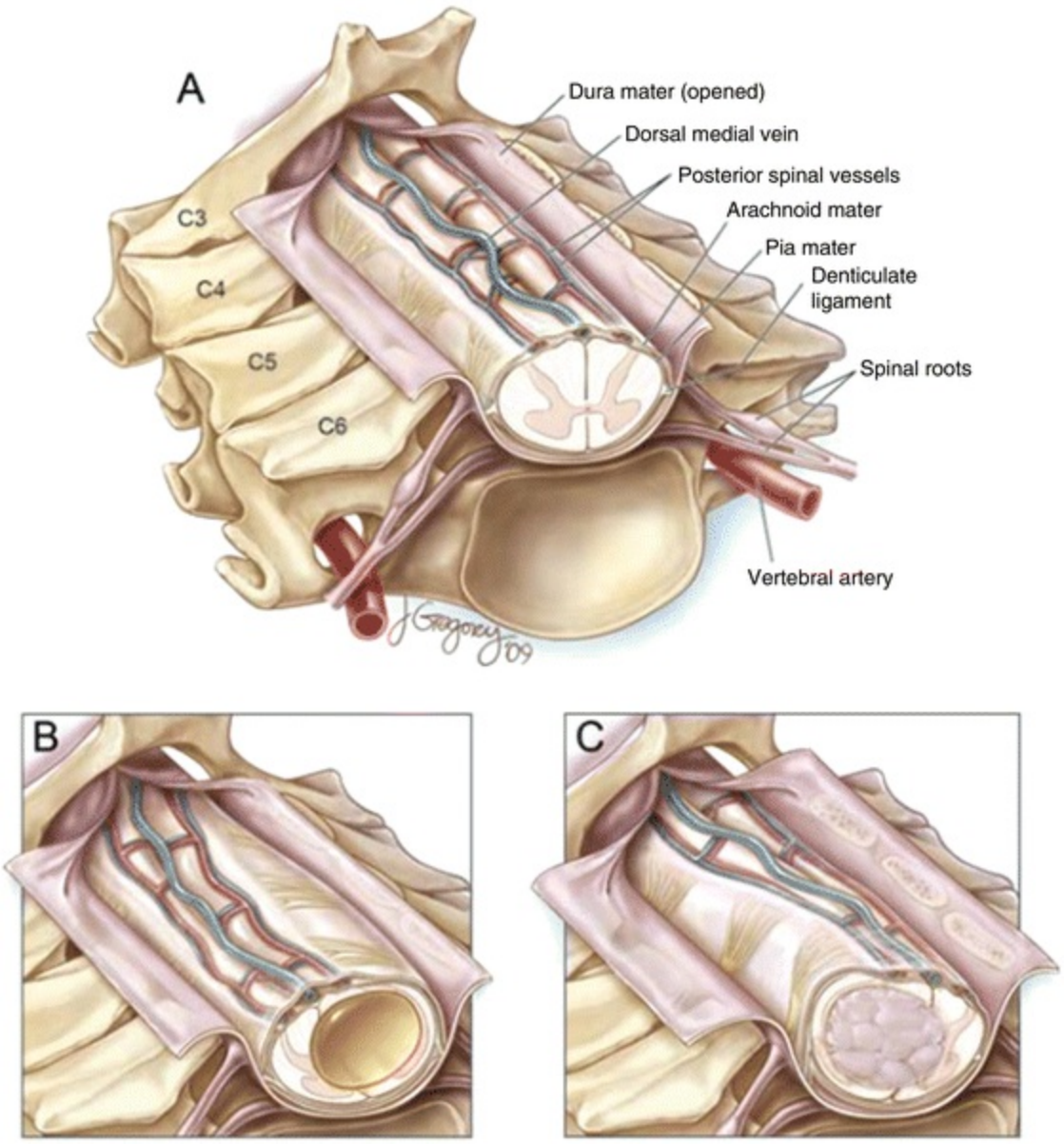

Fig. 9.5 Illustration of normal spinal cord anatomy (**a**) compared with distorted midline anatomy due to an enlarging syrinx (**b**) and an intramedullary tumor (**c**). (Reprinted with permission from Yanni et al. [27])

Fortunately, physiologic mapping techniques can also be used to determine the position of the left and right dorsal columns, and the midline transition between them. In principle, there are four ways to accomplish this. First, peripheral nerves in the four extremities can be stimulated individually, and the location of the maximum evoked response determined with multichannel recordings spanning the dorsal midline [27]. This, however, requires fabrication of small multichannel surface electrodes, which are not

available commercially. The other disadvantage of this technique is that it requires signal averaging, with associated time delays. The second method is to stimulate on the dorsal surface of the cord, using a small monopolar electrode moved systematically across the dorsal columns while recording from the four extremities. Antidromic sensory nerve action potentials can be recorded from surface electrodes placed over ulnar, median, or posterior tibial nerves [28]. Third, synaptically mediated activity can be recorded from distal musculature in each of the four extremities, making use of the connections between sensory and motor neurons that underlie reflex arcs (Yingling and Gardi, unpublished data). This technique is relatively robust and takes advantage of the fact that recording electrodes in distal muscles are typically already in place for EMG recordings. This mapping should be repeated at several levels, to confirm the location of the midline over the extent of the planned myelotomy. A recent paper introduces the fourth method, in which the dorsal columns are stimulated at a low current of 0.2–0.5 mA (0.3 ms pulse width, 3.17 Hz) laterally and then medially on both sides using a bipolar stimulator with prongs held parallel to the longitudinal axis of the spinal cord [29]. Phase reversal is recorded from electrodes placed on the scalp at CP3, CP4, Cpz, and Fz. The midline was identified neurophysiologically as either (1) the site between the mapped right and left dorsal columns based on phase reversal and amplitude changes, or (2) the site where an isoelectric line is recorded. This technique also requires signal averaging to obtain an adequate cortical evoked potential, which may increase the time to identify the midline since the procedure must be repeated at several levels.

Gandhi et al. [30] described a technique for high-resolution mapping spinal cord motor pathways. A concentric bipolar stimulating probe was applied to the tumor cavity, and triggered responses were elicited in specific upper and lower extremity muscles at stimulation intensities between 0.1 and 1.0 mA (1.0-ms pulse width and 60.11-Hz repetition rate). Area(s) in which robust responses were elicited at low stimulation were regarded as unsafe to resect.

It is important to note that these mapping techniques should be used in conjunction with continuous monitoring methods of transcranial MEPs and SSEPs. A remaining issue for future research is to determine the relation between stimulation threshold and distance to the corticospinal tracts at subcortical or spinal levels. Because of the differing anatomical context, the

1-mm/mA calibration described earlier for subcortical pathways at the level of the internal capsule may or may not be applicable to more caudal locations.

Conclusions

In summary, the combination of mapping techniques to identify sensorimotor cortex, continuous monitoring with MEPs elicited by direct cortical stimulation, and mapping techniques to localize motor tracts at subcortical, brainstem, or spinal levels provides a powerful set of tools for the neurosurgeon to minimize new functional deficits while working near motor pathways in the central nervous system.

Questions

1. Why does the SEP reverse polarity across the central sulcus?

2. Why is EMG recording preferable for motor mapping?

3. What are the advantages of performing direct cortical MEPs with brief duration, high-frequency train stimulation compared to bipolar stimulation with prolonged duration, low frequency train using a device such as the Ojemann Cortical Stimulator?

4. Why is spinal cord mapping vital for resection of intramedullary tumors?

Answers

1. The pyramidal cells that generate the N20 to upper extremity stimulation are located in the postcentral gyrus, parallel to the cortical surface, and the initial cortical response is negative at the cell body and positive at the apical dendrites, creating an electrical dipole that is negative posteriorly and positive anteriorly.

2. EMG is more sensitive than observation of overt movement, thus allowing mapping to be done with lower stimulation intensity for greater precision and less concern of eliciting seizures.

3. (1) Significantly lower risk of inducing seizures; (2) less patient movement generated, and (3) corticospinal tracts can be monitored continuously during resection if surgeon places a strip electrode over motor cortex.

4. The physiologic midline may not be in the anatomic midline, and may not be straight, due to distortion by an intraspinal mass. Without physiologic mapping, a midline myelotomy to access the tumor could transect the dorsal columns.

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Footnotes

1 Asterisks indicate key references.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_10

10. EEG Monitoring

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Keywords Basics – EEG monitoring – Cytoarchitecture – Rhythm – EEG signal acquisition – Amplifiers – Filters – Signal processing – Anesthetic drugs impact EEG

Introduction

Monitoring the nervous system begs two questions: what is the function of the nervous system, and how can it be observed to fulfill the promise of monitoring? A simple, yet practical answer to the first question is that the function of the nervous system is to create human behavior. To monitor is to implicitly assume that detecting untoward events in a timely fashion will allow for successful therapeutic intervention. Under the usual circumstances then, the answer to the second question is conversation or visual inspection of behavior (a conventional neurologic exam). During general anesthesia, a novel behavioral state is therapeutically induced to allow safe, tolerable, and meticulous surgery. In this state of general anesthesia, nervous system function is reversibly depressed as are most of the visible signs of CNS function. A few behavioral and physiologic signs can be observed and have long been used as a guide to dosing anesthetics as exemplified by Guedel in 1937. Unfortunately, as the pharmaceutical choices expanded beyond diethyl

ether, these physical signs were found widely between agents making simple observation of outward signs of patient behavior inadequate as a dosing guide. The complete blockade of these signs by the introduction of muscle relaxants further complicated assessment of anesthetic action. During surgery and anesthesia, there are circumstances where the well-being of the brain or spinal cord may be put at risk. Examples include distraction of the spinal column, or clamping of the carotid artery. While tolerated by most patients, some will be injured by these procedures, and early warning may prevent permanent injury. The anesthesia practitioner may also benefit from monitoring because of the possibility of objective control over the state of anesthesia. General anesthesia is a continuum and varies not only with dose vs. a patient's individual sensitivity, but also with dynamic changes in surgical stimulation. Clinical problems result from too little or too much anesthetic. During the past century, using mainly empirical observation, the electroencephalogram (EEG) has been developed as a surrogate for monitoring both the well-being and the degree of anesthetic effect on the central nervous system (CNS). A useful analogy exists between the EEG and the electrocardiogram (ECG) because both provide a remote reflection of the electrical activity of millions of electrically active cells deep in the body. These distant echoes of ionic currents can be interpreted to sense the vitality and function of their originating organs. The cardiogram consists of patterns that we know represent specific underlying physiologic events and sequences; unfortunately, the EEG permits us to link specific wave patterns with underlying physiology only in the special case of evoked potentials. The spontaneous, or background EEG appears to be random electrical variations resembling noise, having no direct connection to known physiologic consequences. This does not imply that the brain's electrical function is random or chaotic, only that it is so complex that it appears so. Indeed, the EEG is widely accepted as being a highly sensitive, moderately specific indicator of CNS ischemia or hypoxia and EEG monitoring has been commonly used for this purpose during carotid surgery [1–3]. The variation in EEG due to drug effect has three applications : a quantitative tool for the pharmacologic study of CNS-active agents [4–6]; the assessment of metabolic suppressive effect (e.g., dose control of thiopental for EEG burst-suppression [7, 8]); and recently, the assessment of CNS functional suppression (depth of sedation or anesthesia [9, 10]).

Historically, the interpretation of EEG waveforms required heuristic and

visual skills obtained only by years of training in neurology and electrophysiology. A breakthrough was achieved a half century ago when it was recognized that while EEG voltage waveforms appear completely random, certain statistics describing the EEG tend to remain roughly the same from moment to moment and even minute to minute over time. The brain's activity whether awake or asleep is not totally stable, or statistically "stationary," but is best described as "quasi-stationary." Thus the brain can be monitored by looking for changes in the compressed graphic trend of some statistical parameters without requiring the continuous, single-minded effort of a trained electrophysiologist. The advent of microprocessors then made it possible to introduce the compact, relatively inexpensive computer-based EEG analyzers that have renewed clinical interest and research in EEG monitoring.

The choice of physiologic or behavioral end-point against which to correlate or test the EEG has proven critical. Prominent changes occur in the EEG during cerebral metabolic failures such as hypoxia or ischemia. After such an insult, the extent and duration [2] of EEG changes usually correlate with the extent of new neurologic deficits. With respect to anesthetic drug effect, the first reported relationship compared EEG with changes in hemodynamics following noxious stimulation [11, 12]. The degree of EEG depression prior to laryngoscopy correlated with the magnitude of blood pressure change following intubation. However, later attempts to correlate EEG with gross purposeful movement in response to surgical incision have not uniformly reported positive results [9, 13, 14]. These inconsistent results may be due to the anatomic and possible pharmacodynamic separation of the neural circuitry responsible for movement responses (spinal cord) from those responsible for the generation of the EEG signal (cerebrum) [15]. EEG, as will be discussed, is a phenomenon of the rostral structures , particularly the cerebral cortex. Anesthetic-induced suppression of spinal function, i.e., surgical immobility, may be independently observable by monitoring spinal responses like F-waves [16, 17]. EEG reliably correlates with behavioral activities linked to the cortex such as awareness or memory, and clinically relevant monitoring may be expected [18–22].

The Genesis of the EEG

The flow of an electric current through an imperfect conductor creates a

voltage consistent with Ohm's law. Bioelectric potentials observed on the skin are created by the flow of ion-based electrical currents within the volume of the body. As in the case of the ECG, EEG voltages detected on the scalp are the gross summation of tiny currents due to dynamic changes in ionic charge distribution across cell membranes contributed by large populations of individual, electrically active neurons.

Living cells use energy to maintain an electrical charge separation (voltage) across the cell membrane in order to segregate useful ion species inside or outside the cell. Sodium, potassium, and chloride are the dominant species of ions involved, and each makes a contribution to the overall membrane potential according to the log ratio of its concentrations, inside vs. outside. Depending on circumstances, this transmembrane voltage is in the range of −60 mV, relative to the outside. Electrically active cells like neurons further utilize the energy stored in this voltage to facilitate communication across distance in the CNS. The dynamic electrical activity of neurons may be divided into two categories : regenerative action potentials (AP) and postsynaptic potentials (PSPs) . PSPs occur when neurotransmitters released by a presynaptic neuron alter the permeability of ion channels in the postsynaptic neuron's cell membrane. The changes in channel conductance alter its transmembrane ionic concentration gradients and thus its transmembrane voltage. The magnitude of an isolated PSP is roughly proportional to the number of postsynaptic receptor channels that have bound neurotransmitter agonist. Because neurotransmitter release is a very localized phenomenon, the resulting changes in resting membrane potential also tend to be focal, with the magnitude of the voltage change diminishing exponentially with distance from the synapse and a membrane constant known as λ. The "length constant," λ, is analogous to a time constant in describing the exponential decay of a perturbation. In this case, λ depends on the characteristics of the cell membrane and describes the distance along the membrane at which the voltage disturbance has decayed to 37 % of the original voltage perturbation. The value of λ is often in the range of 0.1–1.0 mm. The direction of the change in membrane potential can be either positive (depolarizing) or negative (hyperpolarizing) depending on which ionic species has had its membrane permeability altered by the neurotransmitter. Synaptic activity thus creates focal patches of altered membrane potential and ionic current flow occurs between these disturbances. The longer the length constant in a particular neuron, the more focal PSPs will summate and smear

together. PSPs slowly decay over time, bringing the membrane potential back to its resting value. The mechanism of decay is a combination of cessation of ligand-triggered channel activity, either due to removal of the neurotransmitter or inactivation of the ion channels, and the PSP-induced currents that redistribute ionic charge to counteract the PSP. Decay times of PSPs are in the range of 10s of milliseconds to seconds. If the membrane potential of a neuron is depolarized beyond its intrinsic threshold value, an AP is initiated. APs propagate rapidly along the membrane without diminution in amplitude, sustained by voltage-sensitive sodium and potassium channels and the transmembrane concentration gradients of these species. Typically, at a given point on the membrane, the excursion in voltage caused by an AP lasts for about 2 ms and may reach approximately 100 mV in amplitude.

Cytoarchitecture

As isolated activity, the current loops from local membrane disturbances of a single neuron would be quite difficult to detect at the distance of the scalp. Fortuitously, the anatomy of the cerebral cortex provides a means of generating relatively robust signals. Cortical neurons are classified by their morphology [23]. For the purpose of this chapter, the key type is the pyramidal cell that has a long straight apical dendrite extending up through the cortical layers from the cell body directly toward the pial surface of its gyrus. Neighboring pyramidal cells, therefore, have roughly parallel dendrites , as illustrated in Fig. 10.1. These pyramidal dendrites receive thousands of synaptic connections from other neurons, and neighboring dendrites tend to receive inputs from many of the same presynaptic sources and at homologous locations on the dendrite. There often is physical separation of groups of inhibitory and of excitatory PSPs on an individual apical dendrite, which creates bridging current loops between the PSPs. These bridging currents are far larger than might be predicted from the length constants of dendrites (Fig. 10.2). When neighboring millions of pyramidal cells have similar, synchronous areas of altered membrane potentials, their resulting current loops combine additively in the extracellular fluid to create even larger regional current flows, flows which can be detected by the voltage they create on the scalp.

Fig. 10.1 Micrograph of cortical neuropil stained for neurons . The cell bodies of pyramidal neurons project apical dendrites upward and parallel with adjacent pyramidal cells

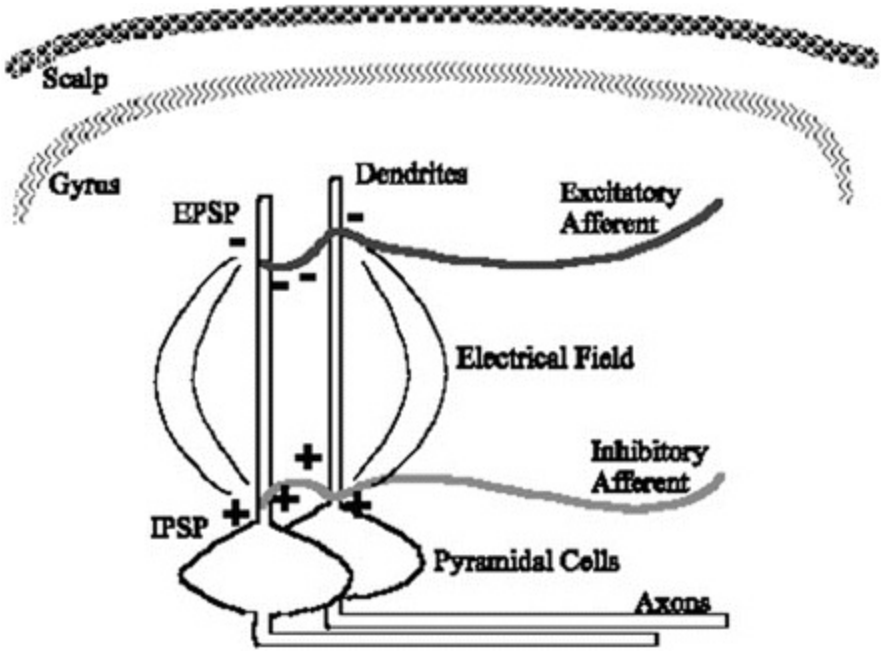

Fig. 10.2 Current flow around parallel dendrites during a period of similar afferent signals produces a larger electric field by summation

Control of Rhythm

As PSPs occur and decay, so the EEG scalp voltage changes over time. Under ordinary circumstances, millions of PSPs are asynchronously firing all over the cortex, creating in summation a complicated composite signal on the scalp. This scalp voltage cannot be decomposed back into component PSPs. As noted earlier, decades of empirical observation indicate, however, that some statistical attributes of the EEG reflect and track some underlying clues as to brain state. EEG monitoring during anesthesia relies on this statistical approach. The most useful correlation revolves around the degree of PSP synchrony in across large numbers of pyramidal cells, which determines the net magnitude and frequency on the EEG. Higher cortical functions like awareness and concentrated thought are usually associated with desynchronization, as neurons act more independently in the creation of conscious human behavior. Anesthesia and other mechanisms that depress consciousness are correlated with increasing pyramidal synchrony. Anatomically, synchrony, and indeed level of consciousness are strongly influenced by neuronal circuit loops involving cortical connection with the brainstem and thalamus [24, 25]. These circuits are sometimes called the EEG pacemakers, although their purpose is by no means clear and several different pacing rates may be present at any one time [25].

Under some conditions, the EEG may contain special stereotypic waveforms that can be used diagnostically. For example, “spikes” or “sharp waves” are sharply featured excursions in the EEG that are created by massive but usually transient synchrony. The presence of repetitive spikes is used in the diagnosis of epilepsy. Another example is burst-suppression phenomena (intermittent electrical activity interspersed with periods of little or no electrical activity), which indicates a nonspecific (e.g., trauma, drugs, hypothermia, etc.) reduction in cerebral metabolic activity.

Once generated, the aggregate postsynaptic current flows must traverse the cerebrospinal fluid (CSF), the skull, and the scalp in order to be detected by skin surface electrodes. The CSF and scalp are relatively conductive compared with the skull, and the overall effect of transmission through these multiple layers is a substantial spatial smearing of regional voltage differences. Physically, this means that the signal from an EEG electrode reflects activity over a wide area, not just the cortex directly under the electrode.

EEG Signal Acquisition

Metal needle or metal/gel electrodes are required to act as transducers, converting EEG (physiologic) ionic currents into electronic voltages, which may then be further processed by the EEG monitoring equipment. Electrodes are not perfectly faithful converters, however, and often contribute to noise and artifact. Just the physical contact between skin and metal generates a voltage potential whose amplitude is many times the size of the EEG. The now standard use of silver/silver chloride skin electrodes for EEG and ECG is an attempt to minimize artifact from electrode potentials.

Voltage signals are always measured as a difference in potential between two points; thus a bioelectric amplifier has two signal inputs, a plus and a minus. Bioelectric amplifiers also have a third input for a “reference” ground electrode, which is discussed below. Because the electrical activity of the cortex is topographically heterogeneous, it is often advantageous to measure EEG activity at several locations on the scalp. In diagnostic neurology, several systems of placement and nomenclature for electrodes have evolved; the most commonly used at present is the International 10–20 system [26]. The 10–20 system is based on meridians crossing the scalp based on key landmarks (the nasion, the inion, and the left and right aural tragus) with additional lines drawn over the midfrontal lobes and the midparietal lobes. The nomenclature uses a letter prefix designating brain site (i.e., C = central, F = frontal, P = parietal, T = temporal) and a number indicating the relative distance from the midline (nasion to inion), where right-sided electrodes are given even numbers and left-sided placement receive odd numbers. Electrodes on the midline are designated “Z,” i.e., FZ is a site overlying the falx between the frontal lobes and P3 is a left parietal site.

Diagnostic EEG as performed in the neurology clinic is seldom recorded with fewer than 16 channels (plus–minus pairs of electrodes) in order to localize abnormal activity. Monitoring 8 or 16 channels intraoperatively during carotid surgery is often recommended although there is a paucity of data demonstrating increased sensitivity for the detection of cerebral ischemia when compared with the 2- or 4-channel computerized systems more commonly available to anesthesia personnel. Although regional changes in EEG occur during changes in anesthesia dose [27, 28], there is little evidence that these topographic features are useful markers of clinically important changes in anesthetic or sedation levels [29]. EEG in the operating room is

most frequently monitored from just the forehead, a hairless area allowing standard saline gel silver chloride electrodes rather than needles or cream-filled cups.

Amplifiers and Filters

The EEG signal is but one of several voltage waveforms present on the scalp. The EEG usually spans a few microvolts in amplitude and most of its energy is in a frequency range of 0.5–40 Hz. In awake subjects, there are at least three other voltage signals generated by physiologic processes in the same range of frequencies: ECG (from the R-wave vector sweeping across the neck), electromyogram (EMG, from electrical activity of scalp muscles), and the electrooculogram (EOG, generated by movement of the electrical dipoles within the eyeballs). There are still more sources of noise: mechanical motion of the electrodes on the skin creates large artifact voltages as noted above. Plus, the body acts as an antenna picking up the powerline 50- or 60-Hz signal radiated by the wiring in nearby walls and ceilings.

While these signals originating outside the brain may contain interesting information, when present, they distort and interfere with the EEG signal. An understanding of the essential characteristics of specific artifacts can be used to mitigate them. A well-designed bioelectric amplifier can remove or attenuate some of these signals as the first step in signal processing. The largest magnitude artifact is the powerline pickup. This artifact possesses two characteristics useful in reducing its impact: it is the same over the entire body surface and it is a single characteristic frequency. Because EEG voltage is measured as the potential difference between two electrodes placed on the scalp, both electrodes will have the same powerline artifact (i.e., it is a “common mode” signal). Common mode signals can be nearly eliminated in the electronics stage of an EEG machine by using a differential amplifier that has connections for three electrodes: “+,” “−,” and a reference. This type of amplifier detects two signals: the voltage between + and reference, and between − and reference, then subtracts the second signal from the first. The contribution of the reference electrode is common to both signals and thus cancels out. Removal of common mode artifacts will be perfect only if each of the + and − electrodes are attached to the skin with identical contact impedance. If the electrodes do not have equal contact impedances, the amplitude of the common mode signals on the plus and minus sides will differ and they will not cancel exactly. Most commonly, the EEG is measured

(indirectly) between two points on the scalp with a reference electrode on the ear or forehead. If the reference electrode is applied far from the scalp, i.e., the thorax or leg, there is always a chance that large common mode signals like the ECG will not be ideally canceled out, leaving some degree of a contaminating artifact.

Some artifacts, like the EMG, characteristically have most of their energy in a frequency range different from that of the EEG. Hence, the amplifier can band pass filter the signal, passing the EEG and attenuating the EMG. Some EEG machines quantify and separately report EMG activity on the screen before filtering it from the EEG.

Signal Processing

Signal processing of an EEG is the massage of the voltage data by a computer to aid the recognition of some message within the EEG that correlates with the physiology and pharmacology of interest. Metaphorically, the goal is to separate this “needle” from an electrical haystack. The problem in EEG-based assessment of anesthetic state is that the characteristics of this needle are unknown, and since our fundamental knowledge of the CNS remains relatively limited, our needle-like constructs will, for the foreseeable future, be based on empirical observation. Assuming a useful quantitative EEG (QEEG) parameter is identified, it must be measured. The motivation for quantitation is threefold: to reduce the clinician’s workload in analyzing intraoperative EEG, to reduce the level of specialized training to take advantage of EEG, and finally to develop a parameter that might, in the future, be used in an automated closed-loop titration of anesthetic or sedative drugs. This section will introduce some of the mechanics and mathematics behind signal processing.

Although it is possible to perform various types of signal enhancement on analog signals, the speed, flexibility, and economy of digital circuits has produced revolutionary changes in the field of signal processing. To use digital circuits, it is, however, necessary to translate an analog signal into its digital counterpart.

Analog signals are continuous and smooth. They can be measured or displayed with any degree of precision at any moment in time. The EEG is an analog signal; the scalp voltage varies smoothly over time.

Digital signals are fundamentally different in that they represent discrete points in time and their values are quantitated to an a priori fixed resolution.

The digital world of computers and digital signal processors operates on binary numbers, which are sets of quantal bits. A bit is the smallest possible chunk of information: a single ON or OFF datum. Useful binary numbers are created by aggregating between 8 and 80 bits. The accuracy or resolution (q) of binary numbers is determined by the number of bits they contain: an 8-bit binary number can represent 2^8 or 1 of 256 possible states, a 16-bit number 2^{16} or 65,536 possible states. If one were using an 8-bit number to represent an analog signal, the binary number would have, at best, a resolution of approximately 0.4 % (1/256) over its range of measurement. Assuming, for example, the converter was designed to measure voltages in the range from −1.0 to +1.0 V, the step size of an 8-bit converter would be about 7.8 mV and a 16-bit converter about 30 μV. EEG monitoring systems usually use 12–16 bits of resolution. By comparison, audio CD recording are 16 bit resolution.

Digital signals are also quantized in time. When translation from analog to digital occurs, it occurs at specific points in time and strictly speaking, the value of the resultant digital signal at all other points in time is indeterminate. Translation from the analog to digital world is known as sampling, or digitizing, and in most applications is set to occur at regular intervals. The reciprocal of the sampling interval is known as the sampling rate (fs) and is expressed in Hertz (Hz, or samples per second). A signal that has been digitized is commonly written as a function of a sample number, i, instead of analog time, t. For example, an analog voltage signal might be written at $v(t)$, but after digitizing would be referred to as $v(i)$. Taken together, the set of sequential samples representing a finite block of time is referred to as an epoch. In statistical theory, the collection of all possible epochs produced from a given EEG state would be known as an ensemble.

The process of analog to digital translation inevitably leads to a loss of fidelity in the resulting digital signal. A realistic digital signal, $x(i)$, can be thought of as the sum of a (an impossibly) perfect digital copy of the true signal xu(i) plus an error term, $e(i)$. The quantization error, $e(i)$, is the difference between the sampled voltage and the true analog voltage. Quantization error can be reduced by increasing the number of bits used to represent the digitized sample. The signal processing designer must trade off increased accuracy against the increased cost of higher resolution hardware (including the A-to-D) converter itself as well as a wider data path in the computing circuits (i.e., the computer arithmetic unit must be expanded to handle numbers with more bits) and more memory to hold the added bits.

When sampling is performed too infrequently, the fastest sine waves in the epoch will not be identified correctly. When this situation occurs, aliasing distorts the resulting digital data. Aliasing results from the requirement for a minimum of two points within a single cycle to identify a sinusoid. If sampling is not fast enough to place at least two sample points within a single cycle, the sampled wave will appear to be slower (longer cycle time) than the original. Aliasing is familiar to observers of the visual sampled-data system known as cinema. In a movie, where frames of a scene are captured at a rate of approximate 24 Hz, rapidly moving objects like wagon wheel spokes often appear to rotate slowly or even backward. An audio music CD is sampled at a rate of 44.1 kHz, which allows artifact-free capture up to 22 kHz, beyond the range of most adult hearing.

Therefore, it is essential to always sample at a rate more than twice the highest expected frequency in the incoming signal (Shannon's sampling theorem [30]). Conservative design actually calls for sampling at a rate 4–10 times higher than the highest expected signal, and to also use an analog low-pass filter prior to sampling to eliminate signals that have frequency components which are higher than expected. Low-pass filtering reduces high-frequency content in a signal, just like turning down the treble control on a stereo system. In monitoring work, EEG signals have long been considered to have a maximal frequency of 30 or 40 Hz, although 70 Hz is a more realistic limit. In addition, other signals present on the scalp include powerline interference at 60 Hz and the electromyogram which, if present, will usually extend above 100 Hz. In order to prevent aliasing distortion in the EEG from these other signals, many digital EEG systems filter out signals above 30 Hz and then sample at a rate above 250 Hz (i.e., a digital sample every 4 ms).

Artifact Mitigation by Software

The problem of artifactual contamination must always be considered in EEG analysis. Artifact is particularly insidious in EEG analysis, since even to the trained observer, much of true EEG resembles noise [31]. Common artifacts include signals that have exceeded the dynamic range of the amplifier (voltage too high due to improper amplifier settings or movement of the electrodes on the skin). These artifacts are easy to recognize, but the epoch containing this artifact must be excluded from the analysis since the original data cannot be recovered. Another common type of artifact, as noted earlier, is caused by the presence of an additional signal that is outside the frequency

range of the EEG. This type of signal might include electromyogram activity or powerline pickup. If the sampling rate is fast enough to avoid aliasing, these kinds of artifacts may be filtered out digitally, leaving a still-usable EEG signal. Some types of artifact including the ECG and roller pump artifact (during cardiopulmonary bypass) occur within the frequency range of interest for EEG and may be recognized by their regularity. Anesthesia equipment such as a train-of-four twitch stimulator, or an evoked potential stimulator may also create a patterned artifact in the EEG. In awake or lightly sedated subjects, eye blinks and rotation of the orbital globes create large, transient slow wave activity that may be recognized based on the pattern of signal amplitude changes. A compendium of techniques for EEG artifact detection and mitigation is provided by Barlow [32]. In commercially available EEG monitors designed for use during surgery, sampled EEG epochs with artifact may be tagged, processed, recovered, or excluded from further processing. Once the EEG signal has been digitized and cleaned up, it is ready to be analyzed to provide clinical guidance.

Time-Domain Methods

EEG is an alternating voltage composed of many wavelets (simple sine waves) superimposed on each other. Analysis of the EEG can be accomplished by examining how its voltage changes over time. This approach, known as time-domain analysis, may use either a strict statistical calculation (i.e., the mean and variance of the sampled waveform, or the median power frequency [MPF]), or may use some ad hoc measurement based on the morphology of the waveform. Most of the commonly used time-domain methods are grounded in probabilistic analysis of “random” signals and, therefore, some background on statistical approaches to signals is useful. Of necessity, the definitions of probability functions, expected values, and correlation are given mathematically as well as descriptively. However, the reader need not feel compelled to attain a deep understanding of the equations presented here to continue on. A more detailed review of the statistical approach to signal processing may be obtained from one of the standard texts [33–35]. Only one class of ad-hoc time-domain methods, burst-suppression quantitation, is currently in use in perioperative monitoring systems and it will be described below.

A few definitions related to the statistical approach to time-related data

are called for. The EEG is *not* a *deterministic* signal, which means that it is not possible to exactly predict future values of the EEG. Even if the exact future values of a signal cannot be predicted, some statistical characteristics of certain types of signals are predictable in a general sense. These roughly predictable signals are termed *stochastic* . The EEG is such a nondeterministic, stochastic signal because its future values can only be predicted in terms of a probability distribution of amplitudes already observed in the signal. This probability distribution, $p(x)$, can be determined experimentally for a particular signal, $x(t)$, by simply forming a histogram of all the observed values over a period of time. A signal such as may be obtained by rolling dice has a probability distribution that is rectangular or uniform (i.e., the likelihood of all face values of a throw are equal and in the case of a single die, $p(x) = 1/6$ for each possible value); a signal with a bell-shaped or *normal* probability distribution is termed *Gaussian* . As illustrated in Fig. 10.3, EEG amplitude histograms may have a nearly Gaussian distribution. The concept of statistics like the mean, standard deviation, skewness, and so on, to describe a probability distribution will be familiar to many readers.

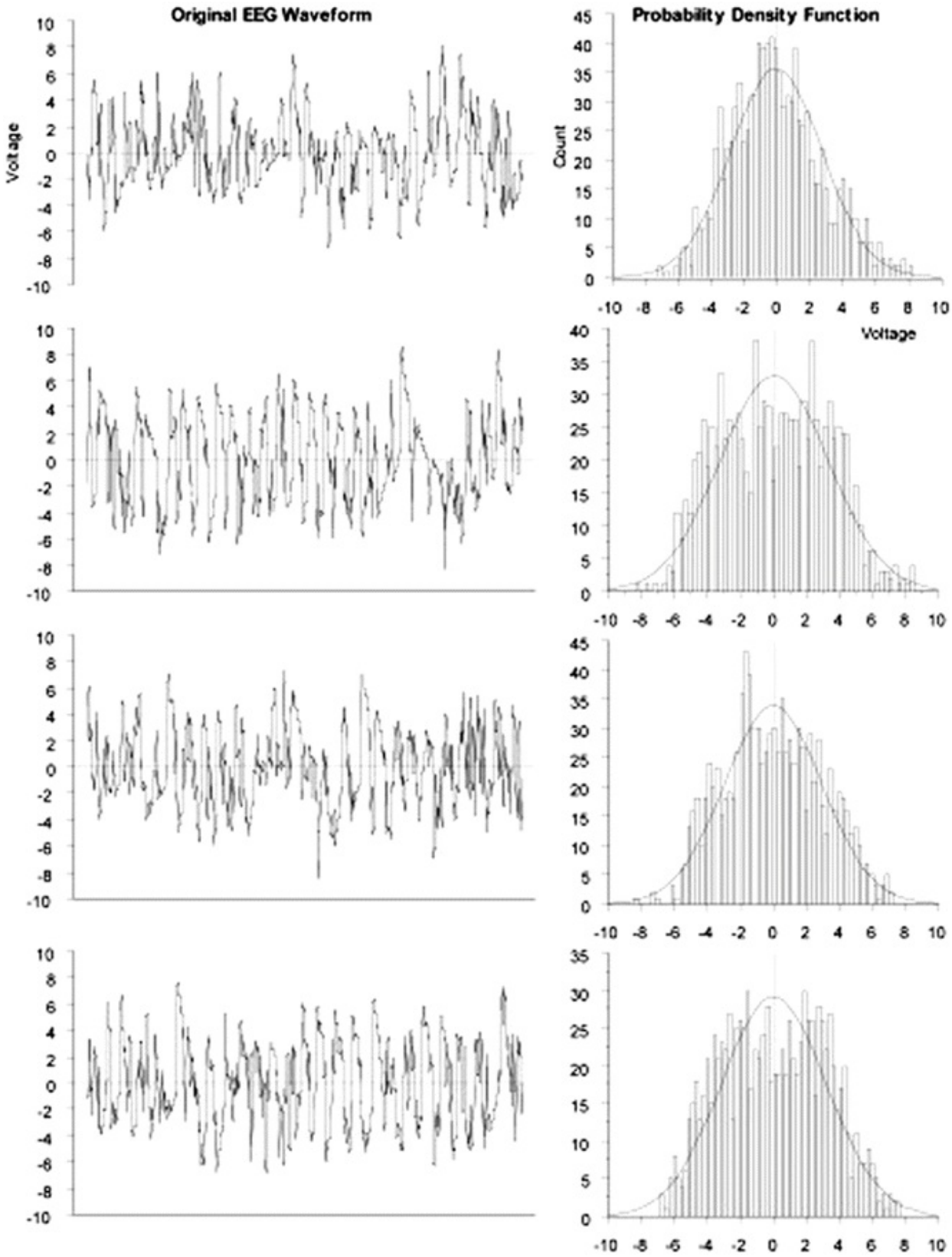

Fig. 10.3 EEG amplitude values sampled over time exhibit a normal distribution . Data recorded from

anesthetized rats by author at 256 Hz with gain of 500 and analyzed as sequential 4-s epochs

If the probability function, $p(x)$, of a stochastic signal, $x(i)$, does not change over time, that process is *stationary* . The EEG is not strictly stationary as its statistical parameters may change significantly within seconds (Fig. 10.3), or it may be stable for tens of minutes (*quasi-stationary*) [36, 37]. If the EEG is at least quasi-stationary, then it may be reasonable to check it for the presence of rhythmicity, where rhythmicity is defined as repetition of patterns in the signal. Patterns can be identified quantitatively using correlation. Usually, correlation between two signals measures the likelihood of change in one signal leading to a consistent change in the other. In assessing the presence of rhythms, autocorrelation is used, testing the match of the original signal against different starting time points of the same signal. If rhythm is present, then at a particular offset time (equal to the interval of the rhythm), the correlation statistic increases, suggesting a repetition of the original signal voltage.

Empirically it is known that the EEG has a mean voltage of zero, over time: any sample is as likely to be positive as it is negative. However, the EEG and its derived statistical measurements seldom have a true Gaussian probability distribution. This observation complicates the task of a researcher, or of some future automated EEG alarm system that seeks to identify changes in EEG over time. Strictly speaking, non-Gaussian signals should not be compared using parametric statistical tests , such as *t*-tests or analysis of variance, that are appropriate for normally distributed data. Instead, there are three options: nonparametric statistical tests, a transform to convert non-Gaussian EEG data to a normal distribution, or higher order spectral statistics (see below). Transforming non-Gaussian data using its logarithm is frequently all that is required to allow analysis of the EEG as a normal distribution [38]. For example, a brain ischemia-detection system may try to identify when slow wave activity has significantly increased. A variable like “delta” power (described below), which measures slow wave activity, has a highly non-Gaussian distribution. Thus, directly comparing this activity at different times requires the nonparametric Kruskal–Wallis or Friedman’s test. However, the logarithm of delta power may produce a nearly normal $p(x)$ curve. Therefore, the more powerful ANOVA with repeated measures test could be used appropriately to detect changes in log (delta power) over time. Log transformation is not a panacea, however, and whenever statistical

comparisons of QEEG are to be made, the data should be examined to verify the assumption of normal distribution.

Clinical Applications of Time-Domain Methods

Historically, the first intraoperative application of EEG analysis used time-domain-based methods. In 1950, Falconer and Bickford noted that the electrical power in the EEG (Power = voltage × current = voltage^2/resistance) was associated with changes in the rate of thiopental or ethyl ether administration. Using analog technology, they computed a power parameter as (essentially) a moving average of the square of EEG voltage and used it to control the flow of diethyl ether to a vaporizer. This system was reported to successfully control depth of anesthesia in 50 patients undergoing laparotomy [39]. Digital Total Power (TP = sum of the squared values of all the EEG samples in an epoch) was later used by several investigators, but it is known to have several problems, including its sensitivity to electrode location and to its insensitivity to important changes in frequency distribution. Arom reported that a decrease in TP may predict neurologic injury following cardiac surgery [40].

Hjorth [41] created a trio of combinations of conventional (time-domain based) descriptive statistics parameters: *Activity*, *Mobility*, and *Complexity*. Activity is defined as the variance of the signal amplitude within an epoch, i.e., the square of the standard deviation of the digitized data points, and provides a measure of the mean power of the signal. Mobility can be considered an approximation of the average frequency of the EEG. It is defined as the standard deviation of the first derivative of the EEG signal (i.e., the intersample slope of the waveform) divided by the standard deviation of the original signal. Complexity is a variable to quantify the degree of curve complexity beyond a baseline sine wave. These parameters of Hjorth are frequently used in the related application of sleep staging [42, 43] but have not directly been tested in perioperative monitoring.

A time-domain-based approach to analysis of the frequency information within the EEG was reported by Burch [44] and Klein [45], who estimated an “average” frequency by detecting the number of times the EEG voltage crosses the zero voltage level per second. Investigators have not reported strong clinical correlations with Zero Crossing Frequency (ZXF) . While simple to calculate in the era before inexpensive computer chips, the ZXF

parameter is not simply related to frequency-domain estimates of frequency content as demonstrated in Fig. 10.4, because not all waves in the signal will cross the zero point. Demetrescu refined the zero crossing concept to produce what he termed *aperiodic* analysis [46]. This method simply splits the EEG into two frequency bands (0.5–7.9, 8–29.9 Hz) and the filtered waveforms from the high and low frequency bands are each separately sent to a relative minima detector. Here, a *wavelet* is defined as a voltage fluctuation between adjacent minima and its frequency defined as the reciprocal of the time between the waves. Wavelet amplitude is defined as difference between the intervening maxima and the average of the two minima voltages. The Lifescan Monitor (Diatek, San Diego, CA) was an implementation of aperiodic analysis; it is no longer commercially available, but its algorithms were described in detail by Gregory and Pettus [47].

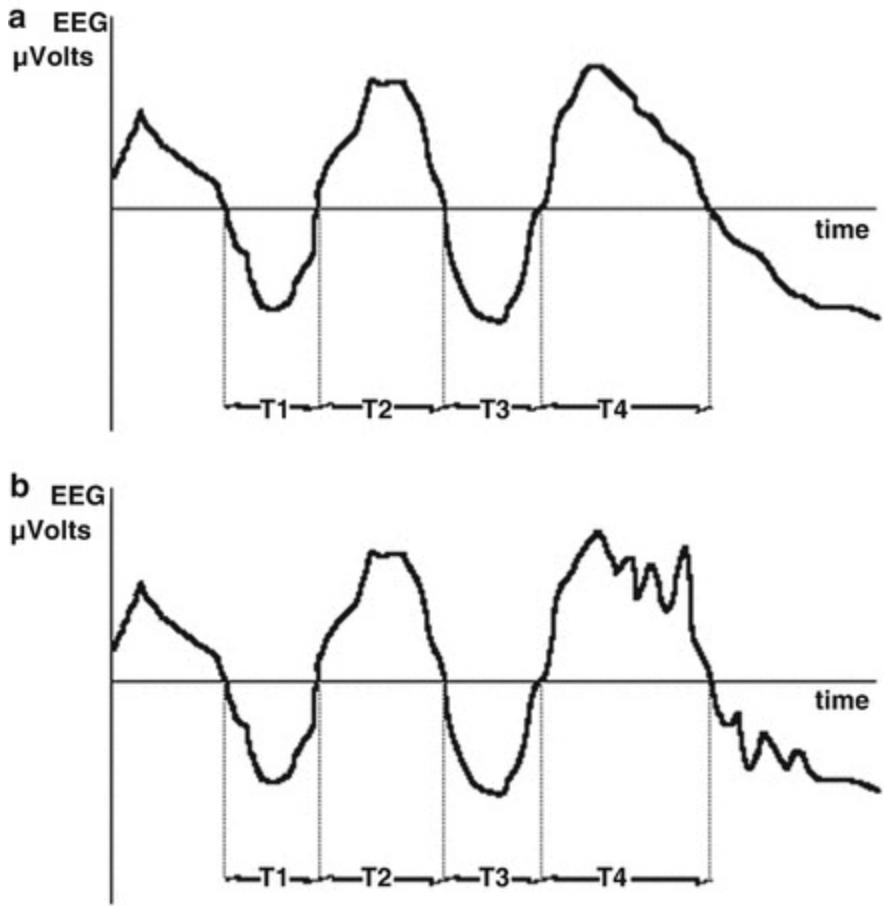

Fig. 10.4 Failure of zero-crossing algorithm to be sensitive to all components of EEG waveform. In interval T4 and beyond, the high frequency, low amplitude activity in waveform B is ignored

Burst Suppression and Its Quantitation

During deep anesthesia, the EEG may develop a peculiar pattern in the time-domain signal. This pattern, known as *burst suppression* , is characterized by alternating periods of normal to relatively high voltage activity changing to relatively low voltage or even isoelectricity, rendering the EEG at the usual degree of amplification inactive in appearance. Following head trauma or brain ischemia, this pattern carries a grave prognosis; however, it is nonspecific as it may also be induced by large doses of general anesthetics, in which case, burst suppression has been associated with reduced cerebral metabolic demand and possible brain “protection” from ischemia. Titration to a specific degree of burst suppression has been recommended as a surrogate endpoint against which to titrate barbiturate coma therapy. The burst-suppression ratio (BSR) is a time-domain EEG parameter developed to quantitate this phenomenon [48, 49]. To calculate this parameter, suppression is recognized as those periods longer than 0.50 s during which the EEG voltage does not exceed approximately ± 5.0 μV. The total time in a suppressed state is measured, and the BSR is reported as the fraction of the epoch length where the EEG is suppressed (Fig. 10.5).

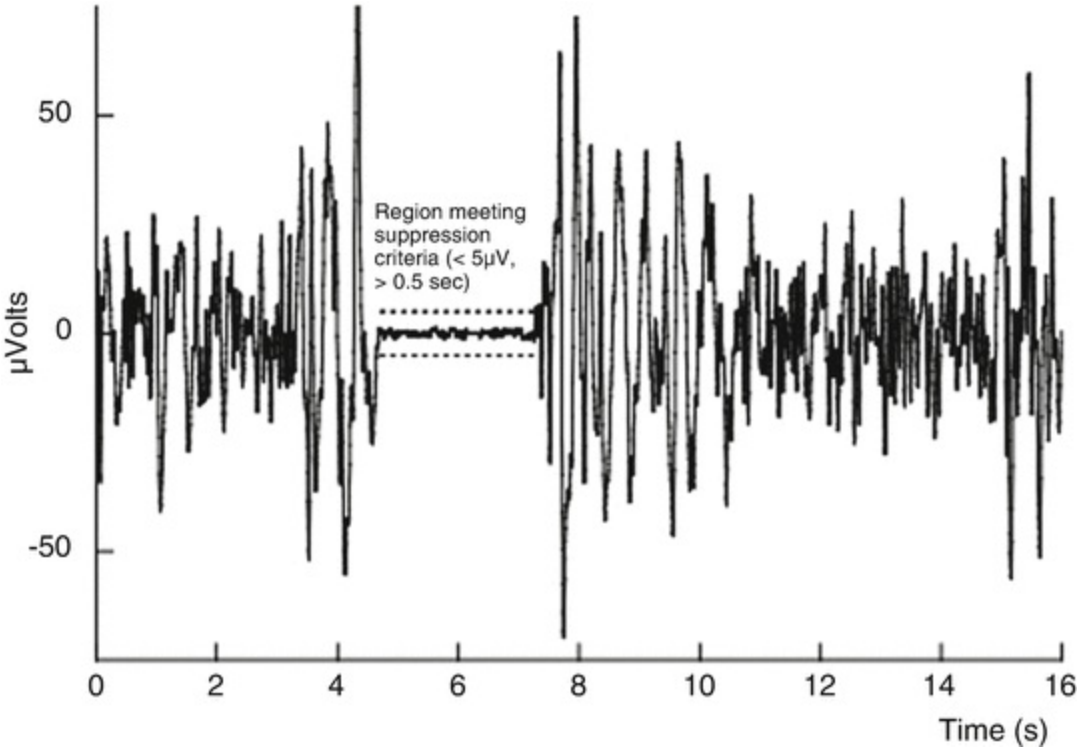

Fig. 10.5 The burst-suppression ratio (BSR) algorithm displayed graphically

The random character of the EEG dictates that extracted QEEG parameters will exhibit a moment-to-moment variation without discernible change in the patient's state. Thus, output parameters are often smoothed by a moving average prior to display. Due to the particularly variable (nonstationary) nature of burst suppression, the BSR should be averaged over at least 15 epochs (60 s).

Frequency-Domain Methods

An important alternative approach to time-domain analysis examines signal activity as a function of frequency. Frequency-domain analysis translates waveforms that are voltage magnitudes as a function of time into spectra that are magnitudes as a function of frequency. This process of conversion is akin to the action of a glass prism, which translates white light into a rainbow spectrum (Fig. 10.6). Each color of light represents a unique frequency photon, and the relative brightness among the colors is a measure of the energy amplitude at each frequency. This type of conversion has its mathematical roots in the work of Baron Jean Baptiste Joseph Fourier who was studying heat conduction and the cyclic variations of tides. He discovered that any time-varying waveform could be decomposed into a series of pure sine waves of differing frequencies, amplitudes, and phases. For each component sine wave, frequency is the number of complete cycles per second, amplitude is one-half the peak-to-peak voltage, and phase angle is the way to describe the starting point of the waveform. However, the manual and even early computer solution of the Fourier transform for a particular set of data points was too time-consuming to be of practical use. Other approaches to frequency-domain analysis included the creation of large banks of analog filters with narrow bandpasses arrayed in parallel to emulate a true spectral analyzer [50]. It was not until Cooley and Tukey discovered a mathematical trick leading to the "fast Fourier transform" (FFT) that frequency-domain analysis became practical for real-time EEG processing [51]. The FFT algorithm results in a set of frequency bins, each containing the magnitude of the signal at that particular frequency. Although this algorithm still requires a great deal of number-crunching, current microprocessor chips can perform real-time EEG FFT analysis on up to four or more simultaneous channels. Special purpose signal processing chips can calculate FFTs with even greater speed.

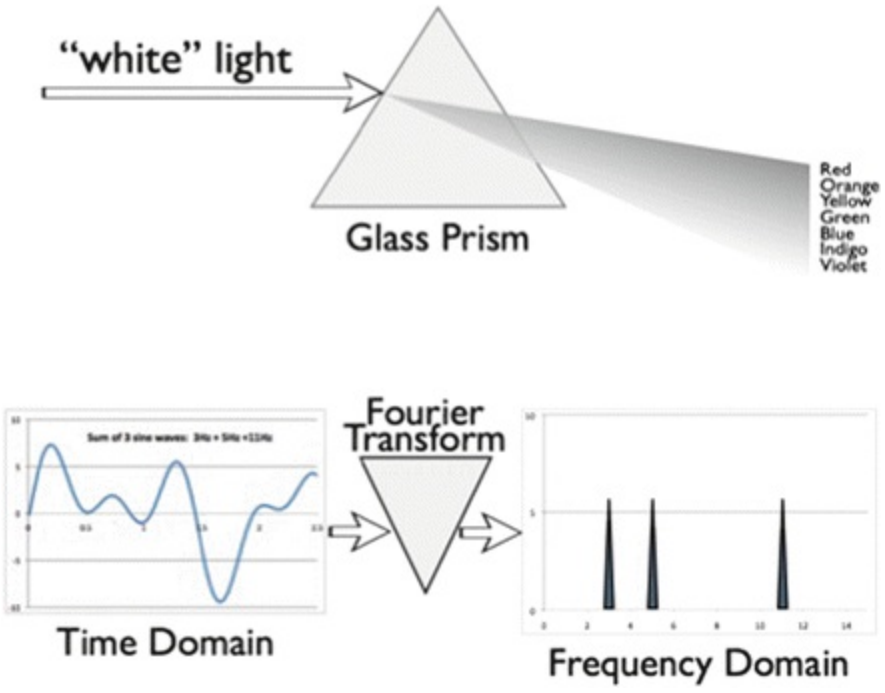

Fig. 10.6 The effect of the Fourier transform on time-varying waveform data is analogous to the effect of glass prism on light: it breaks the input up into component parts

The conversion process of a time-domain voltage waveform, $x(t)$, into its sine wave frequency components, $X(f)$, is known as a Fourier transformation . This transformation, under ideal conditions, does not alter or reduce the information content within the waveform, and an inverse Fourier transformation will reconstitute the original waveform (i.e., the transformation is symmetric). Squaring the values of amplitude spectrum creates the *power spectrum*, which is the commonly used version of frequency-domain data. In typical applications, the so-called *phase* spectrum is discarded.

Early in his survey of human EEG, Hans Berger identified several generic EEG patterns that were loosely correlated with psychophysiologic state. These types of activity, such as the alpha rhythms seen during awake but restful periods with eyes closed, occurred within a stereotypic range of frequencies that came to be known as the *alpha* band. Eventually, five such distinct bands came to be widely accepted.

Using an FFT , it is a simple matter to divide the resulting power spectrum from an epoch of EEG into these band segments, then summate all power values for the individual frequencies within each band to determine the band power. Relative band power is simply band power divided by power

over the entire frequency spectrum in the epoch of interest.

In the realm of anesthesia-related applications, traditional band power analysis is of limited utility, since the bands were defined for the activity of the awake or natural sleep-related EEG without regard for the altered nature of activity during anesthesia. Drug-induced EEG activity can often be observed to pass smoothly between bands as the dose changes. Familiarity with band analysis is still necessary because of the extensive literature utilizing it.

In an effort to improve the stability of band-related changes, Volgyesi introduced the augmented delta quotient (ADQ) [52]. This value is approximately the ratio of power in the band 0.5–3.0 Hz to the power in the 0.5–30.0 Hz range. This definition is an approximation because the author used analog band-pass filters with unspecified but gentle roll-off characteristics that allowed them to pass frequencies outside the specified band limits with relatively little attenuation.

John's group [53] applied a normalizing transformation [38] to render the probability distribution of power estimates of the delta frequency range close to a normal distribution in the CIMON EEG analysis system (Cadwell Laboratories, Kennewick, WA). After recording a baseline "self-norm" period of EEG, increases in delta band power that are larger than three standard deviations from the self-norm were considered to represent an ischemic EEG change [54]. Other investigators have concluded that this indicator may be nonspecific [55].

Another approach to simplifying the results of a power spectral analysis is to find a parameter that describes a characteristic of the spectrum without a priori assumptions from the neurology literature. The first of these descriptors was the peak power frequency (PPF), which is simply the frequency in a spectrum at which the highest power in that epoch occurs. The MPF (median power frequency) is that frequency which bisects the spectrum; half the power is above, half below. The *spectral edge frequency* (SEF) is the highest frequency in the EEG, i.e., the high frequency edge of the spectral distribution. The original SEF algorithm utilized a form of pattern detection on the power spectrum in order to emulate mechanically visual recognition of the "edge." Beginning at 32 Hz, the power spectrum is scanned downward to detect the highest frequency where four sequential spectral frequencies all contain above a predetermined threshold of power. This approach (Rampil and Sasse, unpublished results, 1977) provides more noise immunity than the

alternative algorithm, SEF95. SEF95 is the frequency below which 95 % of the power in the spectrum resides. Clearly, either approach to SEF calculation provides a monitor that is only sensitive to changes in the width of the spectral distribution (there is always energy in the low-frequency range). Many commonly used general anesthetics produce burst-suppression EEG patterns without slowing the waves present during the remaining bursts; thus the SEF of the epoch would not reflect the anesthetic-induced depression. Combining the SEF with the BSR parameter to form the burst-compensated SEF (BcSEF [Eq. (10.1)]) creates a parameter that appears to smoothly track changes in the EEG due to either slowing or suppression from isoflurane or desflurane [11, 48].

$$\mathrm{BcSEF} = \mathrm{SEF}\left(1 - \frac{\mathrm{BSR}}{100}\right) \tag{10.1}$$

Spectral QEEG parameters like MPF or SEF compress into a single variable, the 60 or more spectral power estimates that constitute the typical EEG spectrum. The SEF has been used to predict sensitively new ischemic deficits postoperatively following carotid surgery [2, 56, 57]. Other studies comparing SEF to other EEG parameters (or a neurologist's visual assessment of ischemia), but not patient outcome have found the SEF lacking in sensitivity [58, 59]. As Levy pointed out [29], a single feature may not be sensitive to all possible changes in spectral distribution. However, there is no evidence, to date, suggesting that additional parameters (describing a complex spectrum) improve the predictive clinical utility of simple univariate parameters. Frequency-domain-based QEEG parameters, like their time-domain-based relatives, are generally averaged over time prior to display. The author uses nonlinear smoothing when computing SEF that strongly filters small variations, but passes large changes with little filtering. This approach diminishes noise, but briskly displays major changes, such as may occur secondary to ischemia, or following bolus injection of anesthetics.

The quantitative EEG variables described to this point were all created to measure patterns in the raw waveform or the power spectrum of the EEG apparent by visual inspection. While many of these QEEG variables detect changes in the EEG caused by anesthetic drugs, all suffer from the inability to be calibrated to useful behavioral endpoints such as following verbal command or onset of explicit amnesia [13]. Their performance as anesthetic monitors also suffers due to their sensitivity to the different EEG patterns induced by different drugs.

Spectral Displays in Clinical Practice

In clinical monitoring applications, the results of an EEG Fourier transform are graphically displayed as a power vs. frequency histogram and the phase spectrum has been traditionally discarded as uninteresting. One reason for this opinion is that the frequency spectrum is relatively independent of the start point of an epoch (relative to the waveforms contained); the Fourier phase spectrum is highly dependent on the start point of sampling and thus very variable. More to the point, there has yet to be discovered any clinically actionable information in phase spectra. Spectral array data from sequential epochs are plotted together in stack (like pancakes) so that changes in frequency distribution over time are readily apparent. Raw EEG waveforms, because they are stochastic, cannot be usefully stacked together since the results would be a random superposition of waves. However, the EEG's quasi-stationarity creates spectral data that are relatively consistent from epoch to epoch, allowing enormous visual compression of spectral data by stacking and thus simplifying recognition of time-related changes in the EEG. Consider that raw EEG is usually plotted at a rate of 30 mm/s or 300 pages per hour, whereas the same hour of EEG plotted as a frequency spectral array could be examined in great detail on a single page.

There are two types of spectral array displays available in commercial instruments: the compressed spectral array (CSA) and the density spectral array (DSA) . The CSA presents the array of power vs. frequency vs. time data as a pseudo-three-dimensional topographic perspective plot (Fig. 10.7) and the DSA presents the same data as a gray scale-shaded or colored two-dimensional contour plot. Although both convey the same information, the DSA is more compact, while the CSA permits better resolution of the power or amplitude data.

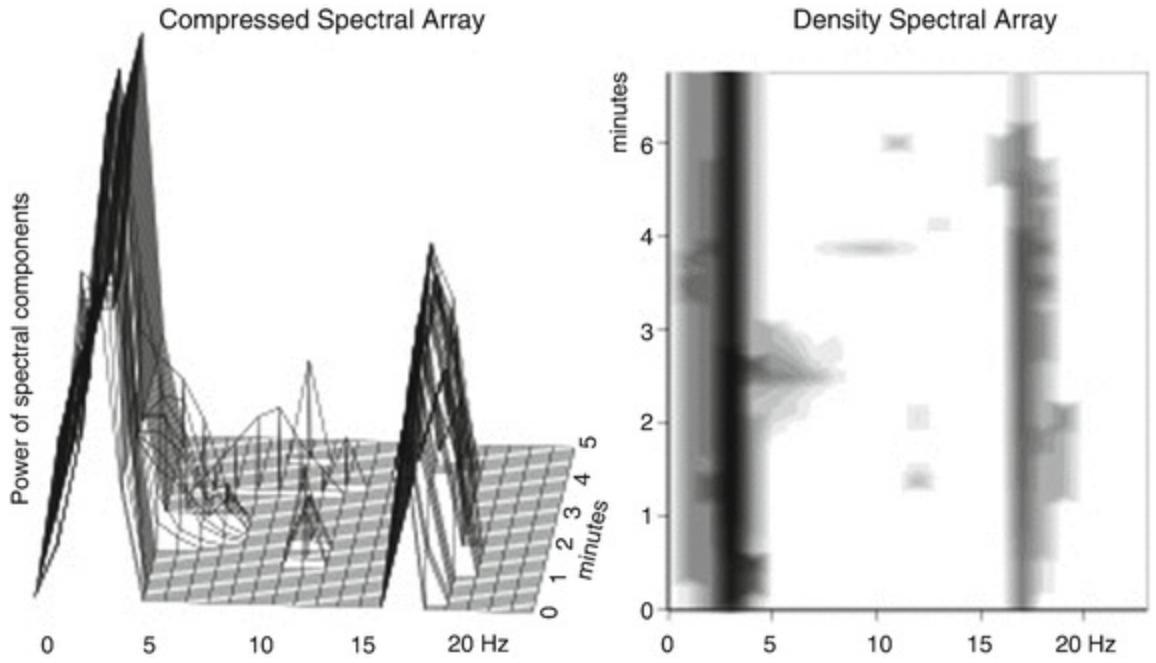

Fig. 10.7 The creation of a spectral array display involves the transformation of time-domain raw EEG signal into the frequency domain via the fast Fourier transform . The resulting spectral histograms are smoothed and plotted in perspective with hidden-line suppression for CSA displays (*left*) or by converting each histogram value into a *gray* value for the creation of a DSA display (*right*)

Bispectrum

The effort to glean useful information from the EEG has led from first order (mean and variance of the amplitude of the signal waveform) to second order (power spectrum, or its time-domain analog, autocorrelation) statistics, and now to higher order statistics. Higher order statistics include the *bispectrum* and *trispectrum* (third and fourth order statistics, respectively). Little work has been published to date on trispectral applications in biology, but there have been many hundreds of papers and abstracts to date related to bispectral analysis of the EEG. Where the phase spectrum produced by Fourier analysis measures the phase of component frequencies relative to the start of the epoch, the bispectrum measures the correlation of phase between different frequency components as described below. What exactly these phase relationships mean physiologically is uncertain; one very simplistic model holds that strong phase relationships relate inversely to the number of independent EEG pacemaker elements. Bispectral analysis has several additional characteristics that may be advantageous for processing EEG signals: Gaussian sources of noise are suppressed, thus enhancing the

signal/noise ratio for the non-Gaussian EEG, and bispectral analysis can identify nonlinearities that may be important in the signal generation process. A mathematical treatment of higher order spectra as applied to clinical EEG applications may be found in a review by Rampil [60]. A survey of clinical monitoring results using commercial high spectral techniques (i.e., BIS or Bispectral Index) is located elsewhere in this volume.

Anesthetic Drugs Impact EEG

Volatile Agents

Induction with halothane [61], enflurane [62], isoflurane [63, 64], sevoflurane [65], desflurane [6], or xenon [66] all are associated with the loss of occipital alpha rhythms and the genesis of frontally maximal, relatively well-synchronized beta activity. In the waveform, this activity may resemble sleep spindles or a fast version of alpha rhythm. In a spectral display, it will create an alpha–beta band of activity, usually separated by a spectral band having little activity from the delta activity also present. Once this anesthetic-induced fast activity appears, its dominant frequency changes inversely with the anesthetic concentration and spreads its distribution over the scalp. This archetypal drug-induced fast activity invites comparison with, but it should not be confused with, alpha pattern coma, a postischemic or trauma pattern with a very poor prognosis. The overall patterns of EEG activity with anesthetic drug dose responses are illustrated in Fig. 10.8. At surgical levels (>1.0 MAC), the volatile anesthetics begin to differ in their EEG effects. Isoflurane and desflurane begin to induce burst suppression above 1.2 MAC without further slowing of the activity within the remaining bursts. Enflurane is associated with epileptiform activity [62], particularly “spike and wave” complexes or even frank seizures above 1.5 MAC. Sevoflurane appears to also predispose to epileptiform activity [67], particularly in pediatric patients [68]. Halothane causes a reasonably linear monotonic slowing in the “fast” activity easily noted in the spectral response to sinusoidal variation in halothane concentration (Fig. 10.9); burst suppression does not occur with this drug at clinically relevant doses. Intense noxious stimulation by tetanic stimulation of the sciatic nerve of dogs receiving less than one MAC of halothane activates EEG with (desynchronization) and increases cerebral metabolic rate for oxygen ($CMRO_2$) but provokes little change in dogs

receiving more than one MAC [69]. Similar changes have been reported in adult humans following skin incision, whereas stimulation in children anesthetized with halothane tended to produce high-voltage slow waves [61].

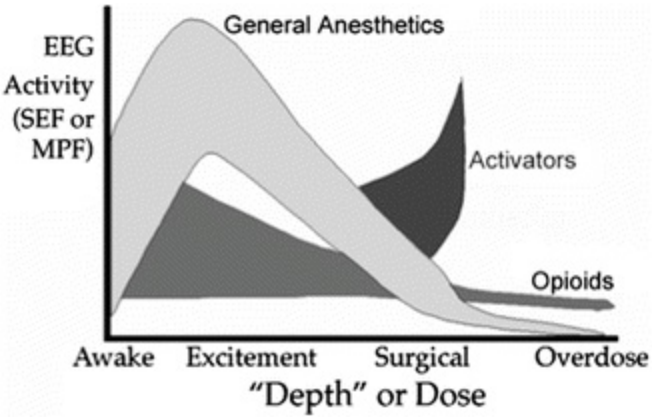

Fig. 10.8 The typical EEG pattern of activation and depression created by various anesthetic drugs

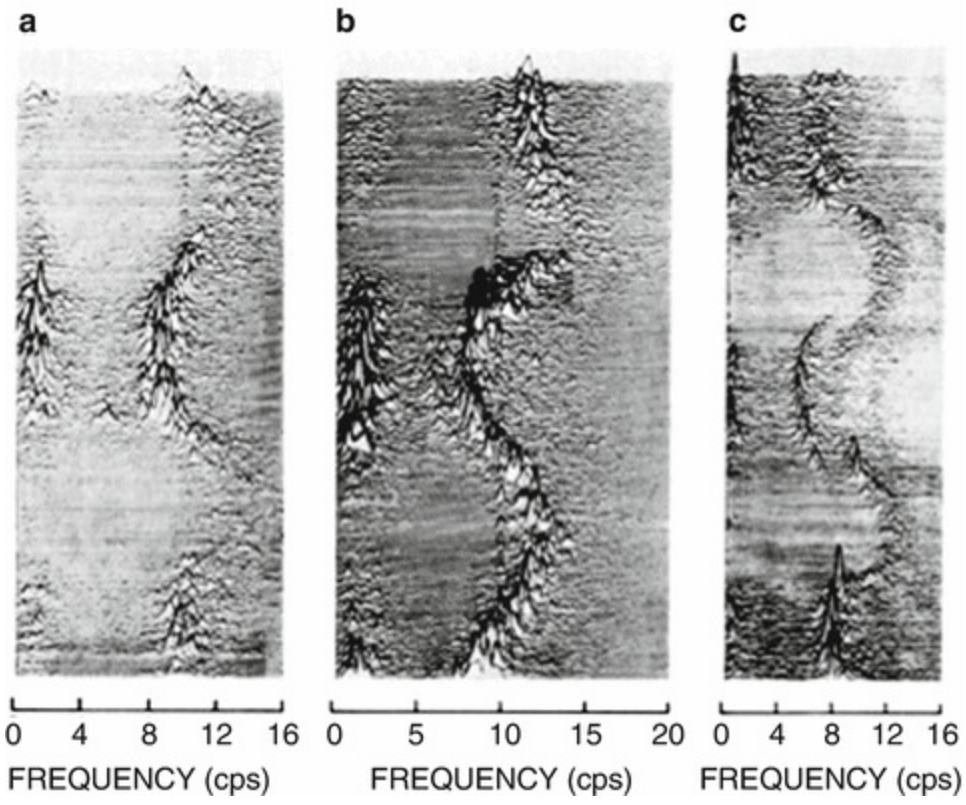

Fig. 10.9 Sine wave response apparent in the compressed spectral arrays of three healthy male volunteers given a sine wave variation (period of 31 min, concentration varying from 0.5 to 3.0 % in oxygen) of halothane. The sinusoidal appearance of the responses implies a linear dose response; however, there is a wide intersubject variation in the slope of the response curve (N. T. Smith, personal communications, UCSD)

Nitrous Oxide

The effects of nitrous oxide on the brain depend on the circumstances of its administration. Given alone, in subanesthetic concentrations (up to 70 %), Yamamura et al. [70] found that nitrous oxide induced a frontally dominant, fast rhythmic activity having an average peak frequency of 34 Hz. Traces of this fast oscillatory activity persisted for up to 50 min following nitrous oxide exposure [70]. Given alone, at subhypnotic concentrations (up to 50 %), nitrous oxide did not alter awake BIS readings, consistent with BIS as a measure of hypnotic effect [71]. When combined with other volatile anesthetics, nitrous oxide usually increases the amplitude and frequency of the anesthetic-induced fast activity in dogs [72] and rabbits [73]. Avramov et al. [74] reported that when nitrous oxide was administered to humans receiving a steady-state concentration of halothane, the sequence of EEG patterns over the course of approximately 1 h changed in a manner suggesting the development of tolerance to the nitrous oxide.

Barbiturates and Propofol

Barbiturates follow the drug response template : small doses cause drug-induced fast activity that is similar to that apparent with other general anesthetics, while higher doses increase EEG depression, culminating in burst suppression, then electrocerebral silence if the dose is high enough [75, 76]. There appears to be a topographic sequence of EEG changes (Fig. 10.10) similar to those seen with volatile anesthetics. The appearance of the fast activity corresponds with clinically apparent excitement phenomena and results in insensibility when substantial delta activity is present [76]. The straightforward pattern of EEG power during barbiturate anesthesia was used by Bickford [39] in the late 1940s to automatically control thiopental anesthesia in surgical patients. Schwilden et al. [77] reported using MPF to control methohexital sedation in volunteers; however, although it was possible to maintain a steady MPF of 2–3 Hz, this EEG pattern was not clearly correlated with an acceptable anesthetic state [77]. Methohexital is interesting in that while it is a potent anticonvulsant like the other barbiturates, it actually enhances interictal epileptiform activity in predisposed patients. It is therefore useful in locating seizure foci during epilepsy surgery [78, 79]. Propofol induces the same biphasic EEG pattern of

excitement followed by depression culminating in burst suppression as the barbiturates [80, 81].

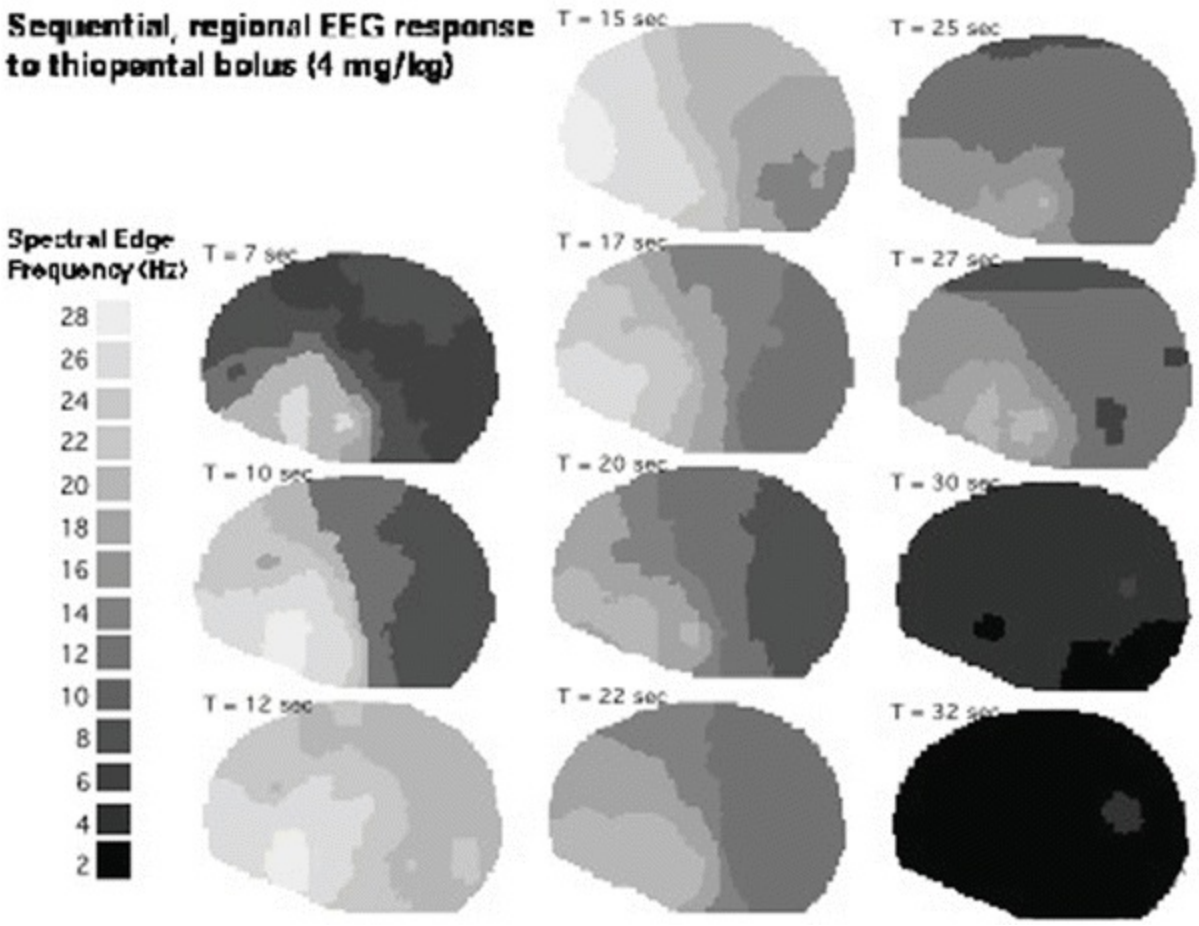

Fig. 10.10 A sequence of "snapshots" at 2.5-s intervals displaying the changing distribution of EEG frequency content (in this case, spectral edge frequency) over the scalp following a bolus injection of 4.0 mg/kg thiopental. In frames $T = 7$–17, there is a prominent focus of frontotemporal fast activity that spread posteriorly during this interval. Starting about $T = 15$, extreme slowing and suppression begins occipitally and spread anteriorly, enveloping the entire cortex by $T = 30$ (Rampil 1985; unpublished data)

Etomidate

Etomidate causes changes in EEG output similar to those induced by barbiturates [82]. Like methohexital, in small doses (0.1 mg/kg), etomidate enhances interictal activity of epileptic foci [83], although the myoclonic activity occasionally observed during induction with this drug is not associated with cortical epileptiform activity [82, 84]. In higher doses, etomidate causes burst suppression and a reduction in $CMRO_2$ similar to that

seen with thiopental [85]. Etomidate also has the interesting property of increasing the amplitude of somatosensory-evoked potentials [86].

Ketamine

Ketamine is a dissociative agent that provides a different EEG pattern than the general anesthetics. The onset of sedation results in high amplitude, rhythmic theta activity, often accompanied by a significant increase in beta range activity. Ketamine can provoke frank seizure activity in patients with epilepsy, but only rarely in normal subjects.

Narcotics

The EEG effects of narcotics differ from those of the general anesthetics, as illustrated in Fig. 10.8. Generally, there is a little or no excitement phase when mu-subtype agonists (morphine, fentanyl, sufentanil, alfentanil, remifentanil) are administered, but, instead, produce a steady decline in frequency content until only delta activity remains [87, 88]. There is no further change in the EEG with increasing dose. Burst suppression does not occur with narcotics. Peripheral muscle rigidity is not associated with cortical seizure activity [89] but, rather, seems to be a direct effect of narcotics on an area of the brainstem, particularly the nucleus raphe pontis [90]. Seizures are not seen during administration of clinically relevant doses of narcotic anesthesia, but have been noted in dogs given extremely high doses (4 mg/kg intravenously) of fentanyl [91], and in the presence of normeperidine, a metabolite of meperidine.

Benzodiazepines

When used in small doses as premedicants or as adjuvants to induction of anesthesia, benzodiazepines, like midazolam or valium, induce significant, predominantly frontal beta range activity [92]. Increasing doses are associated with generalized slowing in the theta/delta range, apparently without burst suppression [93]. Flumazenil promptly restores EEG activity to a prebenzodiazepine state [93]. Aside from their salutary effects on patients, premedication with a benzodiazepine frequently simplifies interpretation of raw EEG during induction and maintenance of anesthesia because additional anesthetics will cause only a decrease in EEG frequency content.

Muscle Relaxants

Although succinylcholine is not usually thought to affect the CNS, intravenous bolus administration appears to cause an increase in EEG activity and cerebral blood flow resembling arousal; persisting far longer (5 min) than might be expected from electromyographic fasciculation artifact [94]. Lanier et al. [94] hypothesize that this effect is due to increased afferent neural traffic from intrafusal fibers in fasciculating muscle.

Atracurium is metabolized to a large extent by nonenzymatic Hofmann elimination. One of the metabolites of this process is laudanosine, a compound long known to be a convulsant and cerebral stimulant [95]. While it is unlikely that a patient will receive a sufficient dose of atracurium intraoperatively for laudanosine to cause convulsions, administered doses may be sufficient to increase EEG activity and perhaps alter the depth of anesthesia [96].

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Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_11

11. Clinical Application of Raw and Processed EEG

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Keywords Electroencephalography – Anesthesia – Awareness – Consciousness – Stroke – Ischemia – Neuromonitoring

Key Learning Points

- Raw EEG waveforms and spectrogram patterns help characterize the neurophysiologic properties of various anesthetics.
- Processed EEG monitoring has not been shown to reduce the risk of awareness with explicit recall (AWR) compared to end-tidal anesthetic concentration (ETAC) monitoring protocols.
- EEG-guided titration of anesthetic depth may help to minimize the risk of cognitive dysfunction after surgery though multicenter trials are

needed to confirm preliminary findings.

- Various EEG markers are indicative of cerebral ischemia , and they tend to demonstrate frequency slowing, decreased power and variability of faster frequencies, and increased regional asymmetry.

Introduction

In 1924, Hans Berger began recording electrical activity from the scalp of humans [1]. His motivation was to prove the existence of telepathy, as he believed his sister telepathically sensed he was in danger when he suffered a military accident in World War I. As he continued to improve electrode technology, Berger ultimately discovered synchronized 10-Hz oscillations in the occipital region after subjects closed their eyes; these oscillations were later called “Berger waves.” Although initially met with skepticism, Berger’s findings were later independently confirmed [2], and different groups of investigators began exploring the neurophysiologic properties of the electroencephalogram (EEG) in the subsequent decades. Since then, the role of EEG has continued to evolve. EEG now has diagnostic and prognostic value for various neurologic conditions, such as epilepsy [3], stroke [4], traumatic brain injury [5], and brain death [6]. Clinical and research efforts have led to the release of guidelines for EEG use in neurologic patients [7] as well as the growth of governing bodies such as the American Clinical Neurophysiology Society.

The clinical application of EEG has been largely confined to the field of neurology, but there is growing interest in the use of EEG for brain monitoring during anesthesia [8]. To date, there is no standard anesthetic monitor for the brain although this is arguably the target organ of anesthetic administration during surgery. Targeted brain monitoring during anesthesia and surgery may improve neurologic outcomes by reducing the risk of intraoperative awareness with explicit recall (AWR) and by enhancing postoperative cognitive recovery. Further research is needed to identify reliable EEG markers that reflect level of consciousness and to explore the ability of EEG to improve such perioperative neurologic outcomes. This approach must begin, however, with a basic understanding of the neurophysiologic effects of various anesthetics as reflected by the EEG. Thus, in this chapter, we will review the anesthetic effects on both raw and processed EEG data and then discuss the clinical utility of EEG for surgical

patients.

EEG Data Acquisition and Interpretation

Raw EEG

Continuous EEG data are collected from scalp electrodes applied in standard locations (Fig. 11.1) that detect spikes in cortical microvoltages at various frequencies. These microvoltage spikes are believed to reflect postsynaptic voltage potentials from pyramidal neurons activated by cortical and thalamic sources [9]. Voltage oscillation frequencies are often divided into gamma (26–80 Hz), beta (13–25 Hz), alpha (9–12 Hz), theta (5–8 Hz), delta (1–4 Hz), and slow-wave (<1 Hz) bandwidths. At any given time (in both conscious and unconscious states), many bandwidths may be contributing to the overall EEG waveform . To deconstruct frequencies into individual components, a Fourier transformation can be performed [10]. This transformation is represented as an EEG spectrogram , which depicts time on the *x*-axis, frequency on the *y*-axis, and power on the *z*-axis (Fig. 11.2). This allows one to more easily analyze frequency bandwidth power for any given EEG segment. The reader is referred to Chap. 10 (“EEG Monitoring”) for further information regarding EEG acquisition and monitoring . As we will see below, each anesthetic is associated with a specific pattern in both the raw EEG and corresponding spectrogram.

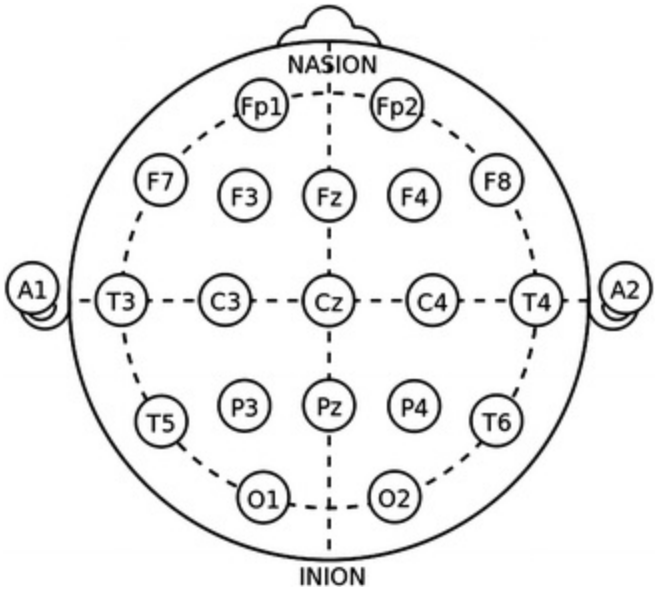

Fig. 11.1 Standard 10–20 system for location of EEG scalp electrode placement (i.e., montage). The number 10 indicates distance in percentage (10 %) from nasion and inion to adjacent frontal and occipital electrodes, respectively. The number 20 indicates distance in percentage (20 %) among remaining electrodes. Leads on the *left side* have odd numbers, and leads on the *right side* have even numbers. *F* indicates frontal; *T* temporal, *C* central, *P* parietal, *O* occipital. *Midline* (vertex) electrodes are denoted with the letter *z*, which indicates zero

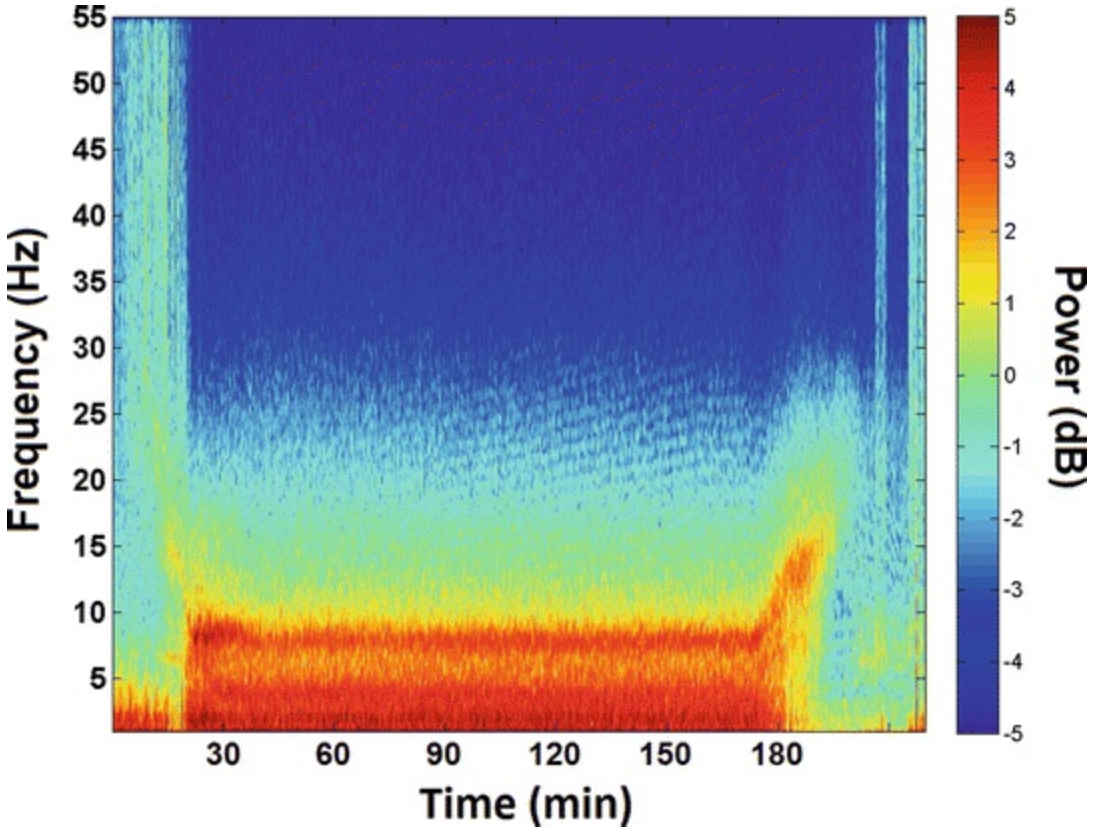

Fig. 11.2 Example spectrogram is depicted, with time (min) on the *x*-axis, EEG frequency (Hz) on the *y*-axis, and power (dB) on the *z*-axis

At depths consistent with general anesthesia , propofol predominantly displays alpha, delta, and slow oscillations on the raw EEG (Fig. 11.3a). On the corresponding spectrogram, high power is demonstrated in these corresponding frequency bandwidths (Fig. 11.3b). Ether-based volatile anesthetics (e.g., isoflurane, sevoflurane, desflurane) demonstrate a similar pattern on the raw EEG, which is characterized by alpha, theta, delta, and slow oscillations (Fig. 11.3a). On the spectrogram, high power is demonstrated in these bandwidths, often with more theta power compared to the propofol spectrogram (Fig. 11.3b). Halogenated ethers and propofol share similar neurophysiologic traits with non-rapid eye movement (NREM) sleep. For example, coherent oscillatory spindle activity is present with both

propofol sedation and NREM sleep, which is believed to reflect a breakdown of thalamocortical processing [11–13]. Asynchronous slow-wave oscillations are also noted during both sleep and propofol anesthesia, which may represent fragmented cortical connectivity [11, 14].

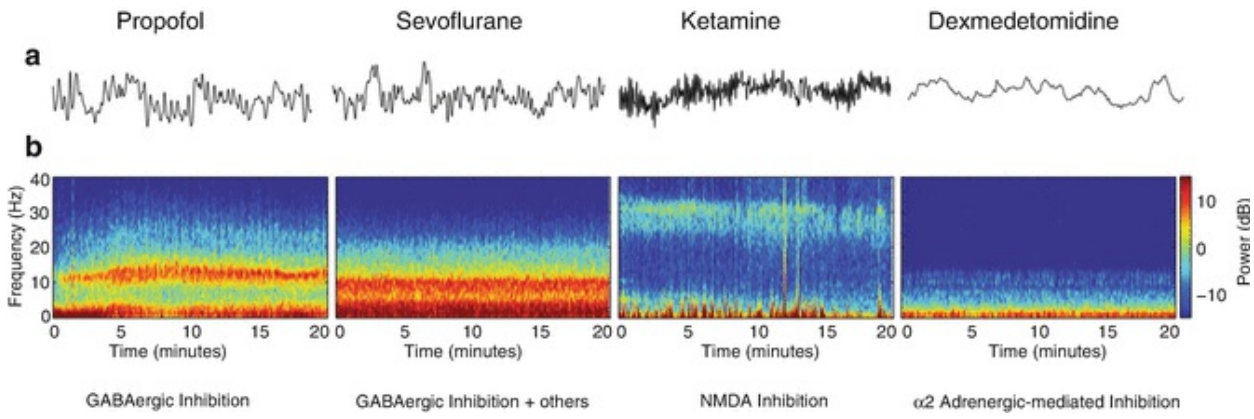

Fig. 11.3 Comparison of raw EEG and spectrogram patterns among different anesthetic classes. (**a**) Raw EEG patterns are displayed for each anesthetic class represented. Faster frequencies are appreciated with ketamine compared to other anesthetics. (**b**) Each anesthetic drug class corresponds to a specific spectrogram signature, which may reflect nuances in molecular and circuital properties in each class (Reproduced from Purdon et al. [56]; with permission)

Uniquely, ketamine anesthesia is associated with increased beta and gamma oscillatory activity on the raw EEG (Fig. 11.3a). This stands in contrast with the lower frequency patterns of propofol and ether-based volatile agents. During general anesthesia with ketamine, increased power is noted in the gamma range, particularly near 30 Hz (Fig. 11.3b). Lastly, dexmedetomidine induces characteristic EEG changes that vary depending on the depth of sedation. For example, during periods of light sedation, increased power is noted in the low-beta range on the spectrogram (Fig. 11.4a), which likely reflects the presence of spindle patterns on the raw EEG also similar to those observed during NREM sleep (Fig. 11.4b). With deeper levels of dexmedetomidine sedation, increased power is noted in the slow-delta bandwidths (Fig. 11.4c), and slow-delta oscillations are noted on the corresponding raw EEG (Fig. 11.4d). This presents a similar pattern to that observed with propofol and ether-based volatile agents but without the alpha oscillation (see Fig. 11.3).

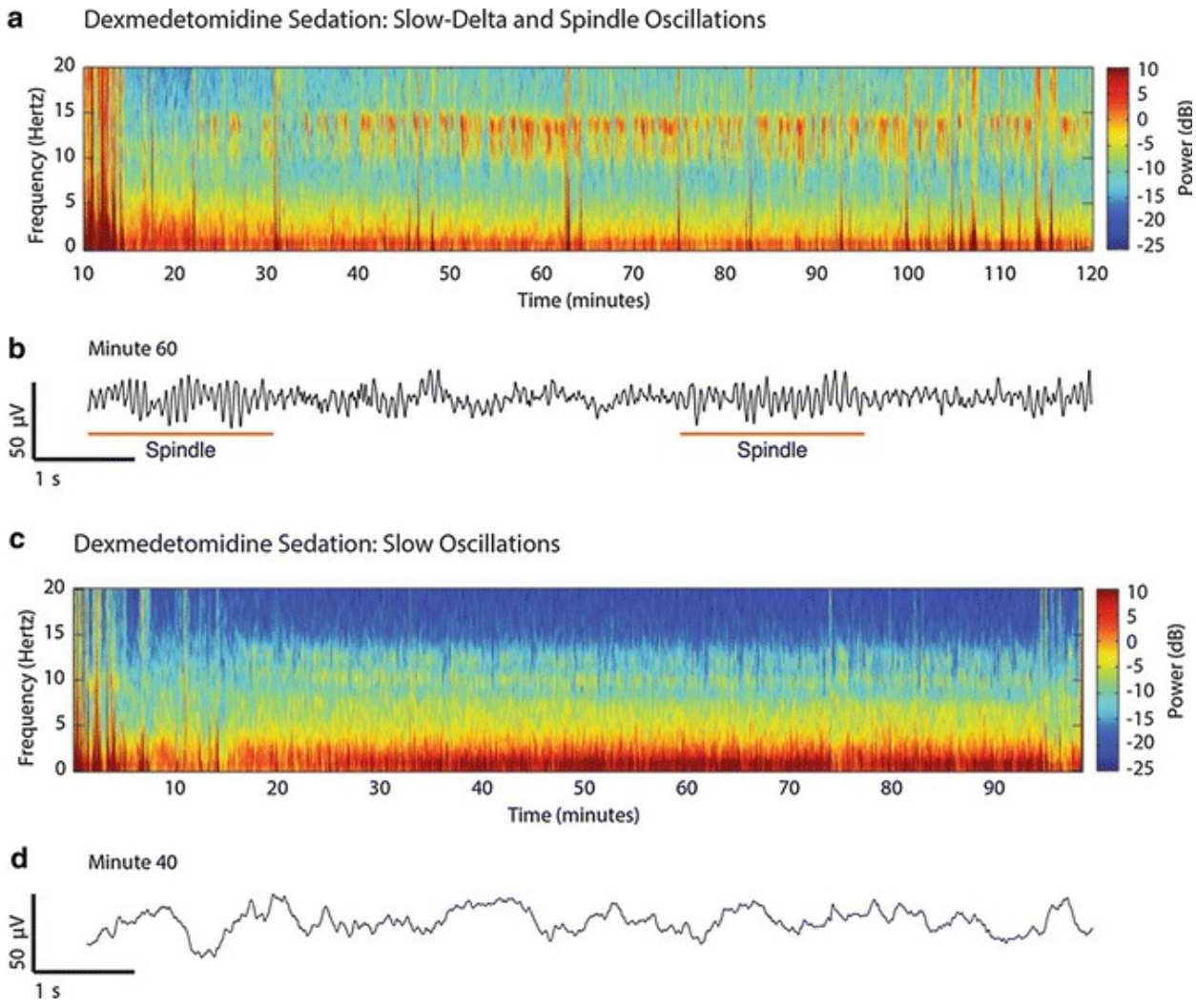

Fig. 11.4 EEG characteristics with light dexmedetomidine sedation . (**a**) Increased power is noted as a red streak in the low-beta range (~13 Hz) under light sedation, likely corresponding to spindle activity. (**b**) Coherent spindle activity is noted during light sedation on the raw EEG, similar to spindle activity appreciated during NREM sleep. (**c**) With increasing doses of dexmedetomidine, increased power is noted in the slow-delta bandwidths. (**d**) Slow-delta oscillations are appreciated on the corresponding raw EEG tracing with higher doses of dexmedetomidine (Reproduced from Purdon et al. [56]; with permission)

Though these EEG patterns reflect neurophysiologic differences among anesthetic classes, they do not necessarily provide insights into the mechanisms behind anesthetic-induced loss of consciousness. For example, propofol-mediated loss of consciousness has been linked with alpha rhythm anteriorization, which may be mediated by γ-aminobutyric acid (GABA) potentiation [12]. This alpha rhythm anteriorization does not appear in the very young or very old [15, 16], and it has not been consistently

demonstrated with sevoflurane- and ketamine-induced loss of consciousness, which involve agents that have known molecular targets other than GABA receptors [17–19]. Despite these molecular and neurophysiologic differences, all three drug classes have the ability to consistently induce loss of consciousness. An emerging explanation for this common functional outcome may be the shared ability of these anesthetics to inhibit communication between anterior and posterior brain regions [17–19]. Specifically, loss of consciousness with propofol, sevoflurane, and ketamine is correlated with reduced EEG measures of frontal-to-parietal directed connectivity [17–19], which is believed to be a surrogate of information transfer involved in conscious experience [20].

Processed EEG

The Bispectral Index (BIS) and SEDLine monitors are two of the most commonly used portable EEG systems for intraoperative EEG monitoring, although many systems are available (Table 11.1). Each system has a set of corresponding electrode channels—or montages—that are applied to the forehead of patients for EEG data acquisition. Both raw and processed EEG data are captured and displayed. In this context, processed EEG refers to the acquisition, integration, analysis, and conversion of raw EEG data—by a proprietary multivariable algorithm—to a dimensionless number meant to reflect anesthetic depth (Table 11.2). With the BIS system, for example, values ranging from 40 to 60 reflect depth consistent with general anesthesia [21], and values ranging from 25 to 50 reflect this same depth with the SEDLine monitor [22]. Processed EEG values have specific limitations, however, which will be discussed further in the next section.

Table 11.1 Commercially available processed EEG systems[a]

Monitor	Data and display features	Index target range[b]
Bispectral Index (BIS)	Raw EEG, processed values	40–60
	– BIS index	
	– Spectral analysis	
SEDLine	Raw EEG, processed values	25–50
	– Patient State Index (PSI)	
	– Spectral analysis	
Narcotrend	Raw EEG, processed values	D, E

	– EEG stage (A-F)	40–60
	– Narcotrend Index	
	– Spectral analysis	
Entropy module	State entropy (EEG-based)	40–60
	Response entropy (EMG-based)	
IoC-View	Raw EEG, processed values	40–60
	– IoC Index	
	– EEG suppression ratio	
SNAP II	High-frequency (80–240 Hz) and low-frequency (0–18 Hz) EEG analysis, processed SNAP Index	50–65
NeuroSENSE	Raw EEG, processed values	40–60
	– Wavelet-based (WAV_{CNS}) index	
	– Spectral analysis	

EEG electroencephalogram, *IoC* index of consciousness, *EMG* electromyogram

[a]The authors do not imply support for any particular device

[b]Number range reportedly consistent with general anesthesia for each device

Table 11.2 Processed EEG steps

Signal sampling
Bandpass filtering
Artifact detection
Suppression ratio calculation
Fourier analysis (γ, β, α, θ, δ bandwidths)
Total power calculation
→ Coherence and power analysis
→ Multivariate analysis
Index value calculated

Clinical Utility of Raw and Processed EEG

Processed EEG has largely been studied with the aim of preventing AWR . Comparative trials have not demonstrated a reduced risk of AWR with processed EEG monitoring compared to end-tidal anesthetic concentration (ETAC) monitoring protocols [23, 24], but processed EEG monitoring does reduce the incidence of AWR compared to routine care and monitoring [24,

25]. Furthermore, this may be particularly helpful during total intravenous anesthesia (TIVA), where ETAC monitoring is not available, and the risk of awareness may be increased [26]. There are several reasons why processed EEG might not be effective in reducing AWR beyond simple ETAC monitoring . For example, anesthetists in these studies used the processed EEG value, rather than raw EEG data interpretation, to gauge anesthetic depth . As such, assessment of anesthetic depth came from a processed algorithm, rather than from direct neurophysiologic assessment. This approach may be problematic, as index values do not take into account the different neurophysiologic properties of various anesthetics. For example, ketamine and nitrous oxide lead to an increased EEG oscillation frequency [27, 28], which may in turn render a higher processed EEG value. Additionally, precise neural correlates of consciousness remain under active investigation. Although certain EEG-based markers such as frontal-parietal disconnection [19, 29] and disruption of thalamocortical connectivity [12, 30] provide insights into causally sufficient mechanisms to induce unconsciousness, the neuroscientific framework that defines consciousness remains incompletely understood. Thus, attempts to distill a patient's level of consciousness to a single number are not yet rooted in complete scientific understanding. A deeper neurophysiologic understanding of consciousness and anesthetic action is likely to be helpful in determining levels of consciousness.

Though intraoperative EEG monitoring has been long examined for the prevention of AWR , EEG may also be useful for appropriately titrating anesthetic depth. For example, EEG allows practitioners to detect burst suppression, a pattern of electrical bursts interspersed with electrical silence (Fig. 11.5). This pattern represents a profound depth of general anesthesia that is not observed during sleep. Longer periods of intraoperative and postoperative burst suppression have correlated with postoperative delirium [31, 32], and a recent meta-analysis of prospective trials has demonstrated a reduced risk of postoperative delirium with BIS-guided protocols [33]. Alternatively, titrating anesthetic depth to achieve burst suppression can be useful in certain circumstances, such as cerebral aneurysm clipping , where burst suppression may reduce the risk of ischemic injury by reducing cerebral metabolism [34]. Thus, EEG-titrated anesthetic depth may be useful in certain clinical scenarios, which would be valuable to anesthesiologists for improving perioperative neurologic outcomes .

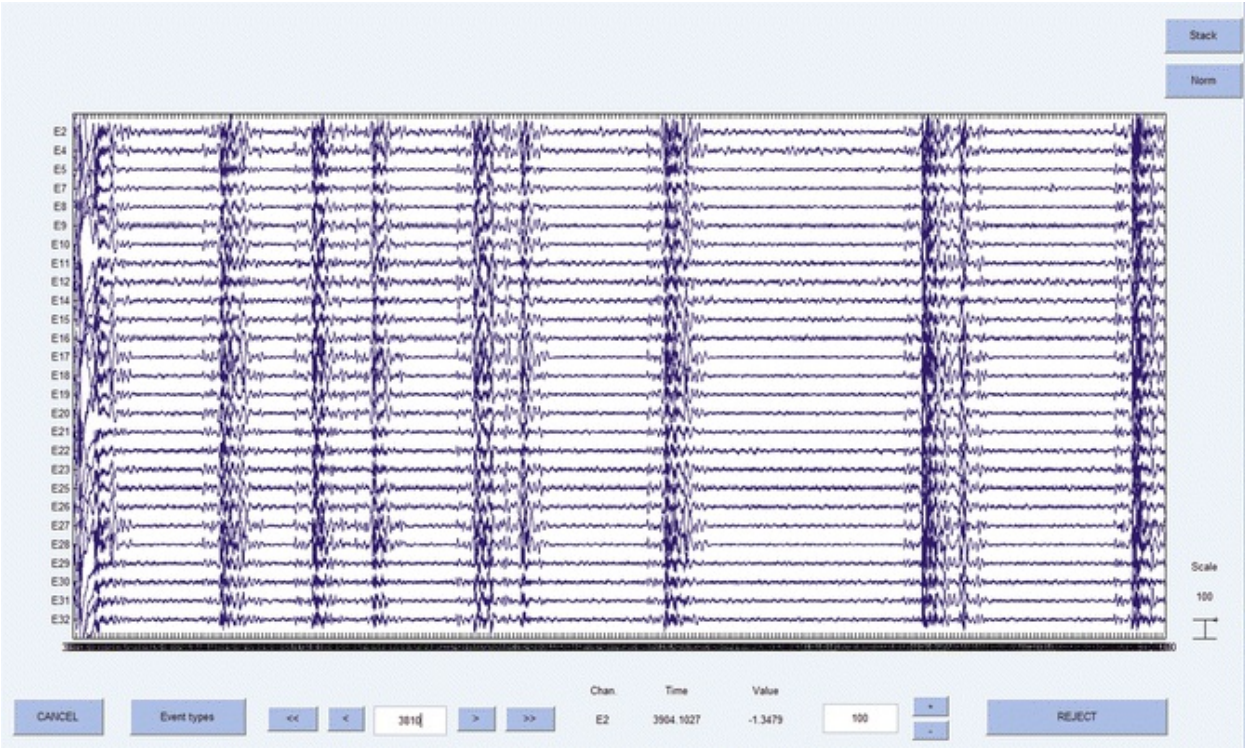

Fig. 11.5 Burst suppression illustrated with continuous EEG data

Lastly, both raw continuous (cEEG) and quantitative EEG (qEEG) findings may be useful for the detection of cerebral ischemia in high-risk settings. Cortical voltage oscillations begin to decrease in frequency once cerebral blood flow (CBF) decreases below specific ischemic thresholds [35, 36]. This slowing results from ischemic damage to neurons, which have high oxygen and glucose requirements to maintain electrochemical gradients across cellular membranes [37]. Frequency slowing is manifested by specific EEG patterns. Intraoperatively, for example, asymmetric oscillatory slowing has been demonstrated during carotid endarterectomy (CEA), marked particularly by irregular delta waveforms [35, 38] (Fig. 11.6). Also during CEA, spectral edge frequencies and relative delta band power are qEEG markers that have helped objectively identify ischemia during carotid clamping [39]. Postoperatively, both cEEG and qEEG have been shown to successfully predict cerebral ischemia in certain pathologic settings. For example, certain features of cEEG and qEEG predict cerebral ischemia from vasospasm after subarachnoid hemorrhage. For cEEG, pathologic delta patterns [40] and regional attenuation of faster frequencies—especially without delta waves present—can help acutely diagnose cerebral ischemia

[41]. Reduced total power [42] and decreased relative alpha frequency variability [43] are qEEG markers that have demonstrated utility predicting cerebral ischemia due to vasospasm. These quantitative markers of the EEG may be particularly useful, as they are easier to interpret and do not require continuous EEG surveillance and expertise to interpret the data.

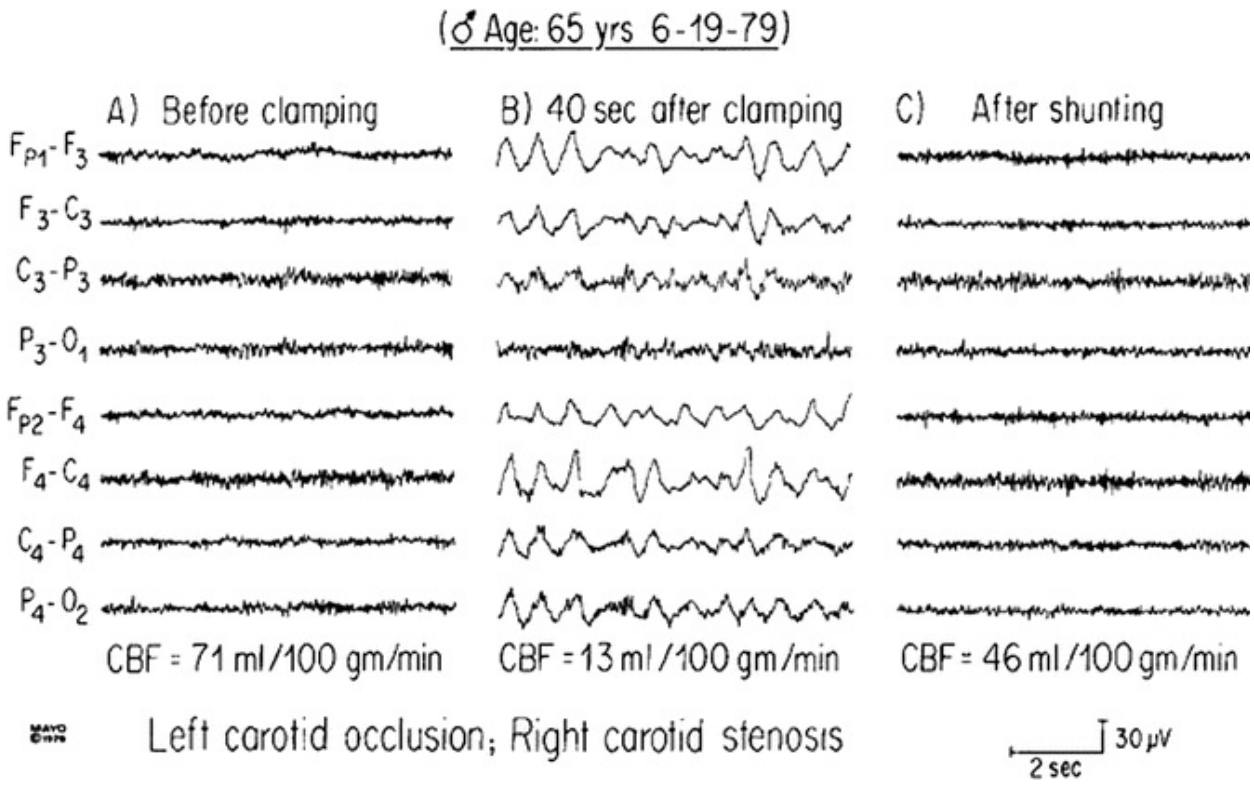

Fig. 11.6 Frequency slowing noted after clamping of the right carotid artery during endarterectomy. Irregular, delta-wave activity is appreciated with attenuation of faster frequencies. Changes are more pronounced on the *right*, which is the side of clamping. EEG waveforms return to baseline after shunt is placed. Reproduced with permission from Dr. Don Schomer and Dr. Fernando Lopes da Silva, Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields, Fifth Edition [57]

Future Directions of EEG Monitoring

Although significant progress has been made since the first suggestion in 1937 that EEG may be used as an intraoperative monitoring modality [44], the current approach to assessing anesthetic depth is still fairly rudimentary. First, it is important to note that the most commonly used metrics of anesthetic depth —hemodynamics and MAC—are flawed. In the case of hemodynamics, there is no consistent relationship between hypertension and

insufficient anesthetic depth or, perhaps more importantly, hypotension and supratherapeutic anesthetic depth. There are numerous determinants of blood pressure and heart rate (e.g., hypovolemia) that are independent of anesthetic dosing or neural activity. In support of this, numerous cases of intraoperative awareness have been identified in the absence of frank hemodynamic changes [45]. In the case of MAC , we have known since the 1990s that the functional endpoint of MAC—movement—is suppressed primarily through anesthetic effects on the spinal cord [46–48]. Thus, MAC is not intrinsically linked to the anesthetic effects on the brain.

In order to advance the field, we need a more sophisticated knowledge of either anesthetic mechanisms in the brain or the neurobiology of consciousness (or both). Current approaches to the EEG are attempting to focus on these two domains of knowledge. Currently available processed EEG monitors display indices that were, primarily, empirically derived through a comparison of the awake EEG and the anesthetized, without necessarily considering whether the differences between the two were related to anesthetic mechanisms or the neural substrate of consciousness. Currently, there are more principled approaches to the EEG. One focuses on linking the systems neuroscience effects of anesthetics to network-level oscillations , searching for drug-specific signatures on the EEG [15]. For example, in healthy adults anesthetized with propofol, a strong alpha oscillation can be seen in the frontal spectrogram, which has been hypothesized to result from a GABAergic effect in the nucleus reticularis of the thalamus that sets up a highly coherent thalamocortical oscillation [49]. Ketamine, on the other hand, does not have strong GABAergic properties and does not result in increased alpha. Rather, slow oscillations and high-frequency gamma activity are observed [19], the latter possibly due to the NMDA antagonist effects on GABAergic interneurons. These entrained oscillations can restrict the normally flexible repertoire of connectivity and communication across the cortex. The other principled approach to the EEG and intraoperative monitoring focuses on the neural correlates of consciousness in the normal state of wakefulness and how these correlate change with anesthetic exposure. It is generally believed that the integration of neural information is a prerequisite for conscious experience [50]; if interrupted, disrupted, or eliminated, conscious processing would not occur. There are various surrogates for connectivity and communication that can be assessed with EEG. Techniques to assess functional connectivity (statistical

interdependence between two brain areas) include coherence and phase synchronization [51]. Techniques to assess directed connectivity (a statistical interdependence that unfolds over time) include transfer entropy and Granger causality [52]. Techniques to assess effective connectivity (the identification of a causal influence of one brain region on another) include dynamic causal modeling [53]. All of these techniques have been examined during general anesthesia. Although a complicated literature, it has been generally found that long-range functional connections and surrogates of communication are broken down during general anesthesia, which presumably reflects the interrupted information synthesis that leads to the breakdown of consciousness. This has been found consistently across all major classes of anesthetics [19]. Thus, while the attempt to link underlying anesthetic mechanisms to EEG features seeks to identify drug-specific signatures, the approach to understanding the neural correlates of consciousness seeks to identify state-specific signatures that are invariant with respect to drug type. The latter approach has many stages of development before real-time monitoring can be attempted. However, there is the promise of a drug-invariant approach that might accurately identify the breakdown or return of consciousness in the operating room and perhaps even disruptions of consciousness in the postoperative period (such as delirium). Furthermore, we must recognize that all of these techniques aim to monitor the sedative-hypnotic effects of general anesthetics. The potent and clinically important amnesic effects are mediated by structures in the medial temporal lobe and may be less amenable to monitoring.

Case Presentation

A 62-year-old man with a pertinent past medical history significant for a right anterior cerebral artery aneurysm presented to the operating room for aneurysm clipping. Intraoperative EEG and somatosensory-evoked potential (SSEP) monitoring were planned to monitor for ischemia during the procedure. Shortly after anesthetic induction, neuromonitoring electrodes were placed for EEG and SSEP signal acquisition, and baseline data were obtained. A balanced technique was employed for maintenance of anesthesia, which included propofol and sufentanil infusions with 0.5 minimum alveolar concentration (MAC) of isoflurane. Shortly after this maintenance regimen was initiated, the following pattern was noted in the EEG (Fig. 11.7). Upon

detection of burst suppression, the propofol infusion dose was decreased, and the pattern returned to slow-wave oscillations. The EEG was used to titrate the anesthetic depth for the rest of the case, and burst suppression was in fact requested prior to aneurysm clipping for ischemic neuroprotection. The aneurysm was successfully clipped, and the rest of the case proceeded uneventfully. The patient was extubated and transported to the neurologic intensive care unit for postoperative recovery and monitoring.

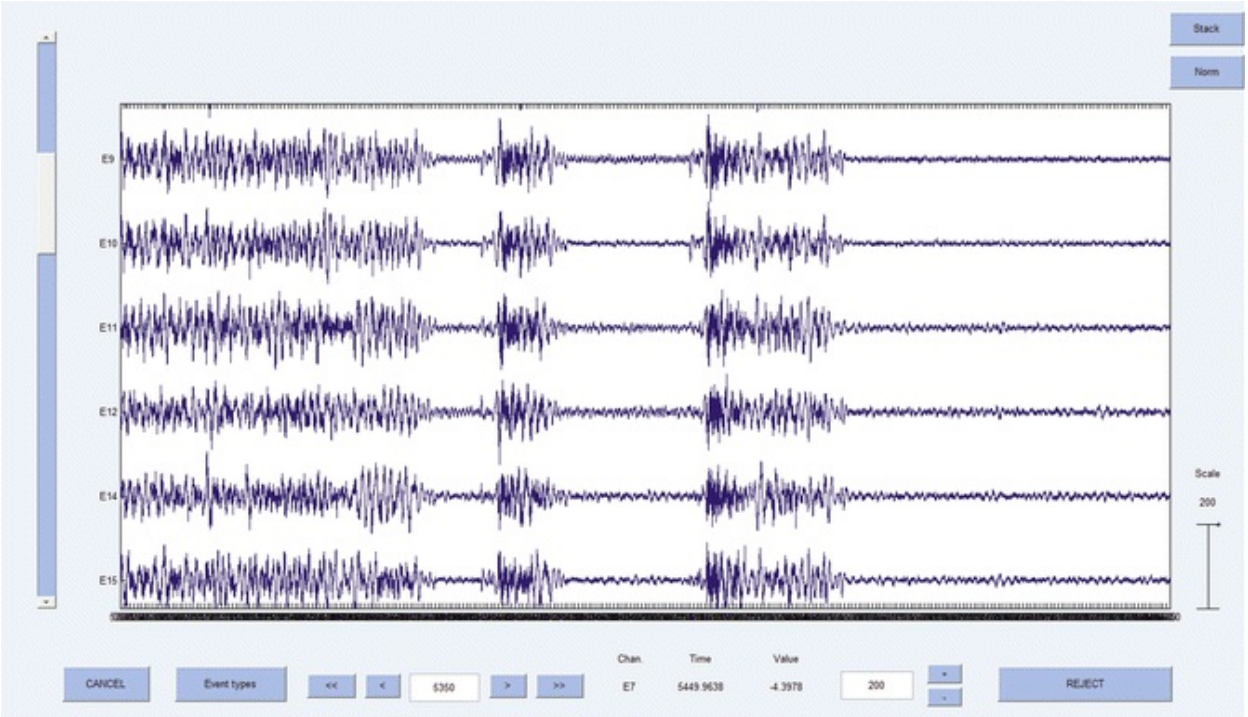

Fig. 11.7 Additional example of burst suppression . This pattern may be noted during periods of deep anesthesia

Conclusion

EEG can serve as a valuable tool for surgical patients in a variety of clinical settings. Although processed EEG monitors do not reduce the incidence of AWR compared with ETAC monitoring protocols , this may be due to an incomplete understanding of EEG markers that reflect the loss of consciousness. Although promising findings are currently being evaluated [17, 54], a further understanding of the neural correlates of consciousness is needed before we can confidently identify true EEG markers of consciousness . Nonetheless, EEG monitoring may play a useful role in other

clinical arenas, such as preventing deleterious neurologic outcomes of surgery and anesthesia. EEG-guided anesthetic titration might minimize the risk of postoperative cognitive dysfunction (POCD) and postoperative delirium; multicenter trials are needed to further explore these possibilities. The amount of time spent in burst suppression and deeper planes of anesthesia, as represented in our case discussion, has correlated with cognitive dysfunction postoperatively [31, 55], and further exploration is warranted to assess whether this has causal significance or if the presence of burst suppression is a marker of a vulnerable brain. Furthermore, EEG monitoring has been shown to detect cerebral ischemia in select surgical and intensive care unit settings. These monitoring strategies may have the potential to detect cerebral ischemia and prevent perioperative stroke in high-risk settings although this requires further exploration. We are presently at an exciting interface between clinical neuroscience and anesthesiology, as technologies for studying the brain continue to improve, and subsequent discoveries continue to shape our understanding of the central nervous system. Anesthesiologists have the first-hand ability to monitor and modulate the brain with ever-improving scientific understanding.

Questions

1. Which of the following allows for EEG frequency decomposition into its individual components?

    A. Fourier analysis

    B. Hilbert transformation

    C. Louvain algorithm

    D. Network analysis

2. Which of the following most correctly describes processed EEG monitoring?

A. Processed EEG is considered a standard monitor in the field of anesthesiology.

B. Processed EEG values consistently reflect anesthetic depth regardless of anesthetic medications used.

C. It has not been shown to prevent awareness with explicit recall (AWR) when compared to end-tidal anesthetic concentration (ETAC) monitoring protocols.

D. The Bispectral Index (BIS) is the only processed EEG monitor commercially available at present.

3. Which EEG pattern, when observed for long periods of time, has been correlated with postoperative delirium?

A. Spindle oscillations

B. Alpha rhythm anteriorization

C. Increased beta and gamma bandwidth power

D. Burst suppression

4. Cerebral ischemia is manifested by all of the following EEG patterns EXCEPT:

A. Cortical symmetry in the alpha frequency bandwidth

B. Regional attenuation of faster frequencies without delta (RAWOD)

C. Reduced alpha frequency variability

D. Onset of irregular delta activity on continuous EEG (cEGG) monitoring and increased delta power during quantitative EEG (qEGG) monitoring

Answers

1. A

2. C

3. D

4. A

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Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_12

12. A Guide to Central Nervous System Near-Infrared Spectroscopic Monitoring

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Keywords Transcranial near-infrared spectroscopy – Hypoxia – Ischemia – Seizures – Neuroprotection – Autoregulation – Vasomotor reactivity

Key Learning Points

- Regional oxygen saturation (rSO_2) represents tissue sample microcirculatory O_2 supply-demand balance.
- Baseline rSO_2 values and intraoperative performance are non-standard and device dependent.
- rSO_2 monitoring aids in determining the:
  - Development of a potentially injurious oxygen imbalance
  - Nature of the imbalance
  - Potential appropriate corrective action
  - Patient response to intervention
- Interpretation of rSO_2 requires additional clinical information.
- Clinical applications of cerebral oximetry include:
  - Detection of preexisting brain oxygen debt
  - Identification of position-related perfusion asymmetry
  - Characterization of vasomotor reactivity, vasoneural coupling and cerebral autoregulation
  - Aiding the determination of blood transfusion need
  - Detection of malperfusion
  - Guidance of supplementary cerebral perfusion

Introduction

Central nervous system oximetry uses transcranial or peri-spinal near-infrared spectroscopy (NIRS) to evaluate changes in neuronal oxygenation non-invasively and continuously. Its operation relies on two basic principles. First, near-infrared light has the capacity to penetrate human tissue , including bone. Second, in these tissues, hemoglobin is the predominant absorbing substance (i.e., chromophore) in the near-infrared range [1].

The binding of oxygen to hemoglobin alters its infrared absorption spectrum . As a result, the concentrations of oxy- and deoxyhemoglobin may be determined by measurement of light absorption at two or more wavelengths. Determination of absolute chromophore concentrations is based on the familiar Lambert–Beer equation and requires knowledge of the optical path length within the tissue sample volume. Claims regarding the accuracy of these measures remain controversial due to the confounding variations in the thickness and light-scattering properties of extraneural tissue and cerebrospinal fluid layers. Despite the continuing uncertainty associated with absolute measurements, close agreement has been shown between brain oxygen level-dependent functional magnetic resonance imaging (BOLD-fMRI) and NIRS estimates of brain stimulation-induced change in deoxyhemoglobin dynamics [2]. Independent direct measures of optical path length and cerebral/spinal chromophore concentrations are currently unavailable. Consequently, the putative “absolute” concentrations of oxy- and deoxyhemoglobin produced by some oximeters appear to be, at best, semi-quantitative estimates [3, 4].

Measurement of the relative concentrations of the hemoglobin moieties (i.e., oxygen saturation) also relies on the Lambert–Beer intensity ratio of incident-to-absorbed light. However, in contrast to attempts at absolute chromophore concentration measurement, the problematic path length factor is eliminated [1]. Because blood within the cerebral vascular bed is typically 70–85 % venous and capillary with the remainder arterial [3], the accuracy of this measure of regional cerebral oxygen saturation (rSO_2) has been validated against the invasive field saturation measurement (i.e., 25–30 % arterial oxygen saturation + 70 % –75 % internal jugular venous oxygen saturation) [5]. However, concern has been expressed that the algorithmic assumption of a constant ratio of arterial and venous blood within the sampled tissue may not accurately represent the inevitable fluctuations in the actual arterial-venous volume relationship [6].

Instrumentation

Medtronic-Covidien (Boulder, CO) currently produces the INVOS™ 5100C cerebral oximeter, the first commercial device to receive US Food and Drug Administration (FDA) clearance for continuous measurement of cerebral and somatic rSO_2 in patients larger than 2.5 kg. It uses two wavelengths of

infrared light generated by broad bandwidth light-emitting diodes. Through a patented process termed “spatial resolution,” the INVOS™ device uses multi-site extra- and intracranial measurements to suppress the influence of extracranial hemoglobin (Fig. 12.1). Independent studies have shown that the source of the resultant rSO_2 metric is approximately 65 % intracranial [7]. More than 700 peer-reviewed articles have characterized performance of INVOS™ systems in a wide range of clinical and experimental settings [8].

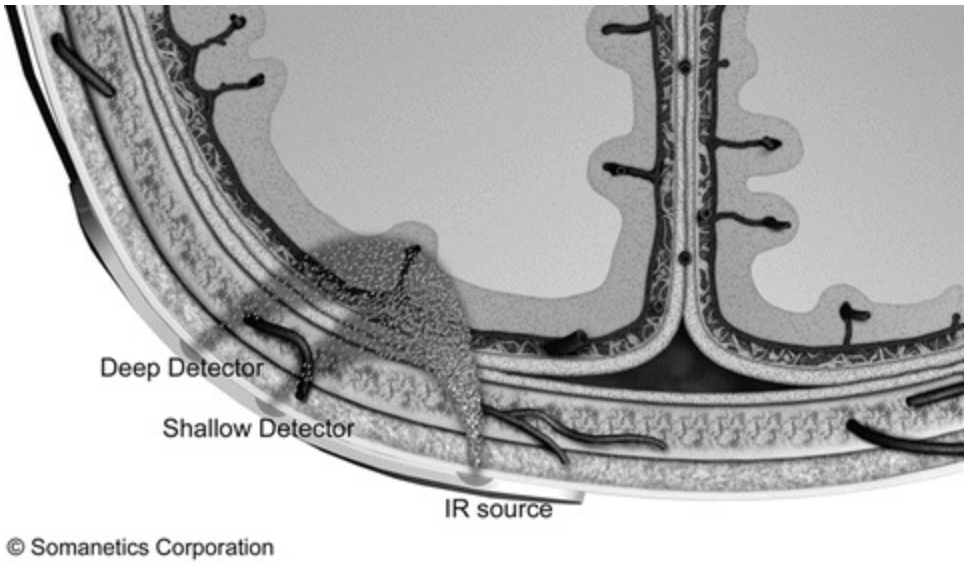

Fig. 12.1 The *shaded parabolas* illustrate the transcranial photon paths from a scalp-mounted infrared (IR) light source to adjacent proximal (shallow) and distal (deep) sensors. The photon paths depicted represent those used with spatially resolved spectroscopy. With this technique, photons arriving at the shallow and deep detectors are reflected by distinct regions of the cerebral cortical microcirculation. Ratios developed from the multi-site intracranial measurements enable suppression of both extracranial reflection and interindividual variability in intracranial photon scatter. The commercial alternative of differential spectroscopy locates the shallow detector much closer to the IR source. As a result, incident photons arriving at this detector have been reflected exclusively from extracortical tissues. The differential shallow vs. deep signal suppresses extracranial reflection. Additional wavelengths of infrared light are used in an attempt to suppress intracranial photon scatter variation

Three other cerebral oximeters have received FDA clearance. The CAS Medical (Branford, CT) Fore-Sight® uses four wavelengths of infrared light with single-site extra- and intracranial measurement to produce a differential rSO_2 signal [9]. Approximately 90 peer-reviewed articles have described device performance in a variety of clinical settings [10]. In addition, several studies have compared Fore-Sight® and INVOS™ performance [11–15]. In general, interdevice measurement disparities led the investigators to conclude

that the rSO_2 values were device specific.

Nonin Inc., (Plymouth, MN) manufacturers the EquanOX® 7600 cerebral oximeter. The analytic approach resembles that of the CAS Fore-Sight® (i.e., four infrared wavelengths and single-site extra- and intracranial differential measurement). The optode contains two light sources, so that the resulting rSO_2 apparently represents an average from pairwise measurements in adjacent tissue samples [16]. About two dozen peer-reviewed articles describe device performance in various clinical settings [17]. The authors of a four-way comparison of INVOS™, Fore-Sight®, and EquanOX® (3- and 4-wavelength) devices concluded that the resultant rSO_2 values were not interchangeable [4]. This situation resembles the discrepant arterial oxygen saturation measurements that have been reported between on-site invasive co-oximetry and laboratory-based complete blood count analysis [18].

The OrNim Inc. (Los Gatos, CA) CerOx® measures brain or peripheral tissue regional oxygen saturation using a combination of multiple wavelength near-infrared light and phase-modulated ultrasound [19]. Currently, there is one peer-reviewed article that characterizes its clinical performance [20]. Comparative studies with competing devices are unavailable.

Additional research instruments without FDA clearance include the (1) NIRO® 100, 200, and 300 (Hamamatsu Photonics KK, Hamamatsu City, Japan) [21], (2) Oxiplex® TSS (ISS, Champaign, IL) [22], and (3) O3® (Masimo, Irvine, CA) [23]. Their clinical application requires an FDA Investigational Device Exemption and/or an Institutional Review Board-approved research protocol with informed patient consent.

Transcranial NIRS Technology

Regional Cerebral Oxygen Saturation Measurement

With the exception of infants, brain mass is too large for transillumination, and as a result, NIRS in adults and children relies on reflectance spectroscopy. An optical electrode or optode, containing both near-infrared and infrared light sources as well as sensors to detect light reflected from the underlying tissue, is fixed on the calvarium. The optode is generally placed on glabrous skin to avoid contamination by environmental infrared light. Light-tight seals around the sensor(s) aid in artifact suppression. In the proximity of intense infrared sources, it may be necessary to drape the

cranium with infrared-opaque material. Disposable optodes contain electroconductive material referenced to the instrument. These optodes should be isolated from electrophysiologic electrodes or ultrasound probes to prevent artifactual contamination or signal degradation.

Large, reusable optodes require fixation and mechanical stabilization with a strap or elastic band, whereas small disposable optodes rely on an adhesive patch that also serves as a light shield. Because of variations in anatomy, skull curvature, and the position of sinus cavities and surface blood vessels, accuracy may be compromised if disposable optodes are placed contrary to the manufacturer's instructions [24, 25]. In particular, placement over the sagittal sinus is potentially problematic due to the large amount of pooled venous blood found there and its confounding effects on photon absorption and scattering [24]. Furthermore, disposable optodes designed for adults should not be used on patients weighing less than 40 kg. Pediatric and neonatal optodes are available from some manufacturers for small patients. Regardless of the optode style, care must be taken to avoid excessive or prolonged compression of the underlying sensitive forehead or scalp tissue. The FDA-cleared optodes have a flat design to minimize tissue compression.

Manufacturers should provide convincing data that the device is actually capable of measuring cerebral as opposed to cranial hemoglobin [7]. Known changes in cerebral perfusion or oxygenation should be manifest by appropriate change in the intracranial oxygenation metric [7]. Evidence should verify that extracranial contamination does not substantially confound interpretation [6]. By measuring optical signals obtained from two detectors placed at different distances greater than 2 cm from the infrared source, oximeter systems utilizing spatially resolved spectroscopy (i.e., INVOS™ and NIRO®) measure the slope of absorption change as a function of photon penetration depth. Their proprietary algorithms partially suppress the confounding influences of interindividual differences in intracranial photon path length and scattering [1].

FDA-cleared cerebral oximeters display rSO_2 trends as a function of time. Research devices may additionally provide estimates of change in the concentrations of oxy-, deoxy-, and total hemoglobin as well as parenchymal cytochrome aa_3. The trends of some devices represent moving averages, while others are a time series of discrete measures. Because smoothing can dramatically affect the responsiveness of the trends to important physiologic perturbations, the averaging time constant should be clearly described by the

manufacturer and understood by the user.

Now it is not possible to directly confirm the accuracy of transcranial measurement of regional cerebral oxygen by an independent analytical method. The closest approximation to this goal has been the comparison with field saturation [5]. As with other neuromonitoring modalities, optimal recording technique dictates that a simple calibration method should be available to confirm that both the optode and recording electronics/software are functioning properly. Although some manufacturers currently provide a calibration device for their recording electronics, none is available for use with individual optodes.

Safety Considerations

Potential users of this technology should ensure that NIRS devices intended for clinical application successfully restrict environmental current flow to patient connections and between optodes. The low-intensity light sources used in these devices are similar to those found in pulse oximeters and do not appear to represent a safety hazard [25]. The higher powered laser light source used in the Ornim oximeter is rated as Class 1, meaning that there is no evidence that its use can lead to potential injury. With any of these devices, care must be taken to avoid undue pressure of the optode against the unprotected forehead or scalp, particularly in infants and young children. Some manufacturers recommend that the skin should be checked for irritation and sensors replaced daily.

Technical Considerations

Cerebral oximeters are relatively immune to motion and electrocautery interference that plague electrophysiologic and ultrasound measurements. The most troublesome artifacts for NIRS are environmental light contamination and light piping. Especially in infants, intense infrared light (i.e., heat source) can readily penetrate the skull opposite the optode and artifactually elevate reflected intracranial light by transillumination. An elevated extracranial signal may occur in adults through the use of a pulse oximeter probe placed on the nasal bridge or forehead, which illuminates the frontal sinuses with infrared light [26]. Contamination may also occur through light piping. Translucent material such as hair, perspiration beads, or moisture condensate in the proximity of the sensors can act as a conduit for

environmental infrared light.

Although rSO_2 measurement is relatively insensitive to melanin and other normal skin pigments [27], anatomic anomalies or underlying pathology in darkly pigmented patients may have a confounding influence [28]. Systems utilizing two wavelengths cannot distinguish between normal and pathologic hemoglobin moieties . The presence of methemoglobin or other abnormal hemoglobins will result in a functional saturation measurement that can be quite different than the fractional measurement. Non-heme chromophores such as bilirubin and biliverdin [29, 30], as well as some intravascular dyes like indigo carmine and methylene blue [31], absorb photons and reduce signal intensity. In contrast, other dyes such as indocyanine green may falsely elevate rSO_2 values [32].

The intracranial presence of extravascular blood (i.e., hematoma or hemorrhage) within the frontal tissue sampled by the oximeter renders the rSO_2 estimate ambiguous [33]. A fundamental assumption of the computational algorithms used in several NIRS devices is that the infrared signal reflects exclusively intravascular hemoglobin. Mixture of this signal with that obtained from a stagnant pool of poorly or unoxygenated blood can result in uninterpretable values. This consideration also influences sensor placement. A midline locus should not be used in order to avoid placement over the sagittal sinus. A superior placement on the forehead also helps to avoid the frontal sinuses [26].

Placement directly over a metabolically inactive cortical infarct may result in indeterminate information because of the lack of oxygen extraction from sequestered venous blood. However, several recent studies have observed abnormally low rSO_2 values sampled from regions containing cerebral cortical infarction [34, 35]. Optode placement over regions of damaged or absent brain tissue (i.e., hemispherectomy) may result in spurious readings. In addition, a postcraniotomy metal plate implant obviously makes monitoring impossible. Conversely, the absence of frontal bone can result in overscaled reflected signals [36]. Skull defects and abnormal frontal sinus anatomy can often be identified simply through transillumination with a flashlight.

Limitations of Cerebral Oximetry

On the basis of current clinical literature and expert opinion, cerebral

oximetry has some limitations as a monitoring tool. First, direct validation of the accuracy of rSO_2 currently is not possible because of the absence of true noninvasive measures of brain oxygen saturation and oxy- and deoxyhemoglobin and cytochrome aa_3 concentrations. Second, baseline brain oxygen saturation measurement appears to be influenced by sensor position on the forehead, and at present, sensor placement is limited to glabrous skin. Finally, because rSO_2 represents focal measurement of prefrontal cortex, regional hypoperfusion affecting large portions of the intracranial anterior or posterior circulations may be invisible to forehead sensors.

Rationale for Cerebral NIRS Monitoring

The generic rSO_2 trend measures change in regional cerebral microcirculatory oxygen supply balance. Currently, this information is not otherwise available in the perioperative or critical care settings. This NIRS technology can prove invaluable as an aid in interpreting electrophysiologic or cerebral hemodynamic data. Change in electrophysiologic signals indicates functional alteration in a specific neural pathway or region, but does not indicate the underlying cause or the most appropriate corrective action . Similarly, transcranial Doppler (TCD) ultrasound documents change in blood flow velocity through the large basal cerebral arteries, but provides no information about the underlying functional status of the neural tissue at risk. In either case, concomitant rSO_2 monitoring aids in determining the:

1. Development of a potentially injurious oxygen imbalance
2. Nature of the imbalance
3. Potential appropriate corrective action
4. Patient response to intervention.

The INVOS™-derived normative median rSO_2 for healthy adults, children, and neonates, respectively, are 65 % [27], 71 % [37], and 78 % [38], whereas lower values have been described for adult (62 %) [39], pediatric (60 %) [40], and neonatal (67 %) [41] patients with cardiac disease.

Because rSO_2 reflects a composite of arterial and venous blood, normative values are higher than published values for jugular venous oxygen saturation ($SjvO_2$) ranges for both healthy adults [42] and cardiac surgery patients [43]. Although conscious baseline rSO_2 values appear to be device specific, currently only limited normative values are available for the other cerebral oximeters [9, 16].

Both noninvasive rSO_2 [44] and invasive brain field saturation [5] are associated with hemoglobin concentration and hematocrit. The relationships appear to be complex and nonlinear [45], such that rSO_2 is independent of hematocrit at fractions greater than 0.3 [46]. Thus, the apparent relationships between these measures and low hematocrit and [hemoglobin] seem to reflect inherent properties of cerebral oxygen saturation that occur with inadequate oxygen delivery.

Kishi et al. [44] observed in adolescent and adult patients that rSO_2 was significantly correlated with patient age. Yet, this apparent age-dependency may be simply a manifestation of underlying pathology (i.e., older patients tend to have more disease and dysfunction). A study by Baikoussis et al. [45] involving adult and geriatric patients supports this interpretation.

This study also documented close interhemispheric agreement in preanesthetic baseline rSO_2 measurements. In contrast, marked asymmetry is the rule with $SjvO_2$. Indeed, $SjvO_2$ right-left asymmetry greater than 10% has been reported to occur in two thirds of patients [46].

In a cohort of more than 2097 adult cardiac surgery patients, INVOS™ preoperative rSO_2 values less than 60 % were associated with increased risk of morbidity and mortality [47]. A similar study involving 1178 patients found even greater risk with rSO_2 baseline below 50 % [39]. Subnormal intraoperative rSO_2 is associated with heightened risk of postoperative delirium and neurocognitive dysfunction [48–53].

Despite the establishment of normative absolute rSO_2 values, it should be appreciated that the number represents exclusively a measure of highly regional intracranial hemoglobin saturation. Individualized static baseline rSO_2 values correlate with cardiac function. However, these static values do not necessarily provide direct information about cerebral well-being [54, 55].

Thus, values within the normative range may be obtained from patients with cerebral infarction or brain death [56]. Cadaveric rSO_2 values may also

lie within the normative range [57] because postmortem cerebral venous oxygen saturation ranges between 5 and 95 %, depending on the cause of death and body storage conditions [58]. Because both the pulse and cerebral oximeters are functionally spectrophotometers, they may generate normative saturation values from illumination of chromophore-containing inanimate objects (i.e., pumpkins) [59].

Preoperative Factors

Interpretation of the clinical significance of cerebral dysoxygenation during surgery or critical care is heavily influenced by underlying patient pathophysiology. There are a number of preexisting factors that affect both the static rSO_2 value and its dynamic response to physiologic change. These factors involve primarily influences on oxygen delivery. Thus, patients with chronic hypertension or diabetes mellitus may have impaired cerebral pressure autoregulation. In such cases, oxygen delivery may be transiently impaired by orthostasis or other positional change. Delivery may also be impaired through vascular stenosis, cardiac dysfunction with low cardiac output, anemia, pulmonary dysfunction, or right heart/pulmonary artery congenital anomalies [60]. These various disorders explain, in part, the wide range of baseline values observed in awake surgical patients prior to preoxygenation.

Systemic Arterial Pressure

The principle of cerebral autoregulation states that cerebral perfusion (i.e., oxygen delivery) is independent of mean systemic arterial pressure over a wide range (i.e., 50–150 mmHg). In healthy individuals, profound hypotension is required to significantly reduce oxygen delivery with a concomitant rSO_2 decrease. However, even a small pressure decrease within the normal autoregulatory range may result in rSO_2 decline if autoregulation is diminished or entirely absent [8]. Cerebrovascular insufficiency from dysautoregulation may be secondary to a preexisting pathology (e.g., stroke) or be iatrogenically induced during surgery (e.g., volatile anesthetics, nonpulsatile perfusion, hypocapnia, hypothermia) [61]. Recently, reports have described the benefit of cerebral oximetry in the detection of position-related cerebral hypoperfusion while systemic arterial pressure remained

within the normally acceptable range [62]. Availability of the arterial pressure trend is essential for interpretation of rSO_2 change.

Systemic Arterial Oxygenation

Delivery of oxygen to the brain depends, in part, on the relative concentration of oxygenated hemoglobin in the arterial blood. An inadequate oxygen supply will thus eventually result in decreased arterial oxygen saturation. However, because systemic oxygen reserves far exceed those of the metabolically active healthy brain [63], a venous-dominant rSO_2 decrease will often precede systemic arterial oxygen desaturation [64].

Oxygen delivery also depends on the availability of hemoglobin. Blood loss or hemodilution can result in an insufficient supply of oxygen to meet brain demands, even though the cerebral perfusion pressure, flow, and arterial oxygen saturation are within normal limits [8]. It is essential to note any marked change in hemoglobin that may accompany sudden rSO_2 changes [65]. Because of the sensitivity of rSO_2 as a measure of inadequate hemoglobin concentration, it has been proposed as a factor to be considered in determining transfusion triggers [66].

Systemic Arterial CO_2 and pH

Normally, cerebral arteries are exquisitely sensitive to hydrogen ion shifts and thus to CO_2 changes. For example, middle cerebral artery flow velocity typically changes approximately 4 % for each 1 mmHg change in the arterial CO_2 partial pressure [67]. This vasomotor reactivity (VMR) may be alternatively measured with cerebral oximetry. INVOS™-determined normal VMR has been defined as approximately 1 % rSO_2 change for each 1 mmHg CO_2 change [68]. Because hyper- and hypocapnea have profound effects on normally reactive cerebral arteries, an end-tidal or arterial carbon dioxide trend may be invaluable in the interpretation of rSO_2 changes.

With rising arterial CO_2 tension , the absence of a parallel rSO_2 increase suggests impairment of both cerebral VMR and autoregulation. Furthermore, an interhemispheric VMR asymmetry warns of a possible vasculopathy (i.e., intracranial stenosis or silent infarct). Anesthesia providers armed with this information may optimize perfusion management to maintain cerebral

perfusion in both hemispheres [68].

Cerebral Blood Flow Obstruction

Systemic arterial pressure reflects perfusion at sites distant from the head. Obstruction to one or more vessels carrying blood to the brain may result in a profound decrease in regional cerebral oxygen delivery without altering either systemic pressure or oxygenation. For example, with bilateral carotid disease and an incomplete circle of Willis, head rotation may obstruct flow by vertebral artery compression [69]. Of course, mechanical carotid occlusion for endarterectomy may produce regional ischemia in the absence of a functionally intact collateral perfusion [70]. Alternatively, during cardiopulmonary bypass, a malpositioned aortic cannula or balloon occluder may block flow to a critical head vessel [71]. Continuous delivery of oxygen to the brain is impeded if venous outflow is compromised (i.e., edema or malpositioned caval cannula). Such obstruction will decrease rSO_2 [72].

Temperature

Changes in rSO_2 cannot be fully understood without knowledge of the cranial temperature fluctuations . Cooling is used for neuroprotection during surgery requiring circulatory arrest because hypothermia, in part, decreases brain oxygen requirement. Thus, during cooling, a nonlinear rSO_2 rise indicative of cerebral hyperoxia may occur despite a decline in cerebral blood flow [69]. Because the magnitude of hypothermic reduction in cerebral oxygen demand varies markedly among individuals, monitoring of cerebral oxygen balance helps to determine the optimal temperature for circulatory arrest. With progressive cooling, rSO_2 typically reaches a plateau with cortical synaptic quiescence (i.e., flat-line EEG) [69]. During rewarming, cerebral blood flow may fall relative to metabolism due, in part, to a cold-induced vasoparesis [73]. The severity of the potentially injurious flow-metabolism mismatch (i.e., vasoneural uncoupling) is manifested by a proportionate rSO_2 decrease [74].

Anesthetic Adequacy

Approximately 60 % of cerebral oxygen consumption is spent on

interneuronal communication [75]. Therefore, rSO_2 is influenced by the choice of anesthetic agent and resulting magnitude of cerebrocortical synaptic depression. Agents such as the opioids exert much of their action at subcortical sites. With these agents, rSO_2 may remain relatively unchanged over a wide dose range. Alternatively, the volatile halogenated agents, propofol and barbiturate hypnotics can virtually eliminate interneuronal signaling (i.e., flat-line EEG). This metabolic suppression typically results in rSO_2 increase [76]. Similarly, inadequate anesthetic may lead to increased oxygen consumption in the waking brain accompanied by rSO_2 decrease. Therefore, intraoperative interpretation of rSO_2 is aided by an objective, quantifiable measure of cerebrocortical synaptic activity (i.e., hypnotic adequacy).

Seizure Activity

With intact vasoneural coupling, increased neural activity produces cerebral blood flow increases that are far larger than associated local metabolic increases [77]. Because this hemodynamic response has variable onset and duration, intermittent activation leads to complex oscillations in hemoglobin saturation, causing a transient rise in the venous-dominant rSO_2 measurement [78]. Based on this phenomenon, a rapidly oscillating rSO_2 trend has been used to detect suspected seizure activity in chemically paralyzed, ventilated patients [77, 78]. This situation is not uncommon, since subclinical seizures are thought to occur in up to one quarter of neurocritical care patients [79].

Supplemental Cerebral Perfusion

For surgery requiring hypothermic circulatory arrest, supplemental cerebral perfusion (SCP), both antegrade (ACP) and retrograde (RCP), appear to provide added neuroprotection [80]. Despite the widespread use of these techniques, optimal management procedures have not been established and vary widely among institutions. Cerebral oximetry has aided management in several important ways. First, it identifies an SCP requirement. As the hypothermia-elevated rSO_2 declines toward a predetermined oxygen debt threshold [81], it warns the surgical team of the impending need to initiate SCP. Second, the rSO_2 trend provides direct objective evidence that cerebral

perfusion actually has been established and is appropriate to avoid either hypo- or hyperperfusion [82]. Absent this evidence, one is typically forced to rely on an unjustified assumption of SCP flow adequacy. The evidence vs. assumption dichotomy may help explain the wide range of published RCP clinical experiences, since many lack either rSO_2 or ultrasonic evidence of retrograde blood flow.

Case reports have documented rapid rSO_2 detection of ACP hemispheric flow asymmetry due to perfusion cannula malposition [83], or an incomplete circle of Willis [82]. Neither of these events is rare [84, 85]. The recent study of Senanayake et al. [86] illustrates the potential clinical value of rSO_2 guidance for SCP management . They found in a series of 27 adult ACP-supported aortic arch repairs that by maintaining rSO_2 at baseline level, postoperative neurodeficit could be completely avoided.

Rationale for Peri-spinal NIRS Monitoring

Recently, a custom-built NIRS optode and an indocyanine green tracer technique were used to validate translaminar peri-spinal oxygen saturation (SsO_2). The neuromonitoring technique demonstrated both local blood flow autoregulation and CO_2 reactivity [87]. SsO_2 monitoring has been achieved by placing FDA-cleared optodes designed for adult transcranial tissue oximetry over the lower thoracic and upper lumbar spine. Badner et al. [88] described the application in two thoracic aortic aneurysm endovascular repairs. In the first, thoracic sensor SsO_2 decline was corrected with mean arterial pressure (MAP) increase and cerebral spinal fluid (CSF) drainage. In the second, an uncorrectable SsO_2 decline of greater than 50 % followed deployment of a thoracic endograft and presaged postoperative paraplegia. A contemporaneous case report examined the SsO_2 vs. MAP relationships before and after deployment of an arch endograft [89]. Postoperatively, SsO_2-guided blood pressure management until autoregulation eventually returned. This observation suggests that SsO_2 monitoring may offer insight into the genesis and prevention of delayed spinal cord ischemic injury. The SsO_2 aortic endograft experience has also been replicated in open thoracoabdominal aneurysm repair [90]. In this clinical population, Etz et al. [91] performed a pilot study using commercial optodes placed bilaterally

over lower thoracic and upper lumbar paraspinous vascular collateral networks (CNs) [91]. Declines in lumbar CN oxygenation appeared to be directly linked to aortic perfusion compromise.

Conclusions

Despite the absence of multiple, positive, large-sample, prospective randomized outcome studies, cerebral oximeters are now installed in the majority of institutions performing adult and/or pediatric cardiac surgery [92]. Yet, a clear consensus on the optimal utilization of this technology by anesthesia providers remains elusive [92–96]. A recent survey highlights the clinical uncertainty [96]. Survey authors attributed the uncertainty to a dearth of both large, randomized clinical trials and nonproprietary educational and training programs and products.

Questions

With each of the following questions, choose the single best response.

1. Which of the following conditions may confound rSO_2 measurement and interpretation?

   a. Skin hyperpigmentation

   b. Skull defects

   c. Cortical infarcts

   d. All of the above.

2. Which of the following statements regarding rSO_2 and arterial blood pressure are correct?

   a. In the autoregulatory range, rSO_2 is independent of blood pressure.

   b. Below the autoregulatory range, rSO_2 is inversely related to blood

pressure.

c. Position-related rSO_2 declines are prevented when blood pressure is maintained within the normal autoregulatory range.

d. All of the above.

3. During the induction of deep hypothermia:

   a. There is an inverse linear relationship between nasopharyngeal temperature and rSO_2.

   b. The nonlinear rSO_2 increase reaches a plateau with cortical synaptic quiescence.

   c. Cooling consistently produces a predictable decline in brain oxygen demand.

   d. None of the above.

4. An abnormally low baseline rSO_2 may be due to:

   a. Cardiac dysfunction

   b. Anemia

   c. Pulmonary dysfunction

   d. All of the above.

5. When measuring cerebral vasomotor reactivity (VMR) with cerebral oximetry,

    a. A normal response is defined as a 4 % rSO_2 change/1 mmHg $PaCO_2$.

    b. It is unnecessary to monitor both hemispheres.

    c. A normal rSO_2 response suggests intact autoregulation.

    d. None of the above.

Answers

1. D
2. A
3. B
4. D
5. C

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Footnotes

1 Asterisk indicates key reference.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_13

13. Transcranial Doppler Ultrasound

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Keywords Transcranial Doppler ultrasound – Cerebral blood flow – Ischemia – Hyperemia – Autoregulation – Vasomotor reactivity – Vasoneural coupling

Key Learning Points

- TCD measures :
  - Cerebral blood flow direction, velocity, and pulsatility within large arteries and veins
  - Cerebral autoregulation
  - Vasomotor reactivity
  - Neurovascular coupling
  - Embolization
- TCD blood flow-velocity changes reflect flow changes if vessel diameter and blood viscosity remain constant.

- High-intensity transient signals (HITS) provide a semiquantitative TCD embolization estimate within a specified cerebral artery.
- The quality of TCD measurements is user-dependent and based on sonographer training, skill, experience, and practice.
- Cranial hyperostosis and cerebrovascular pathology may preclude TCD measure in nearly one quarter of adult patients.

Introduction

The purpose of perioperative and critical care transcranial Doppler (TCD) ultrasonographic monitoring is to assess cerebral perfusion *change*. This is accomplished through noninvasive continuous measurement of blood flow-velocity within the largest intracranial blood vessels. Because normative velocity values may vary widely, the primary monitoring objective generally is the trending of relative velocity. Changes in blood flow and flow-velocity are proportional as long as blood viscosity and vessel diameter remain constant [1].

Technology

Principles of TCD Measurement

Nearly four decades ago, it was first observed that ~2 MHz ultrasound waves often could penetrate the thin temporal bone of the adult human skull and insonate the large, basal intracranial arteries and veins. This finding led to development of the first commercial TCD ultrasonographs. Despite significant improvements, current TCD monitors share basic features common with the original devices (Fig. 13.1). The basic TCD examination and monitoring techniques have been recently reviewed [2, 3]. Scalp-mounted probes, containing both an oscillating piezoelectric crystal and a microphone, generate the high-frequency sound and record its echoes. Blood flow direction and velocity of the echogenic erythrocytes are determined through the use of pulsatile sound and calculation of the Doppler-shift frequency between the transmitted acoustic signal and its echoes. Laminar flow in the largest vessels creates an echo series with the highest shift frequencies (i.e., velocities) in the vessel mid-region.

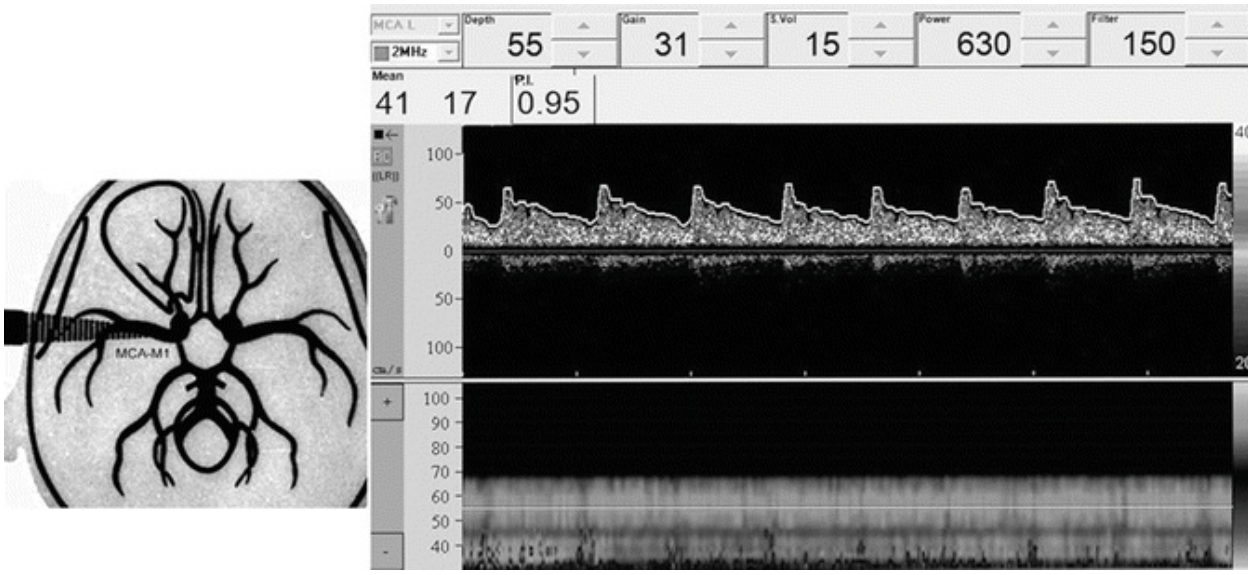

Fig. 13.1 The drawing at the left depicts the transtemporal insonation of the M1 segment of the left middle cerebral artery (MCA) at a depth (i.e., distance) of 55 mm from the ultrasound probe face. Note that at more shallow depths, only MCA branches are generally accessible by the ultrasound beam. On the right is shown a single-depth Doppler spectral trend display in the upper half of the monitor image. The horizontal axis is time, here representing eight cardiac cycles. The vertical axis is instantaneous blood flow-velocity. By convention, positive values indicate blood flow directed toward the probe. The gray-tone scale at the right shows the variation in signal intensity occurring through a cross-section of the insonated artery. Below is the power M-mode Doppler display. Here, the vertical axis indicates depth. The *wide horizontal light*-colored band depicts the velocity of probe-directed blood flow through the entire MCA linear segment. The *thin horizontal white line* shows the specific depth from which the above spectral display was derived

A time series of instantaneous Fourier-derived frequency spectra over a single cardiac cycle produces a pulsatile waveform resembling a blood pressure trace. Monochrome dot intensity or color-coded echo amplitude at each frequency is typically scaled as log change (i.e., dB) above background noise. The highest flow-velocity occurs at peak systole and lowest at end-diastole.

By briefly recording echoes only after each sound pulse (i.e., gating), the velocity spectra may be obtained from a user-defined tissue sample volume at an intracranial locus (i.e., depth below the scalp). Alternatively, the overlapping of multigated spectra creates an M-mode (motion-mode) display simultaneously encompassing velocities over a wide depth range. Because particulate and gaseous emboli have greater acoustic impedance (i.e., reflectivity) than erythrocytes, their presence within the scrolling flow-velocity spectrum or M-mode display is signified as high-intensity transient signals (HITS) (Fig. 13.2). Complexities and uncertainties inherent in

ultrasonic embolic detection render the HITS counts of current FDA-cleared TCD ultrasonographs as semi-quantitative estimates.

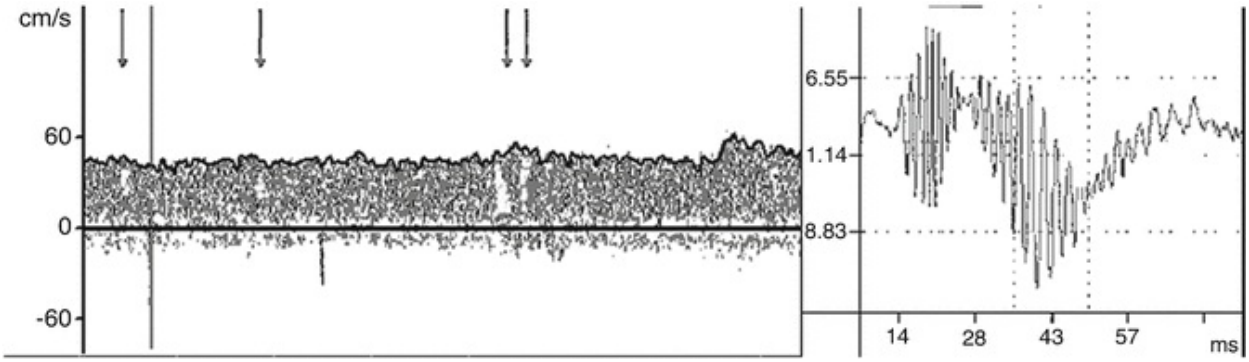

Fig. 13.2 The four *arrows* at the top of this flow-velocity spectral display indicate the presence of emboliform high-intensity transient signals (HITS). Each HIT is shown as a *white spot* within the gray-scale spectral trend. The acoustic signatures of the two most recent HITS are shown in the display on the right. Notice the absence of pulsatility in the spectral trend recorded during nonpulsatile cardiopulmonary bypass

Recently, probe fixation devices have been developed that permit continuous imaging of cerebral perfusion with color duplex sonography [4]. Thus, it is now possible to visualize intracranial vascular pathology procedurally and continuously measure hemodynamically significant changes in large vessel diameter [5].

TCD Limitations

The first and foremost limitation of TCD is that it measures blood flow-velocity, not flow. Because velocity is influenced by vessel diameter, blood viscosity, acid–base balance and temperature, an abnormally high velocity may indicate either hyper- or hypoperfusion. For example, hypercapnia may increase middle cerebral artery (MCA) diameter by more than 20 %, which markedly alters the relationship between flow and flow-velocity.

Second, the quality of TCD information is user-dependent. Correct vessel identification and accurate velocity measurement rely on the training, skill, experience, and practice of the sonographer [6]. Interobserver agreement is high among qualified practitioners who regularly make TCD measurements, but declines substantially among occasional users [6].

Third, effective transtemporal insonation of intracranial vessels is not possible in all patients. Both cranial hyperostosis and the presence of

intracranial vascular disease may prevent monitoring through this cranial site in a significant fraction of patients. For example, successful TCD measurement through all intracranial ultrasonic windows was possible in 78 % of a large series of healthy elderly patients [7]. Alternative insonation sites may be utilized to partially overcome this limitation. Commercially available submandibular probe fixation devices enable continuous simultaneous insonation of the extracranial internal carotid artery (EICA) and internal jugular vein [8]. This approach permits monitoring of blood flow-velocity both toward and away from the brain as well as detection of gaseous and particulate emboli. In addition, intermittent brief transorbital insonation of the carotid siphon with a handheld probe [9] may be helpful in documenting the establishment and maintenance of selective antegrade or retrograde cerebral perfusion during systemic circulatory arrest for aortic arch reconstruction [10].

Fourth, TCD provides no direct information on the cause of observed velocity changes. Sudden signal loss may be caused by flow cessation or unintentional probe movement. Correct causal determination requires input from other monitoring modalities.

Rationale for Cerebral Hemodynamic Monitoring

Transcranial Doppler is most widely used to quantify cerebral hemodynamic function. Measurements include (1) large vessel blood flow direction, and maximum, mean (Vm), and minimum velocity and pulsatility; (2) cerebral autoregulation; (3) vasomotor reactivity (VMR) to ΔCO_2; (4) neurovascular coupling (NVC) and cerebral emboli detection [11].

Cerebral Blood Flow-Velocity Change

For the first application, in diagnostic settings, momentary intra- and extracranial velocity measurements obtained from the patient are compared with vessel-specific age-corrected normative values. During perioperative and critical care hemodynamic monitoring , the potentially profound influences of anesthetic and surgical management on cerebral hemodynamics preclude this approach. Instead, abnormality is inferred from trended changes in flow-velocity referenced to a preprocedure baseline [12]. Because the MCA typically carries approximately 40 % of the hemispheric blood flow, it is generally the preferred monitoring site [13]. The issue of correct vessel

identification may be minimized by using a recording depth of less than 50 mm. With an appropriate probe angle in the adult cranium, at this “shallow” insonation depth, the only arterial signals arise from the MCA or its branches.

When MCA diameter and blood viscosity remain constant, the concept of noteworthy velocity change as an indicator of altered cerebral perfusion has been based on its relationship to the concomitant appearance of clinical signs. In conscious subjects, hypoperfusion-derived syncope appeared with a greater than 60 % decrease in mean flow-velocity or a total signal absence at end-diastole [14]. During general anesthesia, a greater than 60 % flow-velocity decrease coincided with a cerebral blood flow fall to less than 20 mL/100 g/min and pathologic EEG suppression [15]. Flow-velocity declines of greater than 80 % have been associated with a significantly increased stroke risk [16]. However, the clinical correlation with MCA flow-velocity has been less than perfect. In the setting of carotid endarterectomy with regional anesthesia, McCarthy et al. [17] found that clamp-related neurologic dysfunction occurred in just one-third of cases in which MCA flow-velocity declined greater than 60 %.

The rapid detection of a cerebral blood flow obstruction by TCD may be brain- or life-saving. Anesthesia providers often lack data on the functional status of a patient’s intracranial arteries and veins. This paucity of knowledge increases the risk for a generally avoidable and potentially injurious cerebral blood flow obstruction. Despite the limitations described previously [17], TCD can rapidly identify an MCA flow obstruction during carotid endarterectomy or carotid artery stenting associated with head positioning, excessive vascular traction, carotid occlusion [16], dissection [18], or hematoma [19]. The optimal approach to intravascular shunt use remains controversial. Nevertheless, a meta-analysis of 32 studies with pre- and postcarotid endarterectomy brain imaging noted a 38 % reduction in brain infarct incidence in groups utilizing neuromonitoring-based selective shunting [20].

In the repair of an acute aortic dissection , initiation of total cardiopulmonary bypass through a femoral artery may redirect blood flow through the false lumen. Cerebral inflow obstruction may then result in a potentially lethal malperfusion syndrome. TCD can instantly detect its development and guide successful surgical correction [8].

TCD-detectable inflow obstruction may be seen during attempted retrograde cerebral perfusion even with the presence of venous effluent from

open carotid arteries. With an internal jugular functional valve [21], retrograde flow of oxygenated blood from the superior vena cava will be directed upward through extracranial veins and downward through the extensive azygous system. Without a functional jugular valve, momentary complete systemic circulatory arrest may lead to cerebral venous collapse. Initiation of effective retrograde flow may require a brief pressure of more than the oft-recommended 25 mmHg to restore flow in these collapsed vessels [22]. Currently, TCD offers the only direct method to verify the establishment of retrograde cerebral perfusion . Using this approach, Estrera et al. [23] demonstrated the effectiveness of TCD in the management of retrograde cerebral perfusion. Interestingly, the majority of clinical studies describing experience with this perfusion technique used neither TCD nor cerebral oximetry to document successful initiation or maintenance of bihemispheric retrograde flow.

TCD is also invaluable for the documentation of selective antegrade cerebral perfusion during systemic circulatory arrest [8]. Bilateral TCD monitoring can assure the surgeon that both MCAs are appropriately perfused via a single right axillary, innominate, or carotid cannula. Further, Neri et al. [24] showed that selective antegrade perfusion could prevent the cerebral dysautoregulation that typically follows a period of hypothermic total circulatory arrest.

Before or immediately after cardiopulmonary bypass , TCD can detect and guide correction of a cerebral outflow obstruction occurring in response to a malpositioned venous perfusion cannula. The resultant cerebral vascular resistance increase is manifested by a decline or absence of flow-velocity during end-diastole [25].

There are both technical and physiologic explanations for the observed large MCA flow-velocity declines without clinical correlates. With insonation depths of greater than 55 mm, inadvertent insonation of the distal ICA may occur near the bifurcation into the middle and anterior cerebral arteries. Carotid clamping will markedly lower ICA velocity, even with adequate collateral flow through the circle of Willis. Alternatively, vigorous collateral flow through leptomeningeal collaterals may maintain hemispheric function despite MCA hypoperfusion [26].

Currently, TCD provides the only continuous, direct measure of cerebral hyperperfusion . The perioperative monitoring of cerebral perfusion is far from routine. Thus, the incidence as well as the clinical and socioeconomic

significance of this all-too-common problem is under-appreciated. In fact, a surprisingly high (10 %) incidence of postoperative symptomatic hyperperfusion has been reported to occur after carotid endarterectomy [27] or carotid angioplasty and stenting [28]. It should be appreciated that this is at least five times higher than the oft-reported incidence of perioperative hypoperfusion toward which most carotid surgery neuromonitoring resources are directed [29].

Cerebral hyperperfusion is defined as a blood flow increase well in excess of metabolic demand, with flow-velocity increases of higher than 100 % above baseline [30]. Clinical manifestations include severe focal headache, face and eye pain, seizures, focal neurologic deficit, and cognitive disturbances including delirium [27]. Because structural damage and widespread edema are typically absent, diagnostic imaging studies are often uninformative. Without the rare complication of an intracerebral hemorrhage [29], most clinical signs of the hyperperfusion syndrome are transient and self-limiting, albeit expensive for the healthcare delivery system [30]. However, there may be a persistent impairment of cognitive or neuropsychologic function leading to a decreased quality of life [31, 32]. The full economic impact of postoperative or critical care hyperperfusion is incompletely understood (e.g., hospital readmission, rehabilitation attrition, impaired independence, slow return to work) [33], and specific syndrome components are associated with longer and more costly hospital stays [34].

Cerebral Autoregulation

The relationship between cerebral perfusion and systemic perfusion pressure is unpredictable. For example, during adult cardiopulmonary bypass, cerebral autoregulation remains intact in only half of patients [35] and the lower mean arterial pressure limit *range* is approximately 50 mmHg [36].

Optimal patient management requires continuous information on the adequacy of cerebral perfusion. An initially intact autoregulation may be transiently disrupted as a consequence of anesthetic technique, i.e., spinal anesthesia [37], or surgical necessity, i.e., deep hypothermic circulatory arrest [8]. Alternatively, it may be preserved through the adoption of improved perfusion techniques, i.e., supplemental antegrade or retrograde cerebral perfusion [38].

Transcranial Doppler and cerebral oximetry are two approaches to achieving this goal. Information provided by the two techniques may

sometimes be complementary since TCD measures large vessel flow-velocity while cerebral oximetry measures microcirculatory hemoglobin oxygen saturation at the site of tissue gas exchange. Thus, hypoxia decreases MCA blood flow-velocity via vasodilation, while microcirculatory regional O_2 saturation (rSO_2) declines in response to reduced O_2 delivery [39]. However, in other cases, the two measures of cerebral perfusion may appear to be in conflict. For example, the vasopressor phenylephrine increases MCA velocity and decreases rSO_2, while the opposite occurs with administration of the hypotensive agent, sodium nitroprusside. This seeming paradox has been explained by drug-induced changes in MCA diameter [5].

Vasomotor Reactivity

The use of TCD to determine VMR is well established [40]. It describes the cerebral hemisphere-specific relationship between $PaCO_2$ and MCA blood flow or flow-velocity. Early knowledge of the patient's VMR status may be of considerable value during perioperative anesthetic management [40]. First, VMR is a precondition for cerebral autoregulation [41]. With a normal VMR (i.e., 4 % Δ velocity/mmHgCO_2), TCD can define both the lower limit of autoregulation and the zero-flow pressure below which perfusion ceases [42]. A subnormal VMR and associated dysautoregulation identify pressure-passive hemispheric perfusion and an increased stroke risk, which may lead to adjustments in the anesthetic plan [43]. Second, the presence of normal VMR alerts anesthesia providers to the potential hazards of hypocapnia. Aggressive hyperventilation of CO_2-reactive patients following endotracheal intubation may decrease MCA flow-velocity by more than 30 % and produce ischemic EEG suppression [44]. Third, TCD identifies hemispheric asymmetry in VMR, which can lead to blood flow steal from the non-CO_2-reactive hemisphere in the presence of hypercapnia [45]. Fourth, knowledge of the VMR status is important during the planning for deep hypothermia. In both pediatric [38] and adult patients [46], optimal brain cooling with high cerebral blood flow appears to be best achieved through pH-stat acid–base management, while rewarming favors alpha-stat control. Establishment of these ideal conditions requires CO_2-reactive arteries in both cerebral hemispheres.

Vasomotor reactivity and cerebral autoregulation are related, but distinct,

phenomena. Autoregulation requires normal VMR, but may become suppressed while cerebral artery CO_2 responsiveness remains intact. For example, volatile anesthetics [47] and other vasoactive agents [48] may diminish TCD-assessed autoregulation without affecting cerebral artery constriction with hypocapnia. Additionally, it should be appreciated that the widespread notion of a universally intact cerebral autoregulation with a lower limit of 50 mmHg is based on a 1953 study of 15 conscious pregnant women, half of whom were toxemic [49]. In fact, the 1973 article that published the now-familiar sigmoid autoregulatory graph of blood pressure vs. cerebral blood flow emphasized that the lower limit was highly variable and in hypertensive patients often above 100 mmHg [50].

Neurovascular Coupling

Neurovascular coupling refers to the mechanism that adapts local cerebral blood flow to changes in associated neuronal activity in the healthy brain [51]. Van Alfen et al. [52] used TCD and EEG recording to illustrate the maintenance of NVC during brain cooling. In aortic surgery requiring hypothermic circulatory arrest, cooling to 25 °C partially suppressed cerebral metabolic activity and resulted in a burst-suppression EEG pattern. Despite unchanged extracorporeal blood flow, the TCD recording evidenced an oscillating flow-velocity trend, with peaks occurring approximately 5 s after the onset of each burst of EEG activity; velocity nadirs occurred with a similar delay following cessation of each burst.

Circulatory arrest may disrupt NVC due to vasoparesis. Resultant uncoupling observed with TCD monitoring during subsequent reperfusion and rewarming may portend developing brain injury if NVC is not restored [53].

Peca et al. [54] combined TCD with visual evoked potentials (VEPs) to compare NVC in healthy subjects and patients with amyloid angiopathy. During photic stimulation, uncoupling was evident in the patients because flow-velocity responsiveness was suppressed while VEP changes were the same as in healthy subjects [54].

Combined TCD and EEG recording during anesthetic induction demonstrated that NVC was maintained with propofol. In contrast, sevoflurane appeared to disrupt NVC with resulting luxury cerebral perfusion and EEG suppression [55]. Prompt flow adaptation to changing metabolic

needs appears to be caused by an incompletely understood local vasodilation evoked by neuronal activation. The relative contribution of NVC and systemic factors to cerebral blood flow regulation is currently unknown [56].

Cerebral Embolization

Of the currently available neuromonitoring modalities, TCD is unique in its capacity to detect both gaseous and particulate emboli within the cerebral circulation. TCD has detected cerebral emboli associated with cardiac [57], carotid [58], laparoscopic [59], and hip and knee surgery [60]. During postoperative or critical care, such emboli have been observed in patients with (1) new mechanical aortic valves [61], (2) infective endocarditis [62], (3) atrial fibrillation [63], or (4) those with implanted ventricular assist devices [64]. The presence of persistent TCD-detected embolization may lead to the development of focal neurologic deficits. However, the clinical expression of embolic injury appears to be a threshold phenomenon that may require a persistent HITS rate of more than two per minute [65]. With the incorporation of this threshold concept, TCD-guided antiplatelet therapy has successfully reduced particulate-based HITS and associated neurodeficit signs following carotid endarterectomy [66].

To date, TCD monitoring has not been widely used to detect perioperative particulate emboli. The lack of enthusiasm seems based, in part, on the mistaken notion that reasonable therapeutic options are unavailable. In fact, several choices are available to mitigate brain injury once ultrasonic HITS begin to appear. With early detection, the embolic source may be detected and controlled. TCD-guided antiplatelet therapy can mollify the influence of a thrombus formed in the carotid lumen postendarterectomy [66] or in the fibrillating atrium after cardiac surgery. TCD may help minimize the clinical consequences of atheroemboli through a directed reduction in aorta/carotid manipulation [67], enhancement of cerebral emboli clearance, or augmentation of penumbral or collateral perfusion.

Large numbers of HITS representing lipid microemboli have been reported during cardiac and aortic surgery [68]. TCD-guided alterations in surgical and perfusion technique have been shown to markedly reduce aggregate HITS counts and are associated with improved outcome [69].

Finally, TCD aids in the prompt detection of massive cerebral gas embolization. The promptness of the detection and certainty of the cause can facilitate effective therapeutic interventions in a timely fashion [70].

Conclusion

TCD provides the only FDA-cleared method to continuously and directly monitor change in cerebral hemodynamics in the perioperative and critical care settings. The information is clinically valuable and potentially life-saving. However, the quality of the information provided by TCD is heavily influenced by the training, skill, experience, and practice of the sonographer. Therefore, those who interpret TCD findings should have a sound appreciation of both the technology and those who produce the hemodynamic data. Armed with this knowledge, anesthesia providers may confidently use TCD information to improve patient care.

Questions

With each of the following questions, indicate whether the statement is true or false.

1. TCD is a quantitative measure of cerebral blood flow.

    a. True

    b. False

2. Like EEG and cerebral oximetry, TCD monitoring is possible in nearly all patients.

    a. True

    b. False

3. In contrast to EEG, TCD monitoring can promptly detect potentially injurious cerebral hyperperfusion.

    a. True

    b. False

4. Combined EEG and TCD can detect anesthetic-induced uncoupling of cerebral blood from neuronal activity.

    a. True

    b. False

5. TCD can detect both particulate and gaseous emboli within the cerebral circulation.

    a. True

    b. False

Answers

1. B
2. B
3. A
4. A
5. A

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Footnotes

1 Asterisk indicates key reference.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_14

14. Monitoring of Jugular Venous Oxygen Saturation

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Keywords Jugular bulb – Monitoring – Cerebral oxygen saturation – Cerebral ischemia – Hyperemia – Neurocritical care – Intraoperative – In vivo oximetry – Outcomes

Introduction

Maintaining adequacy of cerebral blood flow (CBF) and oxygenation is the cornerstone of neurocritical care and anesthetic management during craniotomy when the risk of cerebral ischemia may be high. Jugular venous oximetry by cannulation of the jugular bulb allows monitoring of cerebral oxygenation. Normal jugular venous oxygen saturation ($SjvO_2$) ranges from 55 to 75 % with values at either extreme reflecting probable global cerebral ischemia or hyperemia [1–3]. Importantly, jugular oxygenation values are reflective of global cerebral oxygenation and may not be able to detect focal

ischemia in the brain. Yet, monitoring of $SjvO_2$ can provide early diagnosis of global ischemia and is useful to guide clinical decisions for optimizing hyperventilation therapy, perfusion pressure, fluid management, and oxygenation in adults as well as children [4–8]. Jugular venous desaturation has been shown to be associated with poor neurologic outcomes after brain injury [2]. Although monitoring of $SjvO_2$ is not a new technique [9], it has evolved substantially from sampling techniques to its utilization both in the operating room and in the ICU. This chapter provides a concise review of relevant literature with focus on the following aspects:

1. Rationale for $SjvO_2$ monitoring

2. Anatomy of cerebral venous drainage

3. Technical aspects of jugular venous oximetry
   - Placement of jugular bulb catheters
   - Fiberoptic versus laboratory co-oximetry
   - Sampling rate from jugular bulb catheters
   - Complications and contraindications

4. Normative $SjvO_2$ values and differential diagnosis of abnormal $SjvO_2$ values

5. Clinical applications of $SjvO_2$ monitoring

6. Limitations (Table 14.1)

Table 14.1 Key to abbreviations and physiologic terms used in the chapter

CBF	Cerebral blood flow
$CMRO_2$	Cerebral metabolic rate of oxygen
O_2ER	Oxygen extraction ratio = (O_2 consumption/O_2 delivery) = $AVDO_2 \times CBF/CaO_2 \times CBF = AVDO_2/CaO_2 = SaO_2 - SjvO_2/SaO_2$
SaO_2	Arterial oxygen saturation

PaO_2	Oxygen tension pressure in arterial blood
$SjvO_2$	Oxygen saturation in the jugular bulb blood
$PjvO_2$	Oxygen tension pressure in jugular venous blood
$AVDO_2$	Arteriovenous difference of oxygen = $(SaO_2 - SjvO_2) \times 1.34 \times Hb + (PaO_2 - PjvO_2) \times 0.0031$
CaO_2	Arterial oxygen content = $(SaO_2 \times 1.34 \times Hb) + (PaO_2 \times 0.0031)$
$CjvO_2$	Jugular venous oxygen content = $(SjvO_2 \times 1.34 \times Hb) + (PjvO_2 \times 0.0031)$

Rationale for $SjvO_2$ Monitoring

The jugular venous oxygenation reflects a balance between cerebral oxygen supply and metabolic consumption , the $SjvO_2$ value being directly proportional to cerebral oxygen supply and inversely proportional to cerebral oxygen consumption. Consequently, $SjvO_2$ monitoring provides a means to indirectly assess the ability of the brain to extract and metabolize oxygen. In the healthy brain, the cerebral metabolic rate for oxygen ($CMRO_2$) is coupled to the CBF such that when $CMRO_2$ increases, CBF increases to match demand. Using the Fick principle, cerebral oxygen consumption can be calculated as:

$$CMRO_2 = CBF \times (CaO_2 - CjvO_2)$$

where $CaO_2 = (SaO_2 \times 1.34 \times Hb) + (PaO_2 \times 0.0031)$ and

$CjvO_2 = (SjvO_2 \times 1.34 \times Hb) + (PjvO_2 \times 0.0031)$.

The dissolved oxygen is negligible and can be ignored. Also, the hemoglobin is constant. As a result, the content of oxygen is, in fact, proportional to the oxygen saturation. Hence, the difference in arterial-venous content of blood ($AVDO_2$) can be determined by the difference in SaO_2 and $SjvO_2$. Rearranging the above equation,

$$AVDO_2 = CMRO_2/CBF$$

Therefore, $SjvO_2$ is a function of the arterial oxygen saturation (SaO_2), CBF, and $CMRO_2$. In a situation in which $CMRO_2$ increases without a concomitant increase in CBF, the $AVDO_2$ increases in conjunction with

cerebral oxygen extraction and decreases in $SjvO_2$. As a result, in the clinical situations, a decrease in $SjvO_2$ indicates either relative increase in $CMRO_2$ or a relative decrease in CBF and can help the clinician make a differential diagnosis of cerebral desaturation. Importantly, during disease states such as traumatic brain injury (TBI) as well as under anesthesia, the normal relationship between cerebral oxygen consumption and cerebral blood flow is often altered (uncoupling). However, the clinical value of $SjvO_2$ monitoring lies in the fact that even in such conditions, the oxygen content of jugular venous blood continues to reflect the relative balance between oxygen consumption and supply. Notably, both hypoxia and anemia can reduce the oxygen delivery to the brain.

Essentially, the $SjvO_2$ monitoring helps in detecting episodes of cerebral hypoxia/ischemia that may lead to poor neurologic outcome [2]. Based on $SjvO_2$ monitoring, appropriate interventions can be made to either decrease the elevated $CMRO_2$ due to seizures or hyperthermia or to optimize hemodynamic and ventilation parameters to increase the reduced CBF in the setting of below normal $SjvO_2$ values. Conversely, in situations of cerebral hyperemia characterized by supranormal $SjvO_2$ values, depending on the clinical setting, either the CBF may be reduced by blood pressure reduction (e.g., after resection of intracranial arteriovenous malformation) or the anesthetic depth/sedation reduced as appropriate.

Anatomy of Cerebral Venous Drainage

Figure 14.1 shows a diagrammatic representation of cerebral venous drainage. The cerebral venous system is composed of superficial and deep venous plexuses . Venous blood from the brain flows via superficial and deep cerebral veins into the venous sinuses (which lie between the outer endosteal and the inner meningeal layer of the dura mater). Venous sinuses drain into the internal jugular veins (IJVs). The cerebral veins can also be referred to as external (superficial or cortical) and internal (deep) groups. The external group drains mostly into the superior sagittal sinus and, to a lesser extent, to the cavernous or the sphenoparietal sinuses . The internal group of cerebral veins drains into the straight sinus that, together with the superior sagittal sinus, joins to form the confluence of sinuses (torcular Herophili). The two lateral sinuses take origin from the confluence and course laterally to reach

sigmoid sinuses and then the jugular bulbs. The jugular veins drain blood predominantly from the ipsilateral side, but also from the contralateral side (minority). Ultimately, all the venous sinuses drain into the IJVs, which comprise two bulbs, the superior and inferior. The superior bulb provides an anatomically viable sampling site. Of the two lateral sinuses, the right is larger in 62 % of the patients, the left is larger in 26 %, and the sinuses are of the same size in 12 % [10]. Cavernous and circular sinuses at the base of the brain have equally free communication from side to side and drain through the petrosal sinuses to the jugular bulbs. Although the dural sinuses join at the confluence of sinuses in most people, the blood from the straight sinus (draining subcortical areas) tends to flow into the left lateral sinus and the blood from the superior sagittal sinus (draining cortical areas) tends to flow into the right lateral sinus [11].

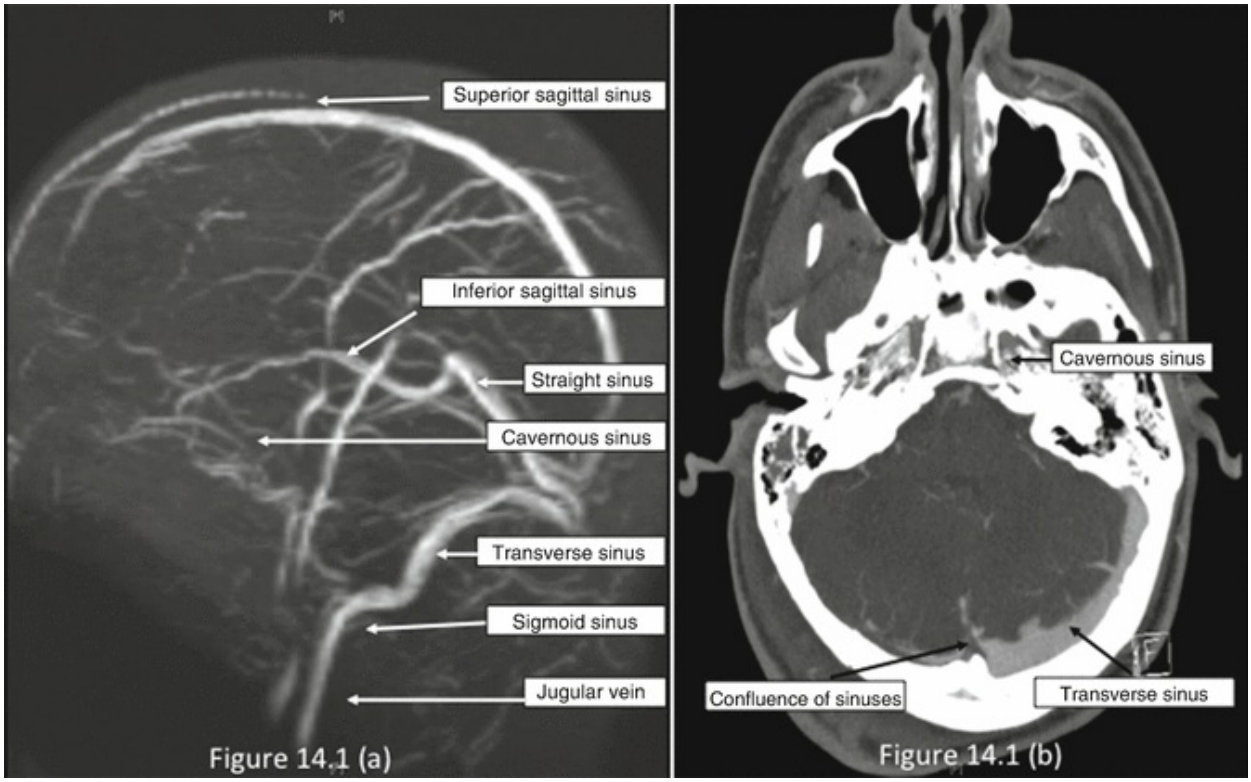

Fig. 14.1 Cerebral venous sinuses : (**a**) superior view. (**b**) Oblique posterior view. Note the convergence of several individual sinuses on the internal jugular vein (IJV) near the jugular bulb (Reproduced with permission from the original author of *Clinical Anatomy Principals* [Chapter 2, page 157] published by Mosby Yearbook Inc. 1996)

On average, two thirds of the blood from a single internal carotid artery is drained by the ipsilateral IJV, and one third is drained by the contralateral

jugular vein [12]. Although the jugular venous blood is derived from both cerebral hemispheres, the venous drainage is usually asymmetrical, with the majority of the patients draining cerebral venous blood dominantly into the right side jugular bulb, some draining dominantly into the left side and a few may drain equally into both jugular bulbs. In patients draining primarily into one jugular bulb, a side-to-side asymmetry of greater than 10 % in $SjvO_2$ values can occur [1]. Hence, it is recommended that a jugular bulb catheter be placed into the IJV on the side of dominant cerebral venous drainage [1, 4] although it is often argued that in the presence of a focal brain injury, the catheter should be placed on the side ipsilateral to brain injury. The cerebral venous dominance can be easily determined by examining the venous caliber on the cerebral angiogram (a larger caliber indicating dominant venous drainage) [4], by ultrasonographic comparison of the size of the IJVs [13], or computerized tomographic assessment of the jugular foramen size [14]. Figure 14.2 shows the venous phase of cerebral angiograms of three different patients demonstrating right-dominant, left-dominant, and right-left co-dominance of cerebral venous drainage. In a series of 32 patients with severe TBI and simultaneous measurements of $SjvO_2$ in the right and left jugular bulbs, the average difference in $SjvO_2$ between the right and left jugular bulb was 5 % [15]. Fifteen patients had a maximal right-to-left difference in $SjvO_2$ of more than 15 % [15]. Three additional patients had differences more than 10 % [14]. It was not possible to predict on the basis of CT scan information which patients would have significant differences in $SjvO_2$ or which jugular bulb would have the most abnormal values [15]. These findings further support selecting the jugular bulb on the side of dominant venous drainage for $SjvO_2$ monitoring [4].

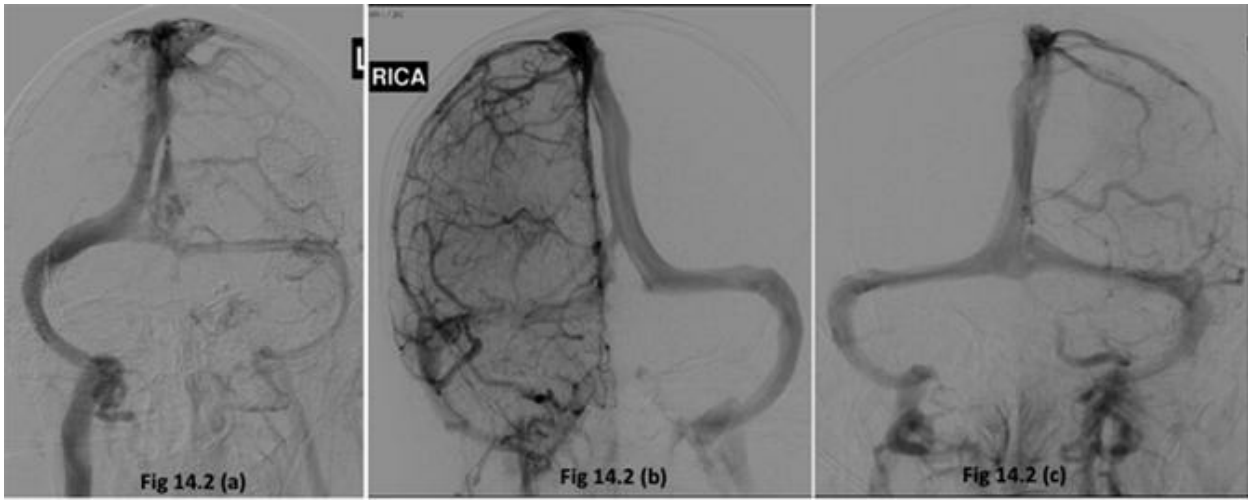

Fig. 14.2 Venous phase of cerebral angiograms of three different patients demonstrating right-dominant (**a**), left-dominant (**b**), and right-left co-dominance (**c**) of cerebral venous drainage

The IJV is a direct continuation of the intracranial sigmoid sinus (see Fig. 14.1). It begins at the jugular foramen of the skull and ends at the thoracic inlet (behind the manubrium sterni where, after crossing the subclavian artery, it joins the subclavian vein to form the brachiocephalic trunk). It thus traverses the entire length of neck, enclosed in the carotid sheath, in close proximity to the carotid arteries. During its course, it lies posterolateral to the carotid artery and crosses it from the lateral to the medial side. The IJV has two dilatations: one at each end, referred to as the superior and inferior “jugular bulbs." The superior (upper) bulb is an outpouching of the venous wall and is more prominent, whereas the inferior (lower) bulb is a dilation of the vein situated about 1 cm above the clavicle and is less defined.

The previously mentioned, anatomic facts have important clinical implications pertaining to extracranial contamination of blood sampled from the jugular bulb. Such contamination can come from multiple sources: (1) emissary and frontal veins drain blood into the superior sagittal sinus; (2) the sigmoid sinus receives blood from the cavernous sinus through petrosal sinuses. The cavernous sinus in turn communicates with the ophthalmic veins and pterygoid venous plexus; (3) influx of blood from pharyngeal venous plexus and facial veins, which can be a source of contamination if the catheter tip migrates caudally, below the superior bulb. Contamination by extracranial blood will give false high readings of $SjvO_2$ because oxygen extraction by extracranial tissues is less than that of the brain.

Technical Aspects of Jugular Venous Oximetry

Placement of Jugular Bulb Catheter

Under careful aseptic precautions, the IJV on the side to be cannulated is typically punctured under ultrasound guidance at the level of the apex of the triangle formed in the neck by the two heads of the sternocleidomastoid muscle and the clavicle. The Trendelenburg position, often used for central venous cannulation for improved ultrasonographic visualization of the IJV, may not be an option in patients with poor intracranial compliance. The Seldinger technique can be used to thread the jugular bulb catheter over a guide wire. An introducer sheath (5–6 French size) is first inserted through which an oximetric catheter (4.5–5 French) is advanced in a cephalad direction until a resistance is felt (15–20 cm in most adults), which generally coincides with approaching the superior jugular bulb where there is a slight bend in the vessel lumen just below the jugular foramen below the base of the skull. The catheter is then pulled back half a centimeter. The cannulation technique is similar to that for central venous catheterization except that the needle, guide wire, and catheter are advanced in a cephalad direction (Fig. 14.3). We routinely use a 16 G, 5.25-in. long venous cannula for intraoperative jugular venous oximetry [4, 6]. We usually insert the catheter to a distance equal to that measured from the point of insertion to the level of the mastoid process until resistance is met. This technique is helpful in adult as well as pediatric patients [4].

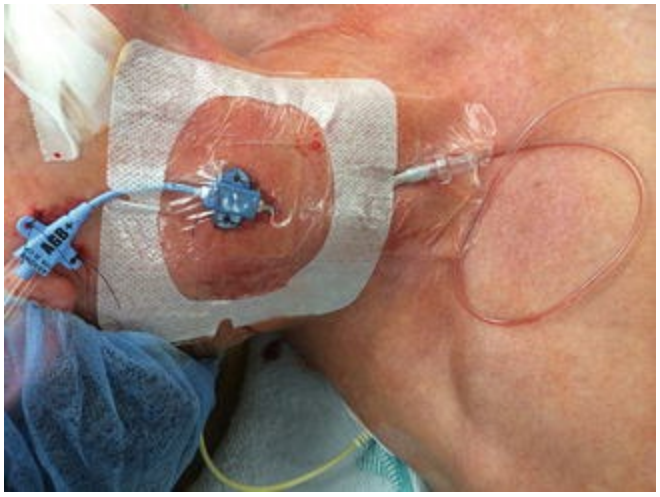

Fig. 14.3 Depicting a central venous catheter and a jugular venous catheter inserted on the same side of the neck. The central venous line is inserted caudad while the jugular bulb catheter is inserted

cephalad

The final position of the cathete r in the jugular bulb should be confirmed by a lateral X-ray of the skull documenting the catheter tip at the level of, and just medial to, the mastoid process. It has been suggested that radiographic assessment of jugular venous catheters is best performed using an overpenetrated Stenvers view (with rotation of the head 15°–20° away from the side of the $SjvO_2$ catheter) and a companion over-penetrated lateral radiograph of the neck. Alternatively, on an anteroposterior (AP) view of the skull, a correctly positioned catheter should lie cranial to the line extending from the atlantoaxial joint and below the inferior orbital margin [16]. Accurate positioning of the catheter tip is essential for dependable $SjvO_2$ data. Even when the catheter is placed in a perfect position, it is not unusual for the catheter tip to migrate leading to falsely high $SjvO_2$ values [10]. Hence, the catheter may need readjustment periodically. The presence of an introducer sheath facilitates such adjustments.

It is recommended that the jugular bulb on the side of dominant venous drainage be cannulated. Different suggested approaches to identify the dominant IJV are:

- If a cerebral angiogram is available, identify the dominance on the venous phase [4] (see Fig. 14.2)
- Use ultrasound to identify the larger caliber IJV, which corroborates with cerebral venous dominance [13]
- Cannulate the side with the larger jugular foramen on computerized tomography [14]
- Cannulate the IJV, compression of which results in a greater increase in the intracranial pressure (ICP) [17]
- In the presence of a focal lesion, cannulate the ipsilateral jugular bulb [18]

Continuous Fiberoptic Jugular Oximetry Versus Intermittent Sampling

Jugular oximetry can be performed either by intermittent sampling of blood or by fiberoptic technology using spectrophotometric catheters that allow

continuous displays of $SjvO_2$ values. The underlying principle is based on the differential absorption of light at different wavelengths by oxyhemoglobin and reduced hemoglobin. The Baxter-Edwards system (Edslab Sat II, Baxter Edwards Critical Care Division, Irvine, CA) uses two wavelengths of light for reflectance spectrophotometry and is calibrated against a sample of the patient's blood. The Abbott system (Opticath Oximetrix, Abbott Critical Care System, Abbott Park, IL) uses three wavelengths of light and may be calibrated in vivo (against the patient's blood) or in vitro (built-in calibration).

A prospective protocol comparing 195 blood gas measurements with simultaneously recorded continuous bedside oximetric monitor values for 31 ICU patients with TBI undergoing jugular venous oxygenation monitoring for an average of 3.4 days reported acceptable correlation between the in vivo monitor (Baxter-Edwards, Santa Ana, CA) and in vitro co-oximetry [19]. Although the sensitivity of the continuous oximetry was somewhat low (45–50 %), the specificity was 98–100 %, indicating that it is less of a concern that patients may be misdiagnosed as having desaturations resulting in unnecessary interventions [19]. Nonetheless, the investigators recommended that suspected jugular bulb desaturation should be verified before taking therapeutic actions [19]. The fiberoptic catheter has also been noted to provide accurate measures of $SjvO_2$ during neurosurgical procedures in a series of 12 patients with 111 readings ranging from 42 to 95 % [20]. However, in another ICU study of patients with TBI, there was a poor correlation for the first in vivo calibration although subsequently, a close correlation between jugular bulb catheter and oximetry values was demonstrated during episodes of jugular bulb oxygen desaturation resulting from a variety of causes including hypocapnia, hypoperfusion, and intracranial hypertension [21]. These investigators also recommended validation with a laboratory oximeter prior to continuous jugular bulb oximetry [21]. Subsequent to calibration with a laboratory co-oximeter, the Edslab catheter (Baxter Healthcare Corporation, Irvine, CA, USA) was also found to provide $SjvO_2$ values that correlated well with co-oximetry with no appreciable drift and negligible bias [22]. Interestingly, the measurement of $SjvO_2$ by the fiberoptic method compared poorly with bench oximetry during cardiopulmonary bypass (CPB) although there was good agreement between the two methods in the 18 h postoperatively [23]. There were wide limits of

agreements (mean difference ± 2 SD) between the two methods during operation (−20.29 to 18.05 %), whereas after operation the limits of agreement were far narrower (−6.39 and 7.45 %) [23]. When indwelling catheters are used for continuous $SjvO_2$ monitoring for several days and/or hemoglobin level is expected to change, it is customary to draw blood samples from the jugular bulb to calibrate the oximeteric catheter at least once daily.

Sampling Rate

Below the jugular bulb, the IJV receives facial and retromandibular venous blood, causing extracranial admixture. Consequently, faster rates of sampling increase the admixture from the extracranial veins, giving falsely elevated $SjvO_2$ values. In mechanically ventilated patients undergoing neurosurgical procedures, Matta and Lam [24] found that sampling at rates faster than 2 mL/min resulted in significantly higher $SjvO_2$ values. Hence, to avoid overestimation of $SjvO_2$, blood samples should be drawn slowly, at approximately 2 mL/min, particularly when the patient is hyperventilated or CBF is otherwise reduced pharmacologically (e.g., during barbiturate therapy) [24]. Importantly, there are no data to prove that the rate of 2 mL/min is free of extracranial blood contamination. Although sampling rates slower than 2 mL/min may further improve accuracy, they may not be practical and may not allow rapid assessment of changes.

Complications

Potential complications are associated with either (1) insertion of the catheters (carotid artery puncture, injury to nerves, injury to lymphatic duct on the left side, pneumothorax) or (2) the presence of an indwelling catheter (infection, thrombosis). In a series of 80 patients, Jakobsen and Enevoldsen [25] had an accidental carotid artery puncture with the Seldinger technique in one patient. Subsequently, Matta et al. [6], in a series of placements of retrograde jugular venous bulb catheters in 100 consecutive anesthetized patients undergoing neurosurgical procedures, reported carotid artery punctures in two patients that were controlled by firm pressure. We have reported our experience of placing jugular bulb catheters in anesthetized pediatric patients and noted no arterial punctures [8]. The use of ultrasound is

likely to further reduce the risk of arterial puncture, especially with experienced providers. Serious consequences involving the development of a hematoma that may follow the insertion of a 5–6 French introducer can be avoided, if the smaller catheter (#18g) is always connected to a pressure transducer to ascertain (from the waveform) the presence of the catheter in the vein prior to insertion of the introducer. In a rare case, inadvertent penetration of the posterior wall of the jugular vein during cannulation has been reported, leading to the placement of the catheter tip in the subarachnoid space [26]. Another rare case of unintentional cannulation of the anterior venous plexus of the cervical epidural space during retrograde catheterization of the jugular vein has also been reported [27]. Other complications such as Horner's syndrome and injuries to the phrenic or recurrent laryngeal nerve may also occur.

The ICP can be increased by obstruction of cerebral venous drainage. Although concerns are sometimes raised about the possible obstruction of cerebral venous outflow by jugular bulb catheters, the size of the catheter used for $SjvO_2$ is very small compared with the size of the vein being cannulated. In fact, Goetting and Preston [28] found no evidence that jugular venous catheterization with indwelling catheters has any significant effect on ICP [28]. Venous thrombosis associated with $SjvO_2$ monitoring has not been reported but could have serious consequences. The risk can be minimized by using the smallest catheter and maintaining patency of the catheter. Infection and sepsis is a known complication with all types of indwelling catheters. Stocchetti et al. [15] reported catheter-induced sepsis in 1.8 % of 45 patients. Strict aseptic technique during insertion and maintenance of catheters is critical.

Contraindications

Absolute contraindications include venous thrombosis. Relative contraindications include hypercoagulable states, coagulopathy, the presence of tracheostomy (due to risk of infection), and unstable cervical spine conditions providing suboptimal patient positioning for placement of the catheter.

Normative $SjvO_2$ Values and Differential Diagnosis of

Abnormal $SjvO_2$ Values

The $SjvO_2$ in normal subjects is reported to be in the range of 55–71 % [9]. A later study reported the lower limit of $SjvO_2$ to be lower than previously reported [29]. In humans, confusion develops with hypoxia or orthostatic hypotension when $CjvO_2$ drops from 3 to 2.7 μmol/mL, which corresponds to an $SjvO_2$ of about 45 % [30]. Unconsciousness develops when $SjvO_2$ reaches a value of less than 24 %. In patients undergoing CPB [31] and in patients with traumatic intracranial hematomas [32], increased anaerobic cerebral metabolism was observed when $CjvO_2$ decreased below 3 μmol/mL. This value of $CjvO_2$ corresponds to an $SjvO_2$ of 50 %. In the first 5–10 days after TBI, the $SjvO_2$ is higher, averaging 68.1 ± 9.7 % (range, 32–96 %) [10]. In general, an $SjvO_2$ less than 50 % indicates cerebral ischemia and an $SjvO_2$ greater than 75 % indicates cerebral ischemia.

Figure 14.4 presents a suggested approach to the management of low $SjvO_2$. Briefly, before any intervention, the low $SjvO_2$ value should be confirmed by a laboratory co-oximetry. Low $SjvO_2$ can result from (1) increased cerebral metabolic activity (due to seizures or fever), or (2) decreased oxygen availability (due to hypoxia, anemia, excessive hyperventilation, hypotension, intracranial hypertension, or vasospasm). The decrease in $SjvO_2$ associated with cerebral ischemia is nonlinear such that a minimal decrease in $SjvO_2$ is seen initially when CBF is near normal, becoming more steep as CBF drops below 35–40 mL/100 g/min. In normal humans, the $SjvO_2$ has been noted to remain unchanged with normovolemic hemodilution decreasing the hematocrit to 26 % [33]. Following brain injury, the lower limit of autoregulation of CBF is shifted to the right, resulting in marked decreases in CBF with relatively minor changes in blood pressure or cerebral perfusion pressure [4]. In anesthetized individuals, the effects of anesthetic agents on CBF also need to be considered in the differential. For example, propofol anesthesia maintains the coupling between CBF and metabolism but in conjunction with hyperventilation can cause jugular venous desaturation [34]. Conversely, volatile anesthetic agents cause flow-metabolism “uncoupling” leading to an increase in $SjvO_2$ [35].

Fig. 14.4 A suggested approach to the management of low $SjvO_2$ value

Cerebral hyperemia ($SjvO_2$ > 75 %) can occur due to intracranial arteriovenous malformations or because of therapeutic hypothermia /sedation to produce burst suppression. High $SjvO_2$ may be treated with controlled moderate hyperventilation or hemodynamic control. Importantly, however, the $SjvO_2$ may be elevated due to cerebral infarction. The therapeutic interventions in response to abnormal $SjvO_2$ values should be made considering information obtained from other monitors simultaneously.

Clinical Applications of $SjvO_2$ Monitoring

Jugular oximetry has important applications in intensive care as well intraoperatively during neurosurgery and cardiac surgery.

Intensive Care Unit Uses of Jugular Venous Oximetry

Monitoring of $SjvO_2$ is a useful part of a multimodal monitoring approach. Because it has a low accuracy to detect regional ischemia, it is most useful in patients with global abnormalities. Select applications of jugular oximetry in the intensive care setting are discussed next.

Traumatic Brain Injury

Patients with severe TBI are susceptible to cerebral ischemia from secondary insults. However, hemodynamic monitoring alone is not sensitive enough to monitor cerebral oxygenation. Consequently, the current guidelines provide a Level III recommendation for the use of $SjvO_2$ and brain tissue oxygen monitoring, in addition to standard intracranial pressure monitors, in the management of patients with severe TBI [36]. Patients with a severe TBI without jugular venous desaturation episodes have significantly lower mortalities and a greater chance of a good recovery compared with patients with one or multiple desaturation episodes [37, 38]. Cerebral desaturation occurs in TBI patients due to treatable systemic (hypotension, hypoxia, hypocarbia, anemia) as well as cerebral (elevated ICP, vasospasm) causes. Episodes of desaturation are common, particularly in the first 48 h after injury, and monitoring $SjvO_2$ provides an early diagnosis of ischemia resulting from either intracranial or systemic causes [39–42]. High $SjvO_2$ values have also been associated with poor outcome [43]. Monitoring $SjvO_2$ also helps optimizing hyperventilation therapy [40, 41], fluid management and oxygenation [40, 44], and cerebral perfusion [4]. Patients with traumatic subarachnoid hemorrhage (SAH) may develop cerebral vasospasm and, in conjunction with transcranial Doppler, jugular oximetry can help differentiate between hyperemia from vasospasm. It is also useful in prognostication [45]. In fact, the number of $SjvO_2$ desaturations might be associated with outcome more strongly than other clinical and radiological features [46]. Importantly, however, while in the brain areas without focal pathology, there is generally a good correlation between changes in $SjvO_2$ and brain tissue oxygenation; in areas with focal pathology, there may be no correlation between the two [18]. Hence, brain tissue monitoring may provide additional information. According to the consensus statement of the Neurocritical Care Society regarding use of multimodality monitoring, $SjvO_2$ monitoring should be part of a multimodal monitoring approach and used at least in combination with ICP monitoring. $SjvO_2$ therapy in isolation does not improve the outcome of severe TBI patients and so $SjvO_2$-based therapy alone should not be used after TBI [47].

Aneurysmal Subarachnoid Hemorrhage

Serial $SjvO_2$ measurements in SAH patients may be helpful in identifying episodes of cerebral desaturation and instituting appropriate therapy. A series of 26 patients with 354 observations reported 10 % desaturation episodes [48]. The ICP was significantly higher during the episodes of low $SjvO_2$ and lower $PaCO_2$ and cerebral perfusion pressures were frequently observed in association with low $SjvO_2$ [48]. Moreover, increases in $AVDO_2$ can be predictive of clinically evident vasospasm in the subsequent hours to days [49]. According to the consensus statement of the Neurocritical Care Society, there are few data on how $SjvO_2$ monitoring may help manage secondary brain damage in patients with coma after SAH, intracerebral hemorrhage, and large ischemic stroke [47].

Intracranial Arteriovenous Malformation

Jugular oximetry is potentially useful in the assessment of adequacy of preoperative embolization in decreasing blood flow through large supratentorial arteriovenous malformations. When $SjvO_2$ decreases after preoperative embolization, indicating a decrease in shunting of blood, hyperemic complications occur less often after surgical resection [50]. Normal perfusion pressure breakthrough and hyperemia can occur after resection of the arteriovenous malformation, and the use of $SjvO_2$ monitoring has been described for timely identification of hyperemia and the institution of antihypertensive therapy to prevent breakthrough bleeding [51].

Intraoperative Uses of Jugular Venous Oximetry

Neurosurgical Anesthesia

Patients undergoing neurosurgical procedures are likely to have impaired cerebral autoregulation and, hence, may be susceptible to intraoperative cerebral ischemia [52]. Despite apparently “normal” blood pressure, cerebral oxygenation may be inadequate if the blood pressure is below the lower limit of cerebral autoregulation [53]. A modest decrease of blood pressure may lead to a significant decrease in $SjvO_2$ and increasing the blood pressure to a level above the lower limit of cerebral autoregulation by titrated infusion of vasopressors normalizes $SjvO_2$ [8]. Jugular oximetry is used to guide the determination of the minimum blood pressure that should be maintained to

avoid global cerebral hypoperfusion during intracranial aneurysm surgery [54]. Moreover, hyperventilation in adult patients with intracranial tumors anesthetized with propofol may be associated with the risk of cerebral desaturation due to synergistic cerebral vasoconstrictive properties [37]. Monitoring $SjvO_2$ is helpful in titrating hyperventilation to accomplish brain relaxation by cerebral vasoconstriction within safe limits [6, 8]. In a series of 100 craniotomies in adult patients, $SjvO_2$ monitoring was helpful in detecting and treating episodes of cerebral desaturation in 60 % of patients with aneurysms, 72 % with intracranial hematomas, and 50 % with tumors [6]. Another series of 19 children who underwent craniotomy for arteriovenous malformation resection, tumor removal, or aneurysm clipping noted that 11 (58 %) patients experienced at least one episode of cerebral desaturation intraoperatively [8]. There were 25 episodes of cerebral desaturation, six of which were attributed to relative hypotension, four to hypocarbia, and 15 to a combination of both [8]. Essentially, intraoperative jugular venous oximetry allows monitoring of cerebral oxygenation during craniotomy without interfering with the surgical field and can guide anesthetic interventions such as hyperventilation, management of perfusion pressure, fluids, and oxygenation to optimize the cerebral physiology [4, 6, 8].

Cardiac Surgery

Postoperative cognitive decline in patients undergoing cardiac surgery is well recognized. Croughwell et al. [55] first reported a 23 % incidence of $SjvO_2$ less than 50 % during normothermic CPB, which was associated with lower CBF [7]. The desaturation is commonly associated with rewarming in preparation for separating from CPB [55, 56]. Subsequently, it was observed that patients who had desaturation during CPB had a greater decline in cognitive function after surgery [55]. During CPB, changes in the ratio between CBF and $CMRO_2$ can be detected by monitoring $SjvO_2$. These changes are largely unpredictable and vary widely from patient to patient. Close monitoring of $SjvO_2$ in individual patients may allow better care of the brain during cardiac surgery [57]. Jugular bulb oximetry enables detection of periods of desaturation, which may indicate the need for appropriate intervention [58]. However, over the last several years, cerebral oximetry using near-infrared spectroscopy (NIRS) has become increasingly popular and preferred during cardiac surgery compared with jugular oximetry.

During CPBSurgery , changes in the ratio between CBF and $CMRO_2$ can be detected by monitoring SjO_2. These changes are largely unpredictable and vary widely from patient to patient. Close monitoring of SjO_2 in individual patients may allow better care of the brain during cardiac surgery. Jugular bulb oximetry is feasible, practical, and beneficial for patients undergoing CPB. It enables detection of periods of desaturation, which may indicate the need for appropriate intervention, and, in combination with arterial oxygen content, allows the calculation of $AVDO_2$.

Limitations

Several limitations of jugular venous oximetry exist.

1. It monitors the balance between global CBF and $CMRO_2$. Regional ischemia can therefore be present despite normal $SjvO_2$. Also, mixing of blood from both sides may not be adequate and the blood from the ischemic areas may drain into the jugular bulb not being monitored.

2. The caudad migration of the catheter may cause false high readings of $SjvO_2$ due to contamination by extracranial blood.

3. As CBF decreases, the amount of extracranial contamination may become proportionately greater resulting in falsely high readings.

Conclusion

Jugular venous oximetry is able to provide valuable information to optimize and individualize hemodynamic and ventilator parameters in patients at risk of neurologic injury and can also guide titration of pharmacologic agents. Careful patient selection and assessment of risk/benefit should be performed prior to jugular bulb cannulation.

Questions

1. Which of the following is correct regarding jugular venous oximetry?

a. Continuous fiberoptic jugular oximetry is more accurate and reliable than sampling by laboratory co-oximetry

b. Jugular bulb catheter should routinely be inserted on the right side

c. There is a high risk of carotid artery injury during the insertion of jugular bulb catheter

d. Jugular bulb catheter does not increase intracranial pressure by obstructing the cerebral venous drainage

2. Which of the following is NOT correct regarding jugular venous oximetry?

a. It is helpful in optimizing blood pressure and ventilation parameters intraoperatively.

b. $SjvO_2$ <50 % predicts poor outcome in patients with severe traumatic brain injury.

c. It is sensitive to focal cerebral ischemia.

d. None of the above.

3. Determination of the dominant cerebral venous drainage to decide the side to be cannulated for jugular venous oximetry should be based on which of the following?

a. Visualizing the venous phase of cerebral angiogram

b. Comparing the diameters of both IJVs using ultrasound

c. Comparing the sizes of both jugular foramen on computed tomography

d. Any of the above

4. All of the following conditions are likely to cause low $SjvO_2$ values on jugular oximetry EXCEPT

   a. Normal perfusion pressure breakthrough after resection of intracranial arteriovenous malformation

   b. Hyperventilation therapy in traumatic brain injury

   c. Hypotension during aneurysm surgery

   d. Severe anemia

5. Differential diagnosis of an increase in $SjvO_2$ value should include all EXCEPT

   a. Cerebral vasospasm

   b. Burst suppression

   c. Caudad drift of the jugular bulb catheter tip

   d. Hypothermia

Answers

1. d

2. c

3. d

4. a

5. a

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Footnotes

1 Asterisks indicate key references.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_15

15. Intracranial Pressure Monitoring

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Keywords Intracranial pressure monitoring – Parenchymal devices – Cerebral pressure reactivity – Intraventricular catheter – Coagulopathy – Herniation – Monro–Kellie hypothesis

Key Learning Points

- The consequences of intracranial hypertension on cerebral perfusion and overall outcome may be severe; patients with prolonged or severe elevations in ICP are at risk for poor neurologic outcome and mortality.
- Several modalities of ICP monitoring exist, the most common being the intraventricular catheter. Risks of intraventricular catheter placement include development of tract hemorrhage, infection, ventriculitis, and upward herniation from overdrainage of cerebrospinal fluid.
- Parenchymal pressure sensors are also commonly used in patients with TBI. There is a reduced risk of infection and bleeding with parenchymal monitors, but no ability to treat hydrocephalus.
- Accuracy of intraventricular and intraparenchymal ICP monitoring is equivalent. Both monitors may fail to identify regional intracranial hypertension, especially in the infratentorium.
- Interventions to reduce ICP should begin when ICP is higher than 15–20 mmHg for more than 5 min, and interventions to raise CPP should begin when CPP is lower than 50 mmHg.
- The ICP waveform contains two arterial pulsations, P1 and P2, and a venous wave, P3. The mean ICP and arterial pulsation amplitude reflect the degree of intracranial hypertension.
- Characteristics of the waveform morphology may suggest subtle changes in intracranial compliance or autoregulatory capacity.
- Rising of the P2 waveform beyond P1 may be an early sign of decreased intracranial compliance that precedes an elevation in the mean ICP.
- The RAP is the correlation coefficient (R) between the amplitude of the arterial pulsation (A) and the mean pressure (P) and reflects compensatory reserve to additional changes in intracranial volume.
- Pressure reactivity (PRx) is a measurement of the response of ICP to slow changes in arterial blood pressure. PRx reflects autoregulatory capacity.
- ICP monitoring is a component of CPP-guided management for patients

with TBI. Other monitors of cerebral perfusion may be utilized such as brain tissue oxygen monitoring and cerebral microdialysis.

Introduction

The cranium is uniquely intolerant to changes in volume. Under normal physiologic conditions, tissue cells, blood, and cerebrospinal fluid (CSF) maintain a consistent presence within the cranium and spinal cord areas. The relationship between components of the cranium and the pressure created by their presence is defined by the Monro–Kellie doctrine [1]. When any single component increases, the other two have a limited capacity to accommodate by shifting into accessory spaces so as to avoid a rise in intracranial pressure (ICP). Once that capacity to buffer is reached, very small increases in volume produce an exponential rise in pressure (Fig. 15.1). When ICP is elevated, the cerebral perfusion pressure (CPP) decreases (CPP = ICP − MAP; MAP = mean arterial pressure), oxygen delivery is compromised, and ischemia may result. With critical elevations in ICP, brain tissue may herniate across dural or bony boundaries and precipitate life-threatening cerebral or brainstem ischemia [2] (Fig. 15.2).

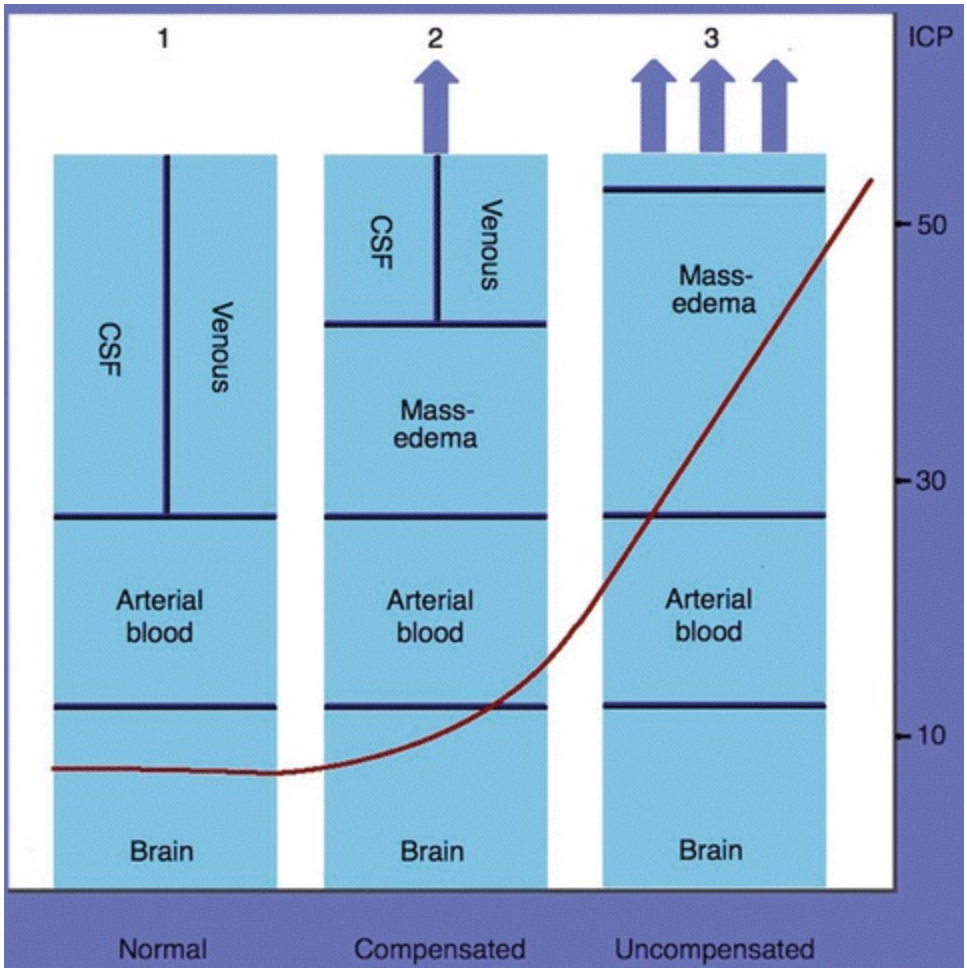

Fig. 15.1 Graphical representation of the Monro–Kellie doctrine . Any increase in a single component of intracranial volume (blood, cerebrospinal fluid [CSF], tissue) must be matched by a decrease in another if intracranial pressure (ICP) is to be maintained. When an intracranial mass or edema expands beyond the buffering capacity of venous blood and CSF, ICP will rise

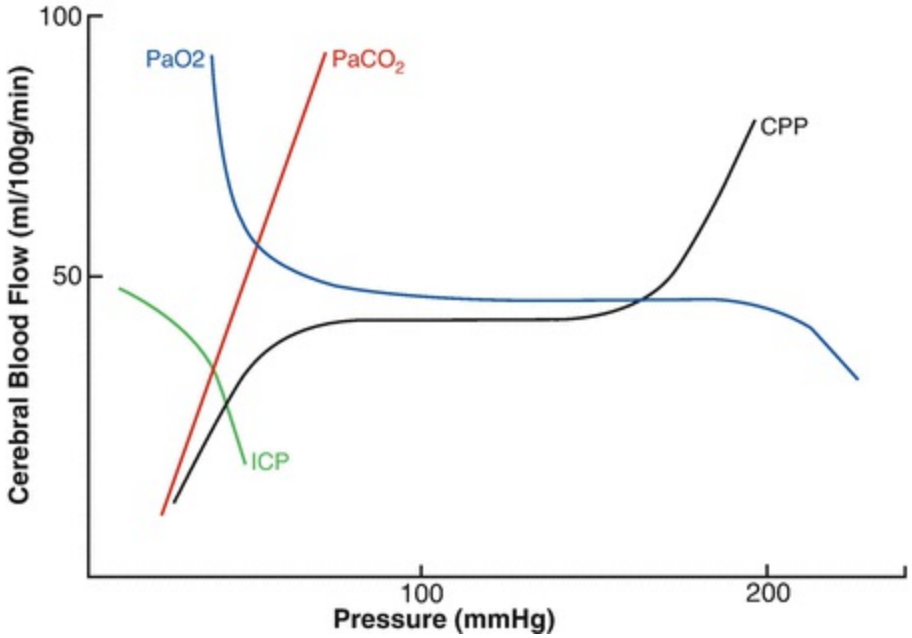

Fig. 15.2 Cerebral blood flow (CBF) is maintained at a constant state when cerebral perfusion pressure (CPP) is between approximately 50 and 150 mmHg. This steady state of flow is provided by an intact autoregulation system. Above or below 50 and 150 mmHg, CBF is proportional to CPP. A PaO_2 below 50 mmHg produces a significant increase in CBF. $PaCO_2$ increases CBF by approximately 1 mL/100 g/min for every 1 mmHg increase in CO_2. Increase in ICP can decrease CBF by decreasing CPP. CPP = MAP − ICP

The question of when to monitor ICP with an invasive device, as opposed to clinical presentation alone, has been a topic of vigorous debate. Numerous studies in recent decades have demonstrated that raised ICP in both adult and pediatric traumatic brain injury (TBI) is associated with poor outcomes [3]. ICP monitoring is also commonly utilized in patients with mass-occupying lesions, hydrocephalus, or cerebral edema , but formal guidelines exist only for patients with TBI. Whether monitoring ICP with a device can change outcomes while avoiding undue risk from the monitor itself is the real question. No randomized controlled trial exists to date that demonstrates a clear outcome benefit for patients with ICP monitoring and ICP monitor-guided therapy. Several cohorts and observational databases have demonstrated a trend toward improved outcome in high-risk populations , which prompted the Brain Trauma Foundation (BTF) to publish guidelines in 2007 for ICP monitoring in TBI based on the benefits seen in this trend [4]. The BTF recommends placement of an ICP monitor in all TBI patients who may be salvageable and who have an abnormal head CT, with the goal of using this information to optimize CPP. In addition, the BTF recommends

establishing a guideline-based approach to treatment of raised ICP. Such a guideline-based approach, or protocol-driven management , has been shown to decrease both mortality and hospital costs while not increasing the numbers of disabled survivors. In recent years, many investigators have questioned the utility of ICP monitoring to guide patient management in subsets of high-risk patients such as the elderly [5]. A randomized trial of ICP monitoring vs. imaging and clinical examination-guided management in 2012 also found no outcome benefit of ICP monitoring [6]. Many have questioned its generalizability to TBI management in the developed world, while others suggest the study indicates that ICP monitoring is an important component of multimodal monitoring of perfusion after TBI [7]. The BTF guidelines continue to recommend ICP monitoring for guiding clinical management.

The intraventricular catheter (IVC), often termed EVD for extraventricular drain, is the commonly held “gold standard” for ICP monitoring. The catheter measures global ICP , which is transmitted to the cerebrospinal fluid (CSF) filled ventricle and from there to fluid-filled tubing, which interfaces with a standard external transducer (Fig. 15.3). Alternatively, the catheter may contain a transducer within the lumen itself. Accurate interpretation of ICP by a ventricular catheter assumes an unobstructed connection between all CSF-containing compartments and free flow of fluid. The intraventricular catheter is introduced into the frontal horn of the lateral ventricle via a percutaneous route through a twist drill or burr hole made at Kocher’s point. Ideal positioning of the tip is in the ventricle, contralateral to the cerebral hemisphere with the disease-producing mass effect (Fig. 15.4). If the disease process leads to significant midline shift and effacement of the contralateral ventricle, then the catheter should be placed in the ventricle located within the hemisphere harboring disease to avoid worsening midline shift. The IVC transducer systems should be calibrated to a zero reference point at the foramen of Monroe, which conveniently coincides with the external auditory meatus. The IVC can be zeroed repeatedly after placement, which is in contrast to some intraparenchymal devices that cannot be recalibrated after insertion. The particular advantage of the IVC results from the option to use the ventricular catheter as a diagnostic and therapeutic tool. For example, in the event of malignant increases in ICP, the intraventricular catheter can be used to drain CSF, thereby decreasing pressure [8]. The dual utility has promoted the IVC to be the favored monitor

in many neuroscience intensive care units. Additionally, the IVC can be used to administer pharmacotherapies such as antibiotics or thrombolytics as well as to provide for easy sampling of CSF for laboratory investigations.

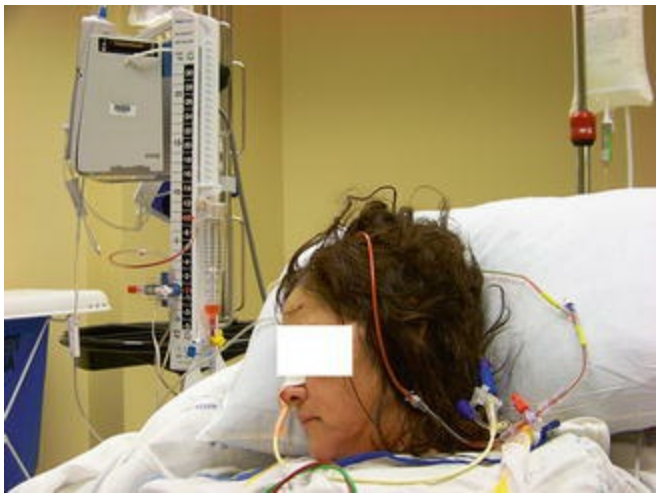

Fig. 15.3 An intraventricular drain placed in a patient following subarachnoid hemorrhage complicated by hydrocephalus

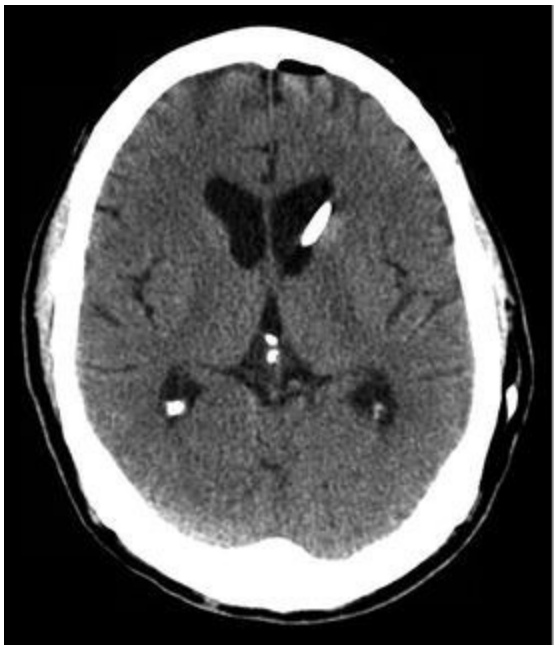

Fig. 15.4 Noncontrasted computed tomography (CT) of the head demonstrating correct placement of an IVC with the tip located in the lateral ventricle. Effacement of the ventricles is a relative contraindication to placement of an intraventricular catheter (IVC) or can be a sign of overdrainage of cerebrospinal fluid (CSF) when an IVC is already present. The IVC tip may also become entrapped in a collapsed ventricle, or displaced into the brain parenchyma, causing inaccurate measurement of ICP

Risks associated with placement of an IVC include bleeding and damage to eloquent tissues along the track toward the ventricle. In a coagulopathic patient, the risk of bleeding could produce high morbidity or even mortality and placement may be contraindicated. Multiple passes, in an attempt to place an IVC, can cause measurable tissue damage and only experienced providers should attempt to place this catheter. Risks also exist in transport or repositioning of a patient with an IVC. Unless a patient is in immediate danger of herniation, the IVC should remain clamped during transport or during significant patient repositioning to prevent inadvertent overdrainage of CSF and subsequent upward herniation (Fig. 15.5). It is best to secure the drain manifold to an IV pole. To prevent infection, the drain should never rest on the floor. Once the patient has been appropriately positioned, the catheter should be leveled to the external auditory meatus, unclamped and the IVC waveform transduced.

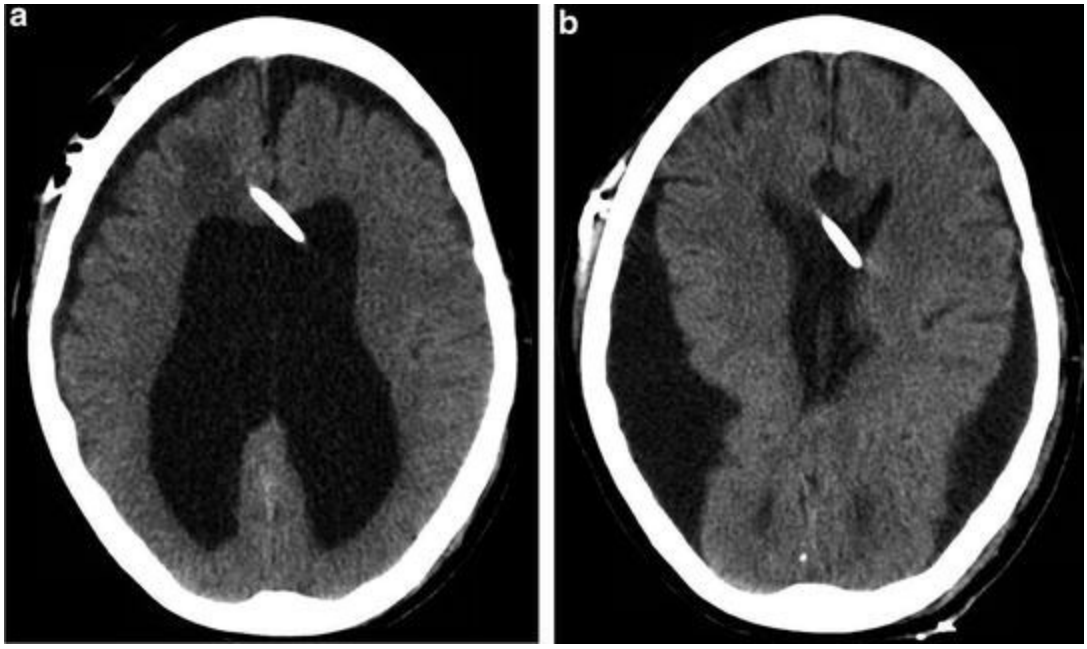

Fig. 15.5 (**a**) An intraventricular catheter (IVC) placed in a patient with a diagnosis of long-standing hydrocephalus . (**b**) The same IVC was left unclamped prior to transport. Neurologic deterioration was noted on examination and an emergent head CT demonstrated significant overdrainage of cerebrospinal fluid and ventricular collapse

Intracranial processes that lead to complete effacement of the ventricular system are considered contraindications to the IVC. In addition to the difficulty and risks with placement, information gathered from IVC

monitoring in such scenario will be of limited value, as accurate ICP measurements via an IVC are dependent on the presence of CSF and unobstructed flow of fluid throughout the ventricular system to deliver accurate information. Risks associated with maintaining an IVC are largely centered on CSF infection. Catheters remaining longer than 5 days are at especially increased risk for infection; some studies report an incidence as high as 1–5 %. As with any device, care should be taken to maintain the highest level of sterility, utilize closed systems, and avoid any unnecessary sampling from the catheter. Compared with the intraparenchymal devices (discussed later), the IVC carries a much higher risk for infection [3, 9]. The added risk for the IVC comes from the column of fluid, which connects the hospital environment to the intraventricular system and provides a pathway for introduction of all manner of pathogens. In addition, the IVC system can be opened for sampling of fluid or administration of drugs , which incorporates risks that can be compared in principle with those of other indwelling catheters, e.g., central venous catheters.

Parenchymal devices to measure ICP can provide excellent diagnostic information and may be favored in clinical scenarios where an IVC is contraindicated. Several intraparenchymal devices are in use today. Each is placed directly into the brain tissue via a support bolt or tunneled subcutaneously before entering the brain via a burr hole. The Codman® microsensor (DePuy Synthes, Massachusetts, USA) is a miniature strain gauge that senses changes in pressure as an alteration in resistance across the tip. The Camino® (Integra LifeSciences Corporation, New Jersey, USA) is a fiber-optic device that senses pressure change as an alteration in a beam of transmitted light (Fig. 15.6). Both systems involve placement of a small system-specific probe into the brain parenchyma and with that carry similar risks and associated errors in interpretation. The risk of infection is much lower with intraparenchymal devices when compared with the IVC. Bleeding risks associated with the intraparenchymal devices may also be lower and therefore preferred when compared with the IVC in a patient with irreversible coagulopathy . Placement of the intraparenchymal device causes much less tissue damage and therefore less of a need for optimal coagulation physiology .

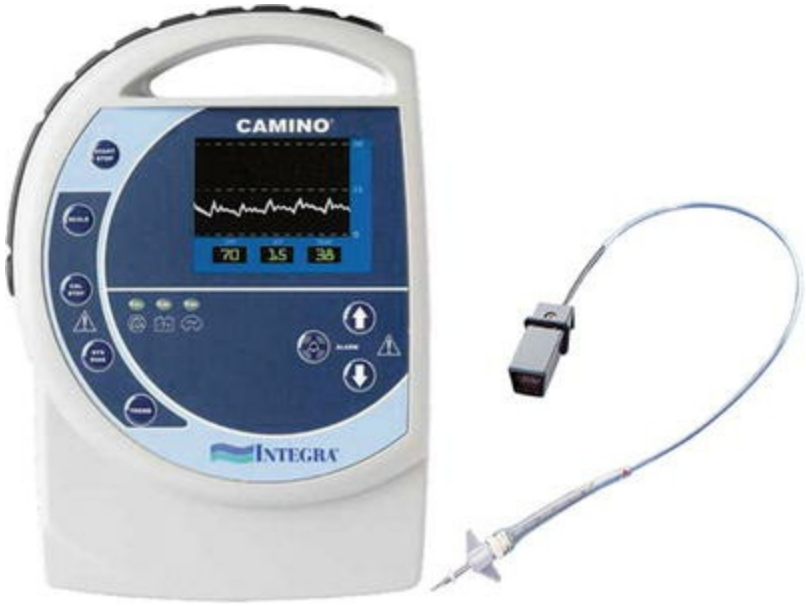

Fig. 15.6 Intraparenchymal fiber-optic monitor Camino® (Integra Lifescience, New Jersey, USA). This monitor is placed through a burr hole with the monitor tip in an intraparenchymal position

Information provided by both the IVC and parenchymal monitors is limited in that ICP is only measured in a relatively localized area of brain tissue [4]. Global ICP may not be reflected evenly throughout the cranium, particularly in the infratentorial vs. supratentorial cavities , as well as between right vs. left hemispheres (e.g., an IVC in the lateral horn may not accurately measure ICP in the posterior fossa). This type of variability has been well documented in studies comparing bilateral vs. unilateral cranial monitoring. Localized ICP provided by a space-occupying lesion may be physiologically devastating while causing little increase in global ICP such as the case in more subtle herniation syndromes.

Each of the two parenchymal systems (Codman®; Camino®) must be zeroed prior to placement of the probe and cannot be re-zeroed again while in situ. Baseline drift was a problem in the earlier versions, but mechanical advances have decreased the importance of this variable. Recent large cohort studies have verified the reliability of these newer models, specifically concluding that the small drift phenomenon that still remains was not clinically relevant for patient management [10]. A third type of device, produced by Raumedic © (Munchberg, Germany), the Neurovent-P, is an advanced probe that provides data on ICP, temperature, and brain tissue oxygenation. This is similar to the LICOX® system from Integra LifeSciences. These multimodality devices may well be the next forefront in

ICP monitoring.

Several intraparenchymal device systems were also designed for possible placement in subdural and epidural locations. These monitors are not widely used clinically due to poor accuracy [4]. Lumbar drains , utilizing the same system as the IVC, are poorly diagnostic of ICPs and in the setting of increased ICP, may precipitate herniation if CSF is drained rapidly. This type of monitor is not recommended for routine monitoring of ICP due to these concerns.

Independent of the technology used, ICP readings are interpreted by both amplitude and waveform. Definitions for normal vs. pathologic ICP are dependent on age, position, and the presence of acute or chronic disease. For an adult in the supine position, an ICP between 2 and 15 mmHg is normal [2]. A TBI patient is considered to have intracranial hypertension above 15 mmHg and demands therapy above 20 mmHg [4]. A patient with chronic hydrocephalus and an internalized shunt should be evaluated further when ICP is 15 mmHg or greater. In traumatic brain injury, sustained ICP above 25 mmHg is predictive of increased mortality [9].

The BTF has published recommendations on ICP and CPP thresholds for treatment. Unfortunately, it may not be as simple as a single goal for either ICP or CPP (CPP is defined as MAP − ICP). Patients with TBI have varying degrees of intact cerebrovascular autoregulation . Blood vessels in contused or ischemic brain tissue, or areas with traumatic bleeding, may have greatly impaired ability to adapt to changes in cerebral blood flow. Uninjured portions of brain may have relatively intact autoregulation. A patient with autoregulation that is presumed to be intact (such as a patient with a traumatic subdural hematoma that has been adequately decompressed) may tolerate a CPP of less than 70 mmHg; this population can be managed with CPP-directed goals of 50–70 mmHg (and greater than 70 mmHg when improvement in neurologic exam is noted), utilizing therapies that increase mean arterial blood pressure. Patients with focally or globally impaired autoregulation will demonstrate increased ICP in response to raised CPP, a reaction termed *pressure passive autoregulation*. This group is better managed with ICP-directed goals of less than 20 mmHg, employing ICP-lowering therapies [9, 11, 12].

Importantly, the ICP waveform can be used as a surrogate parameter for measuring cerebrovascular autoregulation . A more technical approach to ICP and CPP management can be achieved by dissecting the intricacies of this

waveform. Waveform analysis is being used in some neuroscience institutions, and may provide the information needed to tailor therapies in a more patient-specific manner. Advanced waveform interpretation is best done with specialty software. Spectral analysis can break down the ICP waveform to plot each harmonic component independently and determine their respective magnitudes.

The ICP waveform reflects the mean ICP and its change over time in response to pressure changes from parallel-occurring physiologic events transmitted to the cranium (such as from pulsations of blood flow, changes in respiration, and vasogenic reactivity). The normal ICP waveform consists of three peaks each decreasing in height. The component peaks are P1 (percussion wave), P2 (tidal wave), and P3 (dicrotic wave) (Fig. 15.7). It is assumed that P1 and P2 are the result of the pulsation of arterial blood vessels: P1 represents the systolic pulse wave and P2 represents the harmonic reverberation of the pulse against the intracranial compartment. In contrast, P3 is assumed to be venous in origin. A slow sinusoidal pattern will also reverberate the waveform in accordance with changes in intrathoracic pressure during the respiratory cycle.

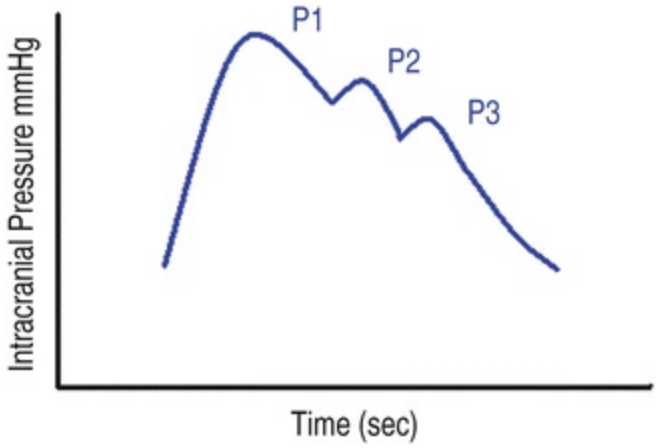

Fig. 15.7 Normal intracranial pressure waveform . Note the three prominent peaks each decreasing in height (P1, P2, P3). P1 and P2 represent the pulsation and counterpulsation of the arterial pressure waveform, where P3 represents venous reverberation

Many physiologic and pathophysiologic states have been identified as modifiers of the ICP waveform: arterial hypotension will decrease both the mean ICP and the amplitude of the waveform, particularly P1. An increase in mean ICP and rising amplitude of both P1 and P2 are seen with arterial

hypertension. A space-occupying lesion will increase mean ICP as well as ICP waveform amplitude. If a mass lesion creates a critical rise in ICP, to the point of decreased CPP, the ICP waveform will change in that P2 will continue to rise beyond its neighbor peaks and P1 will become buried (Fig. 15.8). Increases in CSF volume may also increase both mean ICP and waveform amplitude, but will preserve waveform configuration. Hyperventilation, drainage of CSF, and the head-up position will all decrease mean ICP and waveform amplitude. Cerebral vasospasm will produce little change in mean ICP but may decrease waveform amplitude. Severe hypercapnia or hypoxia will increase mean ICP and produce a rounded waveform appearance, which is due to large increases in the amplitude of the ICP waveform. Early signs of decreased intracranial compliance may be suggested by increased waveform amplitude, P2 elevation, and a rounded out appearance of the overall waveform (see Fig. 15.8) before mean ICP begins to rise.

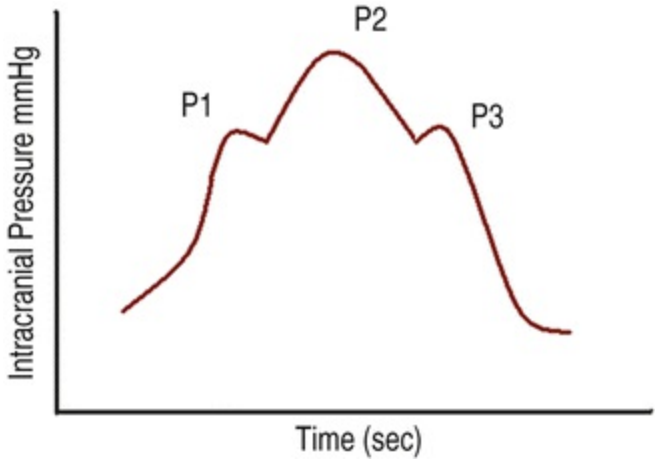

Fig. 15.8 Deranged intracranial pressure waveform with peak P2 higher than P1. Before mean intracranial pressure (ICP) begins to rise, subtle changes in the waveform morphology may indicate reduced intracranial compliance. P2 rising above P1, a widening of the waveform, and an increasing amplitude may all precede a rise in the mean ICP

The P1 and P2 waves provided by arterial pulsation reflect mean ICP and together can be defined as the “fundamental component” of the waveform. This fundamental component is considered to reflect the autoregulatory reserve, that is to say that increases in ICP as a response to increases in arterial BP are evidence of weakened cerebral autoregulation. The amplitude of the fundamental component correlates with mean ICP and is equally

predictive of outcome in patients with TBI.

A measurement of the “compensatory reserve” of the intracranial compartment, or the degree to which changes in intracranial volume effect changes in ICP, has been calculated from characteristics of the ICP waveform: the index of compensatory reserve is calculated from the amplitude of the pulse waveform component and the mean ICP, and is called RAP. Mathematically, RA P is defined as the correlation coefficient [R] between amplitude of the fundamental component [A] and the mean pressure [P].

At low ICP, a RAP of zero indicates little to no change in pressure with an increase in intracranial volume, which represents a state of good compensatory reserve. An elevated RAP suggests diminished compensatory reserve and predicts that even small changes in intracranial volume will result in large changes in ICP. At high ICP, the RAP will be positive and will increase until it reaches a breakpoint after which the RAP will fall below zero, indicating total exhaustion of any remaining autoregulatory capacity, and very low compliance (impending cerebral herniation). Here the cerebral arterioles are maximally dilated in an attempt to maintain CPP and ultimately collapse, leading to a decrease of pulse pressure transmission from arterial bed to cerebral tissue (acute risk for brain ischemia) [6, 8].

Cerebral pressure reactivity (PRx) is another index computed from the ICP waveform and measures autoregulatory capacity: PRx assesses the response of ICP to slow spontaneous changes in arterial blood pressure. A normally reactive cerebrovascular bed will decrease cerebral blood volume (and thus ICP) in response to an increase in arterial blood pressure and PRx will be low or negative. A deranged cerebrovascular bed, denoted by a positive PRx, will increase ICP passively in response to an increase in arterial blood pressure (little to no autoregulatory capacity). The PRx may help to guide the practitioner toward an optimal pressure window of the individual patient in CPP-directed therapy [6, 8].

The high PRx has been associated with poor outcome in patients after traumatic brain injury [13], and guiding CPP management by optimization of the PRx has been associated with improved outcomes [14]. Another index of cerebral autoregulation, the pulse amplitude index (PAx), quantifies the relationship between slow fluctuations of arterial blood pressure and ICP *pulse amplitude*: elevated PAx is associated with poor outcome and mortality. PAx may better reflect autoregulatory capacity than PRx in situations when

compliance *and* ICP are low but when autoregulation remains impaired, such as after a decompressive hemicraniectomy for treatment subsequent to an ischemic stroke or TBI [15].

The goal of ICP monitoring is to gather information to aid the practitioner in the management of physiologic parameters so as to avoid ischemia (low CPP) and hyperemia (high CPP) (see Fig. 15.2). ICP magnitude and waveform analysis can also prove useful when prognosticating based on an assessment of cerebral compensatory reserve and cerebral pressure reactivity. Future areas of investigation will likely focus on the role of ICP waveform analysis in guiding clinical therapies toward optimization of CPP and increased intracranial compliance, and whether the interventions based on advanced ICP monitoring can influence patient outcome.

Clearly, ICP monitoring is not the only established monitor of brain perfusion . Brain tissue oxygen tension, laser Doppler/thermal diffusion flowmetry, positron emission tomography/tissue perfusion CT, jugular venous oxygen saturation, microdialysis, and transcranial Doppler have also been described as methods to estimate brain tissue perfusion and further guide ICP and CPP goals. Multimodality approaches, which integrate ICP monitoring along with additional measures of cerebral physiology, particularly brain oxygen tension, are likely to be the next big step in the management of the brain-injured patient; however, much further research is necessary.

Continuous ICP monitoring is a cornerstone of care of the brain-injured patient, and in the setting of protocol-driven care, appears to benefit patients' outcome. Whether invasive ICP monitoring can benefit an individual patient depends largely on the clinician's interpretation of the data and the selection of medical or surgical therapies.

Questions

1. Which of the following represents the latest sign of decreased intracranial compliance ?

a. Increased waveform amplitude

b. P2 elevation

c. A rounded out appearance of the overall waveform

d. Increased mean ICP

2. Which of the following statements about the RAP is FALSE?

a. RAP is a measurement of compensatory reserve.

b. RAP reflects the relationship between the amplitude and the mean pressure of the ICP waveform.

c. A RAP of zero indicates no remaining compensatory reserve.

d. A negative RAP with high ICP is a poor prognostic sign.

3. Which of the following physiologic value represents the highest risk for cerebral ischemia ?

a. ICP 14 mmHg

b. CPP 46

c. RAP 0

d. PaO_2 65

4. Which of the following statements about cerebral blood flow is INCORRECT?

a. Cerebral blood flow (CBF) is maintained at a constant state when cerebral perfusion pressure (CPP) is between approximately 50 and 150 mmHg.

b. Above or below 50 and 150 mmHg, cerebral blood flow is proportional to CPP.

c. A PaO_2 below 50 mmHg produces a significant increase in CBF.

d. $PaCO_2$ increases CBF by approximately 1 mL/100 g/min for every 10 mmHg increase in CO_2.

Answers

1. D Explanation: An increase in the mean ICP will usually occur after more subtle waveform changes indicating decreased intracranial compliance.

2. C Explanation: At low ICP, a RAP of zero indicates little to no change in pressure with an increase in intracranial volume, which represents a state of good compensatory reserve. An elevated RAP suggests diminished compensatory reserve and predicts that even small changes in intracranial volume will result in large changes in intracranial pressure.

3. B Explanation: Cerebral perfusion pressure lower than 60 is associated with cerebral ischemia in patients with traumatic brain injury. All of the other physiologic values are normal.

4. D Explanation: Small changes in $PaCO_2$ can result in proportional increases in CBF as a result of cerebral vasodilation. $PaCO_2$ increases CBF by approximately 1 mL/100 g/min for every 1 mmHg increase in CO_2.

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Footnotes

1 Key references marked with asterisk.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_16

16. IOM Instrumentation Layout and Electrical Interference

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Electronic supplementary material:
The online version of this chapter (doi:10.1007/978-3-319-46542-5_16) contains supplementary material, which is available to authorized users.

Keywords Basic electrical circuits – Electrical interference – Recording technology – Impedance – Electrodes – Signal-to-noise ratio – Grounding – Signal averaging – Electromagnetic fields – Electrode burns

Key Learning Points

- Electrical interference challenges recording of tiny neurophysiologic signals due primarily to electromagnetic coupling, the relatively large size of electromagnetic fields present in the operating room, and the

large conductivity of skin.

- The team performing IOM, including the anesthesiologist and other professionals, has many tools to effectively battle electrical interference.

Introduction

Performance of Intraoperative Neuromonitoring (IOM) routinely requires up to 50 or more patient attachment electrodes connecting the patient to IOM instrumentation in order to electrically stimulate and record physiologic signals . Finding patient skin locations to apply these many electrodes and laying out the leadwires is only one of the challenges the anesthesiologist and IOM team face.

- ***The physiologic signals are tiny*** relative to other electrical sources nearby, and are sometimes in the low microvolt range. If we assign 1 in. to 1 μV, finding a sensory evoked potential in the presence of 120-V wall voltage is like trying to find a piece of notebook paper somewhere between Miami, Florida and Anchorage, Alaska.
- ***The IOM recording circuitry acts as an antenna*** to the multitude of nearby electrical noise sources in the OR, potentially rendering the IOM ineffective.
- ***The large capacitance of skin*** facilitates coupling of unwanted electrical noise, often into the IOM recording circuitry.
- ***High-energy electrical equipment*** such as the electrosurgical unit (ESU or “Bovie”) in addition to introducing electrical interference in the IOM recordings may, without adequate attention to cabling layout, create electrode burns.

This chapter discusses the physics underlying the electrical and electromagnetic interactions occurring when neuromonitoring is performed in the electrically hostile setting of the operating room. The goal is to demonstrate how electrical interference makes its way to IOM recordings, and to illuminate methods of laying out IOM instrumentation equipment, leadwires, and electrodes for optimal and safe electrophysiologic recordings. The electrical and physics explanations are not intended as a detailed treatise. Rather, it is desired that the OR professional retains helpful mental pictures

and checklists to use in the everyday performance of IOM.

Basic Electronics and Definitions

While the field of electronics is wonderfully complex, the basic concepts necessary to understand how electrical interference can enter the recordings are not difficult to understand. Figure 16.1 shows a circuit that is a simplification of the recording circuit, with a source and three impedance s.

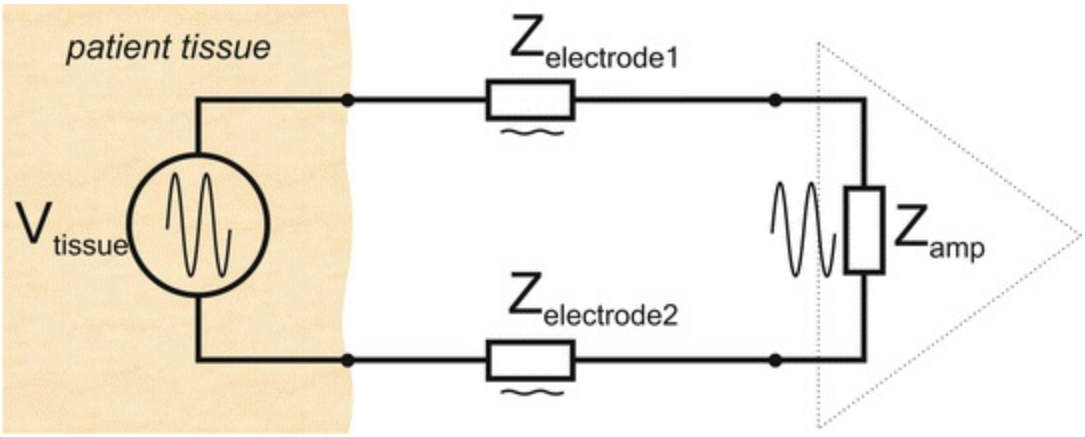

Fig. 16.1 Simplified recording circuit showing tissue voltage source V_{tissue}, two impedances representing electrodes $Z_{electrode1}$ and $Z_{electrode2}$, and the input impedance of the amplifier Z_{amp}

Definition 1

An ***Electrical Circuit*** is a closed loop pathway in which electrical current flows. The amount of current flowing is the same at every point along the circuit. The circuit must be continuous such that it is complete; an opening along the path stops current flow. The source of voltage drives a current through the circuit impedances according to Ohm's law. In electronics, there are many types of voltage sources including constant (or DC for direct current) or alternating (or AC for alternating current). Our IOM recording circuit as shown in Fig. 16.1 has physiologic voltage sources that are alternating with a range of frequency components, designated as V_{tissue}.

Definition 2

Impedance (usually denoted as "*Z*") is the term for devices that resist the flow of electrical current. There are three basic types of impedance as described below.

Definition 3
Ohm's law is a very simple relationship. It takes voltage (*V*) to drive a current through impedance (*Z*) to that current flow (*I*) according to the formula: Current = Voltage/Impedance ($I = V/Z$). A different way to phrase it is that current passing through impedance builds up a voltage across that impedance.

> *KEY POINT: When current flows in the circuits due to some voltage source such as a physiologic signal, that current builds a voltage across every location in the circuit where there is impedance.*

Definition 4
A ***Voltage Divider*** explains that the source voltage divides among the impedances in the circuit. Larger impedances get a larger share of the voltage, but the sum of the voltages building on the circuit impedances always totals the exact value of the source voltage.

> *KEY POINT: We wish the physiologic signal to build up voltage on the amplifier input impedance where it can be amplified. We therefore need to ensure that the electrode impedances are small relative to the amplifier input impedance, as shown in* Fig. 16.1 .

Definition 5
An ***Amplifier*** is an electronic circuit that multiplies an input voltage by a gain factor to deliver an output voltage. IOM equipment generally utilizes differential amplifiers in which the input voltage is the voltage difference between two inputs.

> Technical Note: An ideal differential amplifier would deliver an output equal to the voltage difference across its inputs (or differential voltage) multiplied by the gain. A real-world amplifier also amplifies the voltage common to both inputs (or common mode voltage) though to a much lesser extent. The iso-ground serves as the reference point for this common mode voltage. The measure of an amplifier's ability to reject the common mode voltage is the common mode rejection ratio (CMRR), which is the ratio of its differential gain to its common mode gain. The CMRR of modern IOM equipment can exceed 100 dB or 100,000:1.
>
> *KEY POINTS: Selection of an iso-ground location impacts common mode voltage. Furthermore, imbalances between electrode impedances*

result in one electrode impedance with more voltage buildup and negatively impact the CMRR of an amplifier.

Sources of electrical interference and more details have been added to the simplified recording circuit in Fig. 16.2. Notice that $Z_{electrode2}$ is now shown as a complex of three different parts in parallel. This is because electrical impedance has three components, including a resistive component *R*, capacitive component *C*, and inductive component *L*. For simplicity, the impedance subcomponents are only shown for $Z_{electrode2}$, but exist for all circuit impedances, even if just at the tiniest of levels.

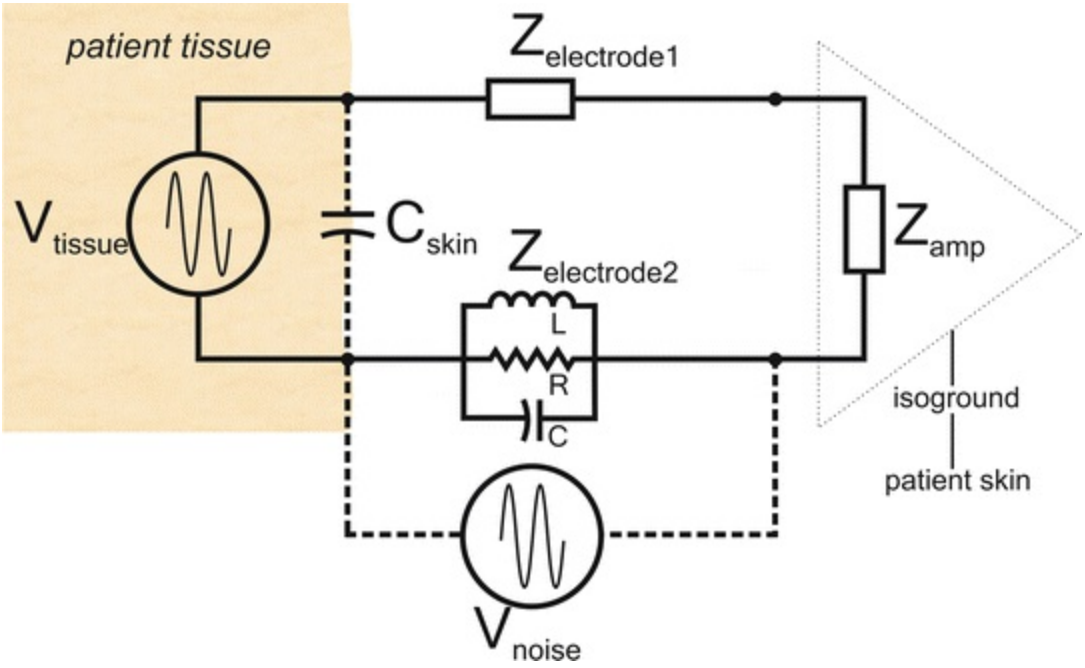

Fig. 16.2 Simplified recording circuit with potential sources of electrical interference

Electrical Impedance is a measure of the opposition to alternating current flow. It is the vector summation of three different impedance components arising from electrical resistance, electrical capacitance, and electrical inductance. This is usually reported in Ohms (Ω).

Electrical Resistance is a measure of the opposition to direct current flow. The resistive component of impedance does not change with frequency.

Electrical Capacitance is a measure of how much charge can be held. The capacitive component of impedance decreases as the frequency of flowing current (or applied voltage) increases.

Electrical Inductance is a measure of opposition to a changing current flow. The inductive component of impedance increases as the frequency of flowing current (or applied voltage) increases.

> *KEY POINT: The capacitive and inductive components of impedance allow nearby sources of electrical interference to couple through the air with the recording circuitry.*

It is the inductive and capacitive components highlighted in Fig. 16.2 that allow for the two most common pathways for electrical interference to enter the recording circuit.

Pathway 1: The Skin of the Patient C_{skin}

The patient's skin has large capacitance (the ability to hold charge). It is this capacitance that allows the skin to build up large static voltages that hurt when they are discharged in the winter. This capacitance aids the skin of the patient in being an attractive antenna for electrical interference nearby. In filling the capacitance of the patient's skin, the charge distributes all over the patient's body surface, inherently bringing this noise to the recording electrodes in contact with the skin and into the recording circuit.

Pathway 2: Ambient Sources of Electrical Noise V_{noise}

A source of ambient electrical interference is shown as V_{noise}. For simplicity, it is only shown to be coupling with the impedance of leadwire 2. However, every part of the circuit is potentially susceptible. As we will see later in the chapter and in many of the videos, the leadwires as well as the patient's skin are particularly vulnerable.

An understanding of how these two pathways enable noise to enter the recording circuit will help us consider electromagnetic coupling mechanisms discussed later.

> Technical note: An essential concept in data acquisition is signal-to-noise ratio (SNR) . We can think of any of the recordings as a combination of two elements. The first is the signal we are interested in. The remainder is what we consider to be noise. Noise is also referred to as interference or artifact and these terms are often used interchangeably. The ratio of the power of the signal to the power of the

noise is the signal-to-noise ratio. The higher the signal-to-noise ratio, the more likely we are to be able to gain useful information from a recording. To achieve these results, we can increase the signal or reduce the noise.

Signal averaging is commonly used when the signal-to-noise ratio is low (e.g., auditory brainstem response where the signal has very low voltage). Averaging improves the signal-to-noise ratio by reducing the noise amplitude by virtue of the fact that the signal in each trial stimuli remains the same, but the noise varies in a random way such that averaging trials reduce the averaged noise, with the signal-to-noise ratio improving by the square root of the number of averaging trials.

While averaging represents an important way to improve signal-to-noise ratio , it does nothing to reduce actual noise. Much of what is presented in this chapter falls on the side of reducing the noise reaching the amplifiers, or else making the noise more common so it is rejected.

The Basic IOM Recording Circuit

The many recording electrodes attached to the patient are but a repetition of the same basic recording circuit many times over. Figure 16.3 shows the basic recording circuit including the instrumentation amplifier, two recording electrodes, amplifier iso-ground, and physiologic signal source (V_{tissue}).

Though the three electrodes shown are subdermal needle electrodes, other electrode types such as hydrogel surface pads, EEG cups, and longer needles may also be used in IOM settings. The concepts discussed here are pertinent regardless of the electrode type used or the IOM equipment used.

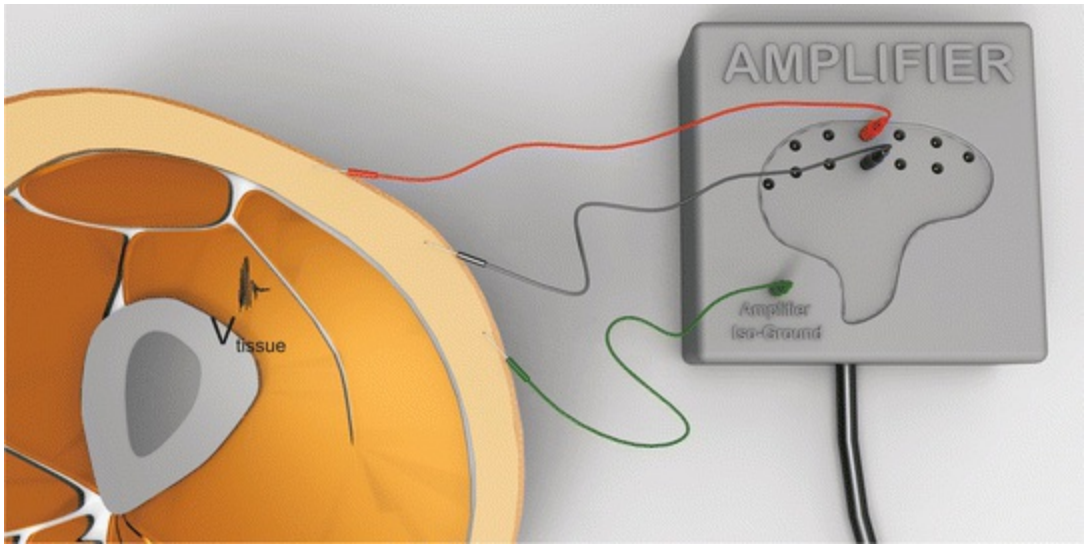

Fig. 16.3 Example of a recording scenario highlighting the basic IOM recording circuit

If the insulation covering the electrodes is removed, it becomes obvious that electrodes contain many materials, even the seemingly simple needle electrodes shown. This is depicted in Fig. 16.4.

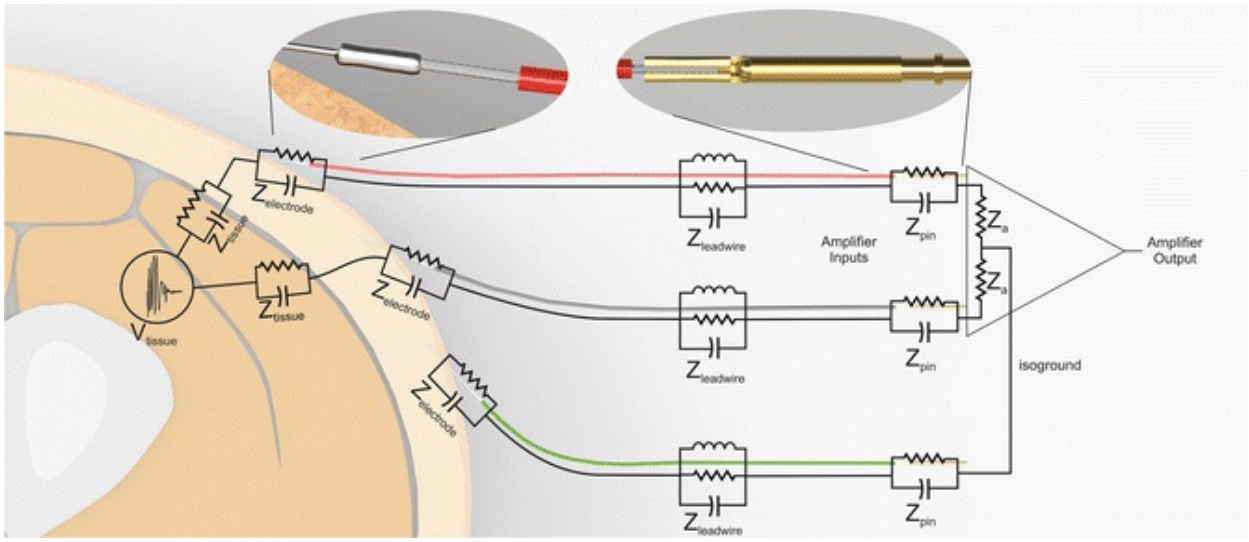

Fig. 16.4 The basic recording circuit electrical schematic showing all electrical connections in the circuit including the resistive, capacitive, and inductive components of impedance. Note the numerous dissimilar metal-to-metal connections (highlighted in the inserts)

The electrical equivalent circuit is shown in Fig. 16.4 with the exposed connections within the electrodes shown. When thinking about electrode impedance, it is common to consider the impedance of the electrode

attachment to skin. However, as Fig. 16.4 shows, at many points on the circuit, we find impedance. The components of the basic recording circuit are listed under the following subheadings.

Tissue Physiologic Generator (V_{tissue})

The physiologic signal volume conducts in three dimensions outward from the neurogenic or myogenic source through the array of tissues surrounding it, losing amplitude exponentially as it migrates outward. A portion of the volume conducted signal electrical field conducts to each recording electrode via a near infinite number of pathways, shown in white outline, in Fig. 16.5. As a result of volume conduction losses as well as signal attenuation traveling through high impedance tissues such as adipose, by the time the physiologic signal reaches the recording electrodes, the amplitude is exponentially lower than at the source.

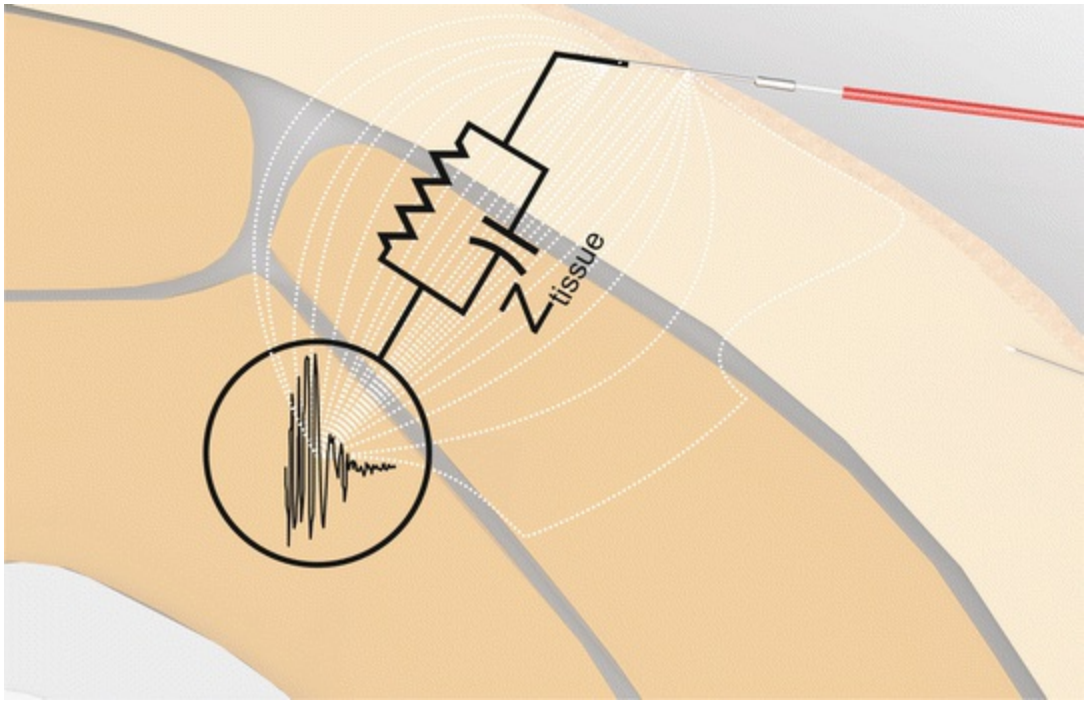

Fig. 16.5 Near infinite tissue pathways from generator to recording electrode. Current flows from the source generator to the recording electrode using a near infinite number of tissue pathways dependent on conductivity of each pathway

Circuit Component: Tissue Between Generator and

Electrode (Z_{tissue})

The signal pathways follow the path of least impedance through the array of different tissues from source to recording electrode. Tissues like muscle, blood vessels, capillary beds, and mucosa have low impedance (below 1 kΩ) [1]. Skin can range in impedance depending on location on the body, thickness, and concentration of sweat and sebaceous glands (typically over 40 kΩ) [1]. Tendon, fat, and bone have the highest impedances though these layers also represent unavoidable pathways to current flow if surface or subdermal needles are used. Note that many of the pathways shown from the source to the recording electrode are surprising, as they may follow unexpected pathways as shown by the far right signal path in Fig. 16.5. These multiple parallel pathways can be considered as an equivalent impedance, shown in black outline in the figure (pathways) and labeled Z_{tissue}. There is no typical value of Z_{tissue}, as the adipose layer thickness in the patients varies dramatically.

> *KEY POINT: Since tissue impedance is frequency dependent, we can assume that the different fundamental frequency components of physiologic signals will attenuate differently when volume conducted through tissue and that is indeed the case. Higher frequency signal components volume conduct through tissue with more amplitude loss on average than lower frequency signal components. Note that this tissue-filtering effect occurs prior to the signal reaching the recording electrodes!*

Circuit Component: Electrode Connection to the Patient + Electrode Components ($Z_{\text{electrode}}$)

Electrode connection to patient: This portion of impedance is due to the connection of the electrode with the patient's tissue. This is typically the impedance many IOM clinicians first think of when asked what their impedances are and why care is usually taken to lower this impedance by attention to skin preparation and electrode placement.

Due to the high impedance of the epidermis, particularly the stratum corneum, it is necessary to either prepare the skin surface by some form of debridement or to use electrodes that bypass this high impedance layer such

as needle electrodes. Exact levels of impedance achieved vary depending on skin preparation and surface area of electrode used, but may be anywhere between a few hundred ohms and 10 kΩ or more. The electrode conductor in contact with patient tissue has the ability to hold charge, therefore it is important to consider this portion of impedance to be a resistance in parallel with a capacitance. Needless to say, it is best to avoid dissimilar electrode types in one amplifier circuit to minimize impedance imbalance between electrodes.

Electrode components at the patient end of the electrode: Excellent volumes have been published detailing patient attachment electrodes for recording and stimulating physiologic signals [2]. Mention of a few details pertinent to the discussion is warranted.

Electrode patient connections may contain many different materials, whether biocompatible metal, conductive plastic, ionically rich hydrogel, carbon or metal foils, glues, solders, and a large list of other possible materials. In the subdermal needles shown, a medical grade stainless steel needle is soldered to a 19-strand tinned copper wire, so many different metals are present in this tiny junction. When placed together to form the patient attachment end of the electrodes, the contribution to impedance is quite low, typically less than a few ohms. However, where there are dissimilar metals, it is possible to have a voltage generated through galvanic corrosion mechanisms, the same reaction used to create voltages in many batteries. All that is needed is ionic fluid to bath the metal-to-metal junction. Ionic fluids such as sweat are readily present around the operating room bed. Any such galvanic voltage generated is added to the recording circuit as electrical interference.

> *KEY POINT: To avoid metal-to-metal galvanic corrosion voltages contaminating the recording circuit, care should be taken to avoid accidentally bathing the electrode and hub in fluids.*

Circuit Component: The Wire Between the Electrode Patient End and Connector End (Z_{leadwire})

The leadwire may have many different types of conductor covered by an electrical insulating material. Some examples of conductors include multistrand tinned copper, copper, carbon fiber, and tinsel wire. Though the

leadwire generally has less than a few ohms of impedance, this portion of the recording circuit plays a large role in electromagnetic interference through the inductive and capacitive components of impedance .

> *NOTE: Though all portions of the basic recording circuit have an inductive component of impedance, for simplicity, only the inductive component of impedance of the leadwire has been shown in* Fig. 16.4 .

Circuit Component: Leadwire connection to safety connector + Electrode to amplifier connection (Z_{pin})

The leadwire connection to the touchproof socket is typically a molded plastic over a metal ferrule crimped to the leadwire conductor. While the metal used in the mechanical crimp that grips the leadwire conductors could be tin, copper, brass, gold-plated brass, or others, this end of the electrode almost universally contains two dissimilar metals, as shown in the insert of Fig. 16.7, where the gold-plated brass ferrule is crimped to the 19-strand tinned copper leadwire. Since the molded plastic overmold keeps ionic fluids away from the dissimilar metal joints, this connection is rarely a source of galvanic voltage. Connection is made at the amplifier via a 1.5-mm diameter pin over which the touchproof socket of the leadwire fits. This metal pin is typically gold-plated brass but could be other conductive metals. As part of electrical troubleshooting, it is important to consider this connection. A loose connection can be a source of intermittent impedance. Though it is very rare, it is possible for the plastic overmold to have plastic slivers down inside the 1.5-mm opening that hinder the electrical connection between the 1.5-mm pin and the touchproof socket conductor.

> KEY POINT: As part of troubleshooting, the IOM team should remember that electrodes may be nonfunctioning right out of the box, though it is very infrequent that this occurs.

Circuit Component: Amplifier Impedance (Z_a)

The input impedance of the IOM amplifier is the combination of the two impedances labeled Z_a. Modern IOM amplifiers utilize ever smaller, more powerful electronics, especially integrated circuitry. The result is a smaller circuitry footprint yielding more sensitive amplifiers with ever higher input impedances of more than 100 kΩ. A technical note is included at the end of this chapter highlighting amplifier characteristics important for the IOM team

to understand.

Circuit Component: Amplifier Iso-ground

The iso-ground position holds as much confusion for the IOM team as any other area of instrumentation. It has an electrode connected to the patient as shown in Fig. 16.4, so it has the same impedance variables and potential to pick up ambient electrical interference as any other electrode position has. Hence the location of the iso-ground placement can influence the amount of noise in the recording. The technical note at the end of the chapter highlights more on iso-ground.

Video 16.7 demonstrates that the efficacy of iso-ground to decrease electrical interference pickup is very location specific.

Basic Circuit Summary Points

- The physiologic signals are often very small in amplitude by the time they volume conduct to the recording electrodes.
- The very high input impedances of modern IOM equipment (>100 MΩ) relative to the much lower electrode impedances (<10 kΩ) ensure that the vast majority of the signal appears across the amplifier inputs.
- The leadwires and patient skin invite coupling with electromagnetic interference.

Understanding Sources of Electrical Interference

The primary method by which electrical interference is introduced to the recording circuits is via electromagnetic coupling , which includes three components: inductive coupling, capacitive coupling, and radiative coupling [3].

Inductive coupling occurs when an electric current is generated in the recording circuit via movement of the recording wires in relation to a magnetic field, either by the leadwires moving through the magnetic field or the magnetic field moving near the leadwires. With the exception of the occasional intraoperative magnetic resonance imaging unit (MRI), there are relatively few stationary magnets in the operating room setting. However, the magnetic component of electromagnetic waves can create inductive coupling with the recording circuit. Since the inductive component of impedance

increases with frequency, this occurs primarily at low frequencies, such as with 60-Hz wall voltage.

Capacitive coupling occurs when a radiofrequency energy source is near enough to the recording circuit to couple with it via the capacitive component of impedance. Since the capacitive component of impedance decreases with frequency, capacitive coupling plays a role in the recording circuit at high frequencies.

Electromagnetic radiative coupling is the principle by which radiofrequency energy from a radio station travels many miles to be picked up by antennas with the sounds heard by a radio. Though the recording leadwire pairs are technically a simple dipole antenna, as shown in Fig. 16.6, the frequencies from RF-radiated signals are generally too high to create visible electrical interference in the recording circuits due to the filter settings used. Although occasionally, IOM clinicians may hear AM radio stations amplified over their speakers when listening to the EMG sounds.

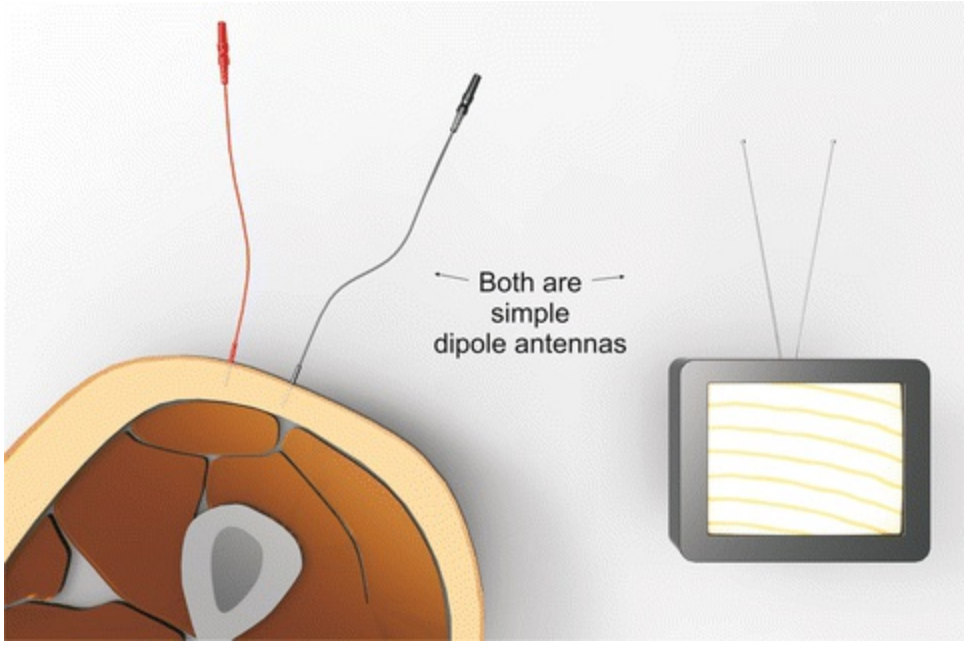

Fig. 16.6 Recording electrodes act similar to the dipole antenna of a radio and can receive electromagnetic signals such as those from radio stations. Fortunately these signals consist of high frequencies that are not usually seen as noise in physiologic IOM signals

The IOM practitioner can use electromagnetic coupling to advantage by creating a leadwire pair to use as a searching coil placed into one recording input of the IOM amplifier. An example of this is shown in Fig. 16.8 later in

this chapter. This wire loop can be valuable in attempting to locate electromagnetic sources when attempting to either mitigate electrical noise at the source or move the source equipment to redirect a directional field away from the recording leadwires or patient skin.

It is critical for the IOM clinician to understand methods of leadwire management to lower the amount of electromagnetic coupling occurring. Figure 16.7 highlights three typical leadwire layouts frequently used, including twisted pairs, ribbon pairs, and loose pairs.

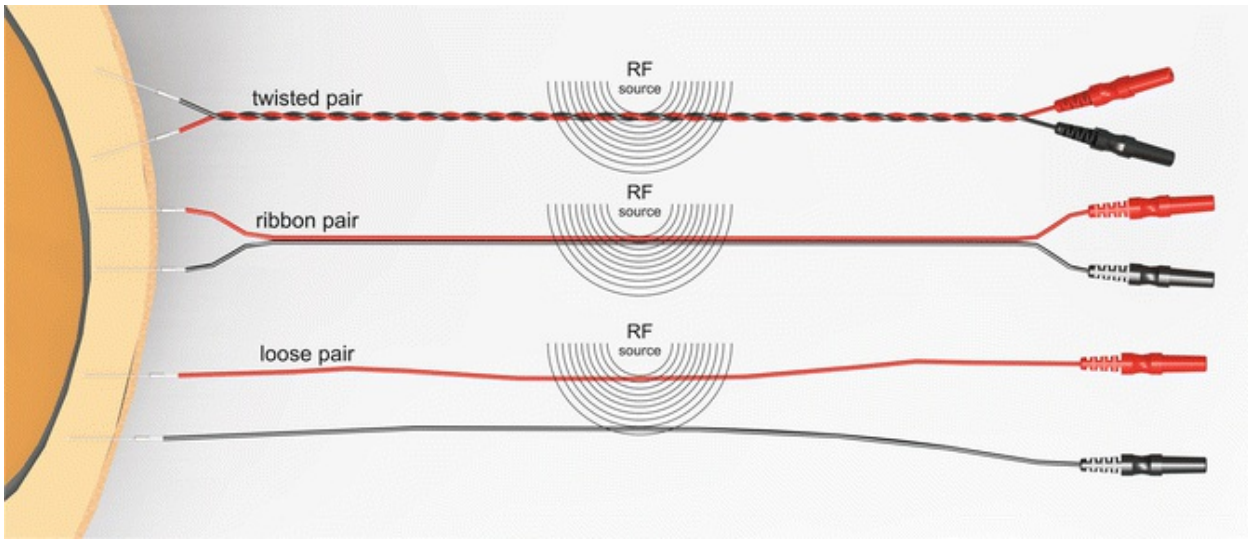

Fig. 16.7 Methods used to manage recording wires in IOM. As described, the twisted pair method reduces the amount of electromagnetic noise more than a ribbon pair, which reduces it more than loose wires

For demonstration purposes in Fig. 16.7, each of the three leadwire configurations has a focused radiofrequency source. The radiofrequency field strength decreases exponentially with distance away from the source, so the closest leadwire will couple an exponentially higher amount of the field.

> *KEY POINT: Electromagnetic fields dissipate inversely with distance squared. As highlighted in many of the video demonstrations, creating distance from these fields can greatly diminish their influence on IOM recordings.*

In the twisted pair leadwire set, the red and black leadwires are, on average, the exact same distance from the RF source, so even though both leadwires couple the exact same amount of electromagnetic interference, the amplifiers will not amplify the interference since it is common mode.

In the ribbon pair leadwire set, the red wire, though very near the black leadwire, is closer to the RF source, so it couples a slightly larger amount of interference. This small difference in coupling between the red and black leadwires of the ribbon, though small, will not be common mode and will therefore be included in the recording as interference.

In the loose pair leadwire set, the black wire is obviously further away from the source than the red wire, leading to an exponential difference in the recorded interference, which will be amplified in the recording as interference.

Interestingly, this twisted pair method is also used to reduce the emission of electromagnetic radiation from power lines. In that case, the twist causes each wire to cancel the effect of its pair. This is often referred to as an old "mariner's trick" to reduce the effect of nearby power cords on magnetic compasses. Unfortunately, most power cords in the OR are not twisted pairs.

> *KEY POINT: Bringing recording leadwire pairs together decreases the amount of electromagnetic interference amplified by making the interference coupled to each leadwire more common than with the recording leadwires separated.*

As the IOM clinician knows, sources of electromagnetic interference are plentiful in the operating room. An incomplete list of electrically noisy equipment components includes wall voltage, fans, pumps, heating elements, and some light bulbs. Once identified, the noise signal can be reduced by moving these sources farther away (or up or down relative to the recording wires) by the square of the distance. In addition, occasionally the device emitting the electromagnetic signal emits it in a relatively unidirectional manner such that if it can be rotated relative to the recording wires, the noise recorded may be reduced.

In addition, it is crucial to identify currents established in patient attachment leadwires due to electromagnetic coupling as they may result in patient burns at the patient attachment electrode. Powerful fields such as those associated with the electrosurgical unit and MRI RF pulse coils are of particular concern. The risk of electrode burns has been documented previously [4–7].

See the addendum to this chapter for videos demonstrating many of the topics discussed including the electromagnetic field s associated with a few pieces of OR equipment. But the more important message is that it is quite

easy for you as the OR clinician to develop a troubleshooting skill set to diagnose electromagnetic interference sources.

Practical Tips

Specifically for the Anesthesiologist

The anesthesia team is in an ideal position to help find problems that can plague the IOM team.

- Watch for dislodged IOM electrodes. The impedance of both needle and surface electrodes increases dramatically when dislodged.
- If possible, try to have anesthesia equipment and power cords as far away from recording electrodes as possible.
- Note when new equipment (e.g., blood warmers) is added to the operating room such that if a search for noise ensues, the new equipment can be evaluated as a new source of noise.

For the IOM Professional

- Ensure that all hydrogel-type patient attachment electrodes (“stick on” electrodes like ECG electrodes) are fresh and within use-by date. This is especially true for the electrosurgical unit return (“grounding”) pad, which plays a critical role in patient safety.
- Prepare your own electromagnetic directional sensing coil to locate sources of electromagnetic noise (Fig. 16.8). A 2.2-kΩ resistor can be purchased in an electronics store or online for pennies. After removing the electrodes from two long leadwires and stripping the insulation off of the ends, twist a leadwire to each end of the resistor wires. By taping the leadwires with resistor to a flat mobile surface with the leadwires widely separate, twisting the extra leadwire together and plugging the two leadwires into a channel of your IOM system yields a directional sensor. Monitoring the free run signal on your IOM system will allow you to view the electromagnetic fields in front of the flat surface.

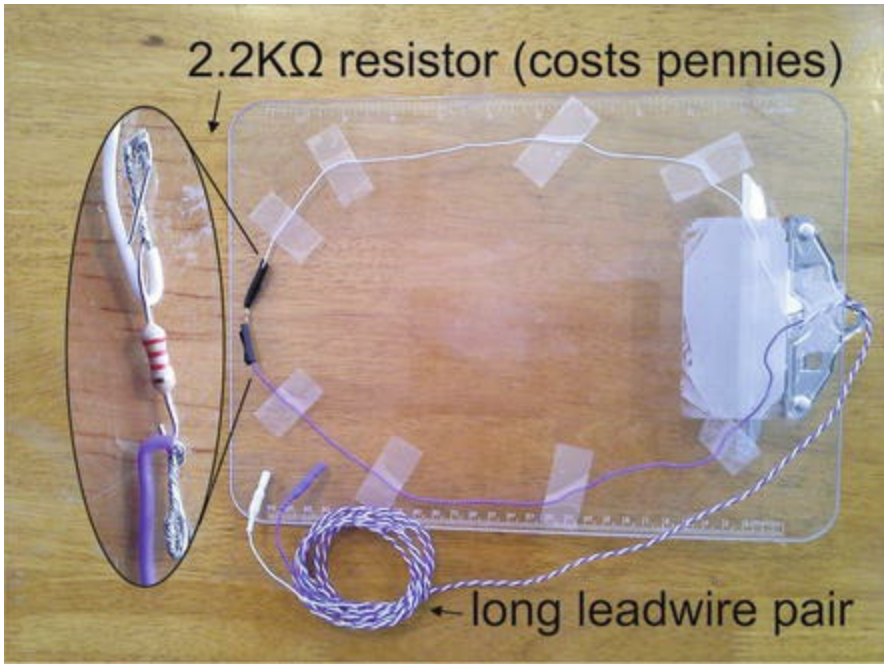

Fig. 16.8 Example of a simple to make noise sensor . This is essentially a wire coil to pick up electromagnetic noise that can be attached to the amplifier to locate the source

- Become adept at identifying electromagnetic interference. Practice monitoring 60-Hz interference using different free run sensitivities and time bases. Remember that the peak-to-peak time of a 60-Hz sine wave is 16.67 ms.

During Patient Setup

- Bundle (twist or braid if possible) all recording electrode leadwires, including the iso-ground
- Keep all leadwires separated from the patient's skin
- Monitor the electrosurgery unit (ESU) return pad placement and interact with the team setting up the ESU. Become familiar with the Association of Operating Room Nurses (AORN) guidelines on electrosurgery [8].
- Ensure that the ESU active and return cables have distance from the skin of your patient and your leadwires. It is probable that your OR team does not know how the ESU can electromagnetically couple with your leadwires.

When Troubleshooting Electrical Noise

- Intermittent noise can be caused by loose safety connectors on the end of the leadwires plugged into the amplifier. Be aware of this because, though rare, it does happen. Jiggling the safety connector can typically reveal this as a source.
- Monitor free run signals to identify the frequency of the electromagnetic interference. This is a simple way to rule out if 60-Hz interference is contaminating the recordings.
- If the IOM instrumentation will allow, unplug the iso-ground electrode from the amplifier input to see if the location of the iso-ground is adding to the noise.
- Be certain to utilize the correct number of iso-grounds. Many 32-channel IOM systems consist of two 16-channel amplifiers. Each amplifier should have a single iso-ground and the iso-grounds of separate amplifiers should not be connected. Check the system documentation to identify this circumstance.
- With the approval of the OR team, physically rotate, raise, or lower electrical equipment in question.
- With the approval of the OR team, selectively unplug electrical equipment in question to identify if it is the source of artifact. If a marked reduction in 60-Hz noise occurs when unplugging, the device may need to be checked by the Hospital Biomedical Department for leakage current or a bad ground (similar to the type of periodic equipment check done on IOM equipment). In addition to increasing noise in the IOM recording, a bad ground on a device may allow dangerous currents to be delivered to the patient or staff.

Technical Note: Modern IOM Equipment and Grounding

There was a time when it was almost necessary to have an engineering degree to be able to operate an intraoperative monitoring system. The various settings and adjustments were controlled by many physical knobs and dials.

Sometimes making changes in the recordings involved moving plugs or cabling. While modern IOM systems have taken many of the technical details involved in the electronics of data acquisition from the forefront and buried them behind slick graphical interfaces, effective troubleshooting still requires knowledge of what is happening behind the scenes. Without that knowledge, troubleshooting can be haphazard and ineffective, resulting in lost time and inadequate patient care.

It is important to understand some basic features of electronics involved in the data acquisition in order to effectively locate and reduce noise in the recordings. Figure 16.9 shows a simplified model of the path of the signal from patient to display. This section will focus on the elements in blue.

Fig. 16.9 Signal pathway of signal acquisition from the patient to the IOM equipment display

Recording Pathway: Input Switching

- Modern IOM equipment is very flexible. It is capable of many stimulating and recording montages, the configurations of which can often be changed on the fly. This has become possible due to advances in electronics that allow electrode switching. It is no longer necessary to connect electrodes to the inputs associated with specific amplifier channels. Electrodes can be connected to headboxes or other input peripherals in ways that are convenient, either in terms of physical layout or simply remembering where to plug the electrodes in. This has effectively eliminated the need for splitters and jumpers to connect a single electrode to multiple inputs.
- With this advancement comes new concerns. Signal pathways within the equipment have become physically closer and the same circuit path may be used in a short span of time for several different signals. This can result in interference or crosstalk between electrodes or channels. Some manufacturers recommend turning off or disabling unused electrodes since an electrode can convey an unwanted signal by acting as an antenna. This coupling can happen internally to the equipment as well as in the environment surrounding the patient.

Recording Pathway: Amplifiers

- The core of the data acquisition system is the amplifier. The basic amplifier used in IOM equipment is known as the instrumentation amplifier. This amplifier has three inputs. These inputs are named in various ways. The first two inputs may be referred to as active and reference or as inverting and non-inverting; the third input is commonly referred to as iso-ground, signal ground, or simply ground.
- It is important to take a step back here and look at the ground input in more detail.
  - The first point to make is that this ground input is not the same as earth ground, the ground pin on the wall electrical outlet, or even the chassis ground on the IOM equipment. For the purpose of this discussion we will refer to the ground input as iso-ground.
  - Iso-ground is an active part of the amplifier circuit. It serves to increase the common mode rejection ratio (CMRR) of the amplifier circuit. While an ideal amplifier circuit's output is the difference between the signals at the two active inputs multiplied by the amplifier gain, a real-world amplifier also amplifies the signal that is common to both inputs. This is the common mode signal. The output based on common mode gain and differential gain is calculated as:

$$V_{\text{out}} = A_D (V_1 - V_2) + \frac{1}{2} A_C (V_1 + V_2)$$

V_{out} is the output of the amplifier

V_1 and V_2 are the amplifier inputs

A_D is the differential mode gain

A_C is the common mode gain

  - Earth ground is important in reducing the risk of injury due to electrical shock from contact with equipment. In modern

equipment, earth ground is electrically isolated from the patient connections, including the iso-ground connection. Older texts taught the importance of grounding a patient for safety and of avoiding ground loops where interference could be caused by currents flowing between various ground connections. This was particularly important with the use of explosive anesthetics such as ether where the buildup of voltages leading to discharge by sparks could ignite the anesthetic. Modern OR design focuses on isolation of the patient from the wall electrical supply [9–11]. The iso-ground lead is no longer subject to those considerations because of the isolation. Isolated patient connections are marked on medical equipment with the symbol in Fig. 16.10.

Fig. 16.10 Symbol used to denote Isolated Patient Applied Part: Type BF

– The current that can flow into the iso-ground is limited for patient safety. Because of this and its isolation from the earth ground, the iso-ground is not able to serve as a sink path to conduct large interference signals away from the patient. For this reason, an iso-ground cannot “sink” large signals in the manner that an earth ground was able to.

– Because of the isolation between an iso-ground and earth ground, the likelihood of noise coming through the earth ground to contaminate signals is far less than in older equipment. An earth ground does still have the ability to sink noise signals and therefore a more common problem with grounding is a poor or open ground on a piece of equipment allowing it to emit

excessive noise (*see* Video 16.6).

Recording Pathway: Antialiasing Filters

- Modern IOM equipment has antialiasing filters to reduce the amplitudes of higher frequency components that are beyond the system's ability to appropriately sample (the Nyquist frequency). These filters are applied to the signal before the analog to digital conversion stage and are independent of the high-cut/low-pass filter settings available to the user and should not be a source of concern.

Recording Pathway: A/D Convertors

- Analog-to-digital (A/D) conversion is the process by which the analog physiologic signals are converted to digital data.
- The resolution and range of an A/D convertor impact the quality of the recorded signals. The resolution is the number of steps that the convertor can discern between its highest and lowest levels (its range or scale). Because of the binary format of the computerized data, the resolution is expressed in bits with the number of steps being 2 to the power of the bits of resolution. The resolution of modern IOM equipment can exceed 16 bits (2^{16} or 65526). Due to the rounding error at the smallest step, the signal-to-noise ratio of an ideal A/D convertor is calculated as 20 * $\log_{10}(2^{N})$ where N is the bits of resolution.
- The amplifier gain is used to match the amplitude of the signal being recorded to the range of the A/D convertors. If the amplitude is too low, then the full resolution of the A/D convertor is not being utilized and the effective resolution of the amplifier is lowered. For every bit the effective resolution is reduced, the signal-to-noise ratio is reduced by 6 dB. In the extreme, this results in signals taking a choppy or staircase appearance. If the amplitude is too high, then the result is "clipping" where the elements of the signal that are at a higher voltage than the maximum that can be processed by the A/D convertor are all expressed as that maximum.

  KEY POINT: It is common to assume that modern A/D conversion resolution is greatly improved over that in older equipment. While that

is true, it is crucial for the IOM team to realize that to fully utilize the capabilities of the IOM system, it is necessary to select a gain setting that utilizes the full range (or scale) of the A/ D converter input.

Recording Pathway: Digital Signal and Computer Processing

- Once the domain of large computer systems, digital signal processing (DSP) is now commonly handled by circuitry in specialized “chips.” The speed and capabilities of these circuits have advanced to the point where most systems no longer have discrete analog filters other than the anti-aliasing and DC blocking filters. Instead, what are still often referred to as analog high-pass (low-cut) and low-pass (high-cut) filters are in fact mathematical models implemented by the DSP circuitry and applied to the incoming data stream in real time. Making a filter change in the software causes parameters to be changed in the model rather than resistors or capacitors changed in a filter circuit. Even though the filters no longer consist of discrete components, they still behave in the same way. A digitally implemented 4-pole 100-Hz low-pass Butterworth filter will still have the same effects on phase and amplitude as an analog filter. Those effects must be taken into account whenever changes are made. The same considerations apply to 60Hz notch filters (50Hz in some countries). It is tempting to use them to reduce the power line noise prevalent in the operating room. These were once separate filters similar to the anti-aliasing filers but able to be toggled on and off. Now incorporated along with the other filters in DSP, notch filters can still produce distortion of the signals. This is considered undesirable and their use is not recommended.

Conclusion

The recording of IOM signals is based on basic electrical principles. Although these are usually in the purview of the IOM recording team, the anesthesiologist plays an important role in helping reduce the unwanted noise and in identifying physical problems with electrode connections.

Questions

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1. Regarding the use of amplifier iso-ground in IOM, which of the following statements are true?

    a. The efficacy of the iso-ground electrode to decrease electromagnetic interference is highly dependent on location where it is placed.

    b. The iso-ground electrode has the same potential to pick up ambient electrical interference as any other recording electrode position has.

    c. It is not a patient safety issue to disconnect the iso-ground electrode from the amplifier to troubleshoot if the iso-ground is contributing noise to the recording instead of decreasing noise.

    d. All of the above statements are true

2. Moving sources of electromagnetic field s such as a fluid warmer can alter the interference picked up in the recording leadwires and patient skin. Which of the following is NOT true?

    a. The electromagnetic field strength decreases exponentially with distance.

    b. Most electromagnetic fields are directional meaning that rotating or lowering/raising the associated equipment may decrease interference pickup.

    c. Radiative coupling such as from an AM radio station is also a dominant component of the interference the IOM equipment picks up from OR equipment.

    d. Any portions of the equipment radiating the electromagnetic field that happen to be in contact with patient skin might physically

conduct the noise straight to skin, so moving the equipment away from patient skin may stop the conduction.

3. The IOM team may, in some instances, be able to unplug the OR table. Which of the following is true about unplugging the OR table?

    a. Always decreases 60-Hz electrical interference being coupled to the leadwires and patient skin.

    b. May decrease 60-Hz electrical interference being coupled to the leadwires and patient skin, but may increase 60-Hz electrical interference since unplugging removes the earth grounding of the bed, allowing the bed to become a giant antenna for nearby 60-Hz noise.

    c. Is always a good idea.

    d. All of the above statements are true.

4. The skin and subcutaneous fat layers of the patient have electrical characteristics challenging to the IOM team. Which of the following is TRUE?

    a. Skin has the ability to hold large amounts of electrical charge (it has large electrical capacitance). Electrical interference signals coupling to skin at one location of the body rapidly conduct to the entire skin surface of the body, including where the electrodes are.

    b. The relatively large impedance of skin not only requires prep for placing surface electrodes, but the combination high impedance of skin and subcutaneous fat drastically attenuate physiologic signal power.

c. Dangerous levels of electrical energy from the electrosurgical pencil cable can couple to electrode leadwires. Having the electrode leadwires or electrosurgical cabling on skin enhances this coupling.

d. All of the above are true.

5. Which of the following is TRUE about electromagnetic coupling in the operating room:

a. Moving magnets near the leadwires presents a changing magnetic field, which will couple interference to the leadwires and patient skin.

b. Equipment-emanating time changing fields such as 60-Hz electromagnetic fields will couple interference to the leadwires and patient skin.

c. Equipment such as microscope lighting emanating an electromagnetic field that is time changing, even if not at 60 Hz, will couple interference to the leadwires and patient skin.

d. Electromagnetic fields in the operating room are generally bipolar or quadruple, meaning they are directional.

e. All of the above are true.

6. Of the three components of electrical impedance, which does not vary with changing the frequency of the current through them?

a. Resistance component of impedance

b. Capacitive component of impedance

c. Inductive component of impedance

d. All vary with changing frequency

e. None of these vary with changing frequency

Answers

1. D

2. C

3. B

4. D

5. E

6. A

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Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_17

17. Signal Optimization in Intraoperative Neuromonitoring

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Keywords Troubleshooting – Electrical noise – Signal acquisition – Technical error – Recording – Stimulation

Key Learning Points

- The root cause(s) of suboptimal neuromonitoring signals can be traced to patient-related, anesthetic/systemic-related, and/or technical issues.
- A systematic approach to identifying underlying causes and applying solutions allows efficient signal optimization

Patient-Related Issues

Even when technical issues are eliminated or minimized, a patient's pre-

existing pathophysiology may hamper the ability to obtain robust baseline data . Logic dictates that for at least a percentage of surgeries, it is exactly these preoperative neurologic deficits that have led to the surgical procedure. As well, patients may exhibit preoperative neurologic dysfunction that may be unrelated to the surgical procedure being monitored, yet hamper the neurophysiologic pathways being monitored. For example, a patient undergoing an intradural spinal cord tumor resection may also present with peripheral neuropathy. Although the peripheral neuropathology in this case is not related to the spinal central nervous system tumor, monitoring standard modalities such as somatosensory-evoked potentials, motor-evoked potentials (MEPs), and/or electromyography may all be affected by the neuropathy.

There is wide variation in the degree of pre-existing neural dysfunction and likewise wide variation in the degree to which this will affect the neuromonitoring. It behooves the intraoperative team not to assume pre-existing pathology is the sole cause of poor signals, but rather to consider that other possible factors discussed in this chapter may be at least partly to blame. We will discuss here several approaches to maximize signals for modalities when pre-existing deficits exist and to cope with signal amplitudes that remain unavoidably poor because of preoperative pathophysiology.

Somatosensory-Evoked Potentials

Peripheral Nerve Disorders

Radiculopathy is a common finding in monitored patients and its effect on somatosensory-evoked potentials (SSEPs) varies greatly from no effect to obliteration of signals depending on the extent and levels of nerve root involvement. For standard SSEP testing, the ascending volley is mediated by at least two nerve roots (e.g., posterior tibial nerve [L4, L5, S1]; ulnar nerve [C8, T1]; and median nerve [C6, C7, ±C8/T1]). If a radiculopathy is limited (e.g., C5 radiculopathy), all standard SSEPs may well be unaffected. Given the mediation by at least two roots, satisfactory SSEPs are often attainable even when a monoradiculopathy directly affects some of the proximal projections of the nerve stimulated.

Neuropathy is also commonly encountered in the operating theater and often has a great effect on obtaining SSEPs. Unlike radiculopathy, polyneuropathies affect the peripheral nerve more widely and thus SSEPs are likely to be hampered. For length-dependent polyneuropathies, SSEP signals

are typically affected symmetrically side-to-side, but longer length pathways are affected to a greater degree (posterior tibial nerve ≫ulnar nerve > median nerve). An effective counter to this phenomenon is to stimulate the nerve more proximally (Fig. 17.1), thereby bypassing the distal segment of nerve that exhibits the greatest dysfunction. Focal neuropathies, on the other hand, may show great asymmetry in SSEPs, including side-to-side asymmetry.

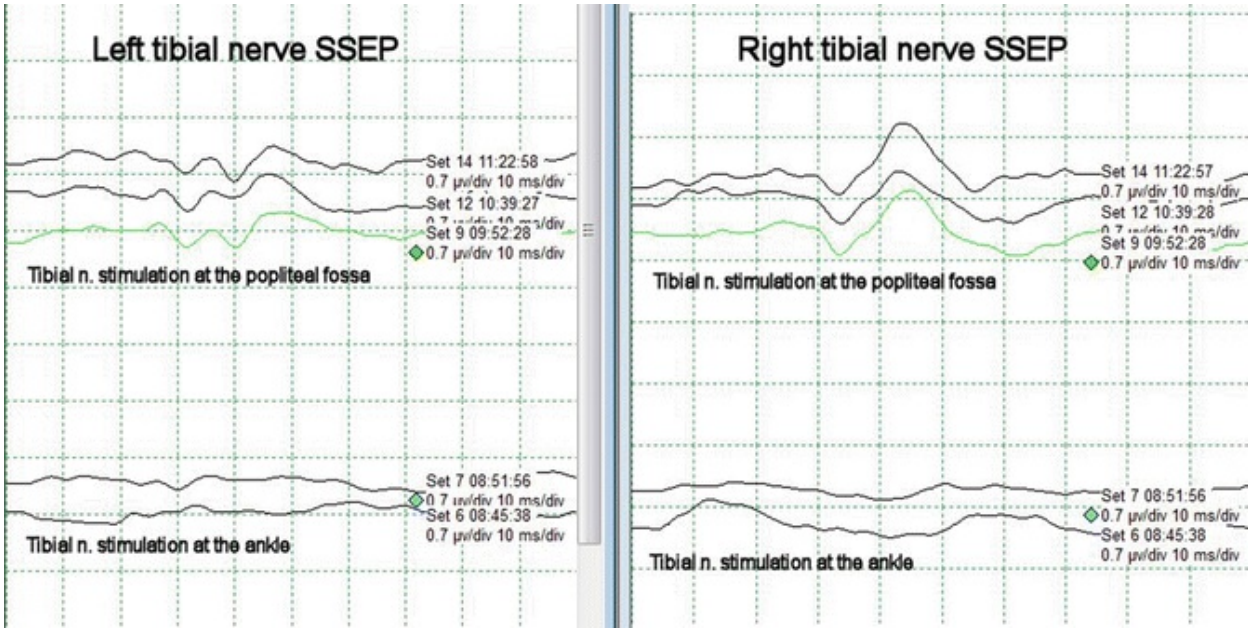

Fig. 17.1 Proximal stimulation with length-dependent neuropathy . Proximal stimulation (popliteal fossa) elicited tibial nerve SSEPs, whereas distal stimulation (ankle) did not in a patient with known diabetes but no documented history of neuropathy. This pattern suggests the presence of length-dependent diabetic neuropathy

Stimulation requirements are often increased in peripheral neuropathy and, as a rule, supramaximal stimulation of the peripheral nerve for SSEP acquisition improves the consistency of the responses. This makes establishing that a supramaximal level is present more important in the presence of neuropathy, and methods to elucidate supramaximal stimulation levels are discussed further in the “Technical Issues” section. It is further important to anticipate that SSEP latencies will be prolonged for patients with neuropathy and displayed time scales may need to be adjusted to avoid missing late-arriving SSEP waveform components. When stimulating more proximally, the relative latency of these components will be shorter than from a distal site, but may still be prolonged if the neuropathy is extensive.

Body habitus can present difficult challenges for the intraoperative

neuromonitoring team. Those with little muscle mass may have a propensity for peripheral nerve compressions and additional padding may be needed to prevent or correct this risk. Conversely, patients with obesity suffer from increased rates of peripheral compression due to their increased body and limb weight and one must again be alert for these factors when evaluating SSEPs. Furthermore, with increased adipose tissue or peripheral edema, the distance from skin to target nerve for stimulation is increased, making it more difficult to supramaximally stimulate. For most stimulation sites, marginal increases in the distance from the site to the nerve can be overcome with simple increases in the stimulation intensity, assuming the underlying nerve remains normal. However, it is not uncommon that the underlying medical conditions that are associated with obesity or edema are also associated with peripheral nerve dysfunction. As a result, obesity or edema may complicate monitoring and more proximal stimulation sites, use of needle-stimulating electrodes as opposed to surface stimulation, or even use of longer-than-standard stimulating needles may be helpful.

Central Nervous System Dysfunction

Central nervous system pathophysiology also presents challenges to SSEP monitoring. Strokes, central demyelinating disorders such as multiple sclerosis, and other central disorders may have varying effects on SSEPs depending on the degree of central impairment. Central conduction delays, poor evoked waveforms, or absent evoked waveforms may result. In patients with demyelinating disease (e.g., multiple sclerosis), temperature management becomes particularly important as increased temperatures may impair neural transmission and therefore degrade signals in these patients (Uhthoff's phenomenon). As such, it is important to document core temperatures and avoid relative hyperthermia in these patients.

Because scalp recording sites for SSEPs are a reflection of the electrode position relative to the brain tissue, any factor that alters this relationship may alter recordings. Scalp hematomas may dampen cortical response amplitudes; especially in patients with bleeding dyscrasia, a hematoma may even result from the placement of SSEP scalp recording needles. Similarly, subdural air, subdural hematomas/hygromas, or other tumors in this location have an even more profound effect and some of these may not be known to the intraoperative team at the time of surgery. When SSEP recordings point to dampening at a specific recording electrode rather than at all recording sites,

one should consider a process possibly being present between the brain and scalp in addition to problems with the electrode itself. Similarly, a shift in the brain may occur after resection of a large tumor or when changing the position of the patient (supine to prone, supine to sitting position, or the reverse). Whereas the SSEP recording electrodes may stay in exactly the same position on the scalp, the underlying brain may shift slightly and therefore the relative orientation between brain and scalp may be altered and thereby affect SSEP signals.

During intracranial procedures, sterile field requirements may alter standard SSEP needle placements and thus changes in morphologies should be expected depending on the degree of displacement from standard electrode sites. In some cases, this alteration may be mitigated if the surgeon places sterile needles in the field. Neuronal migration disorders of cortical tissue (abnormal fetal migration of developing brain) or normal variation may also produce atypical SSEP cortical responses. For example, some patients will present with cortical waveforms following lower extremity SSEP stimulation that have a wider than typical N37 [1] distribution and a small or absent P37, thereby mimicking an upper extremity type of scalp distribution ("N37" morphology). Although this may be identified by its pattern if sufficient recording channels are utilized, verifying that the stimulation and recording electrodes are properly placed is also usually warranted for most atypical patterns (refer also to the section on technical issues in this chapter).

Motor-Evoked Potentials

Patient pathophysiology that affects SSEPs may similarly affect transcranial electrical MEPs . However, given the difference and variability in the central neural pathways that mediate these monitoring modalities, there is a complementary nature between SSEPs and MEPs and one may remain more reliable than the other in the face of preoperative neurologic dysfunction .

Peripheral Nervous System Disorders

As with SSEPs, radiculopathy may affect MEP signals and the degree to which this is manifest will depend on whether the affected myotome is relevant to the acquired motor signals. As muscles selected for MEPs may be innervated by different roots/nerves than those that mediate SSEPs, one can appreciate that MEPs and SSEPs may be differentially affected (Fig. 17.2).

Neuropathies may also affect motor signals and, with the common length-dependent form, commonly used distal muscles for MEPs (i.e., thenar, abductor hallucis) may be disproportionately affected. In addition, neuropathies may be predominantly either motor or sensory, which may also contribute to disparities between MEP and SSEP baselines.

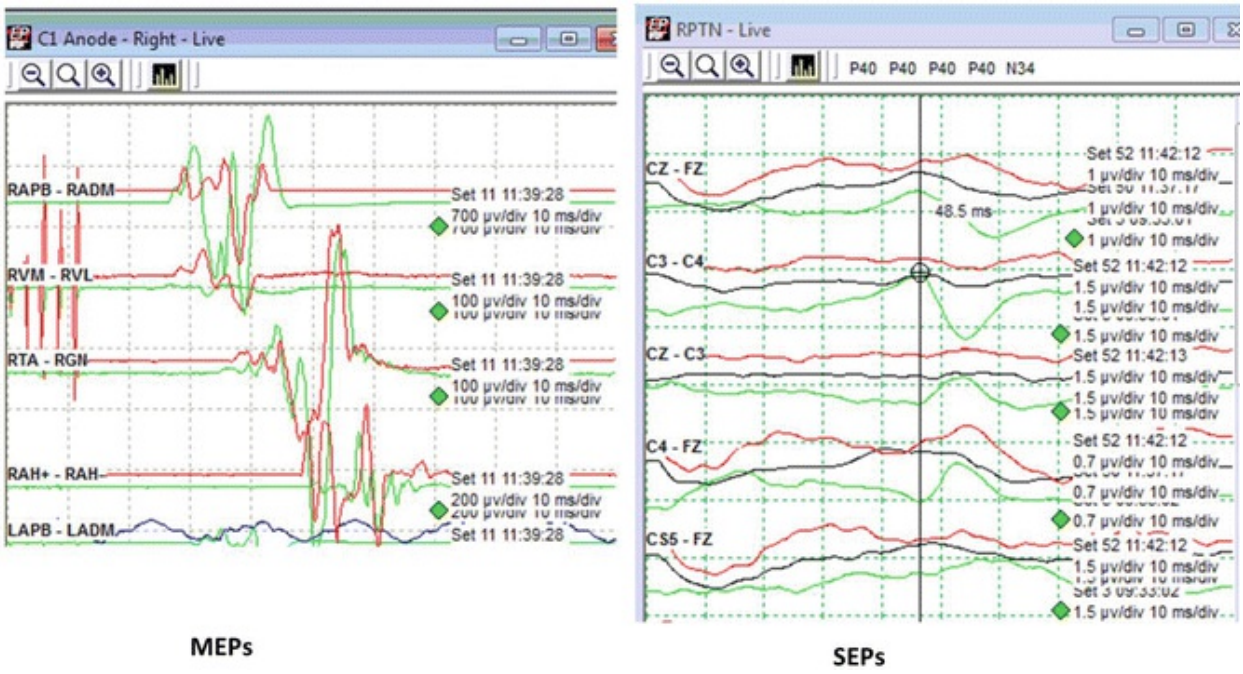

Fig. 17.2 New L5 radiculopathy affecting SSEP more than MEP. Right-sided MEPs (*left panel*) and SSEPs (*right panel*) taken at similar times during a lumbar surgery where a suspected root injury occurred. Note the clear disparity in that MEPs, including the posterior tibial nerve innervated abductor hallucis muscle ("AH"), show reproducibility to baseline levels, whereas SSEPs following right posterior tibial nerve stimulation shows dramatic and sustained decrease (*red* and *black traces*) from that of baseline (*green trace*)

Strategies are limited to address these issues for MEPs, but one should be aware of the surgical level of importance. Muscles used for recordings can be chosen outside of weak myotomes . Likewise, more proximal muscles can be chosen if significant distal motor neuropathy exists, although often proximal muscles are not as reliably monitored for MEPs. If a procedure involves high cervical levels (e.g., C3–4), deltoid muscles (C5 root) may well serve an important role in monitoring even if a severe neuropathy is present that precludes or limits MEPs in distal musculature. Given their reliance on conduction restricted to central white matter, D-wave recordings avoid peripheral nerve issues entirely, much in the same way they avoid anesthetic

and neuromuscular junction issues.

Central Nervous System Dysfunction

Motor-evoked potentials are highly sensitive to a new myelopathy occurring during a surgical procedure, which leads, in part, to their utility in neuromonitoring. Unfortunately, sensitivity to a pre-existing myelopathy is similarly high, presenting a particular challenge for acquiring MEPs in that setting with marginal or absent signals often being the result. When this occurs, ideal anesthetic conditions as well as meticulous placement and adjustment of stimulating electrodes may be required for monitorable MEPs to be present. In addition, facilitating techniques may be required to increase the chance of eliciting a response or to maintain a response in the face of changing conditions or anesthetic fade during a procedure. These facilitating techniques are further discussed in the "Technical Issues" section below under the "Poor signals" subheading.

Electromyography and Nerve Conduction Studies

Electromyography (EMG) monitoring and pedicle screw stimulation testing is reliant on an intact motor unit, and anything that disrupts the motoneuron, root, nerve, neuromuscular junction, or muscle may have an effect. The presence of applicable disease states and particularly weakness in target muscles should warn the neurophysiology team of possible limitations in the use of these modalities. (For more information on nerve conduction studies, *see* Chap. 38, "Surgery in the Peripheral Nervous System").

Radiculopathy or neuropathy may greatly reduce the sensitivity of EMG monitoring as mechanical perturbation of roots or nerves may not be as readily reflected at the muscle in these conditions. The location and duration of the lesion are influential in how these effects are demonstrated. An acute lesion leaves the distal nerve functionally intact, which can be dangerously misleading if the nerve is stimulated distal to the lesion yielding a robust compound muscle action potential (CMAP) and giving the impression it is functionally intact (e.g., in facial nerve testing). Thus, testing as proximal as possible is preferred to assure functional integrity of the nerve. With more chronic axonal lesions, Wallerian degeneration proceeds within a week and the distal nerve will also show dysfunction as well, although in rare cases the distal nerve may remain functional in a nonfunctioning nerve (neurapraxic

conduction block).

Radiculopathy/neuropathy may also significantly impact testing that relies on stimulation thresholds such as pedicle screw electrical testing. In the normal setting, a high stimulation threshold suggests that the screw is well-insulated by bone and thus is appropriately positioned. However, falsely elevated thresholds due to nerve dysfunction may occur during pedicle screw testing in the presence of radiculopathy/neuropathy and, as such, test results involving weak myotomes should be interpreted with caution. If possible, direct proximal root stimulation may help determine if a root has a stimulation threshold in the normal range (e.g., <4 mA using typical stimulation parameters). It may also be helpful to examine relative thresholds if multiple screws are evaluated and the finding of a threshold that is much lower than companion screws should alert suspicion and receive additional evaluation for malpositioning from the surgeon. Similarly, for free run EMG monitoring, it should be kept in mind that sensitivity may be affected depending on the muscles tested and severity/distribution of the radiculopathy/neuropathy.

Pre-existing neuromuscular junction disorders may also influence EMG testing. Depending on the type of disorder, measures of neuromuscular blockade may also yield unreliable results and the response to pharmacologic neuromuscular blockade may be highly exaggerated and prolonged.

Electroencephalography

Electroencephalography (EEG) is typically monitored either by scalp electrodes and/or by direct cortical recordings (electrocorticography) during intraoperative neuromonitoring. EEG may be useful for such intracranial surgeries as aneurysmal or other vascular repair, brain mass excisions, and in epileptic foci excision. It is also useful in extracranial surgeries like carotid endarterectomies to assess for hemispheric ischemia.

Unprocessed EEG is also useful in identifying the deep anesthetic state that exhibits a burst-suppression pattern (Fig. 17.3). This state is easy to identify and may be useful as a surrogate marker of other synaptic suppression affecting neuromonitoring signals (e.g., those related to MEPs) and the deep cortical anesthetic state supplies information to the anesthesia team that they may use to titrate anesthetics. On the other hand, if the goal is to assess through the entire range of anesthetic depth, EEG requires digital processing techniques (e.g., Bispectral Index [BIS] monitor) that are often

imperfect and fall outside the usual realm of the neuromonitoring team (*see* Chap. 11, “Clinical Application of Raw and Processed EEG”).

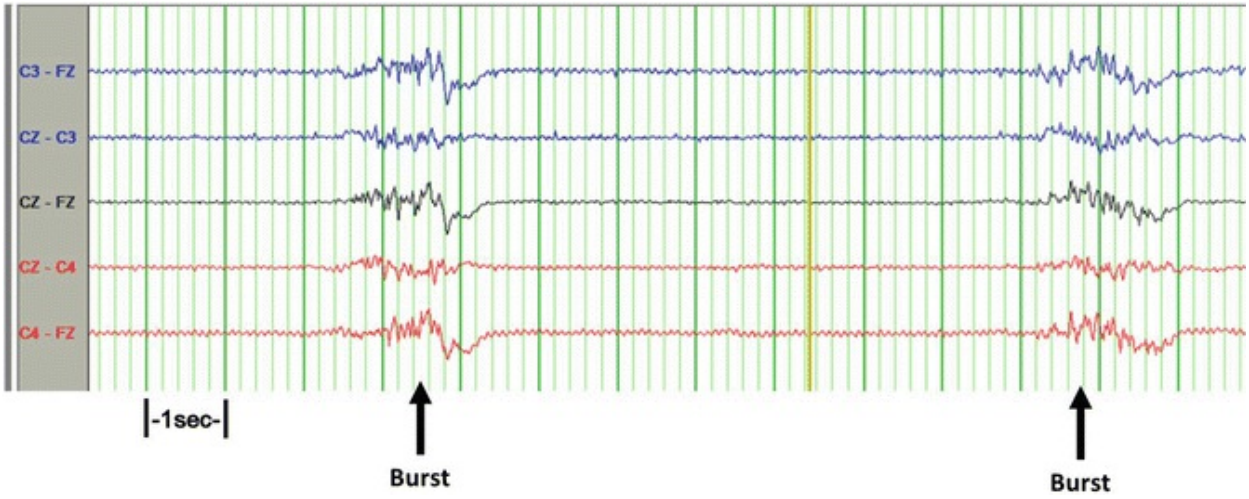

Fig. 17.3 Burst suppression pattern on the EEG. A burst suppression pattern follows a bolus of propofol on this limited EEG montage

Those anatomic barriers that insulate or alter SSEP recording electrodes (as discussed previously) can have the same inhibitory effect on obtaining EEG traces. In particular, hygromas, subdural hematomas, and scalp hematomas are examples of fluid spaces that will insulate scalp needles from underlying cerebral generators of EEG. These and other preoperative abnormalities such as focal attenuation, epileptiform discharges, or rhythmic slowing are likely to be present prior to surgery, making preoperative or preincision EEG a helpful reference to distinguish between these pre-existing displays and new findings (Fig. 17.4).

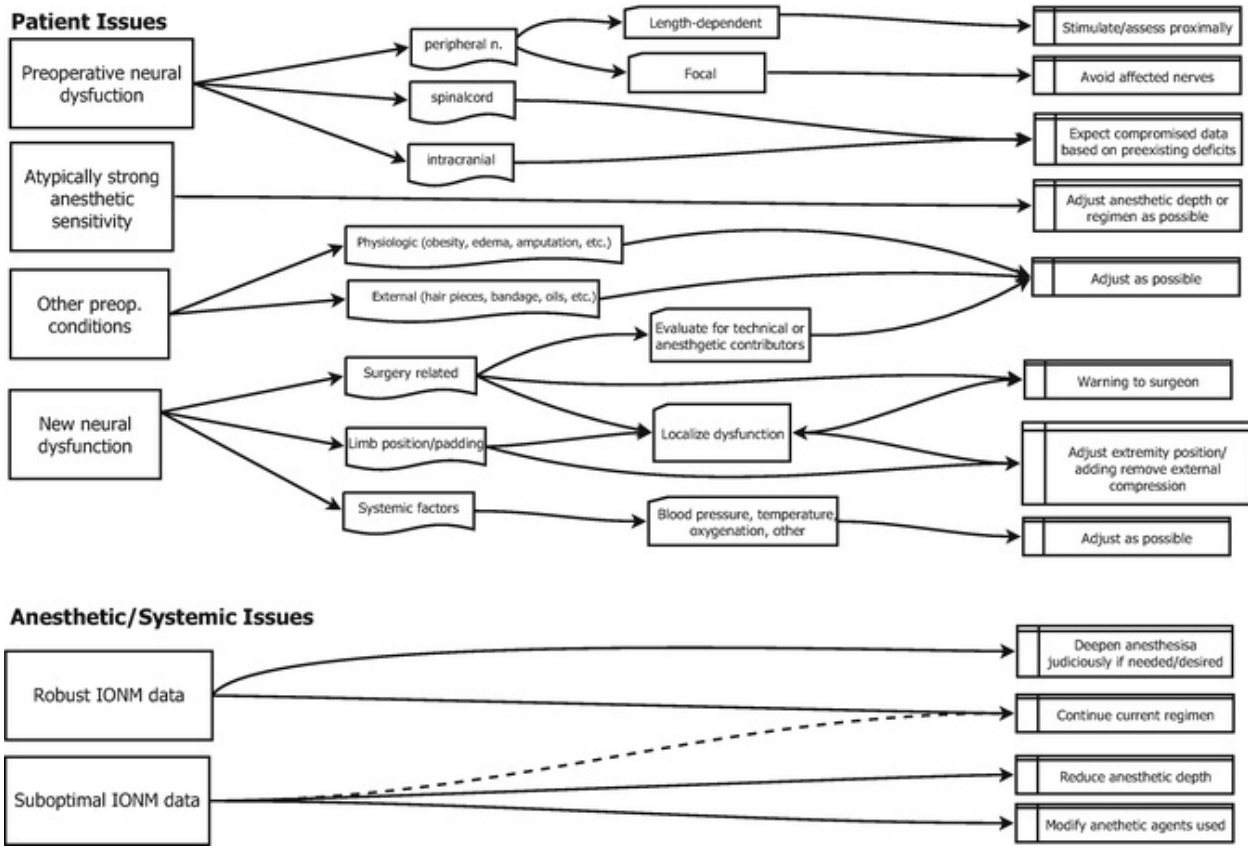

Fig. 17.4 Patient anesthesia chart

Anesthetic and Systemic Effects

The goals of anesthesia, analgesia, and amnesia may at times be in direct opposition to obtaining robust neurophysiologic data . Those neurophysiologic functions requiring more synapses are in turn typically the first to be blunted by anesthesia (e.g., conscious acts) and differential effects are noted within neurologic pathways utilized by common neuromonitoring tests (e.g., MEPs affected to higher degree than SSEPs). Although a bell curve may generally exist for the average anesthetic affect across patients, there is wide variation for an individual patient's responses.

A number of systemic variables may also impact neuromonitoring data both directly and through the patient's reaction to an anesthetic. Temperature, pH, blood pressure, hematocrit, oxygenation, CO_2 levels, blood loss, fluid status, and other factors can impact monitoring signals, which can dramatically change intraoperatively [2]. Stability of anesthetic and systemic parameters improves the stability of neuromonitoring data and allows for a

clearer interpretation. However, the reality is that some degree of variation is inevitable and wide degrees of change may be unavoidable. Understanding the impact that anesthetic/systemic variations have on neuromonitoring data and the ability to differentiate this from new neural dysfunction is part of the art of intraoperative neuromonitoring. For more details, *see* Chap. 19, "Anesthesia Management and Intraoperative Electrophysiological Monitoring."

Somatosensory-Evoked Potentials

Because anesthetics produce their greatest effect on pathways with the greatest number of synapses, SSEPs recorded from cortical generators are affected more than recordings from subcortical sites. As seen in Fig. 17.5, the A1-Fpz subcortical channel recordings are unchanged relative to baseline even though the cortical channel recordings have been greatly diminished with increases in anesthesia. Because the operation in this case was an orthopedic spine case, the stability of the subcortical response helps to provide reassurance that conduction is proceeding normally across the surgical levels despite the large changes from anesthesia. The largest subcortical response typically is generated in a Cerv5-Fpz channel, which adds a small N13 cervical component to what is primarily positive medullary activity (P13, P14) recorded in the Fpz electrode. Additionally, a pure medullary response is purposefully recorded in cervical level cases by foregoing the Cerv5 electrode for one above the neck such as from the ear (A1 in Fig. 17.5).

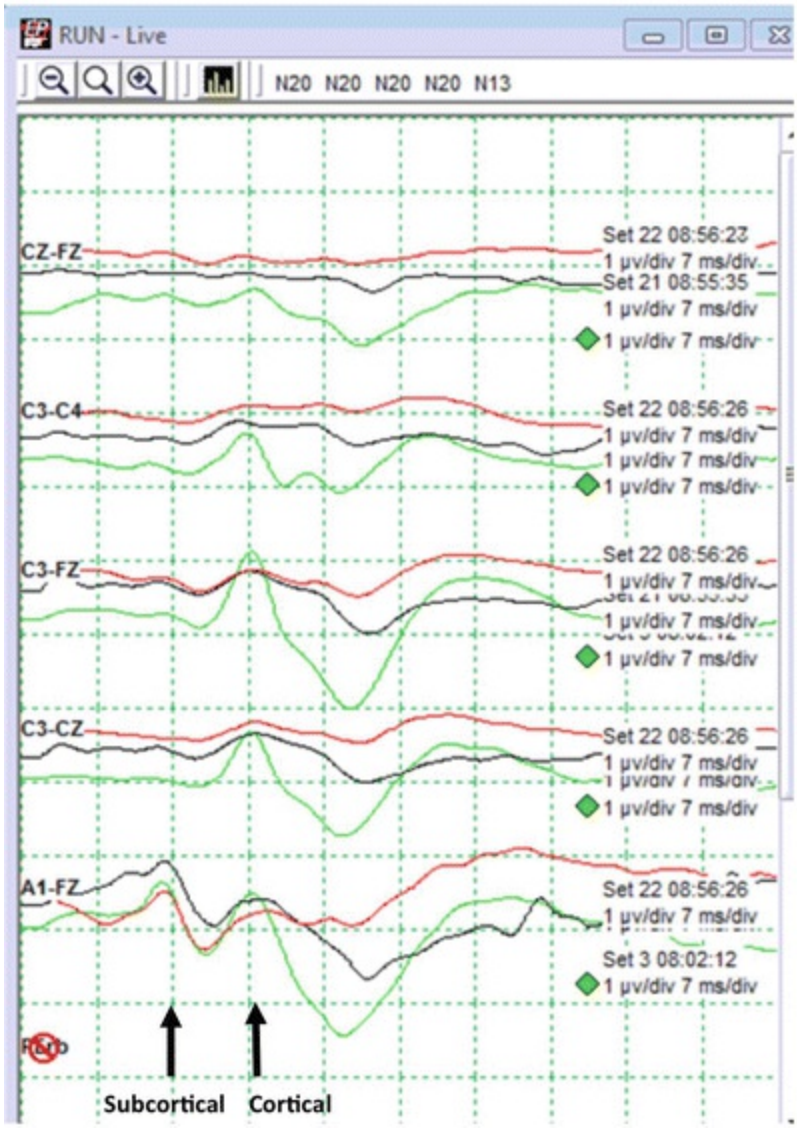

Fig. 17.5 Anesthetic suppression of cortical SSEP responses. Right ulnar SSEP recordings were obtained during a cervical spine fusion using four cortical (Cz-Fz, C3-C4, C3-Fz, C3-Cz) and one subcortical channel (A1-Fz). The *green traces* are baseline responses, *red traces* are current traces, and *black traces* are the previous set. After an increase in anesthetic gas, the subcortical response is stable, whereas all cortical traces are blunted and delayed compared with baseline (a similar pattern was present in left ulnar recordings at the time)

Use of the subcortical response to identify anesthetic effects in lower extremity SSEPs may be more problematic because these subcortical signals are notoriously more difficult to obtain as compared with those from the upper extremities. Thus, for thoracolumbar procedures, when a subcortical response is not available to aid interpretation, one may have to rely on cortical responses that are inherently more affected by anesthetics. In this

situation, stability of the upper extremity subcortical signals in the face of both upper and lower extremity cortical signal decline can still lead to a conclusion that an anesthetic/systemic effect is at play.

Other limiting factors for the acquisition of a subcortical response are its particular susceptibility to electrical noise due to the long interelectrode distances and the presence of myogenic artifact due to the proximity of recording electrodes to muscle. As a result, these signals are commonly degraded when a patient is under relatively light anesthetic and is not under neuromuscular blockade. If these are the causes, the noise may be abated with increased anesthetics and/or delivery of neuromuscular blockade, although these may often not be desirable for other reasons. Alternatively, narcotics and other intravenous agents will typically have lesser effect on the cortical and subcortical components of the signals while still effectively mitigating EMG-induced artifact.

Although stable subcortical responses may confirm adequate dorsal column function across the surgical levels in spine surgeries, intracranial neurologic dysfunction remains possible despite a preserved subcortical response. A not uncommon example exists in the case of anterior cervical procedures where the placement of retractors may impinge on a carotid artery. If adequate collateral flow is not present, hemispheric ischemia may result that will affect cortical responses from the contralateral upper extremity while leaving the associated subcortical response unaffected. Thus, in conditions when cortical responses are diminished and one has to rely on subcortical SSEP responses alone, a change due to carotid retraction could readily be missed.

Increased anesthetics, decreased oxygenation or hematocrit, decreased perfusion pressures, and perturbed pH may all similarly affect SSEPs with a preferential effect on cortical SSEPs. Although one may expect globally similar or at least symmetric bilateral effects on cortical responses with increases of anesthesia, practical experience not uncommonly demonstrates quite asymmetric changes due to anesthetic alterations. These often appear accentuated when baseline asymmetries already exist and patterns may emerge that greatly increase the chance that changes are mistakenly interpreted as arising from a surgical cause.

Motor- Evoked Potentials

Anesthetic agents and systemic changes may have profound and variable

effects on MEPs. Inhalational agents potently suppress the ability to activate motoneurons. As a result, propofol, supplemented at times with ketamine and/or narcotic, has become a widely used agent and its use is more conducive to acquiring MEPs compared with the use of inhalational agents at similar degrees of anesthetic depth. However, it should be kept in mind that any anesthetic agent, whether intravenous or inhalational, is capable of inhibiting MEPs and high-dose propofol can also dramatically suppress MEPs [3]. Measuring the blood's concentration of intravenous (IV) agents is rarely practical, and physiologic measures such as using a BIS EEG-type monitor have been imperfectly reliable. Simpler EEG measures, as noted previously (Fig. 17.3), can identify burst suppression indicating a deep cortical level of anesthesia. This may be used as a guide to the anesthesia team that anesthetics are becoming excessive as a deep anesthetic state is clearly reached with burst suppression. At that point, a reduction in anesthetic delivery might be considered and any further increase in anesthetics would be expected to further suppress neurophysiologic responses, to increase the incidence of propofol infusion syndrome [4] and to increase the likelihood of long wake-up times at the end of the procedure. In addition, bolus dosing of propofol may yield wide swings in MEP suppression, leading to a difficult interpretative environment for the monitoring team.

For practical purposes, some mixture of inhalational gases and IV anesthetics are commonly used in procedures that use MEPs. However, patients exhibit vastly different sensitivities to inhalational agents in terms of the suppression of their MEPs. For patients who are particularly sensitive or for patients who are myelopathic or have other neurologic impairment, MEP signals may not be recordable. When this occurs in the setting of a mixed inhalational and intravenous anesthetic technique, a subsequent shift toward intravenous and away from inhalational agents can improve the likelihood of obtaining useful MEPs in these cases.

When poor or absent MEPs are encountered, a number of steps focused on improving the stimulation delivery may be taken in parallel with efforts to improve the anesthetic environment. These are discussed previously and also in the "Technical Issues" section below under the "Poor signals" subheading.

The level of neuromuscular blockade is obviously an important additional factor in the acquisition of MEPs. However, unlike anesthetic agents, of which the action is on already difficult to activate central synapses, the action of neuromuscular blockade is more predictably linear on the amplitude of the

MEP. That being said, an understanding of the state of this blockade is important and high levels of blockade will prevent MEP acquisition. We find it helpful to utilize train-of-four measures in each limb so as to provide the most accurate assessment of the systemic level of blockade and to assess for focal variability. MEPs are also sensitive to other systemic parameters such as blood pressure, pH, oxygenation levels, and hematocrit. It is not uncommon that MEPs can slowly diminish in their response over the course of a procedure and this is likely a combination of anesthetic effects and the inevitable changes in blood composition that occur during surgery such as blood loss. Resultant decreases in hematocrit and thus oxygenation with concomitant pH perturbations are all thwarting factors to the acquisition of MEPs. An additional adverse systemic factor that is frequently overlooked when attempting to acquire MEPs is rising core temperature with the use of body warmers. Mild hypothermia may actually improve MEPs [5], while extremes of temperature in either direction will impair MEP monitoring. As with SSEPs, all of these systemic parameters may exacerbate the effects of anesthetics and it is common to see these culminating effects with time; especially in longer surgical procedures.

Electromyography

EMG monitoring is relatively immune to the effects of anesthetic agents; appropriate monitoring typically requires only that neuromuscular junction functioning be intact. Inhalational and intravenous agents used for anesthesia do not have a clinically evident effect on this junction. However, paralytic agents are commonly used, and by definition, may have a profound effect on EMG activity. Sensitivity to the effects of these agents varies greatly across patients as does the recovery of neuromuscular junction function. Therefore, the effect of this dosing is not precisely predicted and instead must be measured at the muscle. For pedicle screw testing, a T1 % (amplitude of an evoked supramaximal abductor pollicis brevis [APB] muscle response as compared with preanesthetic baseline) of over 20 % has a minimal effect on threshold testing [6], which translates to the more easily electrically measured train-of-four ratio in the gastrocnemius of 35 % (unpublished data). Visually assessed mechanical measures of ulnar nerve “twitches” has wide inter-rater variability, although, if used, this level of blockade usually corresponds to three or four twitches out of four. Levels of partial blockade that do not affect the sensitivity of free-running EMG are not well-defined, but are likely not

clinically impaired at those parameters discussed before. When in doubt and when possible, erring on the side of less blockade is preferred.

Electroencephalography

Certain anesthetics may have a more pronounced effect on EEG than others, but sufficient concentration of any anesthetic may alter EEG. Boluses of intravenous anesthetics in particular may also influence EEG greater than say SSEPs; if there is a sudden global suppression in EEG while SSEPs remain stable, an anesthetic-related contributor is the usual cause (*see* Fig. 17.3).

Differentiation of effects on our signals from systemic factors versus from new neurologic dysfunction is not always clear cut and some alterations in systemic patient physiology may contribute to new focal neurologic dysfunction. For example, relative hypotension in isolation may affect some signals without expectation of adverse sequelae in most cases. However, if surgical steps result in tissue that cannot tolerate any decrease in perfusion, even mild relative hypotension could cause a critical threshold for tissue ischemia to be surpassed. As such, one often needs to simultaneously take action related to possible new neurologic dysfunction while addressing other factors that may be obscuring the ability to correctly identify potential new dysfunction.

Technical Issues

"Technical issues" is a broad term that concerns the technique used to acquire signals. As noted in the Introduction, these issues have their roots in good basic technique, and a solid working knowledge of neuromonitoring is assumed. Beyond basic technique, we hope to address further coping strategies in response to the patient and anesthesia challenges discussed previously, the sometimes electrically hostile operating room environment, equipment failure, and unintended deviations from usual methods.

As in all areas of signal optimization, a rational step-wise approach to understanding, localizing, and addressing the specific issues at hand will provide the best route to timely and effective optimization. In contrast, inexperienced persons may try steps "because they worked before" (often for a different problem) or in an otherwise illogical way. A moment of thought in these situations will often save valuable time, allowing redirection of

attention to other optimization or even the monitoring itself. One extreme example is someone who wanted to “replace all the electrodes” when encountering a high-amplitude noise problem, but instead, with some quick investigation, showed that this was an external noise source (unplugging the bed solved the problem). Once issues are identified as technically related (as opposed to or in addition to patient/anesthesia-related issues), our goal is to further break down the issues until we come to a specific answer (Fig. 17.6).

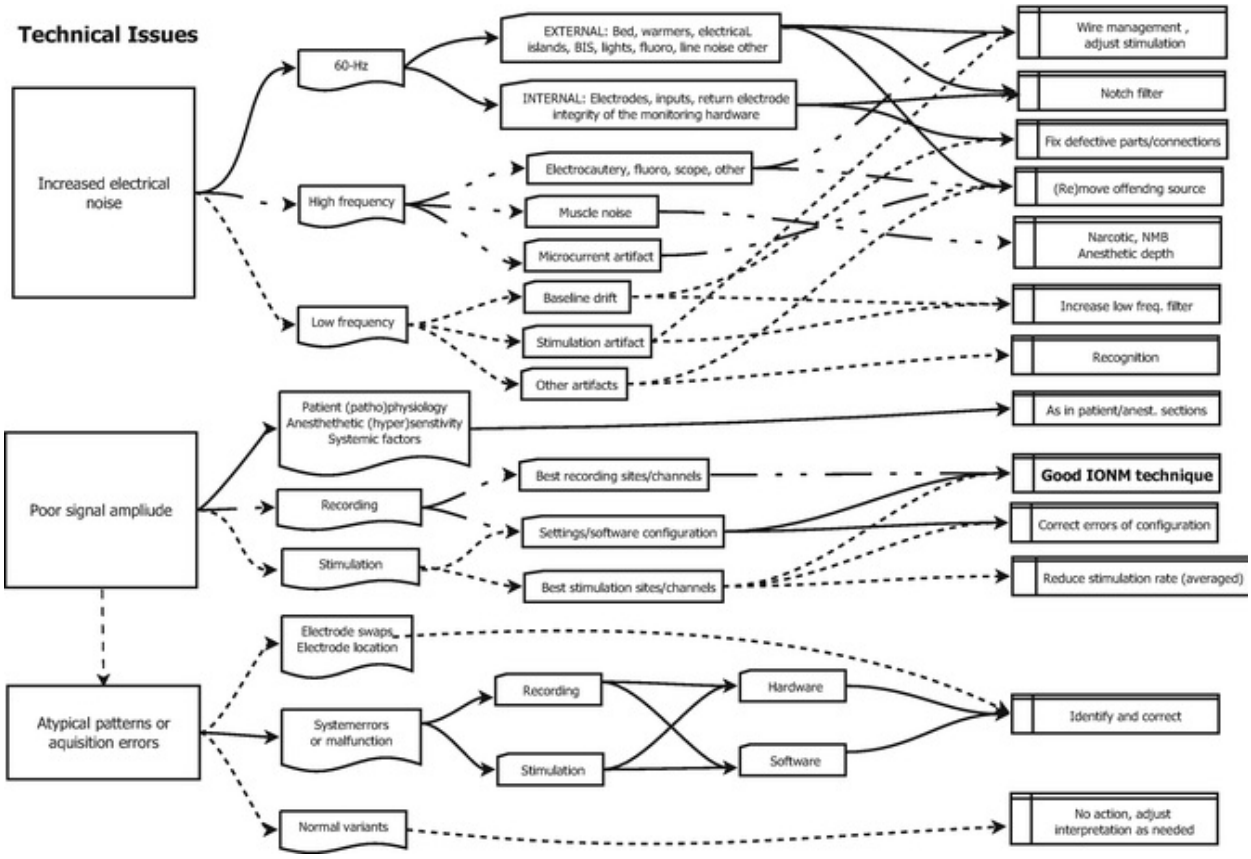

Fig. 17.6 Technical chart

For technical issues, we first decide whether the problem fits into one of three broad areas: increased electrical noise, poor signal amplitude, or atypical patterns of signal response. One will quickly recognize that the first two categories are the two components of the SNR, and deciding the root cause of a poor signal is usually deciding whether the problem is primarily increased noise, decreased signal, or both. This distinction hinges on both an understanding of the usual levels of background noise and the usual response characteristics of target signals. If we encounter a poor SNR and the

amplitude of electrical noise exceeds our expectation for typically sized signals, then we'd expect that electrical noise is our primary issue. If, on the other hand, the level of electrical noise is below the range of typical signals, then we expect that low signal is the primary cause. This may appear trivial, but some common errors demonstrate that this thought process is not universally applied. For example, most of us have probably encountered a situation in which the sensitivity for recording has been increased to a point that universally present intrinsic noise is displayed prominently and the absent signals are described as "noisy." Conversely, with high noise levels, recording sensitivity may be decreased to make the baseline superficially appear to have a reasonable noise level when, in fact, embedded signals would never be recognizable. The key to avoiding these errors is to have an understanding of expected amplitude and latency of the target signal. If one knows their target values, they will adjust their settings to those values rather than to a potentially deceiving "look" and the differentiation between noise and signal issues should be much easier.

The third main category for technical issues primarily deals with errors in the configuration of our monitoring systems or electrodes. This may be due to failure to correctly configure or connect components or it may be due to breakage of the equipment. When these "errors" occur, signals may be present in unexpected patterns/morphology, but possibly with reasonable recording fidelity. At other times, select signals will be absent in patterns that do not make physiologic sense or signals may be completely and unexpectedly absent but possibly with clues such as absence of stimulation artifact.

As is apparent, there is overlap between the "poor signal" category and the signal acquisition error category. In fact, one might logically consider this third category as a subdivision of the poor signal category. For discussion and thought organization purposes regarding the signal acquisition error category, we will focus on frank errors or breakage, whereas in the prior category, we will focus on reasonable but potentially suboptimal aspects of either the stimulation or the recording systems.

Increased Electrical Noise

Electrical noise is a constant accompaniment to neuromonitoring and some level of background noise is omnipresent and must be tolerated. However, a number of routine strategies are used to limit ubiquitous noise such as

common mode rejection amplifiers, signal averaging techniques, and electrical filtering. When, despite these measures, the amplitude of electrical noise increases to the point that it adds variability to or overwhelms the recorded signals, it may interfere with identification and interpretation of neuromonitoring data.

When feasible, the best and most common strategy for dealing with noise is to remove or mitigate (by changing the source's location or the location of recording equipment/wires) the offending noise generator. In order to remove noise, the source must first be identified. One possible strategy is to note where the noise amplitude is the greatest, and if our signals point to a specific area of the body, we can look in that area first. Unfortunately, a clear focality to noise is not always obvious, so we also characterize the frequency of the intruding noise, which may yield clues as to its source (Table 17.1).

Table 17.1 Common sources of elctrical noise

External sources of 60-Hz noise	*Internal sources of 60-Hz noise*
1. The operative bed	1. Poor/partial electrode contact with the body
2. Fluid warmers	2. A damaged electrode
3. Body warmers	3. Poor connection of the electrode to the recording system
4. Electrical islands, extension cords	4. Dysfunctional jackbox, associated cable, or their connection
5. BIS monitors	5. Dysfunction amplifier
6. Fluorescent lights	6. General current leak in the system
7. Fluoroscopy unit	
8. Other electrical device in the vicinity	
9. Power line noise (e.g. nearby heavy equipment use)	
High-frequency noise	*Low-frequency noise*
1. Muscle artifact	1. Stimulation artifact
2. Microcurrent artifact	2. Movement artifact
3. Electrocautery activation	3. High-amplitude noise transients "intrusions"
4. Electrocautery return pad (constant impedance testing)	4. "Baseline drift" from poor electrode contact
5. Operating microscope	5. Cardiac/pulse artifact
6. Fluoroscopy unit	6. Respiratory or ventilator artifact
7. Other electrical devices	7. Compression device activation

Electrical Noise: 60 Hz

Probably the most common noise type is the sinusoidal 60-Hz waveform (in the US and 50 Hz in most parts of the world) due to the alternating current in our power supplies. This noise is easily recognized by its 16.67-ms period and its typical sine wave morphology (Fig. 17.7). For free-running data where the period may not be easy to see, attenuation or elimination of the noise when the 60-Hz notch filter is turned on should help verify its presence. Once noise is identified as exhibiting a 60-Hz frequency, the next step is to identify the source and again the distribution of the noise may yield clues. If the noise is maximal in a specific area of the body, this is more likely to point to an external (room noise) source. If, on the other hand, the noise is restricted to recordings that correspond to a given component of the recording system, this would point to an internal (within the recording system) source. If we can narrow down the possibilities, our search for a source will be far more efficient (*see* Table 17.1).

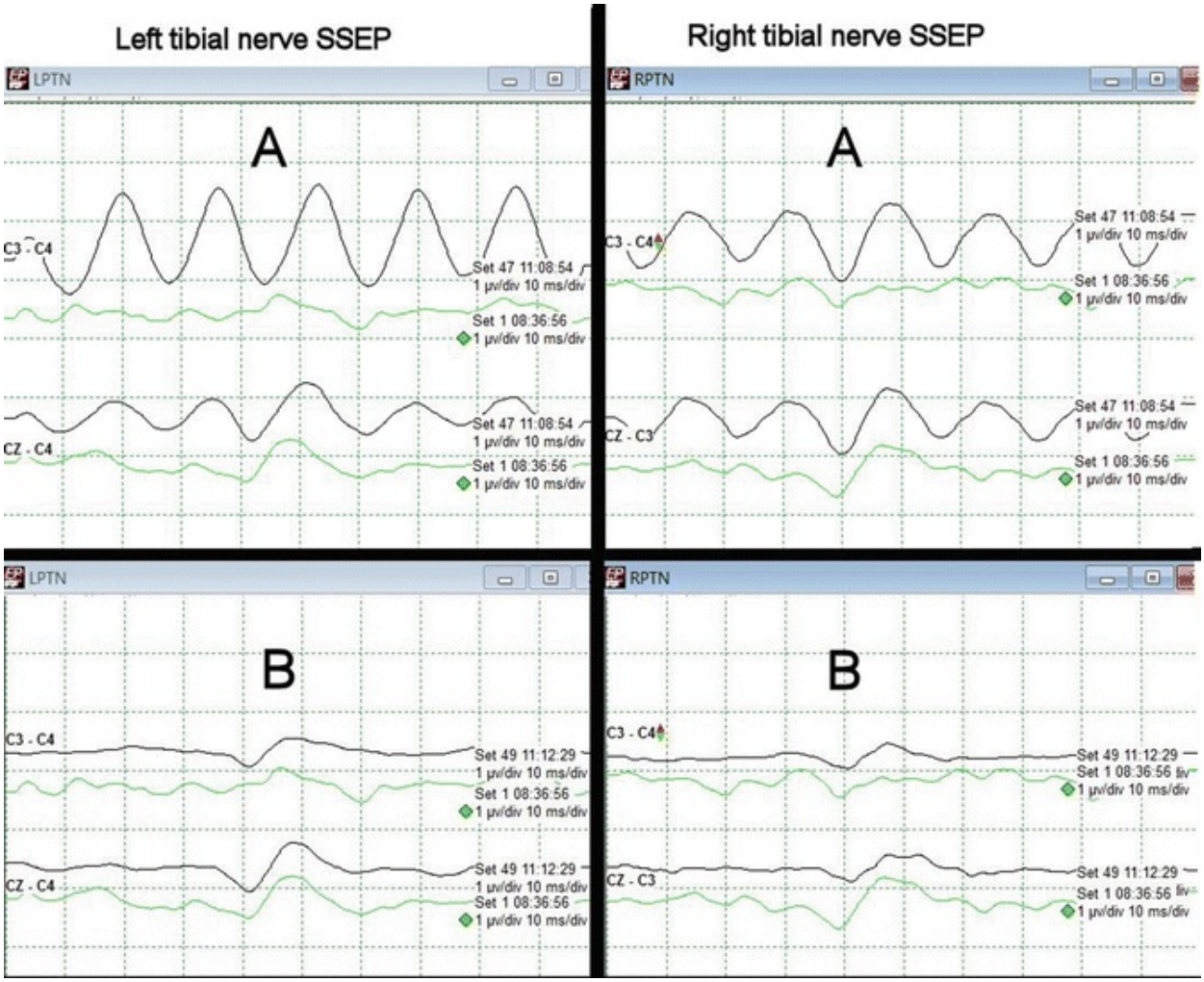

Fig. 17.7 60-Hz electrical noise . Sixty Hertz noise with characteristic 16.67-ms period partially obscuring tibial nerve SSEPs (**a**). Removal of an electrical device resolves the 60-Hz noise (**b**)

Often the 60-Hz noise source may be identified, but the offending device is critical to the procedure and cannot be eliminated or sufficiently mitigated. In these situations, steps may be taken to mitigate the interference; the most common of these is the 60-Hz notch filter. This filter is commonly and appropriately used to reduce electrical noise in our recordings. However, a number of potential pitfalls must be kept in mind. The notch filter, like any electrical filter, can be overwhelmed by electrical noise and if the filter limits are exceeded, the noise may still disrupt the physiologic data. Furthermore, this process may transform electrical noise into waveforms that may mimic physiologic data. For example, Fig. 17.8 shows EEG with notch-filtered high-amplitude 60-Hz noise with bleed-through that may appear as brain-wave activity to the inexperienced electroencephalographer. As is obvious,

this misinterpretation of noise as EEG activity could be disastrous in some c linical situations.

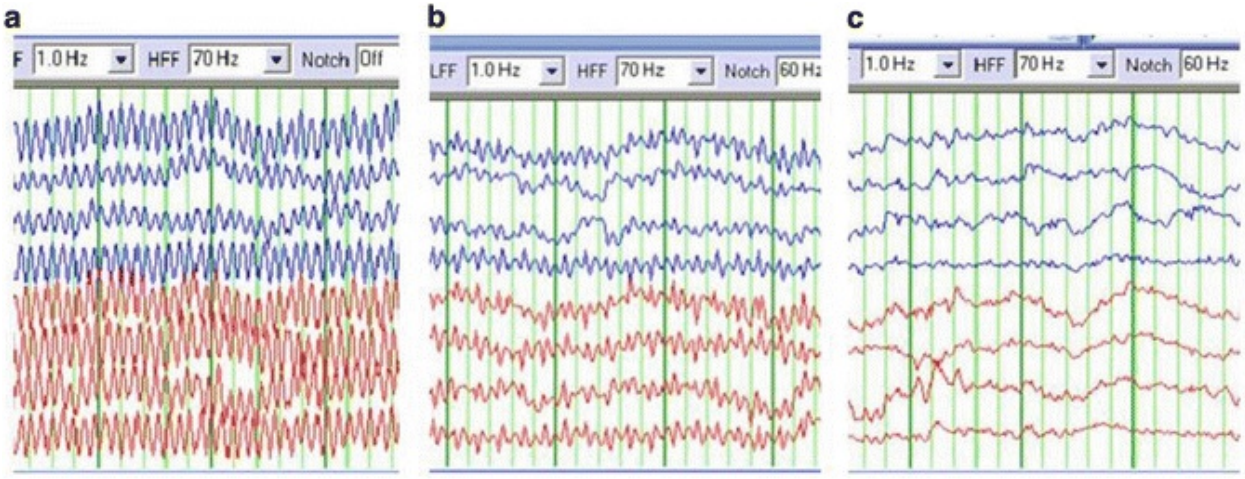

Fig. 17.8 EEG contamination with 60 Hz noise despite use of notch filter. EEG recordings from longitudinal channels of the left hemisphere (*blue*) and right hemisphere (*red*) show high amplitude 60 Hz noise (**a**). Use of the 60-Hz notch filter results in marked attenuation and alteration of the original noise, but residual noise persists (**b**) and obscures the relatively low-amplitude true underlying EEG activity that is revealed after removal of the offending noise source (**c**)

Another pitfall with use of the notch filter is that some of our recorded signals contain 60 Hz as a component frequency and thus the notch filter may lead to attenuation in those recordings. Finally, for averaged signals, the notch filter may cause ringing artifact with introduction of new noise that is sometimes worse than the original 60 Hz offender or, again, may produce a waveform that emulates a physiologic response. Given the above potential pitfalls, we avoid reflexive or routine use of the notch filter, preferring to eliminate the noise source. However, some noise sources cannot be identified or, if identified, cannot be removed or mitigated. Thus, judicious use of the notch filter is appropriate in many situations with the above precautions in mind. In addition, some systems offer notch filters other than 60-Hz that can be tailored to specific frequencies as needed after analysis of the predominant frequency band of the noise. Similar cautions apply regarding signal attenuation, bleed through, and ringing, but these filters may be useful tools if used with these potential problems in mind .

Electrical Noise: High Frequency

High-frequency noise is often the most disruptive and is often difficult to

eliminate. As with any noise, recognition of the source is critical to finding an appropriate means to optimize signals . Table 17.1 notes the most common high-frequency noise sources; each has unique clinical features that allow identification and signal optimization. Myogenic artifact tends to occur as background tone returns to muscles when neuromuscular blockade wears off and anesthetic depth is relatively light. Although additional neuromuscular blockade is typically highly effective, in many situations it has been allowed to wear off for a clinical reason, and re-dosing is not a preferred option. Alternative specific steps can include administration of narcotics (infusion of high doses of short-acting narcotics is effective with little effects on monitoring) or otherwise deepening the level of anesthesia.

Microcurrent noise artifact [7] occurs when metals of different types come into contact in association with a bath of electrolyte solution (typically irrigation fluid or bodily fluids within the surgical field). In most situations, microcurrent artifact can be suspected when surgical instruments are in the field and may be in contact with instrumentation being implanted or with metal retractors (e.g., placing screws to secure a plate after cervical discectomy and fusion). Microcurrent noise can be difficult to distinguish from muscle artifact in some situations, but the clinical situation usually will point to the correct source.

Noise from activation of monopolar electrocautery is typically obvious (especially if the cautery device's alarm is audible) and obliterates all but the highest amplitude electrical signals. Bipolar coagulation is similarly obvious, but is often compatible with acquisition of moderate-amplitude and remotely generated signals. For all electrocautery, the typical response is to suspend signal acquisition during cautery activity. A related source of noise arises from the automated testing of the monopolar electrocautery return pad's impedance (Fig. 17.9) and this high-frequency noise is likely to affect electrodes in the immediate vicinity of the pad. Gaining as much distance between the pad and the recording electrodes is desirable both to minimize this noise and for safety reasons, described in Chap. 16, "Wiring and Electrical Interference in IOM." Electrocautery frequencies are usually well outside the typical filter ranges of our systems and thus no filtering is likely to be useful.

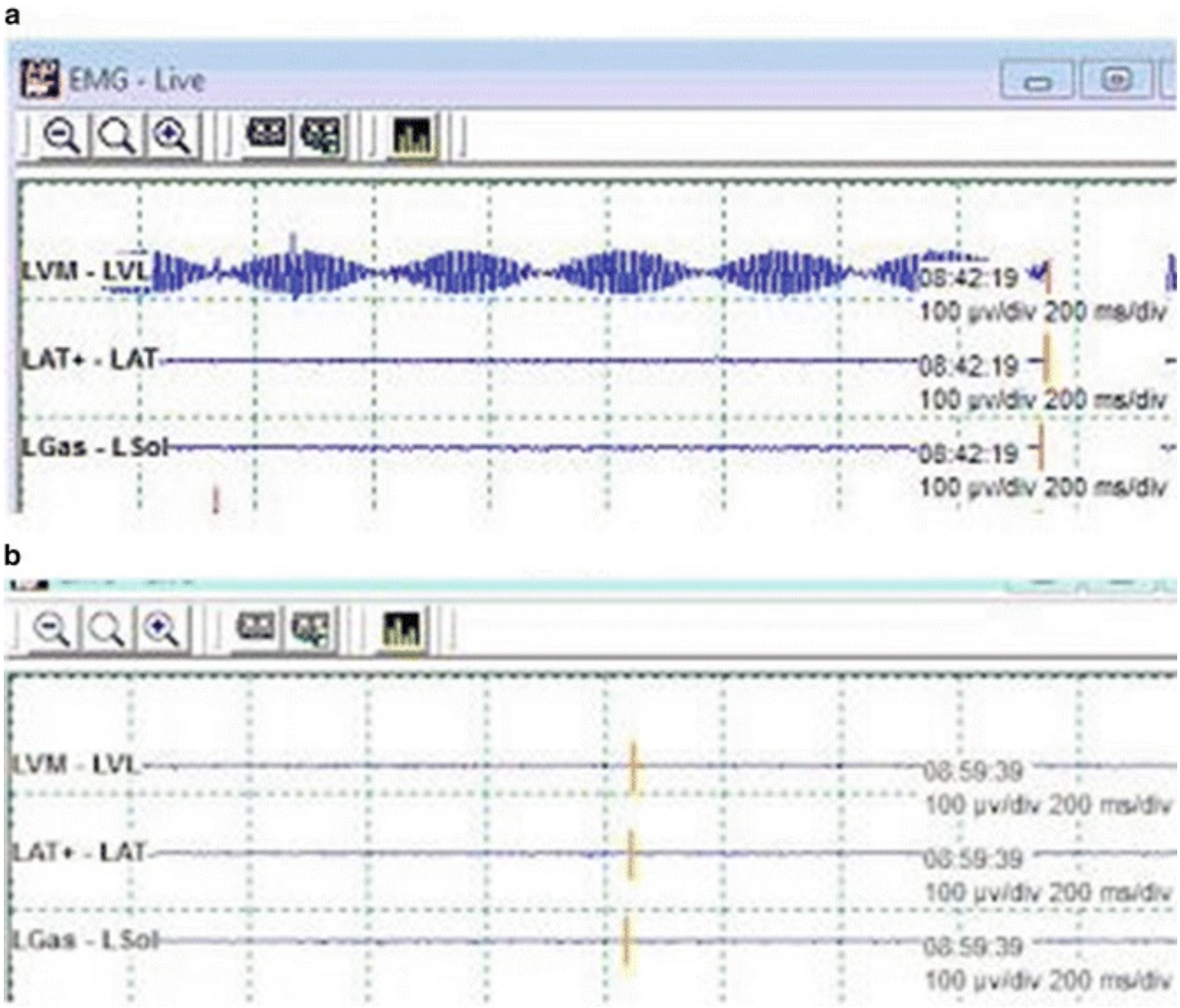

Fig. 17.9 Electrocautery high-frequency noise . EMG monitoring in the left quadriceps ("LVM-LVL") is disrupted by noise from the electrocautery return pad (**a**) during a L3–L4 posterior fusion. Movement of the pad away from recording electrodes resolves the issue (**b**)

Other electrical devices may also introduce high-frequency noise and some, such as an operating microscope or fluoroscopy unit , may be needed in the immediate proximity to the patient and cannot be turned off during specific portions of a procedure. If these cannot be moved to a more favorable location, then the general strategies to deal with electrical noise suggested later are often the only options.

Electrical Noise: Low Frequency or Intermittent

Low-frequency noise tends to be less disruptive in general than the higher

frequency varieties, but can still be troublesome. A common type of low-frequency noise is stimulation artifact ; the sometimes large electrical noise associated with the electrical stimulation we deliver. At times, exaggerated stimulation artifact may result if either the recording or the stimulating electrodes are in poor contact with the body. In addition, proximity of recording electrodes to the stimulation components that generate the electrical charge being delivered (the “stim box”) may introduce artifact.

Even when all components are correctly configured, stimulation artifact may still occur and can be countered with strategies targeted to both the stimulation and recording systems. On the stimulation side, the minimum effective stimulation level should be used and the anode should be in proximity to the cathode but away from the recording target. Recording parameter alterations include increasing the cut-off value for the low-frequency filter, assuming this alteration does not unduly degrade the signal. One such example is an increase in the low-frequency filter setting during motor nerve conduction testing of thoracic roots when recording from the abdominal muscles (stimulation artifact is very common). In this setting, a low-frequency filter as high as 100 Hz has a minor effect on compound motor action potential amplitudes and no discernible effect on measured thresholds under normal conditions. Another strategy that is available in many systems is the incorporation of a delay after stimulation before the recording is triggered. This will prevent the greatest energy from the stimulation from affecting the amplifier and will therefore greatly reduce the subsequent capacitive discharge artifact that otherwise results. This can be highly effective, although of course the triggered physiologic response must have an onset latency that exceeds the trigger delay. Finally, in some cases, stimulation artifact may enter the recording system through electrodes attached to the recording system but purportedly inactive at the time. An example would be testing of transcranial motor-evoked potentials with large artifact entering through the inactive somatosensory potential recording electrodes on the scalp (Fig. 17.10). In such a case, increasing the distance between the stimulation and inactive recording electrodes may help, and if not, temporary physical disconnection of the inactive electrodes during stimulation may be needed.

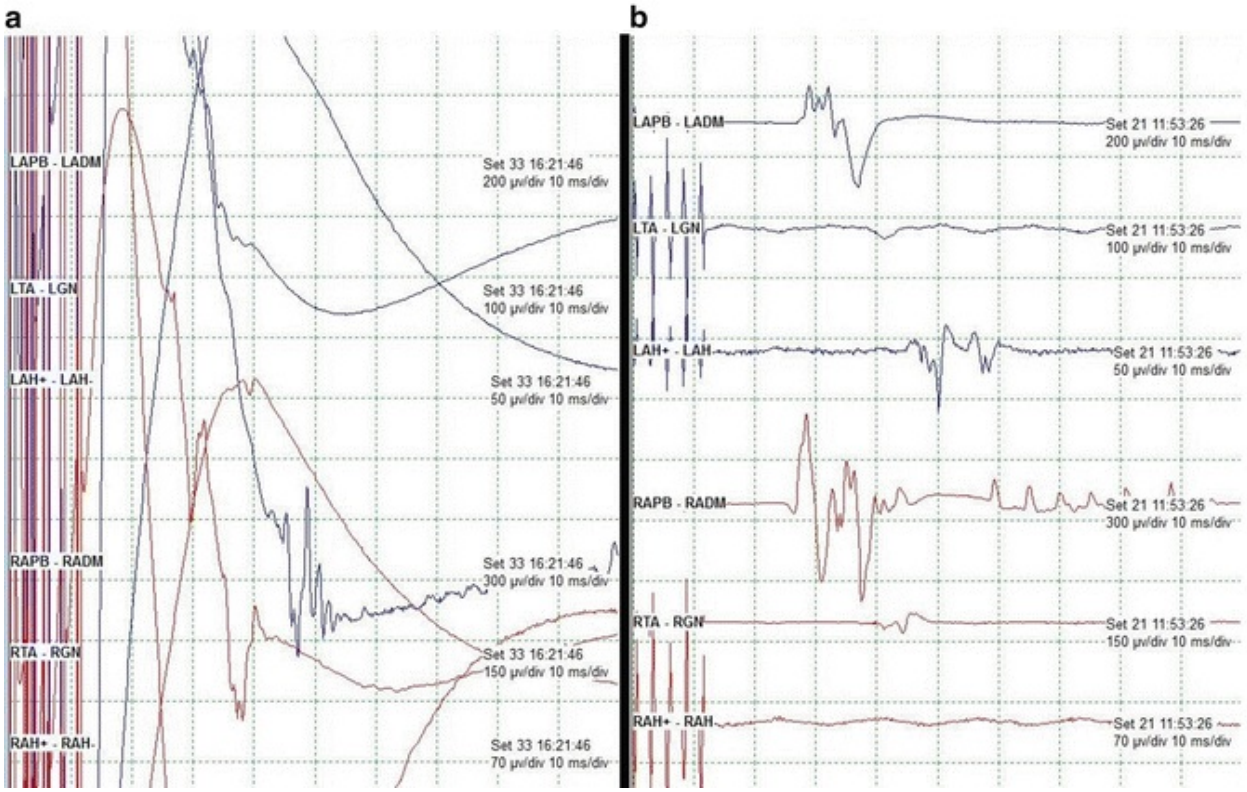

Fig. 17.10 Stimulation artifact entering via inactive recording electrodes. Stimulation artifact obscures MEPs while inactive SEP electrodes are connected to the recording system (**a**). Disconnection of SEP electrodes during testing removes stimulation artifact (**b**)

Movement artifact in our recordings can occur from surgical activity or from other devices in the patient's vicinity. Noise from surgical activity will depend on the surgeon's actions, but often can be seen as delta activity in the EEG. Even if surgical activity is not directly over the recording electrodes, the surgical drapes may also be in contact with these electrodes, thereby focally transmitting the energy of surgical actions. Movement may also be introduced by blood pressure cuff activation, ventilators, sequential compression devices, or pulse artifact. The periodicity of these movements coupled with the lack of correlation to surgical events is the hallmark of these noise sources. If one is not aware of these possible sources of noise, they can be mistaken for physiologic activity such as pulse artifact identified as "focal delta" in the EEG or the noise resulting from an endotracheal tube cuff leak can be mistaken for periodic cranial nerve EMG activity.

One of the more frustrating forms of noise comes in bursts of high-amplitude activity, making it more difficult to identify and counter. These noise intrusions can at times be related to surgical activity, but at other times

may remain mysterious. For averaged signals, common noise strategies such as reducing the stimulation rate or increasing the number of averages in a trial only serve to increase the likelihood that these intrusions wipe out the targeted physiologic signal. In this case, even if signals are imperfectly acquired, short runs of averages in which the intrusions are not captured may be the best strategy. In addition, reduction of the rejection threshold (as discussed later) may be particularl y helpful.

Electrical Noise: General Strategies

The previous discussion about noise focuses on identifying and removing noise sources. Unfortunately, eliminating noise is not always possible in the operating room (OR), and strategies then shift to minimizing the noise while improving the underlying signal such that evaluation of signals can proceed. As always, this is a focus on the SNR.

Strategies to increase the signal are few but can be effective. Actions include optimization of recording sites, avoidance of pre-existing neural dysfunction, and optimization of stimulation. In this latter category, a reduction in stimulation rate produces an increase in the amplitude of responses for many averaged central-evoked potential signals. Finally, attempts to reduce or alter the anesthetic regimen may allow emergence of larger signals that may become adequate despite the presence of noise.

Strategies focused on noise reduction include the configuration and selection of recording channels . In general, the use of small interelectrode distances reduces noise, but this must be balanced against phase cancelation if recording electrodes are so close that they both “see” the same signal. The specific balance of these factors may depend on the specifics of any noise problem, but as a rule, one recording electrode is placed where the target signal is expected to have maximal activity and the reference electrode will be placed as close as possible where there is minimal (or reverse polarity) activity. Such a configuration allows for the greatest difference in electrical potential between electrodes (the signal) while keeping electrodes close to each other so that they “see” roughly similar levels of noise (which will thereby cancel each other), thus allowing for maximization of the SNR.

The ideal recording channel is not always predictable for a given patient, and the best recording channel may change over the course of a procedure. For example, when recording somatosensory-evoked potentials, differential anesthetic effects may alter the distribution of cortical responses, thereby

improving or degrading responses in specific channels and potentially changing which channel might be considered “best.” Similarly, the use of multiple cortical recording channels is often important when coping with electrical noise. We frequently see noise affect some channels more than others and, when it cannot be eliminated, the availability of many channels increases the likelihood that at least one remains adequate and thereby salvages the ability to continue to monitor. More traditional recording channels using electrodes overlying the somatosensory cortex and referenced to Fpz are excellent under good recording conditions, but they are also c ommonly the most sensitive to electrical noise given the relatively long interelectrode distances and the proximity of an electrode at Fpz to potentially excess myogenic noise from the frontalis muscle. In these situations, Cz′-C3′ or Cz′-C4′ (or their inverses) often are the most noise-resistant channels (*see* Fig. 17.7) [8]. Recording adjustments for other types of signals may also be made. When recording auditory-evoked potentials, the C3′ or C4′ sites may provide an alternative recording site when the more commonly used Cz′ site is associated with excessive noise.

The routine and meticulous management of electrode wires will help to avoid electrical noise. Recording wires should be closely grouped/braided. These grouped wires should then run together from their patient attachment to the jackbox inputs. Along this course, the wires should be separated from other electrical wires or electrical devices as much as possible (especially electrocautery wiring) and excess length of wires should never be coiled, as explained in Chap. 16. When noise sources cannot be moved, it is sometimes possible to move the electrodes on the patient to new locations away from the source that allow continued monitoring while minimizing noise.

Averaging signals to improve their SNR is a routinely utilized strategy for many neuromonitoring tests in which target signals are small in comparison to typical background noise. The SNR is improved by a factor of the square root of the number of averages, so one of the easiest ways to improve the SNR is to simply average more. In addition, some signals that are not routinely averaged may be better delineated by the addition of averaging.

The acquisition (stimulation) rate also plays an important role with averaged signals. Any change in stimulation rates can potentially improve signals depending on the frequency of noise present, and one may find that another rate is more suitable for attenuating the noise present. If the predominant noise that is present is in sine wave form and of known

frequency, one can even alter the stimulation rate to attempt to initiate stimulation in a way that "hits" the sine wave at intervals that are half a wave apart (by using a rate that has a stimulation period that is an integer multiple of the noise-period + 0.5 * noise-period). In other words, if the latency of the target response to stimulations 1, 3, 5 … corresponds to the presence of the peak of the sine wave, then the response to stimulation 2, 4, 6 … would arrive along with the trough of the sine wave. The combination of odd and even responses would theoretically then allow more effective cancellation of the noise. Stimulation rates that meet these criteria can be easily calculated for any noise frequency. Examples for 60-Hz noise include 13.333, 10.909, 4.8, 4.444, 3.636, 2.105, and 1.101. Such stimulation rates are therefore described as "ideal" for 60-Hz noise [9]. The exact opposite of the above strategy would be to use a stimulation rate that hits the 60-Hz sine wave at the same sine wave location with every response (e.g., peak every time). Such a "resonate frequency" would dramatically impair the efficacy of averaging. Most will recognize this as what we seek to avoid when following the rule to never use stimulation rates that are even divisors of 60. However, many think of this as only whole numbers while forgetting that rates such as 1.2, 1.25, 1.5, 2.4, 2.5, 3.75, and 7.5 Hz are also divisors in the sense that, when multiplied by integers, they equal 60 and therefore they are just as resonate and just as deleterious to averaged signals as are whole number divisors. Finally, just to complicate this situation further, we have noted that at times, use of "ideal" rates are not the most effective rates for noise elimination and this may reflect times when harmonic frequencies of 60 Hz are also present. It turns out that EVERY stimulation rate that is "ideal" for 60 Hz is resonate for 120 Hz (and selected other harmonics) and thus in some situations use of ideal rates is not as effective. In conclusion, attempts with ideal rates may be helpful but we need to be flexible, and a bit of trial and error with a range of rates may be necessary.

Most modern neuromonitoring systems automatically reject trials that contain too much noise so that these are not incorporated into the completed average. For this function, single responses that contain activity with amplitude in excess of a set level are rejected as excessively noise-filled prior to incorporation into the averaged response. Default levels are typically adequate under usual conditions, but it is often overlooked that the cut-off amplitude for rejection can be adjusted and reduction of the cut-off amplitude (more responses rejected) can reduce noise in the final average. Conversely,

when averaging is effective but too many averages are rejected, then the cut-off level can be increased.

Band-pass electrical filtering is a standard part of all modern monitoring signal acquisition and the addition of notch filtering to counter-specific frequencies is an available addition. Commonly used default band-pass ranges can be altered if it is done with an understanding of what the impact on the recorded signals will be and how comparisons to any baseline data will be affected. Given the potential to impair signals in addition to attenuating noise, this is usually a late attempt to acquire signals when other steps have failed. In addition to simple band-pass filtering, adaptive filtering methods may become incorporated into future systems [10].

Possibly the most important aspect of coping with electrical noise is differentiating noise from physiologic signals. Misidentification of noise as signal may lead to disastrous results if this produces a false suggestion that the nervous system is still functioning as expected (*see* Fig. 17.8). One such case was published as an example of false-negative MEP monitoring in which an automated system identified noise as persisting motor signals after spinal correction in surgery for kyphoscoliosis [11]. Visual inspection of published figures shows possible though, if present, exceedingly small left leg motor signals prior to spinal correction, while on the right leg only sine wave noise was discernible. After spinal correction was performed during the surgery, no leg signals could be visually identified from either side, although clear right leg sine wave noise persisted. Despite this, the amplitude of the noise automatically recorded and measured by the computer was numerically comparable to data obtained earlier for both legs and thus signals were considered “within normal limits.” The potential for disaster with this type of error is apparent.

Poor Signal Amplitudes

When signals are low in amplitude, it is most commonly considered to be caused by the patient’s physiology or due to anesthetic suppression of signals. In addition to attempts to counter these possible causes, an assessment for the contribution of technical causes should always be made. At other times, a neurologically normal patient may unexpectedly have poor amplitudes and a technical cause is suspected. For both of these situations, the logical approach to the assessment is made simpler by splitting consideration into either recording or stimulation causes.

Recording Technique

Meticulous placement of recording electrodes in standard positions and well-conceived basic acquisition parameters will allow high-quality initial signals in the greatest number of cases. When standard technique is closely followed but signals are still lacking, further improvement in some cases may be possible for signals that are sensitive to small recording adjustments (SSEPs > ABRs or myogenic potentials). Adjustments may proceed by trial and error or a systematic approach may be used [1]. It goes without saying that in order to improve signals, they must be correctly identified to start, and for this, a full appreciation of their expected polarities, latencies, amplitudes, and relations to other signals or signal components must be known. These factors as well as an understanding of the expected most active electrodes will also be invaluable in identifying situations in which errors have been made, as discussed later.

Stimulation Technique

Somatosensory-evoked potentials , train-of-four testing , and several additional types of testing are best performed with a supramaximal stimulation level. This is a stimulation level that corresponds to activation of all axons within the targeted nerve that contribute to the elicited response. As indicated by the name, it is also a stimulation level for which further increases in stimulation intensity yield no further increase in the response amplitude. For the appropriate tests, use of a supramaximal level is important for two reasons. First, it yields the largest responses, which will benefit the SNR. Second, the supramaximal level depends on a functional measure rather than a specific stimulator output number. As such, it is reproducible and this level of stimulation can always be reliably reestablished even if stimulation electrodes are altered, thereby leaving comparisons to baseline findings valid. The specific levels of stimulation that achieve the minimum supramaximal level will vary by patient and will depend on the proximity of stimulating needles to the targeted nerves as well as the function of those nerves. These factors imply that even in a given patient, significant left to right asymmetry in stimulation may be entirely appropriate if side-to-side electrode placement varies, anatomy varies, or nerve function varies.

In general, the supramaximal level can be achieved through a relatively wide range of stimulation intensities from the “minimum supramaximal level

” up to the maximum stimulation output of the system. While this full range of stimulation may be safe in most circumstances, a setting near the minimum supramaximal level is generally preferred in order to minimize unnecessary electrical energy delivery and to prevent spread of stimulation outside the targeted nerve. Determination of the minimum supramaximal level can be time-consuming if averaged and sometimes variable signals are assessed such as with cortical SSEP responses, but more stable alternates are often available. An SSEP peripheral nerve response is typically stable and requires little averaging, thus allowing multiple trials at differing stimulation levels over a short period. Similarly, determination of the supramaximal level for the train-of-four test is simple given the large amplitude and unaveraged muscle potentials produced. However, if partial neuromuscular blockade is present, then single stimuli should be delivered and at least 7 s between stimulations should be allowed so that trial-to-trial amplitudes can be compared without introduction of a decremental response due to the presence of nondepolarizing neuromuscular blockade. Often the same nerve used for a train-of-four is used for SSEPs and the supramaximal level found in the train-of-four can suggest a supramaximal level for SSEPs, since the larger fiber sensory axons are typically depolarized before the slightly smaller motor axons. If the stimulation is monopolar (e.g., popliteal fossa), then results directly translate, whereas if bipolar stimulation is used (as is typical at the wrists and ankles) then minor variability may be introduced due to the reversal of stimulation polarity between those two tests (cathode proximal for SSEP and distal for train-of-four). If the limb is visualized, the presence of robust movement with stimulation similarly accomplishes this goal.

For superficial nerves with normal physiology, the precise determination of the minimum supramaximal level is not needed as long as standard stimulation levels are high enough to be supramaximal, while not so high that there is unintended activation of nearby nerves. Spread to nearby nerves occurs most commonly at the wrist when the ulnar nerve is targeted, but high stimulation levels also activate the nearby median nerve. As a general rule, we limit stimulation of the ulnar nerve to 35 mA or less (with 0.3-ms pulse width), which for typically sized patients with normal nerves and stimulating electrodes in our standard position results in stimulation well above the minimum supramaximal level, while still below the point we expect to activate the nearby median nerve. For SSEPs, selective stimulation of the ulnar nerve is important as it represents a lower entry of the ascending

activity into the spinal cord (C8-T1) so that most of the cervical spinal cord is assessed. It is similarly important to selectively stimulate the ulnar nerve to distinguish it from the median nerve when assessing for peripheral nerve dysfunction.

Limiting stimulation to single nerves is typically desired; however, there may be times when purposeful stimulation spread to the median nerve may be useful, such as when an ulnar nerve response is degraded and subsequent assessment of the median nerve is desired. Loss of ulnar signals can occur due to dysfunction at any point in its course, whereas if the median nerve is simultaneously affected, the localization is most likely to be where these nerves travel together (wrist, axilla, or brachial plexus), assuming a peripheral nerve problem is the clinical expectation. For most patients, robust spread to the median nerve from electrodes over the ulnar nerve can be achieved with a stimulation of 65 mA at 0.3-ms pulse width. Another site where stimulation spread is likely to occur is at the popliteal fossa where both tibial and common peroneal nerves are present. However, the deep course of these nerves and higher stimulation intensities routinely needed make it more difficult to isolate just one of these nerves on a routine basis.

There may be some situations where stimulation artifact or excessive patient movement forces use of a submaximal stimulation level where a supramaximal one might normally be chosen. This may introduce less consistent reproducibility of the proportion of axons activated on a trial to trial basis, but can be used if this factor is understood. Twitch threshold is one option for a reproducible submaximal stimulation level, assuming target muscles can be visually assessed and neuromuscular blockade flux is not a factor.

Submaximal stimulation levels are also used for a variety of testing. Motor and auditory-evoked potentials may be elicited at threshold or at higher stimulation levels, although elucidation of a supramaximal level is not necessary in most cases and not desired in others. H-reflex testing requires a submaximal stimulation. Various stimulation techniques for assessing proximity to neural structures (e.g., pedicle screw testing) are performed at or near threshold.

Comprehensive acquisition methods for transcranial motor-evoked potentials can be found elsewhere [12]. Motor-evoked potentials are intrinsically more variable than most other signals we assess, are highly sensitive to anesthetics, and can vary dramatically depending on the

stimulation methods. Effective stimulation depends on the location of the stimulating electrodes, the intensity of each pulse in the stimulation train of pulses, the number of pulses in the stimulation train, the interpulse interval, and any possible priming techniques used. Specific strategies for each of the above parameters are beyond the scope of this chapter, but the primary goal of stimulation is the successful activation of the anterior horn cells in the spinal cord and, when motor signals are poor, a number of maneuvers may be used to improve this activation. With poor signals, only a small minority of the anterior horn cells projecting to muscles used for recording will be activated, but this may be improved by either increasing the number of anterior horn cells that receive synaptic input or by increasing the likelihood that the anterior horn cell is successfully depolarized in response to this synaptic input. An increase in the number of anterior horn cells that receive presynaptic input can be achieved via higher stimulation intensities that are able to activate wider areas of brain and therefore greater numbers of axons. However, one may quickly run out of stimulator capacity or face diminishing returns on further stimulation increases with this strategy alone. In addition, the wider area of stimulation also activates deeper structures in the brain, which may be problematic for intracranial procedures. The other main way to improve motor signals is to increase the likelihood that the anterior horn cells that receive presynaptic input actually depolarize in response to this input. This latter focus may relate to both the stimulation parameters and to the pharmacologic/anesthetic milieu. Alteration of stimulation parameters that improve the likelihood that any given anterior horn cell depolarizes include optimization of the interstimulus interval, an increase in the number of pulses in a stimulation train, or employment of “priming” techniques such as dual trains [13] or preliminary peripheral nerve stimulation [14–16]. As can be seen in the referenced materials, the specific methods for preliminary peripheral nerve stimulation varies, but our preferred technique uses bilateral tibial nerve stimulation, which is interleaved and repetitively activated as they would for an SSEP (supramaximal stimulation, ~4.7 Hz). Repetitive tibial nerve stimulation is maintained for 15 s or more with activation of MEPs i mmediately following. The primary pharmacologic maneuver to improve the probability that anterior horn cells are depolarized is a reduction in anesthetic inhibition either through reduction of the depth of anesthetic and/or through a shift in anesthetics towards ones that less potently inhibit this process. The choice of maneuvers used to improve motor signals should

depend on the time remaining in a procedure and with attention to the likelihood of “anesthetic fade” [17]. In general, at the beginning of a procedure we focus on stimulation electrode location and the anesthetic regimen while keeping priming techniques in reserve to counteract possible “fade” effects that may occur later in the procedure.

Several comments were made previously concerning alteration of stimulation rates in order to combat electrical noise. Independent of noise issues, slowing a stimulation rate improves the synchrony of averaged central-evoked potential signals . This can be a very useful technique to show that signals persist when increased anesthetic requirement or other systemic factors have already impaired comparisons to baseline signals. If noise is a problem and cannot be eliminated, the greater amplitudes will improve the signal-to-noise ratio, although the focus in this case is on the signal portion of the signal-to-noise ratio. Effects on the noise incorporated into averaged signals will be less predictable and will depend on the specific rate chosen. However, be aware that slower acquisition may reduce temporal fidelity and divert monitoring attention away from other important modalities. In addition, the resulting increased signal amplitudes can potentially compromise comparisons to baseline signals and might theoretically reduce the ability to identify a new neurologic insult. While we keep this possibility in mind when reducing averaging rates, we would rarely consider a signal “fixed” by a slower rate as having a “significant” change in the first place. Moreover, reduction of averaging rates is usually used in settings where baseline comparisons are already somewhat compromised (e.g., anesthetic suppression or increased noise) (Fig. 17.11).

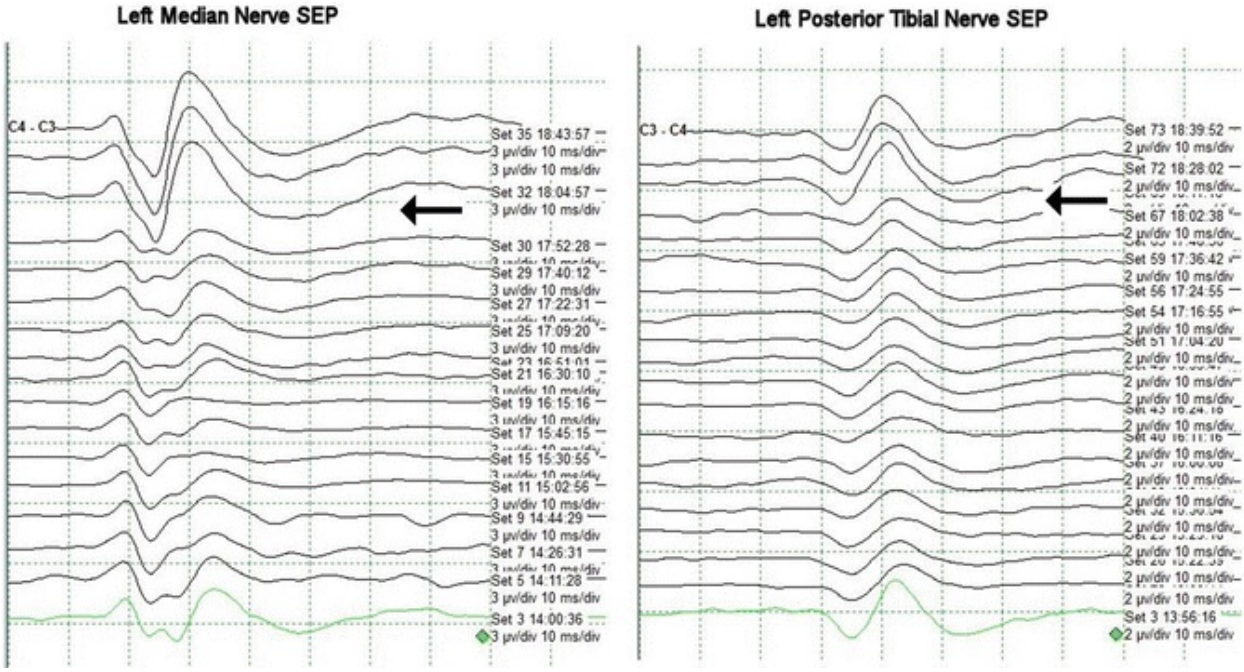

Fig. 17.11 SEP amplitude increase with reduced stimulation rates . Waterfall displays of the left median and left tibial nerve SSEPs are shown with the baseline responses at the bottom (*green*). Gradual reduction in signal amplitudes was noted during the case in association with anesthetic/systemic effects. A decrease in stimulation rate from 4.7z to 1.1 Hz (*arrows*) resulted in increased amplitudes. Similar improvement was seen in right median and posterior tibial responses as well as in ulnar responses bilaterally

Errors of Signal Acquisition

The previous discussions focused on improving signals when faced with challenges that are largely external to the standard neuromonitoring technique. However, constant vigilance must be maintained for errors of configuration of the neuromonitoring system or for malfunction in one of its components.

Electrode Plug-In Errors

Multimodal neuromonitoring involves the placement of dozens of electrodes and each must go in its assigned jackbox or stimulation output slot. To make matters worse, electrodes are often connected to the patient, the wires are all gathered together, the patient is repositioned, and the wires are then covered (drapes, compression devices, warmers, and more) with only the ends accessible. Only then are the wire ends finally plugged into their respective slots. Given the associated challenges of correct configuration, every

neuromonitoring team must have a system to correctly identify each electrode when they are no longer able to easily directly trace it back to its location on the body. Usually these systems utilize a color coding system identifying both location and side of the body, pairing/grouping of electrodes, numbers of knots in the wire, labels, or combinations of these. Particular attention to errors must occur when the usual routine is disrupted, such as when one monitorist takes over for another during or after the initial set-up period, when the patient is not in the usual position during electrode placement, or when needle scarcity alters usual color or grouping schemes.

Greater care, better systems, and better memories all serve to reduce error rates in how electrodes are plugged into the system; unfortunately, the inherent complexity and associated number of chances for error mean that at some point errors will occur. When those errors do occur, we rely on the understanding of our tests and our target signals to identify these problems from clues in the data generated. If electrode swaps occur, it can alter interpretation of signal changes and we may focus on the wrong side of the body or the wrong limbs if the problem is not discovered. A particularly tragic example is one of “false-negative MEPs” in a scoliosis surgery when the upper limb muscles were swapped with the lower extremity muscles. In this case the lower extremity signals appeared to persist through surgery, but since these were in fact signals from the upper extremities, they persisted through the surgery. The falsely labeled upper extremity signals, on the other hand, were lost in association with spinal correction and the patient awoke paralyzed [18–21]. Clues from the data that were missed in this case included earlier latencies in the “feet” compared to the “hands” and an unexplained loss of signals in the “hands” with timing correlated to spinal correction.

Probably, the most common type of plug-in error is a left/right swap of electrodes, and this can affect almost any type of neuromonitoring test with identification depending on the specific test. For free-running activity such as electroencephalography or electromyography, identification often will depend on associated artifact. Movement artifact from surgery, stimulation artifact from other tests, and cardiac artifact should all confirm correct laterality or the electrodes should be re-checked. When myogenic potentials are purposefully elicited (e.g., pedicle screw testing), the side of stimulation should match, and if not, the electrodes should be checked (Fig. 17.12).

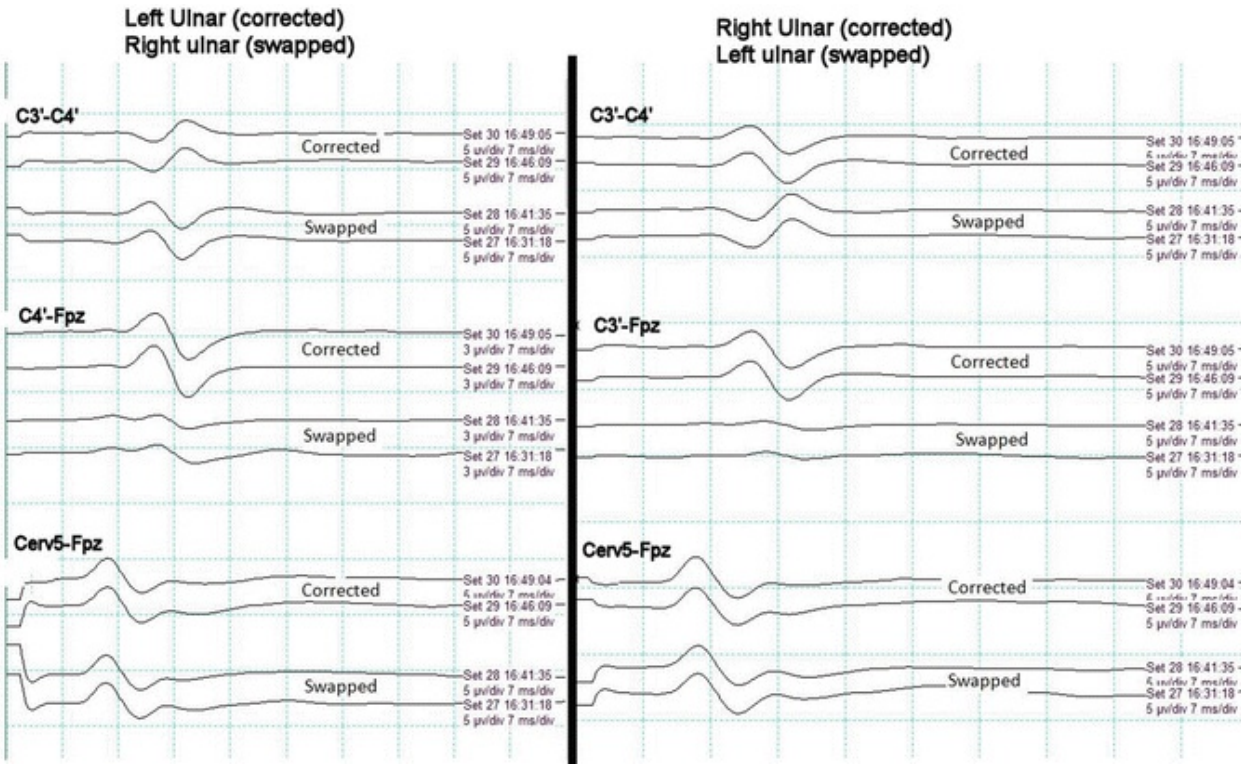

Fig. 17.12 Correction of left/right ulnar nerve SSEP stimulation swap. Four consecutive ulnar SSEP averages are shown spanning the correction of a left/right ulnar stimulation swap. N19 activity is noted at approximately 19 ms on both sides. The intended left ulnar stimulation on the left side of the figure shows initially poor activity in the C4′-Fpz channel and the initially up-going response in the C3′–C4′ channel ("swapped") reflects a greater negative potential in the C3′ electrode as compared to C4′ in conflict with expectations for greatest negativity at C4′. Analogous alterations are noted in the "swapped" responses on the right and the stimulation error was identified and corrected with typical signal morphology thereafter

With evoked potential testing, a left/right swap is expected when signals reflect a pattern for the "wrong" side and the problem may lie with either the stimulation or the recording system. Identification of the "wrong" side is relatively easy for motor-evoked potentials when stimulation electrodes are over each hemisphere and both sides of the body are recorded. In such a case, if the left body activation is intended but only right body responses are observed, the presence of a swap is fairly obvious, although whether the cause is a swap in stimulation versus recording remains to be resolved. Routine bilateral muscle recordings are suggested because if only the targeted side of the body is recorded, signals may be interpreted as small or absent in the presence of a swap when in actuality much better signals are recordable contralateral to those being assessed. For any type of myogenic potential, the presence of a train-of-four response on the expected muscle is a good

indicator that at least that muscle is correctly matched to the stimulation and, if those stimulation electrodes are correct, indicates the recorded muscle is correct. Conversely, a flat train-of-four test with no stimulation artifact suggests a mismatch of the stimulation and recording sites and likely electrode error. Finally, clues from the patient can be very helpful and when (individually) stimulating any peripheral nerve, movement of the corresponding musculature gives an instant confirmation that stimulation laterality is correct.

With auditory-evoked potential testing, the presence of Wave I is a good indicator of laterality and other typical lateralized differences (larger Wave III ipsilaterally, smaller Wave II–III interval contralaterally, greater IV/V separation contralaterally) may be helpful. When signals are poor or these typical differences are not apparent, recording laterality may be indicated by the side with greatest surgical artifact if it is a lateralized approach. It is certainly hoped that errors would be fixed at an earlier stage, but if signal degradation occurs contralateral to an expected side of surgical risk, then a search for a left/right stimulus swap is indicated in addition to usual troubleshooting of the stimulator. Evaluation of the stimulation should be traced from the ear to the computer inputs to confirm laterality when possible, and if doubt persists or as a primary method, use of a stethoscope to confirm the side of stimulation is a useful alternate technique. Failure to identify swaps of the recording electrodes (usually A1 and A2) may be embarrassing on review, but have less of an impact on interpretation.

Recognition of electrode swaps with somatosensory-evoked potentials requires understanding of the expected pattern of cortical signal response over the scalp. For example, a left ulnar nerve N19 cortical response typically has its maximum negativity at or near the C4′ electrode. If we use a C4′-Fpz channel for recording (negative in input 1 plotted up in our system), then we would expect the recorded N19 to be larger than the ones recorded in Cz′-Fpz or C3′-Fpz and this should be assessed. This assessment is made easier for us if we are using a C4′–C3′ channel, as this directly compares the relative activity at these locations. If correctly configured, we would expect an upgoing deflection for N19 (negative) in this channel, whereas if the C3′/C4′ electrodes are swapped or the left/right ulnar stimulation electrodes are swapped, then we would be surprised to see a response that is inverted relative to usual expectations wi th the C3′ electrode showing greater negativity as compared to the C4′ electrode. In such a situation, either the

patient has extremely rare variant anatomy (uncrossed somatosensory pathways); the N19 was misidentified; or, as is most likely, there is a swap. *See* Fig. 17.12 for this phenomenon and its correction. With lower extremity somatosensory-evoked potentials, one must of course incorporate that the targeted cortical signals are typically positive (e.g., P37 for the tibial nerve response) and that the most active electrodes are midline or ipsilateral. Once this is understood, a similar process as above can be applied to identify left/right swaps.

The complexity of multimodality monitoring aids identification of electrode swaps due to the necessary integration of testing. If, for example, ulnar nerve stimulators are utilized to test both somatosensory-evoked potentials and a train-of-four but there is a left/right swap present, then in addition to the cortical response alterations described above, we'd also expect to see a flat, stimulus artifact-free response in the hand train-of-four test. Thus, we obtain another indication of a set-up error from the train-of-four. Of course, this assumes that those hand muscle electrodes were not also swapped (as they might if hand/wrist electrodes are grouped before plugging in), but if that is the case then motor-evoked potentials should show the responses on the "wrong" side. Thus, unless every lateralized electrode is swapped with its contralateral counterpart (a sorry situation indeed!), we should see multiple indications in our signals.

There are an innumerable number of possible electrode swaps that are not simply left/right exchanges, and identifying any signal pattern that is "not right" should prompt evaluation. Clearly all these patterns cannot be specifically discussed, but an understanding of the side, polarity, and latency of an expected response, coupled with information integrated from all test modalities, should a llow identification of a problem in almost all cases.

System Errors

The neuromonitoring apparatus can falter in many ways and when trying to identify the source of an error, a good first step is once again to start by determining if the problem is in the stimulation or recording system. For the recording system, the primary tool is measurement of impedance (explained in more detail in the preceding chapter). A high impedance of a specific electrode initiates a search for a cause. The most common cause and most people's gut reaction is "my electrode came off." If the electrode appears to be in position, however, the search must continue and it is helpful to think in

terms of the most distal to the most central parts of the monitoring system. Moving from most peripheral to most central, we can consider fault in the following elements: electrode disconnection, electrode breakage (may be internal and not apparent), extension pods/extender system (if used), pod/extender cable, inputs to the main acquisition box, or amplifiers. Identifying which of these components is the culprit is one of the more elementary processes of "troubleshooting."

Often simple inspection of these components will not yield an answer and one simple method is to replace components within the faulty electrical chain and then reassess after each replacement. While replacement with a new component is an option (e.g., remove electrode and replace with a new one), it is often more convenient and more efficient (especially if patient access is limited or discouraged) to swap a component that is known to be working with one that is potentially malfunctioning in order to sort out where the problem lies. For example, if inputs for a working electrode are swapped with the one associated with high impedance, then one should quickly be able to determine if the problem is in the needle or is more central within the monitoring setup. If the high impedance "follows the needle," i.e., occurs in previously bad electrode but in a more central input previously shown to be working, then we know the problem is in that electrode. Conversely, if the known "good" electrode now shows high impedance, then we know that some more central component is malfunctioning. In the latter case, swapping more central components can continue along the same vein until the specific problem is identified.

As one moves centrally to the level of potentially broken amplifiers or their projections, we would expect dysfunction to occur in preselected channels rather than associated with specific electrodes. Physically "swapping" out individual amplifiers is rarely an option; however, if an idle system is available, the whole amplifier box might be swapped. If new amplifiers are not an option, tests will often need to be reconfigured to avoid the malfunctioning amplifiers. Unfortunately, some systems automatically assign amplifiers to the prespecified recording channels and deletion of a "bad" channel may result in the reassignment of the dysfunctioning amplifier to a previously good channel. If amplifiers can't be individually chosen and tend to get reassigned, we typically choose to duplicate the channel (thereby forcing use of a new amplifier) without removing the old channel (so the bad amplifier is not reassigned). In addition, with multimodal monitoring, there

may be bad channels in multiple different tests, thereby complicating the picture further. Remedial measures will depend on the equipment used and parts available.

This discussion focuses on hardware issues, but we might consider the "most central" component of our system to be the software. Software or specific patient files can become corrupted and in some cases do not allow monitoring to proceed. There are many system-specific quirks that monitoring teams will learn to counter that are unique to their systems. However, if these do not work, the monitorist (assuming she is a nonexpert in computers) will typically be left with unsatisfying remedial maneuvers such as rebooting the software, rebooting the computer, initiating a new patient test file, or simply swapping out the monitoring computer for another.

Probably, the most common problem with software is incorrect programming by the monitoring team. Innumerable settings may be misapplied, so familiarity with one's specific software system, awareness of appropriate settings, and suspicion of this problem need to be present. This becomes more important if the system was recently updated, used by others, or if it is an unfamiliar system. If one connects an electrode to the jackbox in the "correct" spot but the computer is programmed for a different spot, an error will obviously result. If the programmed electrode input remains empty, then it will show high impedance and in a way this is the most central aspect of our "bad electrode" issue from above. If, instead, a different electrode is erroneously placed in the targeted input slot, then this becomes an electrode swap issue as discussed above and programming errors should remain in mind as potential causes of electrode swaps as well.

System errors in the stimulating system can also be a challenge. When most neuromonitoring systems cannot deliver the prescribed electrical stimulation output, it will give a warning to the user. When such a warning occurs, we can perform a peripheral to central evaluation of the stimulation system similar to the recording system evaluation described earlier. However, when an expected response to stimulation is absent, one should not assume that the absence of these warnings from the system is a fool-proof indication that all stimulation components are functioning properly and that the stimulation was indeed delivered as hoped. In such cases, it is possible that current can flow while not properly being delivered to the stimulating electrodes (electrical short) or to the target tissue (current shunting). These situations may be difficult to recognize and, given coincident absence of

target signals, often must be evaluated in parallel with concerns for neurologic dysfunction.

Stimulator evaluation is often dependent on the testing involved. For nerve root, peripheral nerve, or cranial nerve stimulation, use of positive controls is most helpful when available. For example, in a cerebellopontine angle case, we routinely have recordings available from the trapezius so that the accessory nerve can be stimulated as needed even though that nerve is not commonly at significant risk. Similarly, directly stimulating muscle (usually with higher stimulation output) can yield a direct muscle contraction and demonstrate at least some level of current flow. Failing access to positive controls, changing both the stimulating probe (cathode) and the anode are reasonable steps and if concern of stimulation failure persists, moving those new electrodes to a stimulation output that is known to be working is also worthwhile. For MEPs, some level of patient movement is almost always apparent and lack thereof should prompt evaluation. In addition, if straight needles are used for stimulation, then frequent confirmation that they are fully inserted prevents partial stimulation. For somatosensory-evoked potentials, use of peripheral nerve recording sites is helpful to prove stimulation delivery and, if neuromuscular blockade is not full, then evaluation for movement or of an associated train-of-four test can confirm intact stimulation. For auditory-evoked potentials, the presence of Wave I confirms effective stimulation, whereas absence of Wave I when cochlear function loss is not expected suggests loss of effective stimulation. Click stimulation artifact can be suggestive that a stimulus was delivered, but the presence of artifact should not be considered definitive proof of adequate click stimulation delivery.

General Principles

Timing of Optimization

Signal optimization may be needed at any time during a surgical procedure , but the most common need is at the start of the procedure when signals are first acquired and one sorts through the patient’s specific needs related to their physiology, the anesthetic regimen, and the signal acquisition technique. In general, the time between initial signal acquisition and the exposure of the surgical site is an appropriate time to optimize signals. This represents a time

prior to primary surgical risk, but (ideally) after equilibration of initial anesthetic and systemic variables allowing for the selection of representative baseline signals at that time, which will serve as a basis of comparison through the remainder of the case. Unfortunately, for most cases the initial incision is followed by nearly incessant electrocautery, making further signal assessment difficult or impossible until exposure is complete. Thus, the best time for initial signal acquisition and optimization is mostly limited to the time prior to incision.

Later in the procedure, additional optimization may be needed as both the operating room environment (e.g., new noise sources) and the patient physiology is likely to be in flux. Patient physiology and therefore our signals may be impacted by new neural dysfunction, changing anesthetic regimens, signal fade despite apparently stable anesthetic regimens [17], altered blood pressure, altered temperature, anemia, fluid shifts/edema, and myriad other factors that may not be easily tracked. In addition, new problems with the neuromonitoring system or technique may unfold during the procedure. Attention to all these possible issues is an ongoing process.

Prioritization

Complicated cases, complicated patients, and the frequent use of multimodality monitoring all lead to situations in which multiple tests will need some level of optimization attention. As always, the time window for this is finite and therefore one must both be efficient in this process and prioritize which signals to approach first. Often, the signal optimization process begins as soon as any issue is identified. However, this can be a problem if there are other, possibly yet to be discovered, issues that are more pressing or if that optimization process distracts from ongoing assessment of other more critical tests. One trivial example of poor prioritization in this regard might relate to monitoring a scoliosis procedure with an imminent incision. It would not make sense to repeatedly acquire, over-average, and mark ulnar somatosensory-evoked potentials before even attempting first runs of motor testing or lower extremity somatosensory signals.

Each case will present a unique set of circumstances, so no specific formula for prioritization can be given, but decisions will hinge on some straightforward considerations when time pressures exist. First, the signals that are expected to be most important to monitoring at-risk areas should in general be addressed before control signals or ancillary tests. Second, some

steps toward optimization may require access to the patient and that access will only be available for limited windows. Taking advantage of access will be a priority. Similarly, one type of optimization process may need long noise-free periods, while others might be addressed during or between electrically noisy times such as during surgical steps in which electrocautery is frequently in use (e.g., initial exposure). Third, the degree to which suboptimal signals may impact interpretation should be considered with priority given to those tests where the impact is greatest. Finally, even if some signals requiring optimization may be of lesser importance, their correct acquisition may add insight as to problems with other signals and therefore may merit earlier attention, especially if steps are easy and quick to address.

Prioritization also extends beyond the scope of the neuromonitoring signals. For example, electrical noise from an operating microscope may wipe out target signals. If all efforts to overcome this noise fail and scope replacement is not an option, a decision must be made as to whether the neuromonitoring signals or the microscope is more important to the patient's well-being and, in almost all cases, the microscope wins (at least for some time interval). Less clear situations arise frequently in which surgical, anesthetic, and neuromonitoring goals appear to be in conflict. Again, no formula can be given for the best way to address these conflicts other than a focus on the best interest of the patient. As prioritization spans these areas, it is likely that the surgeon, the anesthesiologist, and the neuromonitorist have an initially incomplete understanding of the issues outside their own realm. When this occurs, communication, flexibility, and creative solutions are paramount for true, patient-centric optimization, which is, of course, the overarching goal.

Conclusion

The process of moving from a determination that "signals are bad" to implementing steps that will improve them is a complex one, but a logical approach will yield the most efficient path to improving signals. The complexity of this process increases dramatically when multiple issues are encountered, but is simplified by realizing that all of these issues can be categorized as patient-related, anesthetic/systemic-related, or technical and this categorization starts a process that can organize thinking and break down

the complexity.

Finally, we would all like to see beautiful neuromonitoring signals in every case. Technical skill and superior monitoring methods can achieve this much of the time, but at times there will simply be factors beyond our control that will impair signals. We must keep in mind that optimized signals imply we have made the best use of the hand dealt to us and it is the ability to cope with the difficult cases that is a true mark of neuromonitoring technical skill.

Questions

1. In the setting of length-dependent peripheral neuropathy, an improvement in somatosensory-evoked responses may result from:

    a. An increase in stimulation intensity

    b. More proximal stimulation sites

    c. Use of the median nerve as opposed to the tibial nerve

    d. All of the above

2. An increase in anesthetic levels is least likely to reduce:

    a. Motor-evoked potential myogenic response amplitudes

    b. Somatosensory-evoked potential cortical response amplitudes

    c. Somatosensory-evoked potential subcortical response amplitudes

    d. Electrical noise from return of muscle tone or voluntary muscle activation

3. Which of the following is not true relating to 60-Hz noise:

    a. It is typically seen as a sinusoidal wave with period of 16.67 ms

    b. It is best eliminated from an averaged signal with stimulation rates that are even divisors of 60.

    c. It can be produced by fluid warmers near the operative field

    d. Notch filters may reduce it

4. Which of the following is most likely to reduce stimulation artifact

    a. An increase in the low frequency filter cut off

    b. An increase in the stimulation intensity

    c. Greater separation between anode and cathode

    d. Greater separation between recording electrodes

5. In the appropriate setting, poor signal amplitudes may be due to

    a. Pre-existing neuropathophysiology

    b. Anesthetic suppression of signals

    c. Incorrect technique

    d. All of the above

Answers

1. d

2. c

3. b

4. a

5. d

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Footnotes

1 Key references marked with asterisk.

Section II
Anesthesia Considerations

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_18

18. Anesthesia for Awake Neurosurgery

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Electronic supplementary material:
The online version of this chapter (doi:10.1007/978-3-319-46542-5_18) contains supplementary material, which is available to authorized users.

Keywords Anesthesia – Monitoring – Awake neurosurgery – Awake craniotomy – Craniotomy – Tumor resection – Indications – Patient selection – Sedation – Analgesia – Cortical mapping – Subcortical mapping

Key Learning Points

- Awake craniotomies are used to maximize resection of tumors near the eloquent area.
- Successful awake craniotomies require: motivated and cooperative patient, skilled and gentle surgical team, and knowledge communicative anesthesiologist to be able to provide good blocks, appropriate sedation while communicating positively with the patient.
- Scalp blocks can easily be performed with bilateral blocks being able to provide stable condition for pinning and surgery.
- The use of modified block of the auricular temporal nerve will decrease the possibility of facial nerve palsy related to the anesthetic agents.
- Awake carotid endarterectomy can be performed with super facial blocks.
- Awake craniotomy patients will experience itching of the nose, dry mouth, and the feeling of the urge to urinate. Patients should be alerted to these ahead of time and to assure the patients about helping to overcome these annoyances.

Introduction

Neurosurgical operations performed in awake patients are increasingly being used. Procedures employing this technique include resection of tumors and epileptic foci in and around the eloquent areas of the brain, localization of the proper nucleus for deep brain stimulation, testing for spinal cord stimulator placement and other pain procedures, carotid endarterectomy, and surgery on the spine and peripheral nervous system [1–6]. Proponents cite easy neurologic evaluation, short recovery, fewer complications, and early discharge from the hospital. In this chapter, we discuss the anesthetic regimen as well as monitoring of neurologic function during these procedures.

Anesthesia and Monitoring for Awake Craniotomy

During Tumor Resection

Indications and Patient Selection

Resection of tumors in the vicinity of the eloquent areas has been associated with a higher risk of neurologic deficit or incomplete resection due to efforts to minimize the deficit. Made possible by the ability of local anesthesia and scalp blocks to allow a craniotomy to expose an insensitive brain, an awake, alert, responsive, and comfortable patient will provide conditions for optimal tumor resection with minimal neurologic deficits [5, 7, 8] This setting enables the team to perform an ongoing neurologic exam to identify the speech center, motor and sensory strips, and the visual center. This allows the surgeon to better identify the tumor margins and thus provide near complete resection of the tumor while sparing the clinical function of the eloquent areas. In addition, some studies show that a craniotomy performed in the awake patient is superior to that under general anesthesia, providing a better clinical outcome and superior chemical homeostasis as it is exhibited by fewer changes in the large neutral amino acids (LNAAs) profiles [9].

The key ingredients for success in these craniotomies include a knowledgeable anesthesiologist; a skilled surgeon; and a motivated, cooperative patient that lacks major psychologic and behavioral problems. The challenges for the anesthesiologist include rapid anesthetic adjustments; maintenance of stable hemodynamics; adequate ventilation while producing minimal interference with the monitoring systems; and managing occasional complications such as nausea, vomiting, and seizures. Verbal communication with the patient is extremely important as it provides a powerful monitor of neurologic function in the awake patient undergoing a craniotomy [10]. A significant language barrier should be considered a relative contraindication to the use of this technique. The anesthesiologist must possess the ability to select the appropriate type and dose of sedatives and analgesics, the skills needed to perform regional blocks, and the ability to effectively interact with the patient intraoperatively. This is indispensable for providing safe patient care. The neurosurgeon may need to inject a local anesthetic to supplement a regional block, use gentle manipulation to dissect dural attachments to minimize pain, and be ready to communicate with the patient as well.

Preoperative Evaluation and Preparation

A thorough evaluation of the patient's medical history should identify the presence of seizures, obstructive sleep apnea, ischemic heart disease, a predisposition for nausea and vomiting, and previous problems associated with local anesthesia administration. The care team should have a thorough discussion of the anesthetic and surgical plans in advance of the surgery. The patient should have a clear explanation of the plan, including an introduction to the operating room environment. The patient should be made aware that the operating room may be cold; that due to the administration of opioids, they may have an intermittent urge to scratch their nose, they may have dry lips; and that due to the presence of an indwelling urinary catheter, they may feel the urge to urinate; and most importantly that they will have the team immediately available to help at all times.

The patient should be positioned on the operating table to minimize discomfort; extra padding on the surface of the table is recommended. The patient's position on the operating room table should enable all members of the team to perform their work and maintain effective communication with the patient. Usually the patient is in the supine position with a small degree of lateral tilt or in the lateral position. In order to keep in constant communication with the patient and to maintain the ability to readily manage the airway, the patient's face should be in direct view of the anesthesiologist. In fact, maintenance of eye contact and intermittent verbal communication with the patient is extremely important and generally serves as a very effective anxiolytic. In a recent paper, Hansen et al. [11] suggested psychologic rather than pharmacologic support and promoted a technique of fully awake patients (awake–awake–awake). This visual contact should be assured by placing a small surgical table ("Mayo") or a special flexible screen at the top of the table around the patient's head and securing the surgical drapes in such a way that access to the patient's face is unobstructed (Fig. 18.1). An unobstructed view of the patient's face is also needed during visual and motor testing and will be discussed later.

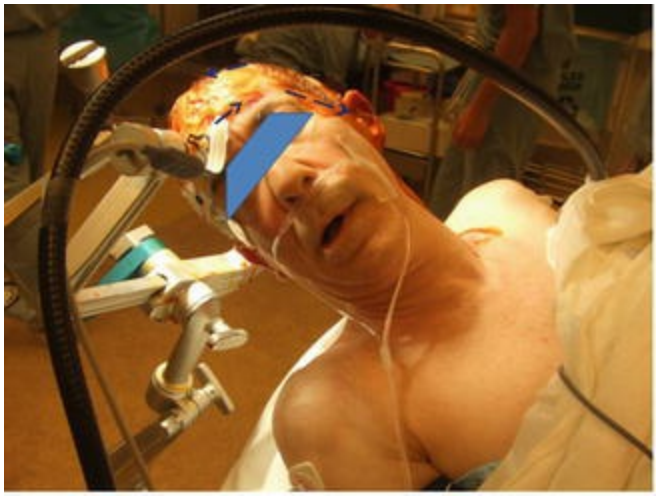

Fig. 18.1 Flexile screen placed at the head of the table serves to protect the face, enable communication with the patient, and to monitor the airway

The anesthesiologist will need to assess the patient after positioning to further plan for management of the airway by inserting a laryngeal mask airway (LMA) or direct laryngoscopy using a flexible fiberscope should the clinical situation arise. In some situations, the use of a nasal airway placed under topical anesthesia may be used to prevent soft tissue obstruction throughout the operation. Some anesthesiologists prefer to manage the airway differently and elect to place an LMA or a nasal endotracheal tube under local anesthesia from the start.

Monitoring

As in general anesthesia , standard monitoring includes electrocardiogram , blood pressure and respiratory rate, end-expiratory CO_2, pulse oximetry, urine output, and a monitor to assess the depth of sedation (*see* Chap. 11, "Clinical Application of Raw and Processed EEG"). Monitoring by direct observation offers valuable information regarding the patient's comfort level, specialized neurologic testing, and fosters trust and allays anxiety.

Throughout the procedure, oxygen is delivered to the patient by nasal cannula or by face mask. Both of these devices should be attached to a line for continuous monitoring of end-expiratory CO_2 and the respiratory rate. Monitoring the respiratory rate will guide the administration of opioids. Should the decision be made to insert an arterial line, it should be done very gently under local anesthesia or under deep sedation in the asleep–awake–

asleep technique (*see* further discussion). Use of an arterial line minimizes discomfort from the frequent inflation of the blood pressure cuff, provides continuous blood pressure measurement, and facilitates sampling for arterial blood gases and other values. Some centers use a simple processed electroencephalogram (EEG) to guide the administration of propofol and other sedatives.

Sedation and Analgesia

Sedative and analgesic medications are generally used in preparation for surgery and during the first and third stages of the procedure [12–15]. A variety of agents may be used for sedation and analgesia. Midazolam is useful as a premedication while short-acting agents that are more easily titrated are used during surgery. Midazolam is frequently avoided if electrocorticography is planned for seizure mapping or in older patients who may not be able to cooperate during testing.

Propofol is the agent most used for sedation during surgery as it is a short-acting drug that has a fast onset of action and a short recovery period [15–18]. At low concentrations, propofol has the added advantage of antiemetic effects by its action on the cannabinoid receptors [19]. The administration of propofol may be guided by the use of continuous monitoring of the processed EEG [16, 17]. Opioids may be administered during surgery to supplement analgesia in the event that there is discomfort from a patchy regional block, positioning, or the urinary catheter. A variety of opioids may be administered either as bolus injections or by infusion. A fast-acting opioid with a short half-life and rapid recovery such as remifentanil has all of these advantages [20] and is our opioid of choice. In our practice, we start remifentanil at 0.1 μg/kg/min and adjust the infusion rate to keep respiratory rate between 8 and 12 breaths per minute before starting a low-dose propofol, which is usually less than 25 μg/kg/min. It is not unusual for some patients to require a higher dose of remifentanil, up to 0.18 μg/kg/min, while some other patients may require a lesser dose. Therefore, it is essential to monitor respiratory rate and reach the proper remifentanil infused dose before the start of the propofol infusion. The use of optimal narcotic dose helps the patient to tolerate surgical position and discomfort of the urinary catheter. Others use higher doses of propofol and lower remifentanil. It is important to have propofol and remifentanil infusions enter the intravenous line at the catheter or to use dedicated intravenous lines

to prevent inadvertent bolus injections.

Dexmedetomidine is a selective alpha-2 adrenergic agonist that works on the subcortical level (locus ceruleus) and has been used to provide sedation and some analgesia without respiratory depression; however, it has no amnesia [21]. Dexmedetomidine acts at the brainstem and in many parts of the body, including the smooth muscles of the blood vessels, thus explaining why higher doses can result in bradycardia and hypotension. Dexmedetomidine has a rapid onset, is metabolized by the liver, and excreted by the kidney. Dexmedetomidine has a distribution half-life of 6 min and a clearance half-life of 2 h, which is longer than propofol . It was first used in functional neurosurgery by Bekker et al. [22] and its use has been supported by others [23, 24]. Typical doses of dexmedetomidine used to achieve the desired level of sedation and analgesia range between 0.2 and 0.6 μg/kg/h administered by continuous infusion [25].

Regional Anesthesia

Regional anesthetic blocks of nerves innervating the scalp are superior to local infiltration to blunt the responses to Mayfield pin placement and surgical stimulation, and to provide postoperative pain control [26–28]. A variety of local anesthetic agents may be used for the regional anesthesia. Long-acting agents with minimal side effects in combination with epinephrine in a final concentration 1:200,000 are often used. The goal is to achieve a block that lasts for the duration of the procedure and afterward to afford postoperative pain relief.

The scalp is innervated, on each side, by six nerves (Fig. 18.2), four of which are branches of the trigeminal nerve and two originate in the cervical region. The four branches of the trigeminal nerve are the Supratrochlear, Supraorbital, Zygomaticotemporal, and Auriculotemporal. The lesser and greater occipital nerves originate from branches of the second and third cervical nerve roots [2, 26, 29–31]. These nerves may be blocked individually or captured in a continuous ring. Individual blocks have longer duration and require the use of less medication and thus lower the risk of possible side effects. The details of regional anesthesia of the scalp are presented in Table 18.1. All injections are done after negative aspiration.

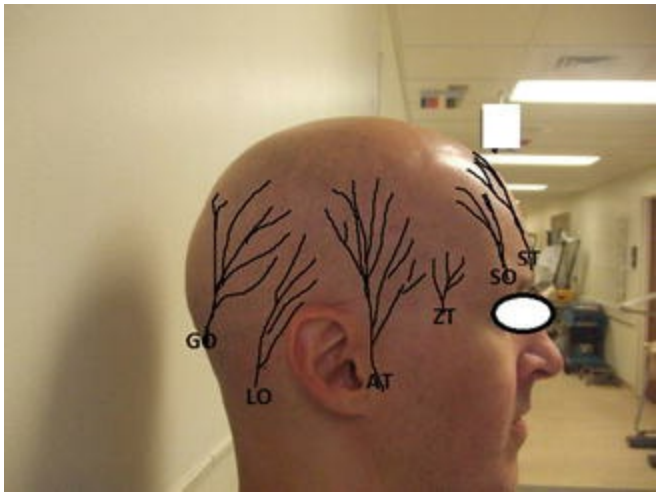

Fig. 18.2 Picture of the head shows drawing of the six nerves that innervate the scalp . GO is greater occipital nerve, LO is lesser occipital nerve, AT is auriculotemporal nerve, ZT is zygomaticotemporal nerve, SO is supra orbital nerve, and ST is supratrochlear nerve

Table 18.1 Regional anesthesia of the scalp, doses used at Northwestern University

Supratrochlear branch Video 18.1-ST	Blocked at the supratrochlear notch, which easily can be palpated where the bridge of the nose meets the supraorbital ridge. The direction of the short 25G needle should be perpendicular to the notch to prevent the needle from sliding down into the orbit or up toward the forehead (Video 18.1)	1 mL
Supraorbital branch Video 18.2-SO	Blocked at the supraorbital notch in the middle of the upper eyebrow usually in direct line with the pupil of the eye. The short 25G needle should be directly perpendicular to the notch to prevent the needle from sliding down into the orbit or up toward the forehead (Video 18.2)	1 mL
Zygomaticotemporal branch	Blocked at a point just above the zygomatic arch lateral to midway between the orbital edge and the tragus of the ear	3–5 mL
Video 18.3-ZT	The 25G needle, 38 mm long, is inserted to the surface of the temporal bone and slides forward toward the orbit. After negative aspiration, 3 mL local anesthetic injected, the needle withdrawn one cm then 1 cm^3 anesthetic injected. Again the needle withdrawn 1 cm followed by the injection of 1 cm^3 more of local anesthetics. This is performed at the side of surgery. The nonsurgical side, only 3 cm^3 are injected	
Auriculotemporal branch Video 18.4-AT	Blocked 1 cm above the tragus just posterior to the superficial temporal artery. This modification is to avoid possible facial nerve palsy [32]	3 mL
Lesser occipital nerves Video 18.5-LO	The lesser occipital nerve is blocked by the injection of local anesthetics in the grove palpated just behind the mastoid at straight line behind the tragus (video 18.2). An alternative method is to perform the block at 2.5 cm lateral to the greater occipital nerve block along the superior nuchal line	3 mL

Greater occipital nerves	Blocked at the superior nuchal line just medial to the occipital artery or one-third of the distance along a line drawn from the greater occipital protuberance and the mastoid	3 mL
Video 18.6-GO		

The choice of local anesthetic for the scalp blocks should be one with a rapid onset and a long duration. Many agents may be used including bupivacaine, lidocaine, ropivacaine, levobupivacaine, and tetracaine. Epinephrine in a final concentration of 1:200,000 may be used in conjunction with these agents to prolong the duration of the block. Our current practice at Northwestern University incorporates the use of 6 mL of tetracaine 1 % (60 mg) mixed with 30 mL of 1 % lidocaine with epinephrine 1:200,000 (300 mg). We perform bilateral blocks of the six nerves. The total volume injected of this mixture, lidocaine/tetracaine , is 30 mL, which contains 50 mg tetracaine and 250 mg lidocaine. This technique reliably enables us to immediately place the three pins head holder comfortably. Also, it is associated with stable vital signs, provides 8 h of surgical time, and up to 22 h of pain relief. In 9 years, we have had no side effects or local anesthetic toxicity to report. In most cases, regional anesthesia of the scalp provides sufficient surgical anesthesia for the duration of the surgery. Should a patient experience pain after the craniotomy while mapping, the scalp blocks may be supplemented with a dural block as described in the following section.

A faster, though less specific approach to anesthesia of the scalp is provided by infiltrating in a line that essentially connects the injection sites of the six branches at their roots in addition to infiltrating the surgical incision site with a field block. This approach leads to a less solid block and is associated with the use of higher doses of local anesthetic.

Anesthetic Management

The anesthetic management for neurosurgical procedures in patients that are awake may be divided into at least three categories. The first may be termed *Asleep Awake Asleep* (AAA). Variations of this technique are used by many anesthesiologists [15, 23, 31–36]. In the early stages of the procedure including provision of anesthesia for the scalp, Mayfield pin insertion, skin incision, craniotomy, and provision of anesthesia of the dura, general anesthesia is provided to assure patient comfort. The patient is anesthetized with a combination of short-acting agents such as propofol, or dexmedetomidine and an ultra-short-acting opioid. Airway management may

be augmented by insertion of an LMA or a nasal endotracheal tube. The nasal endotracheal tube is placed into the trachea in the initial or “Asleep” stage, withdrawn to the level of the pharynx in the second or “Awake” stage, and reintroduced back to the trachea during the final “Asleep ” stage. The anesthetic technique preferred at the second author’s institution, is deep sedation with a nasal endotracheal tube positioned in the posterior pharynx under fiber optic control, which remains in place throughout surgery. This ensures safe airway management with spontaneous ventilation during the craniotomy and allows a smooth transition to an awake patient who is able to participate and speak without airway irritation. It also provides a mechanism for a safe and efficient endotracheal intubation if warranted during closure or at any point in case of emergency.

When an LMA is utilized, it is positioned around the vocal cords during the first and last stages of the surgery. The disadvantages of this technique are the potential for irritation of the airway during endotracheal tube or LMA manipulation, and for paradoxical responses to the anesthetics administered during the intermediate “Awake” stage. Another potential problem is that of movement of the head during the transitions between anesthetic depths with the risk of patient injury.

In the AAA technique , during the “awake” phase, the surgeon may need to anesthetize the dura before incising it. If needed, a short-acting anesthetic agent such as mepivacaine or lidocaine would suffice for the roughly 2 h needed for brain mapping and tumor resection in the awake patient. Dural anesthesia may be achieved during the transition from sedation after the craniotomy has been completed in one of two ways: the meningeal trigeminal branches may be blocked by injecting a local anesthetic into the base of the projected dural flap with a fine (25–30 gauge) needle. In elderly patients or others in which the dura is very thin, this procedure carries a risk of damaging cortical vessels and causing a subdural hematoma. In our experience (Bonn University), a very effective method uses anesthetic-soaked cottonoids or compresses applied to cover the dural flap for 5 min before incision, and on the base of the dural flap until closure. For example, 10–20 mL of 1 % mepivacaine is sufficient for a large craniotomy. This application technique provides rapid anesthesia to the dura, does not interfere with the progress of the procedure, and contributes little to the total volume of local anesthetic with regards to the risk of systemic local anesthetic toxicity.

Another anesthetic management technique, and the preferred method at the first author's institution, is one that provides sedation along a spectrum of different depths while maintaining the patient in an awake or readily arousal state. This is commonly referred to as *monitored anesthesia care (MAC) with sedation*. In this technique, we use remifentanil at higher doses (0.05–0.18 μg/kg/min) to maintain a respiratory rate of 8–12 in addition to a small infusion of propofol, which is usually less than 25 μg/kg/min. The patient will be awake at all times with varying degrees of sedation and analgesia to maintain good ventilation, oxygenation, and a clear airway.

Recently, the complete awake–awake–awake technique without sedation has been advocated by Hansen et al. [11]. In this technique, medication is substituted by psychologic intervention.

Cortical and Subcortical Mapping and Neurologic Monitoring

Surgery performed on a patient who is awake and cooperative allows for testing of all neurologic functions. The utility of the technique is limited, however, by the total duration of the procedure , the patient's position, and the operative setting. Completion of the procedure in less than 2 h is optimal as the patient's position may be difficult to tolerate for extended periods of time. During an awake procedure performed with continuous sedation, the patient often tolerates longer periods of operative time.

The specific test of neurologic function is dependent on the location of the target lesion. Motor function may be difficult to monitor clinically. However, motor and sensory function can be assessed in the anesthetized patient with neurophysiologic methods. Cognitive functions such as language, calculation, spatial orientation, memory, and even emotion may also be tested under awake conditions. However, there are no established intraoperative protocols for these assessments. Typically, surgery in an awake patient is all but required for language preservation in the face of lesions of the left or dominant hemisphere.

Language testing requires some linguistic expertise and is frequently performed by a dedicated psychologist or linguist. Apart from specific expertise in language testing, reassurance and support for the patient undergoing a craniotomy while awake is a key factor for successful mapping and monitoring. An experienced anesthesiologist with interest in and

familiarity with these procedures may perform the testing. There is broad consensus among groups performing awake surgery that a naming paradigm is suited to map and monitor the essential aspects of language function [37]. A picture of an object is presented for 4 s and is named by the patient, often embedded into a carrier sentence such as “This is a banana.” During this time, the surgeon does or does not stimulate the cortex or the subcortical fibers.

Neurologic testing comprises both mapping and monitoring. Using the example of language production, mapping refers to the identification and delineation of eloquent cortical areas and subcortical fiber tracts, which are involved in preserving these structures during lesion resection. Monitoring refers to continuous or intermittent testing of some target function in order to detect and avert functional impairment due to ischemia or other insult. These are complementary aspects of intraoperative functional preservation. Mapping requires electrical stimulation of the cortex or the white matter in order to elicit or, more frequently, inhibit a neurologic function. In these cases, the patient may perceive a “tugging” or motor movement that is not perceptible to the observant anesthesiologist.

Cortical areas where reproducible speech inhibition by stimulation is encountered, are defined as essential for language production. However, there is no reproducible evidence to date that proves that all of these areas are truly indispensable. Typically, bipolar electrical stimulation at a frequency of 50–60 Hz for 1–4 s is employed (Ojemann stimulator). However, stimulation using a high-frequency stimulator, similar to that used for transcranial motor evoked potential stimulation, can be used and is associated with a lower incidence of induced seizures [37–39]. The stimulation parameters are discussed by Szelenyi et al. [40]. It is important to avoid the induction of clinical or subclinical seizures from excessive cortical stimulation [41]. Ideally, the stimulation threshold for after discharges (as a prestage of seizure) is determined by electrocorticography (ECoG) recordings from strip electrodes positioned around the target area, prior to the actual mapping procedure.

Induction of clinical or subclinical focal seizures is rarely dangerous. However, such activity can distort the mapping results, prompting the need for intervention. Irrigating the surgical field with cold Lactated Ringers solution is usually sufficient to interrupt the seizure activity [42]. Sedative drugs such as benzodiazepines should be avoided in order to preserve the

patient’s wakefulness and cooperation for further testing. However, a small dose of propofol (25–50 mg) may be needed if cold irrigation is inadequate. Secondary generalization of seizures hardly ever occurs and can be handled as indicated in the next paragraph.

Complications

Craniotomies, whether they are performed under general, MAC, or AAA anesthesia, are associated with the same complications [2, 31]. As cited, seizures may occur as a result of stimulation during neurologic testing or from excessive use of local anesthetics. Depression of ventilation due to heavy sedation or opioid use may lead to hypercarbia and/or hypoxemia. This may be minimized by careful monitoring and the use of short-acting agents in dedicated intravenous lines. Nausea and vomiting are troublesome intraoperative issues for awake patients and may be minimized by pretreatment with antiemetic medications and the use of low doses of propofol infusion. Nausea related to surgical maneuvers and direct dural irritation may be difficult to prevent and treat pharmacologically and may be relieved only by decreasing surgical stimulation. The ambient room temperature should be adjusted to the liking of the patient and intravenous fluids should be warmed to prevent and minimize shivering. If shivering occurs despite these other maneuvers, it may be effectively treated with medication such as small doses of meperidine, clonidine, or physostigmine. Hemodynamic changes such as hypertension may occur and can be easily treated with beta-blockers and medication to ease anxiety. Pain as a result of poor local anesthesia may occur and should be supplemented by analgesic agents and additional infiltration of local anesthetics, if appropriate. The possibility of local anesthetic toxicity should be kept in mind and the total dose of infiltrated local anesthetics should be calculated and tracked including local anesthetics used during the insertion of the Foley catheter. At times, sedation may yield a paradoxical effect and lead to disinhibition and a lack of cooperation. In this case, the infusion of a sedative or analgesic medication may be decreased or stopped until the patient returns to an appropriate baseline or may require pharmacologic reversal. Seizures may occur during neurologic testing and can be treated as described in the previous section. Significant blood loss may be a complication. The incidence of air embolism is actually increased during awake craniotomies due to the negative intrathoracic pressure, with coughing being the first sign.

Complications related to performing the scalp blocks, such as nerve injury, intravenous and intra-arterial injection, intracranial injection, infection, and facial nerve palsy can occur [43]. To minimize such complications, we modified the auriculotemporal block by performing the block 1 cm above the tragus just behind the superficial artery and decreasing the volume from 5 to 3 mL [32].

Anesthesia for Awake Neurovascular Procedures

Awake craniotomies have been used during cerebral aneurysm surgery, resection of AVMs, and extracranial to intracranial (EC-IC) bypass surgery for Moya-Moya disease to enable the team to perform immediate neurologic exams during surgery [44–46].

Anesthesia for Awake Deep Brain Stimulation

Deep brain stimulation (DBS) is a specific procedure performed in an awake patient. The procedure is performed using a stereotactic technique and has proved beneficial in the treatment of central movement disorders, epilepsy, psychiatric disorders, and obesity [47, 48]. In the case of Parkinson's disease, it has emerged as a therapeutic modality [49–51].

If a deep brain electrode is to be placed on only one side of the brain, then it should be mentioned that clinical motor testing will be conducted on the contralateral upper extremity. For this reason, the intravenous line, arterial line (frequently used to monitor hypertension), and noninvasive blood pressure cuff should all be placed on the ipsilateral arm to avoid interfering with the clinical testing. In the anesthetic management for DBS, infusions of short-acting agents may be used (e.g., propofol, remifentanil). And these agents are avoided during single unit acquisition. Medication administration should be stopped in time to allow recovery before actual neurologic testing so that the nucleus may be identified [52]. Gamma-aminobutyric acid (GABA) receptor-mediated medication (e.g., benzodiazepines) should be avoided because they may inhibit the tremor, which is the endpoint of awake testing. Most anesthetics that act on GABA receptors interfere with the DBS testing and should be used with care [53]. Even ultra-short-acting agents such as propofol and remifentanil should be stopped intraoperatively in time for testing as both agents have been reported to interfere with accurate results

[54]. Certain medications may interfere with the neurologic testing and should not be administered during DBS procedures such as phenothiazine, droperidol, and metoclopramide [55, 56]. The α-2 receptor agonist and to a lesser degree the μ-opioid receptor agonist dexmedetomidine can be used as it has no effect on the microelectrode recording (MER) testing. Frequently encountered, intraoperative hypertension must be aggressively treated to avoid intracranial bleeding (often below 140 mmHg) and hydralazine and infusions of sodium nitroprusside, nitroglycerine, or nicardipine are used (beta-blocking agents are avoided since they may reduce the tremor activity).

Unwanted side effects to the insertion of DBS electrodes may include motor phenomena such as muscle contractions or dysphasia from stimulating the corticospinal or corticobulbar efferent of the internal capsule. In such cases, electrodes are repositioned. Others may include sensory perceptions including transient paresthesia or visual flashes. (For more information on DBS testing and monitoring, *see* Chap. 5, "Deep Brain Stimulation.")

Certain complications may occur during DBS procedures. These include respiratory depression, airway obstruction, hypoxemia, nausea, vomiting, seizures, hypertension, sneezing, bronchospasm, pulmonary edema, angina, and air embolism [53, 57]. Some complications may occur in the postoperative period, such as bleeding, seizures, or a neurologic deficit [57]. In general, there is no one anesthesia protocol, but a variety of methods, often influenced by personal experiences, that are not necessarily supported by solid literature.

Anesthesia for Awake Seizure Surgery

Seizures are found in 5.1 % of the world population. Of the patients treated in the United States , up to 30–40 % are resistant to medical management and require more aggressive surgical treatment. Resections of the seizure focus near the eloquent area carry a relatively high risk of postoperative neurologic deficits. Recent advances in structural imaging, functional testing, and stereotactic surgery, in addition to awake craniotomies, have minimized that risk. Awake craniotomies are considered when the lesion is near the eloquent area and precise resection may spare damage to critical centers [13].

Chronically implanted subdural grid and strip electrodes, as well as stereotactically implanted depth electrodes, can be used for functional mapping as an alternative to awake surgery in children, for example. These

patients have an initial procedure performed under general anesthesia for implantation of the subdural grid and electrodes. The initial postoperative period provides unlimited testing time for more complex cognitive paradigms and higher test–retest reliability [58]. The disadvantage of this approach is that the patient must have two separate surgical procedures with the associated risks. Although it has been adopted for regular brain tumor surgery it has not gained wide acceptance for this application [58]. (For more details, *see* Chap. 45, “Epilepsy and Seizures: OR and ICU Applications of EEG.”)

Anesthesia for Awake Carotid Surgery

Carotid stenosis in excess of 70 % is associated with an increased risk of stroke, especially if associated with a transient ischemic attack (TIA) . To minimize such risk, patients may undergo carotid endarterectomy, carotid angioplasty, or stenting as a preventive measure to decrease the likelihood of a cerebrovascular accident. These procedures are associated with an intraoperative risk of stroke due to either ischemia or embolization. To minimize the risk of ischemia, a shunt may be inserted to provide blood flow to the ipsilateral hemisphere. Placement of the shunt, however, may be associated with stroke due to embolization or carotid dissection. As a result, the question of whether or not to shunt during carotid surgery remains unsettled [59].

Many methods have been used to minimize the risk of shunts yet still be assured of the maintenance of adequate cerebral blood flow [59–61]. These may be divided into two categories: cerebral blood flow measurements and neurophysiologic monitoring. Cerebral blood flow may be measured directly or indirectly by transcranial Doppler (*see* Chap. 13, “Transcranial Doppler”), jugular bulb monitoring (*see* Chap. 14, “Monitoring of Jugular Venous Oxygen Saturation”), near infrared spectroscopy (*see* Chap. 12, “Near-Infrared Spectroscopy”), and measurements of stump pressure. Neurophysiologic testing may be used to assess continued cerebral circulation in the patient that is either awake or asleep. In the awake patient, responses to verbal commands may be used to reflect adequate perfusion. In the patient under general anesthesia, neurophysiologic monitoring using EEG (*see* Chap. 10, “EEG Monitoring”) and/or SSEPs (*see* Chap. 1, “Somatosensory Evoked Potentials”) may be successfully used to assess the adequacy of blood flow to the brain.

Carotid surgery in the awake patient provides a sensitive and specific method for evaluating cerebral circulation and brain function but requires an experienced anesthesiologist; surgeon; and cooperative, motivated patient. The patient's responses to verbal commands by demonstrating their ability to move the contralateral hand is a sensitive method that will identify patients who require shunt placement. While the literature is divided between the use of regional and general anesthesia and the recent large (GALA [General Anesthetic versus Local Anesthetic for Carotid Surgery]) study that failed to show differences with regards to neurologic outcome, there are advantages to the use of a regional technique [62–64]. Those advantages include a lower incidence of shunt placement, shorter hospital stay, cost savings, and fewer cardiovascular and pulmonary complications [62].

Sedation

The ingredients for success in carotid surgery in the awake patient include a gentle and efficient surgical team, an anesthesiologist familiar with performing regional blocks, and an informed and cooperative patient . The entire team, including the patient, should be briefed regarding the planned surgery and anesthetic management as in the case of the awake patient for tumor resection. The patient should be comfortably positioned on the operating room table. The head of the table should be slightly elevated. A flexible screen should be positioned over the patient's head to ensure visualization of the patient's face, access to the airway, and protection from inadvertent pressure on the face by the surgical team. Continuous verbal communication with the patient serves to ease anxiety and assure neurologic monitoring. A propofol infusion of 25–50 μg/kg/min provides both a sedative and antiemetic effect. It may be supplemented with the use of a short-acting opioid such as remifentanil (0.03–0.07 μg/kg/min) to provide analgesia while maintaining adequate ventilation. These patients may experience pain during stimulation of the unblocked recurrent laryngeal nerve or pressure traction against the mandible. Alternatively, an agent such as dexmedetomidine may be used to provide sedation and analgesia but its use may be associated with an increase in the incidence of shunt placement [65]. During carotid cross-clamping, patients may benefit from an enriched inspired oxygen concentration. This benefit may be related to the increase in the amount of dissolved oxygen, which is directly related to the oxygen partial pressure [66].

Anesthesia

Regional anesthesia can be achieved by several methods [62]. Although described in the literature , a cervical epidural block produces anesthesia bilaterally and carries with it a significant risk of cardiovascular compromise. Local infiltration has also been described but is rarely used by surgeons. A deep cervical block is adequate for surgery and may be achieved either in a single injection from the interscalene approach [67] or by individually blocking the C2 through C4 nerve roots [68]. In the single injection technique, a 22-gauge B-Bevel needle is used to enlist a paresthesia at the C3 level. Injection of 20 mL of local anesthetic provides a block of all three nerve roots as the local spreads up and down. For individual nerve blocks, needles are inserted from points behind the sternocleidomastoid (SCM) muscle, and directed medial and caudal to enlist a paresthesia from each of the corresponding nerves . Five milliliters of local anesthetic may be injected at each level. Problems associated with both of these methods include the inadvertent injection of local anesthetic into the intrathecal or epidural space, an intra-arterial injection, blocking the phrenic nerve, or cervical sympathetic blockade with development of a Horner's syndrome.

The superficial cervical block has the advantages of the deep cervical block but with fewer complications. This is the technique we use at Northwestern University (Fig. 18.3). We utilize a mixture of 40 mg of tetracaine and 30 mL of 1 % lidocaine. A needle is inserted at the level of C3, 1.5 cm posterior to the posterior border of the SCM muscle. Subcutaneous infiltration includes 5 mL of local anesthetic infiltrated superiorly to the mastoid process and 10 mL inferiorly to the sternal notch. From an entry point at C3, 5 mL of the local anesthetic are used to infiltrate subcutaneously anterior to the midline. From the same entry point at C3, 5 mL should be injected deep to the belly of the SCM, where the three branches exit from the nerve roots. A total of 25 mL of the local anesthetic is enough to achieve a block.

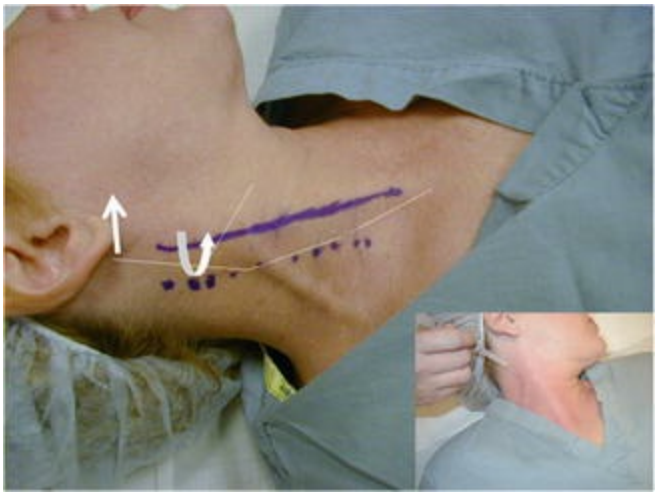

Fig. 18.3 Drawing shows the location of the superficial cervical block

Complete anesthesia is difficult to obtain with the deep and superficial blocks performed alone or in combination. The pain may originate from the inferior alveolar nerve at the angle of the mandible and the patient may experience a tooth ache. This is generally caused by surgical retraction on the lower mandible and may be relieved by adjusting the retractor. An alternative method is to block the inferior alveolar nerve.

Despite the regional technique , the patient may feel some pain during the dissection of the carotid artery or exhibit a profound bradycardia. The deep and superficial cervical blocks do not block the recurrent laryngeal nerve that innervates the carotid body and carotid sinus. Surgical manipulation or retraction about the carotid bifurcation may be the cause. This effect may be blocked by the instillation of 2 mL of local anesthetic directly into the surgical field.

Neurologic Monitoring

An awake, cooperative patient able to respond to questions and to confirm motor strength in the contralateral arm constitutes the best neurologic monitoring [69]. For this reason, sedation administration should be judicious and oversedation avoided. Prior to incision, patients are asked to rehearse a requested motor task, such as squeezing a horn or a device capable of transducing the generated pressure from their contralateral hand. The test should be repeated early in the surgery and then at frequent intervals. Our plan includes periodic verbal instructions for the patient to perform the motor

task every minute for 4 min, every 2 min up to 10 min, and then at 5-min intervals until the carotid is unclamped. Because the patient must understand the directive and perform the task, we are monitoring not only motor strength but mental status. Should the patient not understand the directive or be unable to perform the task in the first 4 min after carotid cross-clamping, then the surgeon may elect to insert a shunt. Overall, the incidence of shunt placement is less than 10 % during awake carotid surgery [60].

Carotid stump pressure higher than 50 mmHg is considered a good indicator for sufficient flow, while a lower stump pressure may indicate poor collateral circulation and the need for shunt placement [70]. The stump pressure measurement is obtained by inserting a small gauge needle into the carotid stump and connecting it to a pressure transducer. Unfortunately, there is no general agreement in the literature regarding the validity of the information obtained from stump pressure measurements [60, 69, 71].

Near-infrared cerebral oximetry can be used to detect a drop in regional cerebral oxygen saturation of the anterior cerebral artery distribution at the time of the carotid cross-clamp. Unfortunately, there is not a commonly accepted threshold for the drop in saturation that would predict the need for shunt insertion [72]. It is recommended to establish a baseline after the monitor is connected and oxygenation established. For more information, *see* Chaps. 12 (“Near-Infrared Spectroscopy” and 30 “Carotid Surgery”).

The monitoring of venous oxygen saturation (SjO_2) from the jugular bulb is not commonly used during carotid endarterectomy surgery. The sensitivity and specificity for SjO_2 is not high enough to make it the sole driver for decision-making with regards to shunt placement [61]. For more details, *see* Chap. 14, “Monitoring of Jugular Venous Oxygen Saturation.”

Conclusion

Regional and local anesthesia in neurosurgery has clear advantages for testing neurologic functions that cannot be monitored easily. Its use provides excellent operating conditions in an awake patient for surgery in or near the eloquent areas, resection of seizure foci, and carotid endarterectomy. This technique also enables the operative team to optimize localization during deep brain stimulation. The awake patient provides one of the best neurologic monitors. The use of this monitor as an adjunct guides decision-making for shunt placement during carotid endarterectomy, minimizes the incidence of

postoperative neurologic deficits, promotes maximal tumor resection, shortens hospital stay, and is associated with fewer complications.

Questions

1. Awake craniotomies can be done in the following methods

    a. Sleep, awake, sleep

    b. Sedated, awake, sedated

    c. Awake, awake, awake

    d. A and b

    e. All of the above

2. Sleep awake sleep is usually done by the following methods except

    a. LMA awake LMA

    b. Nasal intubation awake nasal intubation

    c. Deep sedation, awake, deep sedation

    d. Oral intubation, awake, oral intubation

3. Awake carotid surgery can be performed under the following techniques except

    a. Deep cervical blocks

    b. Super facial cervical blocks

c. Cervical epidural block

d. Cervical spinal anesthesia

e. None of the above

4. During deep brain stimulation, the use of midazolam for premedication is greatly encouraged to help sedate the patient.

   a. True

   b. False

5. In calculating the total dose of local anesthetics, we should add

   a. Local anesthetics used by the anesthesiologist

   b. Local anesthetics used by the surgeon to infiltrate the field

   c. Local anesthetics that may be used for pinning

   d. Local anesthetics used to place the Foley catheter

   e. All of the above

Answers

1. E

2. D

3. D

4. False

5. E

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Footnotes

1 Key references marked with asterisk.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_19

19. Anesthesia Management and Intraoperative Electrophysiological Monitoring

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Keywords Anesthesia management – Intraoperative electrophysiological monitoring – Anesthetic effects – Electroencephalogram – Evoked potentials – Physiological considerations – Halogenated inhalational agents – Intravenous agents

Key Learning Points

- The techniques of IOM can be divided into four groups by whether they depend on muscle responses and are therefore sensitive to the use of neuromuscular blocking agents (NMBA) and whether they are markedly depressed by halogenated agents.
- It is currently believed that the action of anesthetic agents is primarily mediated through changes in synaptic function by their interaction with specific receptors.

- Since the EEG is produced by cortical synapses, anesthetic agents alter EEG monitoring. A regular progression of activation, then drop in frequency and amplitude, burst suppression and electrical silence is typical of many agents.
- In general for each IOM modality, the effects of anesthetic agents can be somewhat predicted by noting the location of synapses within the neural pathway.
- Additional insight into the action of anesthetics on evoked responses is given by examining the neural mechanisms of anesthetics that result in the behavioral goals of amnesia, unconsciousness, immobility, blocking of noxious sensory stimuli (antinociception), and muscle relaxation.
- With unconsciousness, immobility (lack of movement to noxious sensory stimuli) is the consequence of anesthetic action blocking noxious stimuli and interrupting the reflex pathway in the spinal cord.
- MEP is the most difficult technique to record under General Anesthesia with TIVA being the most supportive.
- In some patients MEP can be recorded using TIVA supplemented with ½ MAC desflurane or sevoflurane.

Anesthetic agents used to produce general anesthesia and physiological management during procedures have an impact on the ability of intraoperative neurophysiological monitoring (IOM) to be conducted. The most challenging circumstances are when the monitoring techniques used are sensitive to anesthetic agents, making the agent choice difficult. This chapter will discuss the general principles behind the effects of anesthetic agents and the known effects on electrophysiological monitoring. The specific choice of anesthetic agents will depend on the patient, the effects of the agents, the monitoring techniques used, and the anesthetic goals.

Impact of IOM Technique and Patient Comorbidity

In general, the strategy for choosing a supportive anesthetic begins with the modalities planned for IOM. The techniques can be divided into four groups by whether they depend on muscle responses and are therefore sensitive to the use of neuromuscular blocking agents (NMBA) and whether they are

markedly depressed by halogenated agents (Fig. 19.1). If only sensitive to NMBA, the anesthetic can be designed with the free use of halogenated agents but avoid NMBA. If only sensitive to halogenated agents, these must be severely restricted or avoided (i.e., total intravenous anesthesia [TIVA]) but NMBA can be utilized. Unfortunately, many procedures use multiple IOM techniques such that the monitoring is sensitive to both NMBA and halogenated agents.

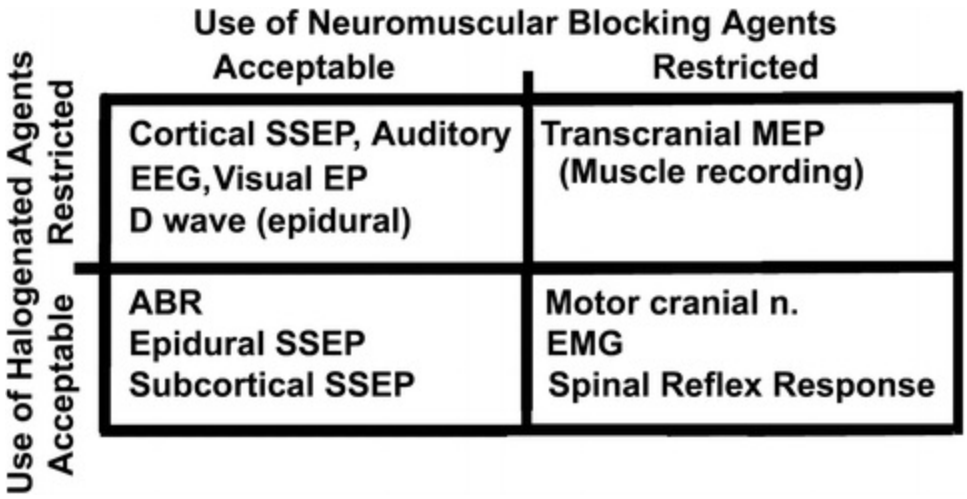

Fig. 19.1 IOM techniques can be divided into four groups depending on susceptibility to the effects of muscle relaxants and to the effects of halogenated anesthetics

The second consideration is how difficult it is to conduct IOM in an individual patient. This is usually a consequence of either immaturity at very young ages or as a consequence of neural pathology, especially in the older patient. This is depicted in Fig. 19.2. Adult patients may have nervous system deficits from age and from neural morbidity such as myelopathy, vascular disease, diabetes, and other primary central nervous system (CNS) pathology. In both of these groups the responses may be difficult to acquire and the anesthesia effects may be more profound. In addition, patients with chronic opioid use can also provide challenges by limiting the effectiveness of opioids, which are usually key agents in the anesthetic. Finally, the chosen anesthetic must address the specific medical comorbidities of the patient and those management aspects necessary for the conduct of the surgery.

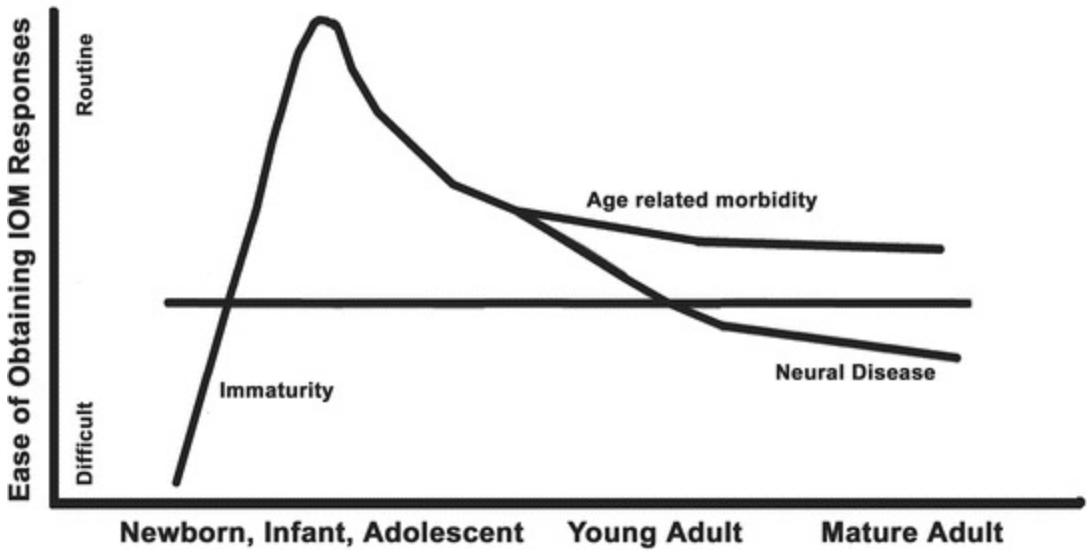

Fig. 19.2 The ease of recording evoked responses varies with patient age, neural immaturity at young ages, and the presence of neural pathology

Mechanism of Drug Action

It is currently believed that although anesthetic agents must have properties of lipid solubility to penetrate into the nervous system, the action of these drugs is primarily mediated through changes in synaptic function by their interaction with specific receptors [1–10]. Differences between agents depend on each one's profile of action on different synaptic receptors, the varying location of those receptors, and the specific subtypes of these receptors involved in their action.

For example, many of these agents increase the inhibitory activity in the major inhibitory synapse by facilitating the effect of γ-amino-butyric acid (GABA) by action at the GABAa receptor [10]. Another common drug effect is inhibition of the major excitatory synapse at the *N*-methyl-D-aspartate (NMDA) receptor [10]. Other synaptic targets include neuronal acetylcholine (nACh), μ opioid receptor, central α2 receptors, potassium, calcium receptors, and the glycine channels (the major inhibitory synapse in the spinal cord) [10]. Muscle relaxation is mediated through acetylcholine receptors located at the neuromuscular junction (mACh) [10]. The combination of effects at these receptors is what gives rise to the effects of general anesthesia as well as the alterations in the electroencephalogram (EEG) and evoked potentials.

Anesthetic Effects on the Electroencephalogram

General Effects

Because the EEG is produced by cortical synapses, anesthetic agents alter EEG monitoring [11] (see Chap. 10, “EEG Monitoring”). Although differences between individuals and anesthetics occur, most anesthetics produce a typical sequence of events with increasing drug levels [12, 13] (Fig. 19.3). At induction, mild activation is seen with rhythmic beta activity replacing the 8- to 10-Hz α rhythm seen in the parietal and superior temporal cortex. With loss of consciousness there is a marked drop in high frequency activity (25–50 Hz gamma-band), an increase in slower frequency theta and delta activity, and a shift in power to the frontal regions. In addition, there is an increase in synchrony of the EEG with variations in activity between regions being reduced including uncoupling of the interaction between frontal and parietal regions and across the midline [13]. As the anesthetic drug effect increases there is a gradual slowing of the frequency and gradual reduction in amplitude and power. Then periods of electrical silence are interspersed with periods of activity (burst suppression) and finally complete electrical silence.

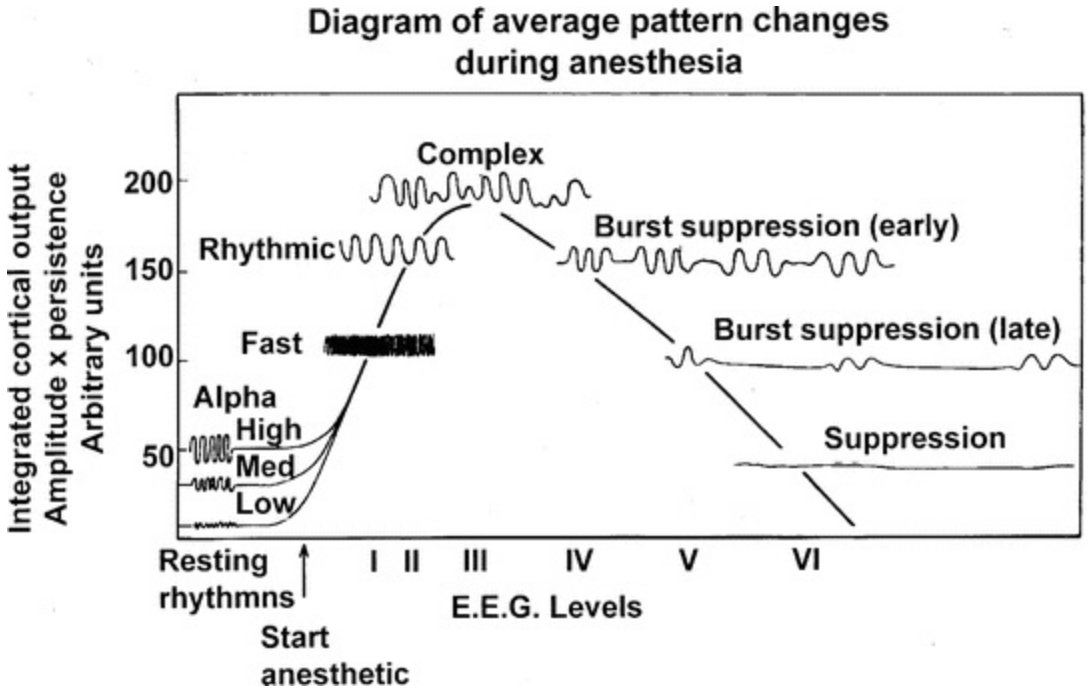

Fig. 19.3 Typical EEG changes with progressively increasing levels of inhalational anesthesia . As shown, the amplitude increases as the variability of the EEG is reduced to synchronous activity in the

8- to 12-Hz range. As anesthesia deepens, the amplitude and frequency decrease, giving way to burst suppression and finally electrocerebral silence. (From Stockard and Bickford [12]; with permission)

The reduction in synaptic activity at burst suppression and electrical silence is associated with a reduction in the associated metabolic activity of approximately 50 % (Fig. 19.4). This depressant effect has been used for the treatment of status epilepticus and for intentional metabolic suppression to improve the balance of nutrient supply and demand such as during surgery in which ischemic injury may occur (e.g., intracranial vascular surgery, cardiac surgery, and carotid surgery). Because burst suppression is associated with near maximal metabolic suppression, this can be used as an end point to monitor the drug administration for metabolic depression.

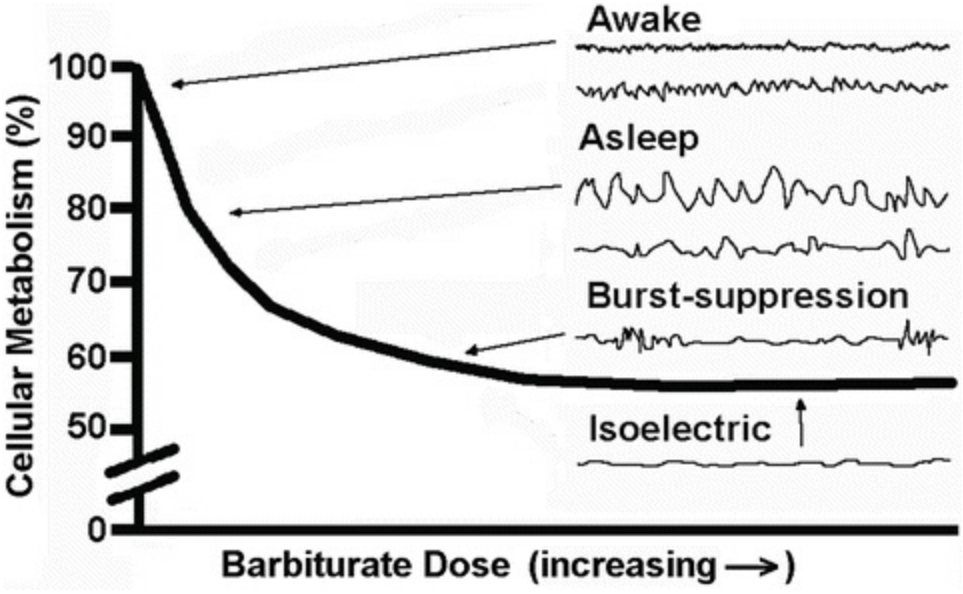

Fig. 19.4 Depiction of the progressive decrease in cerebral metabolism as barbiturate dose is increased until 40–50 % remains. Also shown are typical EEG tracings with increasing doses. Of note is that electrocerebral silence is associated with maximal metabolic suppression and near maximal suppression occurs when burst suppression is seen on the EEG

Specific Drugs and the EEG

Halogenated Agents

The halogenated anesthetic agents produce the typical depression pattern of Fig. 19.3, producing burst suppression at about 1.5 or higher minimum alveolar concentration (MAC) (the MAC of an inhalational agent is the

minimal alveolar concentration of the agent where 50 % of the subjects do not move in response to a painful stimulus) [14]. With increasing age, the brain becomes increasingly sensitive to anesthetics and burst suppression is produced at lower concentrations. Halothane does not follow the typical dose effect of the other agents; it does not readily cause burst suppression but rather a gradual decrease in amplitude with widespread α activity (8–14 Hz) [15].

Not all anesthetic agents produce this general pattern; some can activate the EEG resulting in increased amplitude and frequency with a few ultimately producing epileptiform activity [11]. For example, enflurane and sevoflurane produce EEG changes similar to those of isoflurane but have been associated with increased EEG activity and seizures in some circumstances. With hyperventilation they can produce epileptiform spikes or even electrographic seizures. With these seizures, anesthetic depression of the spinal cord may prevent associated muscular activity (see "Immobility" later) [16]. Sevoflurane can also induce epileptiform activity in patients with epilepsy [17]. Rapid induction with sevoflurane, particularly with hyperventilation and prolonged anesthesia with high concentrations, can produce generalized or focal seizures (even in healthy subjects).

Nitrous Oxide

When used alone, nitrous oxide (N_2O) decreases the frequency and amplitude of α rhythms seen in a restful awake state. It then produces a frontally dominant high frequency (>30 Hz) activity, which coincides with analgesia and depressed consciousness. When combined with halogenated inhalational agents, it can be additive or antagonistic depending on the circumstances and the neurophysiological measure used. Thus, N_2O may be "context sensitive." For example, N_2O has proconvulsant properties or can suppress epileptic spike activity during electrocorticography (ECoG) depending on the other agents used.

Propofol

Propofol produces the typical EEG anesthetic depression described earlier, including burst suppression and electrical silence at higher doses [18]. As such, propofol has been used for the treatment of status epilepticus and to

produce metabolic depression. Despite its seizure-suppressive activity, propofol has become a popular agent for conscious sedation during surgery to identify and ablate seizure foci because its rapid metabolism allows it to be eliminated when awake testing and ECoG is desired.

Etomidate

Etomidate produces the typical EEG anesthetic depression pattern described earlier. Like propofol, it has been used to produce EEG silence and metabolic depression and should be avoided at larger doses during cortical mapping for seizure foci. Different than propofol, at low doses (0.1 mg/kg) it may enhance the detection of seizure foci by evoking native epileptic seizures in patients [19].

Barbiturates

Barbiturates follow the typical pattern of EEG progression described earlier leading to electrical silence. They are the classic agents to produce metabolic depression ("barbiturate coma"). Not typical of all barbiturates, low-dose methohexital (0.5 mg/kg) has been used like etomidate to enhance epileptic spike activity during electrocorticography (ECoG) in surgery to identify seizure foci [19].

Benzodiazepines

Most benzodiazepines produce the typical EEG anesthetic depression pattern but have a less profound effect on the EEG, usually generalized slowing into the theta and delta range at high doses without progressing to burst suppression. They have potent anticonvulsant effects such that they should be avoided if cortical mapping for seizure foci is planned. Midazolam can produce burst suppression and this is used in treatment of status epilepticus.

Dexmedetomidine

Dexmedetomidine activates endogenous nonrapid eye movement sleep-promoting pathways producing an EEG, which is very similar to slow wave sleep [13]. It is not reported to produce burst suppression but has been shown to reduce the thiopental dose requirement for burst suppression by 30 % [20].

Droperidol

Droperidol has little effect on the EEG when used alone; however, it lowers seizure threshold. It does not appear to produce neuroexcitatory phenomena or induce seizures in epileptic patients. When combined with fentanyl ("neurolept anesthesia"), droperidol increases EEG α activity at low doses. At higher doses, it produces high-amplitude beta and delta activity.

Opioids

Opioids do not appear to produce an initial excitement phase in the EEG and do not produce burst suppression or electrical silence. They do produce a dose-related decrease in frequency of the EEG maintaining amplitude with activity in the delta range. They are frequently used during ECoG in surgery for seizure focus ablation. Some clinicians have found alfentanil useful in enhancing epileptic spikes [13].

Ketamine

Ketamine produces initial suppression of awake α rhythms, and then induces high-amplitude theta activity in the EEG, with an accompanying increase in beta activity [21]. At large doses, polymorphic delta with interspersed beta is reported [22]. Ketamine is thus an excitatory agent producing heightened synaptic function and increased motor tone and muscle movement. Seizures have not generally been observed and it is usually anticonvulsive, but it has been reported to provoke seizure activity in persons with epilepsy but not in normal subjects [23, 24].

Anesthesia Selection and EEG

The choice of anesthetic agents depends on the specific application of the EEG [25]. When monitoring for cerebral ischemia, a choice of drugs that keep the EEG active is desired. For the termination of sustained seizure activity or intentional depression of cerebral metabolic activity, intravenous agents (e.g., propofol) have been used. General anesthesia with the halogenated agents has also been used to treat status epilepticus. For the recording of seizure foci during awake craniotomy for the purposes of seizure focus ablation, infusions of short-acting agents have been used (with local

anesthesia for the craniotomy and placement of a Mayfield head holder) (*see* Chaps. 18, “Anesthesia for Awake Neurosurgery”, and 45, “Epilepsy and Seizures: OR and ICU Applications of EEG”). When seizure focus ablation is conducted under general anesthesia, agents that are minimally depressant should be used during ECoG.

Anesthetic Effects on Evoked Potentials

Consistent with a synaptic mediated effect, the effect of anesthetic agents on cortical evoked responses parallels their effect on the EEG. This has been shown by Winters for the midlatency cortical auditory (MLAEP) response [26]. Similar to the EEG, most anesthetic agents cause a progressive depression of the cortical evoked responses, although some agents are excitatory (e.g., etomidate, ketamine). Also like the effects on the EEG, some agents (e.g., opioids) cause much fewer dramatic changes, making them desirable during IOM. Because general anesthetics primarily affect synaptic function rather than neuronal conduction, the majority of anesthetic effects are amplitude changes with smaller changes in latency [27]. For a more in-depth discussion of using the EEG to assess sedation and anesthesia, *see* Chap. 11, “Clinical Application of Raw and Processed EEG.”

Effect Based on Location of Synapses

In general, for each IOM modality, the effects of anesthetic agents can be somewhat predicted by noting the location of synapses within the neural pathway. For example, the somatosensory evoked potential (SSEP) pathway has no synapses until the cervicomedullary junction (near the nucleatus cuneatus and nucleatus gracilis) (*see* Chap. 1, “Somatosensory Evoked Potentials”). As such, recordings of the SSEP response in the peripheral nerve (e.g., popliteal fossa, Erb’s point), along the spinal cord (e.g., epidural), or the subcortical response recorded over the cervical spine show minimal anesthetic effects. Major anesthetic effects are seen at or above the second synapse located in the thalamus (i.e., the cerebral cortex response). These effects are shown in Fig. 19.5 with isoflurane and are typical for most anesthetics, which are depressant on the EEG and evoked potentials.

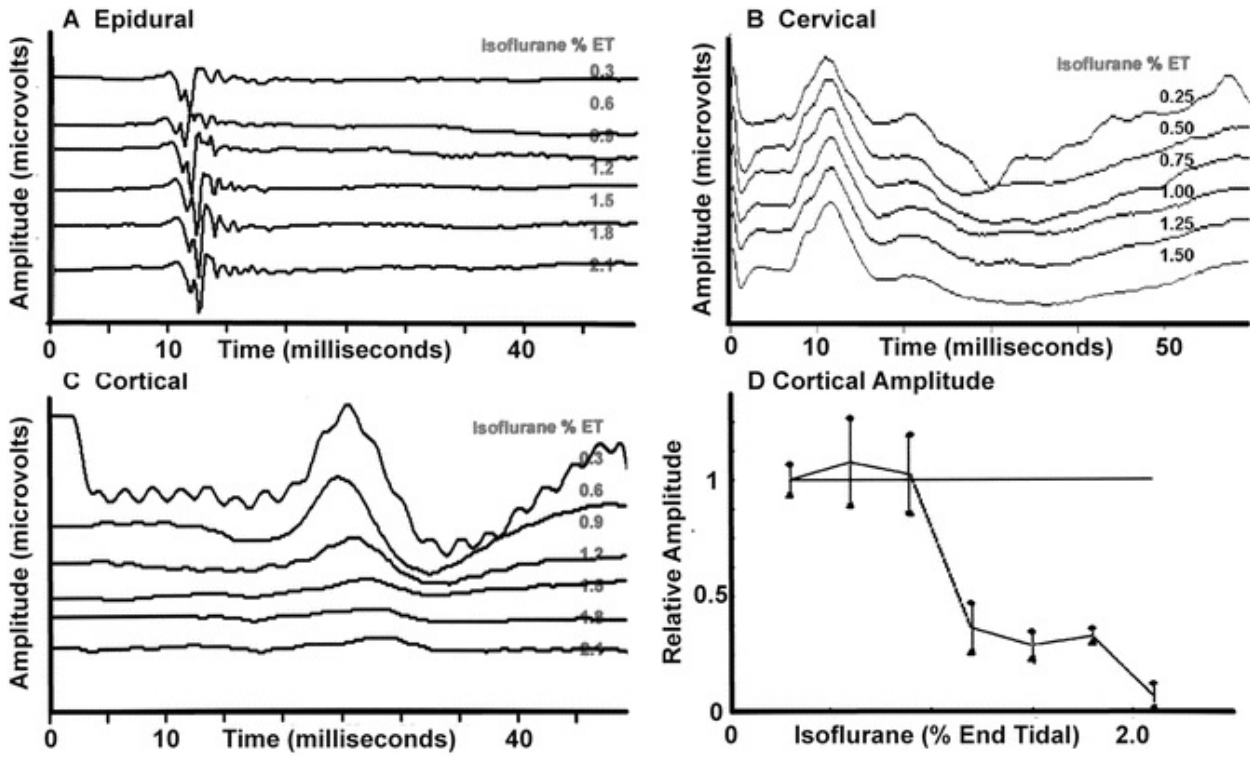

Fig. 19.5 Changes in lower extremity somatosensory evoked potentials recorded at several locations with increasing concentrations of isoflurane in the baboon. (**a**) Recordings from the epidural space that indicate minimal effects. (**b**) Minimal effects in the response recorded over the cervical spine. (**c**) A prominent effect on the response recorded over the somatosensory cortex. (**d**) A plot of the amplitude of the cortical response showing a nonlinear amplitude reduction as the isoflurane concentration is increased

For the auditory brainstem response (ABR), few synapses are involved in the brainstem such that anesthetic effects are minimal (*see* Chap. 3, "Auditory Evoked Potentials"). Because the cortical midlatency response (MLAEP) is heavily dependent on synaptic function, the anesthetic impact is far more substantial.

Motor evoked potentials (MEP) are susceptible to anesthetic agents at several synaptic locations (*see* Chap. 2, "Transcranial Motor Evoked Potentials"). The first location is in the motor cortex where anesthetic depression of internuncial neurons reduces production of "I" waves. Because the "D" waves are the result of direct pyramidal cell stimulation, they are relatively unaffected by anesthetic agents [28, 29]. This maintenance of D waves and loss of I waves with increasing isoflurane is shown in the baboon in Fig. 19.6.

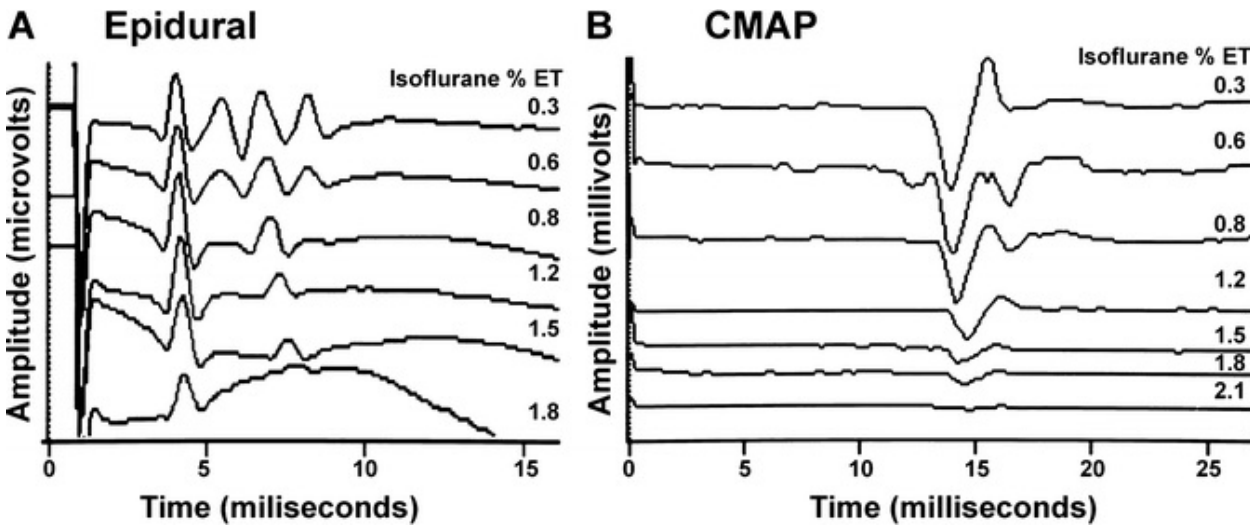

Fig. 19.6 Changes in transcranial motor evoked potentials recorded in the epidural space (**a**) and in the myogenic response (compound muscle action potentials; CMAP) in the hand (**b**) in the baboon. Shown is the maintenance of the single D wave ("D") and loss of the multiple I waves ("I") in the epidural recording and loss of the myogenic response with increasing concentrations of isoflurane

The second location is internuncial synapses within the spinal cord. The anesthetic impact on any given pathway likely depends on the number of these synapses involved. The descending motor tracts follow through lateral and medial pathways with the more distal muscles (i.e., hand and foot) served by the lateral pathway. Because this lateral pathway has fewer synapses, myogenic MEP in these distal muscles (hands and feet) may be slightly less affected by anesthetics than the truncal muscles served by the medial pathway.

Anesthetic action at the anterior horn cell may also impair the generation of a muscle response through synaptic depression. Since the D and I waves must summate temporally to activate the anterior horn cell, the loss of I waves increases the difficulty of obtaining a myogenic response (compound muscle action potential [CMAP]) with a single transcranial pulse stimulation [30, 31]. In addition, other descending tracts (descending suprasegmental systems [corticospinal, rubrospinal, vestibulospinal, and reticulospinal systems] and propriospinal systems) influence the excitability of the anterior horn cell such that anesthetic effect in these pathways could result in additional effect on the myogenic MEP.

This need for temporal summation and the loss of I waves explains some of the success of multipulse stimulation technique, which produces a volley of D waves [32, 33]. At higher anesthetic doses, an even more profound

synaptic block at the anterior horn cell may prohibit synaptic transmission, regardless of the composition of the descending spinal cord volley of activity. The spinal cord has been suggested as the location of the most prominent anesthetic effect on myogenic MEP responses [34].

One additional synapse that may be affected by anesthesia in the motor pathway is the neuromuscular junction. Fortunately, with the exception of neuromuscular blocking agents, anesthetic drugs have little effect at the neuromuscular junction.

Effect Based on Anesthesia Goals

Additional insight into the action of anesthetics on evoked responses is given by examining the neural mechanisms of anesthetics that result in the behavioral goals of amnesia, unconsciousness, lack of movement in response to noxious stimuli (immobility), and blocking of noxious sensory stimuli (antinociception).

Amnesia

Amnesia is thought to be one of the most potent effects of many general anesthetics. It is thought that this involves anesthetic action at the GABAa receptor (with additional contributions at the NMDA and nACh synapses) in the hippocampus, amygdala, and entorhinal and/or perirhinal cortex. Fortunately, anesthetic agents usually block memory formation at or below drug levels that produce unconsciousness [10, 35].

Unconsciousness

Consciousness is likely mediated by a neural network involving the thalamocortical, corticothalamic, and reticulothalamic neurons [36]. Anesthetic action producing unconsciousness is thought to be mediated primarily through the GABAa and central α2 receptors, with additional contributions through the NMDA, potassium channels, and nACh receptors. In general, most anesthetics produce unconsciousness through mechanisms including (1) reducing arousal stimuli to the cerebral cortex by actions at the brainstem (midbrain reticular formation), (2) interfering with cortical processing of information, and (3) blocking sensory information from being received by the cortex through actions at the thalamus (“thalamic gating”)

and at the dorsal horn of the spinal cord [37]. This suggests that the major impact of drugs producing unconsciousness will be depression of the cortical sensory responses (SSEP, MLAEP, and visual evoked potential [VEP]).

It appears that the neural mechanisms producing unconsciousness are nonlinear, similar to an "on–off" system with an abrupt loss of consciousness over a narrow increase of anesthetic concentration [10]. This has been termed a "consciousness switch" and depends on the interaction of two sets of nuclei [36]. One set promotes consciousness (Laterodorsal Tegmental Nucleus, Pedunculopontine Nucleus, Locus Coeruleus, Dorsal Raphe, Ventral Periaqueductal Gray, and Tuberomammillary Nucleus) and the other promotes unconsciousness (Ventrolateral Preoptic Nucleus and Median Preoptic Nucleus). This suggests the anesthetic impact on cortical sensory responses may also be on–off with the major amplitude change occurring over a narrow anesthetic dosage range. The "threshold" for this switch appears to vary with patients as well as with anesthetic agents and may define the ability to use anesthetic agents at concentrations near those that produce unconsciousness.

Immobility

With unconsciousness, immobility (lack of movement to noxious sensory stimuli) is the consequence of anesthetic action interrupting the reflex pathway in the spinal cord. This effect is used to characterize the anesthetic potency of inhalational agents termed "MAC" suggesting halogenated agents will be effective in blocking movement at MAC levels [9]. The major anesthetic effect responsible for this is action of halogenated agents which is thought to be mediated through the spinal cord glycine channels with some contribution at GABAa [38] (which is thought to be the mechanism of etomidate and propofol [35, 39]).

The parts of this reflex pathway include afferent sensory stimuli, which can be effected in the periphery and in the dorsal horn of the spinal cord. The second part is the neural pathways within the spinal cord. This includes interneurons in the reflex as well as the anterior horn cell. The last component is the efferent pathway from the anterior horn to the muscle and includes transmission through the neuromuscular junction. Hence, immobility is a consequence of anesthetic action blocking sensory afferents, reflex pathways in the spinal cord, and motor efferents. In addition, anesthetic action at the neuromuscular junction will affect movement. Although the reflex pathways

can be modulated by descending influences, evidence suggests that immobility is primarily a spinal cord action and is largely independent of drug effect at the brainstem and cortex [40].

The net effect of this pathway is that anesthetic effects on the different parts contribute to immobility. Thus, a balance can be achieved with agents that reduce afferent sensory stimuli, agents that interfere with spinal cord transmission, and agents that reduce the efferent activity. This may allow immobility to be achieved with doses of these agents that allow IOM recording when otherwise higher doses of each agent would be needed and prevent recording.

Antinociception

In addition to blocking sensory transmission to the brain (such as at the thalamus mentioned earlier), the blocking of noxious stimuli ("antinociception") by drug action also occurs throughout the brain and spinal cord. In the spinal cord, sensory stimuli are modulated in the dorsal horn by NMDA and opioid synapses. Descending influences from the midbrain and brainstem also exert an inhibitory or excitatory effect on the dorsal horn transmission. Alpha2 agonists mediate some of the antinociception either directly, modulating descending influences, or by enhancing opioid action [41]. Opioids, norepinephrine, and serotonin play a role in these descending inhibitory pathways [42]. As mentioned earlier, anesthetic effects that reduce sensory transmission through the thalamus and alter cortical processing of sensory information also contribute to antinociception.

Specific Anesthesia Drugs

The differences between drugs are likely a consequence of differing profiles on receptor types (e.g., GABA, NMDA), differing location of drug action (i.e., pre- or postsynaptic effects), the spectrum of effects on individual subtypes of these receptors, and the anatomic distribution of the receptors and subtypes. Hence, the choice of an anesthetic technique becomes a balance of attempting to use concentrations of agents that are supportive of monitoring while accomplishing behavioral goals and the needs of the procedure. Some agents are more supportive of the monitoring techniques and are usually

favored.

Halogenated Inhalational Agents

The most prominent anesthetic effects on evoked responses during clinical anesthesia are those of the halogenated inhalational agents (e.g., isoflurane, sevoflurane, desflurane), which makes them most difficult to use with some IOM techniques (notably myogenic MEP). These agents have a broad action on neural structures and are very effective in producing unconsciousness and amnesia through their action at the GABAa receptor. They are also very effective in producing immobility through their effect at the spinal cord glycine receptor. In addition, they contribute to antinociception via actions at the NMDA, nACh, and potassium channels.

For the SSEP, the predominant anesthetic effect is on responses generated above the level of the thalamus [43, 44] (Fig. 19.5). The blocking of sensory transmission at the thalamus is shown by the reduction of spontaneous and evoked output of the thalamic relay nuclei starting at 0.3–0.5 MAC [1, 37, 44]. This explains why cortical sensory evoked responses can often not be recorded with concentrations above 0.5–1 MAC [45, 46]. Above this level the inhalational agents produce marked effects in a nonlinear, on–off fashion consistent with anesthetic action on consciousness. Hence, the inhalational agents must be limited in most patients to 0.5–1 MAC when monitoring the cortical SSEP. The threshold of the ability to record varies between patients and the presence of neural pathology. In some patients, such as those with very poor responses (e.g., neural degeneration), the halogenated agents may need to be severely restricted (e.g., <0.5 MAC) or not used at all if responses are to be obtained.

Fortunately, responses recorded at peripheral nerves, over the cervical spinal cord, and from electrodes in the epidural space or spinal canal can usually be recorded with only minimal anesthetic effect [47]. Similarly, the ABR can also be recorded without major anesthetic effect. However, the cortical auditory response (MLAEP) is similar to the cortical SSEP with marked anesthetic effect.

The halogenated anesthetic agents decrease VEP amplitude and increase latency [48–50]. Studies of the a and b wave of the electroretinogram show that halogenated agents (and sedatives) decrease amplitude with some agents increasing the response latencies [51, 52]. One study noted with induction with sevoflurane the responses were lost [53].

The effect of the halogenated agents on the spinal reflex mediating immobility is used to determine MAC and is a prominent action of the halogenated agents. Of note, the concentration–effect curve is rather steep with changes in the spinal cord reflex pathway occurring over a relatively narrow concentration range [54]. This may explain the difficulty of finding a suitable anesthetic concentration, which allows recording of myogenic MEP responses.

Because of the anesthetic effect at the spinal cord, the myogenic response of the MEP is the most challenging to record with the halogenated inhalational agents and may require them to not be used (Fig. 19.6). When recordable, the major anesthetic effect may occur at low concentrations (e.g., <0.2–0.5 % isoflurane) with loss of responses above 0.3–0.5 MAC [55–57]. Consistent with the depression of reflex movement by a spinal action of halogenated anesthetics, these agents also depress the Hoffmann reflex (H-reflex) [58, 59]. Studies suggest that the myogenic MEP is depressed more than the H-reflex (50 % vs. 22 % with sevoflurane) [59, 60].

Several recent studies have shown that in some patients, myogenic responses can be recorded with 0.5 MAC of desflurane or sevoflurane [61–64]. In these cases, the amplitude of the MEP is reduced compared with TIVA but monitoring appears to be conducted successfully. In a few patients the MEP could not be recorded until the halogenated agent was eliminated and TIVA used; in one patient it was never recorded. This suggests that the use of 0.5 MAC of a halogenated agent should be reserved for patients with robust responses (i.e., minimal neural pathology) and when used, preparations for converting to TIVA be available when responses cannot be acquired at baseline. At present, it is unclear whether desflurane or sevoflurane is less depressant at these doses [63].

Since the D wave is usually unaffected by anesthesia, it can usually be recorded in the epidural space or spinal canal at anesthetic concentrations of halogenated agents.

Nitrous Oxide

As a nonhalogenated inhalational agent , N_2O is different from the halogenated agents; N_2O is particularly effective in antinociception due to its action at the NMDA receptor with additional contributions at the μ opioid, nACh, and potassium channels. In addition, it contributes to unconsciousness

and amnesia through minor actions at the GABAa and central α2 receptors and contributes to immobility through minor actions at the glycine receptor [65].

The effects of nitrous oxide on the SSEP are similar to the halogenated agents, although the effects vary with the other anesthetic agents being employed. When used alone, nitrous oxide tends to produce graded amplitude and latency changes in a dose-dependent manner [66, 67], with minor or no changes in subcortical responses [47]. Nitrous oxide is a more potent depressant of the P_{15}–N_{20} SSEP response than isoflurane when compared on a MAC basis [68]. Because nitrous oxide is very insoluble, the changes can occur rapidly. Nitrous oxide reduces VEP amplitude with increase in latency at higher doses. When nitrous oxide is added to a halogenated agent, the VEP is lost.

When added to halogenated anesthetics, nitrous oxide may cause additional changes in latency and amplitude [47] or have no apparent additive effect [45]. Studies of equal MAC mixtures of isoflurane and nitrous oxide have demonstrated that the mixture has a more potent effect on cortical SSEP than would be predicted by adding the individual effects of each agent, suggesting a synergism from different mechanisms of action [69]. In cases in which nitrous oxide is added to intravenous agents, amplitude changes predominate, without latency change [70–72].

Studies with MEP [73, 74] show that N_2O produces depression of myogenic responses similar to the halogenated agents [56, 72, 74]. When compared at equal MAC concentrations, nitrous oxide produces more profound changes in myogenic MEP than any other inhalational anesthetic agent [68, 75]. Similar to low doses of halogenated agents, myogenic MEP can be recorded in some patients when N_2O is used in concentrations below 50–60 % [74]. As with other modalities, the effect of N_2O is dependent on the other anesthetics used with marked depression when N_2O is combined with a halogenated agent [76, 77]. Like the halogenated agents, the effects on the epidurally recorded MEP are minimal.

Intravenous Agents

Sedative-Hypnotics: Propofol

When the concentration of halogenated agents must be restricted, intravenous

sedative hypnotics are usually employed to achieve amnesia and unconsciousness. Of the agents available, propofol is currently the most commonly utilized agent. Propofol has potent effects on unconsciousness and amnesia via actions at the GABAa receptor. This action at the GABAa and minor effects at the glycine receptor contribute to immobility during anesthesia. Finally, it makes minor contributions to antinociception through actions at the glycine and nACh receptors.

Propofol induction produces amplitude depression in cortical SSEP, VEP, and MLAEP with rapid recovery after cessation of a short infusion (actual time for longer infusions is dependent on the duration of the infusion, a consequence of the context-sensitive half-time) [78, 79]. Propofol does not enhance cortical responses. When the SSEP is recorded in the epidural space, propofol has no significant effect. At sedative doses, the SSEP is affected at the cortex only. At higher doses (hypnosis), the thalamic response is also affected [80]. At anesthetic doses, the cortical SSEP response amplitude is reduced and is lost at higher doses [56, 81–83].

Propofol induction produces amplitude depression in cortical responses and myogenic MEP with minimal effects on the epidurally recorded D wave with rapid recovery after cessation of infusion [34, 56, 81–83]. Similar to the halogenated agents, I waves are lost during propofol anesthesia consistent with synaptic effects on the brain similar to the depression of the EEG. When propofol is studied without other agents (and without surgical stimulation), MEPs can usually be recorded at burst suppression, although the amplitude is lower than at lighter levels [84].

Different from the steep concentration–immobility effect curve of the halogenated agents, the dose–response curve on immobility is substantially flattened with changes occurring over a wider concentration range [54]. This suggests that it is more likely to identify a concentration where propofol provides adequate anesthetic effect and acceptable depression of the H-reflex and myogenic MEP than with a halogenated agent [58, 81–83, 85].

At doses consistent with adequate anesthesia, patients with neurological compromise and poor responses may not have recordable myogenic MEP with propofol [54]. The same situation arises if higher doses of propofol are needed, such as with chronic GABAa acting drug usage (e.g., ethanol, benzodiazepines) or when an increased effect of propofol is needed to accomplish immobility when opioid tolerance produces poor antinociception [54]. When higher propofol doses appear to be needed, some TIVA methods

have used ketamine or lidocaine to provide additional drug effect so that the dose of propofol can be reduced into an acceptable range [86].

Etomidate

An alternative sedative-hypnotic is etomidate, which also has potent cortical effects on unconsciousness and amnesia via actions at the GABAa receptor. It contributes to immobility via actions at the GABAa and glycine receptors, and has some minor contributions to antinociception through actions on the potassium channels. Of note, its use in TIVA has been reduced in many centers due to concerns of adrenal suppression and worsened outcome, especially in sepsis [87, 88].

At low doses , etomidate also enhances the amplitude of the cortical SSEP [89–94]. Fortunately, the enhancing activity occurs at doses that are consistent with the desired degree of unconsciousness and amnesia needed for TIVA. This amplitude increase appears coincident with the myoclonus seen with the drug, suggesting a heightened cortical excitability (however, no evidence of seizure activity was seen) [95, 96]. A sustained increase with constant drug infusion has been used to enhance cortical SSEP monitoring that was otherwise not recordable [89–94]. A cat study suggests that the location of enhancement is cortical [96], which is consistent with clinical studies showing enhancement of cortical responses with no enhancement in subcortical responses [90]. Higher doses of etomidate cause depression of the evoked responses (similar to the EEG) suggesting a biphasic effect (enhancement followed by depression).

Studies with myogenic MEP have suggested that etomidate is an excellent agent for induction and monitoring of this modality. Of several intravenous agents studied, etomidate had the least degree of amplitude depression after induction doses or with continual intravenous infusion [81, 82, 97–100]. At low doses, etomidate also enhances the myogenic MEP amplitude [89–94, 100]. This appears coincident with the myoclonus seen with the drug, suggesting a heightened cortical excitability [95, 96]. It is interesting that etomidate also increases the H-reflex, suggesting a change in α motor neuron excitability in the spinal cord [101]. This effect may be contributing to the enhancement of myogenic responses of MEP [81, 82, 97–100].

Benzodiazepines

Benzodiazepines , notably midazolam, also act at the GABAa receptor and have been advocated as supplements to TIVA because of amnestic properties and the ability to reduce the chance of hallucinogenic activity with ketamine. Midazolam, in doses consistent with induction of anesthesia and in the absence of other agents, produces a mild depression of the cortical SSEP [81, 93, 95, 102–105]. It has also been used in TIVA, prior to the introduction of propofol, with conditions suitable for anesthesia and cortical SSEP monitoring [90]. As such, when myogenic MEP is monitored, small doses for premedication or occasional supplementation during anesthesia usually allows myogenic MEP recording. Unfortunately, benzodiazepines (notably midazolam) produce marked acute and prolonged depression of myogenic MEP at larger doses [81, 82, 93, 95, 102–105].

In addition to possible cortical locations for the benzodiazepine effect, an effect at the spinal cord has been described as antinociceptive through actions at the GABA receptors in lamina I and II in the dorsal horn [106, 107]. This drug action is thought to be responsible for the depression of the H-reflex by diazepam [106, 107].

Dexmedetomidine

Another agent used to promote unconsciousness is dexmedetomidine , which acts as a central, selective α2 adrenoreceptor agonist drug. Dexmedetomidine has been shown to reduce the amount of propofol, opioids, and halogenated inhalational agents needed during anesthesia [108]. Of note, it does not produce amnesia. Side effects of hypotension and bradycardia relate to its sympatholytic properties and limit the drug to a role as a supplement to other anesthetic agents. The effects on SSEP recordings are minimal, possibly due to selective brainstem action at the locus coeruleus such that thalamic blocking is minimal. But, as with propofol, higher blood levels of dexmedetomidine inhibit MEP monitoring. When used as a supplement to isoflurane or a propofol-fentanyl-nitrous oxide anesthetic, no additional depression to the cortical SSEP is seen [109].

Dexmedetomidine appears compatible with myogenic MEP when low doses are used and in the absence of other agents. However, higher blood levels of dexmedetomidine (or when moderate dosages of other agents such as propofol are used with dexmedetomidine) inhibit myogenic MEP

monitoring [110–112].

Barbiturates

In general, the effects of barbiturates on the cortical SSEP are very small [113, 114], but the effect of thiopental can be rather profound and long lasting on the myogenic MEP at higher doses [77, 82, 97]. Methohexital has been used as a substitute for propofol in TIVA with acceptable cortical SSEP and myogenic MEP monitoring [113–115].

Droperidol

Droperidol appears to have minimal effects when combined with an opioid on cortical SSEP [116, 117].

Intravenous Antinociception: Opioids

To achieve all four anesthetic goals using intravenous anesthetics, opioids or ketamine is usually used to produce antinociception. Of note, these agents also help with immobility due to actions on the afferent portion of the reflex. Like its effects on the EEG, opioid effects on SSEP and MEP are minimal, especially on spinal or subcortical recordings [28, 29, 56, 73, 81, 82, 98, 103, 118–135]. The effects on the SSEP are reversed with naloxone, suggesting that the effect is mediated by the μ receptor [136, 137]. Some transient depression of amplitude and increases of latency in cortical responses can be seen with bolus doses and occasional loss of late cortical peaks (over 100 ms) at higher doses [81, 97, 116]. The spinal application of morphine or fentanyl produces minimal changes in the cortical SSEP [70, 76]. Several studies have shown a minimal depressant effect of clinical doses of opioids on the myogenic MEP [28, 29, 56, 73, 81, 82, 98, 103, 118–135].

Opioids can potentiate the effects of propofol. In addition, bolus doses of these agents will produce transient depression of responses and higher concentrations can persistently produce significant depression. As such, the delivery of opioid by infusion is important during anesthetic maintenance similar to the use of infusions of other agents [138]. Opioids appear to have minimal effects on the VEP, except that pupil constriction can reduce the effectiveness of the stimulation reducing amplitude and bolus doses can transiently reduce the amplitude [137, 139].

Ketamine

As an alternative or supplement to the opioids (particularly when the patient is opioid tolerant), ketamine has very potent antinociceptive actions via its action at the NMDA receptor. In addition, it contributes to unconsciousness and amnesia via minor actions at the GABAa receptor. As seen in the EEG, ketamine is an excitatory agent and has been reported to increase cortical SSEP amplitude [70, 140] and increase the amplitude of myogenic and spinal recorded MEP responses. Ketamine also increases the H-reflex, suggesting a change in α motor neuron excitability may contribute to the MEP enhancement [82, 97, 101, 117, 141–145].

High dosages, however, produce depression of the myogenic response consistent with its known property of spinal axonal conduction block [146]. As such, ketamine can be added to an intravenous technique to enhance the antinociceptive effect while allowing reduction of agents, which produce depression of the evoked responses (e.g., propofol). Unfortunately, increases in intracranial pressure are seen in patients with cortical abnormalities. Hallucinatory activity can also be seen and is minimized by using midazolam and avoiding its use prior to awakening. Of note, ketamine is also thought to minimize acute opioid tolerance through its action at the NMDA receptor [147].

Lidocaine, Magnesium, and Regional Anesthesia

Lidocaine , when infused intravenously at a low dose, has been shown to reduce propofol and opioid doses in TIVA with maintenance of the cortical SSEP and myogenic MEP [148]. It is believed to act via GABA, NMDA, and sodium channels leading to contributions in unconsciousness, immobility, and antinociception. It has been used in patients who are opioid tolerant and is associated with reductions in postoperative pain. Similarly, magnesium infusion offers similar benefits but has not been fully explored with IOM [149]. It is thought to act similarly to ketamine through the NMDA receptor.

When used for regional anesthesia , local anesthetics block conduction in the neural pathways affected, causing loss of sensory and motor responses. This has been shown with epidural anesthesia [150–152], intravenous regional block [153], specific nerve blocks [154], thoracic paravertebral blocks [155], and topical anesthesia where stimulation is being conducted [156].

Neuromuscular Blocking Agents

Despite the controversy associated with the use of NMBA during IOM, a substantial amount of experience has been published. There are certain portions of surgical procedures where neuromuscular blockade (NMB) is routinely requested; in addition to intubation, NMB is often used during transabdominal approach to the anterior lumbar spine, during the initial portions of a posterior thoracic spinal procedure to reduce paraspinous muscle activity, and in interventional suites to facilitate a radiographic background “mask” to be subtracted. In addition, NMB is occasionally requested to prevent patient movement during microscopic surgery [157]. It should be noted that other techniques beside NMB have been used to reduce movement.

Some IOM techniques do not rely on muscle responses such that NMB can be used if they are the only responses measured. These include SSEP, VEP, or ABR [158]. To the extent they reduce electromyographic (EMG) noise in the recording, they may improve the signal-to-noise ratio and improve recording [158, 159].

Motor-Evoked Potentials

Because the myogenic MEP response and H-reflex is dependent on neural transmission through the neuromuscular junction (NMJ) , NMB will reduce the amplitude of the response and complete NMB will prevent monitoring of the myogenic MEP [160, 161]. However, monitoring with the MEP in the spinal canal (D wave) will be possible and relaxation may improve recording because of reduction of the paraspinous muscle artifact from stimulation [29, 131].

Human and animal studies demonstrate that the muscle (M) response from peripheral nerve stimulation is reduced more than the myogenic response to transcranial MEP stimulation (e.g., the myogenic MEP amplitude seen in these studies was 50–60 % of the unblocked value when M response was reduced to 20 % [160–162]). These nonlinearities may be the result of the differences in muscle activation due to repetitive activation of spinal motor neurons, which occurs with centrally applied stimulation due to spatial and temporal summation [163]. Interestingly, several studies show that myogenic MEP responses could be recorded even in the absence of a

mechanical response [160–162, 164]. Because the M wave and myogenic MEP show a parallel reduction with NMB, it has been suggested that the single twitch response might be used to “calibrate” the MEP response should amplitude fluctuations from NMBA be of concern [162].

A large number of clinical studies have been published where myogenic responses of MEP were conducted during partial NMB (pNMB). Successful monitoring has been reported with a single twitch response at 5–15 % [165], 10 % [102, 134], 15 % [166], 10–25 % [128, 133], 20 % [118, 126, 130, 167], 25 % (124), 30–50 % [28, 98, 165, 168], and 80–90 % [130, 133, 162, 168] of the unblocked baseline. When neuromuscular blockade is assessed by train-of-four (TOF) count, acceptable MEP monitoring has been conducted with only one [162, 169] or two of four [121, 129] responses remaining.

As a consequence of amplitude reduction, the ability to record with pNMB will be dependent on other factors, which reduce the myogenic response such as anesthesia or neurologic disease. One clinical study indicated that if the myogenic MEP amplitude is greater than 150 μV, then MEP monitoring should be possible, suggesting the pNMB might be titrated to the MEP amplitude to facilitate monitoring [162]. Hence, if neurologic pathology results in initially small responses, a reduction in amplitude by pNMB may make it difficult to distinguish from background. Similarly, anesthetic choices that reduce amplitude or increase the threshold for stimulation may compound this problem, particularly if pathology in the nervous system increases the anesthetic sensitivity or NMBA effects. This anesthetic effect may also be more profound in young children with incompletely developed nervous systems and the elderly with neural degeneration.

Of note is that partial NMB is associated with higher cortical stimulation thresholds [170]. As such, pNMB may also be problematic in surgery on the cerebral cortex (e.g., cerebral aneurysm clipping) where the MEP is being used to monitor the motor cortex; the higher stimulation voltage needed may cause stimulation to occur deep at the internal capsule or brain stem and render the monitoring less effective in detecting cortical pathology (e.g., ischemia from the placement of temporary or permanent clips) [171].

Because myogenic MEP responses are reduced by NMB, methods to increase the amplitudes would be desirable when pNMB is used. Since transmission across the NMJ is known to be enhanced by prior tetanic stimulation, this effect has been explored [157, 172]. MEP myogenic

amplitude enhancement was seen in the muscles of the peripheral nerve stimulated as well as other muscles, suggesting a central enhancement as well as conditioning of the neuromuscular junction [173]. Myogenic MEP enhancement has also been seen by applying a peripheral sensory stimulus (a train of stimuli in the receptive field of the withdrawal reflex of the anterior tibialis muscle) [174].

Facial Nerve

Studies have been conducted examining the effect of pNMB on facial nerve monitoring when stimulation is used to identify the location of the nerve in the operative field and monitor its integrity [175]. Successful monitoring has been observed when stimulation of the nerve was done proximal and distal to the tumor bed. Consistently the impact on the facial muscles (orbicularis oculi, orbicularis oris) from facial nerve stimulation is less than the impact on the hypothenar muscles from ulnar nerve stimulation (e.g., when the hypothenar muscle was 25 % of baseline the facial muscle response was 50–53 %) [176–178]. When the ulnar nerve response was reduced to 50 % of baseline, 94 % of patients had facial muscle response. This was reduced to 90 % when the ulnar response was 25 % of the unblocked state [176]. No studies have been published examining the effect of pNMB on responses evoked by nonelectrical stimuli or with cranial nerves activated by transcranial stimulation similar to MEP (i.e., corticobulbar responses); however, a reduction in amplitude or increase in transcranial stimulation threshold should be expected.

Recurrent Laryngeal Nerve

The effect of pNMB on monitoring of the recurrent laryngeal nerve during thyroid surgery has shown that responses can be reliably recorded when the accelerometry response was 10 % or better of baseline when measured from stimulation of the ulnar nerve; at this level of pNMB the mean EMG response of the vocalis was approximately 32 % of the response with no relaxation [179]. This is consistent with another study where the effect of NMBA was greater on the thenar muscles than on the vocalis [180].

Peripheral Nerve Monitoring and Pedicle Screw

Testing

Studies of the impact of pNMB on peripheral nerve monitoring have evaluated the impact on stimulation of pedicle screws placed in the spine. One study indicated that pNMB was associated with a higher threshold of stimulation [181]. When the hypothenar response to ulnar stimulation was less than 20–25 % of the unblocked response, the increase in threshold for stimulation of the peripheral nerve could result in falsely elevated pedicle screw thresholds in the L4-S1 nerve root [178, 182]. The authors note that this effect may be more profound with chronically compressed nerves, which are known to be more sensitive to NMBA.

If NMBA Is Used

When NMBA is used it is important to coordinate this with the IOM techniques used. If used for induction, it is key to have it wear off (or be reversed) for baseline recordings (especially if prepositioning values are needed). Similarly, during the portion of procedures where IOM is critical, it needs to be delivered by a carefully titrated infusion and the TOF monitored to prevent the inadvertent loss of the response signaling an alert [160, 161].

Because pNMB will reduce the response amplitude, the ability to record with pNMB will be dependent on the initial amplitude, the effects of the anesthetic management (especially halogenated agents), and neurological pathology in the pathway monitored. In addition, since muscles and nerves may vary in their response to stimulation and NMBA, the impact of pNMB may also vary with the specific nerve and muscle monitored [183]. Hence, it is important to monitor the TOF in the IOM monitored muscle [184]. It is also important to note that halogenated inhalational agents have effects at the NMJ acetylcholine receptor that will enhance the effects of NMBA such that variations in the halogenated agent may change the degree of pNMB [183]. In general, given the complexities and importance of the IOM, avoidance of neuromuscular blocking agents is advised when possible.

Total Intravenous Anesthesia

Given the impact of the anesthetic agents , TIVA without NMBA is often chosen when myogenic MEP responses are monitored. The most common intravenous anesthetic currently involves an opioid and a sedative (e.g.,

propofol) given by infusion. This allows a steady-state anesthetic effect to minimize anesthetic-related changes that could be confused with impending neural compromise. Supplemental anesthetic agents may also be helpful if the effect of the intravenous agents is excessive or opioids are less effective as in patients with opioid tolerance. In this respect, ketamine and lidocaine have been commonly used [86, 185]. The maintenance of a constant anesthetic effect is important (as much as possible) such that baseline drift does not reduce or increase the sensitivity to neural compromise. Both a decrease and an increase in baseline values have been seen and ascribed to anesthesia, although many other variables (including physiology such as temperature) can contribute to the changes [186, 187].

Physiological Considerations in Anesthesia Management

In addition to producing anesthesia, the anesthesiologist also manages the physiological changes induced by anesthetic agents or surgery. Some of these changes contribute to changes in evoked responses and others can help mitigate some adverse circumstances that would otherwise lead to neural injury (*see* Chap. 20, “Monitoring Applications and Evaluating Changes”). For example, during some cases, blood pressure is deliberately lowered to reduce operative bleeding, but excessive hypotension can lead to ischemia. In humans during surgery, SSEP changes have been observed at blood pressures, which would not ordinarily be associated with neural ischemia (e.g., systolic blood pressures above 90 mmHg systolic). This has suggested that the lower limit of autoregulation and acceptable blood pressure may be higher than expected in some patients [188]. This has been thought to be due to individual variability [189] or the result of operative mechanical stress combined with the blood pressure reduction leading to a more profound effect than predicted by blood pressure alone [190]. In several of these patients, an increase in blood pressure restored the response [191, 192].

As such, in many circumstances when a change in evoked responses signals a possible neural compromise, blood pressure is often elevated to treat possible ischemia. In addition to global hypotension, regional hypoperfusion, hypoxemia, severe anemia, excessive hyperventilation, and reduced neural perfusion pressure (e.g., raised intracranial or cerebrospinal fluid pressure) can lead to ischemia. In these circumstances other maneuvers may be

necessary in addition to elevation of the blood pressure.

Hypothermia can alter evoked responses by changing nerve depolarization (increased action potential duration [193], reduced conduction velocity [194], and decreased synaptic function [195]) resulting in increases in latency and decreases in amplitude of evoked responses [196]. Hypothermia can also be regional (e.g., a cold limb or cold irrigation fluids). Since hypothermia has other adverse consequences (e.g., increased operative bleeding, postoperative infection, and cardiovascular complications), maintaining normothermia is usually a desirable intraoperative goal unless deliberate hypothermia is being used as a part of the procedure.

Changes in a variety of other physiological variables may produce alterations in the evoked responses during surgical monitoring. For example, significant reduction in blood volume can alter evoked responses due to changes in blood flow distribution despite the absence of significant blood pressure changes (e.g., extremity ischemia altering the SSEP as blood flow to central organs is spared). An increase in superior vena cava pressure during cardiopulmonary bypass has been associated with SSEP changes [197]. Other physiologic events may occur too slowly to be noted as changes in the evoked response. For example, changes in glucose, sodium, potassium, and other electrolytes important in the neurochemical environment and affecting neural depolarization and conduction can result in evoked response changes [198].

Conclusion

The changes with anesthesia and physiology make the anesthesiologist a key member of the neurophysiological monitoring team. To provide optimal monitoring, the anesthesiologist should choose an anesthetic technique that is acceptable for the patient and supportive of the electrophysiological signals being monitored. In addition, since all anesthetic agents have some effect, keeping the anesthetic levels constant during surgery will reduce the chance that an anesthetic change will be confused with possible neural compromise. Further, providing a physiologically supportive environment is also important, which may involve changing the physiology (e.g., raising blood pressure) when monitoring suggests the change may have a favorable effect on the health of the nervous system.

Questions

1. Which of the following is thought to be the major inhibitory synapse in the cerebral cortex:

    a. GABA

    b. NMDA

    c. Glycine

    d. Neuronal Ach

    e. mu

2. Which of the following is thought to be the major inhibitory synapse in the spinal cord:

    a. GABA

    b. NMDA

    c. Glycine

    d. Neuronal Ach

    e. mu

3. Which of the following agents is least likely to be associated with seizures

    a. Etomidate

b. Methohexital

c. Sevoflurane

d. Ketamine

e. Desflurane

4. Which of the following monitoring techniques are the most difficult to record under anesthesia

   a. Cortical SSEP

   b. Cranial nerve EMG responses

   c. Epidural MEP D waves

   d. Muscle MEP responses

   e. Auditory Brainstem Responses

5. Anesthetic actions which prevent movement under general anesthesia include all of the following except

   a. Muscle relaxants

   b. Antinociception

   c. Spinal cord reflex pathway inhibition

   d. Blocking of sensory stimuli at the thalamus

e. None of the above

6. Which of the following physiological abnormalities is least likely to alter cortical SSEP recordings:

   a. Hypothermia

   b. Hypocarbia

   c. Hypercarbia

   d. Hypoxemia

   e. Hypotension

Answers

1. a
2. c
3. e
4. d
5. d
6. c

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Footnotes

1 Key references marked with asterisk.

Section III
Clinical Applications

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_20

20. Monitoring Applications and Evaluating Changes

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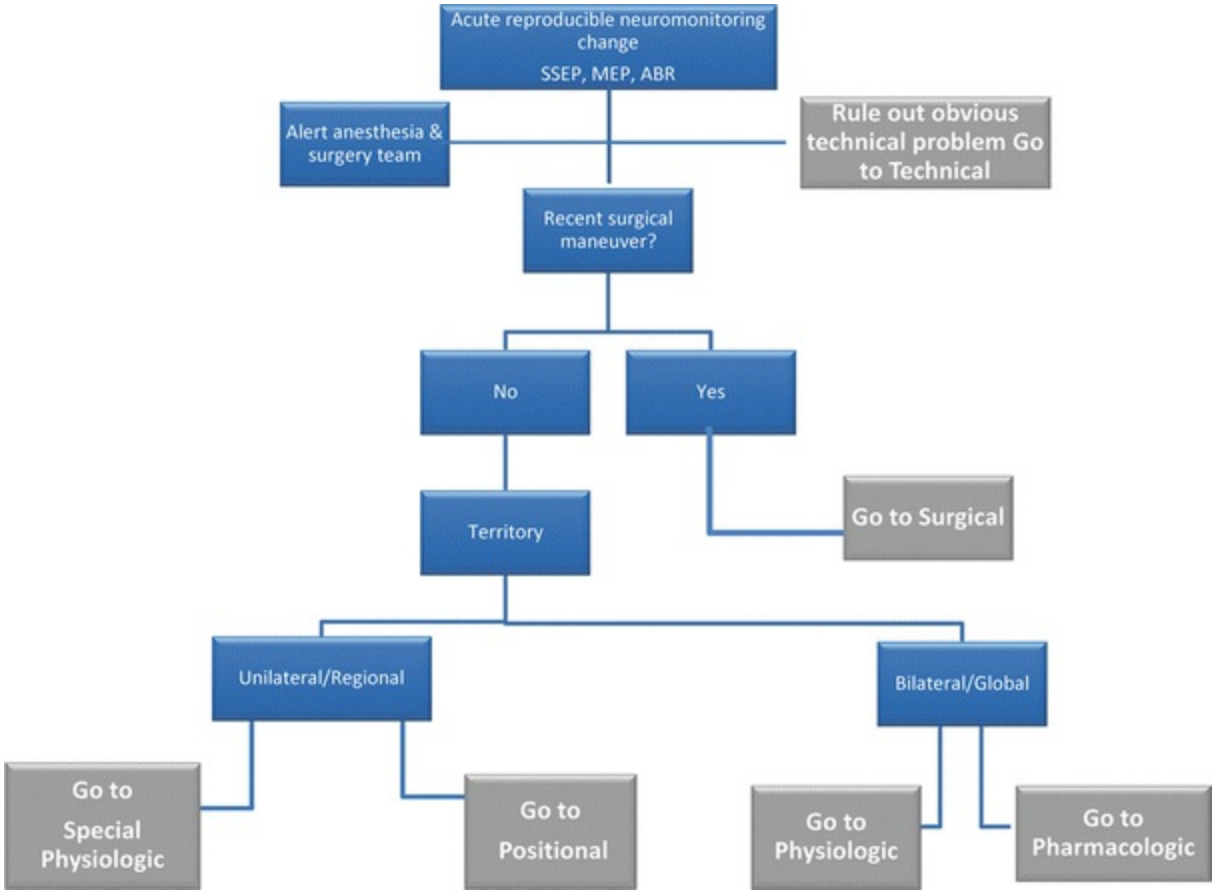
Keywords Monitoring applications – Evaluating changes – Algorithm – Adverse neurophysiological conditions – Acute reproducible neuromonitoring change – SSEP – MEP – ABR

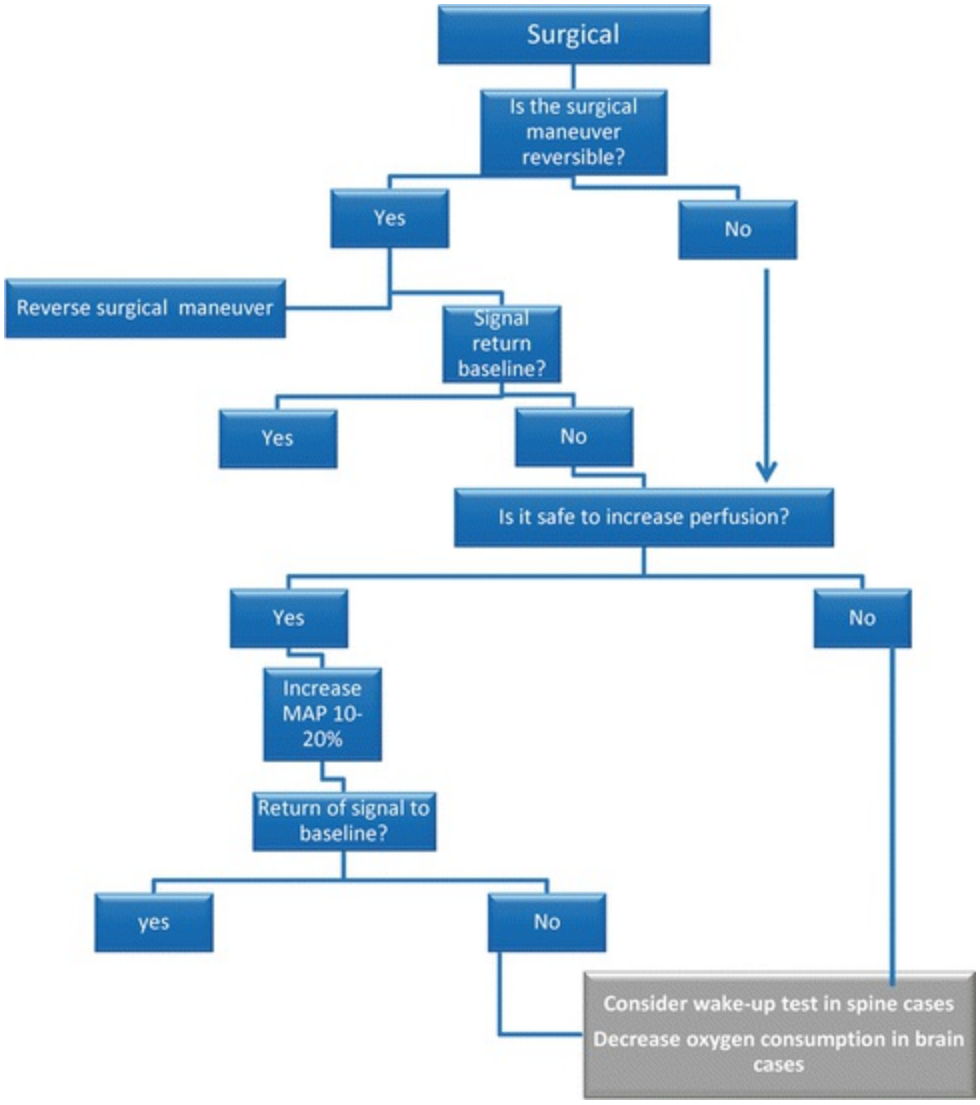
The chapters that follow present case examples of various applications of

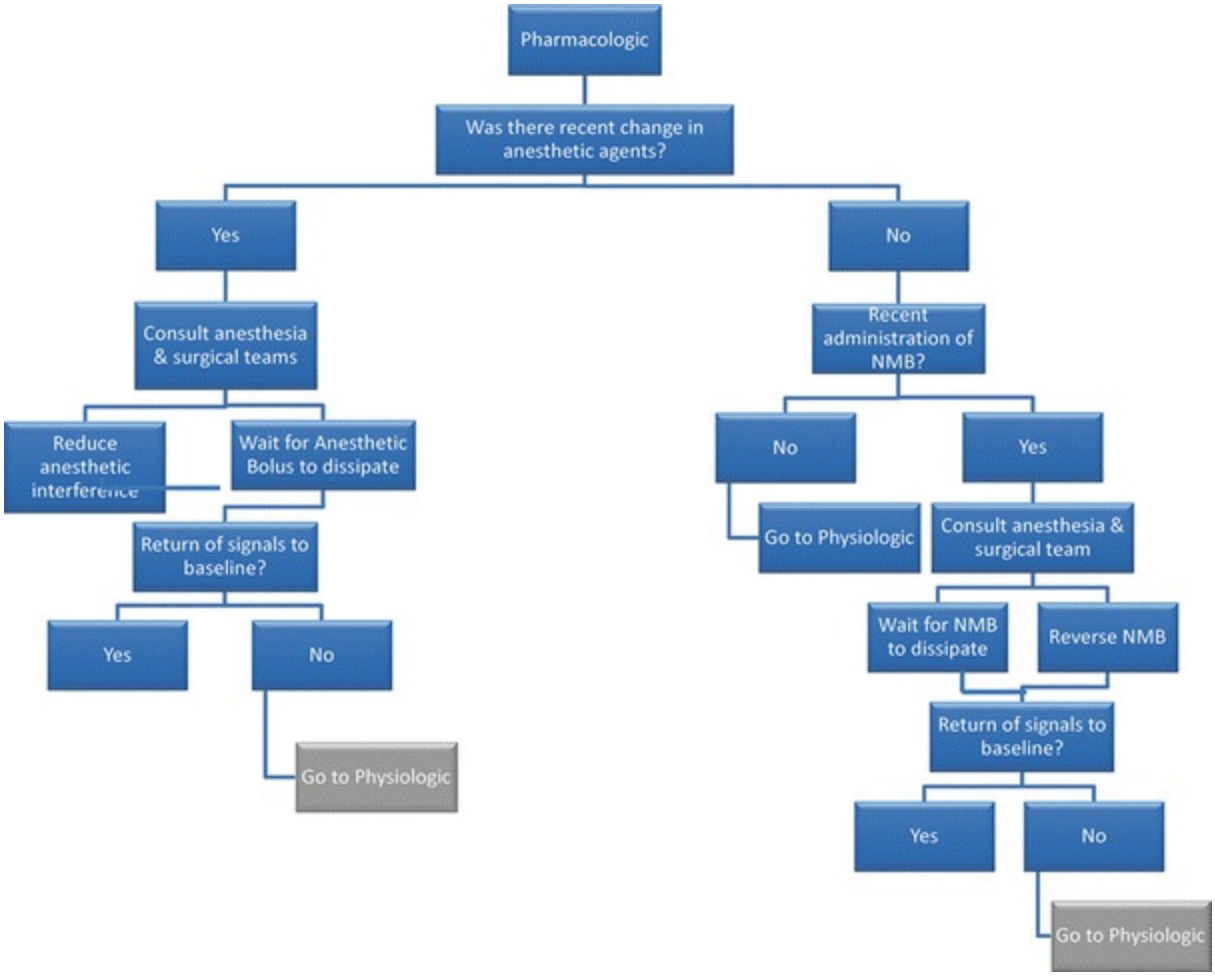
intraoperative monitoring. After a discussion of the patient problem, the application of monitoring is presented. The authors have provided examples of intraoperative monitoring (IOM) changes that may signal adverse neurophysiological conditions . When this occurs, a search for the etiology and possible corrective or supportive measures is important. This introduction attempts to provide an overview of that search since all team members must participate in that endeavor.

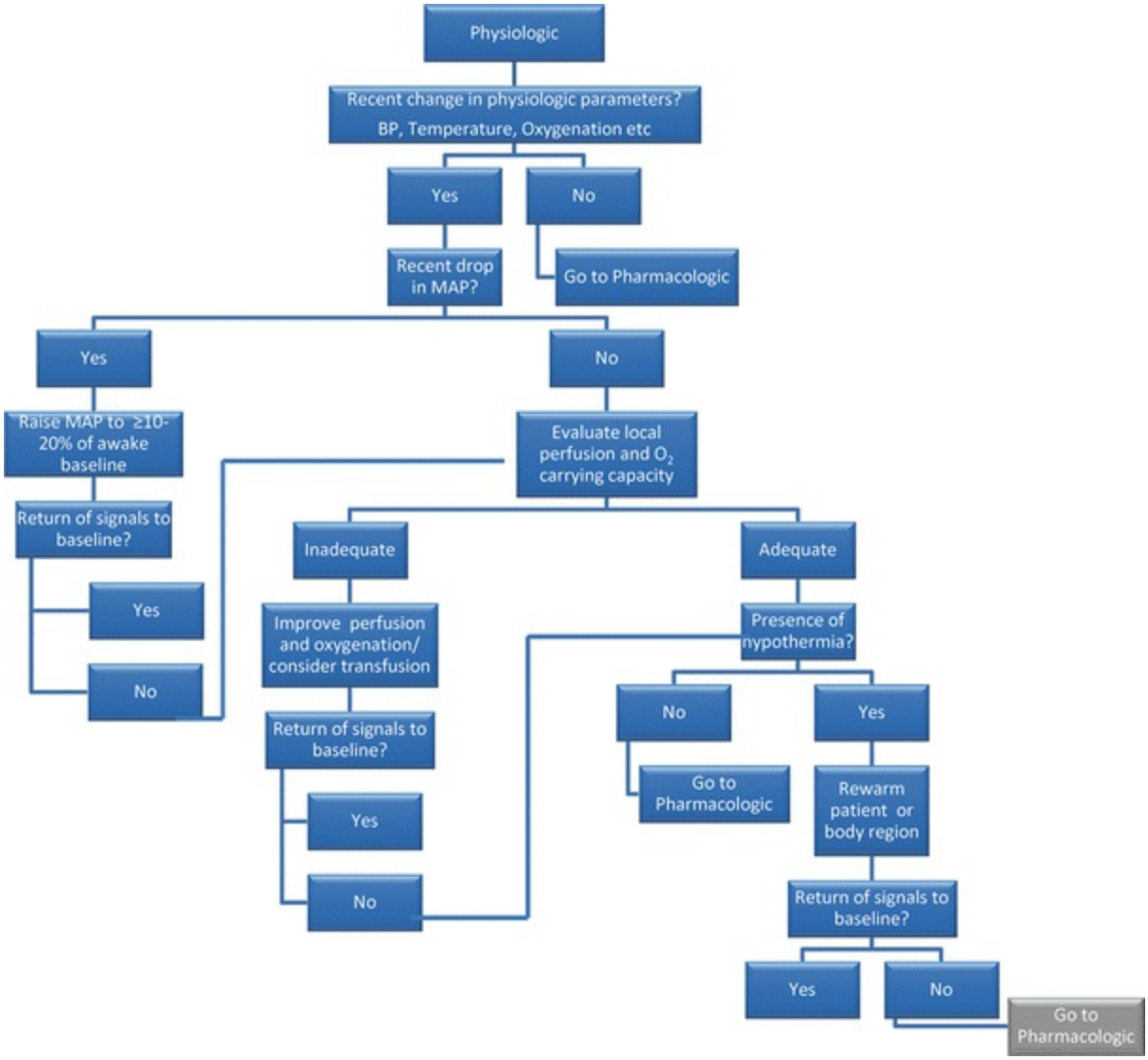
Although the surgeon or professional conducting the procedure (such as in interventional radiology) needs to be alerted if the IOM becomes unreliable or indicative of a possible neurological injury, it is erroneous to always ascribe changes to be procedure related. Frequently, the changes are not the result of the procedure and they indeed “did not do anything.” But while they are evaluating if any part of the procedure could be the etiology of the IOM change, all team members need to search their respective areas for possible contributing factors. For a complete assessment, changes are almost always the result of changes in the five categories (surgical/procedure, anesthesia, physiology, positioning, the technical conduct of the monitoring), or some combination of these factors.

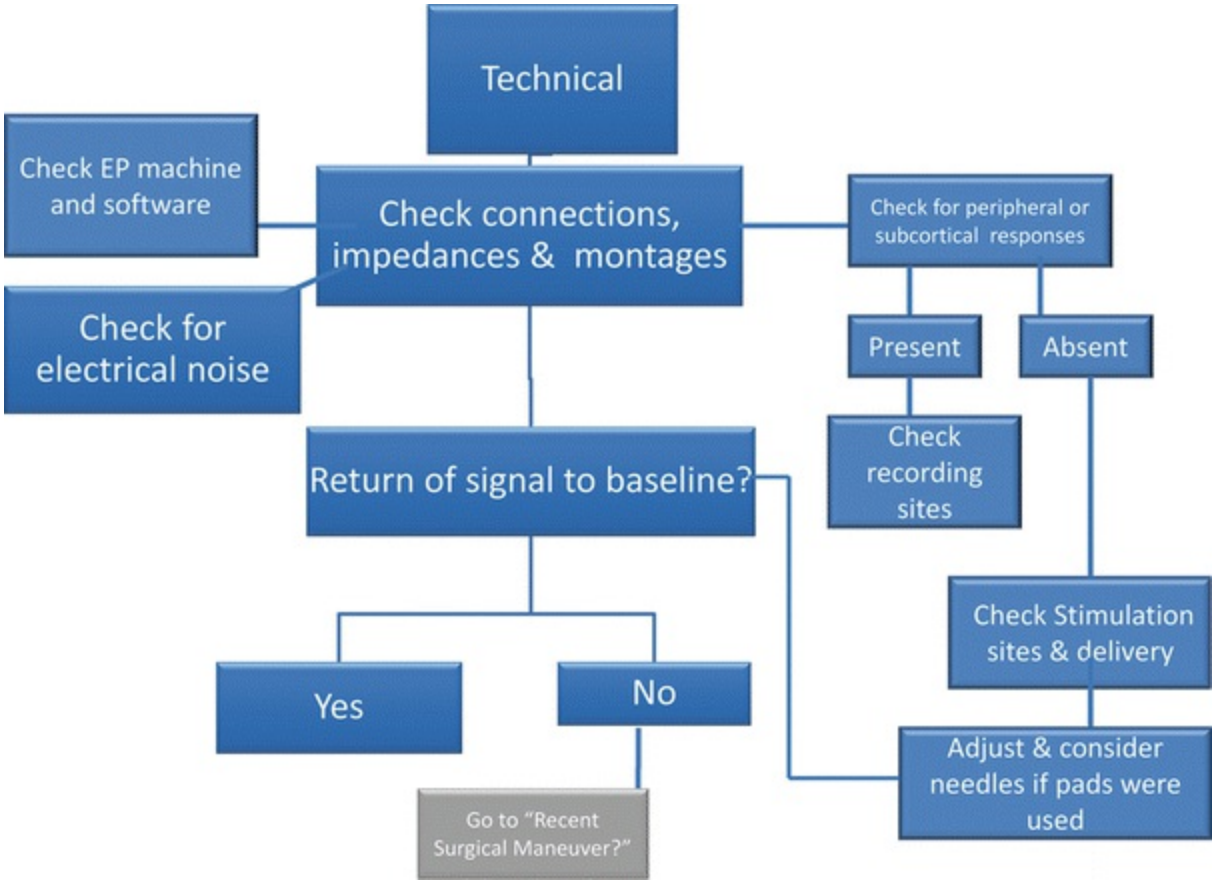
To assist with this assessment, Fig. 20.1 presents a basic algorithm for the anesthesiologist and other members of the monitoring team, to use in evaluating the possible contributions to response deteriorations. This is not exhaustive and clearly the observation and imagination of the operating room team will be necessary to determine the possible etiologies and methods to favorably alter the course of the surgery or procedure.

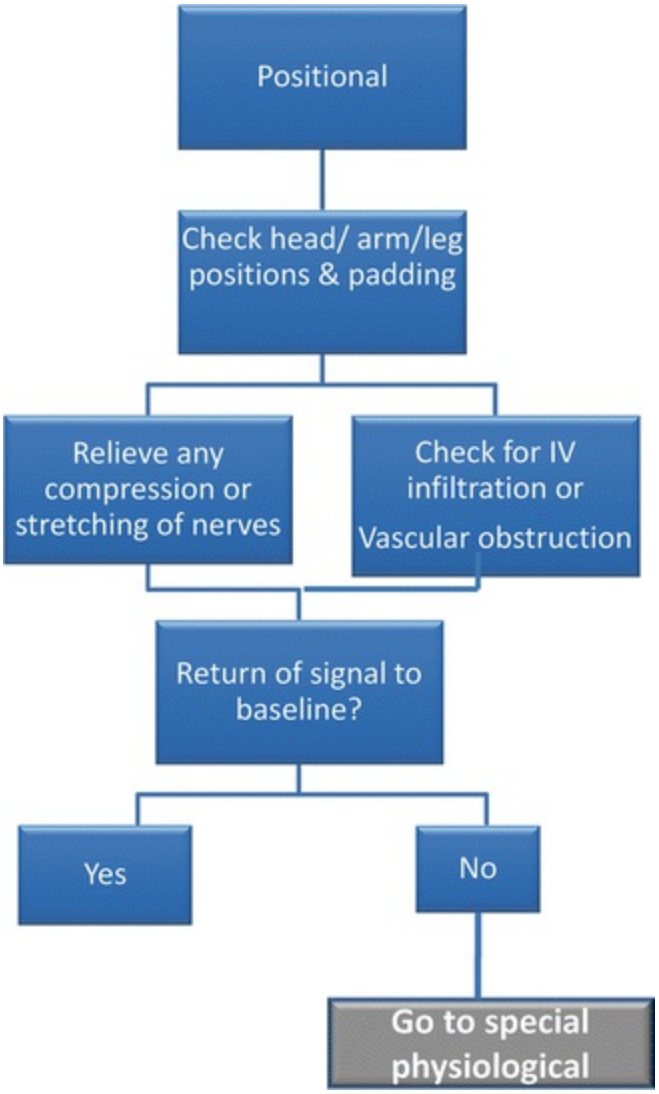

Acute reproducible neuromonitoring change
SSEP, MEP, ABR
Alert anesthesia & surgery team
Rule out obvious technical problem Go to Technical
Recent surgical maneuver?
No
Yes
Go to Surgical
Territory
Unilateral/Regional
Bilateral/Global
Go to Special Physiologic
Go to Positional
Go to Physiologic
Go to Pharmacologic


Surgical
Is the surgical maneuver reversible?
Yes
No
Reverse surgical maneuver
Signal return baseline?
Yes
No
Is it safe to increase perfusion?
Yes
No
Increase MAP 10-20%
Return of signal to baseline?
yes
No
Consider wake-up test in spine cases
Decrease oxygen consumption in brain cases


Pharmacologic
Was there recent change in anesthetic agents?
Yes
No
Consult anesthesia & surgical teams
Reduce anesthetic interference
Wait for Anesthetic Bolus to dissipate
Return of signals to baseline?
Yes
No
Go to Physiologic
Recent administration of NMB?
No
Yes
Go to Physiologic
Consult anesthesia & surgical team
Wait for NMB to dissipate
Reverse NMB
Return of signals to baseline?
Yes
No
Go to Physiologic


Physiologic
Recent change in physiologic parameters? BP, Temperature, Oxygenation etc
Yes
No
Recent drop in MAP?
Go to Pharmacologic
Yes
No
Raise MAP to ≥10-20% of awake baseline
Evaluate local perfusion and O_2 carrying capacity
Return of signals to baseline?
Yes
No
Inadequate
Adequate
Improve perfusion and oxygenation/ consider transfusion
Presence of hypothermia?
Return of signals to baseline?
Yes
No
No
Yes
Go to Pharmacologic
Rewarm patient or body region
Return of signals to baseline?
Yes
No
Go to Pharmacologic


Technical
Check EP machine and software
Check connections, impedances & montages
Check for peripheral or subcortical responses
Check for electrical noise
Present
Absent
Check recording sites
Return of signal to baseline?
Check Stimulation sites & delivery
Yes
No
Adjust & consider needles if pads were used
Go to "Recent Surgical Maneuver?"


Positional
Check head/ arm/leg positions & padding
Relieve any compression or stretching of nerves
Check for IV infiltration or
Vascular obstruction
Return of signal to baseline?
Yes
No
Go to special physiological

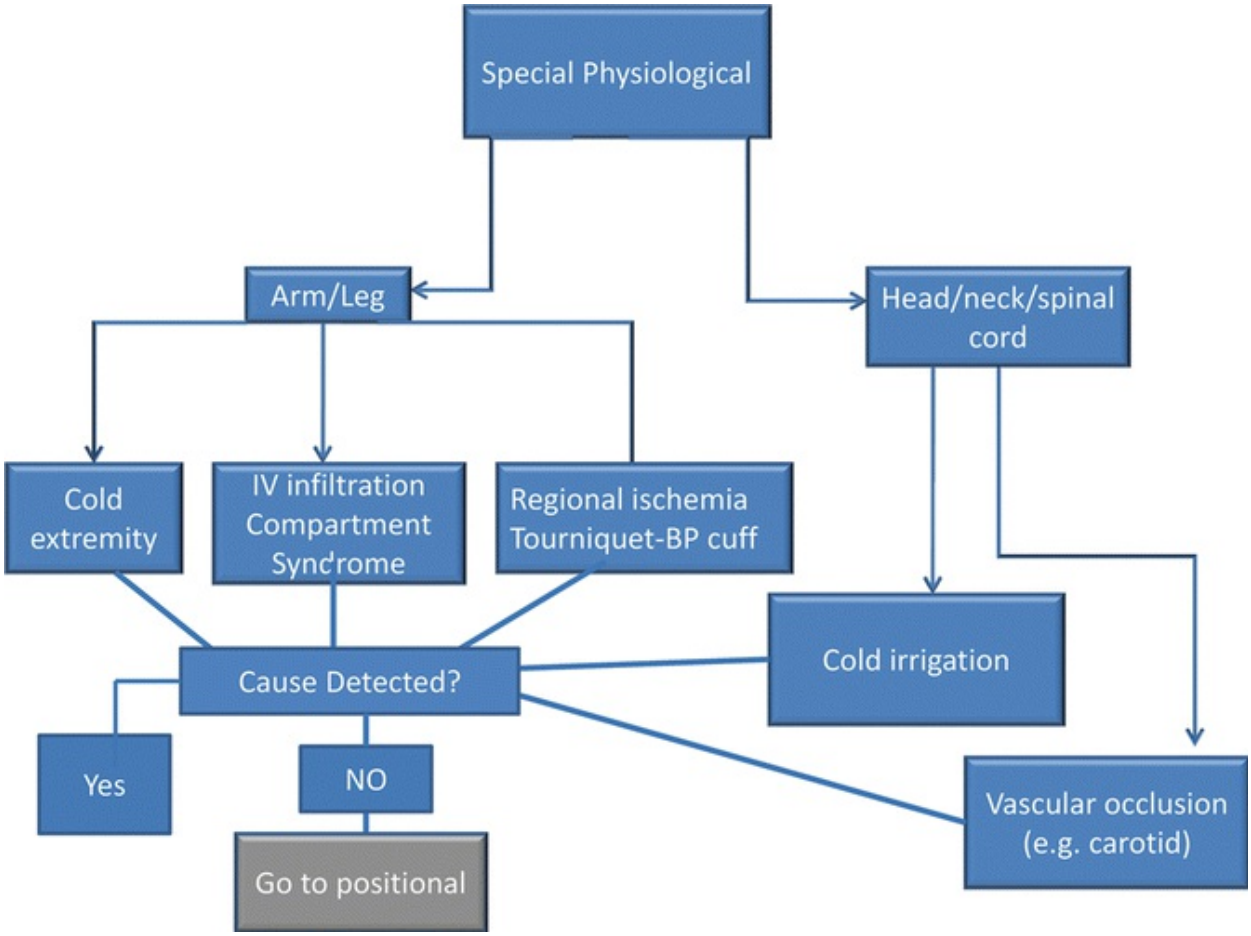


Fig. 20.1 (**a**–**g**) A basic algorithm for the anesthesiologist and other members of the monitoring team to use in evaluating the possible contributions to response deteriorations

The anesthesiologist is in a key position to evaluate the impact of anesthesia, physiology, and positioning, and therefore plays an important role in the search for an etiology . Often the specifics of the change can help identify possible causes. For example, anesthetic causes tend to be global and not to be focal in nature. Although certain IOM modalities are more sensitive to anesthetic agents (e.g., cortical somatosensory evoked potential [SSEPs] or muscle motor evoked potentials [MEPs]) (*see* Chap. 19, "General Anesthesia for Monitoring"), it would be very unusual for anesthetics to alter only one hemisphere or one extremity more than the other. In addition, some modalities are rarely affected by anesthetic agents (e.g., short latency ABRs , subcortical SSEPs, EMG responses [aside from muscle relaxant effects], and spinal recordings of SSEPs and MEPs). Therefore, if the change in the IOM is related to an anesthetic effect, then a quick search for changes in the management becomes essential. Since a steady-state anesthetic protocol is

least likely to produce changes, any abrupt change in drug delivery that may lead to an alteration in drug levels should be considered as a possible etiology. One exception is a slow change in IOM amplitude referred to as “fade ,” which is often ascribed to anesthesia but is not well understood [1]. In addition to being of global nature, anesthesia-related changes tend to occur within a short time (1–15 min) after alteration of the anesthetic levels.

A second category where the anesthesiologist must search for etiologies is that of physiology. Some of these effects are noted in several chapters. Like anesthetic effects, physiological effects may be global in their nature (i.e., they would usually expect to affect both sides of the body). Also like anesthesia, adverse physiology generally has more impact on cortical responses than subcortical responses, and within the spinal cord it has more of an effect on grey matter than white matter (*see* Chap. 40, “Surgery on Thoracoabdominal Aortic Aneurysms”). Hence, a quick scan of the physiological monitoring may help identify a change in blood pressure, heart rate, ventilation/oxygenation, etc. The effects of physiology can also be focal. For example, blood flow to one part of the brain could be reduced by carotid occlusion, hypothermia could occur primarily in one arm due to rapid infusion of cold fluids, and so on. In these cases, the question that must be asked is, what is the anatomic region that is affected based on the IOM responses, and what are the possible physiological circumstances in that region that could be unfavorable for the neural paths involved?

Frequently, the physiological effect is one of ischemia , and this is often amenable to changes in management so as to be supportive to the neural system. Not surprisingly, some surgical maneuvers may be contributing to the ischemia, and it is the combination of factors that leads to the end result of inadequate blood flow. For example, a brain or vascular retractor, an inadvertently misplaced vascular clip, a cannula in the iliac artery, a pledget placed against the spinal cord to tamponade bleeding, and so on, could cause an otherwise adequate blood pressure to be inadequate. For this reason, many anesthesiologists may raise the mean blood pressure when IOM changes suggest possible ischemia even though the specific etiology is unclear.

Also in the purview of the anesthesiologist is consideration of positioning. Evoked potential (EP) changes related to position tend to be associated with regional anatomical sites. Some of the positional changes may be related to the initial body position such as head position during the use of Mayfield pins, while other changes may be related to inadvertent

movements of the body parts. Some positioning changes may be obvious (such as an arm that is pushed by a radiology device or a surgical assistant into an adverse position), but others may be more subtle (e.g., spine sagging from release of intervertebral ligaments). In this case, a good knowledge of vascular and neural anatomy and a review of the patient's position (and any possible changes such as neck or arm movement) may reveal a possible etiology. As with anesthesia and physiology, a review of the specific neural tracts whose function is altered will help point to the specific area of concern if adverse positioning is considered. Not surprisingly, arm and shoulder positioning are frequent sources of concern, as is neck positioning in cervical and cortical procedures.

Finally, searching for technical problems is often a shared responsibility since IOM electrodes and equipment are in a "shared space." Although the IOM monitoring professional will usually take the responsibility for searching for technical problems, the anesthesiologist can also help by looking for changes in electrodes and equipment (e.g., a transcranial Doppler [TCD] transceiver), as well as considering the introduction of new equipment that may have moved IOM equipment or introduced electrical noise that alters the signal.

Experience suggests that there are two major categories of technical aspects in which the anesthesiologist may assist the IOM professional in the search for problems. First is electrical noise that contaminates and degrades the IOM signals. These can be transmitted through the electrical supply that the equipment is plugged into or may be due to electromagnetic signals transmitted through the air. Frequently, this is from a newly added electrical device such as a blood warmer that is near the IOM recording electrodes or recording amplifiers but can also be from a power cord that is moved near the electrodes or preamplifiers. Machines that are used for anticlotting during surgery can also often produce high electrical interference. Twisting the leads that are connected to the patient and lifting those away from the headbox or amplifiers will often help to alleviate the magnitude of this problem. Once identified, the device may be able to be relocated recognizing that the electrical noise may be reduced by plugging into a different electrical socket, rotating the orientation of the device, or moving it farther away from the recording electrodes (radiated noise falls by the square of the distance from the source). If a particular piece of equipment consistently interferes with recording, it may need to be checked by the biomedical department for a bad

ground. Noise could also occur if any of the recording electrodes (especially the ground electrode) are fully or partially dislodged. In addition, dislodged stimulating electrodes could also affect the IOM responses. Hence, examining for obvious electrode or IOM equipment problems near the patient could be helpful. Finally, some equipment may actively supply a test signal to the patient to check their connections, and this could be a source of electrical noise necessitating that an alternate piece of equipment be used for these cases. This has been observed in some electroencephalographic (EEG) recording devices (checking their electrode impedance) and some electrosurgical units (monitoring the grounding pad). For more details on electrical problems and signal optimization, *see* Chaps. 16 ("Wiring and Electrical Interference in IOM") and 17 ("Techniques for the Optimization of Signal Acquisitions").

Technical changes tend to be one-sided; however, bilateral changes can occur if the problem is related to a common lead. Like anesthesia, physiology, and positioning, the identification of technical problems also relates to anatomy—in this case the "anatomy" of the IOM equipment and the stimulating and recording equipment/electrodes.

Just as the team effort must be designed to make the IOM most effective, when changes occur, the team must also work effectively to identify possible etiologies for correction as well as possible changes in management, which may provide a more supportive neural environment; both of which are designed to improve the safety for the patient and facilitate the best possible outcome.

Dedication

Thanks to Carine Zeeni, Dhanesh Gupta, Laura Hemmer, and John Bebawy for their contribution to the Algorithm.

Reference

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Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_21

21. Intraoperative Neurophysiological Monitoring for Intracranial Aneurysm Surgery

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Electronic supplementary material:
The online version of this chapter (doi:10.1007/978-3-319-46542-5_21) contains supplementary material, which is available to authorized users.

Keywords Intracranial aneurysm – Intraoperative neuromonitoring – Clip ligation – Endovascular therapy – Adenosine

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Key Learning Points

- Intraoperative neuromonitoring during intracranial aneurysm clipping acts as a real-time method for detecting ischemia and is effective both for risk warning and assistance with surgical strategy decision making.
- MEPs confer additional monitoring benefit over SSEPs in detecting ischemia in parts of the motor pathway with an intracranially distinct blood supply from the sensory pathway (e.g., subcortical areas/deep structures supplied by perforating arteries). They can also give earlier warning than SSEPs of potential injury, because subcortical pathways can be particularly sensitive to interruption of blood flow.
- Since multiple vascular territories can be affected during intracranial neurovascular procedures, the use of both SSEP and TCMEP monitoring for the upper and lower extremities should be routinely considered. However, it is especially important to monitor the territory most at risk based on aneurysm location (e.g., contralateral upper extremity for ICA and MCA aneurysms, and contralateral lower extremity for anterior cerebral aneurysms.)

Introduction

Primary intracranial aneurysms (i.e., those not associated with infectious or traumatic causes) are found in approximately 1–3 % of the population, although the prevalence is higher in women, smokers, and patients with a genetic predisposition (i.e., autosomal dominant polycystic kidney disease or a family member with subarachnoid hemorrhage [SAH]) [1–3]. The natural

history of intracranial aneurysms is heavily dependent on the location of the aneurysm and the aneurysm geometry (e.g., diameter, aspect ratio, size of the parent artery) at the time of discovery [4–6]. Other factors that may affect the natural history include a previous history of SAH, familial history of SAH, presence of connective tissue disease, cocaine abuse, and heavy alcohol intake [7]. In addition, patient factors, such as smoking, hypertension, and other causes of systemic inflammation, can increase the risk of aneurysmal rupture [8]. Therefore, the incidence of aneurysmal rupture is estimated to be between 0.05 and 6 % per year, depending on patient factors and the aneurysm anatomy and geometry [1–7, 9].

Aneurysmal subarachnoid hemorrhage is a neurologic catastrophe that requires care at medical centers that can not only treat the cerebral aneurysm , but also manage the associated cardiac, cerebral, and pulmonary complications that increase perioperative morbidity and mortality [1]. Approximately 10–15 % of patients experience sudden death, while only 20–30 % return to preoperative neurologic status, often because of the high neurologic morbidity associated with delayed cerebral ischemia. Aneurysmal rebleeding , which occurs in at least 4 % of patients in the first 24 h and then 1.5 % additional per day over the next 2 weeks, is associated with a 70 % mortality. The preoperative neurologic status (measured by the Hunt and Hess Clinical Grade or the World Federation of Neurological Surgeons Grade) is the major determinant of neurologic outcome and mortality from all causes. In fact, neurologic grade as well as the Fisher score is a useful biomarker for the risk of development of delayed neurologic ischemic deficits and subsequent neurologic morbidity and mortality [1]. For the above-mentioned scales, both Hunt and Hess and World Federation of Neurological Surgeons Grade are based on clinical presentation and they grade consciousness or consciousness and motor deficit, respectively, while the Fisher score is based on the hemorrhage pattern on initial head CT scan.

Most aneurysms are asymptomatic until they rupture. For aneurysms found prior to rupture by screening high-risk patients or by evaluation of neurologic symptoms related to mass effect, such as headaches, cranial neuropathies, or seizures, treatment is dependent on the predicted risk of rupture or progression of neurologic symptoms. For patients younger than 60 years of age who have unruptured, small (<7 mm) anterior circulation aneurysms, microsurgical clip ligation offers the benefit of definitive repair with no change in neurologic and cognitive morbidity and mortality at 30

days and 1 year [3]. In contrast, for aneurysms amenable to both microsurgical clipping and endovascular therapy , endovascular therapy may be associated with less mortality and lower incidences of neurologic morbidity and cognitive impairment. However, the risks of aneurysm recurrence and subsequent hemorrhage are higher with endovascular therapy compared with microsurgical clipping [2, 10]. Most ruptured aneurysms should be treated by either microsurgical clipping or endovascular coiling as early as feasible in order to reduce the risk of rebleeding. A decision regarding treatment modality should be made as a multidisciplinary effort between cerebrovascular surgeons and endovascular specialists and based on patient and aneurysm characteristics [11].

Unfortunately, treating a ruptured aneurysm does not decrease the incidence of delayed cerebral ischemia. However, early aneurysm treatment does allow the neurocritical care team to employ all available management modalities, including hemodynamic augmentation and cerebral angioplasty or intra-arterial vasodilator therapy with a significant decrease in the possibility of aneurysm rebleeding [1]. Of note, “triple-H therapy”, consisting of hypertension, hypervolemia, and hemodilution, has long been a mainstay of critical care management of these patients, but evidence of efficacy is lacking and accumulating clinical studies and guidelines now emphasize hemodynamic augmentation with euvolemia maintenance and induced hypertension for delayed cerebral ischemia [11, 12].

Cerebrovascular surgery , from planned temporary arterial occlusion, malpositioned aneurysm clips impinging on the parent vessel or inadvertently occluding a perforating artery, accidental dissection-related trauma, and/or unintended local injury from brain retraction, presents substantial risks of cerebral ischemia that can produce neurologic morbidity and cognitive impairment. As with preoperative aneurysm rupture, intraoperative aneurysmal rupture (or re-rupture) is associated with a substantial neurologic and cognitive morbidity and high mortality. Aneurysms can rupture at multiple key times during the intraoperative period due to abrupt increases in the transmural pressure of the aneurysm wall or as a result of direct aneurysm injury during surgical dissection and aneurysm manipulation. Transmural pressure increases can be seen both with arterial hypertension (such as can occur without adequate anesthesia during tracheal intubation, placement of Mayfield head fixation, and surgical incision), or with intracranial hypotension (such as can occur with aggressive cerebral spinal fluid

drainage). Any perioperative tool that serves as an early warning of cerebral ischemia may decrease neurologic morbidity, cognitive impairment, and mortality.

Although endovascular therapy may be associated with less mortality and lower incidences of neurologic morbidity and cognitive impairment for some aneurysms, endovascular therapy has its own series of potential neurologic insults. Along with catheter-induced inadvertent aneurysm rupture, one of the potentially most devastating endovascular accidents that can occur is inadvertent embolization of a downstream artery. Neurophysiologic monitoring, as used in some centers, serves as an early warning to the interventionalist to detect re-bleed, hemorrhage, or embolic ischemia and may also decrease complications. See Chap. 42, “Interventional Neuroradiology”, for additional details.

Large (10–25 mm) and giant (>25 mm) aneurysms require special perioperative considerations . Often these aneurysms are difficult to treat surgically because they can be calcified, partially thrombosed, and have complex necks. In addition, these large and giant aneurysms are most often located in the posterior circulation, including the basilar apex. This provides its own surgical difficulties because of treacherous surgical access due to the deep location and a plethora of perforating arteries and cranial nerves in close proximity. Endovascular recurrence rates are highest in this subgroup. Hence, there remains a strong rationale to approach these lesions microsurgically [13, 14]. If endovascular therapy is not a viable option, these aneurysms often require a logistically complex surgical approach that includes such techniques as adenosine-induced flow arrest , endovascular balloon suction-occlusion of the parent vessel, deep hypothermic circulatory arrest , and extracranial-intracranial arterial bypass [15, 16]. Each of these techniques is associated with its own neurologic morbidity and mortality, some of which can be mitigated by neurophysiologic monitoring and techniques that might decrease the vulnerability of the brain to injury by prolonging tolerance to temporary ischemia [17, 18].

Case Presentation 1: MCA Aneurysm

A 45-year-old woman without significant past medical history is scheduled for clipping of a right 8 × 5 mm MCA aneurysm at the junction of M1 discovered on MRI done after a minor motor vehicle accident.

Which Monitors Should You Consider for the Aneurysm Clipping?

American Society of Anesthesiologists' standard monitors , including end-tidal carbon dioxide monitoring and temperature, should be used. Because hemodynamic control to minimize risk of aneurysm rupture is imperative, and manipulation of systemic pressure with vasoactive agents is often required, intra-arterial pressure monitoring also is indicated. Central venous access and pressure monitoring may be desired for vasoactive medication delivery and for assistance in determining volume status, particularly in especially complex or ruptured aneurysms. Osmotic diuretics are often used, mandating urine output monitoring. Multimodal neurophysiological monitoring—electroencephalography (EEG), somatosensory-evoked potential (SSEP), and motor-evoked potential (TCMEP) monitoring—should be considered to help identify cerebral ischemia.

What Do We Expect the Selected Neuromonitoring Modalities to Monitor During This Surgery?

The EEG is sensitive to changes in cerebral perfusion and can be used to confirm pharmacologic burst suppression, if this is employed. SSEPs can give a real-time indication of the functional integrity of the sensory system and, due to shared blood supply to the motor cortex, can give an indication of motor function [19]. TCMEPs can detect ischemia in parts of the motor pathway with an intracranially distinct blood supply from the sensory pathway (e.g., subcortical areas/deep structures supplied by perforating arteries). They can also give earlier warning of potential injury, because subcortical pathways can be particularly sensitive to interruption of blood flow [20, 21]. See Chaps. 10 ("EEG Monitoring"), 1 ("Somatosensory Evoked Potentials"), and 2 ("Transcranial Motor Evoked Potentials") for the technical aspects of performing these neuromonitoring techniques, respectively.

Although there are ethical concerns in withholding a potentially beneficial treatment or ignoring warnings of neurological system compromise (making prospective, randomized, blinded trials of neuromonitoring modalities in intracranial aneurysm clip ligation unlikely), there is accumulating literature support for neuromonitoring [22]. SSEP and TCMEP

monitoring together has been found to alter the surgical strategy in 20 % of aneurysm clipping surgeries, with TCMEPs resulting in surgical strategy change in 16 % and SSEPs in 4 % [21, 23]. In a study comparing the motor outcomes at a single center for unruptured anterior circulation aneurysm clipping before and after institution of TCMEPs, Yeon et al. [24] concluded that, with SSEP and TCMEP monitoring, postoperative motor deficits can be minimized to less than 1 %, which is comparable to or better than coiling. In MCA aneurysm clipping, such as for the patient in this case presentation, a prospective cohort study by Yue et al. [25] concluded that patients without intraoperative TCMEPs were nearly four times more likely to experience postoperative motor status decline than patients with TCMEPs (odds ratio, 4.77; $P = 0.042$) [25]. Guo et al. [26] reviewed case series and a permanent intraoperative TCMEP loss was found to have a positive predictive value of 1.0. Transient signal loss or deterioration was found to be associated with a variety of postoperative clinical findings, and the positive predictive value of a transient loss or signal change was 0.31. Application of causality guidelines, as by Holdefer et al. [27], shows very strong association, consistency across settings, and biological plausibility between surgical events and evoked potential changes in aneurysm clipping surgery.

What are Some Drawbacks of Each of the Above Monitors in Relation to This Surgery?

If burst suppression is requested by the surgeon, EEG monitoring for ischemia is then not possible during the critical phases of aneurysm clipping [19]. SSEPs can miss a most feared complication of aneurysm surgery—new motor deficit. In fact, in up to 25 % of cases of new postoperative motor deficit, there were unaltered SSEPs [21]. TCMEPs can be technically complex to employ in microneurosurgery, especially with concerns about patient movement elicited by TCMEPs [28, 29]. Some of the concern about movement with TCMEPs in this patient population may be overstated (although intraoperative movement could be catastrophic), since a retrospective review of 220 craniotomies for aneurysm clipping reported that 3.2 % of patients exhibited unacceptable movement with transcranial TCMEP stimulation, and in all but one case, TCMEP monitoring could be resumed after either deepening the anesthetic or decreasing stimulation intensity (depending on the suspected etiology of the movement), yielding a 99.5 %

monitoring rate [30]. (Also see Chap. 22 [“Intracranial Arteriovenous Malformation Surgery”] for further discussion related to movement with TCMEP signal acquisition.) With use of the minimum necessary stimulation intensity, the microsurgical field movement expected can be seen in Video 21.1. Importantly, too high of a stimulation intensity can also result in false-negative TCMEP results, as described in Chap. 22.

Upon arrival to the operating room and placement of the American Society of Anesthesiologists’ standard monitors, infusions of remifentanil (0.1 μg/kg/min) and propofol (50 μg/kg/min) were initiated and anesthesia was induced with boluses of lidocaine (1.5 mg/kg), propofol (2 mg/kg), and the intermediate acting non-depolarizing neuromuscular junction blocking agent, rocuronium (0.7 mg/kg). After confirming adequate neuromuscular relaxation with a nerve stimulator, the trachea was intubated and the patient was mechanically ventilated with an inspired fraction of oxygen of 50 % (air:oxygen mixture). Desflurane was titrated to maintain an end-tidal alveolar desflurane concentration of 0.5 minimum alveolar concentration or MAC . Anesthesia was maintained with a combination of desflurane (0.5 MAC), remifentanil (0.1–0.5 μg/kg/min), and propofol (0–150 μg/kg/min), and no additional neuromuscular junction blocking agent was administered. The right radial artery was cannulated for invasive arterial pressure monitoring and multiple (at least two) large-bore peripheral intravenous cannula were inserted for intravenous fluid administration, with one IV cannula dedicated to administration of intravenous anesthetic infusions. Since the aneurysm was unruptured, patient was normotensive and did not have history of hypertension, and the noninvasive blood pressure cuff was deemed reliable, the arterial line was placed after induction. After bladder catheterization was completed, the patient’s head was placed in a Mayfield head fixation device and the patient was then positioned supine with the left arm pressure points padded after placing it to the patient’s side while the right arm was placed on a padded arm board, easily accessible to the anesthesia team. Prior to surgical preparation of the head for incision, the neuromonitoring technologist placed the stimulating and recording electrodes in the scalp and the extremities for monitoring the EEG, median nerve SSEPs and TCMEPs, and the anesthesiologist placed a bispectral index (BIS) monitor. There are insufficient data to recommend one specific anesthetic regimen (the anesthetic described above is a common regimen at the authors’ institutions), but hemodynamic control must be maintained to minimize risk

of aneurysm rupture and consideration should be given to strategies to protect the brain against ischemic injury, such as avoidance of hyperglycemia [11].

During surgical field draping, the technologist obtained baseline values for all modalities and reported the following information: the EEG showed profound slowing with some burst suppression activity, the SSEPs showed decreased amplitude of the cortical wave recorded from stimulation of the left median nerve with normal right median nerve SSEPs, and the TCMEP responses were of small amplitude but symmetrical and present in all extremities.

What is the Interpretation of These Neurophysiologic Monitoring Waveforms?

It is clear that because the surgery has not started, none of the observed abnormalities in the neuromonitoring modalities are caused by a surgical insult. Therefore, other etiologies, such as technical problems with signal acquisition, physiologic disturbances to peripheral and central nervous system (CNS) function, and positional and pharmacologic factors, should be entertained. Since none of these factors alone could explain all the abnormalities, each one should be analyzed separately.

Slow EEG activity with periods of burst suppression is most likely related to medications [31–34]. Because the findings are global, they are unlikely related to blood flow irregularity resulting from head position (e.g., jugular venous obstruction from extreme neck rotation or flexion). Although hypotension from extreme head-up positioning can contribute to such changes, it is unlikely to be the cause in this case with the patient's supine positioning and blood pressure within preoperative normal limits. The most likely cause is profound depth of anesthesia induced by the combination of desflurane (0.5 MAC) and propofol infusion (100 μg/kg/min) [35]. In fact, the BIS value is 22. After temporarily decreasing the propofol infusion rate to 25 μg/kg/min for 10 min, the BIS value increases to 35 and burst suppression on EEG disappeared.

The global decrease in TCMEP signals at this stage of surgery is most likely due to residual motor blockade post–muscle relaxant administration for intubation [36]. While inhalational agents do affect TCMEP signals, the concentration used here is usually low enough to allow adequate TCMEP signals in a neurologically intact patient without residual muscle relaxant

present [37]. Although we have identified the likely cause of the abnormal global TCMEP signals, it is important to go through the entire differential to avoid overlooking a second cause of abnormal TCMEPs. A quick scan of the arterial pressure will exclude the other possible (and potentially devastating) cause of global signal changes. If there is concern that global hypoperfusion from systemic hypotension is causing signal change, temporarily increasing mean arterial pressure while not changing any other potential cause of the signal change will serve to test whether the patient had reached her lower limit of pressure autoregulation [38]. In this case, residual partial muscle blockade was confirmed by the neurophysiologist (or could be checked by train-of-four ratio). Over the following 30 min, the TCMEP amplitude improved as motor blockade resolved.

Unlike the global EEG and TCMEP findings, the SSEP signal abnormality is focal. Cortical SSEP changes due to anesthetic agents or physiological causes are usually bilateral and thus this SSEP abnormality is not related to either surgery (which has not commenced yet), anesthetic, or physiologic causes [39, 40]. Therefore, with this focal abnormality, a positioning or technical etiology would be suspected. Obstruction of jugular venous drainage from an extreme rotation and/or flexion of the neck is a possibility, but this is unlikely because the EEG had a global change, ruling out unilateral cerebral hypoperfusion from jugular venous obstruction. Examination of the left arm demonstrated no peripheral compression of the median nerve or any stretch on the brachial plexus—both positioning-related causes of abnormal signals from a single extremity [41]. The last possibility is a technical problem with signal acquisition, either at the stimulation site (left median nerve) or the recording site (scalp over the right lateral sensory cortex). A low stimulation intensity at the median nerve could produce these changes. This could be caused by excessive insulation between the stimulating electrode pad and the median nerve (i.e., obesity, edema, malpositioned stimulation pads far from the nerve). It can also be caused by an error in delivering the appropriate stimulation to the patient. Recording from Erb’s point and subcortical signals from cervical leads could confirm that the stimulus was being correctly delivered (and also confirm that the peripheral positioning was adequate) [42]. A normal Erb’s point and cervical recording with decrease or loss of the cortical responses can be related to blood flow obstruction to the right carotid artery. This possibility is excluded with positive palpation of the superficial temporal artery. A very rare but

possible cause is aneurysm rupture during induction or pinning due to sudden hypertension. However, blood pressure was maintained in normal range, and upon examination, pupils are miotic but equal in size and bilaterally reactive, decreasing the possibility of an intracranial catastrophe. Further inspection of the recording leads revealed a malpositioned C4′ scalp needle electrode and correction of this needle position resulted in normal signals. A similar circumstance could occur during the craniotomy if the brain had pulled away from the skull leaving a layer of air between the brain and recording electrode (Fig. 21.1).

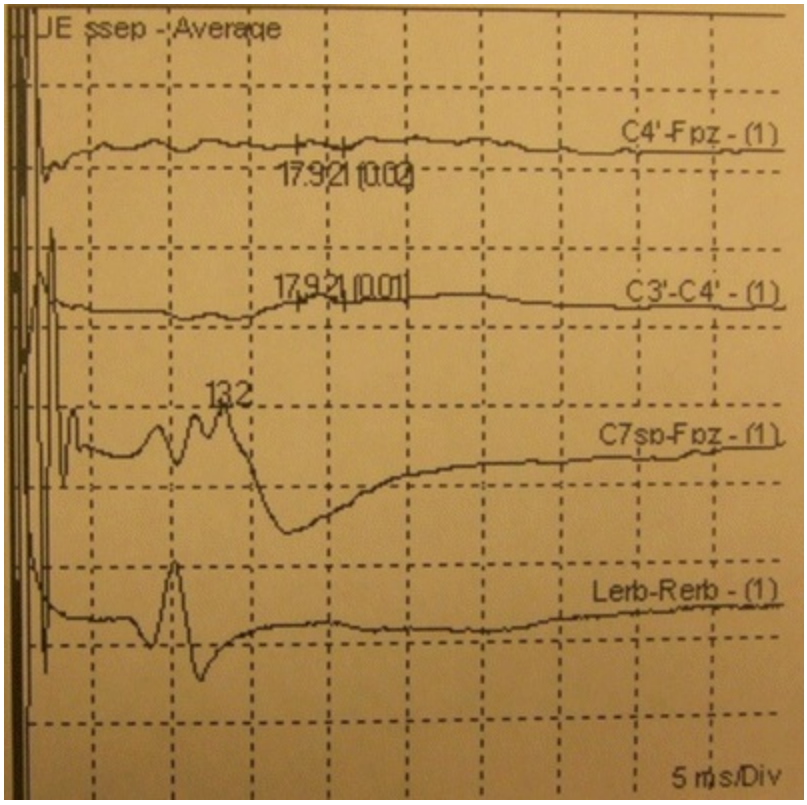

Fig. 21.1 Tracing of SSEPs from left upper extremity, with normal responses from Erb's point and the cervical region, but abnormal from the cortical leads. These abnormal tracing were caused by faulty positional placement of the C4 cortical lead. Normal responses were obtained after proper positioning

As surgery commenced, all neurophysiologic parameters were within normal limits. The dura was opened and the microscopic portion of surgery started. Surgery progressed well and the surgeon performed a few surgical adjustments to the surgical field to facilitate good exposure of the aneurysm. The technologist then announces an isolated but significant drop in the amplitude of the TCMEP signals recorded from the left hand (Fig. 21.2).

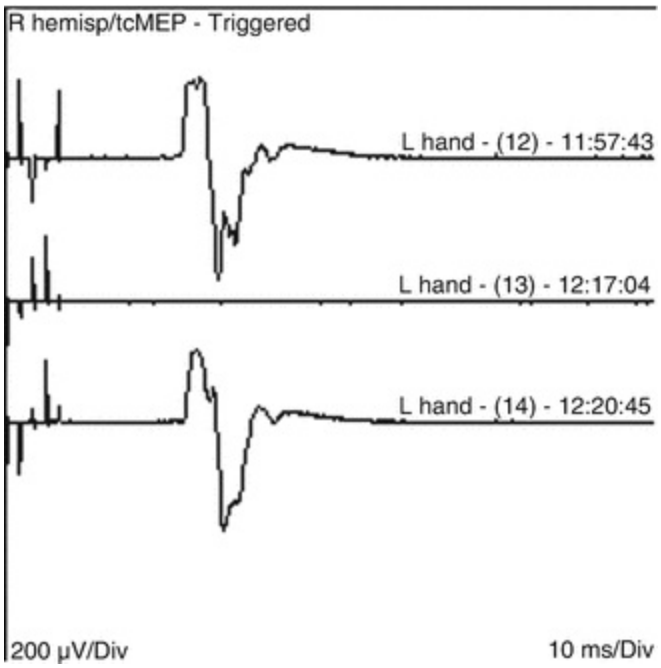

Fig. 21.2 Loss of hand TCMEP due to retractor pressure with prompt recovery after releasing the retractor

What is the Cause of This Change?

With any change in a signal during a surgical procedure, a surgical cause must be sought out quickly and efficiently—surgical causes must be quickly reversed before permanent damage occurs. Since surgical maneuvers were being performed with multiple adjustments of the retractors, this was likely the culprit. Retractor pressure can alter blood flow from the lenticulostriate arteries that supply the deep cortical and subcortical motor and sensory pathways or the branches of the anterior or middle cerebral arteries that feed the motor and sensory strips [43].

As noted above, TCMEP responses are more sensitive to ischemia and precede SSEP changes [21, 29, 44]. While the presence of SSEPs may be assuring of the outcome, the TCMEP changes serve as an early warning system for possible damaging ischemia [45]. In this case, the release of the retractor resulted in fast recovery of the TCMEP signals. To make sure no other source of change in TCMEP is overlooked, it is important, as always, to scan the rest of the possible causes of a unilateral change in a TCMEP. An isolated change is unlikely to be related to anesthesia or physiological maneuvers; since position was not altered, if there is no new pressure on the left upper extremity, this cause can be excluded too. Simple evaluation of the

stimulation pattern and the impedance of the stimulating electrodes, which were unchanged from baseline, can also rule out technical causes.

The surgical exposure proceeded well, and the surgeon requested initiation of pharmacologic burst suppression to, in theory, prolong the tolerance for ischemia in preparation for possible temporary clip placement [18, 46–48]. (Of note, there is no solid clinical evidence that pharmacologic treatment of ischemic brain and/or agents used intraoperatively for burst suppression is effective in these patients.) [11, 18]. Burst suppression was achieved by increasing the propofol infusion to 150 μg/kg/min. New "baseline" neuromonitoring signals should be obtained before critical surgical maneuvers, since high doses of most intravenous anesthetics can affect evoked potentials [49]. The surgeon took a final look and placed two tandem permanent clips. Two minutes later, the TCMEP signals of the left hand deteriorate followed by left median nerve SSEP changes.

What is the Cause of These Changes?

Since these unilateral changes occurred after surgical manipulation, surgical causes for such change are highly likely and should be investigated and managed immediately [21, 29, 45]. All members of the team should be involved in the investigation. The technologist should check the machine to confirm the fidelity of the system and exclude any last minute technical error. The anesthesiologist should induce hypertension (we usually raise blood pressure by approximately 20 %) to increase perfusion via the collateral circulation (i.e., the leptomeningeal pathways). The surgeon will visually inspect the field for potential vascular compromise, use a Doppler to interrogate blood flow, and may use indocyanine green (ICG) to perform a noninvasive angiogram (see Chap. 22). In this case, the ICG angiogram showed clip impingement on one of the blood vessels [50, 51]. The clip was readjusted with immediate recovery of TCMEPs followed by recovery of SSEPs (Fig. 21.3) (Video 21.2).

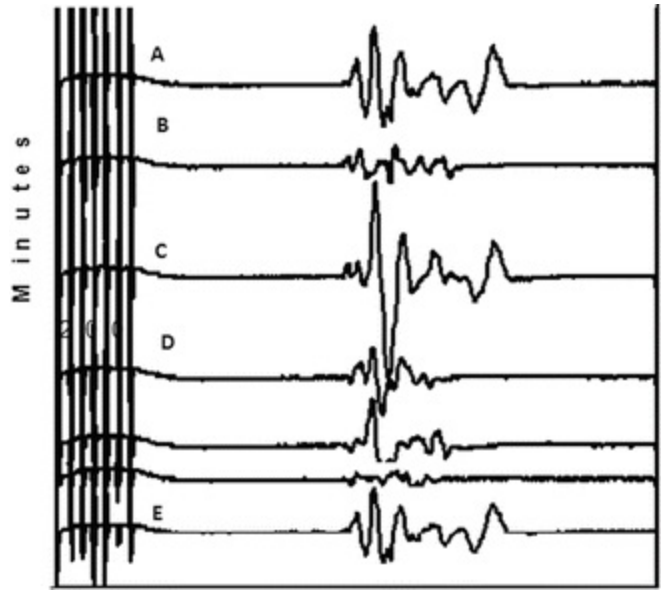

Fig. 21.3 Basilar artery aneurysm ; *A* = baseline, *B* = clip positioned, *C* = clip removed, *D* = clip repositioned, *E* = clip repositioned again

When a permanent clip is placed, there is risk of occluding a perforating artery, decreasing the size of the parent artery or causing severe spasm. Changes in TCMEP/SSEP can help identify such changes related to ischemia and a quick readjustment and treatment may prevent postoperative neurologic deficits [21, 29]. After clip readjustment and recovery of the signals, ICG and the Doppler confirmed good blood flow. The surgery concluded uneventfully. The patient emerged smoothly and was extubated in the operating room with the patient still receiving an infusion of remifentanil 0.05 μg/kg/min. Immediate postoperative exam revealed no neurological deficits. Fentanyl was administered as needed for postoperative analgesia and the patient was taken to the recovery room before proceeding to the ICU for overnight monitoring.

Case Presentation 2: ICA/Ophthalmic Aneurysm

An otherwise healthy 57-year-old female is scheduled for craniotomy for clip ligation of an unruptured 12 mm right internal carotid artery aneurysm just distal to the ophthalmic artery.

Anesthesia proceeded as in the first case, above. The surgical plan included potential placement of a right internal carotid artery endovascular balloon for occlusion with suction decompression to facilitate aneurysm

clipping [52]. Both groins and the right neck were prepped and draped prior to starting the craniotomy.

Should Only Upper Extremity SSEPs and TCMEPs, Only Lower Extremity SSEPs and TCMEPs, or Both Upper and Lower Extremity SSEPs and TCMEPs be Monitored for This Surgery?

With intracranial surgery, it is important to monitor the territory of the vascular structures where ischemia is most likely to occur [53]. For aneurysms involving the internal carotid artery (such as this case), middle cerebral artery, or posterior circulation, ischemia is most likely to involve the vascular territory of the sensory cortex of the contralateral upper extremity [44]. Hence, upper extremity SSEPs and TCMEPs are the most appropriate monitoring modalities. If the aneurysm involved the anterior cerebral artery or the anterior communicating artery, the contralateral lower extremity would be at primary risk [44]. With this surgery, the anterior circulation may also be at risk, and thus, monitoring the lower extremities should also be performed. In reality, since multiple vascular territories can be affected during intracranial neurovascular procedures in general, the use of both SSEP and TCMEP monitoring for the upper and lower extremities should be routinely considered [54].

Baseline-evoked potentials for upper and lower extremity SSEPs and TCMEPs were robust in amplitude and normal in latency and morphology. Surgery proceeded uneventfully with exposure of the aneurysm. The decision was made to proceed and place an endovascular balloon into the intracranial internal carotid artery proximal to the aneurysm via the right femoral artery. This was done with a plan to inflate the balloon, suction deflate the aneurysm, and trap the aneurysm with a temporary clip placed distal to the aneurysm on the intracranial internal carotid artery.

Trapping an aneurysm refers to the temporary occlusion of both antegrade blood flow from the upstream, parent artery, and retrograde blood flow from the distal, collateral arteries, in order to allow tension in the aneurysm neck to decrease enough for clip ligation and possible parent artery clip reconstruction. For anterior communicating artery aneurysms and middle cerebral artery aneurysms, trapping involves placement of three to four

temporary clips. In contrast, for intracranial proximal paraclinoid carotid artery aneurysms, either a temporary cross clamp has to be placed on the extracranial internal carotid artery after exposure by neck dissection, or an endovascular balloon tip catheter has to be placed in the internal carotid artery, proximal to the aneurysm, and the balloon inflated to occlude antegrade blood flow (Fig. 21.4). A more distal intracranial internal artery temporary clip is still required to occlude retrograde blood flow into the aneurysm. Suction can be applied in this scenario via the endovascular catheter to decompress the aneurysm while retrograde blood flow continues [52]. These maneuvers will enable the surgeon to safely clip the aneurysm, but with the risk of ischemia to any territory that is perfused by perforator arteries within the trapped arterial segment (e.g., the recurrent artery of Huebner during trapping for an anterior communicating artery aneurysm or the opthalmic artery during trapping of a paraclinoid carotid artery aneurysm). There is also the potential for ischemia to the territory normally supplied by the trapped parent artery, unless collateral flow via the Circle of Willis and/or the leptomeningeal pathway arteries is adequate.

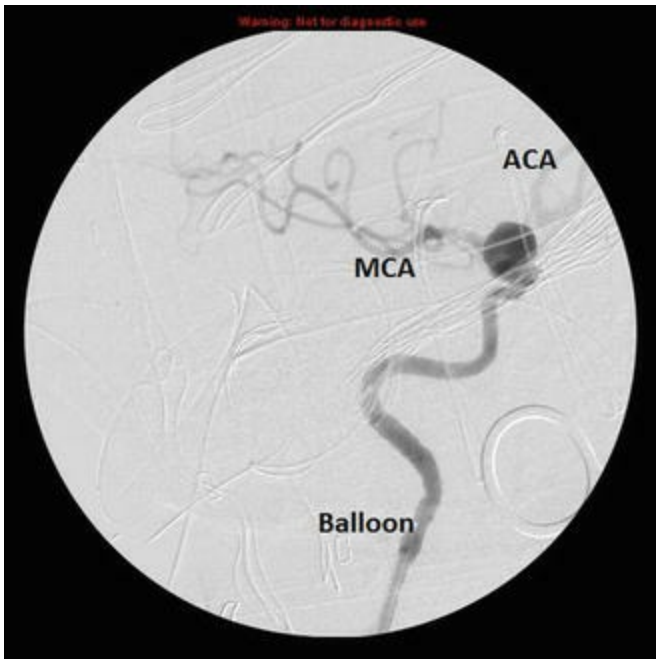

Fig. 21.4 Angiogram showing the placement of the balloon in the ICA, the aneurysm and both the MCA and ACA

Although traditionally both burst suppression and hypothermia would have been applied for this case, there is a dearth of literature support for these

activities. In theory, decreasing the oxygen consumption of the brain, along with increasing collateral blood flow, may prolong the time that the brain can tolerate ischemia [18, 47, 48]. Administering an intravenous hypnotic or a volatile anesthetic decreases oxygen consumption of neuronal tissue associated with electrical activity. However, once the EEG achieves a burst suppression ratio of 0.8 (i.e., an EEG pattern of 80 % electrical silence and 20 % bursts of activity), there is little additional decrease in the cerebral metabolic rate and the cerebral blood flow [55]. Hypothermia can also decrease cerebral oxygen consumption, with the added benefit of decreasing both the cellular metabolism associated with electrical activity and the energy requirements for nonelectrical cell processes [56]. Therefore, hypothermia may produce additional tolerance to cerebral ischemia as the temperature is lowered below the point of electrical silence [57]. Unfortunately, mild intraoperative hypothermia (33.5 °C) did not change the neurologic or cognitive outcomes in patients who had World Federation of Neurologic Surgeons Grade I or II SAH when compared with normothermia in a large international, multicenter, double-blinded, randomized-controlled study (Intraoperative Hypothermia for Aneurysm Surgery Trial [IHAST]) [58]. In addition to prolonging the tolerance to ischemia during aneurysm trapping, hemodynamic maneuvers that increase the collateral blood flow (e.g., increase systemic mean arterial pressure, decrease brain bulk, increase brain luxury perfusion) may prevent the onset of ischemia [18]. In this case, we achieved burst suppression and increased the blood pressure.

Surgery proceeded with the balloon inflated. The EEG demonstrated a burst suppression ratio of 0.8, and both the TCMEP and SSEP signals were stable. The aneurysm was difficult to clip and it took extra time to be completed. Twelve minutes after initiating the trapping, TCMEP signals from both the left arm and the left foot deteriorated, followed by SSEP signal deterioration at 15 min. Signal deterioration was thought to be related to cerebral ischemia from trapping. The surgeons were notified; unfortunately, they had opened the aneurysm dome and therefore reperfusion at that time was not an option (Video 21.3). The mean arterial pressure was increased approximately 20 %. Surgery proceeded with complete loss of both TCMEP and SSEP signals after 2 more minutes despite further induced hypertension. With completion of the aneurysm clip ligation and clip reconstruction of the parent artery, the balloon was deflated and the distal temporary clip was removed. The TCMEP and SSEP signals gradually recovered to baseline

morphology. Visual inspection, Doppler testing, and ICG angiograms demonstrated satisfactory reconstruction of the parent artery and no areas of inadequate dye or Doppler flow. Surgery proceeded and the patient was awakened at the end of surgery. On wake-up, it was noted that the patient had mild weakness on the left side, more in the arm than the leg, and both improved within 30 min.

In this case, the TCMEP and SSEP changes occurred at minutes 12 and 15, respectively. These late occurring post-trapping changes are likely better tolerated than changes that may occur within the first 4 min after temporary arterial occlusion or aneurysm trapping [21, 29, 44]. The changes seen in both TCMEP and SSEP are due in this case to surgical maneuvers consistent with the aneurysm trapping. In general, all other causes should be contemplated and excluded. However, because of the temporal relationship to the known surgical insult, we needed to concentrate on the surgical cause. It is important to have a stable anesthetic and hemodynamic course and to avoid changes in technical parameters at this point of surgery in order to avoid producing false-positive signal deterioration.

The initial weakness in the first 30 min after emergence from anesthesia may be related to regional ischemia caused by blood flow interruption and alterations in regional cerebral blood flow, especially in areas of ischemia. Reduced reperfusion may result in slower washout of the anesthetic drug, thereby prolonging the time course until the region at risk recovers from anesthesia [59].

Case Presentation 3: Basilar Apex Aneurysm

A 64-year-old woman is undergoing an orbitozygomatic-pterional craniotomy for microsurgical clipping of an unruptured 15-mm wide-neck basilar apex aneurysm.

How Does This Aneurysm Location Influence the Choice of Neurophysiologic Monitoring Modalities to be Used?

Part of the large morbidity and mortality associated with surgical correction of basilar apex and posterior circulation aneurysm is due to the proximity of multiple brainstem and subcortical perforator arteries as well as the limited

surgical corridors, which make visualization challenging [17]. Although SSEPs and TCMEPs provide information regarding the integrity of the subcortical and brainstem pathways with regard to direct neurologic injury or injury secondary to ischemia, brainstem auditory-evoked responses (ABRs) provide additional monitoring more specific to the brainstem integrity, and ABRs are very resistant to anesthetic effects (see Chap. 3 [“Auditory Evoked Potentials”] for additional information). Therefore, ABRs are often included to give complimentary information to help determine the specific location of neurologic trespass that may produce permanent neurologic injury from trauma or ischemia. In addition, because it is difficult to obtain a panoramic view of basilar apex aneurysms and the perforators at risk for injury, using these neuromonitoring modalities provides better functional evaluation of the possibility of clip impingement of perforators (Fig. 21.5). Electromyography (EMG) for cranial nerve monitoring of any cranial nerve with a motor component at anatomic risk may also be used for posterior circulation aneurysms (see Chap. 7, “Electromyography”, for additional information.)

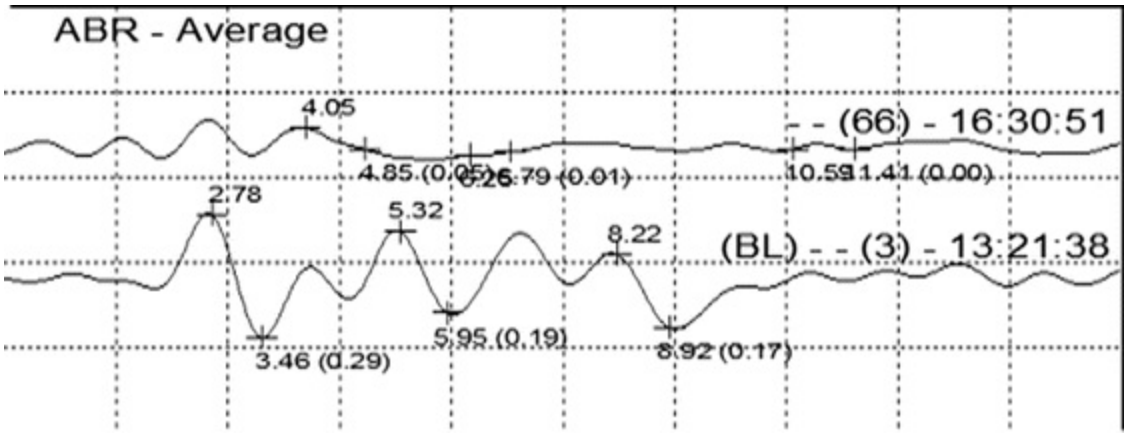

Fig. 21.5 ABR tracing showing the changes in waves IV and V

After isolating the aneurysm, the surgeon determined that the aneurysm neck was extremely tense and that there was no safe location to place a temporary arterial clip to soften the aneurysm neck. After the aneurysm had been exposed and the patient demonstrated an EEG with a burst suppression ratio of >0.8, as requested by the surgeon, the surgeon manipulated the aneurysm to inspect possible clip placement and inadvertently ruptured the aneurysm. The microsurgical field filled with blood and it was impossible for the surgeon to identify any anatomical structures to control the bleeding. The

anesthesiologist administered 0.4 mg/kg of adenosine as a rapid intravenous bolus and this produced a 15 s sinus pause and a total of 45 s of profound hypotension (systolic blood pressure <60 mmHg), allowing a bloodless field and permanent clip placement [15] (Video 21.4 and Video 21.5).

All neurophysiologic signals were stable. The surgeon evaluated the position of the clip and was satisfied. As the surgeon irrigated the field to prepare to begin dural closure, the left upper extremity TCMEPs became attenuated.

What are the Most Likely Etiologies for This Signal Change?

The operative team again follows a systematic approach to determine the etiology of this focal change. Physiologic and anesthetic etiologies are improbable for a focal change and technical causes were ruled out. Because the change occurred only a few minutes after surgical manipulation that has a high probability of causing a neurologic injury (placement of a permanent aneurysm clip), a surgical etiology is most likely. After communication with the surgeon, an ICG angiogram was performed and a small perforator deep to the aneurysm neck was found to be occluded by the permanent clip. An additional dose of adenosine was administered and the surgeon repositioned the permanent clip. A second ICG angiogram, after the background ICG had dissipated, was performed and the perforator appeared patent. The TCMEPs began to normalize 2 min after clip repositioning and returned to baseline levels before completion of the dural closure [21, 29, 44, 45].

Questions

1. Question (True or False): Motor-evoked potential signal that is lost and then recovers during surgery after intervention taken to reverse the deleterious effect still indicates the patient will awake with neurological deficit.

2. Question (True or False): MEPs offer little additional information as long as EEG and SSEP are monitored during aneurysm clipping.

3. Question (True or False): For an anterior cerebral artery aneurysm,

monitoring EEG and SSEPs and MEPs of bilateral lower extremities is important for detecting comprise to a critical neurological structure.

Answers

1. False. Signals that are lost and then recover after intervention during surgery can lead to a range of clinical findings postoperatively from no deficit, transient deficit, to mild permanent deficit. As noted above, Guo et al. [26] found the positive predictive value of a transient loss or signal change was 0.31.

2. False. MEPs are able to monitor parts of the motor pathway with separate blood supply than the sensory pathway. This is particularly important for perforating artery compromise that could be undetected by EEG and SSEP, but could result in hemiplegia for the patient. Furthermore, MEPs often give earlier warning of potential injury than SSEPs.

3. True. It is important to at least monitor the anatomic area most at risk during surgery. For aneurysms involving the anterior circulation, the contralateral lower extremity is at most risk. For aneurysm involving the internal carotid artery, middle cerebral artery, or posterior circulation, ischemia is most likely to involve the vascular territory of the sensory cortex of the contralateral upper extremity.

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Footnotes

1 Key references marked with asterisk.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_22

22. Intracranial Arteriovenous Malformation Surgery

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Keywords Intraoperative neurophysiological monitoring – Intracranial arteriovenous malformation surgery – Normal perfusion pressure breakthrough

Key Learning Points

- There is evidence from both an adult and pediatric patient series that neuromonitoring intraoperatively is useful to help prevent morbidity in surgical and endovascular management of cerebral AVMs.
- Particularly for intracranial surgeries, transcranial motor-evoked potentials are made more accurate by decreasing stimulation intensity. If

stimulation intensity is too high, myogenic MEPs from contralateral limbs could be obtained despite presence of cortical ischemia or even deeper subcortical ischemia, and this would lead to a false-negative MEP result.

- Advances in neuroimaging, neuromonitoring, and microsurgical technique are allowing more surgical treatment of AVMs located in close proximity to eloquent areas when treatment once would have been limited to more conservative management. Neuromonitoring advances facilitating this surgery include application of EEG, SSEPs, MEPs, as well as mapping techniques for patients under general anesthesia. There is also some more recent promotion of awake anesthetic techniques to facilitate monitoring and mapping for resection of AVMs in or near eloquent areas.

Introduction

Arteriovenous malformations (AVMs) are tangled anastomoses of blood vessels in which arteriovenous shunting occurs in a central nidus (the area where feeding arteries converge and from which enlarged veins drain) [1, 2]. AVMs are the most common type of vascular malformation, with autopsy data suggesting an overall frequency of about 1–4 % [3]. However, only about 12 % of AVMs become symptomatic [1]. The mean age at presentation is 35 years old, and the majority present with intracranial hemorrhage (usually intracerebral hemorrhage) [1, 4]. There is an overall risk of initial hemorrhage of about 2–4 % per year. The next most common presentation is seizure, followed by headache and focal neurological deficit [1]. In young children, presentation can also include congestive heart failure and hydrocephalus [3].

The most commonly used grading scale for AVMs is the Spetzler-Martin AVM Grading Scale , a five-point scale that considers AVM size, pattern of venous drainage, and location [5]. Other important factors in determining management include surgical accessibility, number of feeding arteries, flow velocity through lesion, steal from surrounding brain, and presence of associated aneurysms [3, 5]. With the Spetzler-Martin scale, higher-grade lesions have a higher treatment associated morbidity [5].

Arteriography is the “gold standard” for defining the arterial and venous anatomy of AVMs (Fig. 22.1). Magnetic resonance imaging is also used for

localizing and defining AVM topography [3]. High-flow, angiographically identifiable AVMs are considered “giant” if their size is greater than 6 cm [6].

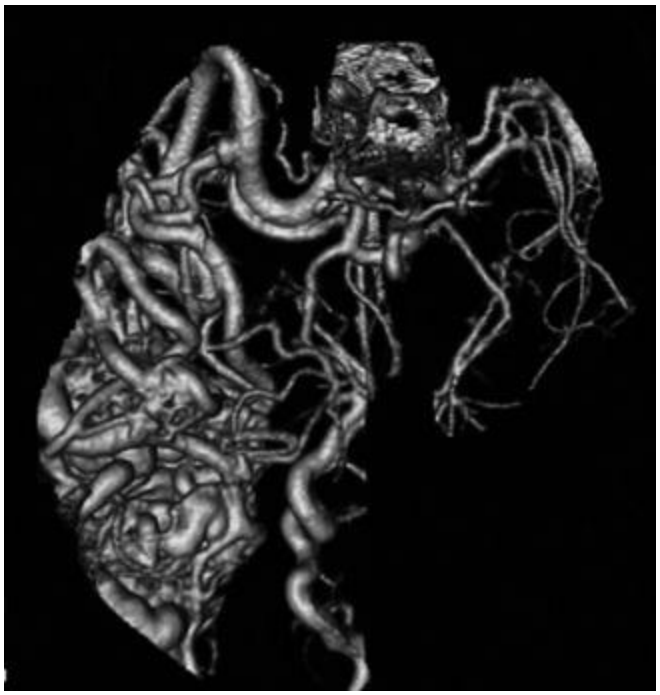

Fig. 22.1 Angiogram of an arteriovenous malformation (AVM)

Treatment options for AVMs include expectant monitoring versus complete obliteration using microneurosurgery, endovascular techniques, or radiosurgery. Embolization can be employed presurgically or preradiosurgically for progressive flow reduction and decrease in nidus size, to occlude deep/inaccessible arterial vessels and to eliminate related aneurysms. It can also be used palliatively for worsening neurological deficits in large AVMs not suitable for surgical management. Radiosurgery is usually employed to destroy small AVMs, especially if they are poorly accessible or if they are in an eloquent brain location [3]. In patients who undergo radiosurgery that then fails, surgery is usually facilitated, since deep and fragile arteriolar feeders tend to become fibrotic and easier to manage [7]. Surgically, AVMs are usually excised with routine microsurgical technique by ligating arterial feeders and then excising the nidus and resecting the draining vein(s) [1, 3] (Fig. 22.2).

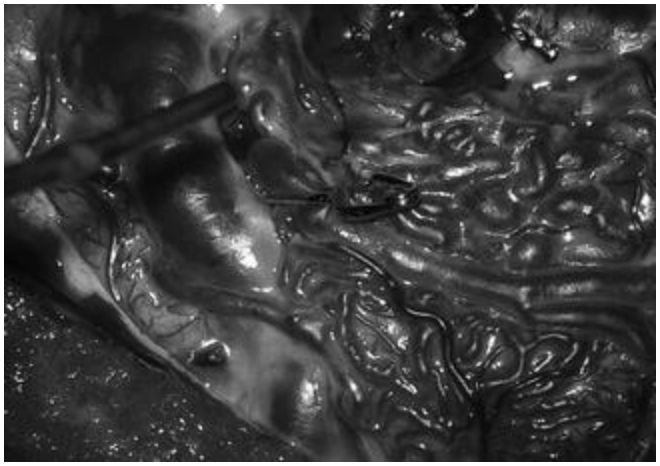

Fig. 22.2 Microsurgical excision of an arteriovenous malformation with a temporary clip in place

Prior to management, it is sometimes necessary to perform Wada testing with intracarotid injection or superselective Wada testing in the neurointerventional suite with specific arterial injection of usually the short-acting barbiturate amobarbital to inhibit gray matter structures and the local anesthetic lidocaine to inhibit white matter structures to detect eloquent brain tissue perfused *en passage* by AVM feeding arteries to better preserve function [8]. For embolization , materials used include Gelfoam (from purified skin gelatin), polyvinyl alcohol particles, *N*-butyl cyanoacrylate, Onyx (a non-adhesive liquid polymer), and a variety of coils [9]. Although the patient is awake for Wada testing, general anesthesia is preferred at many centers for AVM embolization to facilitate imaging and prevent patient movement. Depending on the agent deployed, some specific anesthetic maneuvers may be undertaken. For example, transient profound-induced hypotension may be necessary to aid in correct embolic glue setting, and temporary apnea is sometimes requested to improve visualization [10] (see Chaps. 20 and 21 for discussion of potential physiological effects on neuromonitoring as well as later in this chapter).

Routine neuroanesthetic management for intracranial lesions applies to AVM surgical resections. Because AVM resections are generally elective, the patient should be medically optimized prior to surgery. There is the potential for rapid and massive blood loss, so adequate intravascular access and blood availability is mandatory [3, 11]. Risk of AVM rupture during induction is low, but it should be remembered that the incidence of a coexisting intracranial aneurysm is at least about 10 %, so blood pressure control in the

range of the patient's normal pressures is warranted [1, 3, 11]. The selected anesthetic regimen must maintain hemodynamic stability, provide amnesia, prevent patient movement to noxious stimulation, facilitate neuromonitoring, and allow rapid emergence, but no specific regimens have demonstrated superior safety in intracranial surgery [12, 13]. Anesthetics that decrease cerebral metabolic rate and vasoactive agents that do not promote cerebral vasodilation are usually selected. Maintenance of normothermia or a mild decrease in body temperature resulting from general anesthesia is generally accepted. Patients should be rewarmed in preparation for emergence [3, 11, 14].

Case Presentation

A 35-year-old woman with no significant past medical history presents for craniotomy for AVM resection after the AVM was incidentally discovered on an MRI performed for the patient's complaint of headaches. The AVM is located in the middle cerebral artery territory, and it has a maximal diameter of 4 cm.

What management could be considered to potentially decrease blood loss prior to surgical resection of the AVM?

Staged reduction in blood supply to the malformation via intra-arterial embolization is often recommended to decrease the size of the arteriovenous shunt [3, 6]. (For information on neuromonitoring for interventional neuroradiology procedures, see Chap. 42, "Interventional Neuroradiology".) To avoid development of collateral blood flow, surgical resection of the AVM should occur within several days after embolization of the final feeding artery [3].

Which monitors should you consider for the surgical resection ?

Monitoring for cerebrovascular surgery is aimed at all the physiological influences on cerebral blood flow [15]. American Society of Anesthesiologists' standard monitors including end-tidal carbon dioxide and temperature monitoring should be used. Because manipulation of systemic pressure with vasoactive agents is often required, intra-arterial pressure monitoring also is indicated. Central venous pressure monitoring may be desired for assistance in determining volume status. Osmotic diuretics are often used, mandating urine output monitoring. If the operative site is above heart level, a precordial Doppler probe to monitor for air entrainment should

be employed (and placement of a multiorifice catheter for air aspiration should also be considered). Finally, especially if deliberate temporary arterial occlusion is planned, multimodal neurophysiological monitoring—electroencephalography (EEG), somatosensory evoked potential (SSEP) , and motor-evoked potential (MEP) monitoring—should be considered to help identify cerebral ischemia (and therefore identify feeder vessels to eloquent areas) [16]. (See Chaps. 10 [“EEG Monitoring”], 1 [“Somatosensory Evoked Potentials], and 2 [“Transcranial Motor Evoked Potentials”] for the technical aspects of performing these neuromonitoring techniques, respectively.)

What are potential benefits of combining SSEP and MEP monitoring?

There is a dearth of prospective and randomized trials of neurophysiological monitoring in intracranial surgery. However, there is evidence, from both adult and pediatric patient series, that neuromonitoring intraoperatively is useful to help prevent morbidity in surgical and endovascular management of cerebral AVMs [17–20]. Because SSEPs and MEPs provide complementary information about the neurological system, combining these modalities may give a better reflection of the patient’s actual neurological status [21]. In fact, in up to 25 % of cases in which a new postoperative deficit manifests in intracranial neurovascular surgery (especially intracranial aneurysm surgery), intraoperative SSEP recordings were unchanged. This is not surprising since anatomically distinct arteries not supplying sensory pathways supply parts of the motor pathway (e.g., subcortical portions) [22]. MEPs also can give earlier warning of potential ischemic injury compared to SSEPs [23]. Finally, if there is difficulty in obtaining signals from one of the modalities, combining SSEPs and MEPs can increase the number of patients who can be successfully monitored [21]. Of course, it is especially important to ensure the anatomic area most at risk from the particular surgery is monitored, as discussed in Chap. 21 (“Intracranial Aneurysm Clipping”).

Although the majority of AVMS are suptratentorial in location, what additional neuromonitoring would be helpful if the AVM involved the posterior fossa/vertebrobasilar circulation ?

Posterior circulation and brainstem ischemia can be identified by using a combination of SSEPs, MEPs, and auditory brainstem-evoked potentials (ABRs) [17, 24] (see Chap. 3, “Auditory Evoked Potentials” for additional information). Electromyography for cranial nerve monitoring of any cranial nerve with a motor component at anatomic risk may also be added to the

neuromonitoring regimen (see Chap. 7, “Electromyography”, for additional information).

When should neuromonitoring be performed during the case?

Recordings should be obtained after anesthesia induction and once a steady state of anesthesia is achieved (but before incision) as a baseline. Obtaining a baseline before incision allows time for troubleshooting if technical difficulties are encountered, and, if evoked potential changes occur, it could help identify (and allow correction of) patient malpositioning while a surgical cause is a nonfactor. Recordings should be obtained at regular intervals during the procedure, even when there is minimal risk of neural injury. Anesthetic agents and levels, physiological parameters (mean arterial pressure and temperature), and surgical events should be noted with each reading. If burst suppression is initiated, a new “baseline” should be obtained before critical surgical maneuvers are undertaken, since high doses of most intravenous anesthetics can affect evoked potentials [25]. During critical surgical manipulation, neuromonitoring should be performed continually.

Transcranial MEP stimulation can cause movement of the patient. What can be done to minimize this movement?

Naturally occurring field movement can be limited with transcranial MEP stimulation by minimizing stimulus intensity to the lowest amount that results in reliable MEPs [26]. To avoid movement of the microsurgical field during critical surgical work, brief surgical pauses for monitoring should be coordinated with MEP testing. Often, MEP stimulation can be facilitated by the anesthesiologist noting a pause in surgery and initiating communication between the technologist and surgeon to efficiently acquire MEPs. Most MEP acquisitions can be timed to coincide with surgical instrument exchange. In addition, some stimulation locations used for MEPs may be associated with less movement. (To not sacrifice SSEP and/or MEP head electrode position when craniotomy site interferes with ideal electrode positioning, sterile electrodes can be placed by the surgeon.) Video monitoring can also be used to assist the neurophysiology team in timing stimulation with surgical pauses.

Spontaneous movement of the patient under anesthesia without muscle relaxation, which could occur with MEP stimulation, can be largely avoided by keeping the patient adequately anesthetized. We routinely use a maintenance anesthetic technique of moderate opioid dosing (≥0.1 μg kg $^{-1}$ min^{-1} remifentanil, 0.5 minimum alveolar concentration (MAC) of volatile anesthetic, and 0–150 μg kg^{-1} min^{-1} propofol). We pay close attention to

volume status and phenylephrine (10–50 μg min^{-1}) is added, if needed, to maintain adequate hemodynamics. Since much of the anesthetic regimen is via intravenous infusion, diligence is required to ensure that drug delivery problems, such as extravasation or mechanical obstruction, do not occur (which could result in the patient being "light" and spontaneously moving).

After initial baseline MEP recordings are obtained, you note detectable signals from bilateral upper and lower extremities. However, you notice that both contralateral and ipsilateral waveforms are obtained with stimulation of one hemisphere. What is happening and what can be done to correct this?

The stimulation intensity should be decreased. Otherwise, during surgery, cerebral ischemia could be missed, resulting in false-negative findings . This is because too high of a transcranial stimulus intensity can activate deep subcortical motor pathways and bypass ischemic higher cortical levels, resulting in myogenic MEPs from the contralateral limbs being generated despite cerebral ischemia [17, 27]. Deep subcortical motor pathway ischemia could also be missed if activation of the corticospinal tract occurred even more caudally [26, 28]. In other words, as the intensity of stimulation is increased, the activation site of corticospinal fibers is shifted deeper into the brain. There appears to be a limit to how deeply the site of activation can be displaced by increasing the transcranial MEP stimulation intensity, and this limit appears to be similar to the site activated by stimulation at the level of the brainstem (likely at the pyramidal decussation) [29]. Higher stimulation intensity is required to overcome muscle relaxation, so avoiding muscle relaxant post-intubation can help minimize stimulus intensity [30, 31]. In summary, transcranial MEPs are made more accurate by decreasing the stimulation intensity [27].

The stimulation intensity is decreased to the point where only contralateral extremity waveforms are obtained. However, now there is no signal from one foot. Surgery has not yet begun. What can be done to improve the signal knowing that increasing the intensity results in bilateral limb stimulation?

The monitoring team can increase the number of stimulus pulses in the stimulation train. Often, lower extremity MEP responses require more train pulses than upper extremity MEPs [28]. Since the threshold intensity of MEPs depends on the number of pulses, the duration of each pulse, and the locations of the stimulating and recording electrodes, the amplitude of muscle responses generally can be increased by increasing the number of pulses, the

duration of each pulse, and/or the stimulation intensity and by optimizing electrode locations [32]. (However, as noted above, increasing the stimulation intensity can have the undesirable effect of incorrect localization.) In this patient, with the increase in stimulus train count, detectable signals in all four extremities return with bilateral stimulation.

What nonradiographic intraoperative method could be used to help delineate the vasculature while the surgeons are dissecting around the AVM?

Although digital subtraction angiography is the "gold standard" for evaluating vascular flow in AVM surgery, distinguishing AVM vasculature also can be facilitated by several nonradiographic methods, including Doppler ultrasound imaging and fluorescent angiography [33, 34]. Indocyanine green (ICG) video angiography is one of the fluorescent techniques, and it is based on the different timing of vessel fluorescence. After intravenous injection, ICG leads to arteries fluorescing first (within 3–12 s), then arterialized veins, and then nonarterialized cortical veins. Images are viewed using a near-infrared video integrated microscope. The light source includes the ICG excitation wavelength, and the images are viewed through an optical filter that allows only fluorescence in the ICG emission wavelength. The recommended dose of ICG for angiography is 0.2–0.5 mg kg^{-1}. ICG is cleared by the liver, and it has a mean half-life of 3–4 min. Of note, viewing ICG fluorescence is hindered by blood, so, if a hematoma is present, it should be removed as much as possible before ICG injection [34]. ICG video angiography can be used not only to distinguish AVM vasculature, but also serial imaging during dissection can be useful in identifying feeder vessels and in assessing nidus perfusion, as well as confirming complete removal after lesion resection [35]. At our institution, we routinely use a lower dose of ICG (approximately 0.1–0.2 mg kg^{-1}) with good success, allowing for faster "washout" to facilitate repeat imaging quickly if needed. See a video of intraoperative use of ICG in aneurysm surgery in Chap. 21, "Intracranial Aneurysm Clipping."

The electrophysiologist reports to the surgery and anesthesia teams that the amplitude of the MEP response from one lower extremity has decreased significantly. The surgeons state that they are not working in the territory of the anterior cerebral artery, so they do not expect to see changes in the MEPs from the lower extremities. The surgeons also recently had noted that the brain was "tight", so the patient currently is being more aggressively hyperventilated. What should you do to determine the etiology of the MEP

change and possibly mitigate any neurological problem?

Since the change is unilateral, a technical, positional, or surgical etiology is suspected (instead of a physiologic or pharmacologic etiology which should cause a bilateral change). The electrophysiologist should repeat the MEP stimulus to ensure the problem is reproducible. Once reproducibility is confirmed, the electrophysiologist should check for possible technical problems by checking electrode impedances and stimulation parameters. As this technical check is occurring, the anesthesia team should check the patient's position and padding while paying special attention to the affected extremity and any monitors or intravenous lines in that extremity. In this case, if no technical or positional problems are detected, a surgical problem could remain; especially since the patient is being hyperventilated because of increased brain bulk, some local cortical injury from retractor pressure could be occurring [36]. Brain retraction injury can be caused by focal pressure from the retractor blade on brain tissue. The deformation of brain tissue from the retractor causes a reduction in blood flow to the area, and this can lead to ischemia. Local direct tissue trauma to the neurons, their processes, and/or glia is also possible. Resulting injury is likely dependent on the number and shape of retractors and on the pressure and duration of retraction [37]. Upon questioning, the surgeons state they do have a retractor that they can reposition, and they do so. To lessen potential ischemia to the area, raising the systemic blood pressure and less aggressive hyperventilation (since hyperventilation is decreasing cerebral blood flow) could be undertaken by the anesthesia team [36, 37]. Approximately 15 min after these maneuvers, the signals return to baseline. Of note, although prolonged hyperventilation has been shown to be detrimental in instances such as traumatic brain injury, intraoperative hyperventilation has been shown to improve operating conditions and moderate hyperventilation to facilitate surgery seems reasonable and is still routinely employed [13, 38].

What affects the speed with which MEPs can detect potential ischemia?

The different speed with which MEPs can detect potential ischemia is likely due to differences in the amount of collateral circulation to the vulnerable area. For example, the subcortical motor pathways are especially sensitive to interruption of blood flow—encroachment on the lenticulostriate arteries results in a change in MEPs within about 60 s, while interruption of the middle cerebral artery branches to the motor cortex results in changes in MEPs often within 10 min [23].

During AVM resection, EEG slowing is noted, then a global decrease in MEP amplitude occurs, and then this is followed by a global increase in SSEP latency of greater than 10 %. The surgeons are notified of these changes. What do you expect is the cause and what should you do?

A global change is likely to have a pharmacologic or physiologic etiology. After confirming that there have not been any recent changes in your anesthetic, including no change in hypnotic anesthetic, a physiologic change should be suspected. Physiologic factors that could influence evoked potentials include blood pressure, hematocrit, temperature, acid–base balance, and oxygen and carbon dioxide tensions [25]. After quickly insuring adequate oxygenation and ventilation, the mean arterial pressure (MAP) should be checked. You find that the MAP is now below 20 % from the patient's baseline. While starting to augment the patient's blood pressure, the most recent hemoglobin value is obtained, and it shows the patient is now anemic. You realize there has been more blood loss than initially recognized. Thus, the change in neuromonitoring is likely due to the combined effects of hypotension and decreased oxygen carrying capacity of the blood [39].

Oxygen carrying capacity should be improved by transfusing packed red blood cells, and, in the meantime, mean arterial pressure should be increased to aid cerebral perfusion. With aggressive volume resuscitation, the patient's neuromonitoring parameters return to baseline.

For neuromonitoring changes to have occurred, what was the likely cerebral blood flow?

EEG changes appear quickly with cerebral ischemia , and ischemia is first seen as EEG slowing. As ischemia worsens, loss of voltage also occurs [40, 41]. EEG changes can be seen under general anesthesia with cerebral blood flow (CBF) of 10–25 mL/100 g/min; major EEG changes occur with CBF of less than 10 mL/100 g/min [17, 40]. SSEPs are unchanged until cortical blood flow is reduced to about 20 mL/100 g/min, and they change and then are lost at blood flows between 15 and 18 mL/100 g/min [36]. Deleterious effects of cerebral ischemia are potentially reversible at these levels if CBF is improved, since experimental levels associated with cerebral infarction are 10–12 mL/100 g/min [17].

MEPs, as utilized in the case above, give real-time assessment of primary motor system integrity. What additional monitoring could be utilized if the AVM was located within or in very close proximity to the primary motor cortex and/or the corticospinal tract?

Advances in neuroimaging, neuromonitoring, and microsurgical technique are allowing more surgical treatment of AVMs located in close proximity to motor cortical areas or motor projection systems that once would have been limited to conservative management or radiosurgery [20]. Cortical and subcortical bipolar or monopolar mapping intraoperatively is standard for identification of motor neuron assemblies, particularly since mass lesions can distort normal anatomy, making it difficult to locate specific brain functions relying solely on anatomic landmarks. Initially during surgery, neuronavigation based on preoperative images is often used for the craniotomy approach and for lesion localization prior to dural opening. As surgical resection nears the interface of lesion and functional motor tissue, mapping is repeatedly performed to determine a safe plane for resection, with lower motor thresholds indicating a closer location of eloquent tissue. Similar to the concerns of too high of a stimulation intensity causing false-negative results for transcranial MEPs, as discussed above, too high of a stimulation intensity for mapping can lead to a false-positive MEP result from current spread [19]. EEG monitoring is performed during mapping to monitor for epileptic activity.

What would an alternative anesthetic technique be for a patient with an AVM located in or very near the motor and/or language cortex ?

Since AVM resection is generally more technically challenging, slower, and has a greater risk of significant bleeding than tumor resection, awake craniotomy techniques have not traditionally been offered for AVM resection. However, with the cooperation of neurosurgeons, neuroanesthesiologists, and neurophysiologists at our institution (unpublished data) and others, there have been advances in awake craniotomies for AVM resections [42]. Seizure activity, as can occur in these patients especially during the mapping phase of surgery, can be treated first by prompt flooding of the field with sterile ice-cold saline by the surgeon and then, if needed, intravenous administration of propofol and/or benzodiazepine by the anesthesiologist.

Postoperatively, if the patient's mental status deteriorated, what cause particular to AVM obliteration should be considered? What type of neurological monitor might you consider at this point?

Brain edema and hemorrhage postoperatively can complicate successful AVM resection [1]. Although controversial, there are two main hypotheses for the cause of brain edema and hemorrhage during or after surgery—normal

perfusion pressure breakthrough (NPPB) and occlusive hyperemia.

According to the NPPB theory, there is preferential shunting of blood to the AVM and away from normal brain because of lower blood pressure within the AVM's arterial feeders. Arteries within adjacent brain respond to this hypotension by dilating to maintain as much flow as possible. Once increased (but normal) flow is reestablished through these vessels after AVM resection, a loss of autoregulatory compensation from the chronic dilation results in surrounding brain edema and hemorrhage [6, 43]. According to the occlusive hyperemia theory, arterial stagnation and/or venous outflow obstruction from the AVM resection causes the swelling and hemorrhage [44, 45]. There continues to be little understanding of the actual pathophysiology of these deleterious events that can occur after AVM resection [46]. To help evaluate and manage the patient, an intracranial pressure monitor could be considered. (For types of ICP monitors and their technical aspects, see Chap. 15, "Monitoring Intracranial Pressure.")

What precautions should be taken to avoid NPPB?

Swelling and hemorrhage can be limited by tight blood pressure control postoperatively, staging of the surgical resection if the AVM is giant, and with presurgical embolization and/or radiosurgery to reduce the size of the arteriovenous shunt [6, 43]. In addition, since venous thrombosis is also a risk postresection or postembolization, euvolemia should be maintained after treatment [6, 45].

Would the management of an AVM differ if the patient was pregnant, and what additional monitoring should you consider?

Data suggest that the risk of AVM hemorrhage to the parturient is similar to that of the nonparturient [47]. Data also suggest that increased venous pressure during a Valsalva maneuver is not directly transmitted across the AVM nidus, and in most cases, vaginal delivery does not carry a higher risk of hemorrhage than cesarean section delivery [3, 48]. (Although forceps delivery for a passive second stage of labor is sometimes still planned [49].) Thus, if a woman with a known AVM anticipates pregnancy, treatment should be considered before pregnancy. Once pregnancy is established, elective treatment would generally be delayed until after pregnancy [3]. However, if AVM hemorrhage occurs during pregnancy, the risk for rebleeding may be increased compared with the nonparturient [47]. In this case, early definitive therapy may be warranted [3]. If the fetus is viable (≥24 weeks' gestation) at the time of neurosurgery, three options can be

considered in consultation with the surgical and obstetrical teams: neurosurgery performed with a plan to maintain the fetus in utero; cesarean delivery followed immediately by the neurosurgical procedure; or cesarean delivery followed by later neurosurgery.

In addition to the patient monitoring discussed above, perioperative fetal heart rate and myometrium tone monitoring would need to be discussed with the obstetricians [47]. It should be noted that the safety of SSEP and MEP monitoring in pregnant patients has not been established. Use of SSEPs and MEPs in a late-stage pregnant patient has been reported, but there is some concern, especially with the higher electrical energy delivered by transcranial MEPs, that uterine contractions could be stimulated [50]. Finally, if the neurosurgical procedure immediately follows a cesarean delivery, arrangements for intraoperative checks of uterine tone and bleeding during the neurosurgical procedure need to be made [47].

Questions

1. Question (True or False): It is now considered standard of care to perform evoked potential monitoring for intracranial AVM resections.

2. Question (True or False): If, soon after intubation, there is difficulty obtaining baseline MEPs in both upper and lower extremities, concern for AVM rupture during intubation must be high.

3. Question (True or False): Assuming MEP responses are present and reproducible, the stimulus intensity is unimportant as long as it is within generally recommended ranges.

Answers

1. False. There is a lack of prospective and randomized trials of neurophysiological monitoring in intracranial surgery, and evoked potential monitoring is not considered “standard of care” for this surgery. However, there is growing evidence from case series that neuromonitoring intraoperatively is useful to help prevent morbidity in management of cerebral AVMs.

2. False. Risk of AVM rupture during induction is low. Since there can be a coexisting intracranial aneurysm, blood pressure control in the range of the patient's normal pressures is warranted, however. Assuming a hemodynamically smooth induction and continuing stable vital signs, AVM rupture is not likely to be the culprit of poor MEPs. (Concern for intracranial bleeding would be elevated in the presence of bradycardia and hypertension, i.e., Cushing response). The globally poor MEPs are likely the result of residual muscle blockade used to facilitate intubation.

3. False. The lowest possible stimulus intensity should always be used. Too high of a stimulus intensity can lead to false-negative intraoperative monitoring results if stimulation occurs deep to the area of ischemia, increases the potential for patient movement intraoperatively, and increases the risk of adverse events such as bite injury.

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Footnotes

1 Asterisk indicates key references.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_23

23. Intraoperative Neurophysiologic Monitoring During Surgery for Supratentorial Mass Lesions

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Keywords Intraoperative neurophysiologic monitoring – Surgery – Supratentorial mass lesions – Neuronavigation – Electrocoagulation – Risks – Evoked potentials – Resection – Vascular supply – Ischemia

Key Learning Points

- Postoperative neurological deficits after resection of brain tumors are caused by either direct track insult or ischemic insults from proximal and distal arteries.
- Sensory evoked potentials are used during surgery for resection of brain tumors to identify the central sulcus and can detect cerebral ischemia .
- Motor evoked potentials can detect ischemia ahead of the sensory evoked potentials and may detect ischemia occurring in a pure motor structure.
- Intraoperative monitoring for resection of brain tumors is possible under general anesthesia in most cases. Only when speech is desired to be tested, then an awake craniotomy is better suited.

The supratentorial space consists of both cerebral hemispheres and is separated from the infratentorial space by the tentorium (see Chap. 24, “Surgery for Infratentorial Mass”). Two-thirds of all adult central nervous system (CNS) tumors occur in the supratentorial space [1–], whereas in children, about only one-third of CNS tumors occur here. Common primary brain tumors in adults are gliomas (45–50 %), meningiomas, pituitary adenomas, primary CNS lymphomas, medulloblastoma, and ependymomas. By far the most common brain tumors are metastases, notably lung cancer, breast cancer, and malignant melanoma. Fifty percent of patients with metastases have multiple lesions, and up to 50 % of patients with cancer have brain metastases. However, only a small proportion of patients with brain metastases undergo neurosurgical treatment. Primary brain tumors rarely metastasize outside the CNS.

Supratentorial mass lesions can be located in close proximity or attached to functionally important cortical areas and to subcortical fiber pathways. New neurological deficits, after surgery for such lesions, may occur in two ways: directly from a resection close to or within those functional areas or indirectly by inadvertent compromise of their remote vascular supply . Preserving their functional integrity with a maximum surgical resection requires both intermittent identification and delineation of critical regions (mapping), and continuous functional monitoring [4–6]. The continuous examination of language and cognition during surgery requires awake surgery (see Chap. 18, “Anesthesia for Awake Neurosurgery”), while

primary motor and somatosensory functions can be tested with neurophysiological methods in patients under general anesthesia and several recent studies support their use [7–11]. These methods are employed for brain tumors and likewise for vascular and epilepsy surgery. Here, we discuss a pertinent case of functional preservation during surgery for a glioma of the insula of Reil. This case illustrates typical conditions and methods for neurophysiological monitoring during brain surgery.

Case: Resection of an Insular Glioma

A 50-year-old man presented with a history of partial seizures and a mild sensorimotor right-sided hemisyndrome. Magnetic resonance imaging (MRI) showed an enhanced mass lesion of the left insular region without extension into the adjacent opercula (insular glioma Yasargil type 3b) [12]. Resection was performed with neurophysiologic motor mapping and monitoring as detailed below. Histology revealed a glioblastoma. There was a transient moderate postoperative aggravation of the hemiparesis that resolved by discharge. Early postoperative MRI revealed an ischemic lesion close to the corona radiata. The patient underwent radiochemotherapy and repeated cycles of temozolomide thereafter [13].

Risks of Surgery for Insular Tumors and Other Supratentorial Mass Lesions

The major neurological risk of surgery for insular gliomas (about 10 % of supratentorial gliomas) and many other deeply seated tumors is new hemiparesis. Those brain tumors are critically related to the primary motor system in two ways. Typically, they are near to the corona radiata at their dorsoapical extension [14]. In addition, insular and other tumors are surrounded by a variety of vessels, mainly branches from the middle cerebral artery, which supply the motor fibers along their supratentorial course [14–16]. The sylvian branches supply a major part of the motor cortex, the proximal perforating vessels supply the basal ganglia and the internal capsule, and the peripheral insular and also the opercular perforators supply the corona radiata. Monitoring and preservation of the primary motor pathways is crucial because there is no functional substitute for the primary corticospinal projections as opposed to parts of the language and somatosensory networks. Secondary motor areas (supplementary motor area, premotor cortex) and their projections can be sacrificed unilaterally without significant permanent sequelae.

In general, similar risk factors apply to many deeply seated and even superficial supratentorial tumors. They are frequently located close to the corticospinal tract at its extended course. These tumors may also be adjacent to arteries that supply the corticospinal tract, including the lesser known

opercular perforating vessels [17]. For example, temporomesial tumors may encroach on the cerebral peduncle and the vessels of the ambient cistern.

Preservation of Nonmotor Function Using Mapping and Monitoring Techniques

Nonmotor functional systems may require functional mapping and monitoring, depending on the location of the target lesion and the surgical approach (see Chap. 9, “Cortical Mapping”). Mapping the cortex with cortical stimulation and functional monitoring during awake surgery for language and other functions is discussed in Chap. 18 [18]. The somatosensory fibers may be continuously monitored by SSEPs, which are reliable indicators of central cortical perfusion. Limited resections of somatosensory cortex and its afferents are possible without permanent deficits. Supratentorial auditory pathways might be monitored by cortical auditory evoked potentials (ABRs). However, this is hardly ever required due to the extensive bilateral crossover connections of the auditory system. In contrast, significant damage of the visual pathways results in visual field deficits that can be quite debilitating. Unfortunately, intraoperative monitoring of visual evoked potentials (VEP) under general anesthesia has proven technically difficult and they are still of questionable clinical usefulness, although some progress seems to have occurred recently [19, 20] (see Chap. 4, “Visual Evoked Potentials”). For preservation of the visual pathway, diffusion tensor imaging-based tractography may be useful, particularly if it is fed into a neuronavigational, frameless stereotaxic system . This method is suitable for displaying other fiber tracts as well, including the pyramidal tract. However, there are still technical uncertainties regarding this method, in particular with large, space-occupying lesions (brain shift) and peritumoral edema. Likewise, functional imaging (fMRI) may be useful for a rough allocation of functional areas, but is not suited for sharp resection guidance. Recently, awake stimulation-based mapping has been shown to reliably identify optic radiations, which may be preserved depending on the goals of oncological and functional goals of surgery [21]. At present, electrophysiological methods remain the “gold standard” for functional mapping and monitoring.

Motor Mapping and Monitoring

In centrally located tumors, safe resection requires initial identification of the primary motor cortex. Moreover, with insular and other deep lesions, motor mapping is a prerequisite for adequate positioning of the stimulating electrode for continuous motor monitoring. Neurophysiological mapping is achieved mainly in two ways: (1) *Stimulation mapping* (either with the parameters described in Chap. 18 [22] or as described below for the elicitation of motor evoked potentials [23]) is required for the direct identification of the motor cortex and corticospinal tract, but can be time-consuming and may be misled by premotor or even postcentral corticospinal projections. Interestingly, recent data indicate that one may tailor the approach to motor cortex and corticospinal tract mapping using either low-frequency or high-frequency stimulation depending on the clinical scenario [24]; and (2) In most cases, fast and unambiguous results can be obtained easily by the indirect method of S*SEP phase reversal mapping*. Median nerve SSEPs are recorded from an electrode array positioned perpendicularly across the central sulcus over the motor hand area. The tangentially orientated overall source current of the primary postcentral cortical SSEP response generates a polarity-reversed mirror image at precentral recording positions, thus allowing unambiguous identification of the central sulcus and, indirectly, of the primary motor cortex [25]. In some cases, direct motor stimulation mapping usefully complements the SSEP phase reversal recordings [26]. For some deeply seated tumors, mapping of the motor cortex is not necessary. Instead, MEP stimulation is performed transcranially at predefined positions according to anatomical landmarks [27].

After identification of the motor cortex , stimulation for eliciting motor evoked potentials is repeated every 5–10 s throughout the resection via the cortical surface electrodes employed for phase reversal recording. Stimulation at higher frequencies of up to 2 Hz is mainly employed in spinal surgery, but does not yield very stable MEP amplitudes. On the other hand, longer intervals between consecutive MEP recordings do not allow for continuous functional assessment. Every stimulus consists of a short train of four to seven electrical anodal pulses (of 300–1000 ms pulse duration) at an intensity of up to 200 mA. The cathode (subdermal needle electrode) is placed at a frontal midline position. This pulse train elicits a series of action potentials that descend the corticospinal tract. Temporal summation of the burst of excitatory postsynaptic potentials at the alpha motoneuron overcomes the inhibitory effects of general anesthesia so as to elicit motor

responses that can be recorded via surface or subdermal needle electrodes from the target muscles (muscle MEPs) [28]. Obviously, muscle relaxation must be avoided in such cases, although MEPs may still be recordable if the train of four has two responses present. Total intravenous anesthesia with propofol and opioids (e.g., remifentanil) is best suited for MEP monitoring, but balanced anesthesia with low-dose (≤0.5 MAC) halogenated agents in combination with an opioid (e.g., remifentanil) is also acceptable in many patients. MEP amplitude is the target parameter to be monitored in supratentorial surgery. In our experience, a decrease of 50 % is a significant warning sign for impending motor damage. Other groups rely on tighter criteria (a decrease in amplitude of up to 70–80 %) with a higher risk of false-negative results [29]. Latency prolongation without amplitude decrease rarely occurs [30].

Monitoring Results and Surgical Intervention

In the present case, arm muscle MEPs were monitored (Fig. 23.1). There were highly stable responses in two out of three muscles (I). During medial tumor resection, a significant drop of MEP amplitudes (II) occurred. Causes unrelated to the resection, such as positional, technical, physiological, and pharmacological, were examined and excluded. Once these causes were excluded, the surgeon was informed about the MEP changes. Resection of the tumor was temporarily halted and the site was inspected and irrigated; papaverine-soaked gelfoam was applied, and the self-retaining retractor in the sylvian fissure was loosened and readjusted (III). After stabilization of the MEP responses (IV), the tumor resection was safely completed.

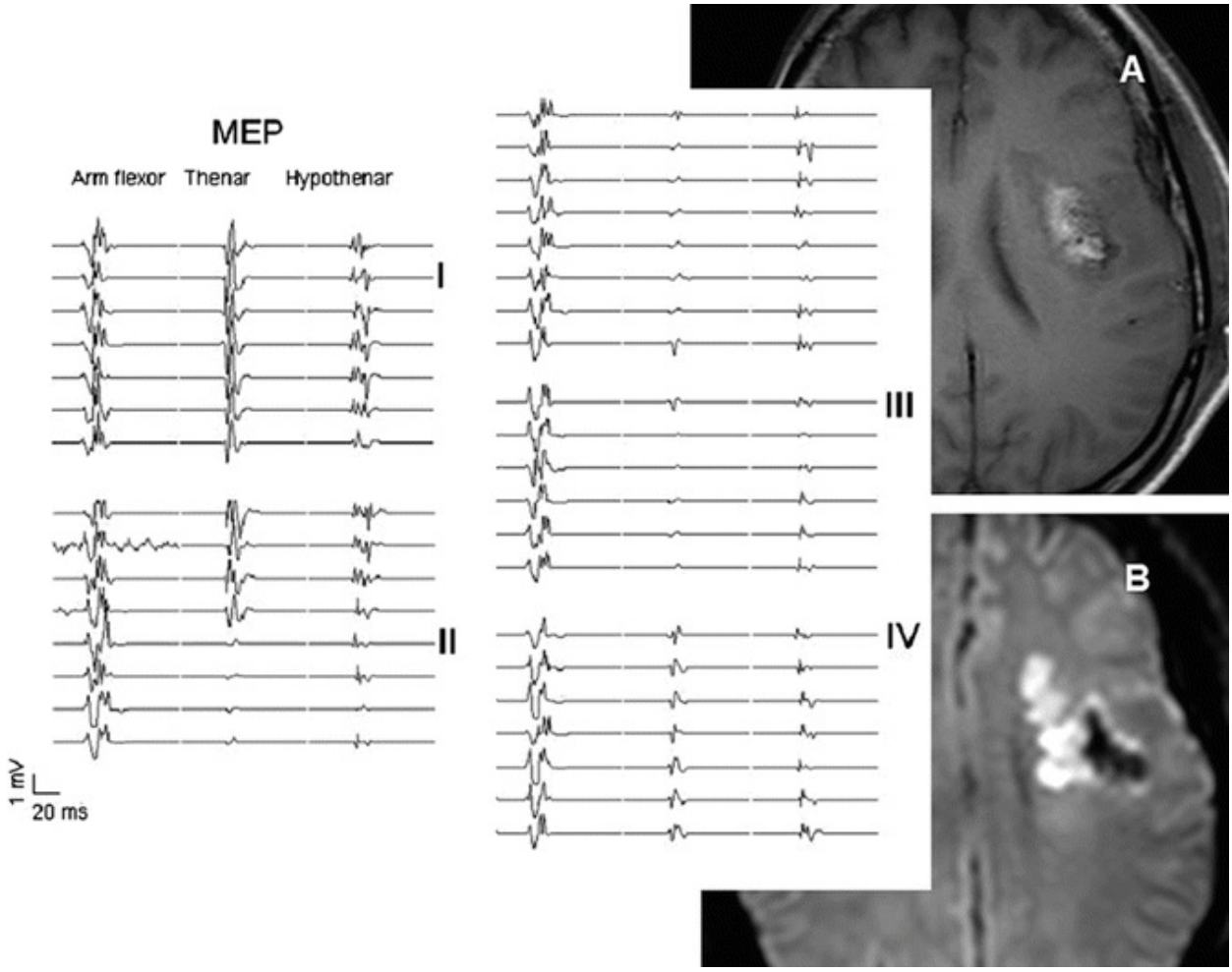

Fig. 23.1 MEP monitoring during surgery for supratentorial tumor surgery with MEP changes

Possible Causes of the MEP Change and the Role of the Surgical Interventions

First, inadvertent bolus injections of anesthetics or muscle relaxation must be excluded, as well as a drop of blood pressure and body temperature, which all may significantly affect MEP amplitudes. In particular, a slow, gradual decrease of blood pressure and body temperature must be taken into account. The MEP parameters are not linearly related to cerebral perfusion but can change abruptly in a more stepwise fashion. When individual threshold values are encountered, MEP amplitude may have a sudden deterioration at an unpredictable point in time. For example, there is no absolute blood pressure threshold value. However, any mean arterial pressure below 70 mmHg may be critical, and significant drops in blood pressure must be

avoided and reported when they do occur. Body temperature should be maintained above 36 °C by air-warming systems, if necessary. After this check for nonsurgical causes, a warning must be issued to the surgeon. Typically, resection or dissection is halted at this point. At the same time, inadvertent decreases of blood pressure or body temperature are reversed and these measures should be communicated to the surgeon. The surgeon must exclude technical causes for MEP changes such as displacement of stimulation electrodes; poor contact of an electrode with the result of high impedance (subdural irrigation and wet cottonoids on top of the electrode are helpful); subdural air collection; or a shift of the motor cortex away from the stimulation electrodes after removal of a mass lesion.

With the possibility of a surgically related cause for the MEP change , the surgeon's attention must be directed at specific surgical conditions that may have caused the monitoring event. Obvious causes may be detected such as resection and electrocoagulation in close vicinity or within the motor tract as revealed by neuronavigation or anatomic criteria. The intervening activity is halted and may be resumed only after MEP changes have stabilized or recovered, or if further resection appears to be possible and safe according to anatomic or other external criteria. Frequently, no specific reason can be found for MEP deteriorations. However, a temporary halt of dissection and readjustment of the brain retraction is often sufficient to enable MEP recovery and further safe resection. However, the previous surgical course of the procedure must be taken into account at this point. Extensive manipulation of remote blood vessels supplying the motor tract at some previous step of dissection is a typical cause of inexplicable MEP deterioration. It may be useful to place pieces of gelfoam or cottonoids soaked with papaverine or nimodipine at sites of (previous) vascular manipulation.

Why Is Neurophysiologic Monitoring Useful?

Clinical case series have shown that MEP deterioration occurs at stages when motor damage is imminent but still reversible. The clinical correlation of MEP recordings—motor function—is not assessable at the time of monitoring unless an awake craniotomy is being performed. Thus postoperative motor outcome is the best surrogate parameter. In large case series, the following correlation has been repeatedly confirmed: If MEP amplitudes recover or there is partial recovery as a result of surgical

intervention, there is no deficit or only transient/minor new motor deficits postoperatively. Fortunately, MEP deterioration is reversible after surgical intervention in the majority of cases. In many of those cases, diffusion-weighted MRI reveals ischemic lesions but not definite stroke affecting the corticospinal tract [15].

If there is an irreversible amplitude decrease and in particular an irreversible MEP loss, there is a high probability of permanent new paresis, frequently associated with a stroke comprising the corticospinal tract. Conversely, stable MEP recordings point to a favorable motor outcome and allow for safe completion of critical steps of the procedure. Therefore, there are three reasons for the use of monitoring: (1) prevention of new permanent deficits; (2) safe completion of critical procedures in order to achieve maximal tumor cytoreduction; and (3) an educational reason, which is to steepen the surgeon's individual learning curve and to improve the surgical skills for future cases. Monitored cases seem to have both a lower incidence of new postoperative deficits and better surgical resections, which lead to favorable results [15, 31, 32].

Conclusion

Resection of supratentorial mass lesions is associated with considerable functional morbidity, particularly when the lesions are located near blood vessels or near the eloquent cortices (e.g., motor cortex). New paresis is of particular concern due to the extended course of the motor system in the brain and the lack of clearly identifiable primary corticospinal pathways. New functional deficits are frequently caused by ischemic lesions that occur during tumor resection, and not very often by cutting into functional cortex and fiber tracts. This applies in particular with insular and other deeply seated tumors as in the present case. Therefore, motor preservation requires both mapping of the motor cortex (cortical stimulation, SSEP phase reversal) and continuous monitoring using MEP recordings, which can be performed with the patient under general anesthesia. Other functions such as language, vision, and somatosensory perception may be mapped and monitored in awake procedures or by other neurophysiologic and imaging methods. The causes of MEP changes may include nonsurgical conditions such as technical, physiological, pharmacological, and positional causes that need to be identified and excluded. Stable MEP recordings allow for safe completion

of surgery whereas deterioration due to surgical causes should lead to early surgical intervention. Restoration of the MEP signals may prevent the occurrence of permanent new deficits.

Questions

1. Under general anesthesia, all of the following can be monitored except

    A. Motor function

    B. Sensory function

    C. Speech function

2. True or false: Brain tumors often metastasize to other parts of the body.

3. MEP changes during surgery may be due to:

    A. Anesthesiologist using muscle relaxants

    B. Technical cause by the technologist

    C. Surgical causes by the surgeons

    D. Technical factors caused by the surgeon

    E. All of the above

Answers

1. C

2. False

3. E

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Footnotes

1 Asterisk indicates key reference.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_24

24. Surgery for Infratentorial Mass

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Keywords Intraoperative neurophysiological monitoring – Infratentorial surgery – Anesthesia management – Resection – Meningioma – Cerebellopontine angle – Potential problems – Risks – Retractor

Key Learning Points

- Surgery in the infratentorial space most commonly involves tumors affecting the brainstem and cranial nerves.
- Monitoring commonly involves EMG of cranial nerves at risk. ABRs, SSEPs, and MEPs may be used in addition to monitor brainstem integrity.

- Injury to the facial nerve and auditory nerve are common complications which prompts monitoring of ABRs and EMG.
- The most common tumors are in the cerebellopontine angle and are often acoustic neuromas (vestibular schwannomas).
- An NIH panel noted facial nerve monitoring during acoustic neuromas improves outcome.
- Surgical approaches to CPA tumors vary with the size and location of tumors and the risk of hearing loss.

Introduction

The infratentorial space is that region of the intracranial space including the posterior cranial fossa below the tentorium cerebella. The tentorium cerebella are an extension of the dura mater which separates the basal surface of the occipital lobe and temporal lobes from the cerebellum and brainstem. This region includes all of the brainstem with the exception of the superior portion of the mesencephalon, which extends through an opening in the tentorium. The tentorium is a rather rigid structure such that volume expansion above or below can lead to transtentorial herniation often noted clinically by pressure on the third cranial nerve and a dilated pupil (mydriasis) on the affected side.

Several aspects of the central nervous system here make surgery risky. For example, this region has a large number of important neurological structures and contains every efferent pathway in the CNS. The blood supply is distinct from the supratentorial space (paired vertebral arteries form the basilar artery), which can be occluded by neck extension or rotation and there are large venous sinuses within the dural folds of the tentorium, which can entrain air resulting in air embolism (especially with surgery in the sitting position).

A variety of surgical procedures are conducted in this space. These include microvascular decompression for trigeminal neuralgia (see Chap. 25), surgery for hemifacial spasm (see Chap. 26), as well as removal of tumors and vascular malformations. The same vascular abnormalities that occur in the supratentorial space also occur in the infratentorial space. In addition, spontaneous hemorrhage can occur, particularly in the cerebellum where 20 % of all hypertensive bleeds occur [1].

Tumors are the most common reason for surgery in the posterior fossa

[1]. The tentorium demarcates the incidence of brain tumors in adults and children. In adults, one-third of all tumors are located in this region whereas two-thirds of childhood tumors are located here [1–3]. For tumors located below the surface, mapping techniques have been developed to locate safe-entry zones for surgical access (Chap. 7). In adults, the most common primary tumors are acoustic neuromas which are also called vestibular schwannomas and often are associated with neurofibromatosis NF II. Metastases are also common and usually come from primary lesions in the lung or breast. In children, the most common tumors under age 1 year are astrocytomas, cerebellar primary neuroectodermal tumors, meduloblastomas, ependymoma, and brainstem gliomas. For children under the age of 2 years, 70 % are meduloblastomas or low-grade gliomas.

Because there is little space for swelling within the tumor (especially with metastases which are usually highly vascular), obstruction of the cerebrospinal fluid (CSF) drainage from the cerebrum is common resulting in hydrocephalus and abnormalities of cranial nerve function (such as diplopia, loss of airway protective reflexes) or changes in respiratory function or consciousness and may prompt emergent surgery for CSF diversion or decompression. This may be particularly urgent when bleeding into the space occurs.

Most infratentorial tumors are benign but the density of vital neurologic structures in the posterior fossa requires a thorough preoperative assessment and careful surgical technique to avoid brainstem damage. Tumors located in the space between the cerebellum and pons, known as the cerebellopontine angle (CPA) , are the most common neoplasms in the posterior fossa of the adult patient, accounting for 5–10 % of intracranial tumors. Eighty-five percent of CPA tumors are acoustic neuromas which are a benign tumor of the covering of the vestibular component of the auditory nerve (cranial nerve VIII), usually starting in the internal auditory canal and growing outward into the posterior fossa eventually affecting the cerebellum and brainstem. This often presents as tinnitus, hearing loss, or vertigo and unsteadiness. Acoustic neuromas and other tumors in the CPA can also cause signs and symptoms secondary to compression of nearby cranial nerves, particularly cranial nerves V and VII (facial nerve) [1].

Although facial nerve dysfunction is not a common presenting symptom, it is of particular note with surgery for acoustic neuromas because, in addition to compression with tumor growth, the facial nerve’s visual identity may be

obscured by the tumor. Facial nerve palsy is one of the two most common postoperative complications of surgery for acoustic neuromas (the other is a CSF leak) [1]. Experience has noted that if monitoring can assist in keeping the nerve structurally intact during surgery, facial nerve function has a good chance of recovery even if weakness is noted immediately postoperatively. In these cases, over 60 % of patients with intact nerves at the conclusion of surgery will regain at least partial function several months postoperatively [4].

Because of the improvement in outcome in posterior fossa surgery seen with facial nerve monitoring [5, 6], a National Institutes of Health (NIH) consensus panel concluded, “the benefits of routine intraoperative monitoring of the facial nerve have been clearly established [in vestibular schwannoma]. This technique should be included in surgical therapy” [7]. Thereafter, facial nerve monitoring became a standard of care in surgery in the United States for acoustic neuroma and is commonly monitored in other surgeries in the CPA [7].

The functional integrity of the facial nerve and its corticobulbar pathway can be evaluated using electromyography (EMG) after direct stimulation of facial nerve (mapping), free running EMG (monitoring), and corticobulbar motor-evoked potentials (coMEP) after transcranial stimulation. EMG techniques can be used to monitor cranial nuclei and cranial nerves which may be at risk, as well as differentiating EMG responses from nerves which might be confused with responses from the facial nerve. For mapping, stimulation of brainstem tissue can be used to identify the facial nerve in the operative field and also identify the location of multiple cranial nuclei to allow “mapping” of the brainstem surface to find the safe-entry zones for surgery on tumors located deep to the surface [8].

In addition to the facial nerve, a large number of other structures are at risk for injury. If not already damaged, hearing loss may occur due to damage to the adjacent auditory fibers of cranial nerve VIII. Hence, salvaging hearing on the operative or nonoperative side using auditory brainstem response (ABR) may be part of the surgical and monitoring strategy. The choice of other electrophysiological tests strongly depends on the specifics of the surgical approach and plan. This includes the positioning of the patient, placement of retractors, tumor resection, and preparation of nerve tissue or blood vessels. As such, neurophysiological considerations for monitoring cases of CPA surgery include the assessment of sensory (SSEP, ABR) and

motor pathways (MEP and cranial nerve EMG).

Knowledge of the particular steps of the surgical procedures and efficient communication with the neurosurgeon is essential for the neurophysiologist to focus on appropriate intraoperative neurophysiological monitoring (IOM) modalities. For example, there are three basic surgical approaches to surgery in the posterior fossa and each has implications for monitoring [1]. The midline suboccipital approach is the most common and offers good exposure to the midline structures (including the vertebral and basilar arteries) and cerebellum. The middle fossa approach is suitable for small tumors when hearing preservation is desired. A variety of other approaches have been used depending on the need for access to specific structures. For surgery on tumors in the CPA, the retrosigmoid and translabyrinthine approaches are also common [9]. The retrosigmoid approach is a versatile approach which allows good access to the midline and the CPA region and reduces the amount of cerebellar retraction needed compared to the midline suboccipital approach. The translabyrinthine approach provides excellent access to the entire CPA region and excellent exposure for acoustic neuromas (but provides poor access to the inferior aspect of the posterior fossa). The translabyrinthine approach can be used for tumors larger than 3 cm or for smaller tumors when preservation of hearing is not attempted because this approach sacrifices hearing on the operative side. It is thought to have lower morbidity for these surgeries (notably headaches) and better exposure of the facial nerve in some circumstances.

Resection of a Meningioma in the Right Cerebellopontine Angle

A 64-year-old woman presented with a history of walking difficulties, dizziness, and right-sided scotoma. She was scheduled for suboccipital craniotomy and resection of a meningioma in the right CPA (Fig. 24.1). The procedure was planned in the sitting position.

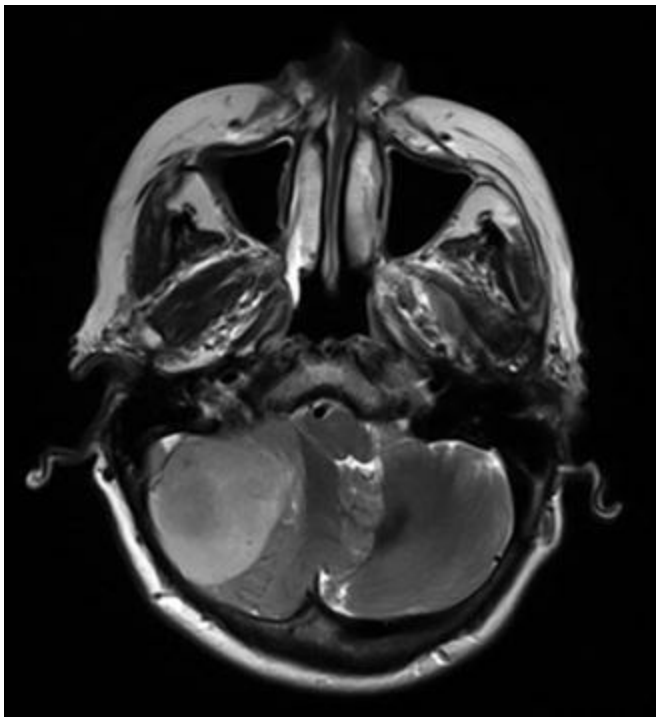

Fig. 24.1 MRI of 64-year-old woman that shows a large tumor mass in the right cerebellopontine angle (CPA). The cerebellum is shifted to the left hemisphere and the brainstem is compressed

Anesthesia management. General anesthesia was induced using continuous infusion of remifentanil (0.4 μg/kg/min), a bolus of 20 mg etomidate and 35 mg rocuronium.

Total intravenous anesthesia (TIVA) was used to maintain general anesthesia (infusion of 5 mg/kg/h propofol (83 μg/kg/min) and 0.4 μg/kg/min remifentanil). Additional neuromuscular blockade (NMB) was avoided because of intended monitoring of the corticobulbar tract (pathway of cranial nerve VII).

The level of hypnosis was monitored using the EEG-based bispectral

index (BIS) recorded from the left forehead. A transesophageal Doppler probe was inserted after positioning of the patient to detect air embolism.

Potential Problems and Structures at Risk

Brain surgery in the sitting position bears the risk of air embolism. In addition, sufficient perfusion pressure must be maintained.

The sitting position has some potential benefits. It allows a better exposure of the surgical field, improved drainage of CSF, reduced blood loss, less tissue damage, reduced ICP, and decreased rate of cranial nerve damage. Potential risks of the sitting position include postoperative quadriplegia, damage to peripheral or cranial nerves, postoperative pneumocephalus, and venous or paradoxical air emboli.

Sudden alterations of the cardiovascular and respiratory systems may occur during or after brainstem manipulation with surgery in the posterior fossa or as a result of the patient's pathology due to the tight space. The size of the posterior fossa is limited and a small increase of infratentorial volume may produce high pressure on the brainstem with dramatic changes in the vital signs and mental status. This may produce sudden apnea without previous warning signs, e.g., changes in alertness or consciousness. Isolated pathology in the posterior fossa will not lead to dilatation of the pupils. Preoperatively, posterior fossa tumors are associated with the risk of hydrocephalus, damage to cranial nerves, and pressure to the brainstem. Intraoperative manipulations of the brainstem may induce sudden changes in heart rate, blood pressure and arrhythmia (pons, roots of cranial nerve V (trigeminus), IX (glossopharyngeus), and X (vagus)), or bradycardia (periventricular gray, reticular formation). Postoperative complications can occur as sequelae of damage to the cranial nerves. Damage to the trigeminal nerve (V) may lead to lesions of the cornea and damage to the facial nerve (VII) may lead to exsiccation of the eye. Impairment of the vestibulocochlear nerve (VIII) may induce postoperative dizziness and hearing loss and injury to the caudal brain nerves (IX, X, XII) impairs swallowing and increases the risk of aspiration.

Postoperative complications may occur due to swelling or bleeding and can be manifested as sudden apnea or alterations in mental status. Hyperperfusion or clotted blood vessels, leakage of CSF or disruption of CSF circulation, and pneumocephalus are typical postoperative complications.

Monitoring

The goals of hemodynamic monitoring are to ensure adequate central nervous system perfusion, maintain cardiorespiratory stability, and detect and treat air embolism. Blood pressure should be measured at the head level to ensure adequate cerebral perfusion pressure while central venous pressure is measured at the heart level. For monitoring air embolism, transesophageal echo (TEE) is the most sensitive method of detection. However, precordial Doppler is the most widely used method.

Neurophysiological Monitoring

A. *Positioning of the patient in the sitting position* requires flexion of the head and may lead to a dramatic decrease in the perfusion of the cervical spine. This is due to different perfusion zones, especially of the posterior spinal arteries at the cervical and upper thoracic levels. Since the dorsal columns are served by the posterior cervical arteries, monitoring of the somatosensory tract via SSEPs is useful for detecting regional ischemia. Figure 24.2a, b shows recordings of the SSEPs after stimulation of the left and right median nerves during positioning of the patient's head. Only a few minutes after flexion, the amplitudes of the cervical (C7 level) and cortical responses from both sides were dramatically reduced. Following correction of the head position, all the SSEP responses recovered. Some teams also monitor motor-evoked potentials to assess ischemia in the motor tracts with positioning.

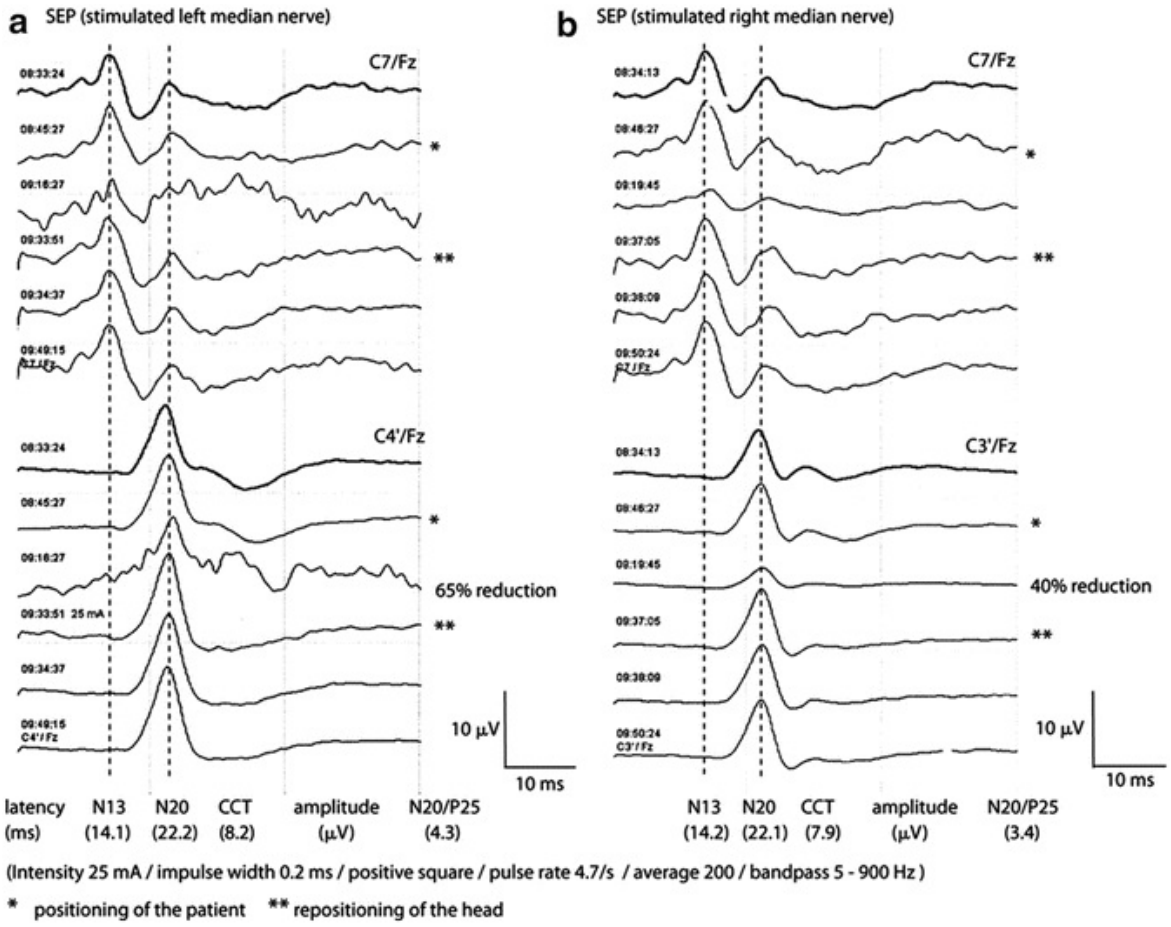

Fig. 24.2 Cervical and cortical SSEP recordings after stimulation of the left (**a**) and right (**b**) median nerve during positioning of the patient in the sitting position. Anteflexion of the head (*) led to dramatic depression of cervical and cortical amplitudes. Recovery of all responses after repositioning of the head (**). No remarkable change of latencies was found

A global reduction in the amplitude of both cervical and cortical responses may also be due to a global change of the patient physiology or systematic technical errors and such causes should be ruled out. Appropriate stimulation can be verified by assessing the evoked response at the level of the Erb's point. Appropriate positions and contact impedances of the recording electrodes must be verified. General anesthesia should be maintained at as steady a state as possible to minimize amplitude changes as a result of the anesthetic agents. In this case, there was no SSEP recording at the Erb's point and therefore a systematic technical error cannot be excluded (e.g., electrical disturbance of the reference electrode). Therefore, the electrodes were rechecked. With bilateral stimulation and symmetric changes, an error at

the stimulus level is very unlikely. There was no change of the continuous propofol infusion and no bolus doses were given.

B. *The placement of retractors* for approaching the tumor can cause shifting of cerebellar tissue which can either involve direct compression of the vestibulocochlear nerve (CN VIII) or indirect impairment of the brainstem. Auditory brainstem responses (ABRs) provide excellent information about the integrity of the auditory pathway and are sensitive to ischemia or tissue damage to the brainstem.

Ipsilateral recordings of ABRs after stimulation of the right and left ear are shown in Fig. 24.3a, b. In contrast to ABRs acquired on the left, the initial recordings from the right side show unstable waves I–III. In addition, the latency of the IV/V complex and the interpeak latencies of I–V were prolonged on the right side (Table 24.1). It is likely that the large size of the tumor and chronic compression of the brainstem led to instability of particular waves and prolongation of the conduction time.

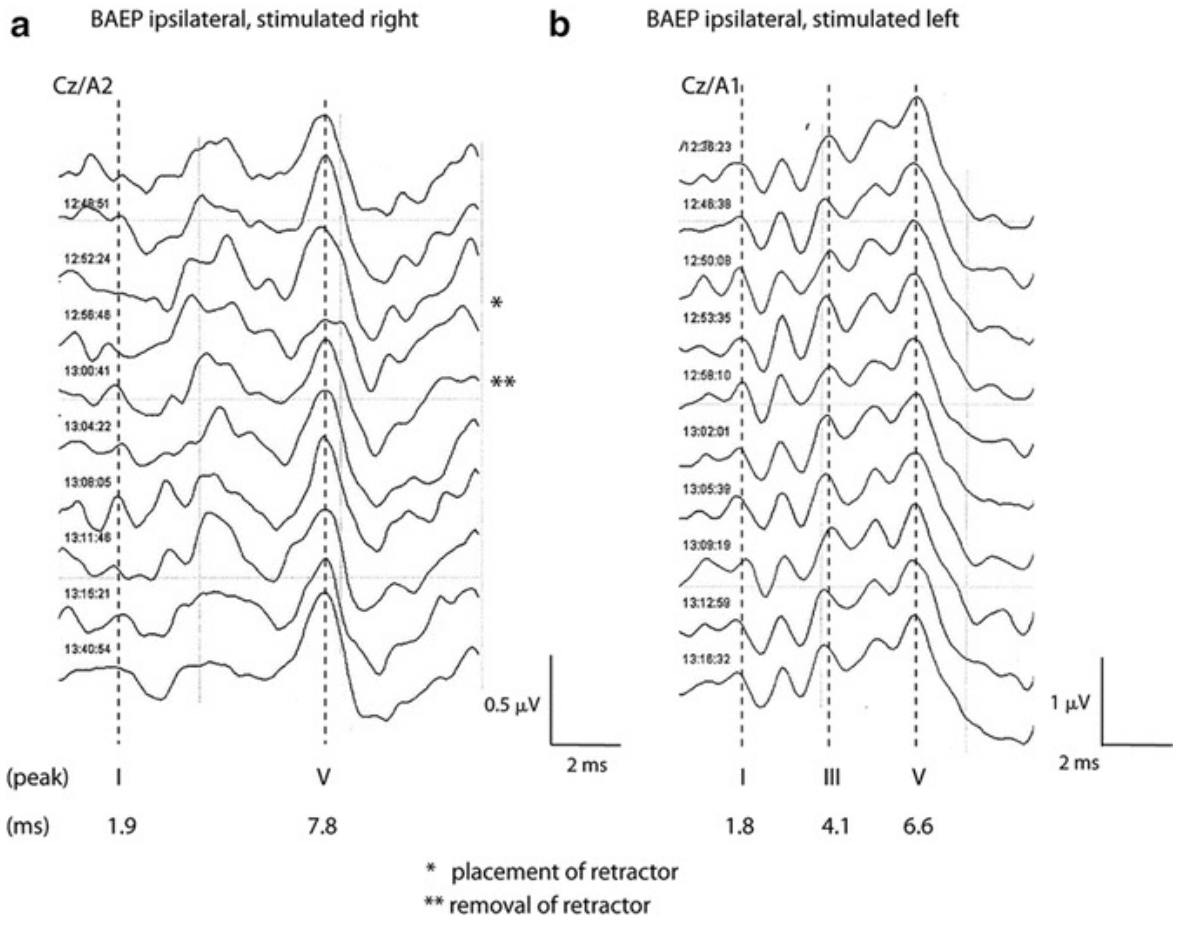

Fig. 24.3 Recordings of ipsilateral ABRs after stimulation of the right (**a**) and left (**b**) ear monitoring the episode of retractor placement. Notice the initially prolonged latency of peak V in the right (tumor side) and the unfavorable signal-to-noise ratio with unstable recordings of peak I and III. Peak V is reproducible and stable. Immediately after positioning the retractor (*), the amplitude of peak V (right) dropped about 40 %. The surgeon was informed by the neurophysiologist and with the removal of the retractor (**), the response completely recovered. In contrast, no change was observed in the left-sided response

Table 24.1 ABR ipsilateral recordings

Side of stimulation	**Right**			**Left**		
Peaks	I	III	V	I	III	V
Latency (ms)	1.9	n.r.	7.8 (↑)	1.8	4.1	6.6
Amplitude (nV)			328			564
IPL I–III (ms)	n.r.			2.3		
IPL (I–V) (ms)	5.9 (↑)			4.8		
IPL III–V (ms)		n.r.			2.5	

Listing of initial latencies of peak I, III, and V as well as the amplitude of peak V and interpeak latencies (IPL) I–III, I–V, III–V of ipsilaterally recorded ABRs after stimulation of the left and right ear. Latencies of peak V right and IPL I–V are prolonged. Peaks I–IV are not reproducible on the right side. Amplitude of peak V from the right ABR is about half the size of peak V of the left ABR
Peak III, IPL I–III, and IPL III–V are not reproducible (n.r.) on the right side

The increase of latencies of waves III–V can also be caused by systemic hypothermia and to a much lesser degree, by general anesthesia (TIVA or balanced anesthesia). But in those cases, the increase of latencies should be bilateral and should have reached their maximum at the time of positioning the retractor. To be able to separate those effects, it is helpful to set a second referential baseline prior to the opening of the dura.

As seen in Fig. 24.3a, the IV/V complex from the right side, which initially remained stable, changed during the placement of the retractor. The neurosurgeon was immediately informed when the amplitude dropped almost 50 % even though the latency did not change. After removing the retractor, flushing the surgical field with warm saline and then repositioning the retractor, the amplitudes of the IV/V complex

recovered. In cases when the latency of wave V increases more than 0.5 ms, the surgeon should also be informed.

As seen in Fig. 24.3, visual analysis of the waveforms indicates an unfavorable signal-to-noise ratio of the right-sided ABRs in comparison to the left ABRs. This is not uncommon because of changes of local temperature and manipulation around cerebellar tissue.

C. *Identification of the facial nerve* : Depending on the position and the size of the tumor, the surgeon should try to localize the facial nerve prior to resection in order to establish a baseline for later assessments during surgical resection (Fig. 24.4d). Sometimes the facial nerve is pushed behind the tumor so the surgeon has to start resection first. Mapping of nerve tissue may even be impossible before large parts of the tumor mass have been removed.

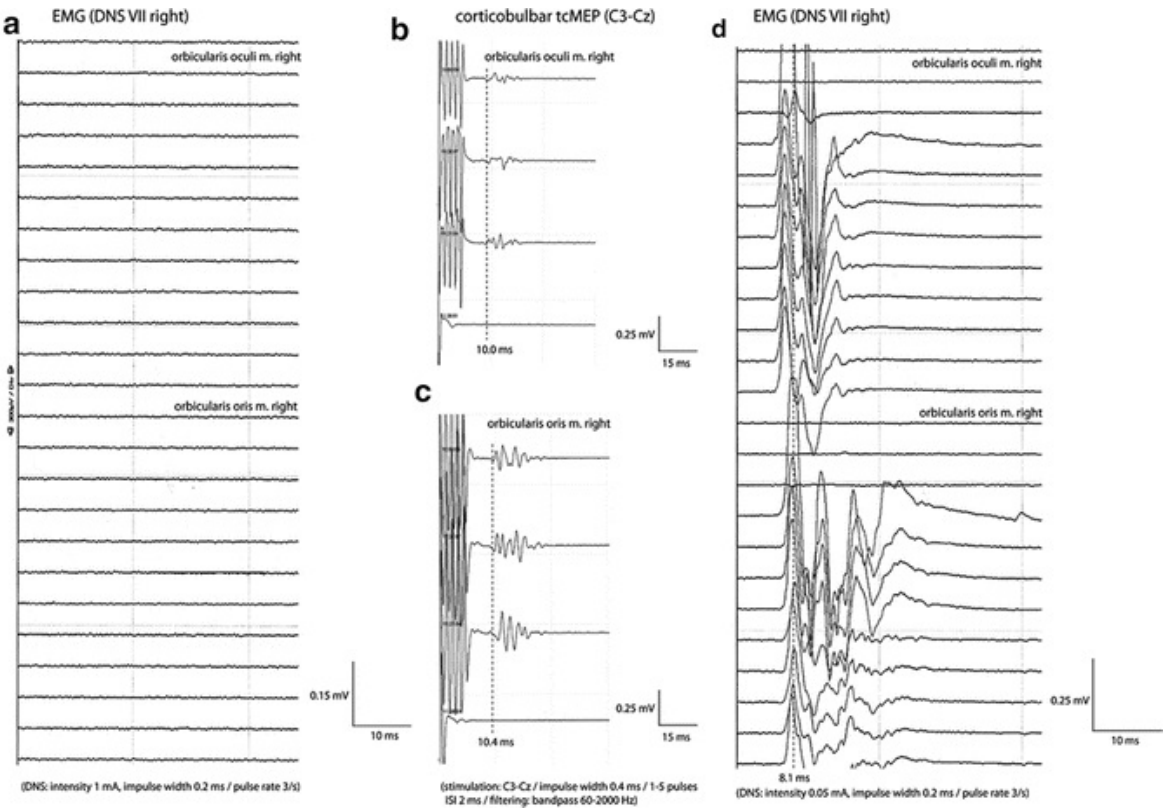

Fig. 24.4 (**a**) Recordings demonstrate the situation of difficult identification of functional facial nerve fibers . After stimulation of a questionable structure (intensity 1 mA, bipolar concentric hand probe electrode), the surgeon was not sure whether they had damaged facial nerve tissue. Unchanged corticobulbar motor-evoked potentials (coMEPs) presume an intact corticobulbar pathway and suppose no lesion of the facial nerve (**b**, **c**). Identification of the facial nerve (**d**)

after final resection of the tumor (intensity 0.05 mA)

D. *The tumor resection* is the most dangerous part of the procedure in which iatrogenic damage of the vestibulocochlear, trigeminal, and facial nerve can occur. This is seen if the facial nerve, clinically intact, is fanned out by the tumor mass. In these cases, the surgeon has to frequently switch between resection and mapping of the facial nerve. A characteristic recording of EMG responses of the orbicularis oculi and oris muscle is shown in Fig. 24.4d. Since mapping by direct nerve stimulation (DNS) only provides information about the peripheral part of the pathway, it can be beneficial to evaluate the entire corticobulbar tract by the monitoring of coMEP of the facial nerve (Fig. 24.4b, d). Figure 24.4a illustrates a situation where the surgeon was concerned about possible damage to questionable fibers. There was no response to DNS even with an increased intensity of 1 mA (concentric bipolar hand probe). However, unchanged recordings of the coMEP would suggest that the pathway was intact and if responses of the coMEP were also reduced, damage to the facial nerve would be very likely. Note that transcranial stimulation of the corticobulbar pathway can also result in direct stimulation of the facial nerve extracranially. A single pulse control stimulation is used to differentiate this extracranial activation because a single pulse will not activate the corticobulbar pathway like multipulse stimulation (Fig. 24.5).

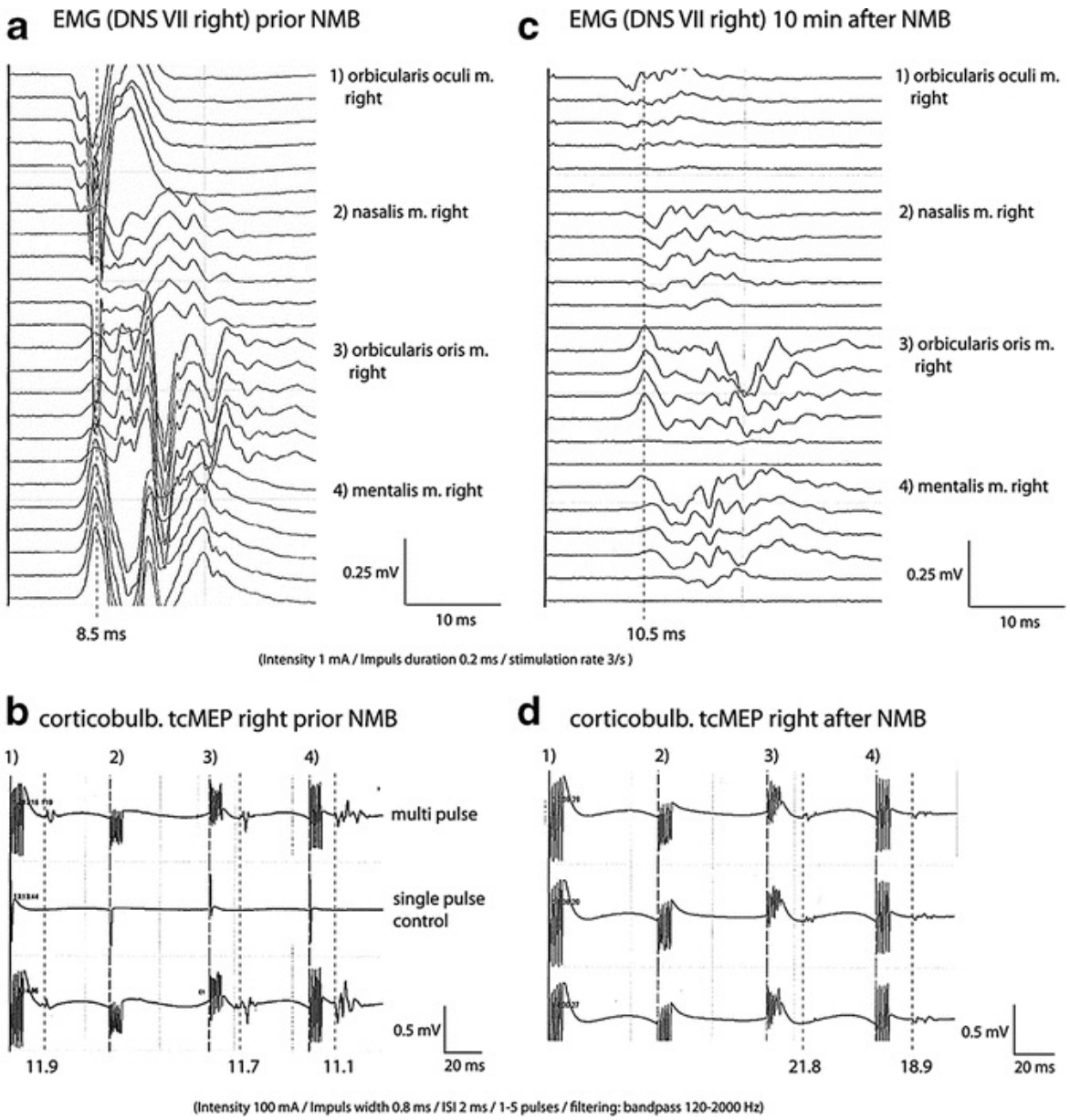

Fig. 24.5 Demonstration of the dependence of electromyography (EMG) and coMEP recordings on neuromuscular blockade (NMB) . Traces of EMG (**a**) and coMEP (**b**) recordings from different facial muscles in the absence of muscle relaxants. All coMEP responses could be recorded after transcranial electrical stimulation (C3-Cz, impulse duration 1 ms (alternating impulse), five pulses with a multipulse rate of 0.2/s). No response was recorded from the nasalis muscle. To evaluate the possibility of superficial stimulation of facial muscles, a single pulse control was applied next to multipulse stimulation. After administering 40 mg rocuronium (train of four (TOF) = 0/4), EMG responses were dramatically diminished and (**c**) coMEPs recorded from the orbicularis oculi muscle were abolished. There also was almost no response from the orbicularis oris and mentalis muscles (**d**)

Unfortunately muscle relaxants and, to a much lesser degree,

anesthetic agents may cause similar changes in EMG and coMEP recordings. Both methodologies strongly depend on the level of NMB. In addition, coMEPs are influenced by intravenous (e.g., propofol) and inhalational agents, especially if boluses are administered.

Traces from a different patient, seen in Fig. 24.5a–d, demonstrate changes in amplitude of EMG responses after DNS of the facial nerve and coMEPs under the influence of NMB. These results emphasize the deteriorating effect of muscle relaxants on EMG recordings. It is recommended that NMB be avoided when EMGs or MEPs are monitored. However, some investigators report the ability to monitor facial muscle activity under partial NMB. In the latter case, it is recommended to control the level of NMB by using train of four (TOF) monitoring and maintaining a level of *at least two responses during* TOF stimulation. If required, this may be reached by continuous infusion of a short-acting muscle relaxant.

False-negative results of EMG recordings after DNS of the facial nerve can occur, especially in patients with large tumors due to accidental stimulation of motor fibers of the trigeminal nerve. This leads to contractions of the masseter muscles and this EMG activity can spread and may be recorded by electrodes that are placed for recording the EMG of the facial muscles. In this case, the latencies of the EMG responses will help in the differential diagnosis. Usually, the peak latencies of EMG responses after DNS of the trigeminal nerve are less than 6 ms whereas the peak EMG latencies from stimulation of the facial nerve are longer than 8 ms.

In cases of chronic compression of the trigeminal nerve by the tumor mass, we observed longer latencies of the trigeminal EMG than the facial nerve EMG. Thus, unless trigeminal activity is separately recorded (e.g., from the masseter muscle), false-negative results cannot be completely ruled out by recognition of latencies only.

The patient was extubated immediately after surgery in the operating room and there was no clinical sign of damage of cranial nerves V, VII, and VIII. No somatosensory or motor deficits were detected as well.

Questions

1. The most common monitoring technique(s) used in infratentorial surgery include EMG of muscles innervated by cranial nerves and

    a. ABRs

    b. SSEPs

    c. tcMEPs

    d. A and B

2. The facial nerve can be monitored using EMG from the

    a. Temporalis muscle

    b. Orbicularis oculi muscle

    c. Masseter muscle

    d. Orbicularis oris muscle

    e. B and D

3. The ABR can be monitored using all of the following EXCEPT

    a. Scalp electrodes

    b. Recordings from c.n. VIII

    c. Electrodes on the cochlear nucleus

d. Corticobulbar responses

4. Which of the following surgical approaches to CPA tumors involves loss of the hearing apparatus preventing salvage of hearing

   a. Retrosigmoid

   b. Translabyrinthine

   c. Suboccipital

   d. None of the above

   e. All of the above

Answers

1. d

2. e

3. d

4. b

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Footnotes

1 Asterisk indicates key reference.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_25

25. Trigeminal Microvascular Decompression

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Keywords Trigeminal neuralgia – Microvascular decompression – Trigeminal cardiac reflex – Auditory brainstem – Monitoring – Cranial nerve monitoring – Motor evoked potentials – Sensory evoked potentials

Key Learning Points

- Trigeminal neuralgia is unilateral, recurrent episodes of severe pain can be triggered by minor stimulation.
- More common in females, right side and the distribution of V2 and V3.
- Microvascular decompression is effective management when medical treatments fail.
- Surgery may be associated with complications related to position, retractors, ischemia to the brainstem, 8th cranial nerve and other cranial nerves.

- Bradycardia, asystole, and trigeminal cardiac reflex can be associated with surgery.
- The causes of evoked potentials changes can be related to technical, positional, pharmacological, physiological, or surgical factors.

Introduction

Trigeminal pain is described as sudden, severe, unilateral, brief, recurrent episodes of sharp shooting pain in the distribution of one or more of the trigeminal branches. It is more common in females, the right side of the face, and in the maxillary and mandibular branches of the trigeminal nerve, V2 and V3 [1]. The incidence is five in 100,000. Pain can be a sequel to normal stimuli such as eating or shaving. This pain is thought to be related to nerve compression by an artery or vein at the nerve dorsal root entry zone. Multiple vascular contacts including veins are common and not identifying all the contacts can be the reason for surgical treatment failure. In theory, the compression produces demyelination of nerve fibers that can affect transmission, processing, and the interpretation of impulses. The entry zone was first observed by Dandy in 1929. Later, Dodd proposed demyelination at the entry zone as the cause of pain that Gardner described as a short circuit of afferent stimuli. In addition, King suggested a central mechanism for pain in the trigeminal distribution. Jannetta reviewed the above information and promoted microvascular decompression (MVD) as an effective treatment [2]. Left untreated, the patient with trigeminal neuralgia proceeds to have shorter intervals free of pain and may progress to have another more complicated type 2 pain syndrome. Patients who fail medical management either because of pain control or excessive side effects are candidates for surgical treatment . An extensive radiological examination may include reliable three-dimensional (3D) high-resolution magnetic resonance imaging (MRI) with constructive interference in steady state (CISS) or fast imaging employing steady state acquisition sequence (FIESTA) that can identify the location and degree of compression at the entry zone [3]. The clinical diagnosis combined with this expanded radiological examination and the intraoperative use of indocyanine (IC) green will lead to better preoperative planning and an improved surgical outcome [4–6].

Early surgical strategies were performed in the prone position with the goal of partially or completely cutting the trigeminal nerve. Since then, the

surgery is commonly performed in the lateral position with the goal of decompressing the nerve through a small suboccipital, retromastoid craniectomy utilizing the microscope and more recently using an endoscopic technique [2, 7–9]. The use of endoscopy offers several advantages: a smaller incision, less tissue manipulation, excellent visualization, fewer complications, less postoperative pain, and a shorter hospital stay [10]. Other treatment modalities have been added to the management of trigeminal neuralgia such as stereotactic radiosurgery, percutaneous balloon compression, glycerol rhizolysis, percutaneous radiofrequency lesioning and the newly, albeit experimental, gasserian ganglion neuromodulation. In this chapter, we discuss a MVD done in the lateral position. However, there are complications that include incisional infection (1.3 %), hearing loss (1.9 %), brainstem and cerebral infarction, CSF leak (1.6 %), facial nerve palsy (2.9 %), facial numbness (9.1 %) and to lesser degree diplopia, ataxia, meningitis, and hydrocephalus [1, 7]. The observed complications after MVD of the cranial nerves directly involved in the surgical approach, and specifically the cochlear cranial nerve, gave rise to cranial nerve monitoring during such surgical procedures [11, 12]. Monitoring select portions of the nervous system to minimize such complications is the essence of this book.

Presentation of Clinical Scenarios

Surgical success starts before incision. Proper positioning will make it easier to perform surgery and improper positioning may compromise the results. The patient is usually placed in the lateral position after induction of anesthesia and needed lines are secured. Pressure points should be padded, a pillow should be placed between the legs, and an axillary roll should be utilized. The patient position is secured using a bean bag, bolsters, or another mechanism. The head should be positioned and stabilized using a three-pin holding device, and rotated 10° away from the surgical side so that the plane of the surgical field is kept parallel to the floor. The neck is flexed so as to preserve at least a 2-cm distance between the mandible and sternum. Positioning is a shared responsibility between the anesthesiologist and surgeon to ensure adequate access into the superior posterior fossa and to maintain a line of sight to the 5th cranial nerve while not compromising intracranial arterial blood flow, venous drainage, or airway patency.

Attention must be paid to the positioning of both upper extremities. The

dependent arm is at risk of vascular compromise and as a result an axillary roll must be carefully placed so that the pulse oximeter can be placed on this arm to detect vascular compromise. The nondependent arm is actually at a higher risk of nerve injury due to positioning. In order to provide more working room, the shoulder of the ipsilateral arm should be gently and carefully pulled inferiorly so as to avoid any excess traction on the upper brachial plexus. Monitoring during MVD will include all American Society of Anesthesiologists (ASA) standard monitors in addition to the neurophysiologic monitoring. Neurophysiologic monitoring should be directed to the structures at risk. The most commonly used monitoring modality is the auditory brainstem response (ABR), which is used to detect hearing loss. (For more information about ABRs, see Chap. 3, "Auditory-Evoked Potentials"). A recent review of the literature of MVD operations found the occurrence of facial nerve palsy to be 2.9 % (0.5–6.2), facial numbness to be 9.1 % (1.3–19.6), and postoperative mortality to be 0.1 % (0.02–0.2). As a result, in addition to the use of ABRs during MVD procedures, such complications support the use of somatosensory evoked potentials (SSEPs) and/or motor evoked potentials (MEPs) and cranial nerve monitoring as well [1]. Monitoring using these modalities allows for the detection of compromised circulation to the brainstem as well as functional changes due to positioning. Laser evoked potentials and trigeminal evoked potentials have been used as research tools but are not routinely used [13, 14]. The rest of this chapter includes six cases: five MVD cases monitored with only ABRs, and one case (#2) monitored with ABRs and MEPs.

Case #1

A 60-year-old, 80-kg woman with left-sided trigeminal neuralgia refractory to medical management was admitted for MVD. She was brought to the operating room, moved onto the surgical table, and ASA standard monitors were applied. Induction of anesthesia included lidocaine (100 mg); propofol, 1.5 mg/kg; and rocuronium, 0.7 mg/kg, with simultaneous initiation of infusions of remifentanil, 0.1 μg/kg/min, and propofol, 25 μg/kg/min. Direct laryngoscopy and endotracheal intubation was performed with a 7.5-mm endotracheal tube secured to the right side of the mouth. A soft bite block was inserted between molars on the left side. A radial arterial line, an additional intravenous line, and a Foley catheter were placed after induction

of anesthesia. The patient was securely placed in the right lateral position. Monitoring included ECG, both arterial and noninvasive blood pressure monitoring, end-expiratory CO_2, oxygen saturation, temperature, and compressed EEG using a bispectral index (BIS) monitor, respiratory rate, tidal volume, peak airway pressure, and urine output. Neurophysiologic monitoring was performed using brainstem auditory evoked potentials (ABRs). (For more details, see Chap. 3). The pulse oximetry probe was placed on the dependent arm to monitor blood flow to that arm. A BIS monitor was used to guide the depth of anesthesia and to adjust the infusion of propofol. The mean arterial blood pressure was maintained within 20 % of baseline values. Manipulation of the blood pressure was accomplished by adjusting the dose of remifentanil or the administration of phenylephrine. Maintenance of anesthesia consisted of infusions of remifentanil (0.1–0.5 μg/kg/min) and propofol (25–150 μg/kg/min) and ≤0.5 MAC of the inhalation agent desflurane. After positioning the patient and obtaining an ABR baseline, a second set of responses were obtained while the surgeon was draping the surgical field. This second set revealed a complete loss of ABR responses to left ear stimulation (Fig. 25.1).

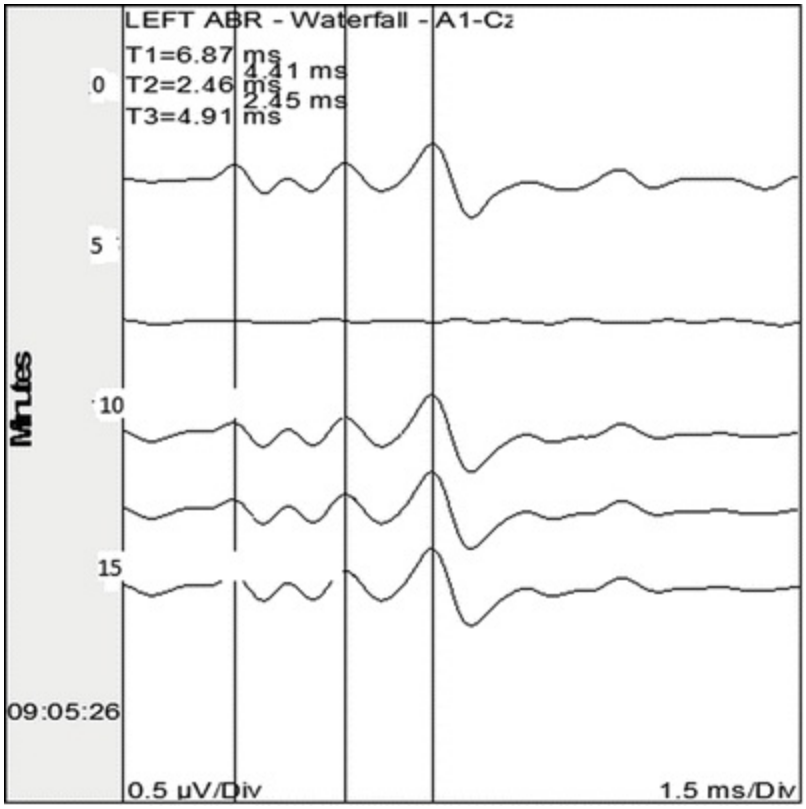

Fig. 25.1 Technical ABR changes . The first tracing on the top is the baseline while the second set (second from top) was taken during obstruction of the silicone earpiece tube. The lower three traces are taken after the release of obstruction

What was the Cause of This Change? Was it Surgical, Pharmacologic, Physiologic, Positional, or Technical?

A surgical cause could be easily eliminated since the change occurred prior to surgical incision. Changes related to anesthetic agents are usually bilateral. However, because the ABR changes were unilateral (the responses to right ear stimulation were normal), an anesthetic-related cause was unlikely. In addition, short latency ABRs (those measured early in the first 10 ms after stimulation) are generally resilient to anesthetic changes. When changes do occur in the presence of inhalation anesthetic agents, they are limited to small increases in latency that do not exceed 0.75 ms. Nitrous oxide has no effect on ABRs, and narcotics, propofol, and barbiturates minimally affect ABRs [15]. Midlatency ABRs (≥50 ms) are affected by anesthetics, but these were not monitored in this case. The anesthetic agents used for this particular patient had very little effect and could be excluded as the cause of the change.

Physiologic changes related to hypothermia may occur while surgery is in progress—when the brain is exposed to a relatively cool ambient temperature and cold solutions are used for irrigation. The effect of hypothermia has been reported to either increase or decrease the amplitude of the ABR. Some reports state that in the face of hypothermia, latency increases of about 7 % for each 1 °C will affect wave I of the ABR, and below 26 °C this effect will double [15]. This did not occur in this case. Other physiologic factors such as hypotension, hypoxemia, and low arterial CO_2 concentration can cause bilateral changes. In this case, there were no such changes in any of these physiologic parameters. In rare situations when a major pathological condition is present in one ear, a physiologic change may lead to bilateral signal changes, with the changes more pronounced on the side with pathology.

We are left with the possibility of either a positional or technical etiology for the encountered change. Because the normal first tracing was done after the patient was positioned with the head fixed without any head or position readjustment, positioning as the cause of the ABR change could be excluded as well.

Technical reasons for ABR changes may include the failure to generate or

deliver proper stimulation or the inability to collect and analyze the signals [15]. Disconnected and broken wires and operator errors account for some of the technical changes. Fluid in the ear canal, kinking of the silicone extension tube, or complete or partial dislodgement of an earpiece can all interfere with stimulation intensity and result in decreased amplitude or completely obliterated responses. Placing cotton and wax or ointment over the earpiece protects against such a problem. The inability to properly collect signals may be related to high impedance, broken wires, noise artifacts, and the use of electrical cautery. The use of an ultrasound aspirator or monopolar cautery can saturate the amplifier and lead to poor signal acquisition. In addition, the use of an integer number for the stimulation rate can cause the acquisition system to lock onto rather than to cancel out 60/50 Hz interference commonly associated with the frequency at which power is being delivered and thus interfere with signal acquisition. For more information about technical problems, see Chap. 16, “Wiring and Electrical Interference in Intraoperative Monitoring”.

In this case, a review of the potential technical causes for loss of the ABR response revealed that a near complete kink of the silicone extension tube following draping was the cause. The signals recovered immediately after releasing the kink, allowing the appropriate intensity sound stimulus to be applied.

Case #2

In another scenario similar to Case #1, a 58-year-old man with left-sided disease was placed in the lateral position. The surgeon requested IOM monitoring, to include ABR, cranial nerves 5 and 7 in addition to MEP. Baseline responses revealed normal ABRs on both sides. The MEP baseline responses revealed an absent left hand, but present left foot responses and the presence of both hand and foot responses from the right side (Fig. 25.2).

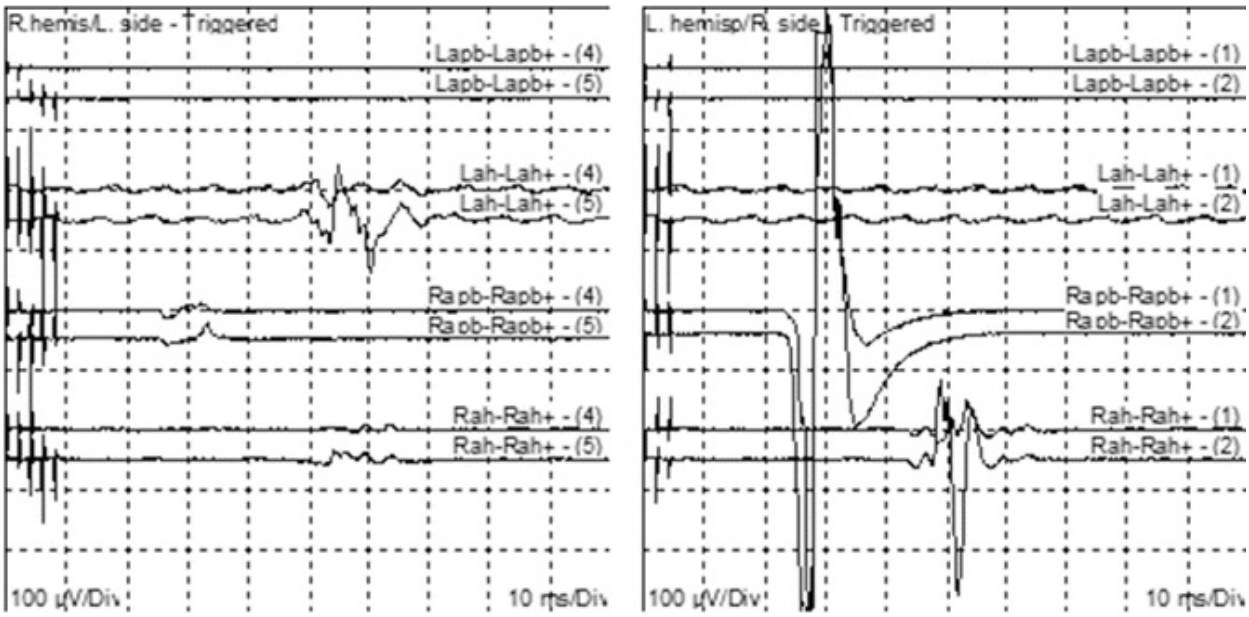

Fig. 25.2 Left panel is tc-MEP from the right hemisphere, showing the missing left hand responses and present left foot response. The right side panel is left tc-MEP with both hand and foot responses

What Could Be the Cause?

In this case we have normal ABRs with absent left hand MEP responses. As in the first case, the surgical procedure had not yet begun, so a surgical cause for the absence of the response was excluded. Anesthesia could be ruled out as a cause since there were no changes in the anesthetic delivery or depth of anesthesia. In addition, changes due to anesthetics are usually bilateral. Physiologic changes such as those due to hypotension, hypothermia, hypocarbia, and hypoxemia are usually bilateral as well. Because there were no changes in any of these parameters, physiologic causes for the absent left hand MEP response were eliminated. However, localized ischemia in the left arm due to a tourniquet is possible, but none had been used. The possibility of a technical cause for the absent response exists. A technical cause would involve either stimulation or recording. Two needles were used for MEP stimulation and because responses were present from the right side and the left lower extremity, stimulation can be excluded as a cause for the absent response. The other possibility to explain this absence is the recording needles in the left hand. These were examined and found to be fine. Low-intensity stimulation is not a possible cause since there were small responses from the other side indicating that the stimulation intensity was strong enough to elicit responses from both sides. In addition, if responses were

absent, it would usually be the foot rather than the hand response if the stimulation intensity was too weak. We are left with positioning as the cause of the absent response. Could this be caused by head position and ischemia-related changes? This is unlikely since the ABRs were normal bilaterally and the right side and left foot MEP responses were normal as well. A very localized ischemic event or a stroke is possible but these cannot be diagnosed based on a clinical examination only. A close examination of the left arm revealed that the arm had been stretched backward by the tape used to keep the arm away from the surgical field. Releasing the tape and moving the arm slightly forward resulted in an immediate recovery of the MEP signals. Their absence may have been due to stretching of nerves or ischemia produced by the abnormal position. A pulse oximeter had been placed on the fingers of the right rather than the left hand to monitor for possible ischemia resulting from the lateral positioning, and therefore we were not able to confirm ischemia as the cause of the absent signals. The fast signal recovery points to ischemia as the cause of the absent responses rather than stretching. Left uncorrected, the positioning may have resulted in nerve injury.

Changes in the ABR due to extreme head positions have been reported by Grundy et al. [16]. Severe flexion and twisting of the head resulting from a patient being positioned in the lateral position may alter the relationship of intracranial structures, increase intracranial pressure, decrease cerebral blood flow, and disturb blood flow to the 8th cranial nerve and other areas of the brain, which can result in changes of the ABRs and MEPs. Such changes are generally corrected with readjustment of the head position and restoration of normal blood flow. Inspection of the head position in this case indicated a slight distortion of the head position but major distortion of the arm. After repositioning of the arm to a more neutral position, the signals readily recovered (Fig. 25.3). This patient may also have had abnormal anatomy or some pathology accentuated by the extreme position that led to changes in the MEPs . If the ABR, SSEP, and MEP baselines are obtained after a patient’s positioning is completed and if the signals are severely abnormal, it may be necessary to readjust the position of the head and extremities.

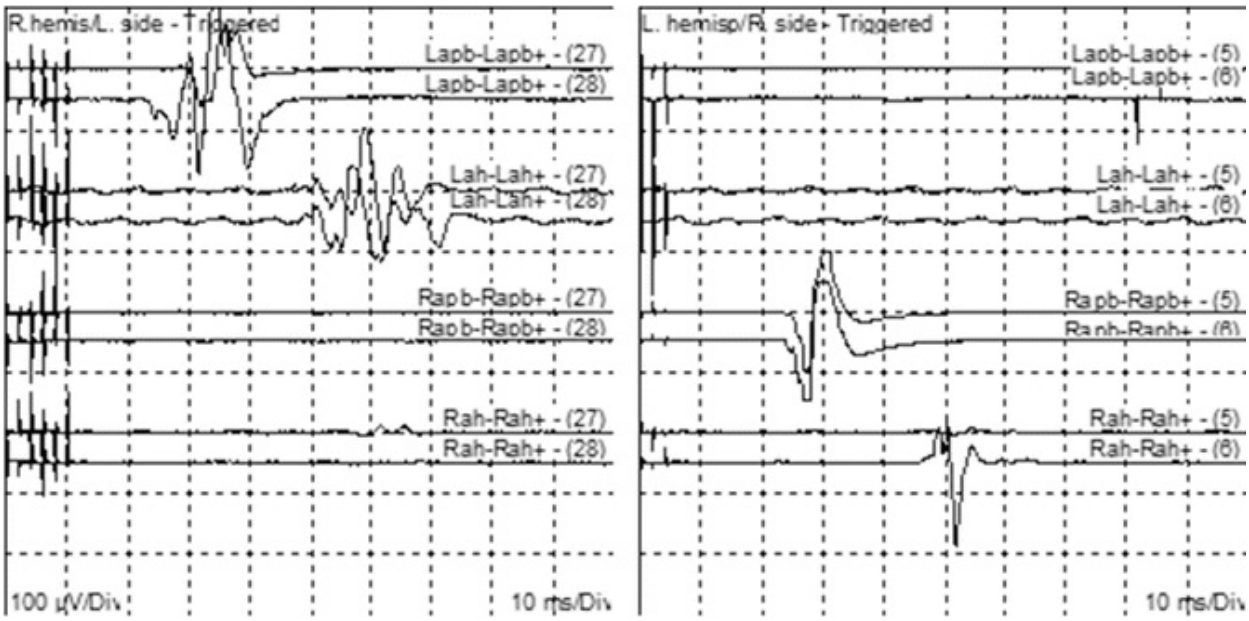

Fig. 25.3 Left side panel is stimulating from right side tc-MEP showing recovery of the left hand responses after adjusting the arm position. The right side is normal responses from left tc-MEP

Case #3

This case is similar to the first case. Baseline values were obtained and the signals were stable before and after positioning of the patient. The surgical procedure began, the dura was opened, and the surgical microscope was used. The surgeon placed and then adjusted a self-retaining surgical retractor several times in order to facilitate surgical exposure and to decompress the trigeminal nerve. During this period, the technologist observed gradual changes of the ABR signals, which included a 5–15 % increase in wave V latency and a 40 % decrease in wave V amplitude from the ipsilateral ear (Fig. 25.4).

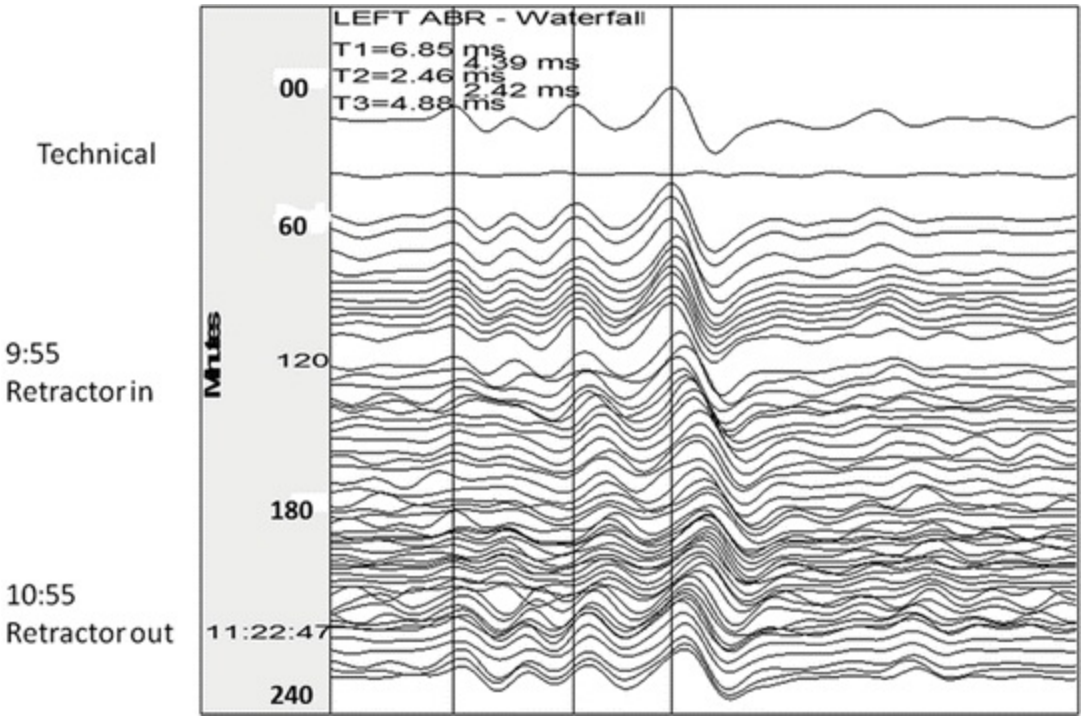

Fig. 25.4 Technical and surgical (retractor ABR changes). The trace on the top is the baseline. Technical change is the second tracing (from top). Cerebellum retractor was placed at 9:55 and released at 10:55. Changes in waves I, III, and V can be seen between these times

Is This a Significant Change?

Polo et al. [17] designated a 0.4-ms (7 %) change in latency of wave V as an early warning sign, a 0.6-ms (10 %) change in latency as the time to alert the surgeon, and a 1-ms (17 %) latency change as serious enough that it needed to be addressed—especially if it was associated with a change in amplitude [17]. In contrast, in 2006, Ramnarayan and Mackenzie [18] found a 0.9-ms latency increase and 50 % amplitude drop to be significant and associated with postoperative hearing loss. Our in-house criteria for alerting the surgeon of a potentially significant change is a progressive 5, 10, and 15 % increase in latency. Some authors depend on latency alone, but Hatayama and Moller [19] believe changes in wave V amplitude are important and should be used as warning criteria when they decrease by 40 %. The changes observed in this case did reach a significant level that required the surgeon's attention.

What is the Cause of This Change?

Technical and positional causes were excluded, as the patient remained in a

stable position and proper functioning of the monitoring system was verified. Both the ambient temperature and the patient's measured temperature were unchanged, no cold irrigation had been used, and the vital signs were stable. Physiologic causes were therefore unlikely to be the cause of the observed ABR changes . Since the changes were unilateral, pharmacologic- and anesthetic-related causes were doubtful, so surgical factors remained as the likely potential etiology.

Surgical causes of ABR changes can be divided into three categories [20]. The first group includes gradual changes in ABR signals from stimulation of the ear on the operative side that recover with surgical maneuvers such as repositioning of the retractor. These are usually not associated with hearing loss. The second group includes ABR changes where there is an abrupt loss of all waves except wave I on the operative side that do not recover with surgical maneuvers. Such changes are usually associated with postoperative hearing loss. The third group of changes consists of a loss of all ABR signals after wave I on the contralateral side of surgery. This change is usually associated with brainstem dysfunction and may result in severe postoperative neurological deficits beyond just hearing loss.

Surgical causes for ABR changes may be due to mechanical or thermal irritation or injury to the 8th cranial nerve or its blood supply, which result in abrupt loss of the signals [15]. Coagulation of small blood vessels that provide blood flow to the cochlea or of veins that drain from the brainstem may result in such changes. Slower changes in the signals without complete loss may be a consequence of direct compression or traction on the nerve or indirect traction on the nerve through cerebellar retraction and tension on the bridging arachnoid bands. Indirect interference with blood supply to the cochlear nerve caused by compression, coagulation, spasm, or intentional occlusion can lead to varying degrees of ABR changes. Retraction of the cerebellum to improve surgical exposure may lead to stretching and potential damage of the 8th cranial nerve, and be associated with an alteration in ABR signals. Such damage can be more critical in MVD than in cases of tumor resection. During cases of tumor resection, distortion of the nerve by stretch or compression may be better tolerated having occurred over time, whereas during MVD, this anatomical stretch represents an acute insult. Changes related to traction of the cerebellum recover soon, often within minutes after retractor adjustment. If abnormal signals persist, the retractor should be completely withdrawn, and the 8th cranial nerve checked for any evidence of

compression including from the Teflon pledgets utilized by the surgeon to isolate the trigeminal nerve from surrounding structures impinging on it.

A clinical situation in which there is wave I delay or loss, with wave V delayed but present, may be the result of mechanical or thermal damage to the cochlea. The presence of wave I associated with equal changes in waves III and V is related to a more proximal injury to the 8th cranial nerve and could be attributed to causes such as cerebellar retraction, nerve compression, or small vessel vasospasm. Preserved waves I and III with delay or loss of wave V may be caused by mechanical, thermal, or vascular injury in the mid to upper pons. Injury to the auditory pathways cephalic to the lower mesencephalon may be associated with normal ABRs. A vascular injury in the posterior fossa that spares the auditory pathway can be associated with normal ABRs.

Of note, an interesting phenomenon is vasospasm , which may be seen in the vascular loop surrounding the cranial nerves during MVD. Successful treatment of spasm of the loop by the application of topical papaverine either directly or via a papaverine-soaked pledget yields immediate improvement of blood flow in the loop but may be associated with decreased blood flow to the cochlea and a loss of the ABR signals within a few minutes. The cause of this change is not clear, although the low pH of papaverine has been suspected [21]. In this case, the changes were gradual, ipsilateral, and involved waves I, III, and V. Delayed latency changes were equal for waves III and V, which pointed to an issue with the 8th cranial nerve proximal to the cochlea and related to the retraction on the cerebellum. The changes in wave I could be related to a compromise in blood flow to the internal auditory artery, either by partial obstruction or spasm. The surgeon inspected the operative site and decided to reposition the retractor. Soon after repositioning, the signals started to recover back to baseline. The most likely cause of such changes was retractor pressure on the cerebellum , which decreased blood flow to the 8th cranial nerve. Strategies to improve the signals include relaxing the retractor, dividing the arachnoid tension bands between the 8th cranial nerve and the cerebellum, and pharmacologically raising the blood pressure. Raising the blood pressure could help by increasing collateral blood flow to the area, especially if retractor repositioning alone did not provide recovery of the signals.

Case #4

In this case, a healthy 45-year-old woman who failed medical management for trigeminal neuralgia was scheduled for MVD . Anesthesia and surgery proceeded in similar fashion to the previous cases. The patient was quite stable, signals were normal and consistent, and the surgery began and progressed without incident. The surgeon was far into the dissection around the 5th cranial nerve to isolate it from the artery when adhesions were noted between the compressing artery and the sensory portion of the 5th cranial nerve. The anesthesiologist noticed an increase in blood pressure and heart rate and thus administered a bolus dose of 0.5 μg/kg of remifentanil and increased the remifentanil infusion rate to 0.2 μg/kg/min. Vital signs stabilized over the next 10 min followed by a period of fluctuating blood pressure during which the pulse varied 20–30 % from baseline. The BIS monitor was stable and the surgical procedure proceeded at a slow pace. Suddenly, the heart rate dropped to 30 beats per minute followed by 8 s of asystole with a precipitous drop in systemic blood pressure (Fig. 25.5).

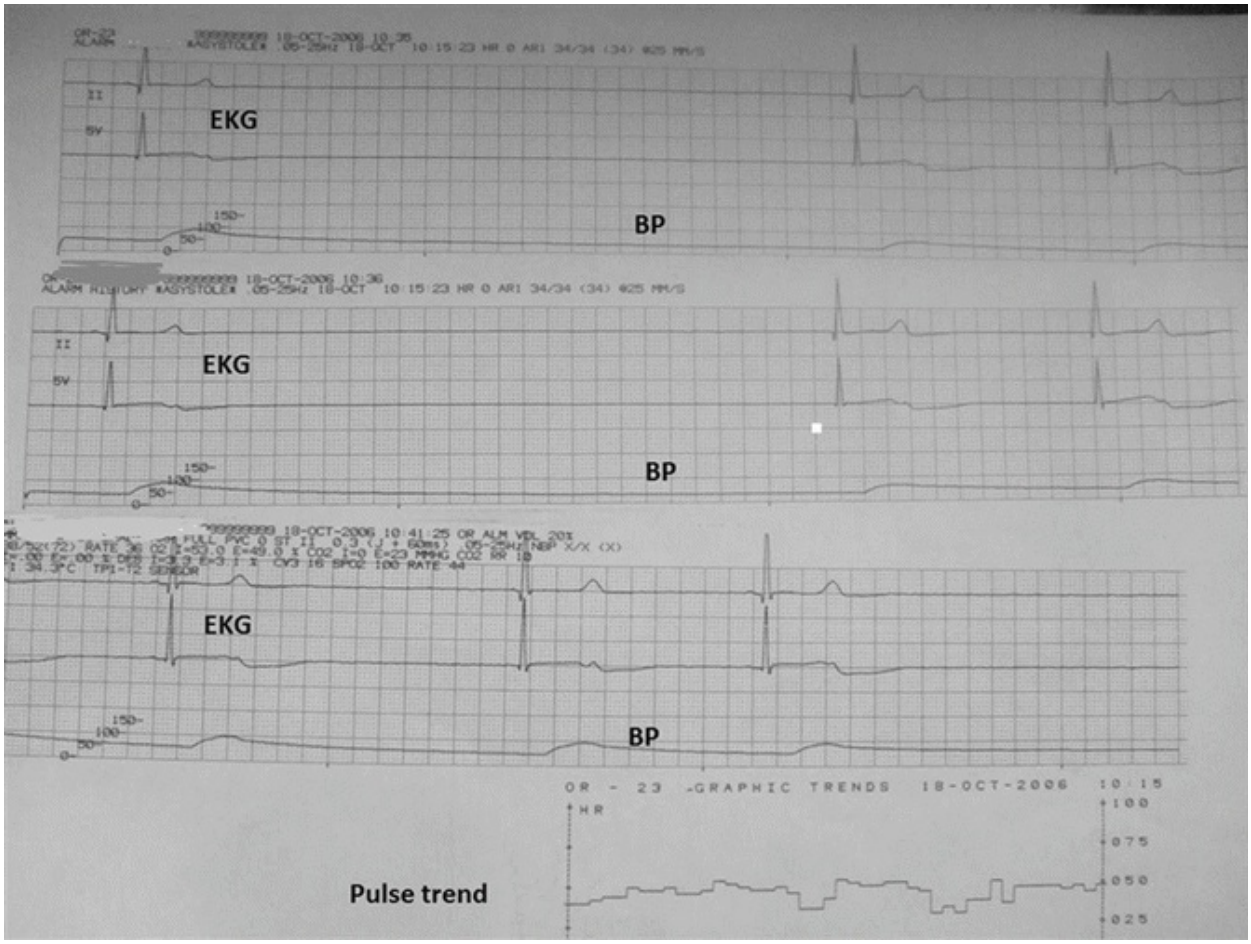

Fig. 25.5 Trigeminal cardiac reflex. EKG changes with severe bradycardia leading to asystole. Three strips with each strip showing two EKG traces on the top and middle, the blood pressure tracing is at the bottom of the strip. Graphic trend is seen in the bottom of the figure

What Happened? Is This Related to the Remifentanil Infusion, a Cardiac Incident, Brainstem Manipulation, or Something Else?

Remifentanil is associated with production of a sympathetic blockade that may lead to indirect bradycardia and hypotension. In rare situations, the change in vital signs may resemble those in the case at hand. Such changes in pulse and blood pressure usually follow a bolus injection and recover spontaneously over a short period of time. Cardiac incidents may also occur in patients with coronary artery disease or other comorbidities. Direct brainstem manipulation can be associated with abrupt fluctuations in pulse and blood pressure that may exceed a 20 % change from baseline values.

This etiology should be considered and reported to the surgeon who may adjust the amount of direct contact with the brainstem. The clinical picture could also be the result of the trigeminal cardiac reflex. It is a well-described phenomenon that may be triggered during surgical procedures at the cerebral pontine angle area or skull base, an MVD, or a sudden and significant manipulation of the dura. In addition, the trigeminal cardiac reflex may also be elicited during ophthalmologic surgery, surgery of the maxilla, and other areas innervated by the trigeminal nerve [22]. Release of surgical traction or cessation of the trigger stimulation will allow the reflex to cease and the vital signs to return to normal without further intervention. However, if the stimulation resumes, the reflex may reoccur. On occasion, the reflex may produce such a profound change in heart rate and blood pressure that the clinical picture progresses to cardiac arrest. The mechanism for this reflex was described in The *Journal of Neurosurgery* in 1999 [23]. In summary, stimulation of the trigeminal nerve sends an afferent signal to the sensory nucleus at the brainstem, which then crosses to the motor nucleus of the vagus nerve. The signal then travels through the efferent arm to the heart, lungs, and stomach to cause bradycardia, apnea, and hypergastric secretions. This reflex may be a cerebral oxygen conserving reflex [24].

In this patient, the trigeminal cardiac reflex was suspected and the surgeon was alerted to stop any manipulations. The surgeon was not in direct contact with the brainstem but was manipulating a blood vessel adhering to the trigeminal nerve near the brainstem. Blood pressure and heart rate returned to normal soon after the surgeon stopped the manipulation.

Case #5

The following case depicts a rather rare scenario for MVD in an otherwise healthy patient with refractory medical management. The anesthesia, positioning, and surgical course followed the same regimen as the previous cases. The surgical course proceeded without incident during which the MVD was completed. The ABR remained stable throughout the procedure and the surgeon started to close. Upon closure of the dura , the ABR signals started to deteriorate and were completely lost with the closure of the fascia.

What is the Problem and What Should Be Done?

Unilateral ABR changes at this stage of the operation are not characteristic of those caused by anesthetic depth, physiologic causes, or patient positioning. Occasionally, irrigation with cold saline in the surgical field just before dural closure can cause a decline in signals, but these occur immediately. In this case, the changes occurred after the dura was closed. The two most likely causes for this change were technical or surgical. In this case, no technical cause could be identified. Since the dura was closed, neither direct manipulation of the 8th cranial nerve or low blood flow from retractor pressure could be implicated. Indirect factors related to intradural anatomical changes that could decrease blood flow to the 8th cranial nerve at different locations remained a possibility. Bleeding, hematoma, and clot formation could affect the integrity of the nerve. Changes and loss of ABRs, caused by these factors, after the closure of the dura have been reported previously [11, 25–27].

Bleeding and cerebral edema may be the result of movement caused by light anesthesia, high blood pressure, or inadequate hemostasis by the conclusion of surgery. In some patients, coagulation and cutting of a petrosal vein larger than 2 mm in caliber may lead to obstruction of drainage from parts of the brainstem. In turn, this can result in venous congestion, edema, and an increased intracranial pressure (ICP) and may be the cause of the ABR changes. Contralateral hearing loss has been reported due to vascular congestion causing brainstem shift, edema, and high ICP, and has been associated with ABR changes [28]. Before disruption of such a vein, an occlusion test with a temporary aneurysm clip placed on the vein in conjunction with ABR monitoring may be helpful to prevent such a complication [29].

In this patient, the decision was made to reopen the surgical field and explore the operative site. The surgeon looked for a possible source of bleeding either in the CP angle or within the cerebellar parenchyma, some limitation of blood flow related to vascular kinking, or malpositioning secondary to shift of the Teflon felt. During this time, the anesthesiologist raised the blood pressure to increase collateral circulation. The surgical exploration revealed a small blood collection engulfing the 8th cranial nerve. This was related to a bleeding stump of a branch of the petrosal vein, which had been sectioned on the approach. Once the blood was evacuated, ABR signals started to recover.

Case #6

A 46-year-old 85-kg woman is having right-sided MVD surgery for trigeminal neuralgia. As in previous cases, the patient was positioned in the lateral position and the surgery progressed very well without any noticeable changes in the ABRs. After the main procedure was completed and while securing hemostasis, the technologist noticed significant changes of the right ABR at 10:35 and complete loss at 10:39 (Fig. 25.6). No changes in the left ABR were observed.

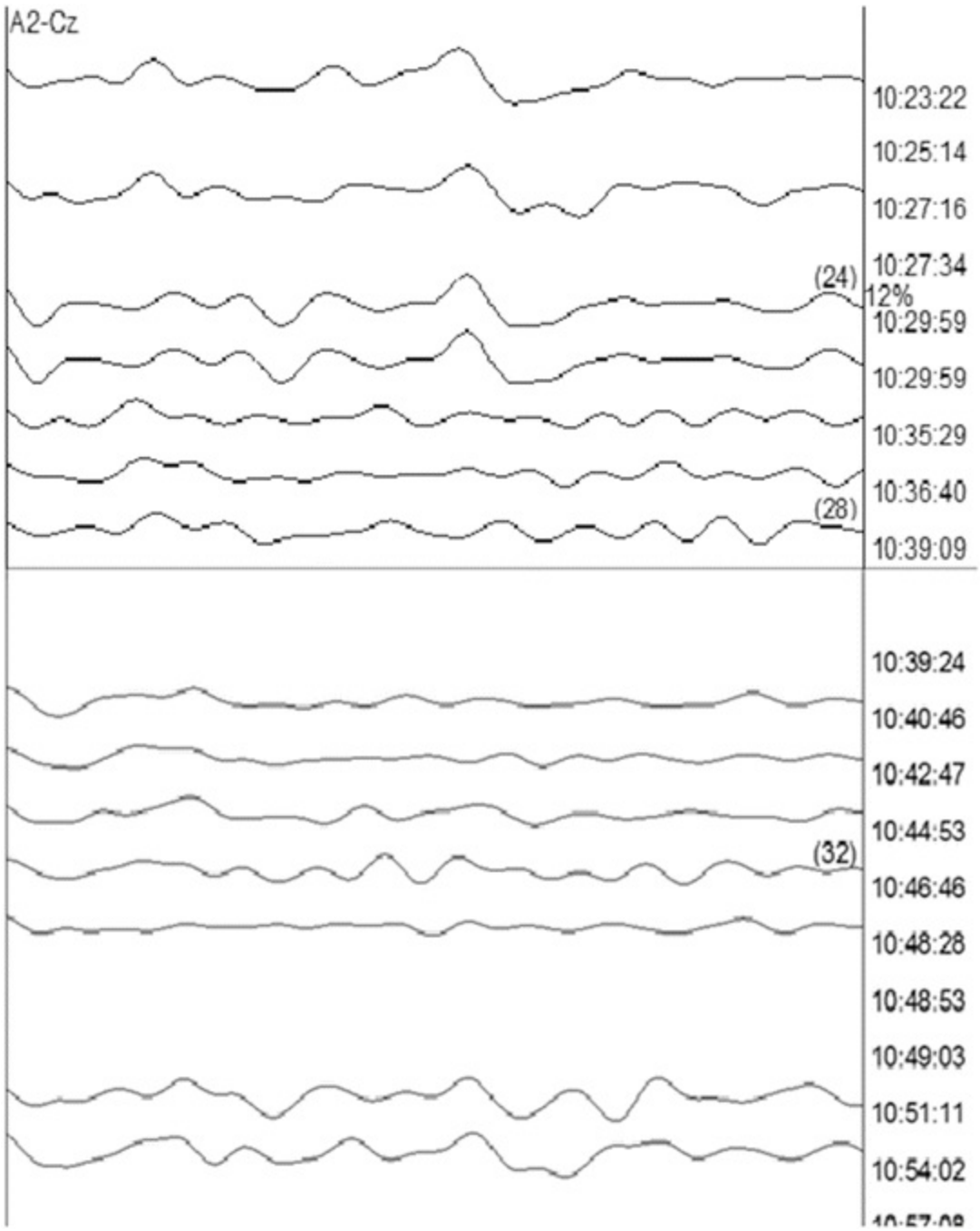

Fig. 25.6 ABR tracing . Papaverine was used at 10:30 and resulted in the loss of ABR responses on the right side which recovered by 10:51 after aggressive irrigation with warm saline to dilute and clear papaverine. No postoperative complications

What happened? What is the cause? If we go through the differential diagnosis and review all five causes of EP changes—technical, physiological, pharmacological, surgical, or positional—we should get the cause. Changes on one side are unlikely to be due to anesthetic agents or physiological

alterations. Special physiological conditions such as regional hypothermia, while possible, are unlikely to be a cause, since only warm irrigations were used for the hemostasis. Severe regional ischemia that affects the distribution of the 8th cranial nerve is possible, but why? No clips or retractors were used at that time. Technical causes should always be considered when localized changes or losses occur. A survey of all technical possibilities did not reveal any cause. Changes due to positioning are unlikely to have occurred since no such changes occurred since the start of the case. At the time when the changes occurred, the surgeon was only performing hemostasis; there were no retractors, no major manipulations, and the dura was not closed with overinfusion of saline [30]. It seems that none of the five causes of EP changes can be easily identified. What is the cause? In this case, the author was walking into the room when he heard the neurosurgical chief resident announcing the use of papaverine to reverse spasm. The surgical team was alerted to its potential effects and stopped any further usage. While the anesthesiologist was talking to the surgeon, the technologist announced that signal changes were occurring. The chief resident was instructed to flush the field with warm saline to minimize the effects of the papaverine. The signals gradually recovered and were back to normal by 10:51. The possible cause of this effect is the low pH of papaverine, which can affect the 8th cranial nerve [21]. If papaverine is needed, its use should be limited to a precise location.

Conclusion

In these six cases we reviewed different clinical situations in which changes of ABRs and MEP signals occurred during MVD surgery. In each case, we followed an algorithm with a stepwise approach to identify the etiology and management. It is critical for both the anesthesiologist and surgeon to work in concert to identify changes, analyze their cause, start treatments, and to perform surgical maneuvers that may reverse changes in a timely fashion in order to optimize the surgical outcome.

Questions

1. Which of the following can result in unilateral evoked potentials during MVD?

a. Retractors

b. Papaverine

c. Technical problems

d. All of the above

2. Trigeminal cardiac reflex is the result of:

a. Injection of medication by the anesthesiologist

b. Irritation of the 8th cranial nerve

c. Irritation of the facial nerve

d. Irritation of the trigeminal nerve

3. Unilateral absence of ABR at the start of the operation may be caused by

a. Bolus of anesthetic drugs

b. Hypotension

c. Surgical manipulation

d. Abnormal head position

Answers

1. D

2. D

3. D

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Footnotes

1 Asterisk indicates key references.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_26

26. Surgery for Hemifacial Spasm

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Electronic supplementary material:
The online version of this chapter (doi:10.1007/978-3-319-46542-5_26) contains supplementary material, which is available to authorized users.

Keywords Neuromonitoring – Microvascular decompression – Hemifacial spasm – Electrophysiology – Pathophysiology – HFS – Operative technique – Facial nerve – Complications – MRI

Key Learning Points

- HFS consists of unilateral facial nerve dysfunction resulting in spasms of the ipsilateral facial muscles. MVD is a surgical procedure that addresses a proposed etiologic cause of HFS, vascular compression causing ephaptic transmission, and is successful in the majority of well-selected patients.
- Electromyography revealing characteristic, spontaneous activity and an abnormal motor response of the facial musculature and MRI confirming vascular compression of the facial nerve are important tools for distinguishing the disease and determining the role of operative intervention.
- Compression of the facial nerve along any portion of the centrally myelinated root nerve is the target for decompression during MVD and is achieved by use of shredded Teflon implants or, in some instances, “slinging” of the artery away from the nerve.
- Considerations for anesthesia specific to MVD for HFS include optimal positioning, avoidance of nondepolarizing agents, and minimization of fluid overload.
- Intraoperative use of abnormal motor response monitoring can be used as a guide for adequate facial nerve decompression and has been shown to correlate with increased odds of symptom resolution postoperatively.
- Due to the proximity of the vestibulocochlear nerve to the facial nerve, hearing loss following MVD for HFS is a possible complication of MVD for HFS, and the use of brainstem auditory evoked responses to mitigate the risk of hearing loss should be considered.

Introduction

Hemifacial spasm (HFS), a syndrome of unilateral facial nerve hyperactive dysfunction , is a severe and disabling condition that causes impairments in a patient’s quality of life [1–4]. Spasms begin insidiously in the orbicularis oculi muscle and spread over time to the muscles of the face with variable involvement of the frontalis and platysma muscles. Ultimately, the patient

may develop prolonged contractions of all the involved muscles, causing severe, disfiguring grimacing with partial closure of the eye and drawing up of the corner of the mouth, the so-called tonus phenomenon [5]. The majority of patients also exhibit the reverse Babinski sign, which is appreciated as paradoxical raising of the eyebrow during closing of the eye [6, 7]. The best available data suggest that the prevalence rate of HFS is ten patients per 100,000 in the population of the United States and Norway [8, 9].

Electrophysiology and Pathophysiology of HFS

The diagnosis of HFS can largely be made clinically, but electromyography (EMG) and magnetic resonance imaging (MRI) may help in distinguishing the disorder from other abnormal facial movement disorders, such as blepharospasm, tics, partial motor seizures, synkinesis, craniocervical dystonia, neuromyotonia, and facial myokymia [10, 11]. The electrophysiologic hallmarks of HFS consist of spontaneous, high-frequency (as many as 150 impulses per second), synchronized firing of EMG activity. In addition, an abnormal motor response (AMR) , also known as the “lateral spread response,” can be elicited by electrically stimulating one branch of the facial nerve and recording triggered electromyographic (t-EMG) responses from muscles innervated by other branches of the facial nerve. Specifically, electrical stimulation of the zygomatic branch of the facial nerve will result in an AMR recording from the mentalis muscles when the t-EMG response should be limited to only the orbicularis oculi muscle.

There remains no consensus regarding the etiopathogenesis of HFS. One hypothesis asserts that symptoms are caused by ephaptic transmission at the location of the vascular contact along the facial nerve [12, 13]. Ephaptic transmission refers to the “crosstalk” between axon fibers as a result of axon demyelination. Alternatively, it has been submitted that the symptoms are secondary to hyperactivity of the facial nucleus [14]. While the hypothesis of ephaptic transmission was popularized for many years, the hypothesis of facial motor nucleus hyperactivity has been supported by intraoperative electrophysiological recordings made during MVD [15, 16], clinical studies [17], and the results of intraoperative blink reflex testing. The blink reflex is elicited by stimulation of the supraorbital nerve and consists of afferent and efferent pathways along the trigeminal and facial nerves, respectively. In anesthetized patients without HFS, the blink reflex is typically suppressed.

However, in the anesthetized HFS patient, a blink reflex can be elicited ipsilateral to the side of facial spasm [18]. The hypothesis is that the pathological hyperactivity in the facial motor nucleus compensates for the suppression typically induced by general anesthesia.

A third proposed contributor is facial nerve depolarization from supraorbital nerve stimulation via axono-axonal ephapsis in the periorbital region. Axono-axonal depolarization of these terminal facial nerve axons would carry the signal antidromically to the site of presumed demyelination (ostensibly at the area of vascular compression) and induce an ephaptic response in the lower facial muscles [19]. The term “lateral spread” is often used interchangeably with the term “AMR.” The term “lateral spread,” however, should be reserved for describing the AMR in relationship to the theory of ephaptic transmission, as the term “lateral spread” neglects the theory of motor nucleus hyperexcitability.

It is certainly possible that all three mechanisms contribute in part to the generation of abnormal reflex responses. As the AMR often disappears with vascular decompression of the centrally myelinated facial nerve, ephaptic transmission is thought to be a more likely, or more common, cause of the AMR. Isolated facial motor nucleus hyperactivity may account for a minority of HFS cases refractory to MVD or, alternatively, to a continuum of disease severity (i.e., motor nucleus hyperexcitability follows ephaptic transmission at the site of vascular compression).

Anatomy of the Facial Nerve and Etiology of HFS

A discussion of anatomy requires a consistent vocabulary. The anatomical terms, hereto used, were first proposed by Tomii et al. [20] and subsequently expanded by Campos-Benitez and Kaufmann [21]. The facial nerve emerges from the brainstem at the nerve’s root exit point from the pontomedullary sulcus. Along its course, it adheres (i.e., the attached segment of the facial nerve) to the pons for 8–10 mm. The nerve then separates from the pons at the so-called root detachment point . The next segment of the nerve is termed the transition zone or the Obersteiner-Redlich zone where the oligodendrocyte-derived central myelin transitions to the peripheral Schwann cells. A study by Tomii et al. [20] of this transition zone revealed that (1) the maximum length from the root detachment point to the most proximal portion of the transition zone is 1.4 mm and (2) the maximum length from the most

proximal to the most distal portion of the transition zone is 2.1 mm. In practice, our group uses 4 mm as the maximum distance from the root detachment point to the end of the transition zone (Fig. 26.1). Beyond the transition zone, the seventh nerve lies adjacent to the anterior rostral border of the CN VIII complex and continues into the acoustic meatus. Rostral and anterior to the VII/VIII complex, the trigeminal root is visible as it emerges from the pons, eventually traveling laterally toward the petrous apex to Meckel's cave. Caudal to the VII/VIII complex, emerging from the lateral surface of the medulla, are the rootlets of the glossopharyngeal and vagus nerves . Our experience with HFS suggests that vascular compression along any portion of the centrally myelinated facial nerve may contribute to symptoms. This portion extends from the root exit point to the distal transition zone. As of note, our group hesitates to use the term "root entry zone" or "root exit zone" as (1) it is imprecisely defined but approximately corresponds to the root detachment point and the transition zone, and (2) does not include the root exit point or the attached segment, which is the most common site of nerve compression [22, 23]. The most common offending vessels are the anterior inferior cerebellar artery (AICA) and the posterior inferior cerebellar artery (PICA) , which occur in the setting of a tortuous vertebrobasilar tree in half of affected patients [24].

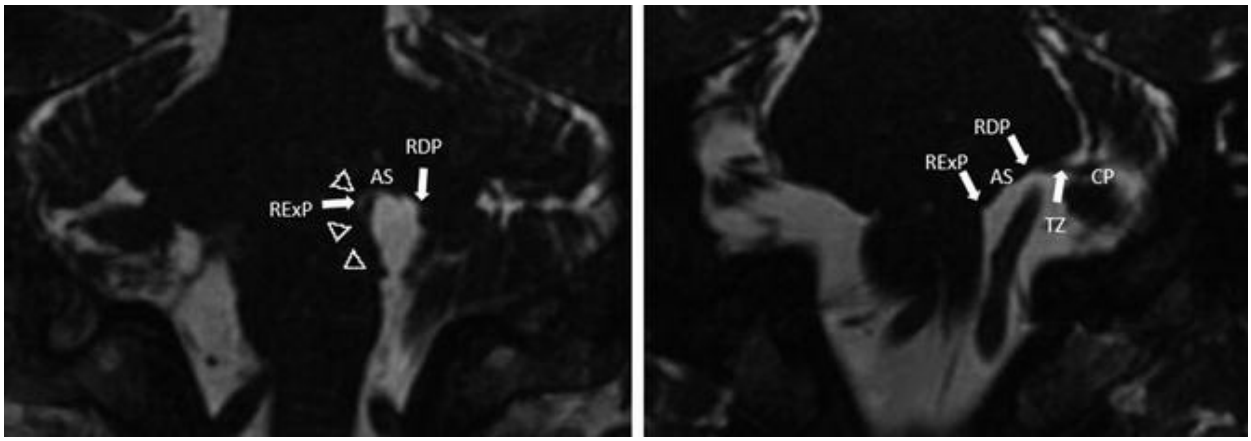

Fig. 26.1 Coronal SSFP image showing facial nerve anatomy: root exit point (RExP), attached segment (AS), root detachment point (RDP), transition zone (TZ), and cisternal portion (CP)

Imaging in HFS

Imaging of patients with HFS who are considered for MVD is intended to

delineate the facial nerve and adjacent vessels. Studies should include thin-section multiplanar steady-state free precession (SSFP) MRI sequences, which are heavily T2 weighted and provide excellent contrast between CSF and adjacent tissue [25]. The role of SSFP imaging in the evaluation of vascular compression syndromes has been described [26–29] and recently optimized for HFS by our group [22, 23]. Studies are performed on either 1.5 or 3 T MRI scanners (Optima and Discovery; GE Healthcare, Milwaukee, WI) and include whole-brain sagittal T1, axial fluid-attenuated inversion recovery (FLAIR) , and diffusion weighted imaging (DWI) sequences. Thin-section axial, coronal, and sagittal SSFP images through the brainstem are obtained. It is important to note that the role of imaging in HFS is supportive and not diagnostic. As reported by our group, imaging has a sensitivity of 75–92.9 % and a specificity of 28.6–75 % [30]. The high sensitivity warrants appropriate counseling in patients deemed clinically favorable for surgery but have no vascular compression on thin-slice T2-weighted MRI . Furthermore, the low specificity does not warrant justification of surgery for positive imaging findings in clinically unfavorable surgical candidates.

Operative Technique of Microvascular Decompression of the Facial Nerve

Medications have been shown to be largely ineffective in treatment of HFS [31–34]. Serial botulinum toxin injections of the facial musculature may provide a temporary respite but are not curative. In addition, prolonged use of botulinum toxin may result in persistent facial nerve paresis or palsy. For this reason, MVD, the only etiological therapy for HFS, is the preferred treatment [33, 35].

Microvascular decompression is performed under general anesthesia with the patient in the contralateral decubitus position (Fig. 26.2, utilizing auditory brainstem-evoked potentials [ABRs]), facial EMG, and monitoring of the AMR in a previously described manner [35]. A retromastoid incision is made behind the hairline, and a small craniectomy below the asterion is performed. The edge of the sigmoid sinus is identified, and the dura mater is opened. After appropriate brain relaxation is achieved with cerebrospinal fluid (CSF) drainage, the facial nerve is exposed from the root exit point to the transition zone and examined for vascular contact. In concert with our neuromonitoring

team, arteries are decompressed from the facial nerve using shredded Teflon® implants. Occasionally, our surgeon (RS) transposes or “slings” the artery away from the facial nerve. ABRs and facial EMG are used to monitor the patients in all cases. Direct monopolar facial nerve stimulation is used in selected cases (Videos 26.1 and 26.2).

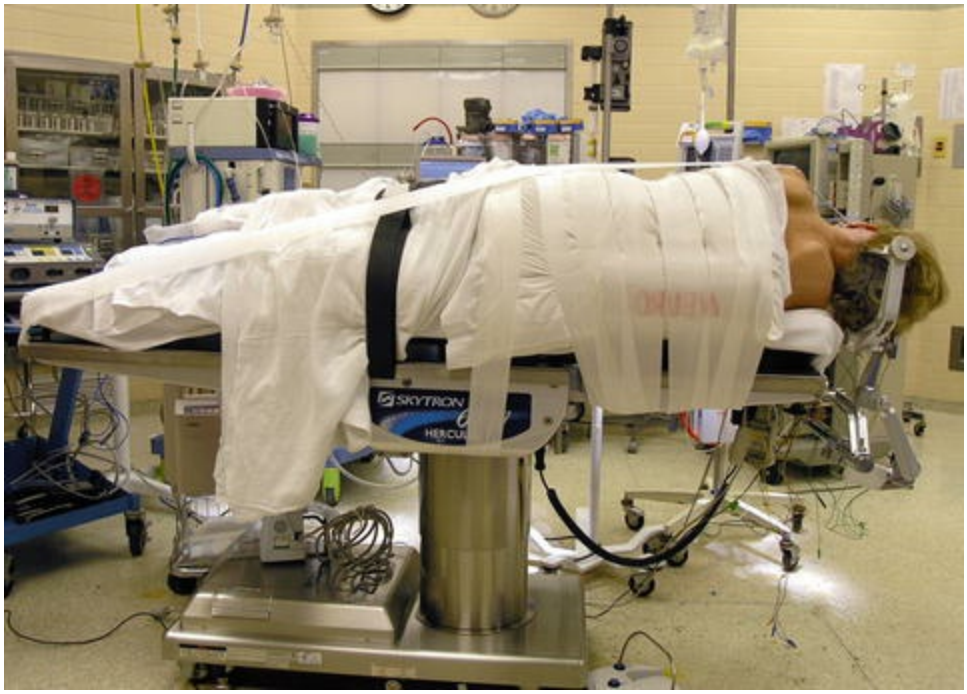

Fig. 26.2 Photograph of patient in the lateral decubitus position. Patient’s head is placed at the foot of the operating table to allow more leg room for the surgeon during the microsurgical portion of the procedure. The head is secured with three-point fixation and the patient is turned in the lateral decubitus position. The head is rotated slightly away from the affected side and flexed to allow approximately two fingerbreadths from the sternum

Anesthetic Considerations During MVD for HFS

Induction of general anesthesia may begin with propofol or etomidate. A depolarizing muscle relaxant is often used for the intubation. It has been our experience that even a small defasciculating dose of nondepolarizing muscle relaxant used during the intubation period is enough to obscure the detection of the AMR at the beginning of the case. Maintenance of general anesthesia can be achieved with a variety of techniques as long as the patient remains motionless without the use of muscle relaxants. Some patients may require only an inhalational agent while others may require inhalation as well as an

infusion of either propofol or narcotic such as remifentanil. Meticulous attention to proper positioning takes into consideration avoidance of extreme head and neck flexion or rotation, proper placement of an axillary roll, as well as proper padding of both upper and lower extremities to prevent peripheral nerve injury. There should always be a final confirmation of bilateral breath sounds to confirm the absence of endotracheal tube migration.

Principles of Intraoperative Neuromonitoring for HFS

The AMR can be elicited in nearly every patient with HFS. Nondepolarizing muscle relaxants can obscure results. Bipolar subdermal needle recording electrodes are placed in the orbicularis oculi and mentalis muscles. Paired electrodes are placed approximately 0.5–1 cm apart. Bipolar stimulating electrodes were inserted subdermally over the zygomatic branch of the facial nerve midway between the outer canthus and tragus. Monophasic pulses were delivered at an intensity of 1–20 mA, a frequency of 4.0 Hz, and a pulse width of 0.2 ms. Final positioning of the stimulating electrodes is based on the location that maximizes the orbicularis oculi response and the AMR recorded from the mentalis muscle group. Once identified, suprathreshold stimulation intensity is utilized throughout the procedure. Electrodes are then affixed to the skin in their optimal position with tape.

To avoid nerve fatigue, the AMR is evoked at approximately 5-min intervals until dural opening. Once the dura is opened, the AMR should be recorded continuously throughout the dissection and decompression and then again periodically during closure to detect the potential reappearance of the AMR. Occasionally, the AMR disappears as CSF is drained, ostensibly as a result of relaxation of vascular compression of the facial nerve. Of note, our group has not used brain retraction in the past 5 years [36]. An attempt is made to restore the AMR by increasing the current intensity (up to 20 mA), increasing the stimulation frequency, and finally by increasing pulse widths in increments of 50 μs. After decompression of suspected arteries and veins from the facial nerve and disappearance of the AMR, a further attempt is made to “drive” or stimulate the AMR by increasing the frequency to 30 Hz. If the AMR cannot be elicited, we consider the AMR to have completely resolved.

Monitoring for Complications

Cranial nerve injuries during MVD may result in facial weakness, hearing impairment, vestibular dysfunction, and dysphagia and/or hoarseness, which can affect satisfaction with MVD despite the absence of HFS postoperatively. ABRs are used to monitor cochlear nerve function throughout the procedure. In addition, continuous monitoring of the AMR (Fig. 26.3) and occasional monopolar facial EMG are performed during the procedure. Indeed, neuromonitoring in MVD surgery has been shown not only to improve patient outcome in terms of symptom resolution, but also to decrease the occurrence of hearing loss and facial nerve weakness after surgery [37–39]. Monitoring of somatosensory evoked potentials (SSEPs) used to detect brainstem stroke secondary to vascular manipulation may be considered but is not routinely performed by our group. Monitoring of the ninth and tenth cranial nerves is not performed.

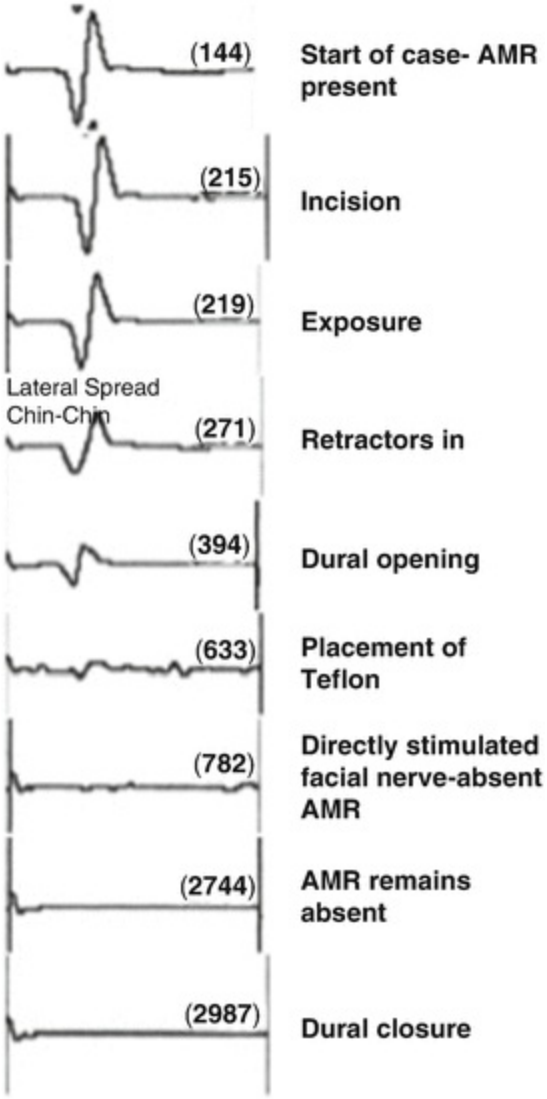

Fig. 26.3 Tracings of the AMR showing changes during MVD for HFS

In the following examples, we review cases from our experience over the past 30+ years of MVD for HFS.

Case Illustrations

Case 1: Understanding the AMR During MVD of the Facial Nerve

A 42-year-old woman with right-sided HFS underwent an MVD after serial botulinum toxin injections resulted in unsatisfactory results. During the

operation, the AICA and PICA were noted to be tightly compressing the right facial nerve. During decompression of the PICA, the AMR resolved and could not be elicited (Fig. 26.4). The patient awoke from the operation with much reduced spasms, which gradually decreased and resolved entirely 4 months after the operation.

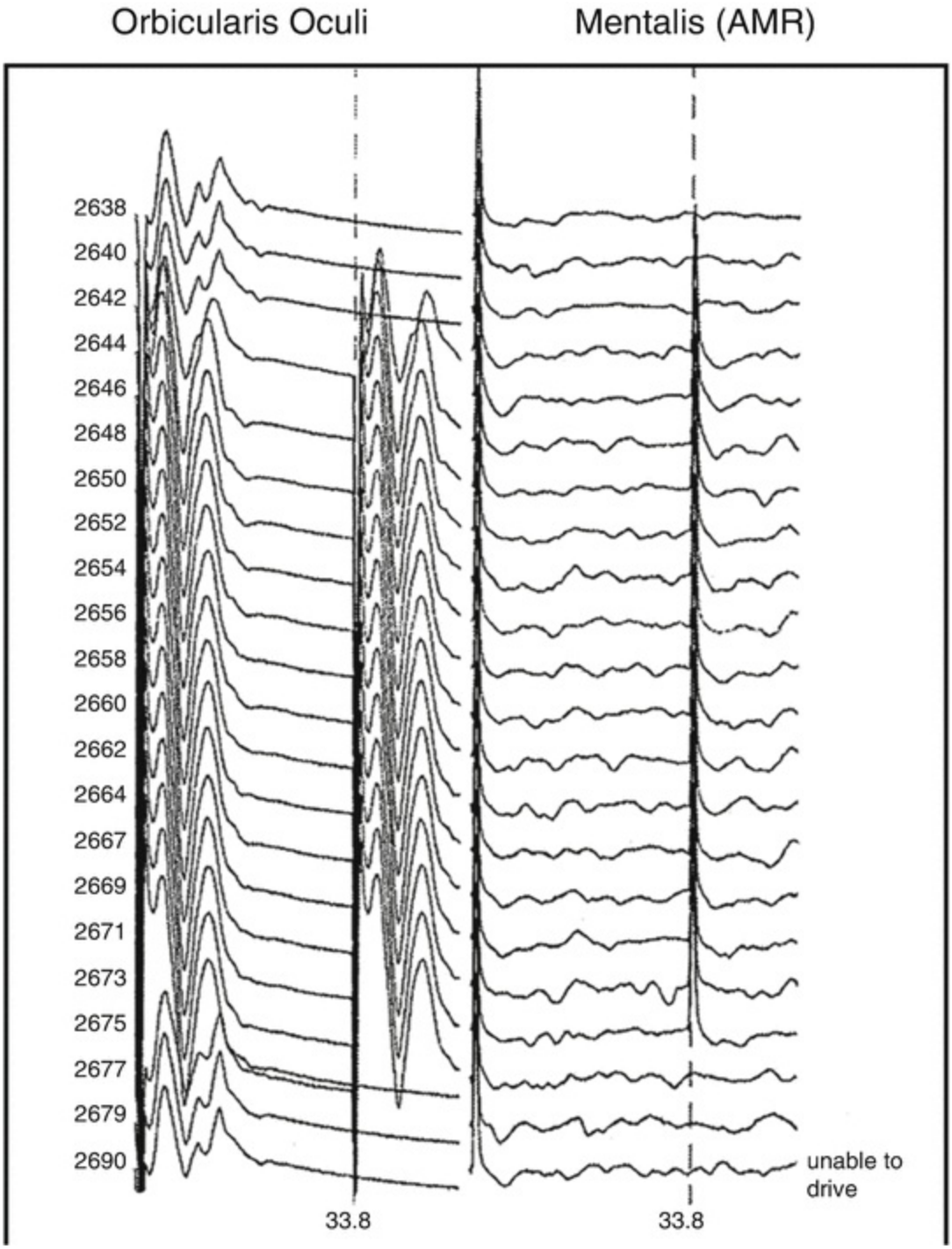

Fig. 26.4 Disappearance of the AMR with successful microvascular decompression of the facial nerve (*Y*-axis represents time in seconds following MVD of facial nerve). The compound action potential is being recorded at the mentalis muscle while the facial nerve branch to the orbicularis oculi is stimulated

Team notes: Even after appropriate decompression of the facial nerve, as many as half of the patients have persistent spasms, which resolve over the course of a few weeks to 23 months [35]. Since the AMR often disappears when the offending vessel is lifted off of the facial nerve in a microvascular decompression procedure, its use has been suggested as an intraoperative guide to success [18, 40–43]. Because HFS disappears or gradually resolves over time in many patients in whom the AMR persists intraoperatively, many authors have questioned the utility of intraoperative EMG [44–47]. In a large study evaluating 300 patients, Kong et al. [43] found a statistical difference at 1-year follow-up in the outcomes between two groups based on whether the AMR resolved or persisted [43]. Their report is the only one to show a statistically different outcome in cases where the AMR did not resolve. A meta-analysis by Sekula et al. [35] of the data concerning the relationship between resolution or persistence of the AMR after MVD and the resolution or persistence of HFS showed that the chance of a cure if the AMR was abolished after MVD was 4.2 times greater than when the AMR persisted. Thirumala et al. [48], reporting on 259 patients undergoing MVD with intraoperative monitoring of the lateral spread response (LSR), found that abolishment of the LSR during surgery was associated with statistically significant rates of spasm relief immediately postoperatively and at discharge. This increased rate of spasm relief was not observed at later follow-up between the two groups [48]. Furthermore, reoperation for persistent symptoms and botulinum toxin treatments prior to surgery does not affect rates of intraoperative abolishment of the LSR [49, 50]. Based on these results, we support that AMR should be monitored routinely in the operating room, and surgical decision-making in the operating room should be guided by the absence or presence of the AMR.

Case 2: “Frozen Shoulder” or Adhesive Capsulitis of the Glenohumeral Joint after MVD in the Contralateral Decubitus Position

A 52-year-old woman with right-sided HFS underwent an MVD after serial botulinum toxin injections resulted in unsatisfactory results. During the

operation, the PICA was noted to be tightly compressing the right facial nerve. During decompression of the PICA, the AMR resolved and could not be elicited. No change in SSEPs was noted. The patient awoke without spasms but complained of pain, stiffness, and limited range of movement of her *left* shoulder.

The surgeon recommended observation and increasing use of the left shoulder for the first 6 weeks following the operation. During those 6 weeks, the patient's shoulder pain increased to the point that she did not use the left shoulder and upper extremity and required assistance with dressing. The surgeon referred the patient for physical therapy, which was ineffective. The patient was then referred to an orthopedic surgeon who diagnosed her with a "frozen shoulder " or adhesive capsulitis of the glenohumeral joint. MRI of the left shoulder confirmed adhesive capsulitis. The surgeon performed "manipulation" of the left shoulder under a general anesthetic in the operating room, and the patient awoke with reduced pain and improved range of motion. Over the next few weeks, the pain resolved entirely and range of motion was restored.

Team notes: The pathophysiology of adhesive capsulitis is elusive. Although this complication is rare with the contralateral decubitus position, it should be considered in the differential diagnosis of those patients complaining of pain and reduced range of motion of either shoulder. Additionally, extreme care should be taken when retracting the nondependent shoulder inferiorly due to the potential for stretching of the brachial plexus. This is true when shoulders are taped and pulled away from the operative field (see Fig. 26.2) whether in the supine (such as in an anterior cervical discectomy and fusion), prone (such as in a suboccipital decompression), or in lateral position, as in this case, a retromastoid approach for microvascular decompression .

Case 3: Inability to Access Brainstem Due to Intravenous Fluid Overload

A 35-year-old man with right-sided HFS was taken to the operating room for an MVD . After a retromastoid craniectomy was achieved, the dura was opened. The surgeon noted that the brain immediately "herniated through the dural opening." After a dose of mannitol and 20 min of head elevation, the brain relaxed to the point that the dura could be closed. MVD was aborted,

and the operation was rescheduled.

Team notes: Accessing the brainstem and cranial nerves requires communication between the surgeon and the anesthesia providers. Particularly in younger patients, the brain can be “full,” making the brainstem difficult to access. When possible, intravenous fluids should be limited prior to dural opening. In general, most patients receive a total of about 1 L of crystalloid or less for the entire perioperative period.

Case 4: Technical Difficulties with the Inserted Earpiece for Acquiring ABRs

A 57-year-old woman with left-sided HFS underwent an MVD after serial botulinum toxin injections resulted in unsatisfactory results. During drilling of the retromastoid craniectomy, the neuromonitoring technician became concerned because of reduced amplitude and prolonged latency of the left ABR . After confirmation that the patient was hemodynamically stable, the neuromonitoring technician checked the left earpiece and noted that the earpiece had become dislodged. The earpiece was adjusted and the ABR returned to baseline.

Team notes: Kinking of the ear insert tubing occurs infrequently and can be minimized by making sure the tubing is run away from the operative field. When the ABRs change without good reason, the insert and tubing should always be checked for proper delivery of the click stimulus (Fig. 26.5).

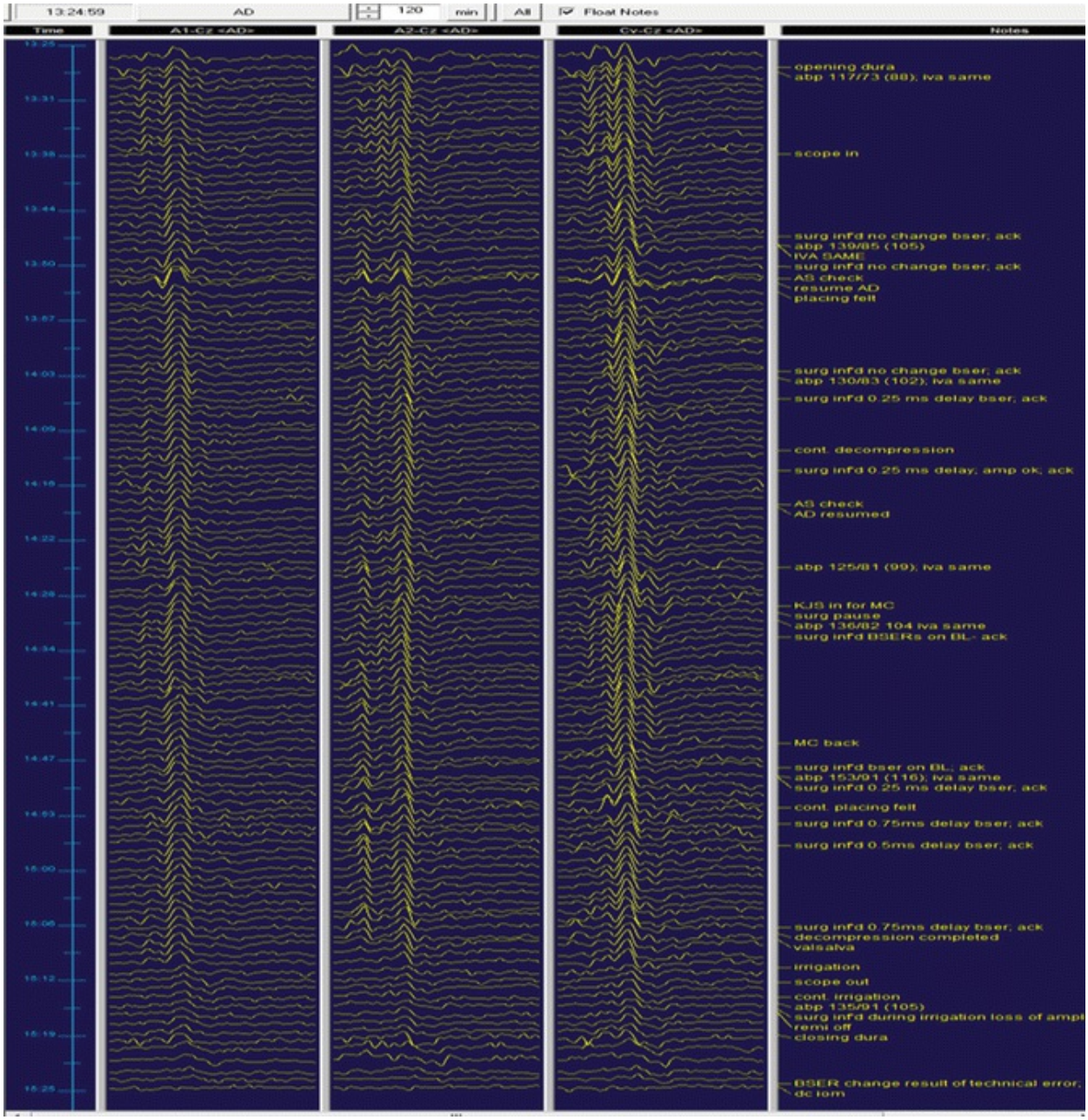

Fig. 26.5 Tracings of the ABRs depict dislodged insert earpiece

Case 5: Hearing Loss as a Result of MVD for HFS

A 67-year-old woman with right-sided HFS underwent an MVD after serial botulinum toxin injections resulted in permanent facial weakness (House-Brackmann grade II/VI) [51]. After dural opening, a brain retractor was used to elevate the cerebellum away from the brainstem for exposure of the facial nerve. During this maneuver, the neuromonitoring technician advised the

surgeon that waves III and V of the right ABRs had increased in latency by 0.8 ms. Within a few minutes, the neuromonitoring technician advised that the amplitude of the ABRs had decreased by 50 %.

After notification of a reduction in amplitude of the ABRs, the surgeon removed the retractor and stopped dissection. The anesthesiologist increased the mean arterial blood pressure 10 mmHg to a MAP of 80 mmHg. Within 2 min, the latency improved and the amplitude increased. Within 5 min, the ABRs had returned to baseline, and the surgeon resumed exposure of the facial nerve.

Team notes: Hearing loss remains a significant risk with MVD of the facial nerve for HFS, with partial hearing loss ranging from 0.5 to 9.5 % and complete hearing loss ranging from 0.7 to 7.6 % [2, 33, 52, 53]. Polo et al. [53] have provided data concerning a stepwise reduction in hearing with progressive latency increases of Peak V of the ABR during microvascular decompression. In their study of 84 consecutive patients undergoing MVD for HFS, they report that in the group with more than a 20-dB loss in pure tone audiogram, delays in the latency of Peak V were on average 1 ms. To this end, a recent study by our group showed that intraoperative loss of wave V resulted in significantly increased odds of hearing loss [38]. Recently, our group attempted to address this with avoidance of a fixed, self-retained cerebellar retractor in favor of dynamic retraction and subsequently demonstrated a reduction in ipsilateral high-frequency hearing loss (HFHL) from 50 to 7.4 % [36].

Case 6: Anesthesia and the AMR

A 54-year-old woman with a 10-year history of right-sided HFS is brought to the operating room for MVD of the facial nerve. After positioning the patient in the contralateral decubitus position, the neuromonitoring technician reports an inability to obtain an AMR of the right facial nerve.

After confirming that the AMR was documented in the Cranial Nerve and Brainstem Disorders Clinic, discussion among the team revealed that a nondepolarizing muscle relaxant had been given during induction for intubation. The team waited 30 min before beginning the procedure, allowing the agent to wear off.

Team notes: Although the evidence is anecdotal, we believe that there is no role for the use of nondepolarizing muscle relaxants in cases involving microvascular decompression for HFS. It has been our experience that a

small defasciculating dose of a nondepolarizing muscle relaxant used during the intubation period is enough to obscure the detection of the abnormal spread at the start of the case. The return of the AMR after the use of a nondepolarizing agent becomes unpredictable.

Case 7: Stroke During MVD for HFS

A 35-year-old woman with right-sided HFS underwent MVD of the right facial nerve. After exposing the facial nerve, the anterior inferior cerebellar arteries as well as multiple perforators of that vessel were noted to be tightly compressing the facial nerve. A preoperative MRI had revealed right-sided dolichoectasia of the vertebrobasilar system with clear compression of the right facial nerve. During the operation, the AICA with perforators and the vertebral artery were decompressed without incident. The AMR was abolished. SSEPs were not measured during the procedure.

Upon awakening, the patient was free of spasms, but, within an hour, she noted contralateral trunk and extremity hypalgesia and thermoanesthesia, ipsilateral Horner syndrome, ipsilateral hypohidrosis, and gait ataxia consistent with a Wallenberg syndrome [54, 55]. Stroke involving the PICA, vertebral artery, or their respective perforators was suspected [56], and a postoperative MRI of the brain confirmed a small infarct involving the lower lateral medulla and posterior cervical spinal cord. Because intraoperative videos did not indicate an avulsion of a perforator or major vessel during decompression of the vertebral and posterior inferior cerebellar arteries (including a complicated tangle of arterioles compressing the facial nerve likely representing PICA medullary perforators), occult compression or vasospasm of perforators was suspected. Although some authors have suggested the use of papaverine to prevent vasospasm-related ischemia [44], we do not routinely use papaverine during MVD due to concerns of vestibulocochlear toxicity [57]. The patient was discharged from acute rehabilitation on postoperative day 13 with improved and independent ambulation. At 10.3-month follow-up, ipsilateral hypohidrosis and gait ataxia had improved significantly with moderate improvement of contralateral extremity thermoanesthesia. The patient notes some incoordination with jogging and persistent difficulty with high humidity due to hypohidrosis.

Team notes: Because of the low incidence of stroke with MVD of the facial nerve (i.e., <0.2 %), we have not utilized SSEPs for MVD for any cranial neuralgia in recent years. It is likely, however, that a change in the

SSEPs would be noted, at least in a delayed fashion, in the event of an ischemic event involving the brainstem. If so, application of papaverine to the affected blood arterial vessels (see above explanation), repositioning of Teflon pledgets, and increasing the mean arterial blood pressure (particularly with hypertonic saline) may have been valuable in this patient.

Case 8: Facial Weakness and MVD for HFS

A 42-year-old man with right-sided HFS underwent MVD of the facial nerve at another institution. Although the operative record noted a significant latency increase of the ABR, specific details were not provided. The patient awoke with persistent spasms and a deaf right ear. Because as many as half of patients awake from MVD for HFS with persistent but reduced spasms and proceed to a spasm-free state over the course of a few weeks to as long as 24 months, the patient was observed by the surgeon for 1 year. At 1 year, the patient was referred to our center with no improvement in spasms.

A repeat MVD was offered. During the MVD, a vein tightly compressing the facial nerve was noted. Prior to and after coagulation of the vein with low-power bipolar cautery, the facial nerve was stimulated at 0.2 mA. Prior to coagulation, the nerve responded robustly. After coagulation, the nerve did not respond at 0.2 mA but did respond at 0.5 mA. The patient awoke with weakness (House-Brackmann, Grade V/VI), which improved completely within 9 months [51].

Team notes: Facial weakness following MVD of the facial nerve for HFS may occur immediately or be delayed. Facial weakness detected immediately following MVD indicates dysfunction occurring at operation (e.g., mechanical dislocation/pressure, thermal trauma or ischemic injury by vascular occlusion, vascular compression, or vasospasm) whereas facial weakness, which develops in a delayed manner, is less well understood. The incidence of delayed facial palsy has been reported to be between 2.8 and 8.3 % [3, 58–60]. Although the phenomenon of delayed facial weakness following MVD for HFS is well known, no explanation is entirely satisfactory, and the evidence is incomplete. Some have suggested reactivation of a dormant virus or delayed facial nerve edema [61, 62]. Fortunately, resolution of delayed facial weakness following MVD for HFS is almost uniformly complete [58–61]. The prognosis of immediate facial weakness is less auspicious. In their series of 1524 operations, Huh et al. [52] reported that 11.4 and 1 % of patients undergoing MVD for HFS developed

immediate transient and permanent facial weakness, respectively. It should also be noted that many patients who present for surgical evaluation of HFS have peripheral weakness caused by botulinum toxin injections, and many others (those with tonus phenomenon, in particular) have mild to peripheral weakness.

Over the years, we have learned that the removal of veins near the facial nerve is better achieved with purposeful avulsion using a microhook rather than bipolar electrocautery. Facial nerve EMG can be used to thoroughly identify the centrally myelinated portion of the facial nerve before and after decompression of arteries or removal of veins in selected cases. In our experience, an intact facial nerve will respond at 0.2 mA.

Case 9: Vestibular Nerve Dysfunction (After MVD for HFS)

A 68-year-old woman underwent MVD for HFS. During the MVD, dissection rostral to the superior vestibular portion of the vestibulocochlear nerve was required. During exposure of the rostral portion of the facial nerve, the latency of the ABR increased by 1.2 ms. After the decompression, the ABR slowly returned to baseline over 10 min. Upon awakening, the patient was free of spasms with preserved hearing, but complained of vertigo and disequilibrium requiring assistance with ambulation. The patient's condition improved slowly over a few months.

Team notes: Data regarding vestibular nerve dysfunction following MVD for HFS are scarce. Because the centrally myelinated portion of the facial nerve lies in proximity to the vestibulocochlear nerve, complete decompression of the facial nerve may result in transient or permanent injury to the vestibular portion of the vestibulocochlear nerve. Samii et al. [2] reported transient and permanent vestibular nerve dysfunction following MVD of the facial nerve for HFS in 9.6 and 2.7 % of patients, respectively, and the authors hypothesized that the dysfunction "was probably attributable to direct mechanical trauma or temporary reduction of the blood supply to the vestibular nerves" [2]. Our own group reports 2.7 % occurrence of transient vestibular dysfunction in the elderly with no permanent symptoms and 3.7 and 1.9 % occurrence of transient and permanent vestibular dysfunction in non-elderly patients, respectively [3]. Because the vestibulocochlear nerve is intimately associated with the facial nerve at the brainstem, vestibular nerve

dysfunction can occur particularly with HFS where rostral compression is the norm [63, 64]. In our experience, risk of vestibular nerve dysfunction following MVD for HFS is increased when decompression is rostral to the facial nerve, adjacent to the vestibular portion of the vestibulocochlear nerve, and dissection of adhesions about the vestibulocochlear nerve in reoperations is required. The ABR can be used as an indirect guide to potential injury of the vestibular portion of the vestibulocochlear nerve. When the latency of the ABR increases (particularly beyond 0.5 ms), the team should consider potential causes such as excessive retraction, systemic hypotension, compression of the cochlear portion of the vestibulocochlear nerve by Teflon, and others. As of note, in the past 5 years, our surgeon (RS) has abandoned decompression rostral to the vestibulocochlear nerve with no diminution in positive outcome.

Case 10: Dysphagia/Hoarseness Following MVD for HFS

An 82-year-old woman with right-sided HFS underwent MVD of the facial nerve. During the operation, a dolichoectatic vertebrobasilar system had shifted into the lower cranial nerves including the facial, vestibulocochlear, glossopharyngeal, and vagus nerves. After decompression of the vertebrobasilar system away from the lower cranial nerves, the patient awoke spasm free but with obvious hoarseness and inability to swallow on the right side. Physical examination showed left uvular deviation and minimal movement of the left side of the pharynx. Flexible laryngoscopy revealed good mobility of the vocal cords. After a few days of intravenous fluids and oral restriction, the patient's swallowing improved to the point that she could safely resume oral intake.

Team notes: Infrequently, patients awaken with hoarseness and/or dysphagia after MVD of the facial nerve due to manipulation and/or stretching of the glossopharyngeal and vagus nerves. Neurogenic dysphagia can involve dysfunction of any of the three phases of deglutition [65]. In the past, we have noticed that some patients, particularly elderly patients, experience significant transient dysphagia and/or hoarseness following microvascular decompression of the facial nerve. Because the facial nerve lies in proximity to the glossopharyngeal and vagus nerves, complete decompression of the facial nerve may result in transient or permanent injury

to those nerves.

A study previously published by our group of 131 HFS patients undergoing MVD showed that 14.8 % of elderly patients experienced transient dysphagia and/or hoarseness with no patients experiencing permanent symptoms. No elderly patients required a feeding tube or medialization of the vocal cords; 2.9 and 1.9 % of young patients experienced transient and permanent dysphagia and/or hoarseness, respectively. One young patient required medialization of a vocal cord. Resolution of transient dysphagia and/or hoarseness may be protracted, and in this series of patients, resolution of transient dysphagia and/or hoarseness ranged from 1 to 10 months in the elderly cohort and 2 weeks to 6 months in the young cohort [3].

Questions

1. Which theory describing the etiology of HFS best explains the phenomena of an intact blink reflex in the anesthetized HFS patient ipsilateral to disease?

   A. Ephaptic transmission at the site of vascular contact

   B. Hyperactivity of the facial nerve nucleus

   C. Axono-axonal ephapsis in the periorbital region

   D. Abnormal excitation of the ventral posterolateral nucleus of the thalamus

2. What imaging modality is best to delineate cranial nerves and adjacent vasculature?

   A. Diffusion weighted imaging with high-resolution fiber tracking

   B. Thin-slice steady-state free precession MRI

   C. 18F-FDG positron emission tomography

D. Fast fluid-attenuated inversion recovery MRI

3. Which of the following would not account for absence/loss of AMR?

   A. Dislodgment of bipolar electrodes from orbicularis oculi and mentalis muscles

   B. Application of nondepolarizing agent during intubation

   C. Overstimulation of facial muscles prior to access to the cerebellar pontine angle

   D. Kinking of the ear insert tubing

4. Which of the following cranial nerve deficits is the least probable complication of MVD for HFS resulting from indirect manipulation?

   A. Dysphagia/hoarseness

   B. Loss of high-frequency hearing

   C. Ipsilateral facial pain/numbness

   D. Loss of pupillary reflexes

Answers

1. B. Explanation: Anesthesia suppresses the blink reflex in nondysfunctioning facial nerves. The ability to elicit a blink reflex in HFS patients is best explained by hyperactivity of the facial nerve

nucleus.

2. B. Explanation: SSFP MRI are heavily T2 weighted, resulting in contrast between CSF and adjacent nerves and vasculature.

3. D. Explanation: The ear insert is used for auditory brainstem response audiometry and not for monitoring of the abnormal motor response.

4. D. Explanation: The fifth, eighth, ninth, and tenth cranial nerves are in close proximity to the seventh cranial nerve and are often visualized during MVD. Loss of pupillary reflexes is unlikely to occur from indirect manipulation but may be a sign of posterior fossa edema/hemorrhage requiring immediate surgical intervention.

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Footnotes

1 Asterisk indicates key references.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_27

27. Skull Base Surgery

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Keywords Skull-based tumor – Intraoperative neuromonitoring – Posterior fossa – Somatosensory-evoked potentials – Motor-evoked potentials – Brainstem auditory-evoked potentials

Key Learning Points

- Due to the complex nature of skull base procedures involving limited surgical exposure and the proximity of vital neurological and vascular structures, utilization of IOM can facilitate surgical progress, reduce recovery times, and help prevent unwanted morbidity.
- Multiple modalities of IOM, such as EMG, evoked potentials, and EEG may be used for surgery of the skull base to help identify neuroanatomical structures and also to detect potential trauma due to

mechanical, thermal, or ischemic insults.

- Positioning requirements for skull base surgery may put the patient at risk for peripheral nerve injuries that may be detected and potentially prevented through the use of IOM.
- Proper interpretation and evaluation of IOM recordings and their changes are imperative to benefit both the patient and the practitioner.

Introduction

Over the past several decades, advancements in many areas of clinical medicine have facilitated the progress and application of surgical intervention for lesion of the skull base. The skull base is composed of the ethmoid, sphenoid, occipital, frontal, and parietal bones, as well as the petrous portion of the temporal bone. Traditionally, this anatomical area has been divided into three compartments: the anterior, middle, and posterior cranial fossae. Located or coursing through this area are a number of vital structures including the pituitary gland, cranial nerves, cavernous sinuses, and the internal carotid arteries. Lesions of the skull base lesion can be defined as those invading a skull base bone or one whose location requires resection of a skull base bone for surgical exposure. Surgical intervention must take into consideration potential damage to the cranial nerves and vascular structures . Improvements in surgical techniques, the development of precision tumor removal instruments, and the advent of modern neuroimaging such as magnetic resonance imaging (MRI) now permit more frequent consideration of invasive treatment and palliative intervention for lesions of the skull base that were previously considered either inoperable or associated with unfavorable morbidity. In conjunction with the increased popularity and complexity of skull base surgery, the utilization of neuromonitoring modalities during these invasive procedures has proven to be of benefit to both the practitioner and the patient. Intraoperative neuromonitoring (IOM) provides the surgeon with a tool to identify and map neuroanatomical structures, assist in the early detection of trauma during the procedures, and predict neurological preservation at the end of the procedure. Additionally, IOM benefits the patient with shorter surgical times, a more precise and complete lesion removal, and an improved chance at avoiding neurological morbidity.

Perioperative Considerations

In addition to the routine concerns of providing anesthesia for patients undergoing operative procedures, skull base surgery presents some unique considerations for the anesthesiologist. These include variations in patient positioning, the possibility of venous air embolism, significant blood loss, and prolonged operative times. Positioning patients for skull base surgery may involve a range of possibilities depending on the surgical considerations and the planned operative approach. In addition to being placed in the supine position, skull base surgery may require the patient to be placed in a sitting or park bench position. These positions are associated with an increased risk of venous air embolism due to the operative site being elevated above the level of the heart. The risk of venous air embolism may also be increased in this patient population since many patients with intracranial tumors are hypovolemic, resulting in a decreased central venous pressure that increases the risk for venous air entrapment. Additionally, skull base surgery can involve resection of the jugular vein and cavernous sinus, which often is performed with the operative site elevated above the level of the heart. Due to the complexity of these operations, their positioning requirements, and their prolonged duration, peripheral nerve injuries may occur even with meticulous attention to details of proper positioning and padding. Significant blood loss also needs to be anticipated during skull base surgery. Preoperative assessment of the lesions location, size, and presumed histological type can help determine the potential for significant intraoperative hemorrhage. For example, meningiomas and glomus tumors are highly vascular lesions frequently located in the skull base associated with significant blood loss during resection. Additionally, lesions involving the cavernous sinus or associated blood vessels are also likely to be associated with substantial blood loss. In select cases, preoperative embolization of the lesion can significantly decrease intraoperative blood loss. The role of controlled hypotension during these surgical procedures needs to be balanced with the risks of potentially ischemic conditions.

Goals of IOM During Skull Base Surgery

The use of IOM during skull base surgery may help reduce the risk of significant neurological sequela that has burdened this type of surgery in the

past. Historically, limiting surgical exposure with the goal of preservation of adjacent vital neural and vascular structures often impeded surgical progress and was associated with prolonged surgical times. IOM reduces incision length and allows a smaller craniotomy to be made by providing the surgeon a means by which identification of anatomical structures is permitted through a smaller exposure area. This, in turn, reduces trauma to the surrounding tissue decreasing morbidity and reducing recovery time. The surgeon can rely on IOM to detect, in real-time, trauma to the adjacent tissue from mechanical forces such as retraction or electrocautery. IOM may facilitate the identification of neuroanatomical structures under conditions where the neural structures are grossly misplaced and hinders the progress of lesion extirpation. Furthermore, IMO may also aid the surgeon when morphological changes to the neural tissue due to local inflammation or lesion invasion make identification of such structures difficult. Finally, the preservation of neurological function may be tested in an anesthetized patient undergoing skull base surgery at a time when clinical examination is otherwise impossible. This allows the surgeon to alter the surgical technique or approach with the goal of minimizing or reversing damage to the monitored structures.

Modes of Neuromonitoring

Lesions of the skull base arise from a heterogeneous mixture of histological structures such as bone (osteochordoma, osteosarcoma), vascular structures (hemangioma), neural tissue (schwannoma, neurofibroma, meningioma), and skin (epidermal cyst). Due to the confinements of the skull base, extirpation of these lesions is often technically challenging. As a result, several types of IOM may be utilized to assist the surgical intervention. The use of IOM and the type of modality employed are dictated not only by the location of the lesion and involved tissue, but also by the structures at risk during the procedure. Furthermore, the concomitant use of multiple modalities during the procedure allows more sensitive detection of the pathophysiological process of concern.

Electromyography

Commonly, electromyography (EMG) is employed to identify and help

detect injury to cranial nerves via measurement of the electrical activity of innervated muscle. At baseline, muscle activity in an anesthetized patient is relatively silent and the detection of muscle activity permits the surgeon rapid feedback of direct stimulation or mechanical manipulation such as stretching or thermal injury to the corresponding nerve [1–3]. Due to the location of lesions around the brainstem, skull base surgery typically necessitates the direct or indirect EMG monitoring of the lower cranial nerves. Selection of which cranial nerves to monitor by EMG is determined by the relationship of the nerve to the lesion and also by the clinical significance that damage to the nerve may cause to the patient. Surgery involving structures in the middle fossa such as the orbits or cavernous sinus poses risk to cranial nerves II, IV, and VI, all of which may be monitored with EMG recordings of the extra-ocular muscles. Lesions of the posterior fossa such as cerebellar pontine angle (CPA) tumors or acoustic neuromas require EMG of the lower cranial nerves (V, VII–XII). However, consideration is also given to the clinical significance that an injury to a given nerve will have on a patient. For instance, while injury to cranial nerves V, VII, and X may lead to significant morbidity in the patient, injury to cranial nerve IX (glossopharyngeal) has little clinical significance to most patients and therefore EMG monitoring of this cranial nerve is less common.

EMG monitoring of the facial nerve (VII) is probably the most documented of all the cranial nerves given the morbidity associated with injury and the common involvement of the facial nerve with acoustic neuromas. Intraoperative EMG monitoring of the facial nerve may help in the preservation of facial nerve function and can be used to prognosticate facial nerve postoperative function [1, 4–7]. These findings are likely related to using EMG to identify the facial nerve as well as for the detection of pathophysiological changes during tumor exploration and resection. Therefore, use of EMG monitoring of the facial nerve during CPA tumor resection remains a common entity by itself, or in a multimodal capacity with evoked potentials [8]. The glossopharyngeal nerve (IX) innervates only one muscle, the stylopharyngeus, which is not readily accessible for direct EMG monitoring. When monitoring is desired, neural stimulation of the glossopharyngeal nerve can be detected by electrode placement into the ipsilateral soft palate, which then detects activity of the stylopharyngeus muscle by proxy. Concomitant monitoring of the vagal nerve (X) is also required with this technique to differentiate activity between the two nerves.

Dysfunction of the vagal nerve can lead to significant hoarseness and dysphagia. Therefore, EMG monitoring of cranial nerve X is frequently performed during skull base surgery involving lesions located near the jugular foramen. Electrode placement directly into the vocalis muscle requiring direct laryngoscopy can often be avoided with the use of modified endotracheal tubes with surface electrodes positioned at the level of the vocal folds. While less invasive, the surface electrode technique is more susceptible to positional changes and poor electrode contact. IOM of the accessory nerve (XI) is frequently performed due to the relative ease of reliable recording in the trapezius muscle and due to the fact that elicited muscle activity of the accessory nerve often indicates that nearby cranial nerves are also at risk.

Evoked Potentials (SSEP , MEP, VEP, ABR)

In order to monitor neural structures that do not have significant motor innervations, or whose motor innervations would be difficult to monitor via EMG, other IOM modalities are needed during skull base surgery. Evoked potentials such as somatosensory-evoked potentials (SSEP) and motor-evoked potentials (MEP) are modalities used to assess various functional changes due to the compromise of neural structures as well as vascular structures [9, 10]. For instance, potential ischemic insults may be detected with a loss or change of evoked potential recordings of electrodes placed over the corresponding motor or sensory cortex. Additionally, SSEP changes may be seen during concussive (hammering) injury or compression of the surrounding neural tissue. Another modality, brainstem auditory-evoked potentials (ABRs), is used to detect potential injury to the auditory nerve ipsilateral to the lesion as well as potential injury to the brainstem when bilateral pathways are monitored [11]. While IOM with ABR has been shown to reduce postoperative morbidity in posterior fossa surgery [12], ABR may also be utilized to assess the efficacy of surgery such as during microvascular decompression of the facial nerve. Finally, reversible ischemic injury during skull base surgery may be monitored by electroencephalogram (EEG) that can detect changes in the metabolic rate of the cerebral cortex.

While IOM for skull base surgery has become invaluable, limitations of its use should be considered. Most of these limitations are not unique to skull base surgery and should be assessed in any surgery in which IOM is employed. First, the use of IOM techniques comes with an added cost of the

hardware used as well as the technical supervision required for reliable application and interpretation. Second, many modalities of IOM are sensitive to inhalational and intravenous anesthetic agents that may decrease the sensitivity and specificity of the recordings [13]. Third, the clinical significance of IOM recordings is often debated among practitioners.

Case 1

A 42-year-old woman with well-controlled hypertension and anxiety/depression who presented with headaches, vertigo, and tinnitus was diagnosed with left-sided hemangioblastoma in the cerebellar pontine angle and scheduled to undergo surgical resection with a lateral suboccipital approach. Her preoperative assessment revealed a normal neurological examination without cranial nerve deficits. The patient was anesthetized with boluses of lidocaine, propofol, rocuronium, and fentanyl, after which an endotracheal tube was placed. Anesthesia maintenance was provided by intravenous infusions of propofol, lidocaine, and remifentanil. A right radial arterial line was placed and a urinary catheter incorporating a temperature probe was inserted. IOM was then established with EMG recordings of cranial nerves VII, X, and XII. Additionally, bilateral ABR and four-limb SSEPs were established. The patient was placed in right lateral position and her head secured in Mayfield pins. A warm-air temperature regulation blanket was placed on the patient. After the surgical site was prepped and draped, baseline recordings of EMG, SSEP, and ABR were normal. After incision and craniotomy, retractors were placed and resection of the lesion progressed. After 10 min, retraction was increased and a shift in latency of the ipsilateral ABR waveform of about 0.4 ms was observed (Fig. 27.1). Low-grade facial nerve EMG firing was also noted. There were no deviations from baseline in SSEPs.

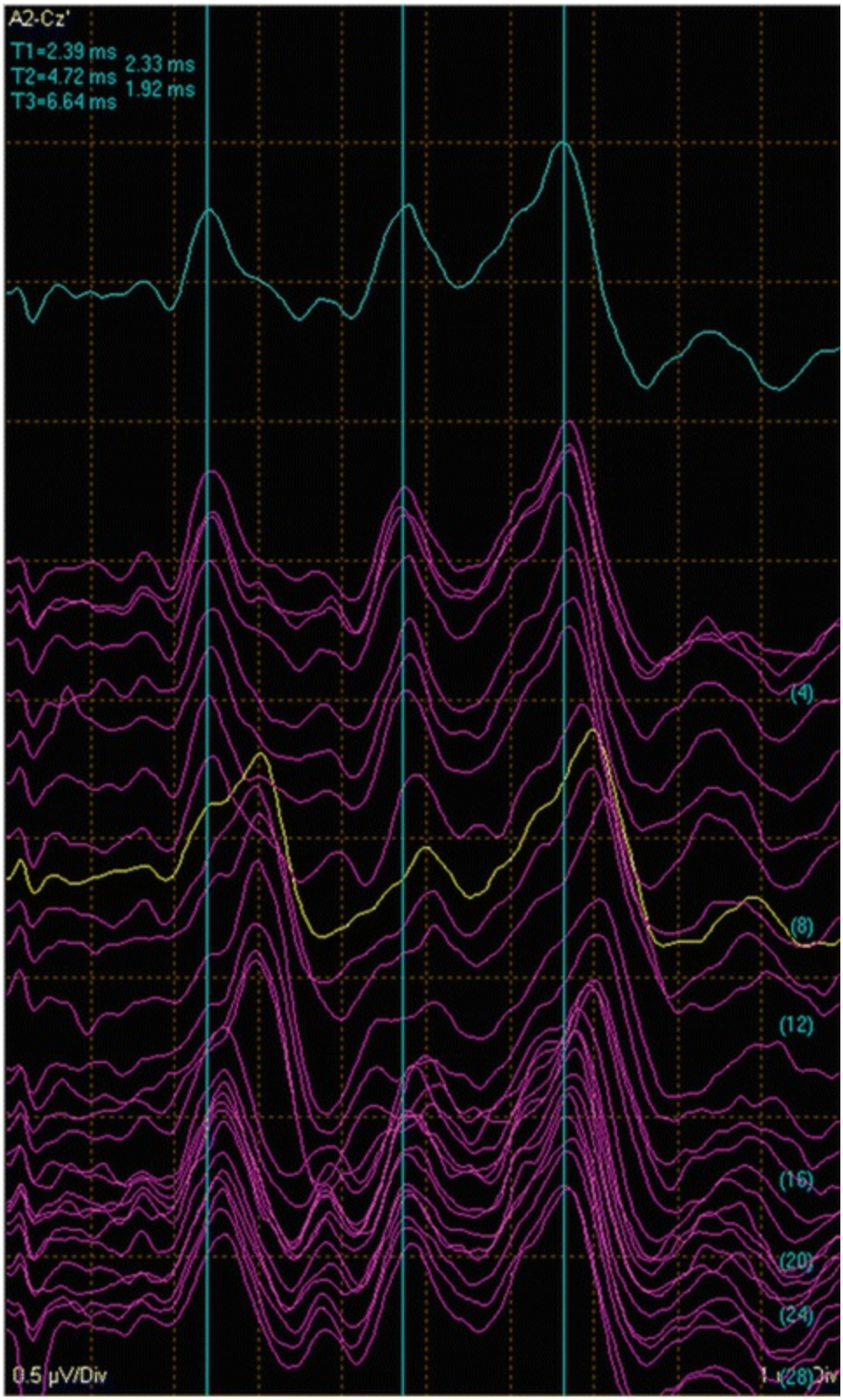

Fig. 27.1 ABR responses with changes due to retractor effect

Differential Diagnosis of ABR Findings

Several nonphysiological processes may contribute to changes in ABRs during IOM [14]. Inherent to any IOM, ABRs are susceptible to mechanical failure and operative errors such as malfunctioning equipment, accidental removal of the stimulating earpiece, or an obstruction in the tubing connected to the earpiece. These conditions may artificially produce increases in latency, decreases in amplitude, or even an entire loss of signal recordings. Other possible nonphysiological processes that can affect ABR signal recording include artifact created by electrocautery or ultrasonic aspirating devices. In the present case, all the data collection and recording equipment was inspected and determined to be working properly. The use of electrocautery was infrequent and no cavitational ultrasonic surgical aspirator devices were being utilized. We therefore determined that changes in ABR recordings were not caused by a nonphysiological etiology.

Short-latency ABR recordings are relatively resistant to the effects of intravenous and volatile anesthetic agents even at levels of anesthesia that attenuate or abolish other forms of IOM (EEG, SSEP, etc.). However, ABRs become more susceptible to anesthetic agent levels when the patient is hypothermic or hypotensive. While reversible prolongation of peak latencies have been observed in patients undergoing induced hypothermia during cardiac procedures [15], unintended mild hypothermia during a prolonged surgical case or even localized hypothermia due to room temperature irrigation baths may produce some degree of latency change in ABR wave peaks. In our case, the patient's core temperature had not changed and only warm saline was used as irrigation for the operative site. Therefore, it was unlikely that the changes in ABR latency observed in our patient were due to hypothermia. Invasive blood pressure monitoring ruled out any contribution of hypotension to the ABR changes as the patient's mean arterial pressure was not significantly lower than baseline measures. In examination of the changes seen in Fig. 27.1, the waveforms in the figure are clearly present and few, if any, changes are seen in the amplitude of the evoked responses. However, a gradual increase in latencies is seen in all wave peaks and between peaks. This observation would argue against the direct mechanical manipulation or dissection of the auditory nerve since such an injury would elicit an abrupt change in the ABR waveform and, when severe, is often accompanied by loss of wave peaks. Additionally, ischemia to the cochlea via damage to the anterior inferior cerebellar artery or the internal auditory artery

would also cause an abrupt change to the responses and potential loss of wave peaks. Alternatively, stretch or excessive retraction of the auditory nerve would cause a gradual increase in wave latencies consistent with the finding in our case. Finally, ischemia or injury to the brainstem may also cause changes in ABR recording, and often these changes are bilateral. However, ABRs may not show any changes during ongoing brainstem or cerebral ischemia if there is sparing of the auditory region. In our case, the lack of baseline changes in concomitant SSEP and EEG recordings indicated that a more pronounced ischemic event was not occurring.

Case Progression

The surgeon was notified that the ABR changes were most consistent with stretch or retraction of the acoustic nerve. At that point, the surgeon temporarily removed the retractors and then reapplied the retraction intermittently throughout the remainder of the case. As seen in Fig. 27.1, the latency of the ABRs improved and approached baseline measurements by the end of the case. Additionally, EMG activity of the facial nerve gradually resolved. The patient was extubated in the operating room and transported to the neurosurgical intensive care unit. Postoperative evaluation revealed no new neurological deficits.

Case 2

A 67-year-old man with coronary artery disease, diabetes, and hypothyroidism presented with diplopia and was diagnosed with a right-sided sphenoid wing meningioma . He was scheduled for a frontal temporal craniotomy after undergoing preoperative embolization of the tumor a day prior to surgery. Preoperative examination revealed a normal neurological evaluation except for mild diplopia with lateral gaze. The patient was anesthetized with induction boluses of lidocaine, propofol, rocuronium, and fentanyl. The patient was intubated and maintenance of anesthesia was provided by intravenous infusions of propofol, lidocaine, and remifentanil. Additional monitoring included left radial arterial line and a urinary catheter with temperature probe. IOM was established with EMG recordings of cranial nerves III, IV, VI, and VII along with four-limb SSEP. The patient was placed in supine position with slight rotation of the torso. His head was

secured with Mayfield pins. A warm-air temperature regulation blanket was placed on the patient. After the surgical area was prepped and draped, baseline EMG and SSEP recordings were normal. The craniotomy proceeded uneventfully with nominal blood loss. As the tumor was being resected, a marked decline in amplitude of the right upper extremity SSEP recordings was noted. Cranial nerve recordings were unchanged from baseline (Fig. 27.2).

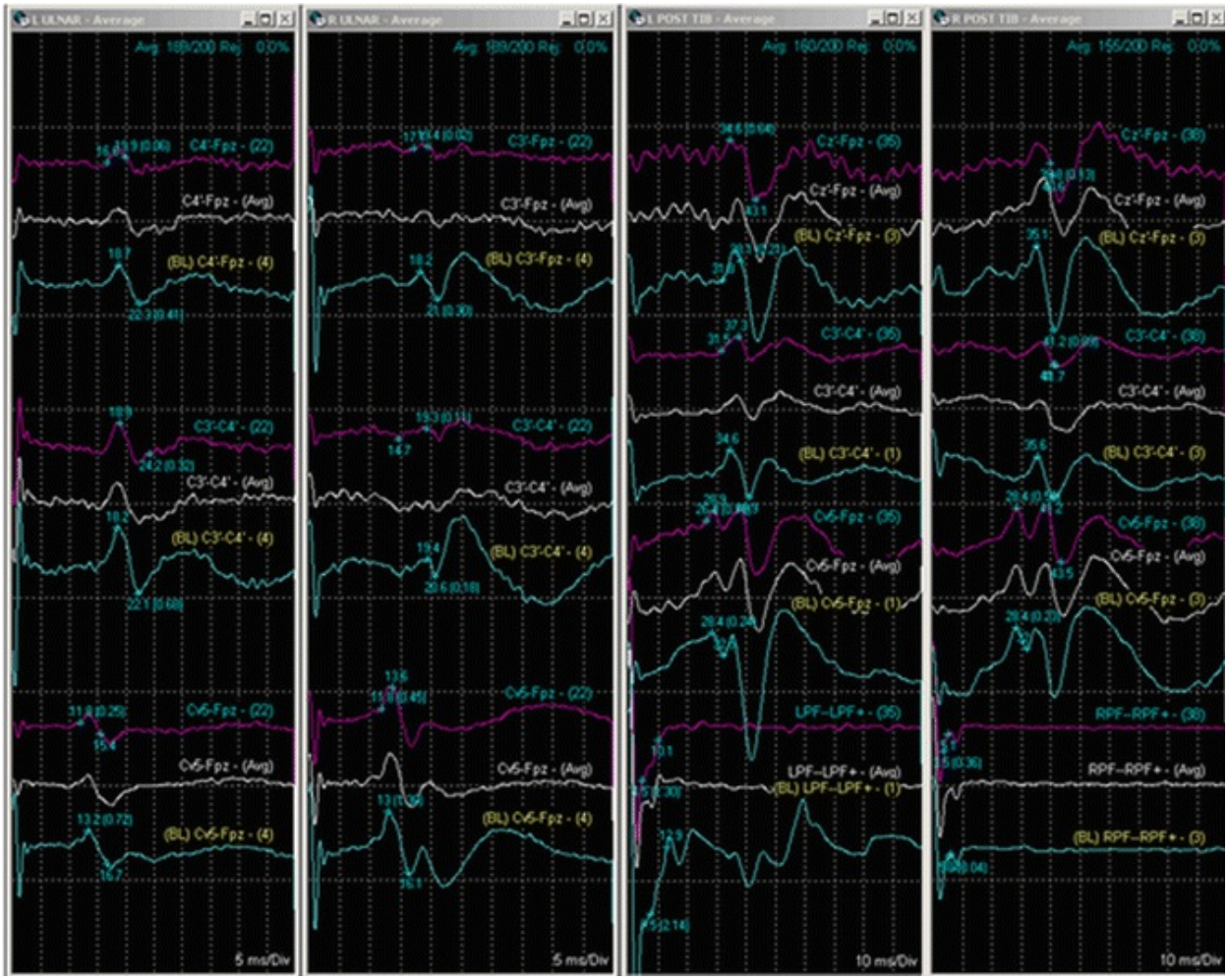

Fig. 27.2 SSEP recording from the four extremities with changes in upper right extremity that was related to positioning

Differential Diagnosis of SSEP Findings

The decrease in amplitude of the right upper extremity SSEP recordings prompted an investigation of both a physiological and nonphysiological etiology to the change from baseline. Technical issues related to the

monitoring were less likely given that the recordings from the other extremities were unchanged and after verifying the integrity of the electrodes placed in the right upper extremity. The maintenance anesthesia regimen had not been changed nor had the patient experienced significant hemodynamic or temperature variations. Due in part to the preoperative embolization of the tumor, minimal blood loss has occurred at this point, which made it unlikely that anemia was contributing to the changes in amplitude. Furthermore, since the findings were isolated to a single extremity, this suggested that the changes in amplitude were not systemic in nature, but rather directly related to the surgical procedure or to the patient's positioning. Given that the findings were ipsilateral to the operative site, it was determined that the positioning of the right upper extremity was most likely the cause of changes in SSEP.

Case Progression

After being notified that the right upper extremity SSEP recordings had changed, the surgeon was able to stop operating while the IOM findings were verified and investigated. Examination of the patient's right arm revealed that it had moved when the Mayo stand had been repositioned during the operation. Once the placement of the Mayo stand was corrected, the SSEP recordings returned to baseline values over the next 20 min. Upon conclusion of the operation, the patient was extubated in the operating room and transported to the intensive care unit. Postoperative examination revealed no sensory or motor deficits in the right upper extremity. Cranial nerve functions were also found to be at preoperative baseline.

Conclusion

In the first case, changes in baseline ABRs were interpreted correctly, reported to the surgeon, and the appropriate action was implemented to resolve the findings. While the sensitivity and specificity of intraoperative ABR changes are often questioned [16, 17], our case outlines an example where utilization of IOM may have prevented unwanted neurological morbidity. This is consistent with other data that suggest that the use of ABR in skull base surgery may improve patient outcomes [18]. In the second case, changes in SSEP recordings were evaluated and lead to an intervention that might have prevented peripheral nerve injury due to an alteration in the

patient's position. While not isolated related to the operative site, positional neuropathies are a common morbidity associated with prolonged surgical times often found with skull base surgeries. IOM during skull base surgery is a valuable tool that benefits both the patient and the practitioner. Correct implementation of various IOM modalities and proper interpretation of their recordings may help with the identification of neuroanatomical structures, the detection of mechanical and thermal injury, and facilitate progression of the surgery.

Questions

1. Reducing the possibility of complications due to the proximity of vital vascular and neurological structures during skull base surgery can be achieved through the utilization of IOM. Which of the following modalities have been shown to be useful during these operations?

   A. Evoked potential (SSEP, MEP, and ABR) monitoring

   B. Processed EEG (e.g., Bispectral Index) monitoring

   C. EMG monitoring

   D. Transcranial Doppler

2. The most commonly monitored cranial nerve during skull base surgery is which of the following:

   A. The glossopharyngeal nerve (CN IX)

   B. The facial nerve (CN VII)

   C. The hypoglossal nerve (CN XII)

   D. The occulomotor nerve (CN III)

3. Which monitoring modality is most likely to detect the potential for injury as a result of the patient being malpositioned?

    A. Somatosensory-evoked potentials

    B. Auditory brainstem response monitoring

    C. Electromyography monitoring

    D. Motor-evoked potentials

4. Which of the following monitoring modalities is most resistant to the effects of anesthetic agents?

    A. Somatosensory-evoked potentials

    B. Auditory brainstem response monitoring

    C. Electromyography monitoring

    D. Motor-evoked potentials

5. While the potential benefit for IOM during skull base surgery has been recognized for many years, determining which modality or combination of modalities to utilize is determined by careful consideration of a number of factors. Limitations to a uniform approach for these cases are dependent on the evaluation of which of the following factors?

    A. The technical and supervisory requirements for the implementation of IOM in a particular surgical procedure can be very challenging. Appropriately trained staff may not be readily available in all

operating locations.

B. The potential impact of anesthetic selection on the patient's physiological state must be balanced with the impact that these drugs have on the ability of the IOM team to obtain reliable readings in order to properly guide the surgeon.

C. The clinical importance and relevance of intraoperative changes is at times subject to considerable debate. Making clinical decisions under these circumstances requires a careful consideration of the patient's clinical condition, the changes that were noted, and the skill and experience of the members of the team including the surgeon, anesthesiologist, and neurophysiologist.

Answers

1. Both A and C are correct. While electromyography can aid in detecting and thus preventing injury to cranial nerves, the addition of evoked potentials helps assess various functional changes due to the compromise of neural structures as well as vascular structures.

2. B is correct. The facial nerve (CN VII) is the most commonly monitored cranial nerve during skull base surgery.

3. A is correct. Positional neuropathies can be the result of patient malpositioning during the often prolonged surgical times associated with skull base surgery.

4. B is the correct answer. Somatosensory-evoked potentials are impacted by the choice of anesthetic agents, but not nearly as much as the motor-evoked potentials. Electromyography is not susceptible to anesthetic agents, under clinically relevant conditions, but is sensitive to the effects of neuromuscular blocking agents. Auditory brainstem response measurements are relatively resistant to anesthetics and are not impacted by the use of neuromuscular agents.

5. All of the above. As with many aspects of medicine, evaluation of difficult clinical situations requires a careful consideration of the risks and benefits along with the analysis of findings that may not always be straightforward to interpret.

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Footnotes

1 Asterisk indicates key references.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_28

28. Surgery for Chiari Type I Malformation

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Keywords Neuromonitoring – Chiari I malformation operation – Pathophysiology – Symptomatology – Diagnosis – Anatomy – Operative technique – Potential structures – Positioning considerations

Introduction

The constellations of neuroanatomic findings and clinical sequelae related to congenital hindbrain herniation currently known as Chiari malformations first began finding predominance in the medical literature in the nineteenth century [1, 2]. While physicians prior to Dr. Chiari had acknowledged anatomic findings consistent with Chiari malformations, it was Dr. Chiari who—based on his descriptions of postmortem anatomic findings–developed the classification system that stands today [3]. Although the cases described by Chiari and colleagues varied considerably, the essential condition was that of a herniation of a tongue-like process of cerebellar tissue into the cervical canal. This description is consistent with Chiari malformation type I (CM-I) . Both type II and III Chiari malformations are congenitally acquired and associated with neural tube defects in a caudal and craniocervical distribution respectively. Chiari II patients exhibit downward displacement of the cerebellar vermis, brainstem, and fourth ventricle through the foramen magnum, boney abnormalities within the calvarium, and are frequently associated with spinal dysraphism. Type III Chiari malformations are rare and severe, involving significant morbidity and mortality related to varying levels of hindbrain herniation into associated cephaloceles. Type-V Chiari malformations are also rare and associated with hypoplasia or absence of the cerebellum. Classically, Chiari malformations as a group have been reported to have an incidence of roughly 1:1000 births—with the majority of cases coming to medical attention as a result of clustered, nonspecific clinical findings such as headache or abnormal gait [4]. With the advent of increasingly refined neuroanatomical imaging modalities, however, increasing numbers of patients are coming to medical attention in the absence of clinical findings or with variants of classically described pathology, leading to modifications of the Chiari classification system in modern literature. Patients presenting to the operative arena for any variety of reasons and also carrying a diagnosis of Chiari malformation are therefore becoming more common, in turn bearing unique considerations in perioperative management. This chapter will focus on only one Chiari malformation subtype: the type I classification.

Anatomy and Pathophysiology

CM-I patients often demonstrate reduction in size of the posterior cranial fossa. As the cerebellar tonsils descend through the foramen magnum and enter the cervical canal, they may cause direct compression of the brainstem structures in this area. Bony abnormalities of the posterior fossa and upper cervical spine may exacerbate compression of the neural elements. Cerebral spinal flow can be altered, leading to a spinal cord syrinx in the cervical spine [5, 6]. Whether or not the compression of cerebellar tissue within the fossa is an impetus for or result of pathologic sequelae, however, remains a topic of controversy [7]. Although all patients with CM-I share the anatomic characteristic of caudal tonsillar displacement of the cerebellum through the foramen magnum, the embryologic pathways leading to such herniation *vis a vie* abnormalities in neural crest and somite activity are likely varied and complex [8, 9]. Subsequently, additional structural and functional defects of the central nervous system frequently associated with Chiari I malformation are not ubiquitous among all patients. Additionally, subsets of populations exist where CM-I is acquired later in life secondary to connective tissue disorders or trauma—a feature unique to CM-I patients.

Symptomatology of Chiari I Malformation

Many patients with CM-I do not have any symptoms and are brought to medical attention due to incidental radiographic findings. When symptoms do occur, however, headache is frequently involved, often described as Valsalva-induced and suboccipital in nature. The headache is exacerbated by increases in intracranial pressure, typically occurring when patients strain for any reason. Other symptoms can include visual abnormalities, hearing and equilibrium difficulty, swallowing dysfunction, apnea, nausea, palpitations, gait ataxia, and a host of other seemingly nonspecific complaints. Unlike patients with the more severe CM-II, which typically manifests in infancy, patients with CM-I may remain asymptomatic or present in adulthood with subtle clinical findings related to brainstem compression. The symptoms gradually worsen over time, and it is not uncommon to see a college student with formerly good grades beginning to have increasing troubles in his or her studies due to the debilitating headaches. In cases of CM-I associated with a syrinx , patients may develop motor or sensory abnormalities of the extremities.

Diagnosis of Chiari I Malformation

The diagnosis of Chiari I malformation is made, in part, with the use of magnetic resonance imaging (MRI). Sagittal MRI images will show the presence of tonsillar descent below a line drawn from the basion to the opisthion (i.e., at the level of the foramen magnum). While it is generally accepted that greater than 5 mm caudal displacement of the cerebellar tonsils is pathologic, tonsillar displacements between 3 and 5 mm may also be considered pathologic if grouped with other findings. Such findings include neurologic deficits, signs of structural compression, or presence of a syrinx. Additional consideration must be given to the patient's age at the time of the study, as less than 6 mm herniation is considered within normal limits if presenting as an isolated finding in the first decade of life [10]. In severe cases, cerebellar tonsils may descend to the level of the second or third cervical vertebrae. On these images, particular attention should be paid to the location of the vertebral artery and the course of the posterior inferior cerebellar artery adjacent to the cerebellar tonsils. Syringomyelia may be appreciated with supplemental imaging of the spinal cord.

With advances in imaging over the past 20 years, tonsillar ectopia, as it is largely used today, is a poor sole criterion for diagnosis of CM-I [11]. Barkovich et al. [12] demonstrated that 14 % of normal control patients had tonsils below the foramen magnum and one in 200 normal control patients had tonsils projecting 5 mm or more below the foramen magnum by MRI imaging. Further, extent of tonsillar herniation in CM-I has never been satisfactorily correlated with severity of symptoms. In the 1980s, the advent of MRI made it possible to make an accurate, noninvasive diagnosis of this disorder for the first time. In the largest series to date, Elster and Chen [13] reviewed MRI images from 12,226 patients and found that a large percentage (31 %) of patients with tonsils herniated 5 mm or more below the foramen magnum were asymptomatic [13]. Today, quantitative analysis of cerebrospinal fluid dynamics is increasingly used in the workup of patients with CM-I [14–16]. Therefore, a comprehensive review of the imaging findings and clinical symptoms is used to make the diagnosis.

Operative Technique for Chiari I Malformation

The classic operation[1] for Chiari I malformation involves decompression of

the posterior fossa via a suboccipital craniectomy, laminectomy of the atlas, and expansile duraplasty with or without cerebellar tonsillar resection. The patient is positioned to provide the surgeon access to the posterior fossa. Most teams prefer the prone position, but the lateral position can provide acceptable access as well. An incision is made in the back of the neck from the inion to the upper cervical spine. A high-speed drill is used to perform a suboccipital craniectomy with laminectomies of the atlas and sometimes the axis. The dura is opened from the cerebellum down to the cervical spine just under the level of the tonsillar descent. Many methods (subpial suction and electrocautery, laser, etc.), based on surgeon's preference, are available to reduce the size of the tonsils. The tonsils re-reduced to the level of the obex. At this point, the entry into the fourth ventricle is exposed, and an autologous or synthetic patch graft is often sewn into the dura to provide expansion of the area available for the hindbrain structures. Meticulous closure follows.

Potential Structures at Risk During Surgery for Chiari I Malformation

Exposure of the craniocervical junction must be performed with great care. Figure 28.1a, b depict the anatomy of the area and structures at risk. As the vertebral arteries emerge over the C1 laminae and turn anteriorly to pierce the dura before entering the foramen magnum, they are vulnerable to injury. Special care must be taken during cervical laminectomy and suboccipital craniectomy not to compromise these vessels. During tonsillectomy, the surgeon must take care not to injure the posterior inferior cerebellar artery (PICA), which underlies the cerebellar tonsils. The PICA supplies blood to the lateral medulla, inferior aspect of the posterior lobe of the cerebellum, cerebellar tonsils, and portions of the choroid plexus . Injury can cause ischemia and infarction, leading to the Wallenberg syndrome. The nuclei of the sixth and seventh cranial nerves are found in the floor of the fourth ventricle; however, given their deep location, injury is rare. Finally, manipulation of the eleventh cranial nerve through the foramen magnum lateral to the spinal cord provides brisk excitement of the trapezius muscles in the absence of blockade. True injury to the spinal accessory nerve, however, is also unusual.

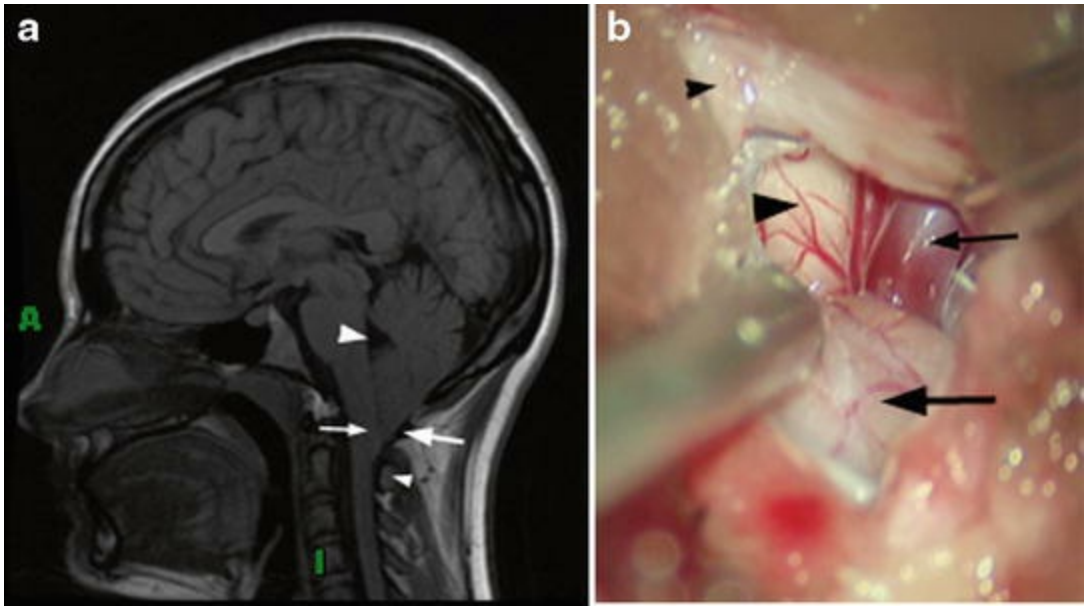

Fig. 28.1 Anatomy of the posterior craniocervical junction in Chiari malformation (**a**). Sagittal noncontrast T_1-weighted MR image in a patient with Chiari I malformation demonstrating herniation of the cerebellar tonsils (*large arrow*) below the foramen magnum. Also shown is the lamina of the second cervical vertebra (*small arrowhead*), the obex (*small arrow*), and the fourth ventricle (*large arrowhead*). Intraoperative posterior view of Chiari malformation surgery (*top of photograph is caudal*) (**b**). After a suboccipital craniectomy is performed and the posterior arch of C1 is removed, the posterior dural band (*small arrowhead*) is divided, revealing the descended cerebellar tonsil (*large arrow*) over the cervicomedullary junction (*large arrowhead*). The tonsillomedullary segment of the left posterior inferior cerebellar artery (*small arrow*) is shown coursing between the cerebellar tonsil and cervicomedullary junction

Positioning Considerations During Surgery

For the prone position, the head is held in three-point fixation. The neck is flexed to increase the working area in the craniocervical junction. It is imperative to recheck endotrachial tube positioning and ensure that bilateral breath sounds are present following neck flexion, as migration of the endotracheal tube leading to mainstem intubation is possible. An appropriate amount of neck flexion allows for surgical exposure without compromising adequacy of ventilation, arterial inflow, or venous outflow. The definition of excessive neck flexion may vary from patient to patient based on variability in boney anatomy or degree of preexisting neural structural compression. If arterial inflow is restricted, ischemia can result. If venous outflow is restricted, macroglossia and intracranial hypertension may occur. In general, there should be at least two to three fingerbreadths of space between the

anterior mandible and the sternal notch. The shoulders are often gently pulled inferiorly and taped into position. Careful attention to the amount of traction on the shoulders can minimize the chance of brachial plexus injury. If somatosensory-evoked potentials are utilized for the case, the brachial plexus can be monitored.

Principles of Intraoperative Neuromonitoring for Chiari I Malformation Surgery

The body of evidence supporting mandated use of neuromonitoring during surgical decompression of Chiari I malformation is lacking. Clinicians have, nevertheless, demonstrated some utility in somatosensory-evoked potential (SSEP) and brainstem auditory-evoked potential (BAEP) monitoring during positioning and in assessing adequacy of surgical decompression respectively [17]. After establishing baseline SSEP signal values, changes during SSEP monitoring can indicate a problem with positioning of the patient due to compression of the brain stem or cervical spine. Prompt recognition and correction of the problem by repositioning can avert a potentially disastrous outcome. SSEP monitoring can also provide information about the dorsal sensory elements of the spinal cord and brainstem during the procedure. Likewise, direct mechanical surgical insults and ischemia of the brainstem due to compression, spasm, or injury to the PICA can be detected by changes during SSEP monitoring. Correction of the surgical insult, blood pressure manipulation, addition of corticosteroids, administration of rheologic agents, or repair of the injury may provide benefit if actively pursued in response to monitoring changes. Monitoring of MEPs is infrequently used during CM-I decompression as no clear advantage has been demonstrated beyond that offered by SSEP or BAEP monitoring. The use of MEPs in this setting should therefore be relegated to surgeon preference.

Case Illustration

Stroke During an Operation for Chiari I Malformation

A 28-year-old female presented with progressive debilitating Valsalva-induced suboccipital headaches and unilateral upper extremity weakness. She underwent MR imaging and was subsequently diagnosed with Chiari I

malformation with cervical syringomyelia. The tonsils were noted to descend 7 mm below the foramen magnum, and a syrinx extending from C2 to C7 was appreciated. She elected to undergo suboccipital craniectomy, cervical laminectomy, cerebellar tonsillar reduction, and allograft duraplasty. The patient was positioned prone on laminectomy rolls, with the head and neck fixed in a three-point pin-based head fixation device. Two hours after skin incision, at the time of the cerebellar tonsillar resection, the posterior spinal radicular arteries on the dorsal aspect of the upper cervical spinal cord appeared blanched. This finding was believed to be unrelated to cauterization. Also within this time period, the neuromonitoring technician reported that the SSEPs were decreased in amplitude. With blood pressure elevation and the direct application of papaverine, vasodilation and reperfusion of the posterior spinal radicular arteries were noted within minutes of the above vascular changes. However, following reperfusion of the posterior spinal radicular arteries, the SSEPs remained reduced from baseline. The operation was completed and the patient awoke with weakness and incoordination of her lower extremities. During the first few months after the operation, the patient's strength and coordination improved, but she continues to struggle with ambulation at a follow-up period of 36 months.

Team Notes

The pre-positioning baseline traces are represented in Fig. 28.2a. Figure 28.2b represents tracings 1 h after the baseline traces were recorded, coinciding with the patient having just been placed in the prone position, neck flexed with the head held in a fixation device. During surgery, an amplitude decrease and a latency shift in the tracings should prompt a differential diagnosis including excessive surgical retraction, hypotension, ischemia, or positioning injury. After the operation, a closer review revealed increasing latency and a diminution in amplitude of the SSEP traces , particularly pronounced in the lower extremity SSEPs, shortly after initial positioning (i.e., after flexing the neck). These circumstances should have immediately raised suspicion of a positioning-related problem. The events of this particular case provide a strong argument for prepositioning baseline neurophysiologic testing as well as postpositioning testing. Baseline traces become invaluable when the practitioner is confronted with patients with neuropathy caused by a comorbid condition such as diabetes mellitus or elderly patients with fewer active nerve fibers and, hence, SSEPs of

potentially lesser amplitude. In the case of this 28-year-old woman undergoing an operation for Chiari malformation, detecting the SSEP changes after initial positioning would have allowed for early correction and adjustment of the surgical position.

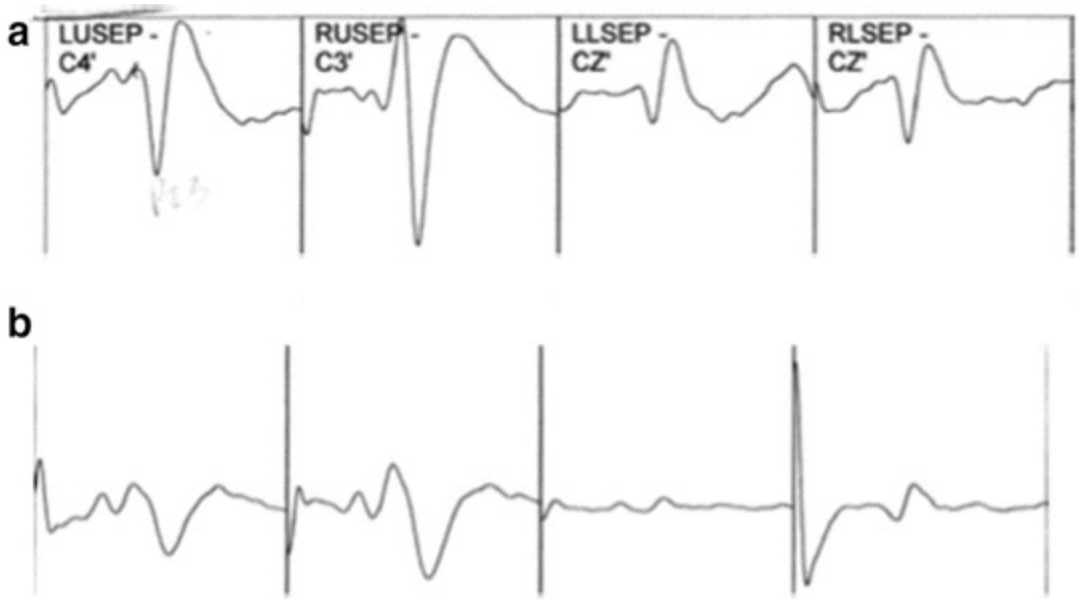

Fig. 28.2 Pre-positioning baseline SSEP traces (**a**). SSEP traces 1 h after positioning (**b**)

In principle, both the surgeon and anesthesiologist should agree on the amount of neck flexion acceptable for surgical exposure as well as adequacy of ventilation and adequacy of venous outflow of the head and neck to prevent macroglossia and intracranial hypertension. When possible, two to three fingerbreadths of space between the anterior mandible and the sternal notch is suggested. In this case, the patient's neck was likely overflexed, which led to chronic stretching and vasospasm of the posterior spinal radicular arteries with presumed diminution in perfusion. Vigilance and attention to monitoring traces are important at all stages of the operation in order to detect a correctable insult early.

To review the information on somatosensory-evoked potentials from Chap. 1, stimulation of the median nerve leads to an evoked potential at the brachial plexus. This P9 response is recorded at Erb's point (slightly above the midportion of the clavicle) and is generated from the nerves of the brachial plexus near the point at which they enter the spine. The recordings at Erb's point indicate brachial plexus activity and confirm appropriate electrical stimulation of the median nerve. Prolongation of the interval

between the P14 and the N20 peaks is referred to as the central conduction time. This interval indicates changes in the integrity of the primary somatosensory system. Thus, a prolonged central conduction time is a sign of ischemia. Recall the P14–P16 waves are generated in close proximity to the dorsal column nuclei while the N20 wave is generated in the primary somatosensory cortex. Whereas the conduction time in the median nerve may be increased in a cool upper extremity during a lengthy surgical procedure, central conduction time is not affected. Factors affecting central conduction time include surgical retraction, anesthetic depth, hypothermia (drop in core temperature), and hypotension—the last three of which affect SSEPs bilaterally.

A comprehensive differential diagnosis for decreased amplitude of SSEPs along with a latency shift should include consideration of physiologic factors, technical causes, responses to anesthetic drugs, surgical events, and patient positioning. Physiologic factors such as hypotension or a decrease in core temperature can cause changes in the SSEPs. Timely assessment of the patient's vital signs can confirm the absence of hypotension contributing to ischemia or a decrease in body temperature. Hypotension, in general, leads to a more global decrease in amplitude, whereas hypothermia causes a slowing of the neural conduction velocity in peripheral nerves and a gradual increase in the latency of the SSEPs [18]. Mean arterial blood pressure should be increased if a hypotensive or hypoperfusion insult is suspected. Upon discovery of hypoperfusion in the spinal radicular arteries in the case above, direct application of papaverine was used in addition to pressor medications. Interestingly, the use of papaverine hydrochloride as a vasodilator to treat vasospasm has been implicated in transient cranial nerve dysfunction. Its application has been reported to affect the oculomotor and facial nerves, as well as cause auditory dysfunction [19].

Technical causes for response changes can sometimes be detected by increases in electrode impedance. Electrode placement, optimal stimulus intensity, and stimulus rate are important factors that can affect the measured responses during any operation. Such issues as sweat and oil on a patient's skin can lead to changes in contact impedance if surface electrodes are utilized. Environmental (electrical) interference can also influence response waveform morphology.

Anesthetic drugs, particularly the halogenated agents, can produce a dose-related increase in latency and decrease in amplitude of SSEP tracings.

Although SSEPs are not as sensitive to such changes as are motor-evoked potentials, it is best to maintain a steady state of anesthesia and avoid giving a bolus of a drug. Nitrous oxide can also increase the latency and decrease the amplitude of cortical SSEPs. In the above case, nitrous oxide was avoided and anesthesia was maintained with sevoflurane, propofol, and remifentanil infusions. Sevoflurane remained constant at 0.5 minimum alveolar concentration (MAC) in order to minimize drug-induced SSEP changes. Although halogenated inhalational agents produce a dose-related increase in latency and decrease in amplitude of the SSEPs, intravenous agents have minimal impact on SSEPs at low to moderate doses. (For more information, see Chap. 19, “General Anesthesia for Monitoring”.)

In a suboccipital decompression surgery for Chiari malformation, during the resection of the cerebellar tonsils, it is not uncommon to see “noise” on the SSEP tracings (Fig. 28.3). After the “noise” has resolved, it is imperative to establish whether or not there has been any change from baseline. If a change in SSEPs persists, the team must perform a timely analysis of the problem, taking into account the aforementioned variables.

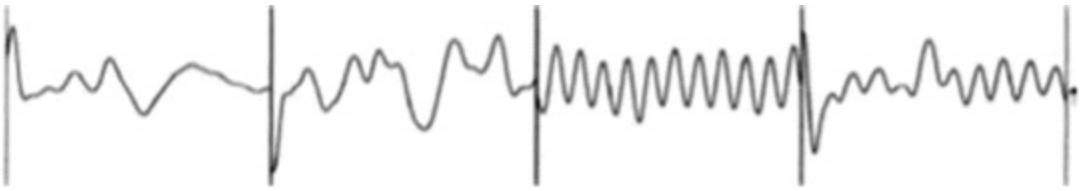

Fig. 28.3 SSEP noise during reduction of cerebellar tonsils with bipolar electrocautery

Finally, possible complications associated with patient positioning in posterior fossa surgery are extensive (Table 28.1). In the presented case, timing of when the SSEP changes occurred and the fact that the changes persisted despite efforts to maintain temperature, blood pressure, and steady anesthetic state make a strong case for SSEP changes being induced by head and neck flexion.

Table 28.1 Complications associated with surgical positioning in posterior fossa surgery

Complications	**Sitting position**	**Prone position**	**Lateral, three quarter prone position**	**Park Bench position**
Nervous system				
Cerebral ischemia	++	+	0	+
Cerebral spine ischemia	++	+	0	+

Palsies				
Cranial nerve	+	++	++	
Brachial plexus	+		++	++
Sciatic nerve	+	0	0	0
Peroneal nerve	+	0	?	
Airway				
Edema of face, tongue, neck (posterior obstruction)	++	++	+	0
Endotracheal tube migration	++	++	+	+
Pulmonary				
Ventilation/perfusion abnormalities	+	++	+	+
Increased airway pressures	0	++	0/+	0
Tension pneumocephalus	+	+	0	0
Cardiovascular				
Hypotension	++	++	0	+
Dysrhythmias	++	++	±	++
Need for blood transfusion	+	++	±	+
Miscellaneous				
Eye compression	0	+++	++	+
Venous air embolism	+++	++	+	++
Paradoxical air embolism	++	+	?	?

Smith [20], © Mosby Elsevier, 2010; with permission
0,+,++,+++ indicate relative probability from no risk to high risk

Questions

1. True/False: Chiari I malformation presents an absolute contraindication to epidural anesthesia in the setting of labor.

2. A 7-year-old girl is brought to her pediatrician by her parents with complaints of acute on chronic worsening of suboccipital headaches and difficulty with schoolwork. An MRI is obtained revealing 5-mm caudal displacement of the cerebellar tonsils through the foramen magnum.
   Which of the following statements is true?

a. 5-mm caudal displacement of the cerebellar tonsils confirms the diagnosis of Chiari I malformation in this patient

b. Headache is a relatively uncommon presenting symptom for Chiari I malformation

c. Isolated 5-mm displacement of the cerebellar tonsils through the foramen magnum is consistent with a diagnosis of Chiari II malformation

d. Diagnostic criteria for Chiari I malformation in the first decade of life include 6-mm caudal displacement of the cerebellar tonsils. Given the symptomaticity of the patient, however, CM-I malformation is high on the differential diagnosis in this patient's case

3. A 19-year-old female patient weighing 65 kg presents to the operating room for posterior fossa decompression of CM-I malformation. Anesthesia is induced with 150 mg of propofol, 40 mg of rocuronium, and 100 μg of fentanyl. The patient is intubated without event. An additional 18 g IV and a left-radial arterial line are placed. The patient is transitioned to a prone position with her head secured in Mayfield pins, and baseline SSEPs are established. Just prior to incision, the anesthesia resident administers 2 g of cefazolin, 10 mg of rocuronium, and 50 μg of fentanyl. Maintenance anesthesia is provided with propofol and remifentanyl gtt. Within 10-min of incision, the neuromonitoring technician reports an increased latency and reduction in amplitude of SSEPs. Particular attention should be paid to:

   a. Dosing of paralytic agent, as residual neuromuscular blockade is likely affecting the SSEP reading

   b. The effect of hypothermia on evoked potentials

c. Patient positioning

d. Excessive blood loss in the surgical field

Answers

1. False Although much of the literature describing laboring CM-I patients is limited in terms of case numbers, safe and successful use of epidural and combined spinal-epidural anesthetics in the setting of labor have been described. Clearly, elevated intracranial pressure puts the patient at risk for herniation in the setting of dural puncture with an epidural needle should it exist. In the hands of an experienced provider, however, the risk of inadvertent dural puncture can be minimized. Moreover, early neuraxial intervention in the setting of active labor may minimize the increases in intracranial pressure associated with painful contractions. Once placed, catheter rates should be titrated slowly to avoid rapid changes in blood pressure and subsequently cerebral perfusion pressure.

2. d Although diagnostic criteria for CM-I includes 6-mm caudal displacement of the cerebellar tonsils during the first decade of life and 5-mm caudal displacement thereafter, the sensitivity of tonsillar displacement as a sole criteria for the diagnosis of CM-I is quite low. Even in the setting of cerebellar tonsil displacement of 3–5 mm, neurologic signs or symptoms at the time of presentation can be a strong indicator of disease. Subsequently, diagnosis of CM-I malformation is often multimodal in nature, with the clinical picture at the time of presentation playing an important role.

3. c Although use of SSEP monitoring is not ubiquitous during posterior fossa decompression, some studies have indicated a benefit in detecting neuronal compromise during patient positioning. SSEP monitoring can detect vascular perturbations to nerve structures secondary to excessive compression. Given the time course in the vignette above, excessive neck

flexion with compromise of vertebral artery flow or brachial plexus damage related to excessive shoulder traction are areas of particular concern. Neuromuscular blockade has no effect on SSEPs. While hypothermia and major blood loss could lead to diminished amplitude and increased latency of SSEP signals, it is unlikely that either of those factors would be an issue this early in the procedure.

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Footnotes

1 *Note:* The senior surgeon [R. F. Sekula] prefers his own variation on the classic operation, which includes a limited skin incision [1 in.], limited suboccipital craniectomy and cervical laminectomy, with cerebellar tonsil reduction and expansile duraplasty.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_29

29. ENT and Anterior Neck Surgery

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Electronic supplementary material:
The online version of this chapter (doi:10.1007/978-3-319-46542-5_29) contains supplementary material, which is available to authorized users.

Keywords ENT neck surgery – Anterior neck surgery – Electrocochleography – Electroencephalogram – Auditory brainstem responses – Neurophysiologic monitoring – Facial nerve – Vagal nerve EMG

Key Learning Points

- Monitoring for each type of otolaryngological anterior neck procedure will depend on what structures are involved or could be compromised by the surgical approach.
- Cochlear potentials have advantages over other auditory potentials because they are faster with more rapid acquisition of waveforms. They can also monitor changes in cochlear blood flow.

- Facial nerve EMG monitoring has some critical limitations. It is only applicable when exposed areas of nerve are present and is hard to use if the nerve is covered by tumor. Nerve activation by stimulation is not uniform and could be affected by flattening or expansion of the normal shape of the nerve.
- Facial MEPs and EMG fulfill different neuromonitoring needs. FMEP provides information on overall nerve integrity and correlation with functional status, while EMG is best used for nerve identification and mapping.
- Recurrent laryngeal nerve monitoring is best done with an ET tube fitted with stainless steel electrodes which make contact with the vocal cords when the ET tube is properly positioned. Preoperative use of a drying agent such as glycopyrrolate will reduce salivation and pooling of saliva which could produce loss of signal from salt bridging.

Introduction

This chapter describes the types of monitoring modalities that may be used for ear, nose, and throat (ENT) and anterior neck surgery, the structures at risk, and the methods to monitor these structures to prevent iatrogenic damage and injury caused by surgical trauma. The different monitors that may be used for these particular procedures are suggested, as the type of monitoring used depends on the particular approach or procedure.

The case is that of a 51-year-old white man presenting with squamous cell cancer of the temporal bone with extension of the tumor to the left neck and throat. The patient will undergo a left auriculectomy and temporal bone resection. He will have a middle fossa craniotomy, parotidectomy, with an accompanying left neck dissection. He will have a subsequent anterior lateral free flap to close the anticipated defect.

Different monitoring modalities may be used during the procedure to protect the structures at risk from surgical trauma. The area of surgical dissection could disrupt or traumatize several cranial nerves as they exit the skull base and extend into the neck to innervate muscles of the face and the upper pharynx. Vascular structures may also be at risk for tumor involvement. Blood supply to the brain and cerebral blood flow could be compromised during the neck dissection. Multimodality recordings from a

combination of various generators provide an effective method to reduce the morbidity associated with intracranial or extracranial surgery in the region of the third through twelfth cranial nerves. Electromyography (EMG) and compound muscle action potentials (CMAPs) are helpful when monitoring nerve function. This tumor is also tracking down the neck, and the mass involves a portion of the carotid artery with possible recurrent laryngeal nerve involvement. Tumor involvement of the carotid artery may necessitate cross-clamping of that structure with possible temporary cerebral hypoperfusion. Cerebral function will be monitored using electroencephalography. Recurrent laryngeal nerve function will also be monitored using EMG and compound motor action potentials recorded with a NIM™ EMG endotracheal tube (Medtronic Xomed, Inc., Jacksonville, Florida).

The selection of which monitoring technique to use is best made on the basis of each individual's clinical situation and the structures at risk. Eighth cranial nerve involvement by the tumor was minimal, but the close proximity of the tumor to the nerve will necessitate the measurement of auditory brainstem responses (ABR) (see Chap. 3, "Auditory Evoked Potentials"). Because the ratio of surface electrical signal to noise is low, especially in the operating room where there is high acoustics and electrical noise, long signal averaging is needed [1]. Also, the patient does have some hearing loss on the operative side which could reduce ABR amplitude. Direct nerve monitoring of the acoustic nerve was considered, but exposure would have been a problem with the operative electrode interfering with the surgical field. An alternative monitor to record auditory potentials could be the use of tympanic electrodes placed on the promontory to record near field cochlear-auditory nerve activity or electrocochleography (ECochG) . This auditory measure provides relatively large amplitudes (5–10 mV) and requires only a small number of sweeps to achieve a compound action potential. The auditory potentials can be recorded by means of a noninvasive electrode placed in the extratympanic intrameatal canal or adjacent to the tympanic membrane.

Difficulties are routinely experienced when monitoring eighth cranial nerve function because of the compressive effects of the tumor on neural and vascular structures. Once a mass is discovered, test parameters should be adjusted with the goal of producing the best evoked responses possible. Optimizing auditory evoked potentials during preoperative testing is beneficial for intraoperative monitoring. Obtaining evoked potentials just

before surgery maximizes the chance that significant decrements have not occurred in the interim. A good baseline response is essential for reporting any change that occurs during surgery. Evoked otoacoustic emissions may play a role in the estimation of cochlear health, gauging cochlear vascular supply, and differentiating cochlear versus sensory components of hearing loss in patients with tumors in close proximity to the nerve. Eighth nerve monitoring techniques have inherent strengths and weaknesses and may be affected by pharmacologic agents or physiologic events during surgery (Table 29.1). A commonly encountered problem with ABRs involves the temporary deterioration of waveforms which results from masking of the responses by noise produced by temporal bone drilling and suction irrigation [2]. The ABR represents the response of the distal auditory nerve to the brainstem's lateral lemniscus following auditory stimulation and is the most commonly employed method for monitoring the eighth cranial nerve . For patients with large tumors or elevated hearing sensitivity, an adequate ABR often takes 30–60 s of averaging. The intraoperative ABR analysis consists largely of the calculation of interwave latency values between wave components. The latencies usually monitored are between waves I and II, I and III, III and V, and I and V. The precise latency values of interest, however, depend on the purpose for monitoring. Since tumor involvement was distal and involved components of the vestibular apparatus, primary emphasis was on calculation of the latency intervals between waves I and II or waves I and III. Simultaneous recordings of ECochG can provide information about the involved ear more quickly because the recording electrode is placed closer to the response generators. Cochlear potentials have several advantages over other auditory potentials which include faster, nearly online acquisition of waveforms as well as the ability to monitor changes in cochlear blood flow. ECochG monitoring was difficult in this patient because of the problems with placing an electrode in the ear canal or within the middle ear space along with high electrode impedance. The use of smaller ear probes, coupled with the use of anchoring wax, has allowed for easier and quicker response acquisition due to better electrode contact. ECochG-evoked responses can provide an early indication of changes in the neurophysiologic status of the peripheral and central nervous system during surgery. These changes can occur because of both physiologic and surgical factors such as hypotension, hypoxia, and compression or retraction of nerves or brain structures. A shortcoming of the ECochG, a representation of very early

evoked potentials from cochlear hair cells and the distal eighth cranial nerve, is that it provides little information regarding the proximal nerve or the surgical effects on its function.

Table 29.1 Effects of pharmacologic agents and physiologic events on intraoperative neurophysiologic monitoring

Pharmacologic agent	**Effect**
Modality: electrocochleography	Resistant to effects of anesthesia
Modality: auditory brainstem response	
Inhalation anesthetics (enflurane, halothane, isoflurane)	Delay of 0.5–1.0 ms prolongation of wave V; I–V interpeak latency prolonged when end-tidal concentration exceeds 1.5 %
Thiopental	≥20 mg/kg dose, wave V prolonged; amplitude reductions noted with larger doses
Pentobarbital	>9 mg/kg, latencies prolonged, amplitudes reduced
Modality: facial electromyography	
Local anesthetics (lidocaine, bupivacaine, cocaine, tetracaine)	Latency and amplitude of CMAP following impaired propagation of potentials
Neuromuscular blockade (succinylcholine; atracurium, mivacurium, vecuronium; pancuronium, doxacurium, pipecuronium)	Spontaneous and triggered EMG abolished until worn off or reversed (can be a lengthy time period)
Physiologic event	
Local or systemic hypothermia	ABR absolute, interpeak latencies prolonged, wave amplitudes diminish; neurotonic stimulation of EMG activity
Tissue compression, retraction	Averaged auditory responses degraded, abolished
Inadequate ventilation, hemodilution, systemic hypotension, regional ischemia	Reduced oxygen affects endocochlear potentials, decreases cochlear output

ABR auditory brainstem response, *CMAP* compound muscle action potential, *EMG* electromyogram

To record or monitor ECochG, preoperative plans should be made for placing a reference electrode deep in the external ear canal (or through the tympanic membrane onto the promontory) along with other monitoring leads before the patient is prepped for surgery. Intraoperative ECochGs are made using an FZ to promontory recording electrode array. The FZ site is located in the midline approximately halfway between the bridge of the nose and vertex. A well-formed response is characterized by the presence of all major

wave components such as the ECochG summating potential (SP), the action potential (AP), and often ABR waves I, II, III, and V [3]. Intraoperatively, the ECochG components of interest are almost always the SP and the AP waves. Both the latency and amplitude of each component are regularly calculated and monitored. The latency is typically defined as the time in milliseconds between the click stimulus presentation and the peak of the wave. Amplitude values of SP and AP are calculated from a common baseline. The major advantage of intraoperative ECochG is that it has improved surgical technique. Intraoperative ECochG instantly confirms to the surgeon which vessel or which maneuver caused a loss of response and this immediate feedback has resulted in significantly improved surgical technique for hearing preservation.

Parotid resection will also necessitate the need for facial nerve monitoring (see Chap. 7, “Electromyography”). The absence of clinically detectable facial nerve deficits does not rule out the presence of subclinical nerve damage. The facial nerve was embedded in fibrous tissues of the tumor; therefore, continuous EMG monitoring of facial muscles during parotidectomy was performed to reduce the incidence of facial paresis or paralysis. To assist with the identification of the facial nerve and the mapping of its branches and to protect against inadvertent surgical damage, subdermal needle electrodes were placed to record EMG from the frontalis, orbicularis oculi, orbicularis oris, and mentalis muscles. This provided continuous intraoperative nerve monitoring of the four peripheral branches of the facial nerve: frontal, zygomatic, buccal, and marginal mandibular using free run and triggered EMG. The EMG activity was monitored continuously to ensure anatomical integrity of the facial nerve pathways and to correctly identify the distal branches prior to dissection. Spontaneous EMG activity during surgical manipulation was promptly communicated back to the surgeon to ensure that it was only transient and not sustained, which would be consistent with nerve injury.

There is a growing body of evidence that supports the value of cranial nerve monitoring in a variety of surgical environments. Intraoperative facial nerve monitoring is an important adjunct to enhance neural preservation, particularly when tumor, infection, trauma, or anatomic variation places the nerve at increased risk. Contemporary intraoperative facial nerve monitoring is based on facial muscle electromyographic activity . Recording evoked electromyographic activity from the muscle rather than the nerve itself takes

advantage of the amplification that occurs at the neuromuscular junction. This form of monitoring is used to provide the surgeon with information regarding the location and extent of the facial nerve contour, surgical trauma, and nerve function.

Surgically evoked facial EMG activity may be classified as either nonrepetitive or repetitive depending on whether single or repetitive discharges occur with a given response. Nonrepetitive activity or phasic bursts may be observed with electrical, mechanical, or thermal stimulation [4]. Surgical manipulation of the facial nerve may result in elicitation of nerve fiber action potentials. An important feature of nonrepetitive evoked EMG activity is the apparent lack of temporal delay between the stimulus and the observed response. Repetitive firing of facial nerve fibers or train activity may be elicited by nerve traction and particularly lateral, nerve compression. Facial nerve EMG activity such as this evoked during surgery has been referred to as an injury potential or neurotonic discharge. There is typically a significant temporal delay, up to a minute, between the provocative or stimulus event and the onset of repetitive activity. Because of this, the identity of the initiating event may be unclear.

Electrical stimulation of the nerve may be an important addition to the surgeon's ability to assess the anatomic location of the facial nerve. Monopolar stimulation is best used to map the general vicinity of the nerve with regard to the tumor mass. After localization of the facial nerve has been accomplished, microtrauma during dissection may result in significant nerve injury. Surgical manipulation often provokes a mechanically evoked facial nerve response that results from rapid neural deformities producing ionic depolarization. Traction responses tend to occur as multiple asynchronous potentials in contrast to a synchronized potential seen with brief direct mechanical contact. Drilling adjacent to the nerve using high-speed pneumatic drills may elicit mechanical and thermal evoked potentials. Even if bone overlies the nerve, vibration can be transmitted through the bone, which could affect nerve firing. Thermal changes can also evoke train potentials. Cold irrigation fluid causes asynchronous potentials to occur, which will subside as the irrigation fluid temperature increases. With drilling, heat buildup may also occur, which could cause aberrant nerve firing. Care should be taken to irrigate the drill to avoid heat buildup during boney dissection. Other techniques to help reduce intraoperative artifacts are listed in Table 29.2. It is imperative to have an adequate baseline with minimal electrical

activity.

Table 29.2 List of ideas designed to help decrease intraoperative artifacts [19][a]

Remove grease and abrade skin before applying scalp electrodes
Glue electrodes down with collodion
If electrodes are on overnight, regel, and abrade scalp in the operating room
Keep electrode impedances at approximately 2000 Ω
Use short electrode wires
Use short interelectrode distances between pairs of recording electrodes
Braid the recording electrode wires with each other
Have backup stimulus and recording electrodes available and already in place on the patient
Keep recording and stimulating wires and cords far away from one another
Do not cross cables or wires over other cables, especially power cables
Do not kick, jar, or sway the wires
Keep the low filter above 1 Hz whenever possible
Unplug unused equipment
Avoid appliances with two-pronged power plugs (ungrounded)
Stop averaging whenever amplifiers are blocking (e.g., after electrocautery)
Adjust sensitivity so that some trials cause artifact rejection
Use enough neuromuscular junction blocking agents
Delay recording until several milliseconds after stimulus

[a]For more information, see Chap. 16, “Wiring and Electrical Interference in IOM.”

Facial nerve (FN) EMG monitoring , though almost a care standard for these types of surgical procedures, has some critical limitations. The method is applicable only to exposed portions of the nerve and is hard to utilize if the nerve is covered by tumor. Also, the activation of the facial nerve by direct stimulation is not uniform. The nerve structure may be altered with spreading of nerve fascicles and flattening or expansion of the normal shape of the nerve due to tumor compression. The motor action potential proximal and distal to the tumor is not reliable, and the prognostic value of the compound muscle action potential amplitude at the end of surgery is of limited predictive value. Transcranial electric stimulation for eliciting motor evoked potentials of the facial nerve (FMEPs) and vagus (vagal MEPs) along with other cranial nerves, (collectively termed “corticobulbar MEPs”) have been

introduced as an adjunct to EMG monitoring [5]. The use of FMEPs allows the activation of motor pathways proximal to the site of the lesion and enables checking the condition of the facial nerve before its visualization. Despite positive reports of their use, FMEPs and corticobulbar MEPs have not yet become a routine tool in neurosurgery or otolaryngology. This may be due to difficulties in application and interpretation of signals. There is considerable artifact and interference associated with CN MEPs. Artifact suppression is improved using insulated head holder pins and by short interstimulus intervals less than 2 ms. Stimulating electrode position can influence waveforms and response latencies. Some authors report placement of the stimulating electrodes at C3 or C4 and others 1 cm anterior near the motor strip at M3 or M4 [6]. Also, a correlation is observed between the extent of tumor size and the quality of the MEP response. MEP latency is shorter with small tumors but increases significantly with increasing tumor size [7]. This could be due to edema or stretch of the nerve by the tumor. MEP amplitude is decreased with increasing tumor sizes corresponding to a reduction of active nerve fibers. Using MEPs, facial nerve status can be assessed even before the surgery has started. FN function can also be predicted by the use of an amplitude ratio that measures waveform amplitudes at the end versus the start of surgery. Patients having good FN function, House/Brackman (HB) 1 or 2, had a ratio of 85 % or greater. The HB facial nerve grading system is a commonly used, standardized, and reliable method to assess facial function. Grade 1 is normal, whereas Grade II is slight weakness only noticeable on close inspection. Grade III is gross and obvious facial dysfunction; it is not disfiguring but weakness is noted. Grade IV is more severe, with disfiguring asymmetry with incomplete eye closure and mouth asymmetry. Grade V is severe dysfunction with barely perceptive movement of the affected side, while Grade VI is complete paralysis. With HB3 function, the amplitude ratio was found to be in the 60–70 % range, and with a more severe FN deficit, HB4, the ratio is around 30–35 %. With severe FN injury corresponding to HB 5 or 6, the FMEP is below 15 % or lost completely. FMEPs are identified by their shape and latency. Physiologically, an appearance of a centrally mediated FMEP before 12-ms latency is not realistic. In the case of space-occupying lesion, longer latencies are expected. Contralateral function of FMEP is also important. Recording of the healthy side serves as a technical control at the start and during all stages of the operation. By contralateral stimulation, the neurophysiologist may verify

whether stimulation itself is deficient, whether air accumulation prevents reliable motor cortex activation, or whether the problem is related to the surgical site.

FMEPs and EMG fulfill different tasks in neuromonitoring. FMEP provides information on overall facial nerve integrity and correlates well with functional status. EMG and CMAP are best used for focal nerve identification and mapping. Either method does not affect the other but compliments their respective information. FMEP helps to identify nerve integrity and overcomes the specific limitations of stimulation intensity and reliability when using EMG. FMEP latency and amplitude provide relevant information on the functional status of the FN before the start and throughout surgery. A preserved FMEP end-to-start ratio above 55 % predicts preserved eye closure.

After the tumor is removed, nerve integrity can be assessed by stimulating it at an area that is proximal to the dissection. Nerves that require elevated stimulus current to reach a firing threshold will demonstrate some degree of postoperative weakness [8, 9]. The presence or absence of a facial evoked response must be interpreted within the context of the surgical procedure. Electrical silence may occur from an absence of facial nerve stimulation, a severe insult which precludes depolarization, transection of the nerve, or technical problems with the equipment. Nerves that have been significantly manipulated during the dissection may demonstrate fatigue. In these instances, stimulus current may need to be increased. Ultrasonic aspiration of the tumor creates low-level artifacts or triggers the autonomic muting circuitry. The use of monopolar cautery may charge the stimulator probe, which can result in a false-positive response. Severe neuropraxic nerve injury can prevent depolarization, just as axonal injuries do. Most surgeons will not resect nerves solely on the basis of the lack of an ability to stimulate. A complete list of problems that could be present with monitoring and possible solutions is found in Table 29.3.

Table 29.3 Checklist for intraoperative nerve facial monitoring problems [20]

Problem	Possible solution
Current jump	Bipolar stimulator
Current shunting	Insulated stimulator
Cautery artifact noise	Muting circuit
Cautery precludes monitoring	Visualize face

Laser heating effect	Monitor baseline amplitude
Saline cooling	Heat saline with “blood warmer”
Stimulus artifact	Increase “stimulus ignore” time
Static discharge	Insulated instruments
No response to stimulation	Power off
	Current intensity too low
	Current measured too low
	Electrode impedance too high
	Electrode disconnect
	Current shunting
	Threshold setting too high
	Volume too low
	Muscle relaxant used
	“Stimulus ignore” too long
	Seventh nerve not contacted
	Other cranial nerve/tissue
	Facial nerve injured

Monitoring the lower cranial nerves also necessitates strict control of muscle relaxants and the elimination of mechanically evoked responses with the presentation of electrically evoked responses. Long-acting muscle relaxants should be avoided. Although low doses may not have a significant effect on the responses to electrical stimulation, they may diminish the ability to monitor small amplitude responses associated with mechanically evoked potentials of the facial nerve. Thus, muscle relaxants should be avoided altogether, if possible, during surgical manipulation with short-acting agents only used to facilitate intubation. Anesthetic agents such as N_2O, opioids, barbiturates, and halogenated agents have minimal, if any, effect on these electrically evoked responses [10]. General anesthesia was maintained with an inhaled agent and an infusion of opioid without the use of muscle relaxants. All standard respiratory and hemodynamic anesthesia monitors were placed. Body temperature was continuously monitored and special measures to maintain normothermia during this prolonged surgical procedure included the use of a forced-air heating blanket and intravenous fluid warmer. The goal was to maintain stable, normal physiological functions including oxygenation, ventilation, arterial blood pressure, body temperature, and to provide a steady level of anesthesia using a drug combination favorable to

neurophysiologic monitoring.

With the present case, tenth cranial nerve monitoring was important since the tumor also involved portions of the recurrent laryngeal nerve. There are optimal essential elements for intraoperative nerve monitoring of the vagus and recurrent laryngeal nerves (RLNs) that are important. Preoperative laryngoscopy is necessary to assess the functional integrity of the RLNs bilaterally before the beginning of surgery to obtain accurate preoperative information on glottic function. Presurgical dissection suprathreshold vagal nerve stimulation allows for verification of the intraoperative neural monitoring (IONM) system function and therefore allows for subsequent neural mapping for the RLN with accuracy. Postsurgical suprathreshold vagal stimulation allows for the most accurate prognostic testing of postoperative glottic function. It has been noted that vagal stimulation has higher sensitivity, slightly higher specificity, and higher positive predictive values to determine vocal cord paralysis as compared to RLN stimulation [11]. Vagal stimulation allows for testing of the entire neural circuit and avoids the potential false-negative scenario of stimulating a damaged RLN distal to the injury site.

The vagus nerve is monitored using electrode pairs placed into the intrinsic laryngeal structures on the side ipsilateral to the tumor. Placement of these electrodes is made with the use of a diagnostic laryngoscope. An even better, less invasive, technique to monitor the recurrent laryngeal nerve innervation of the oropharyngeal space and vocal cords is with the use of an endotracheal tube-based system with embedded electrodes. The ET tube is a flexible silicone elastomer with an inflatable cuff. The tube is fitted with four stainless steel wire electrodes (two pairs) that are embedded in the silicone of the main shaft and exposed superior to the cuff only for a short distance (30 mm). The electrodes are placed to make contact with the vocal cords when the ET tube is properly positioned below the vocal cords. A video laryngoscope is ideal for correctly positioning these monitoring tubes. It is also important to avoid the use of lidocaine spray or other local anesthetics applied to the trachea before intubation or these could interfere with nerve function and monitoring. Alternatively, standard ET tubes may be made into monitoring tubes by placement of a thin adhesive pad containing the paired electrodes. The lower tip of these electrodes is placed approximately 7–10 mm above the upper edge of the ET tube cuff. The endotracheal tube electrode when correctly placed will make contact with the medial surface of

the bilateral cords to allow for monitoring of the bilateral thyroarytenoid/vocalis muscle's surface depolarization.

Proper positioning of the tube is important to achieve a good signal, and tube size is chosen that provides optimal contact with the vocal cords. These endotracheal tubes have outer diameters that are larger than standard ET tubes, so usually a size smaller than normal is chosen. The largest tube considered safe should be used to intubate the larynx, as this will provide optimal contact with the vocal cords. The tube should be placed with a stylet because they are less rigid than standard ET tubes; however, newer versions of these recording NIM tubes seem to be of similar stiffness to regular ET tubes. Preoperative use of a drying agent such as glycopyrrolate is utilized to reduce salivation and pooling of saliva at the cuff. This pooling could produce a reduced signal due to salt bridging at the electrode interface. Care must be taken during the intubation process to assure that the electrodes are properly aligned relative to the vocal cords. The amount of inadvertent rotation of the endotracheal tube during intubation, especially with right-handed anesthesiologists, could be as much as 30°. This rotational error could produce improper placement of the tube, thus reducing the signal [12]. In some instances, the tube is marked at the 12 o'clock position at the upper margin of the exposed electrodes to help with a counterclockwise adjustment of the tube for proper electrode alignment.

With patient positioning, if the head is extended and shoulder rolls are placed, monitoring tube malpositioning can occur. The ET tube may be displaced relative to a neutral intubating position by up to 21 mm inward and almost 33 mm outward as the patient is moved into full neck extension. All tests to assure ET tube vocal cord contact are made after the patient is in the final position for the surgery. In this case, the neurophysiologist looked for the development of respiratory variation, which is a coarsening of the monitoring baseline. Once this was observed, both the monitoring technician and anesthesiologist were assured that the tube was in the correct position.

The latency of the EMG responses to tenth nerve stimulation varies depending on the site of stimulation. Monitoring of the vagus is especially important because of the neurologic deficits that result from its functional loss. Owing to the extensive visceral communication of the tenth cranial nerve , disturbances in autonomic function may be encountered during surgical stimulation; especially reflex bradycardia or sudden asystole. Physical traction applied to the nerve may generate a massive response

compared to the low-level constant current stimulation normally seen during monitoring. When this type of response is anticipated, the anesthesiologist may have to administer prophylactic anticholinergic agents to obtund the response.

There are numerous factors that affect cranial nerve EMG and evoked responses. During the surgical dissection, the physician must identify the track of the nerve and also its anatomic structure as it is involved with the tumor. There are several situations that could mimic facial nerve injury. These should always be assessed during the surgical procedure. While resecting the tumor from the facial nerve, this first train activity was noted (Fig. 29.1). This is surgical irritation of the nerve during the dissection. It is considered nonrepetitive asynchronous activity, which is referred to as an injury potential or neurotonic discharge. The surgeon should be made aware of this activity and adjust the surgical dissection to reduce the neural irritation. As the dissection of the tumor continued, surgical isolation of the nerve from the tumor was accomplished by drilling the mastoid with irrigation of the surgical site to improve exposure. Immediately after irrigation of the site, facial nerve firing occurred that had the activity pattern observed in Fig. 29.2. The surgeon felt that he had caused damage to the nerve from drilling the bone to expose it. Prior to this, no irritation or injury potential was observed. The anesthetic agents had remained constant and hemodynamically the patient was stable with no evidence of light anesthesia. The irrigation fluid was noted to be cold. After replacing the fluid with a solution at body temperature, the firing dissipated. Cold irrigation causes nerve irritation and produces continuous firing of the nerve, which appears similar to traumatic injury. After the temperature to the surgical area had been normalized, the aberrant firing of the nerve diminished. Traumatic nerve injury will continue to produce asynchronous nerve firing that is not normalized by physiologic changes in temperature or blood flow. The surgery progressed and both the facial nerve and tenth cranial nerve were localized within the tumor bed. The surgeon began to debulk the tumor using the CUSA ultrasonic aspirator. The debulking procedure continued and low-amplitude high-frequency activity was noted (Fig. 29.3).

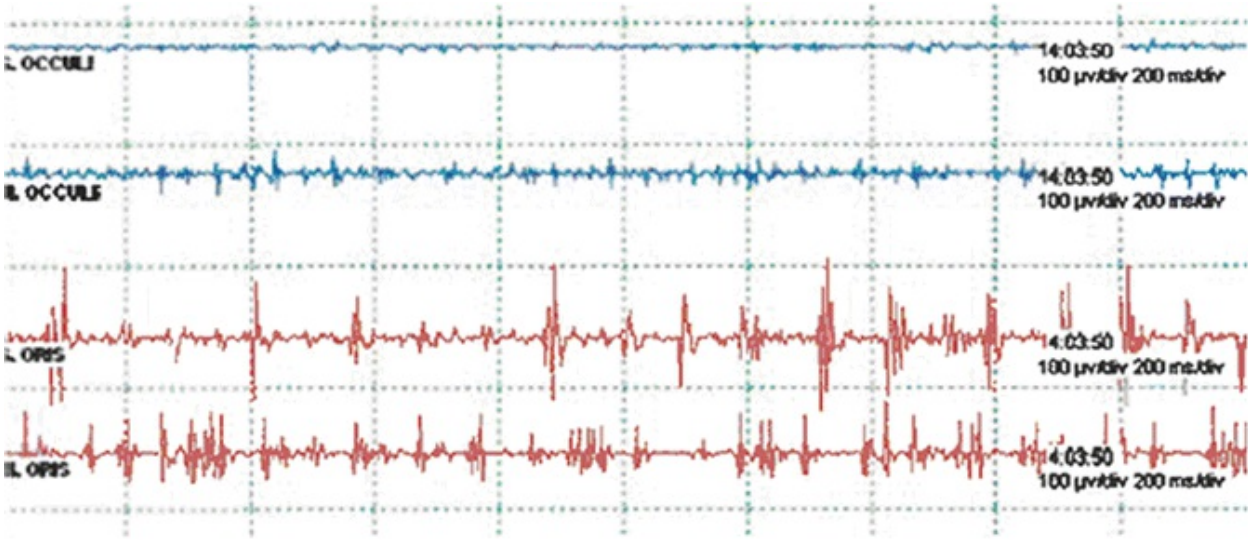

Fig. 29.1 Asynchronous train activity while resecting the tumor from the facial nerve

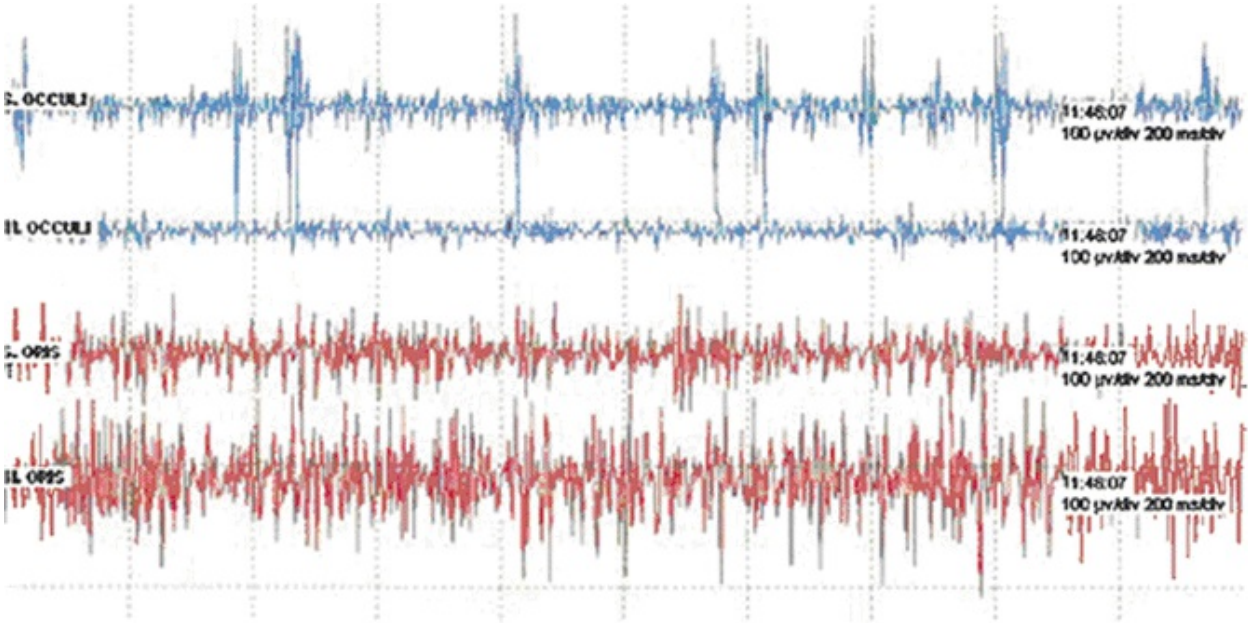

Fig. 29.2 Facial nerve firing immediately after irrigation of the site

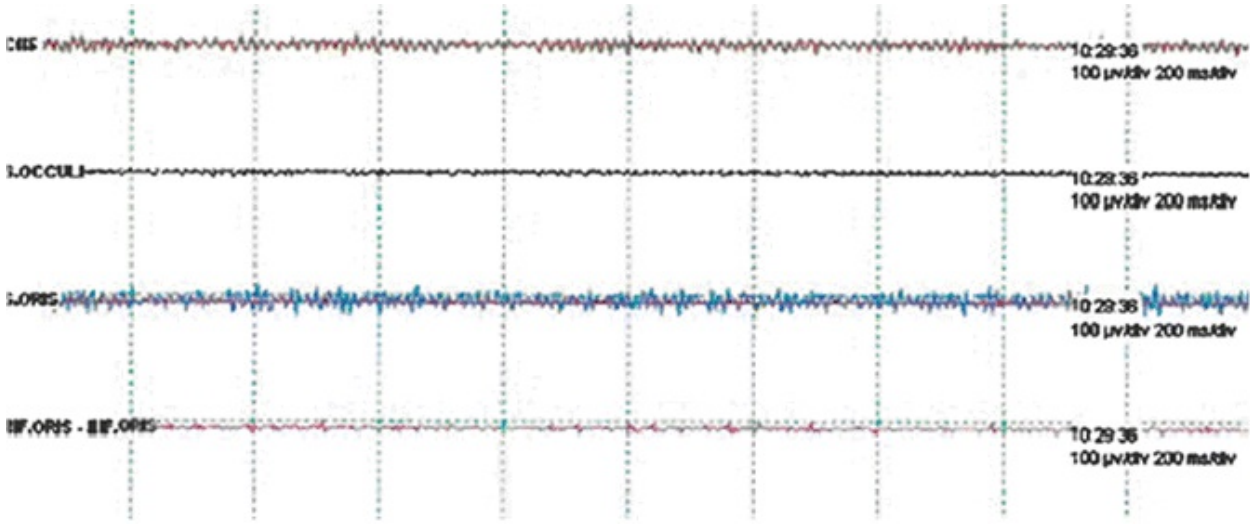

Fig. 29.3 Low-amplitude high-frequency activity as debulking procedure continues

Nitrous oxide, other inhalational anesthetics, and intravenous narcotics do not affect EMG readings. However, anesthetic depth from these agents must be sufficient to negate spontaneous activity from the vocal cords or facial nerve. With this patient, increased coarsening of the monitoring baseline was observed with small waveforms typically varying from 30 to 70 mV. This type of activity can occur immediately before the unparalyzed patient moves, and the neurophysiologist was worried that the patient was awakening [13]. In addition, the surgeon was concerned because it was becoming difficult to differentiate spontaneous activity from evoked activity.

The anesthetic concentration of both inhaled anesthetic and opioid infusion were increased, but a low level of activity was still noted and the surgeon wanted a quiet baseline to detect any nerve irritation during tumor debulking. The inhalational anesthetic was changed from sevoflurane to desflurane since sevoflurane has been associated with higher baseline EMG activity at the level of the larynx. In addition, the opioid infusion was further increased and additional 2 mg IV midazolam was administered (Videos 29.1 and 29.2). The background nerve rumble continued but it was noticed to have periodicity. After closer observation, it was determined to be associated with the use of the ultrasonic aspirator. The surgeon was informed and the ultrasonic power was reduced during the dissection. The background artifact was diminished and the surgical resection proceeded without incident.

As the tumor debulking continued, the vagal nerve EMG signal , which had waveforms noted at greater than 100 mV after stimulation, dropped to

less than 20 mV with stimulation of 2 mA. Latency was noted to be unchanged, and the results of evoked glottis movement with stimulation were equivocal. The surgeon began to assess the course of the nerve to determine any evidence of a lesion or if a clip or suture had entrapped the nerve. There was assurance by the anesthesiologist that no additional paralytic agent had been administered. The stimulating probe was checked and replaced and the stimulus current was noted to be at 1 mA. The endotracheal NIM tube impedance was also noted to be good. It was finally found that the monitor event threshold was set too high to produce stimulation artifact suppression. It was noted that, while stimulating the distal segment of the RLN, the evoked response occurred within this stimulus suppression artifact period and was falsely suppressed. The monitor was adjusted to shorten the stimulation artifact suppression and the signal returned with stimulation. This demonstrates that there are numerous reasons for intraoperative RLN stimulus errors and loss of signal. Once noted, the problem should be evaluated to assess that the monitors are working properly so that no false-positives or false-negatives are present (Fig. 29.4).

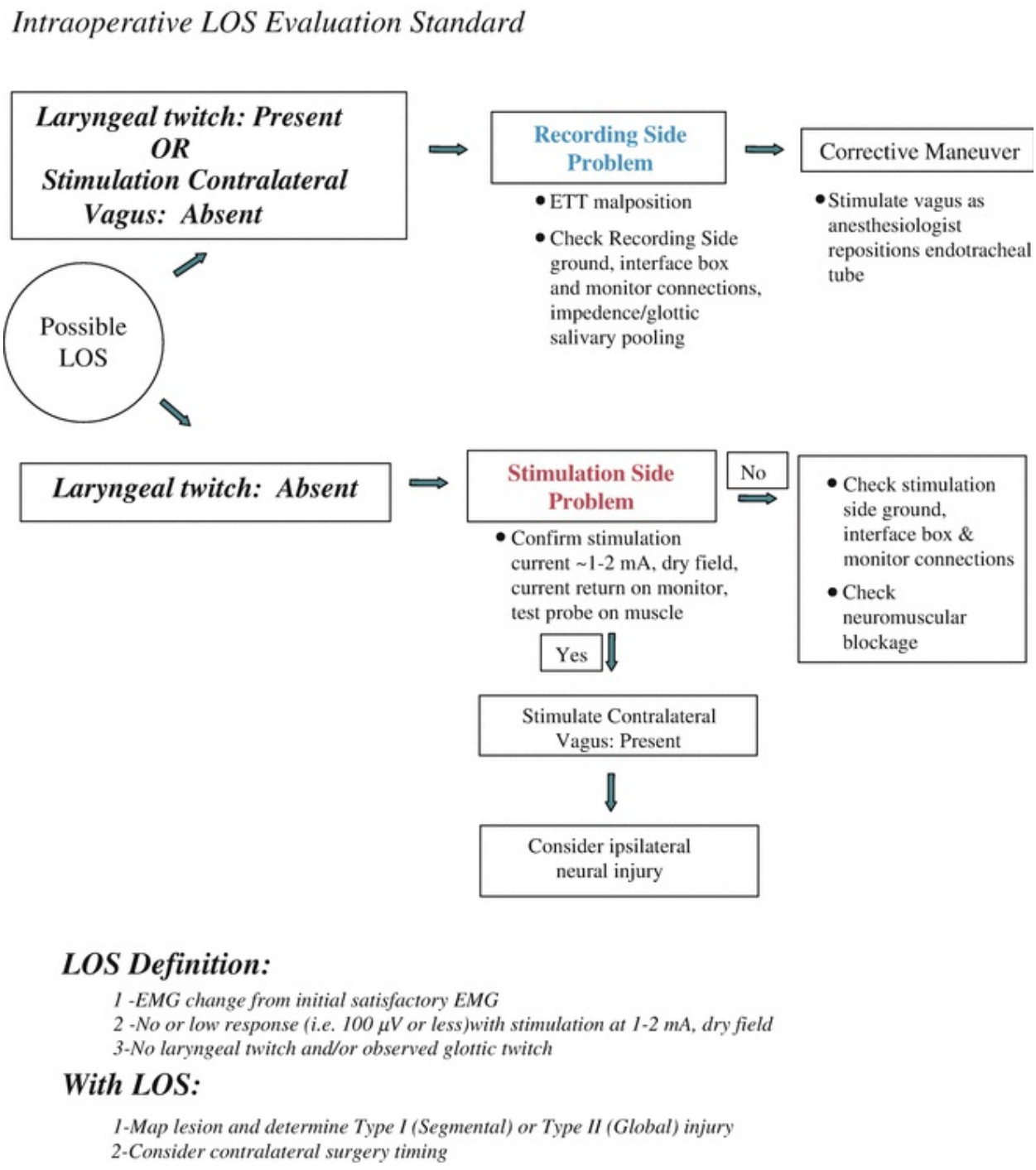

Fig. 29.4 Intraoperative loss of signal evaluation standard

The electroencephalogram (EEG) was continuously recorded from needle electrodes in an eight-channel bipolar montage to help with the assessment of anesthetic depth and to monitor cerebral responses in case of surgical compromise to the cerebral blood supply during neck dissection. The EEG

undergoes predictable pattern changes during anesthesia. This has been the basis for the introduction, over the last 20–30 years, of a considerable number of different processed, or quantitative, EEG-based anesthesia monitors, e.g., more recently, bispectral index (BIS) , patient state index (PSI) , and spectral entropy (SE) . Presenting the information as a single number is helpful for the clinical anesthesiologist. In the case of the BIS index scale of 100 to 0, decreasing values are associated with deeper planes of anesthesia. Thus, the primary utility of BIS is to ensure adequate hypnotic state during anesthesia and a lack of intraoperative awareness. Although processed EEG has been extensively used intraoperatively, the expert visual inspection of contemporaneous raw EEG in this specific clinical setting is still considered as clinically the most critical and superior “gold standard.” This is the reason why a real-time raw EEG must always be simultaneously displayed with any processed EEG index-based neuromonitoring [14].

The EEG responds to cerebral ischemia and if profound global ischemia is present for a sufficiently long period of time (e.g., longer than 10–20 s), EEG changes are readily observed. The EEG response to transient events and incomplete ischemia is not as robust and the arguments pro and con concerning its use in these circumstances have persisted. However, it is notable that in a survey of neuromonitoring for carotid endarterectomy, the EEG was the most commonly used neuromonitoring modality in over 67 % of all cases [15]. In our patient, tumor extension to the carotid artery carries the risk of arterial surgical injury or need for clamping during the neck dissection, which may result in transient cerebral hypoperfusion. In such a case, one approach may be the placement of a shunt to the internal carotid artery, but this has the inherent iatrogenic problems of increased risk of cerebral embolization of atherosclerotic debris and air, potential intimal damage with postoperative thrombosis, technical problems with shunt kinking or occlusion, and obstruction to surgical exposure during the tumor dissection. The EEG response to temporary carotid clamping provides a rationale for the use of selective shunting, i.e., based on the specific patient needs at the time, which improves its risk-benefit ratio. In the circumstances of carotid endarterectomy, selective shunting based on major changes in the EEG pattern has been reported to reduce the incidence of stroke tenfold [16]. Alternative monitors for adequate cerebral circulation and neuronal function such as transcranial Doppler measurements of cerebral blood flow velocity in the middle cerebral artery or oxygen saturation measurement using jugular

oxygen saturation or noninvasive cerebral oximetry are available, but during cranial base and neck surgery they are cumbersome and have found limited use.

The predominant EEG change with the onset of ischemia is one of progressive slowing with attenuation of fast activities and the (usually) sudden appearance of high-amplitude delta waves that ultimately transforms to an isoelectric pattern. Variants of theta prodrome or blockade of prior delta activity have also been described [17]. During carotid endarterectomy, a significant EEG change has been defined as a greater than 50 % decrease in amplitude of 8- to 15-Hz activities (fast alpha/slow beta) [18]. Ultimately, the key to utilizing the EEG as a monitor of cerebral hypoperfusion and ischemia is to associate a possibly deleterious intraoperative event (carotid clamp or injury, profuse blood loss, hypoxemia) with a rapid transition in the ongoing EEG pattern.

It is important to compare the symmetry of EEG pattern changes since unilateral frequency and amplitude changes ipsilateral to the occlusion occur twice as often as bilateral changes. If BIS is used, the EEG slowing is reflected by a rapid decrease in the index values with recovery when cerebral perfusion is adequately restored [19]. However, the BIS sensor is typically unilateral, which precludes interhemispheric comparison and consideration must be given when placing it on the side of the surgical procedure. In addition, BIS monitoring will only detect ischemia in the frontal lobes and may miss evidence of poor perfusion or ischemia in other brain regions. In some instances, SSEP monitoring may be used to detect both cortical and subcortical ischemia.

During neck dissection of the tumor in the vicinity of the carotid artery, ipsilateral augmentation of delta activity was noted in the frontal EEG of our patient. The asymmetry of these EEG changes and their association with surgical dissection adjacent to the carotid artery suggested intermittent obstruction to cerebral blood flow. It was also noted that arterial blood pressure had drifted below baseline pressure at that time. Normotension was promptly restored and the surgeon proceeded with gentler tumor manipulation. Thereafter, the EEG pattern returned to baseline and remained symmetric.

When neuromuscular relaxants are not used, the appearance of EMG “contamination” in the recorded EEG may also signal the presence of more intense surgical stimulation and the need to adjust the anesthetic level. Prior

studies have also found facial nerve EMG to be a better predictor of patient movement than BIS [12]. During tumor debulking, an increase in background EMG activity was reported. It was also observed at that time that higher frequency EMG activity was superimposed on the ongoing EEG pattern. Considering the possibility of a lighter plane of anesthesia, after a small bolus of propofol and an increase of the opioid infusion, the EMG and EEG changes subsided.

Outcomes

Postoperative care for each patient varies as to the extent of surgery. Patients with small lesions and minimal reconstructions can be done as same day surgical procedures with early discharge. If the facial nerve has been mobilized or extensive soft tissue dissection performed, the patient can be observed overnight with discharge the following day. This patient had dissection of vascular structures, extensive surgical intervention with free flap reconstruction of the surgical defect. The patient was observed in the neurological intensive care unit for several days for intensive wound care and observation of both hemodynamic and neurologic status. Temporal bone neoplasms are usually associated with high complication rates and prolonged recovery times. The surgery involved both the vagal nerve and portions of the recurrent laryngeal nerve. The patient had the potential for severe swallowing deficits and passive aspiration. He underwent a bedside vocal cord and swallowing evaluation as part of his postoperative assessment using a flexible fiber optic laryngoscope. Some patients will require adjunctive therapy including thyroplasty and possible palatal adhesion. Rehabilitation of the facial nerve and eye began immediately. A paralytic eyelid risks exposure keratosis and possible blindness. This patient suffered temporary facial paresis requiring the eyelid to be lubricated and taped at night. The postoperative facial paresis was managed conservatively. After several months without return of function, a nerve substitution procedure or static suspension procedure may be attempted.

Refinement in conducting biomaterials and stimulus generators has enhanced the safety of direct neural stimulation and recording. The application of intraoperative monitoring for neurotologic surgery should achieve the following objectives:

- Distinguish cranial nerves from soft tissue and tumor through selective

neural stimulation

- Expedite tumor excision by identifying regions of tumor not containing neurologic structures
- Provide early indication for surgical trauma
- Confirm neural responses at the end of surgery
- Identify and assess the degree of neurologic injury resulting from the surgery
- Maintain functional hearing if possible and identify the site of the lesion along the auditory pathway
- Maintain neurologic integrity after tumor removal

The past experience with intraoperative monitoring suggests that reduction of the CMAP response obtained with electrical stimulation of the nerve proximal to the tumor site loosely correlates with postoperative dysfunction. These observations require that more exacting correlations be obtained of electrophysiologic findings with ultimate prognoses.

In terms of outcomes, there are few controlled studies comparing monitored to unmonitored cases. However, the experience of most clinicians would favor that the preservation of neurologic function after anterior neck and skull base tumor surgery is improved with the use of these monitors. Most of these monitors have inherent strengths and weaknesses and may be affected by pharmacologic and physiologic factors that occur during surgery. Several drugs used clinically in the operative setting may interfere with the propagation of potentials along motor nerve and muscular membranes. The anesthesiologist must have an intimate knowledge of what effect these agents and physiologic events have on these monitoring modalities and must work in close collaboration with both the surgical and monitoring teams in order to produce an optimal outcome.

Questions

1. Which intraoperative neurophysiologic monitoring method is least affected by anesthetic agents?

   A. ABR

B. Corticobulbar MEP

C. Electrocochleography

D. EMG

E. SSEP

2. Which is not an objective for monitoring the cranial nerves?

A. Provides early recognition of surgical trauma

B. Monitors neurologic integrity after tumor removal

C. Expedites tumor excision by identifying regions of tumor not containing neurologic structures

D. Assessment of irrigation fluid used during the procedure

E. Identify the site of the lesion along neural pathways

3. Should long-acting muscle relaxants be used during FN EMG monitoring?

A. Yes

B. Only if partial paralysis used

C. No

D. Only if used with TIVA anesthesia

E. Only if used with warm irrigating solution

4. Which two selections below should be assessed after RLN loss of signal?

A. ETT position

B. Stimulation current at 1–2 mA

C. Neuromuscular blockade

D. All of the above

E. None of the above

Answers

1. C

2. D

3. C

4. D

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Footnotes

1 Asterisk indicates key reference.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_30

30. Carotid Surgery

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Keywords Carotid surgery – Anesthetic considerations – Neuromonitoring considerations – Anesthetic management – Carotid – Endarterectomy – Cerebral blood flow – Electrophysiological examination

Key Learning Points

- Ways to monitor for cerebral perfusion during CEA include: intraoperative clinical exam, electrophysiological exam, cortical cerebral blood blow, and cerebral oxygenation.

- The clinical intraoperative examination requires that the patient be fully awake in order to perform an accurate examination of mental status.
- The level of anesthesia should remain constant prior to clamping the carotid artery so that changes in TCD cerebral blood flow velocity and/or changes in the EEG can be attributed to changes in cerebral blood flow exclusively, without having pharmacological or physical changes interfering with assessment.
- When significant changes in the EEG are seen upon application of carotid artery clamping despite managing blood pressure, a shunt should be inserted to prevent global hemispheric ischemia. Similarly, >60 % decrease in cerebral blood flow velocity as seen with TCD should also necessitate insertion of a shunt.

Introduction

Patients have carotid artery surgery most commonly due to extracranial stenosis at the bifurcation of the common carotid artery into the internal and external carotid artery branches. Patients undergo carotid surgery if they are symptomatic to prevent fatal or disabling strokes. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST) have shown the benefit of carotid endarterectomy (CEA) in symptomatic patients with greater than 70 % stenosis at the internal carotid artery; CEA reduced the risk of fatal ipsilateral stroke by 80 % over the 2–3 years after surgery [1–3]. However, decisions about treatment for patients with moderate level of stenosis (50–69 %) must take into account recognized risk factors for a small benefit. Exceptional surgical skill is obligatory if CEA is to be performed on these patients [4]. Patients with stenosis of less than 50 % did not benefit from CEA [4].

There remains debate regarding the necessity of performing this type of surgery on asymptomatic patients. The Asymptomatic Carotid Atherosclerosis Study (ACAS) recommended addition of CEA to best medical therapy for asymptomatic carotid stenosis if CEA could be performed with a less than 3 % perioperative major morbidity and mortality rate [3]. Current American Heart Association/American College of Cardiology/American Stroke Association/Society for Vascular Surgery guidelines recommend (class IIa, level A evidence) CEA in asymptomatic

patients who have greater than 70 % stenosis of the internal carotid artery, if the risk of perioperative stroke, myocardial infarction (MI), and death is low [5]. These guidelines further recommend that selection of asymptomatic patients be guided by an assessment of patient comorbidity, life expectancy, and other individual factors and should include a thorough discussion of the risks and benefits of the procedure with an understanding of patient preferences [5]. Indexes for determining risks of complications that have been developed include age, dyspnea on exertion or rest, previous peripheral revascularization or amputation, chronic obstructive pulmonary disease (COPD), recent angina, and functional status [6].

Since 2000, there has been increasing interest in performing carotid artery angioplasty and stenting as an alternative to CEA; however; which patients are appropriate for this therapy is still unclear. Comparative studies have only recently been reported. The Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) showed that endovascular treatment decreased cranial nerve injury and hematoma risk compared with CEA [7]. The 30-day risk of stroke or death was high in both groups. In contrast, the Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy (SPACE) study was a European, multicenter study that showed a higher rate of ipsilateral stroke and death within 30 days after treatment in the patients randomized to stenting [8]. The Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA 3S) was terminated early due to safety concerns, and showed a significantly lower rate of stroke and death in the CEA group [9].

The International Carotid Stenting Study (ICSS) is a multicenter, international, randomized controlled trial that investigated the safety of endovascular treatment as compared with CEA in symptomatic patients. The results showed an increased risk for stroke, death, or procedure MI after 120 days in the endovascular treatment group [10, 11].

The Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST) is also a multicenter, international (the USA and Canada), randomized controlled trial that, in contrast to the ICSS trial, investigated symptomatic and asymptomatic patients. Their primary endpoints included the periprocedural risk of stroke, death, and MI, as well as the risk of ipsilateral stroke over a 4-year time frame [12]. The study concluded that CEA and endovascular therapy both have similar composite outcomes, long-term safety, and efficacy; however, endarterectomy had a lower rate of

perioperative stroke whereas the rate of coronary infarction was lower with endovascular treatment. However, younger patients had slightly better outcomes with endovascular therapy and older patients had better outcomes with endarterectomy, possibly due to technical factors: increased vascular tortuosity and calcification in elderly patients. The association of older age and increased risk of complications with endovascular therapy was also noted in the SPACE and ICSS trials [8, 10].

Therefore, trials thus far have shown that both endovascular and endarterectomy treatment are effective procedures, each of which may prove to be more beneficial to patients in specific subgroups.

In the remainder of this chapter, we will discuss two cases of typical patients undergoing a CEA, and the anesthetic and neuromonitoring considerations specific to maximize and measure cerebral perfusion. We will then discuss the neurophysiological changes that occur during the clamping of the carotid artery during surgery, two possible neuromonitoring changes associated with the carotid clamping, and the intraoperative management when these changes arise. Finally, we will analyze the possible causes of changes during neuromonitoring.

Case 1

The patient was a 72-year-old man with a 1-week history of left-sided hemispheric stroke affecting his right arm more so than his leg. The weakness had improved, but he still noted awkwardness of his right hand, especially when writing since he was right-handed. His past medical history was significant for coronary artery disease, status post coronary artery bypass surgery 1 year ago, and peripheral vascular disease, status post femoral-popliteal bypass on the right for claudication. He had a history of hypertension, for which he inconsistently took hydrochlorothiazide and amlodipine and a history of hypercholesterolemia, for which he took simvastatin. He did not complain of dyspnea on exertion, chest pain, or paroxysmal nocturnal dyspnea. He smoked one pack per day of cigarettes for 60 years.

On physical examination, his vital signs were a blood pressure of 160/90 mmHg (bilateral arms), a pulse of 80 beats per minute and regular, an oxygen saturation of 97 % on room air, and a respiratory rate of 16 breaths per minute. He weighed 85 kg and was 178 cm tall. Examination of his chest

demonstrated clear breath sounds bilaterally, and normal S1 and S2 heart sounds, without murmurs or extra heart sounds. Neurological examination was normal except for problems with naming, right arm drift, and impaired fine finger movements of the right hand. There was hyperreflexia on the right side, arm and leg, and a Babinski sign on the right. No sensory findings were elicited.

In preoperative examinations, magnetic resonance angiography demonstrated greater than 80 % stenosis of the left and a 30 % stenosis of the right internal carotid arteries (Fig. 30.1). Magnetic resonance imaging and cerebral Doppler further confirmed the identification and location of stenosis in the left internal carotid artery. The examination using a cerebral angiogram was not done for a couple of reasons: angiography does not provide adequate information into the physiological response of the cerebral vasculature to identify those patients at the greatest risk of hemodynamic ischemia [13]; in addition, studies have found a correlation between the use of cerebral angiography and neurological complication (stroke or transient ischemic attack), permanent neurological deficit, and even mortality [14–17].

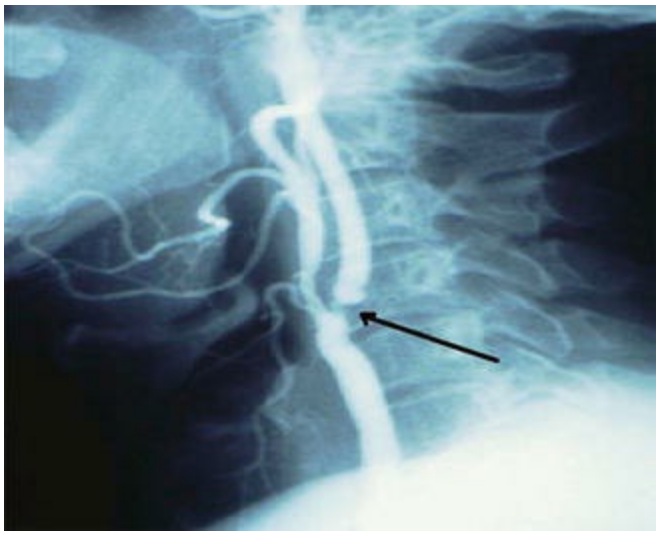

Fig. 30.1 This MRI angiogram is from a patient with left carotid artery stenosis just above the level of the carotid artery bifurcation (*arrowhead*)

The neurologist discussed the two possible treatment options of CEA, and carotid artery angioplasty/stenting with the patient. The patient elected to have CEA due to the decreased risk of periprocedural stroke.

Preoperative: Anesthetic and Neuromonitoring Considerations

Specific Goals in the Anesthetic Management of a Carotid Endarterectomy

Patients presenting for CEA typically have diffuse vascular disease, involving the heart and peripheral vascular circulation [18]. Because of significant stenosis of one or more major vessels supplying blood flow to the brain, maintaining normal arterial blood pressure, and avoiding hypotension are particularly critical to ensure adequate blood flow to the brain. These patients have more recently had blood pressures of 200/120 rather than 120/60. Therefore, a higher blood pressure is much more clinically typical of the patient's baseline physiology than a low one. Although avoidance of hypotension is a fundamental anesthetic goal during general surgery, the maintenance of adequate cerebral perfusion despite anesthetic pharmacological effects and surgical manipulation is especially critical during CEA. The rule of "high is good, low is bad" becomes particularly applicable for these patients having CEA.

Different Possible Monitoring Techniques to Assess Cerebral Blood Flow

There are four methods to monitor the brain for adequate cerebral perfusion : two are functional and two relate to cerebral blood flow. The two functional methods are (1) clinical intraoperative examination of an awake patient (see Chap. 18, "Anesthesia for Awake Neurosurgery"); (2) electrophysiological examination by evoked potential monitoring (see Chap. 1, "Somatosensory Evoked Potentials") or monitoring of spontaneous electrical activity from the cortex (see Chap. 10, "EEG Monitoring"). Monitoring spontaneous electric activity by electroencephalography (EEG) monitors activity that arises from the cortex (see Chap. 19, "General Anesthesia for Monitoring"). Evoked potential monitoring such as somatosensory evoked potentials (SSEP) evaluates both subcortical and cortical regions. Motor evoked potential monitoring (MEPs) can also monitor for blood flow to subcortical areas of the motor tract. The two blood flow-related methods are (1) cortical cerebral blood flow measurements, and (2) oxygen saturation of the cortex. Cortical

cerebral blood flow measurements can be determined directly with techniques utilizing xenon, but this technique has the associated technical difficulty of environmental removal. More commonly, a surrogate measure of cerebral blood flow is used such as transcranial Doppler (TCD) ultrasonography, which evaluates cerebral blood flow velocity in major cerebral arteries that are subcortical (see Chap. 13, “Transcranial Doppler”). Oxygen saturation of the cortex is based on the adequacy of cerebral blood flow and uses near-infrared spectroscopy (NIRS) to measure oxygen saturation of the cortex (see Chap. 12, “Near-Infrared Spectroscopy”).

The clinical intraoperative examination requires that the patient be fully awake in order to perform an accurate examination of mental status including language, as well as motor and sensory functions. The other techniques can be performed with patients under general anesthesia. Commonly, awake patients require the surgical area to be anesthetized using a regional technique with either a superficial or deep cervical block. The patient has to understand and agree with the expectation that they will be awake during their surgery, subject to the sounds of the operating rooms, and be able to participate upon request with neurological testing. In addition, the possibility of sudden airway compromise must be considered. A major advantage to awake neurological testing is the lack of needed equipment and expertise in using it to perform testing.

Although at our institution, EEG and TCD monitoring is considered the standard, at other institutions, SSEP and MEP monitoring are performed. Changes in median nerve SSEPs during carotid clamping is a sensitive marker of ischemia of the middle cerebral artery (MCA) territory. A limitation of this monitoring technique is false-negative SSEP results, reported in up to 3.5 % of patients [19]. However, to identify ischemia of the anterior cerebral artery and subcortical territories, tibial nerve SSEPs and MEPs should be used and decreases this false-negative rate [20]. It may be possible that triple monitoring (monitoring EEG, SSEP, and MEP) could improve sensitivity and specificity in finding ischemia during carotid clamping; however, studies addressing this question are limited and there is no evidence in the literature to support doing so as of yet [21, 22]. NIRS is also an assessment of cerebral flood flow by measuring oxygen saturation of the cortex. Although this measurement correlated with changes on EEG and awake testing, the positive predictive value of this modality of measurement is low [23, 24].

Agents used for achieving general anesthesia affect the various monitoring techniques differently. For example, SSEPs are significantly reduced when nitrous oxide is administered, whereas spontaneous electrophysiological activity from the cortex measured with EEG is enhanced with nitrous oxide due to its sympathomimetic properties [25].

Intraoperative Course

In the operating room, routine monitors were placed in addition to a preinduction left radial arterial line. The time during general anesthesia when intraoperative hypotension most commonly occurs is with and immediately after induction; therefore, a preinduction arterial line allows for rapid blood pressure monitoring and control during this interval. Two neuromonitors were placed: a transcranial Doppler ultrasound was placed on the left temporal area insonating on the left MCA (Fig. 30.1), and an EEG cap (Electro-cap International Inc., Eaton, OH) was applied with 16 electrodes placed according to the International 10–20 electrode placement system (Fig. 30.2). The EEG montage was a bipolar "double-banana" montage (Fig. 30.3).

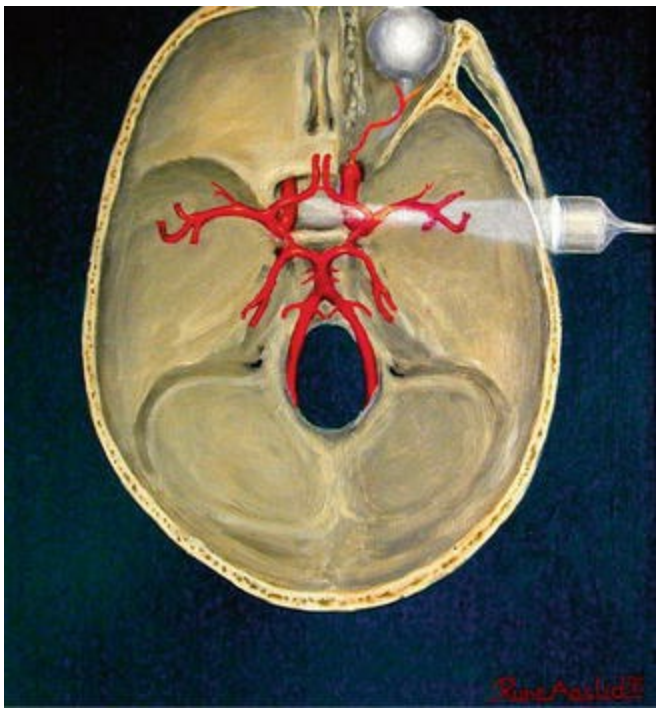

Fig. 30.2 Electroencephalography . *Top panel* depicts the International 10–20 System from (**a**) left and (**b**) above the head. This is a standard way of placing and naming electrode positions based on landmarks and distances between them on the patient's head: the anterior to posterior distance is from

nasion to inion, and the lateral distances from preaurical point on the left to preaurical point on the right. The “10–20” refers to percentages of these distances where electrodes are placed. All even-numbered electrodes are on the right and odd-numbered electrodes are on the left. “F”, “C”, “T”, “P”, “O”, and “A” are frontal, central, temporal, parietal, occipital, and ear lobe, respectively. The subscripts refer to F_P, and “Z” is midline. The “double banana” montage is a bipolar montage where two strings of electrodes are arranged anterior to posterior parallel to the midline and parallel to the circumference. Viewed from above, the electrodes form a shape that looks like two bananas. *Bottom panel* depicts Montage: Bipolar and Referential. All electrical potentials are potential differences. These differences are generated from differential amplifiers by comparing pairs of neighboring electrodes called a bipolar montage, shown on the left, or by comparing pairs of electrodes all referred to the same reference electrode, called a referential configuration, shown on the right. This figure was made available at http://www.bem.fi/book/13/13.htm#03 under the terms of GNU Free Documentation License, Version 1.3

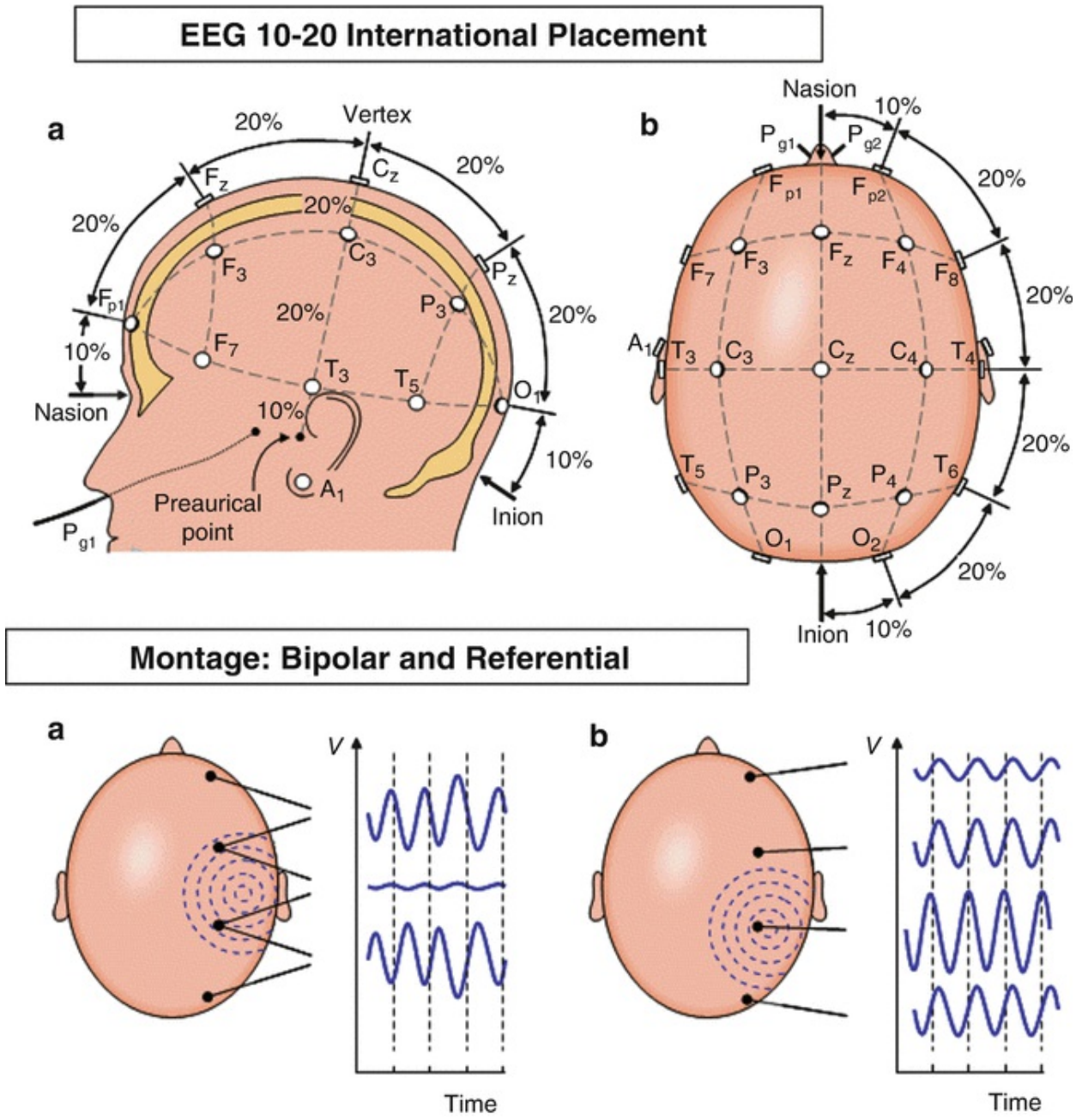

Fig. 30.3 Transcranial Doppler ultrasonography . This figure is a horizontal view of the head with the TCD probe on the left temporal area insonating on the ipsilateral middle and anterior cerebral arteries. It demonstrates where our TCD was placed on the patient to obtain the tracings shown below. This figure was made available at http://en.wikipedia.org/wiki/File:Transcranial_doppler.jpg under the terms of GNU Free Documentation License, Version 1.3 by Rune Aaslid

The patient was sedated with fentanyl, 100 μg, and midazolam, 3 mg. He was pre-curarized with rocuronium, 10 mg, 3 min prior to induction. He was induced with etomidate, 20 mg, and succinylcholine, 140 mg. Intubation was

with a Macintosh size 3 blade and the vocal cords were seen. A #8.0 endotracheal tube passed without difficulty. Anesthetic maintenance for the patient was with 0.7 % isoflurane and 50 % N_2O. Since his blood pressure decreased after induction, a phenylephrine drip (40 μg/mL) was started at 30 mL/h to maintain his blood pressure at 150/90 mmHg. Five minutes before clamping the carotid artery, 6500 mg of heparin was administered (0.08 μg/kg) intravenously and the resultant activated clotting time (ACT) was 254 s. The phenylephrine drip rate was increased to 60 mL/h and the arterial blood pressure increased to 185/100 mmHg during this pre-cross clamp interval.

Clamps were applied sequentially to the superior thyroid artery, the common carotid artery, internal carotid artery, and the external carotid artery.

Transcranial Doppler Ultrasonography

TCD was monitored throughout the procedure . In addition to temperature, blood pressure, and end-tidal carbon dioxide ($PeCO_2$), TCD measurements (peak and mean MCA flow velocities), pulsatility index (PI), and delta %, which is the change in mean cerebral blood flow velocity compared to baseline, were obtained at specific times during surgery as part of our research protocol. These times are:

- baseline (before induction)
- pre-clamp (at heparin injection)
- clamping, shunt insertion (if required)
- post-clamping (15 min after clamping)
- clamp release
- 5-min post-release
- 10-min post-release

At each event, the surgeons were informed of relevant TCD information.

To measure the MCA flow velocity, a 2-MHz Doppler probe was placed over the temporal bone ipsilateral to the operative side (left); the MCA at a depth of 50 mm was the main detected target. Prior to surgical draping, a headframe (Model 600, Spencer Technologies, Seattle, WA) was placed around the patient’s head to hold the Doppler probe transducer firmly in

position throughout the procedure.

At baseline, the patient's MCA velocity and PI were within normal range, varying from 57 to 63 cm/s (normal, 35–100 cm/s) and 0.90 to 1.05, respectively (Fig. 30.4a, Table 30.1). This broad velocity range can be explained by decreasing blood flow to the brain with age, the dependence of cerebral blood flow on the partial pressure of CO_2 and the level of cerebral metabolism [17]. Right after clamping, MCA velocities quickly dropped by 64 % from the pre-clamp value, resulting in timed average mean velocity (TAMV) of 21 cm/s and PI of 0.5 (Fig. 30.4b, c). In comparison to TAMV, PI is usually more sensitive measurement for detecting changes in cerebrovascular resistance due to clamping. This significant decrease in MCA velocity demonstrated the patient's poor collateral blood flow. No shunt was used despite the fact that there was more than 50 % decline in flow velocity from the baseline. Cerebral tolerance to carotid clamping was assessed by an equation by mean velocity MCA% (mv MCA%):

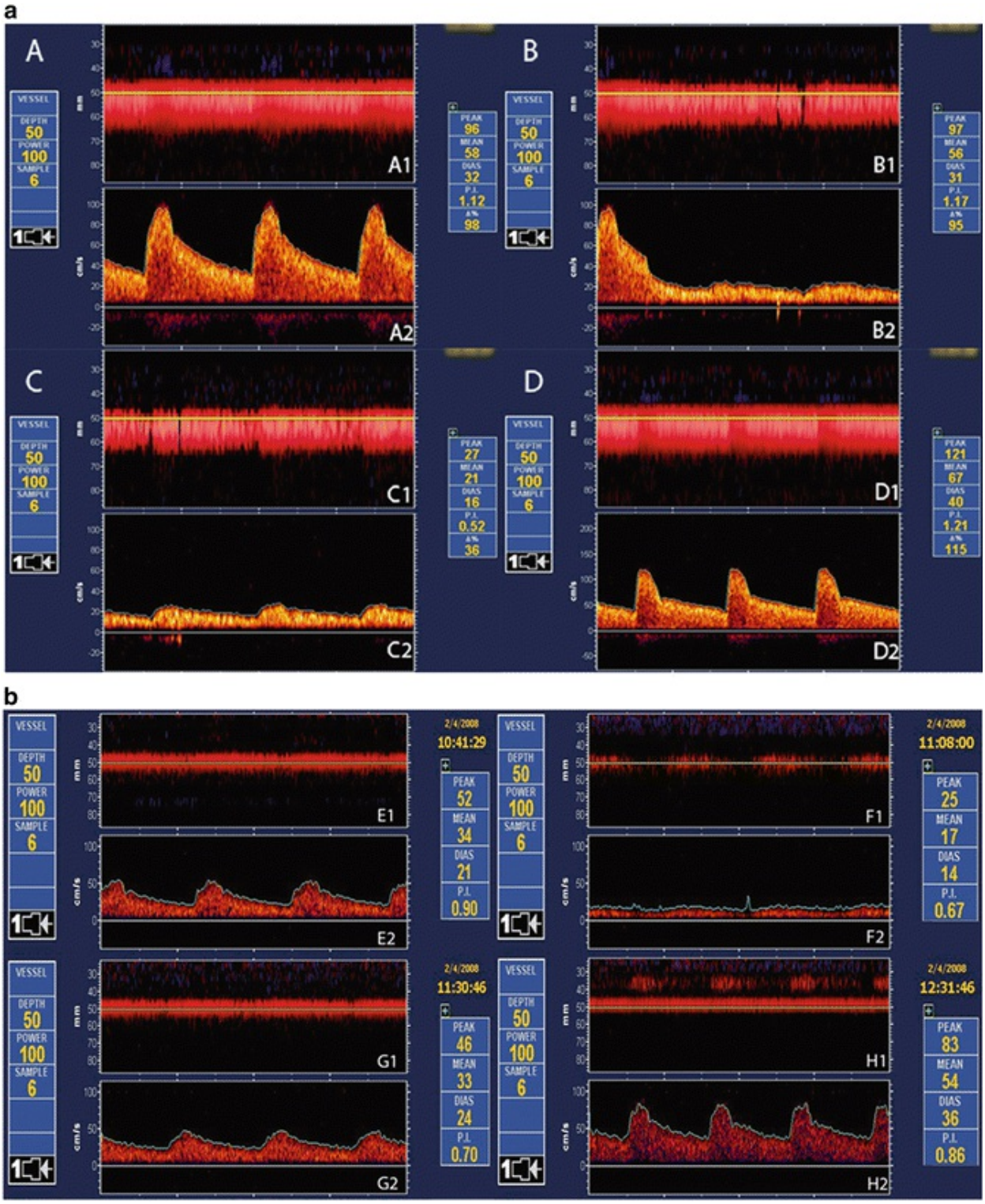

Fig. 30.4 Transcranial Doppler ultrasound tracings . Patient 1: TCD tracings at four different time points relative to cross-clamping the carotid artery: (**a**) before, (**b**) immediately at, (**c**) during, and (**d**) after unclamping the carotid artery. Each tracing consists of two frames, "1" and "2". "1" is the Power M-mode tracing (analogous to the ultrasound mode) on the "y-axis" in mm and visualizes flow from 30

to 80 mm from the surface of the scalp. “2” is the Doppler velocity in cm/s on the “y-axis” at a distance indicated by the yellow line in the Power M-mode. The “x-axis” is in seconds between the time markers. The boxed numbers to the left of each tracing show the depth in mm, power, and sample volume. The boxed numbers on the right of each tracing show the peak, mean, diastolic velocities, pulsatility index (PI), and the percentage change from baseline of the mean cerebral blood flow velocity. Patient 2: TCD tracings at four different time points relative to cross-clamping the carotid artery: (**e**) before, (**f**) immediately at, (**g**) after shunt insertion, and (**h**) after shunt removal and unclamping the carotid artery. Each tracing consists of two Fig. 30.4 (continued) frames, “1” and “2”. “1” is the Power M-mode tracing (analogous to the ultrasound mode) on the “y-axis” in mm and visualizes flow from 30 to 80 mm from the surface of the scalp. “2” is the Doppler velocity in cm/s on the “y-axis” at a distance indicated by the yellow line in the Power M-mode. The “x-axis” is in seconds between the time markers. The boxed numbers to the left of each tracing show the depth in mm, power, and sample volume. The boxed numbers on the right of each tracing show the peak, mean, diastolic velocities, and pulsatility index (PI)

Table 30.1 TCD monitoring data from patient 1, who did not have a shunt placed[a]

	Peak velocity (cm/s)	**Mean velocity (cm/s)**	**Pulsatility index**
Baseline	86	60	0.90
Clamp on	28	21	0.50
Post-shunt	N/A	N/A	N/A
Post-clamp	33	25	0.54
Clamp off	113	60	1.32
5 min post-release	74	44	1.39
10 min post-release	96	56	1.17

[a]MCA velocities and PI at post-clamp were measured

$$(\text{mvMCAclamping}/\text{mvMCApre-clamping}) \times 100$$

Generally, a shunt is placed when mv MCA % is less than or equal to 15 % [13]. In this case, the calculated mv MCA% was 33 % and therefore a shunt was not placed.

After release of the clamps, MCA velocities rapidly increased above pre-clamp value (TAMV, 60 cm/s; PI, 1.32) and then decreased toward the pre-clamp value (TAMV, 44 cm/s; PI, 1.39 at 5 min after clamp release; TAMV, 56 cm/s; PI, 1.17 at 15 min after the release) (Fig. 30.4d).

Case 2

We also present another patient, with an 80 % stenosis of the left internal carotid artery demonstrated by magnetic resonance angiography. Overall, the TCD monitoring during the procedure demonstrated a similar trend of

changes in MCA velocity and PI to that seen with the first patient. In comparison to the first patient, his baseline peak and mean MCA velocities were lower (peak, 52 cm/s; mean, 34 cm/s) (Fig 30.4e, Table 30.2). After clamping, these velocities instantaneously and drastically went down to 19 and 30 cm/s, respectively (Fig 30.4f). Although mv MCA% calculated using the formula provided above indicated 35 % decrease (which is above the suggested cutoff number; 15 %), a shunt was still placed in order to add sufficient blood flow that had not been reached previously due to inadequate collateral flow. The problem was quickly fixed by shunt placement, and the velocities were raised closer to his baseline values (Fig. 30.4g). Once the clamps were released, MCA velocity increased above pre-clamp value (TAMV, 52 cm/s) and then dropped toward the baseline value (TAMV, 40 cm/s; PI, 1.01 at 5 min after clamp release; TAMV, 41 cm/s; PI, 0.98 at 15 min after clamp release) (Fig. 30.4h), similar to what we saw in the first patient.

Table 30.2 TCD data on patient 2, who underwent shunting[a]

	Peak velocity (cm/s)	Mean velocity (cm/s)	Pulsatility index
Baseline	52	34	0.90
Clamp on	19	12	0.52
Post-shunt	42	30	0.72
Post-clamp	N/A	N/A	N/A
Clamp off	80	52	0.84
5 min post-release	67	40	1.01
10 min post-release	66	41	0.98

[a]The velocities and PI at post-shunt replaced the values of post-clamp

EEG Monitoring

EEG monitoring for a CEA can be performed with either needle electrodes placed subcutaneously on a patient's scalp, or with surface EEG electrodes—either using an EEG cap with electrodes sown into a standard configuration that is then applied to the patient's head like a swim-cap, or with surface electrodes placed on the scalp and held on with collodion adhesive. Needle electrodes have an advantage of having very low resistance, which improves the recording. The disadvantages of needle electrodes include pain upon

insertion, which necessitates a post-induction placement, needle-stick safety hazard, and minor bleeding at the insertion sites. Likewise, the major advantage of the EEG cap is a comfortable application, which can be done pre-induction. The major disadvantage is the potential of having high resistance due to the fact that the electrodes sit on top of the scalp and are connected to the scalp EEG via conductive gel (Electro-Gel, Electro-Cap International, Inc., Eaton, Ohio). Another disadvantage is getting the collodion out of the patient's hair after surgery.

In this patient, as mentioned above, an EEG cap (Electro-cap International Inc., Eaton, OH) was applied with 16 electrodes placed in according to the 10–20 International placement positions (Fig. 30.2). The EEG montage was a bipolar "double-banana" montage (Fig. 30.2).

The agents used for anesthetic maintenance are important to consider when monitoring the EEG. N_2O is sympathomimetic and increases the frequencies recorded on the EEG, allowing for a greater difference in the event of ischemia and slowing of the EEG [25]. Likewise, avoiding a high concentration of volatile agent, in our case isoflurane, avoids a dose-dependent slowing of the EEG [26]. Most importantly, it is important to maintain a steady level of anesthetic agents during the period of clamping to avoid changes that may be attributable to changes in agent, as opposed to changes in cerebral blood flow.

Upon clamping the carotid artery, changes in velocity were noted in the TCD recording, the EEG recording was closely monitored. No changes were seen on the EEG in this patient. The surgeon was informed and surgery proceeded without the placement of a shunt.

In contrast to this patient, we present an example of a third patient who had similar changes on TCD, but had marked unilateral slowing of frequency on EEG (Fig. 30.5). The surgeon was informed, and a shunt was placed.

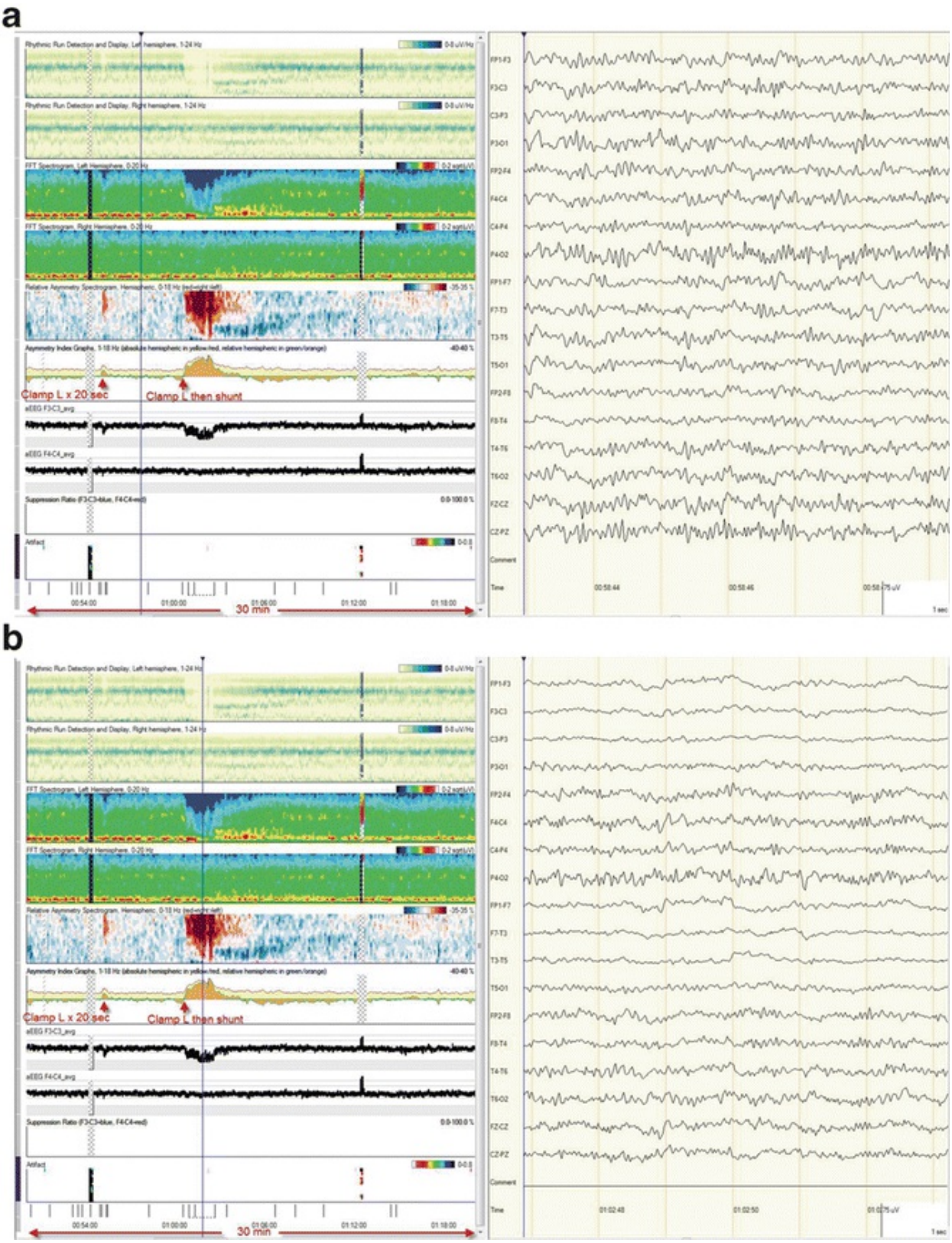

Fig. 30.5 Electroencephalogram with processed EEG . Electroencephalogram from a patient showing

the 30-min processed EEG before, during, and after clamping the carotid artery in left panels (**a**) and (**b**). The "raw" EEG is shown on the right panels without EEG changes in (**a**) and with EEG changes in (**b**). *Both* (**a**) *and* (**b**) *are indicated by the vertical line on the processed EEG*. The processing is performed using software from Persyst Development Corporation (Prescott, AZ, http://www.persyst.com). "Raw" EEG is shown with odd numbered electrode on the left and even on the right. A complete description is provided in Fig. 30.3

Analysis of the Cause of Intraoperative Neuromonitoring Changes

There are various possible explanations for a change in EEG and TCD at the time of carotid clamping. Broadly, these include physical changes, e.g., hypothermia; pharmacological changes, e.g., the administration of lidocaine, induction agents, or an increase in volatile agents; as well as ischemic changes due to decreased blood flow after clamping of the carotid. As previously mentioned, the reason the level of anesthesia should not change prior to clamping the carotid artery is that we would like to attribute changes in TCD cerebral blood flow velocity and/or changes in the EEG to changes in cerebral blood flow exclusively, without having pharmacological or physical changes interfering with assessment.

Since the brain has a rich vascular supply, reduction of cerebral blood flow by more than 60 % is needed to change the EEG predictably. Changes in cerebral blood flow velocity of this magnitude greatly increase the likelihood of developing new neurologic findings after surgery [27].

Changes in cerebral perfusion are accompanied by compensatory changes in cerebrovascular resistance. In the TCD, this is reflected in a decrease in cerebral blood flow velocity initially greater than is seen a few minutes later. The change in cerebral vascular resistance is also seen in the PI is a calculated measurement of the systolic cerebral blood flow velocity minus the diastolic cerebral blood flow velocity divided by the mean cerebral blood flow velocity [28]. It reflects changes in peripheral cerebral resistance. Normal values of this unit-less variable are 0.6–1.1. Changes in cerebral blood velocity occur immediately and can be observed immediately by the TCD, in contrast to changes of the EEG, which can have a time delay after the clamping of the carotid artery. Decreases in cerebral blood flow velocity reflect percentage decreases in cerebral blood flow without indicating what the actual value of cerebral blood flow is if the diameter of the insonated vessel remains constant. In addition to monitoring the percent decrease in cerebral blood flow, the TCD can be clinically useful in ensuring blood flow

in patients with shunts. Some surgeons who always place shunts across the surgical site still use TCD monitoring to indicate that the shunt is actually working well [29, 30, 53].

While an absolute absence of cerebral blood flow causes significant delta waves to be seen in less than 10 s, generally clamping of the carotid artery reduces but does not eliminate cerebral blood flow [31]. Therefore, insufficient cerebral blood flow may take a minute or more to develop. Depending on the collateral flow present, decreased cerebral blood flow less than 20 mL/100 g of brain tissue/min results in ipsilateral or bilateral decrease of fast frequency EEG waves (>5 Hz), and a predominance of high-amplitude slow frequency waves less than 4 Hz [32–35].

While one might be inclined to think that one monitor more likely predicts neurologic outcome than another, the purpose of the TCD and EEG is to address the issue of the adequacy of collateral circulation when the carotid artery is clamped. Dr. Rampil demonstrated that patients who had normal baseline EEG prior to surgery and experienced greater than 9.5 min of cerebral ischemia (as indicted by the EEG) developed new neurologic deficits [36]. However, most patients who develop new neurologic findings after CEA do so because of emboli [37]. The effect of emboli cannot be determined by the EEG, but the presence of emboli can be seen by TCD. Gaunt presented evidence that most emboli are gaseous, but greater than ten particulate emboli are associated with both incipient carotid artery thrombosis and the development of major neurological deficits [4].

Management of Changes

If there are changes in cerebral blood flow reflected by any of our cerebral perfusion monitors, after letting the surgeons know, arterial blood pressure should be increased [38]. While in theory the mean arterial pressure should be the parameter to be followed, this is a calculated variable and reflects changes in systolic blood pressure. Therefore, our rule of thumb is to look to the systolic blood pressure as the variable we increase. Remember, almost all of our elder patients have seen systolic arterial blood pressures greater than 200 mmHg more recently than 120 mmHg. Systolic pressure is increased while the surgeons complete insertion of a shunt from below the surgical site to above the site. An infusion of phenylephrine is commonly used to increase peripheral vascular resistance and increase systemic arterial pressure without constricting cerebral vessels [39].

When significant changes in the EEG are seen upon application of carotid artery clamping , a shunt should be inserted to prevent global hemispheric ischemia. Similarly, a greater than 60 % decrease in cerebral blood flow velocity as seen with TCD should also necessitate insertion of a shunt. We have seen clinical cases where there were no significant EEG changes with significant decreases in cerebral blood flow velocity and patients awoke with transient neurologic and neuropsychometric changes [40]. These two modalities look at different components of cerebral perfusion. Emboli can be clearly seen with dissection of the carotid artery and its bifurcation when using TCD, and particularly when the internal carotid artery clamp is released [29].

Outcome

Prior to unclamping the carotid artery, and particularly the internal carotid artery, systemic arterial blood pressure is reduced to normal or in a range up to 20 % below normal. This is frequently achieved by stopping the phenylephrine infusion. If cerebral ischemia had been seen by TCD or EEG when the carotid artery was occluded, then it is seen again when the carotid artery is reclamped to remove the shunt. There is increasing concern that of the 10–15 % of patients who develop hyperperfusion with release of the carotid artery clamp, many of them will also develop significant neurocognitive changes [41–48]. It may be that the usual definition of hyperperfusion of twice baseline cerebral blood flow is too stringent and that small increases also produce neurologic problems.

Fortunately, the incidence of new neurologic deficits after CEA surgery is less than 5 % [1, 49]. Some of us (EJH) have made a career defining more subtle changes in cognitive functioning [50–52]. However, in most patients these findings resolve by 6 months [50].

The patients, in both scenarios described in this chapter, awoke quickly in the operating room at the end of the surgery without any new neurological deficits.

Conclusion

During CEA, neuromonitoring is critical to ensure adequate cerebral perfusion. Neuromonitoring can be used to determine if a shunt is necessary

to increase global perfusion when the carotid artery is clamped. Alternately, if shunts are routinely used by the surgeon, then neuromonitoring can be used to determine that the shunt is working correctly. Our primary tool to prevent ischemia is systemic arterial blood flow: keep it where the patient normally is, or higher. Remember the golden rule: low is bad, high is good.

Questions

1. During a carotid endarterectomy, which of the following changes are suggestive of ischemia?

    A. Ipsilateral increase in frequency of EEG

    B. Ipsilateral decrease in frequency of EEG

    C. Increase in MCA flow velocity on TCD

    D. Patient continues to talk and squeeze contralateral hand

2. During carotid clamping during an endarterectomy, EEG frequency is noted to decrease and MCA flow velocity decreased by 60 %. Appropriate management includes:

    A. Surgeon notification

    B. Blood pressure increase to an MAP 20 % above baseline

    C. Shunt placement by surgeon

    D. All of the above

Answers

1. B

2. B

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Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_31

31. Anterior Cervical Spine Surgery

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Keywords Anterior cervical discectomy and fusion – Recurrent laryngeal nerve – Somatosensory-evoked potentials – Motor-evoked potentials – Electromyography – Erb's point

Key Learning Points

- The safety of ACDF for patients with cervical radiculopathy, with or without neurophysiologic monitoring, is extremely high, with very low rates of temporary or permanent neurologic sequelae.
- The risk of neurologic injury during an ACDF for those patients with myelopathic symptoms and requiring a cervical corpectomy, laminectomy, or foraminotomy, while unknown, is thought to be higher than that for patients with a radiculopathy alone. For these cases, multimodality neurophysiologic monitoring (SSEP, MEP, EMG) may play a significant role in detecting, and hopefully averting, impending neurologic injury.
- While EMG monitoring is beneficial in detecting mechanical insults to the nerve roots or spinal cord, it lacks the ability to detect changes related to ischemia.

Introduction

An anterior cervical discectomy and fusion (ACDF) is a routinely performed surgery to relieve spinal stenosis, remove intervertebral disk and bony matter that may be impinging upon neural elements, and also to mechanically stabilize the cervical spine after such material is removed. Herniated intervertebral disk material or osteophytes in the spinal canal or intervertebral foramina may cause compression of the spinal cord or nerve roots, respectively. Such compression may lead to radiculopathy, myelopathy, or both, and patients can present with significant symptoms such as pain, numbness, paresthesias, weakness, or paralysis.

The ACDF procedure can be performed at one or multiple levels with varying amounts of complexity depending on the extent of neural tissue compression. An anterior approach in the cervical spine is often preferred to a posterior approach for discectomy due to anatomic favorability. However, in more extensive anterior surgeries, a posterior cervical fusion may also be warranted to stabilize the cervical spine (*see* Chap. 32, “Posterior Cervical Spine Surgery ”). The safety of an ACDF for patients with cervical radiculopathy, with or without neurophysiologic monitoring, is extremely

high, with very low rates of temporary or permanent neurologic sequelae [1]. One exception to this is the occurrence of a C5 palsy , which may have an incidence of up to 5.9 %. While it is unclear why the C5 nerve root is at higher iatrogenic risk than other nerve roots, this complication seems to be associated with more profound spinal cord compression and possibly ischemic axonal injury secondary to microvascular trauma [2]. Other rare forms of injury include hypoglossal nerve injury , C6 injury causing a Horner's syndrome due to sympathetic chain injury, and basilar artery ischemia due to excessive cervical extension.

In contrast, the risk of a neurologic injury during an ACDF for those patients with myelopathic symptoms requiring cervical corpectomy, laminectomy, or foraminotomy, while unknown, is thought to be higher than that for patients with radiculopathy alone [3]. Likewise, upper cervical spine surgery is often considered more risky than surgery at lower cervical levels [4]. For any of these cases, and particularly for those requiring complex reconstruction, multimodality neurophysiologic monitoring may play a significant role in detecting, and hopefully averting, impending neurologic injury [5–7]. The most frequently used modalities of neurophysiologic monitoring in these cases are somatosensory-evoked potentials (SSEPs), spontaneous electromyography (EMG), and transcranial motor-evoked potentials (MEPs) [8, 9], with dermatomal sensory-evoked potentials and direct epidural (D wave) MEP recordings being used to a lesser degree. Transcutaneous, mid-thoracic D-wave recording has been advocated due to the false-positives that may arise from SSEP recording alone and in circumstances in which transcranial MEPs may be difficult or impossible [10].

Neurophysiologic monitoring has generally been accepted during the surgical management of scoliosis, but has mixed acceptance during cervical operations such as ACDF [11, 12]. The value of SSEPs alone has been questioned in these cases; however, the combined usage of SSEP, EMG, and MEP monitoring is gaining support [13, 14]. When SSEPs are used for ACDF, median nerve responses are generally thought to be more helpful when higher cervical levels (C3–C6) are operated on, while ulnar nerve responses are more frequently favored when lower cervical levels (C6–T1) are the operative target [15].

Because SSEPs function specifically as a monitor of the posterior elements of the spinal cord (i.e., dorsal columns), and nonspecifically as a

monitor of the entire spinal cord, they are prone to false-negatives in the detection of injuries to the anterior spinal cord (e.g., corticospinal tracts) [3, 12] and/or nerve roots. Hence, spontaneous EMG monitoring has been advocated in these surgeries, in combination with SSEPs and MEPs, as a way to specifically monitor the motor component of the nerve roots [4]. Identification of muscle-specific spontaneous EMG discharges would be the most efficient indicator of mechanical irritation of a nerve root, preceding the more concerning changes in SSEPs and MEPs, which might be related to ischemia.

While EMG monitoring is beneficial in detecting mechanical insults to the nerve roots or spinal cord, it lacks the ability to detect changes related to ischemia [16]. Therefore, many authors have advocated the routine use of MEPs in those patients thought to be at high risk for intraoperative ischemia due to compression (e.g., severe myelopathy due to critical spinal canal stenosis, severe spondylolisthesis) [13, 17]. SSEPs may be less sensitive than MEPs in this regard, as anterior (motor) spinal elements tend to be at higher risk during anterior spinal surgery. In all reported case series, MEPs were employed in conjunction with SSEPs in order to improve both sensitivity and specificity of the neurophysiologic monitoring being performed. In most published reports, SSEPs have a low but finite incidence of false-positives (Taunt et al. [12] reported 1.8 %), and an even lower incidence of false-negatives [1]. MEPs and EMG may serve a confirmatory role in these cases.

A study by Cole et al. [5] revealed that for single-level spine surgery , neuromonitoring was only helpful in lowering neurologic complication rates for lumbar laminectomies, with no added benefit for lumbar discectomies, lumbar fusions, or ACDFs. Furthermore, a large prospective study by Helseth et al. [6] found that outpatient microsurgical cervical decompression was feasible without neuromonitoring and with a very low overall complication rate. Others, however, advocate for multimodality neuromonitoring, even in single-level ACDFs. Epstein argues that because quadriparesis/quadriplegia is one of the more common reasons for malpractice suits after single-level ACDFs, neuromonitoring (and specifically MEP monitoring) should be employed in these cases.

Another consideration related to nervous system injury during ACDF, and also a concern during thyroid and parathyroid surgery , is injury to the recurrent laryngeal nerve (RLN). This is the most common type of neurologic injury related to ACDFs and can be caused by direct surgical trauma to the

nerve, nerve compression between a retractor and the shaft of the endotracheal tube, high endotracheal tube cuff pressure, or a combination of these elements [18]. RLN injury usually occurs on the side of the surgical approach. The incidence of injury has been shown to increase with the number of cervical spine levels operated on, when the lowest level instrumented is T1, when the surgical approach is from the patient's left side, when the Cloward retractor is opened greater than 3 cm to expose the spine, and with previous surgery at that location [19, 20]. Although the incidence of postoperative vocal cord dysfunction is 2–5 %, most vocal cord injuries resolve within several months.

The RLN is often monitored using EMG, specifically by employing an endotracheal tube adapter or commercially available endotracheal tube with surface electrodes that contact the true vocal cords. Direct visualization of the vocal cords and the electrodes on the endotracheal tube is necessary to ensure proper positioning of these devices (depth and tube rotation). A new method for monitoring RLN function is the use of corticobulbar track motor-evoked potentials with recording from the vocal cords [21]. Many practitioners use succinylcholine, rather than a longer acting muscle relaxant, to facilitate intubation in these cases so that muscle function will recover before the time that monitoring is necessary (although this practice is not always required, since the vocal cords are relatively resistant to the effects of intermediate acting muscle relaxants when given in judicious doses) [22]. An alternative method for intubation if succinylcholine is contraindicated is to use ephedrine, 15 mg; remifentanil, 4 μg/kg; and propofol, 2 mg/kg. Dimopoulos et al. [23] have gone further to describe a method by which they objectively quantify the amount of RLN irritation in ACDFs by the amount of EMG activity, and determined that longer surgeries, multilevel surgeries, previous surgical intervention, and the use of self-retaining retractors are all associated with more RLN irritation. Also, it is important to be cognizant of the use of topical lidocaine on or near the vocal cords, as might be performed during an awake intubation, as this might preclude adequate monitoring of the RLN [24]. Despite this, RLN monitoring is used more commonly in thyroid and parathyroid surgery, being used less frequently for ACDF surgery where other neuromonitoring modalities predominate. Another and long used way to minimize laryngeal nerve is to deflate the cuff of the endotracheal tube. However, there is concern about aspiration in addition to circuit leak.

Case 1

A 68-year-old male, 85 kg, ASA PS 3, with a past medical history of poorly controlled DM and HTN, presents for an ACDF of C4–C7 (right-sided approach) for severe myelopathic and radiculopathic symptoms . The patient has been complaining of bilateral upper extremity weakness, numbness, and bilateral lower extremity paresthesias. A cervical MRI examination reveals critical spinal canal stenosis at C5 and C6, and extensive osteophytic lesions throughout.

The patient was monitored with standard ASA monitors , and multimodality neurophysiologic monitoring was employed, including SSEPs, MEPs, and EMG. Because of the patient's myelopathy, an awake fiberoptic intubation was planned so as to clinically examine the patient after intubation. Intubation proceeded smoothly, a neurologic examination was performed with no change from preintubation status, and anesthesia was then induced. Induction consisted of propofol, remifentanil, and rocuronium. Rocuronium was chosen to facilitate positioning because prepositioning responses were not deemed necessary and its relatively rapid metabolism would allow MEP and EMG monitoring as soon as possible. If monitoring of the patient's neck position had been required (such as with an unstable cervical spine injury), the avoidance of muscle relaxants could have been planned. A radial arterial line was then placed to facilitate close monitoring of the patient's hemodynamic status. Maintenance of anesthesia consisted of propofol, 50–150 μg/kg/min; remifentanil, 0.05–0.5 μg/kg/min; and desflurane end-tidal 3.3 % (0.5 MAC) in oxygen and air (FiO_2 0.5); no muscle relaxant was used after intubation. Stimulating and recording electrodes were placed for the planned neuromonitoring, and the patient's arms were padded, tucked at his sides, and wrapped firmly with sheets. Baseline SSEPs and MEPs were obtained after a "steady state" of anesthesia, with slightly diminished amplitudes in the upper extremity SSEPs, more diminished amplitudes and increased latencies in the lower extremity SSEPs, and slightly diminished MEPs in all four extremities.

What are the possible causes for the diminished baseline SSEP and MEP signals in this patient?

The diminished responses, involving both SSEPs and MEPs, observed at baseline (i.e., before the start of surgery), were not caused by surgical maneuvers, since surgery had not commenced. Moreover, because a global

diminishment in signals was seen without complete loss of the signals, a positional or technical cause was unlikely. Physiologic factors such as hypothermia and hypotension may produce such changes; however, these too are unlikely reasons for the changes because both parameters were within normal limits. In some patients, blood pressure that is borderline-low may lead to a global decrease in signals. Because hypotension is a common cause of SSEP changes in these patients [25], the anesthesiologist will often raise the blood pressure by 20 % while continuing to troubleshoot for a cause. In this case, raising the blood pressure did not significantly correct the observed low signal parameters.

At this point, we are left with whether anesthetic effects, underlying pathology, or a combination of the two is responsible for the decreased signals. Certainly, the diminished MEP signals could be partially related to the residual effects of the muscle relaxant used during intubation. A train-of-four (TOF) nerve stimulation test would help identify such a cause. This was done in this case and showed 80 % TOF recovery. Increasing the MEP stimulation intensity by 50 V produced a better global MEP signal. Other anesthetic drugs may also be contributory, especially in the presence of a volatile anesthetic. Sedatives/hypnotics (e.g., propofol) and opioids tend to have minimal effects on SSEPs and MEPs unless they are given in large doses. Volatile anesthetics, however, may cause more depression of evoked potentials; nonetheless, when given at 0.5 MAC or less as part of a balanced anesthetic technique, the volatile anesthetics are usually compatible with adequate evoked potential tracings unless the patient has significant neurologic dysfunction (e.g., myelopathy). To test the possibility that the volatile agent was responsible for the decreased SSEP and MEP signals in this case, the desflurane was turned off and the propofol infusion was increased to maintain anesthetic depth. No sizable improvement was seen in either the SSEP or MEP amplitudes after sufficient time to remove the volatile agent. During the following 20 min, SSEP signals remained stable, whereas MEP signals improved slightly; consistent with near-complete recovery from the muscle relaxant.

Most likely in this patient, severe cervical canal stenosis coupled with severe peripheral neuropathy secondary to poorly controlled diabetes are the major contributing factors to the globally diminished evoked potentials seen at baseline.

The surgery was begun and proceeded uneventfully throughout exposure.

During the course of deeper dissection, however, a slight decrease in the amplitude of the SSEP of the left arm was noticed. Repeated testing confirmed further SSEP deterioration by more than 50 % in amplitude in both the left arm and left leg although the left Erb's point waveform was not changed (Fig. 31.1). No changes were seen on the right side. EMG activity was also negative. The surgeon was notified and MEPs were tested, which revealed a complete loss of signals of the left hand and left leg with normal right-sided responses.

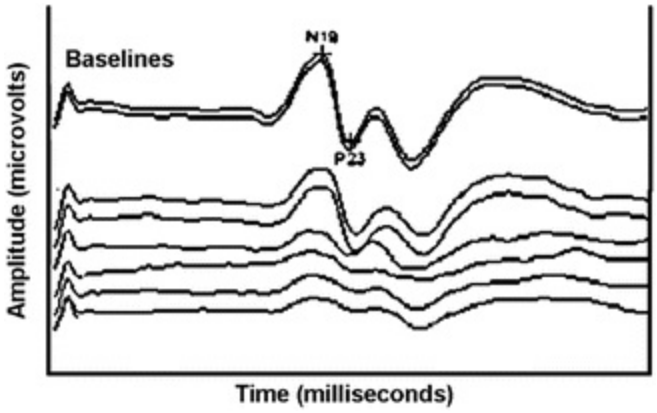

Fig. 31.1 Representative of cortical SSEP changes caused by unilateral carotid occlusion due to retractor malposition

What are the possible causes for the diminished left-sided SSEP and MEP signals at this point in time?

Given that this change is focal (not global) in nature, anesthetic and physiologic causes for the diminished signals are less likely. Hence, surgical, technical, or positional causes should be sought to explain this evoked potential change. In this case, the anesthesiologist raised the blood pressure by 20 % above its current level while troubleshooting other causes. The position of the arms was checked while the neuromonitoring technologist was assessing the technical fidelity of the signals. There were no apparent technical or positional problems, leaving us only with a potential surgical cause for these changes. The surgical causes for signal changes may be related to mechanical stress, thermal injury, surgical injury, or ischemia. Mechanical stresses are usually associated with EMG discharges and are related to either nerve root irritations or dural insults. Neither instrumentation nor thermal devices were being used on any of the neural structures at this time. Ischemia to the left arm could explain MEP changes but it would not

explain the SSEP changes in the lower extremity nor those in the upper extremity (since the response from Erb's point was normal). In fact, occlusion of the right-sided cerebral blood supply is a more likely cause of the changes that were seen. An ischemic or hemorrhagic stroke to the right hemisphere, caused by manipulation of an atherosclerotic right carotid artery, is a possibility. Even more likely is cerebral ischemia caused by obstruction of the right carotid artery, which is in close proximity to the surgical field and may be distracted by the surgical retractor.

Absent blood flow within the right carotid artery was confirmed by the anesthesiologist by palpation of the right superficial temporal artery (transcranial Doppler could also have been used for this indication). The surgeon was informed and repositioned the retractors, which resulted in an immediate restoration of the right superficial temporal pulse as well as both the MEP and SSEP waveforms.

Case 2

A 36-year-old, ASA PS 1, woman without significant past medical history is scheduled for a C5–C7 ACDF for disk herniation and removal of an osteophyte. Anesthesia is performed with standard ASA monitoring and neurophysiologic monitoring consisting of EMG recorded from the deltoid, biceps, and triceps, SSEPs, and MEPs for the upper and lower extremities. Normal baselines of all monitoring parameters were obtained prior to surgery. Discectomies at the C4–5, C5–6, and C6–7 interspaces were performed and significant bony overgrowth along the pedicles of the vertebral canal was removed. At one point, during shaving along the pedicle of C5, there was a burst of spontaneous EMG activity recorded from the biceps (Fig. 31.2).

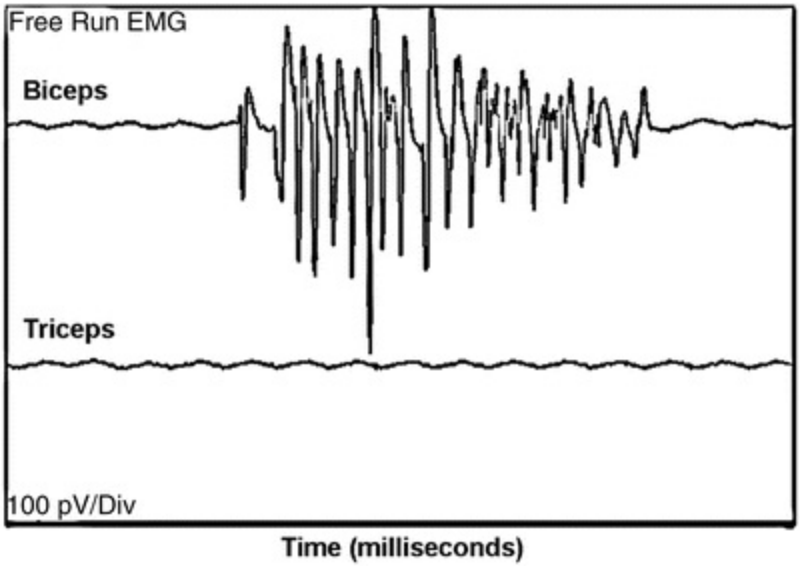

Fig. 31.2 Spontaneous EMG firing at the biceps, with minimal noise in other muscles

What could be the cause of this EMG change ?

EMGs are used during such operations to continuously monitor for mechanical irritations to the spinal cord or nerve roots induced by the different surgical instrumentation used. EMG discharges are related to mechanical insults that cause depolarization, and are not related to ischemia. The premise of using EMG monitoring is to alert the surgeon to changes related to such mechanical irritation before a greater insult occurs that can lead to more permanent neuronal damage. Notably, “light” anesthesia can be a cause for abnormal EMG discharges that are not surgically related (however, light anesthesia usually produces activity in multiple muscles rather than the one muscle noticed here). The use of other electrical devices, such as cautery, may also produce “false” EMG discharges. EMG discharges have been graded in intensity according to a four-level system [16]. In this case, the discharges were mild, the surgeon was notified, and the discharges disappeared immediately thereafter. The surgeon continued to work but a few minutes later severe discharges reappeared (which might indicate the potential for a larger mechanical and/or ischemic insult). The surgeon was again notified and paused surgical activity while MEPs were obtained. During this time, SSEPs were also being acquired. These modalities were used as confirmatory tests in the presence of the EMG changes, testing for any potential spinal cord injury that might be caused by ischemia as a result of mechanical distortion.

MEPs were acquired and revealed no changes. SSEP responses were also stable. How should we proceed?

Because the only change seen in the neurophysiologic monitoring was an increase in EMG activity at C5 or C6, there is most likely a surgical reason for the observed change. In this case, the most likely scenario is that the C5 or C6 nerve root emerging from the intervertebral foramen has been mechanically irritated during attempted decompression at the foramen. EMG provides a real-time alert for impending neurologic deficits related to a mechanical insult. The SSEP and MEP waveforms were most probably not affected because they tend to transmit along major peripheral nerves, which originate from many individual nerve roots, thus masking irritation or impending injury to a single nerve root.

A disadvantage of EMG monitoring compared to MEP monitoring is that it can be "contaminated" by artifact from various sources, including patient movement, Bovie interference, etc., while this is not the case with the relatively high amount of stimulation needed to generate MEPs. A potential advantage of EMG monitoring compared with MEP monitoring, as was seen in this case, is the continuous nature of EMG signal acquisition, which might detect compression/injury to a nerve with greater sensitivity than an evoked MEP, whose acquisition is intermittent and would require deliberate acquisition at or after the time of the insult to the nerve to detect it. Most importantly, as illustrated in this case, EMG also has the advantage of being able to detect irritation to a single nerve root, which is less likely with either SSEP or MEP monitoring, because these modalities monitor major mixed sensory/motor nerves and muscles that have overlapping nerve root innervation.

The surgeon stopped working in the C5–C6 nerve root area and the EMG recording returned to a silent state. The surgeon proceeded to complete the surgery without any further changes in the neuromonitoring signals. The patient was awakened, extubated, and examined neurologically, with no change in the examination as compared with her preoperative status.

Case 3

A 47-year-old woman, 140 kg, ASA PS 2 with a past medical history of morbid obesity, is scheduled for a C3–C5 ACDF (right-sided approach) for intermittent and nonreproducible radiculopathic symptoms in her left upper

arm. Her clinical examination is not consistent with any myelopathy, and a cervical MRI seems to confirm this (no spinal cord impingement). Of note, on her physical examination, the patient has a Mallampati Class IV airway with a thyromental distance of 4 cm. Previous anesthetic records indicate that she was easy to ventilate by bag/mask but difficult to intubate, requiring fiberoptic intubation.

How should the airway be secured in this patient? Should an awake or asleep technique be used? Would neuromonitoring, after induction but prior to intubation, be of any value in this case? What neuromonitoring modalities should be used for this case?

Based on the patient's previous airway history, anawake or asleep fiberoptic technique would seem prudent. The advantage of an awake fiberoptic intubation, besides maintaining spontaneous ventilation, would be to retain the ability to examine the patient for evidence of new radiculopathic/myelopathic symptoms during and after intubation. An asleep fiberoptic intubation could also be performed, with SSEPs and EMG acquired pre- and postintubation (under "steady state" anesthesia), to confirm that neurologic injury from intubation had not occurred. Whether intubation is performed awake or asleep, the use of flexible fiberoptic bronchoscopy should limit the amount of neck movement and cervical subluxation compared to a direct laryngoscopy.

For this surgical procedure, any combination of the neuromonitoring modalities mentioned above could be used depending on the level of concern for spinal cord, nerve root, orperipheral nerve injury .

Because no myelopathy is suspected in this patient, and because of a known ability to mask ventilate her in the past, an oral asleep fiberoptic intubation is chosen to secure the airway.SSEPs of the median and posterior tibial nerves are obtained as well as EMG of the deltoid, biceps, and triceps muscles. All of these neuromonitoring modalities remained unchanged before and after intubation under a "steady state" of anesthesia, being careful to record signals after recovery from the succinylcholine (i.e., no residual effect on EMG) used to facilitate intubation. A small amount of rocuronium (20 mg) was then given to assist during positioning and exposure. Anesthesia was maintained with propofol, 100–150 μg/kg/min, and fentanyl, 1–5 μg/kg/h (TIVA), which were infused through a dedicated intravenous (IV) catheter placed in the left arm. Fluids and bolus medications were injected into the IV catheter placed in the right arm. SSEP baselines were obtained from all four

extremities and were found to be robust and reproducible. Before surgical incision, the neuromonitoring technologist reports a greater than 50 % decrease in the amplitude and an increase in the latency of the SSEP signals recorded from the right arm (Fig. 31.3).

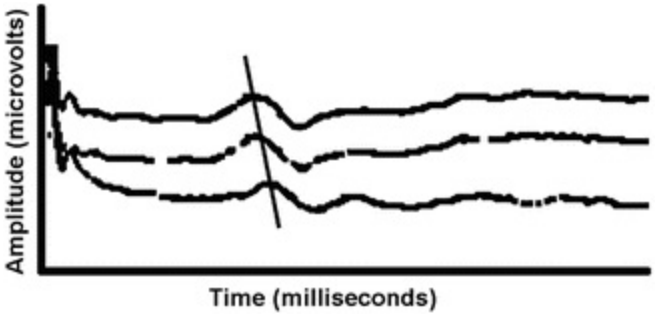

Fig. 31.3 SSEP changes at the cervical level due to excessive traction on the shoulder caused by taping too tightly

What could be the cause of these right arm SSEP changes ? What should be done to correct these changes and avoid injury?

Since surgery has not yet begun, surgical causes for the observed changes are eliminated, and because this is a unilateral change, anesthetic and physiologic causes are unlikely. The possibility of a technical cause exists (e.g., due to a decrease in stimulation intensity caused by partially dislodged stimulating pads). All stimulating and recording pad placements were checked, and all other technical parameters were within normal limits. On further evaluation of the right shoulder position, the shoulder was found to be taped down to the table rather tightly, placing it in undue traction. The tape was somewhat released, which resulted in the return of the SSEP signals to baseline. Presumably, the observed change was related to stretching of the brachial plexus, and if left uncorrected might have led to a longer-lasting neurapraxia. A similar effect could result from straps attached to the wrists to allow traction, which would improve visualization of the spine under fluoroscopy. Other causes of a change in the SSEP responses from the upper arm were also excluded (such as a tourniquet effect of the noninvasive blood pressure cuff or drapes used to hold the arm or a cold arm from infusing cold intravenous fluids).

As surgery proceeded, the anesthesiologist noticed a few episodes in which the blood pressure and heart rate suddenly and inexplicably rose in association with an elevated Bispectral Index (BIS) value, seeming to

indicate periods of “light” anesthesia. These were treated with IV boluses of medication. However, after three such episodes, the anesthesiologist added desflurane, 6.6 % end-tidal concentration (1 MAC), to control these episodes. The patient’s vital signs and BIS value promptly returned to those of a “normally” anesthetized state, and the case continued. The surgeon continued to work near the spinal cord and a few minutes later the neuromonitoring technologist noticed a decrease in the amplitude of all the cortical SSEPs without any changes to the cervical or Erb’s point SSEP waveforms and without any EMG discharges.

What could be the cause of this global change in cortical SSEPs alone?

This is a global change that is isolated to the cortical leads with normal signals from both Erb’s point and the cervical spinal cord. Technical, positional, and surgical causes for such a change are unlikely because of the global nature of the signal aberrations. Physiologic factors are a possibility, but none can be identified, as blood pressure and temperature were found to be within normal limits. Hence, an anesthetic cause, namely the addition of a volatile agent at 1 MAC, seems to be the most likely candidate for the observed changes. Inhalation agents administered at less than 0.5 MAC can be used in most patients with good SSEP signal acquisition. Levels higher than this may be problematic in some patients, especially in those patients who have pre-existing diminished baseline SSEPs. In this case, the inhalation agent was decreased to 0.5 MAC and the SSEP signals recovered to baseline.

Near the completion of surgery, the cortical, cervical, and Erb’s point SSEP responses from the left arm began to deteriorate, while the right arm signals remained stable (Fig. 31.4).

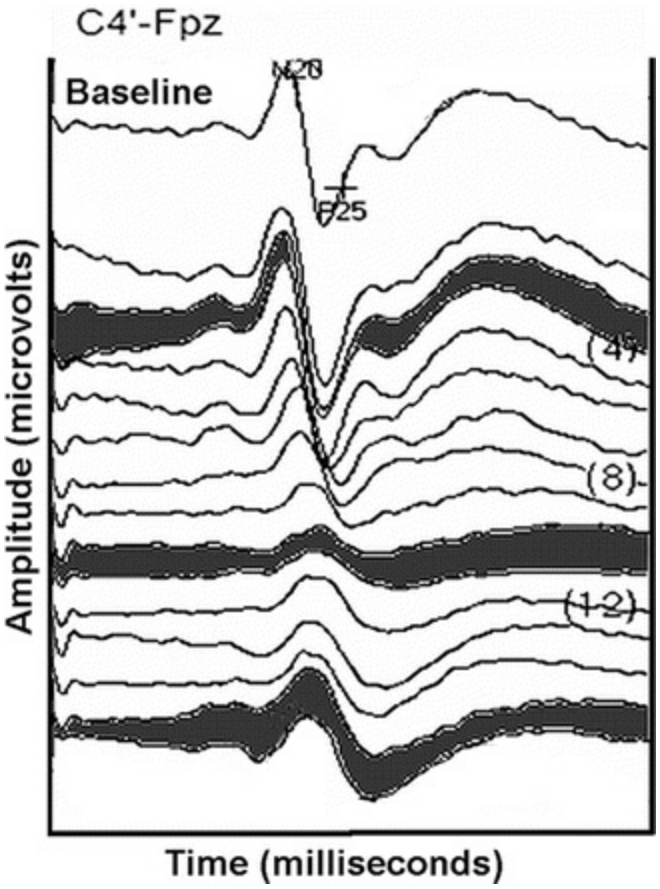

Fig. 31.4 SSEP changes during intravenous infiltration of the extremity

What might be the cause of this type of change in SSEPs?

Since this was a unilateral change, it is unlikely to be caused by anesthetic agents or physiologic alterations (with the possible exception of regional hypothermia causing a cold arm). A positional cause might be possible, but the timing of the changes does not support this as there was no recent change in thepatient's position . Technical causes for the change were checked by the neuromonitoring technologist and were ruled out. Furthermore, a surgical cause for the changes was deemed unlikely as the surgery was at the stage of closure with no direct manipulation of the spinal column, and no bleeding or hematoma on the spine was visualized.

In this case, the disappearance of theleft upper extremity SSEP waveforms seems to coincide with "light" anesthesia, as evidenced by the previously mentioned changes in hemodynamic vital signs, necessitating the addition of a volatile agent. These changes, when taken together, should prompt the anesthesiologist to examine intravenous lines, drug infusion

pumps, and so on for appropriate drug delivery. If drugs or fluids have extravasated into an extremity, a decrease in SSEP signals from that extremity might be expected. This would be due to expanding tissue planes and, subsequently, to a greater distance between the stimulating electrode and the peripheral nerve being stimulated.

To counteract this problem, stimulation intensity can be increased at the peripheral nerve site that is stimulated. Another option to improve signal strength is to exchange the surface transcutaneous stimulating electrodes for needle stimulating electrodes, which can be quite helpful in cases in which there is a significant amount of adipose tissue or edema (or extravasated fluid), causing the nerve to be more distant from the skin surface.

The left upper extremity was examined and appeared to be in a good position without any excessive extension, abduction, or external pressure. The extremity, however, was noted to be somewhat tense in the forearm, and drug extravasation was suspected. The pulse oximeter was placed on the left hand and obtained a strong signal.Radial and ulnar pulses were confirmed as being present on the affected side. The intravenous catheter on the left arm was removed, and the intravenous medications were subsequently connected and delivered to the IV catheter in the right hand. The transcutaneous stimulating electrodes were exchanged for needle stimulating electrodes in the affected extremity, and the SSEP signals gradually but dramatically improved. The remainder of the case was uneventful.

Conclusion

An ACDF is a commonly performed surgical procedure with a generally low, but finite, incidence of nervous system injury. Neurophysiologic monitoring is often employed for these cases, especially in complex operations so as to avert neurologic injury. Because of the potential for central as well as peripheral nervous system injury during these cases, it is important to apply a systematic approach when troubleshooting changes in neuromonitoring signals, paying close attention to how the different modalities of the neuromonitoring interact to paint a picture of the status of the nervous system at any given point in time.

Questions

1. What is the value of recording the Erb's point waveform on SSEPs when performing an ACDF?

2. Why might MEPs be an especially useful monitoring modality, in addition to SSEPs and EMG, in ACDF?

3. What differences exist in the anesthetic regimen that can be used when SSEPs are used alone versus when SSEPs are used in conjunction with MEPs?

Answers

1. Changes in the Erb's point waveform (increased latency or decreased amplitude) without changes in cortical or subcortical signals may signal a problem with conduction through the upper extremity due to localized effects.

2. MEPs will monitor the anterolateral spinal cord (corticospinal tracts) for ischemia, which may be more at risk than the posterior spinal cord (dorsal columns) during anterior cervical surgery.

3. The use of MEPs prohibits or severely limits the amount of muscle relaxant that can be used, whereas with SSEPs alone, muscle relaxant may actually help to improve the signal obtained. In both cases, 0.5 MAC or less of volatile anesthetic should be used to allow signal acquisition.

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Footnotes

1 Asterisk indicates key reference.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_32

32. Posterior Cervical Spine Surgery

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Keywords Posterior cervical fusion – Posterior – Cervical – Fusion – Cervical pedicle – Lateral mass screw indications – Decompression

Key Learning Points

- Cervical Spondylotic Myelopathy

A. Most common cause of progressive neurologic decline in patents over 50.

B. Primarily affects C5–7

C. Relatively minor neck injuries can result in devastating spinal cord injury

D. MRI T2-weighted spinal cord enhancement represents spinal cord damage due to ischemia, edema, or compression.

E. Extensive spinal cord decompression variably results in improved neurologic function, but does prevent further decline.

- Long-term complications of extensive posterior decompression include

A. Development of thick fibrous scar causing spinal cord compression

B. Progressive cervical kyphosis in decompression without three column stabilization

- Lateral mass and pedicle screw fixation with rods has become the technique of choice for posterior stabilization due to:

A. Superior deformity correction

B. Improved immediate and long-term three-column stabilization

C. Versatility for application in many conditions

- Laminoplasty is an alternative to decompression and fusion in patients with spinal stenosis with intact cervical architecture and limited pain due to degenerative changes.
- Intraoperative neurologic monitoring with somatosensory, transcranial motor-evoked and nerve root EMG monitoring is helpful in preventing devastating intraoperative injury.

A. Pre-positioning baselines are helpful in detecting issues with

surgical positioning

B. Responses to intraoperative degradation in signals include examining technical, physiologic, surgical, and anesthetic factors.

C. Communication and rapid action are imperative to decrease complications.

Introduction

Posterior cervical spine surgery is usually performed for multilevel compression, instability of the spine, fracture, degenerative disk disease, or stabilization for tumor removal. In addition, candidates for surgery include patients who have progressive neurologic changes with signs of severe spinal cord compression and neurologic changes that include:

- Weakness in the arms or legs
- Numbness in the hands
- Fine motor skill difficulties
- Imbalance issues
- Gait changes

Common posterior surgical procedures include laminoplasty, laminectomy with or without instrumentation and fusion, and laminotomy.

A laminoplasty relieves spinal cord compression by cutting one side of the lamina completely and the other partially, enabling it to swing open like a door, relieving compression on the spinal cord. It is then held open with titanium spacers or bone graft and plates.

A posterior cervical laminectomy and decompression with/without instrumentation and fusion is most commonly performed for patients with deformity, instability, cord compression and other spinal conditions, such as tumors, and infections. This surgery extensively removes the lamina, thickened ligament, and/or bone spurs that are putting pressure on the spinal cord and nerve roots and instrumentation restores three-column stability while bone fusion takes place.

Cervical laminotomies are limited procedures performed to relieve pressure on a compressed spinal nerve. Only a portion of the lamina is excised to relieve compression of nerve roots.

Intraoperative neurologic monitoring is frequently performed in conjunction with laminoplasty and multilevel laminectomies. Important monitoring modalities to detect spinal cord compromise include somatosensory-evoked potentials, transcranial motor-evoked potentials, and selective nerve root EMG monitoring.

Posterior cervical stabilization and fusion with or without decompression is a commonly performed procedure for fracture and/or dislocation of the cervical spine, to stop the progression of spinal deformity, or to decompress the spinal cord and/or nerve roots (tumors, infections, deformity, and stenosis). While fracture repair and nerve root decompression s are usually limited to one or two levels, decompression of the spinal canal for tumors, infections, and cervical spinal stenosis can be multilevel procedures (Fig. 32.1).

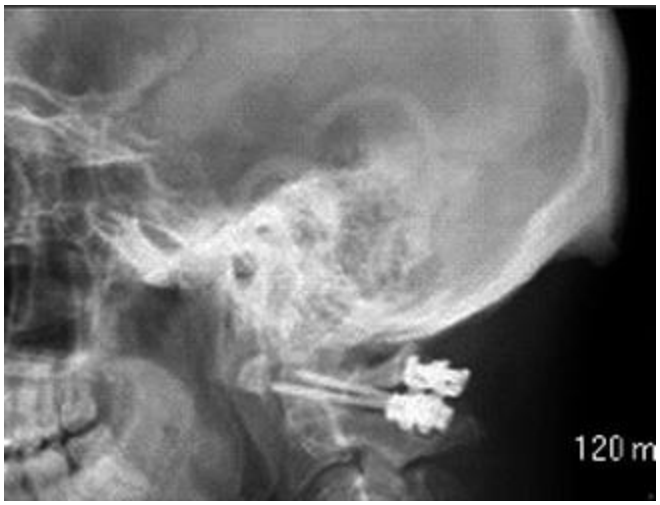


Fig. 32.1 Posterior cervical instrumentation and fusion of C1 ring fracture

In preparation for these surgical procedures, a thorough evaluation of the bony and ligamentous anatomy guides the surgical approach and technique. This evaluation is accomplished with standard radiologic evaluations (anterior, lateral, flexion, and extension views of the cervical spine), computed tomography (CT), and magnetic resonance imaging (MRI).

X-ray and CT scan are used primarily to evaluate bony abnormalities, while an MRI allows for evaluation of discoligamentous pathology and

provides clear visualization of the spinal cord with any impingement or compression. If severe, spinal cord damage can be visualized with the MRI T2-weighted and STIR (short tau inversion recovery) images, spinal cord enhancement on the T2-weighted images may reflect pathologic changes due to inflammation, edema, ischemia, gliosis, or myelomalacia [1, 2] (Fig. 32.2). MRI with intravenous contrast can also help to assess blood flow as well as tumor margins.

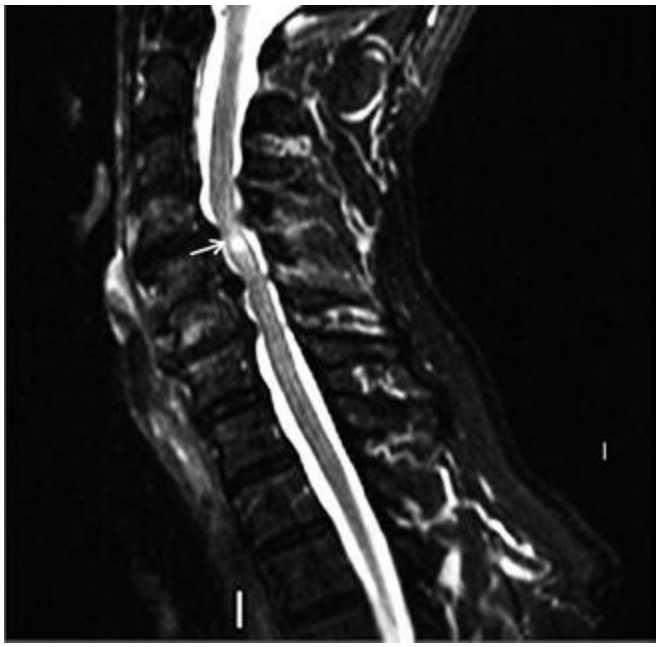


Fig. 32.2 MRI T2-weighted image with enhancing cord lesion (*arrow*) behind C5

Many surgical options have been described for posterior spinal fixation for fractures of C1 or C2, lateral mass/laminar fractures of C3–C7, or posterior decompression and stabilization for extensive spinal stenosis. These techniques include interspinous or sublaminar wiring, laminar hooks, lateral mass, and pedicle screw fixation [3]. Recent studies, however, have shown that three-column stability is best preserved with lateral mass and pedicle screw fixation because they provide (1) superior deformity correction, (2) greater immediate and long-term stabilization, and (3) can be used in almost all conditions requiring posterior stabilization or reconstruction of the occipitocervical spine, midcervical spine, or cervicothoracic junction [4, 5] (Fig. 32.3). Table 32.1 reviews the major indications for instrumentation with pedicle/lateral mass screws.

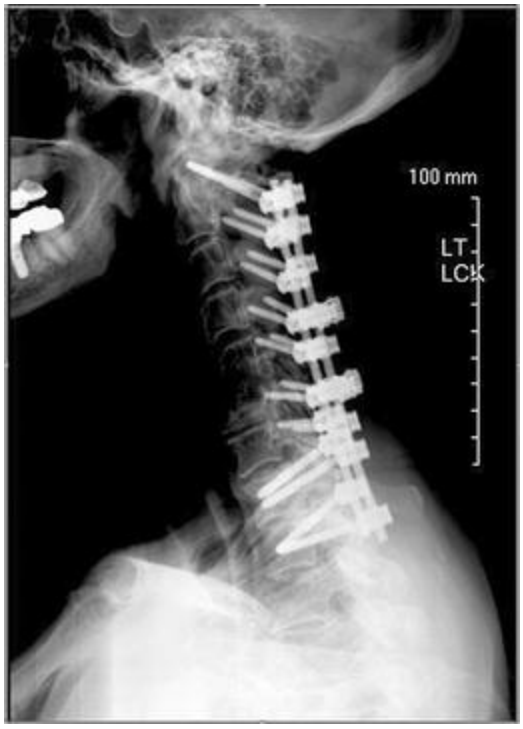


Fig. 32.3 Posterior laminectomy and fusion with pedicle screw instrumentation, C1, T1–T2 with lateral mass screw instrumentation C2, C3, C4, C5, C6, and C7

Table 32.1 Cervical pedicle /lateral mass screw indications

Posterior disruption or anterior/posterior disruption without severe vertebral body injury
Cervical spinal instability caused by nontraumatic lesions (metastatic tumor, rheumatoid arthritis, and destructive infectious lesions)
Correction of cervical malalignment in the sagittal plane, including postlaminectomy and posttraumatic kyphosis spondyloarthropathy
Stabilization of the segmental motion caused by posterior decompression
Posterior reduction and stabilization at the cervicothoracic junction
Salvage of previous anterior surgeries
Rigid stabilization of the craniocervical fixation

In comparison to lateral mass screws, pedicle screws have a higher pullout force and the greatest capacity for restoring sagittal alignment of the cervical spine with correction of malalignment in the occipitoatlantoaxial region [6–8]. However, because of the size of the pedicle screws in relation to the pedicle and the narrow trajectory required, they also have a greater chance of nerve root or vertebral artery injury. Since the risks of neurovascular complications caused by malaligned screw placement into the

cervical pedicle cannot be completely avoided, they are often placed in the higher cervical and cervical-thoracic levels where the pedicle has sufficient size for screw placement [9–14].

Cervical spinal myelopathy (CSM) is another common indication for a posterior cervical surgical procedure. In contrast to cervical fractures, which occur mostly in males younger than 40 years old, CSM is the most common cause of progressive neurologic decline in patients more than 50 years old [15, 16]. In most cases, myelopathy develops slowly due to spinal cord compression from progressive degenerative arthritis (osteophytes), ossification of the posterior longitudinal ligament (OPLL) or hypertrophy of the ligamentum flavum. The lower extremities are usually affected first with patients presenting with gait disturbances caused by the degeneration of the spinocerebellar and corticospinal tracts. Further compression or acute injury can result in upper extremities, loss of coordination, and difficulty with fine motor tasks [15].

In general, CSM most commonly affects the C5–C7 region of the cord with a variable clinical presentation. Often patients will have neck pain and stiffness and can experience deep aching or burning in the upper extremities (brachialgia). Motor and sensory dysfunction may be unilateral or bilateral depending on the extent and location of cord compression.

Patients with mild signs and symptoms of CSM are usually followed clinically. However, surgical decompression from an anterior or posterior approach is indicated in patients with progressive moderate to severe neurologic deficits. While the optimal surgical strategy (anterior vs. posterior or a combined procedure) for CSM) remains controversial, there is no clear evidence that either approach more reliably results in recovery from a compressive myelopathy [3, 14, 17] (Fig. 32.4). The goals of the surgical procedure are to decompress the spinal cord to avoid either static or dynamic compression, restore sagittal alignment, stabilize the spinal column, and avoid kyphosis. While the surgical procedure itself inconsistently improves myelopathic symptoms, it does prevent further decline of neurologic function [18, 19]. Thus, in many cases the surgery is prophylactic to prevent continued spinal cord damage and loss of function.

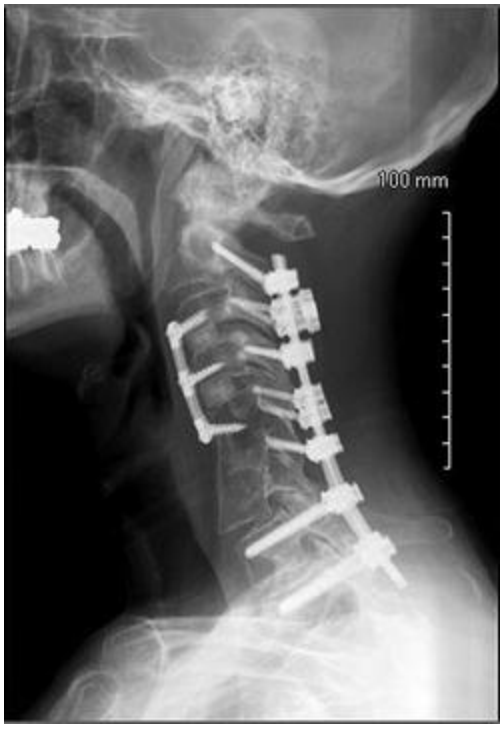


Fig. 32.4 Combined anterior (C3–C5) and posterior fusion with lateral mass screws, C2, C3, C4, C5, C7, and bilateral pedicle screws, T1 and T2

Because the majority of the abnormal anatomy-producing spinal cord compression is located anteriorly, the procedure most commonly chosen is an anterior cervical discectomy/corpectomy and fusion (ACDF; see Chap. 31). However, in multilevel compression and/or progressive deformity, posterior decompression with instrumentation may be indicated, often in combination with an anterior procedure. In the past, posterior decompressions alone often led to progressive kyphosis. With modern fixation techniques and the increased use of cervical instrumentation and fusion, this is much less common [4] (Fig. 32.5).

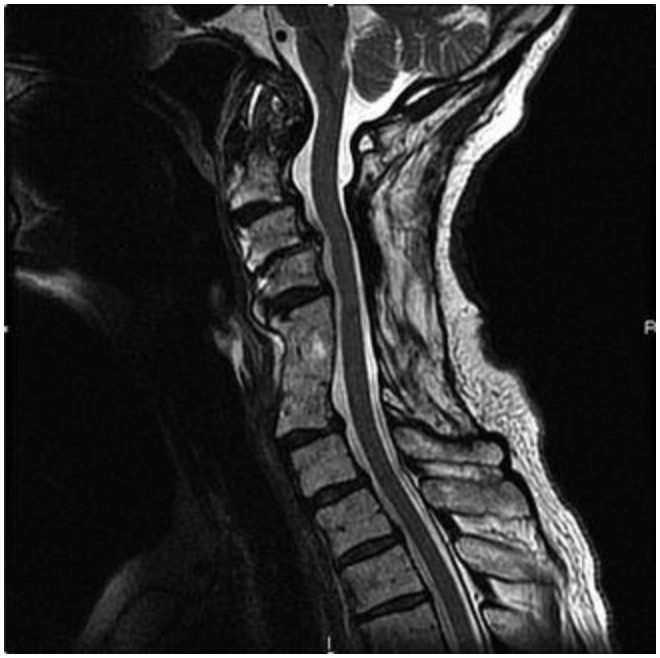


Fig. 32.5 Previous anterior cervical fusion at C4–5 with posterior laminectomy C3–5. The patient now presents for posterior cervical instrumentation secondary to spondylolisthesis at C2–4 and progressive kyphosis

With improvements in posterior instrumentation (screw and rod fixation) in the past decade, there has been an increased use of posterior decompression and instrumentation for the treatment of extensive degenerative cervical myelopathy. One complication of the extensive laminectomy is the formation of a thick fibrous scar at the operative site that replaces the bony compression and with progressive kyphosis reproduces the original symptoms in the extended postoperative period. An alternative technique to a laminectomy is a laminoplasty, which provides for relief of the pressure on the spinal cord with surgical reconstruction of the posterior vertebral elements to increase space for the neural structures while maintaining aspects of the bony posterior arch [20]. Thus, muscle reattachment is also possible to help maintain a posterior tension band and reduce the risk of postoperative kyphosis. A laminoplasty involves cutting through the lamina of the vertebrae on one side and merely cutting a groove on the other side and then “swinging” the freed flap of bone open to relieve the pressure on the spinal cord. The spinous process may be removed to facilitate the process. The bone flap is then propped open using small wedges or pieces of bone such that the enlarged spinal canal will remain in place [3, 21, 22] (Fig. 32.6). Mini-plates can also be used to maintain the open canal

and increase stability.

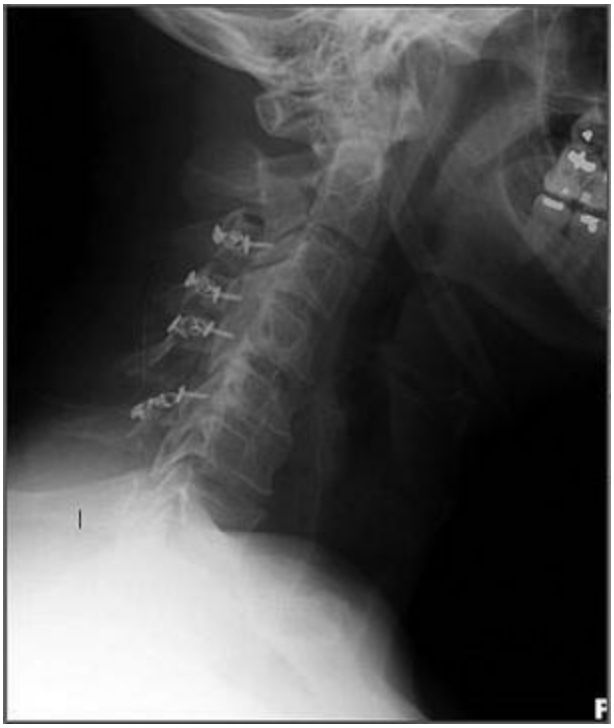
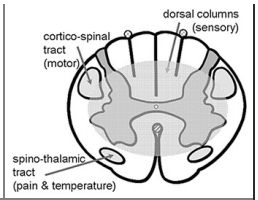
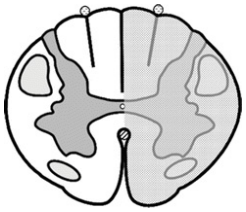
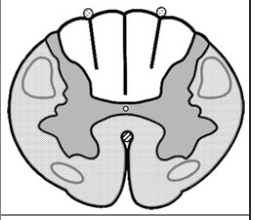
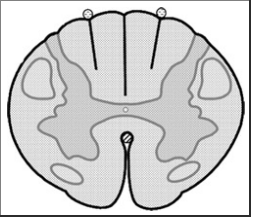


Fig. 32.6 Posterior cervical laminoplasty C3–C6

While the progression of CSM is highly variable, major neurologic injury from even relatively minor spinal cord injuries can manifest as one of four clinical syndromes (central cord syndrome, anterior cord syndrome, Brown-Sequard syndrome, and a transverse lesion syndrome). The most common location for spinal injuries from trauma is in the flexible regions of the cervical spine (e.g., C4–C5). The central vascular region of the spinal cord is the most easily injured, with progressive degrees of injury extending the injury radially until the entire cord is injured (transverse lesion syndrome). Anatomic knowledge of the spinal pathways of the syndromes helps guide the approach to interpretation of intraoperative neurophysiologic monitoring during posterior cervical decompression (Table 32.2).

Table 32.2 Cervical spinal cord injury syndromes —clinical findings and anatomic correlation

Syndrome	Clinical findings	Anatomy
Central cord syndrome	Injury to central grey matter (anterior horn cells) or lateral columns with greater weakness or paralysis, pain and temperature loss of the upper extremities compared to the lower extremities	
	Light touch and proprioception is usually spared	

		
Brown-Sequard syndrome	Injury to the corticospinal tract, dorsal column, and spinothalamic tract resulting in:	
	Ipsilateral weakness or paralysis	
	Ipsilateral loss of proprioception and light touch loss	
	Contralateral pain and temperature loss below the lesion	
Anterior cord syndrome	Loss of motor, pain and temperature, with preservation of fine touch and proprioception	
Transverse lesion syndrome	Loss of all function below the level of injury	

During posterior cervical procedures , the application of somatosensory- and motor-evoked responses is frequently helpful in the evaluation of intraoperative compromise of the spinal cord during the procedure and during positioning of the patient. While the use of intraoperative neuronavigation systems and fluoroscopy aids in placement of the pedicle screws, cortical perforation still occurs in 20–25 % of pedicle screw placements [11, 14]. A recent small study (n = 26) evaluated the sensitivity and specificity of pedicle/lateral mass screw stimulation thresholds for the determination of cortical perforation [23]. A stimulation threshold of 15 mA or greater provided a 99 % positive predictive value (89 % sensitivity, 87 % specificity) that the screw was within the lateral mass or pedicle. However, stimulation values of 10–15 mA provided an intermediate sensitivity and specificity (66 and 90 %, respectively); whereas a stimulation value of less than 10 mA was highly predictive that a screw is malpositioned (70 % sensitivity, 100 % specificity). Thus, the addition of the intraoperative evoked EMG monitoring is a valuable tool in the evaluation of lateral mass and pedicle screw placements with stimulation values below 10 mA triggering evaluation, repositioning, and possible removal of the pedicle screw.

Case Presentation

A 32-year-old man suffered a spinal cord injury at C3/4 after a fall down a flight of stairs. He had a severe central cord injury with loss of strength and sensation in bilateral upper extremities. He was not able to squeeze his hands. He did have 1/5 strength in his upper extremities and 4/5 strength in all muscle groups of his lower extremities. Sensation was intact in the lower extremities. CT scan showed a comminuted fracture of the right C3 lamina and left posterior lateral C3 vertebral body/pedicle junction that extended into the facet joint. The MRI showed an abnormal bright signal on T2-weighted sequences within the gray and white matter of the spinal cord at the C3/4 level consistent with a contusion. There was mild subluxation of the C3 facet on C4 with intact anterior and posterior longitudinal ligaments and 5 mm of anterior spinal space (Fig. 32.7). After review of the surgical options and analysis of the risks and benefits, the patient opted for posterior stabilization and fusion.

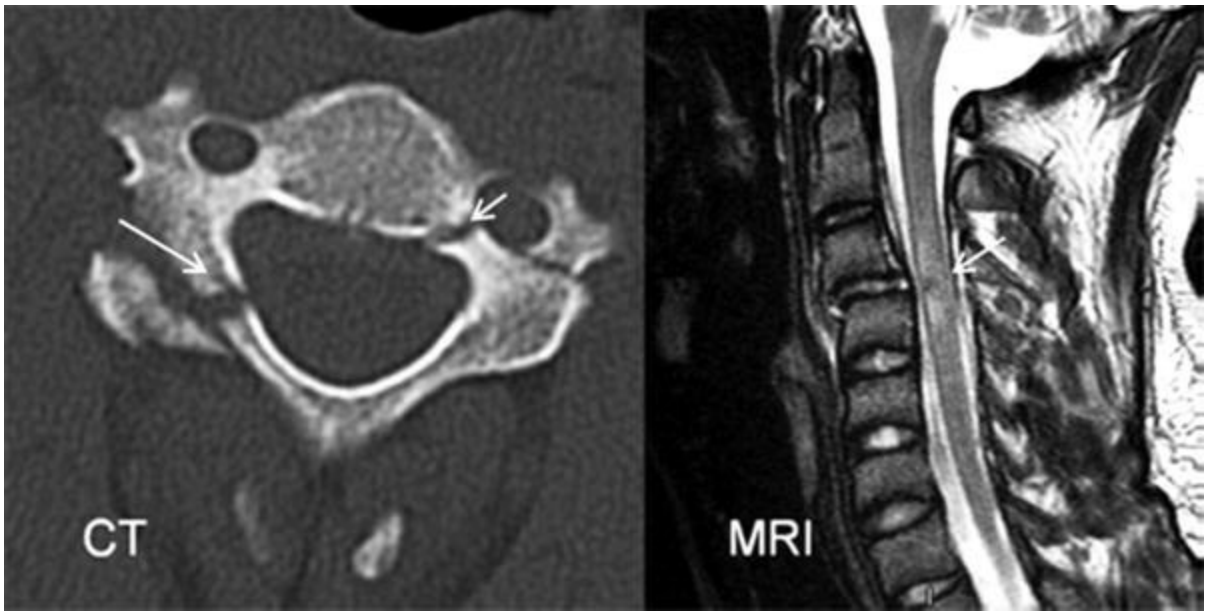


Fig. 32.7 CT scan with a comminuted fracture of the right C3 lamina (*long arrow*) left posterior lateral C3 vertebral body/pedicle junction (*short arrow*). MRI with abnormal bright signal on T2-weighted sequences within the gray and white matter of the spinal cord (*arrow*) at the C3/4 level

The patient was brought to the operating room. After local anesthetic topicalization of the nasal, oral, and laryngeal mucosa, a nasal fiberoptic intubation was performed with minimal sedation and minimal movement of

the head and neck. General anesthesia was induced with propofol and maintained with infusions of propofol and sufentanil. Neuromonitoring electrodes were placed and baseline somatosensory- and motor-evoked potential signals were obtained. All of the waveforms exhibited significant prolongation in latency. The amplitude, though small, was easily discerned from background noise and these findings were consistent with the central cord syndrome. The Mayfield head holder was placed and the patient turned prone on the Wilson frame with the neck slightly flexed. Evoked potentials immediately after positioning showed significant diminution of both the somatosensory- and motor-evoked responses (Fig. 32.8). The blood pressure was immediately increased to 20 % above baseline and positioning was evaluated with fluoroscopy. Repositioning of the cervical spine with the head flexed forward and translated posteriorly improved alignment of C3 in relation to C4. Recovery of the evoked responses occurred within 15 min and the decision was made to continue with the procedure.

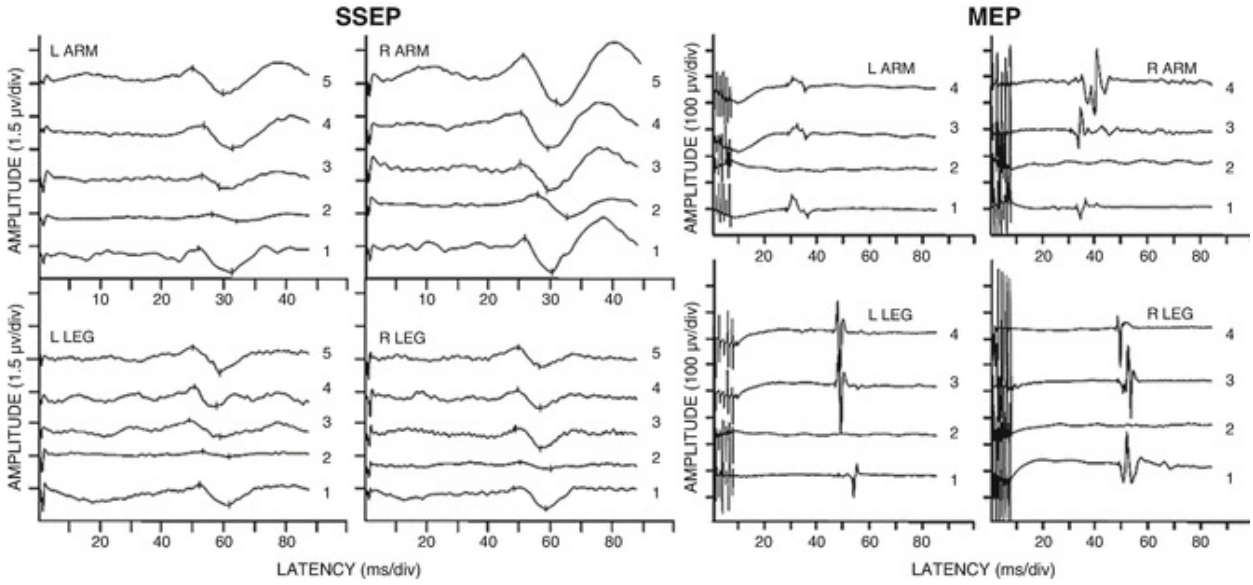


Fig. 32.8 Somatosensory (SSEP) and transcranial motor-evoked (MEP) responses. Waveform 1 represents the baseline tracing after induction and intubation, but before prone positioning. After initial positioning the SSEP responses were significantly diminished and the MEP responses were not present (waveform 2). After repositioning of the cervical spine under fluoroscopic guidance, there was prompt return of both the SSEP and MEP responses (3) that persisted for the duration of the procedure (waveforms 4 and 5)

After surgical exposure, lateral mass screws were placed at C2, C3, and C4 on the left side and C2 and C4 on the right side. No screws were placed at

C3 on the right side as the facet was fractured and it was unlikely to provide any stabilization. Stimulation of the lateral mass screws resulted in EMG responses that were all greater than 15 mA. The lateral mass screws were secured with rods that provided reduction and distraction of the facet and subluxation at C3–C4. The evoked responses did not change significantly over the duration of the procedure and the patient awoke with no new neurologic deficits.

Discussion

When presented with a patient with an unstable cervical spine fracture, intubation and positioning are critical times of the procedure that can result in neurologic injury. The first major decision is how to proceed with securing the airway since this may impact spinal cord perfusion . There is no objective evidence that one method is safer than any other. The critical consideration is to prevent excessive motion of the cervical spine. In a patient with a normal airway examination, a direct laryngoscopy with inline stabilization is an option and may be required in an uncooperative patient. A large retrospective series of patients (n = 3000) at the University of Maryland Shock Trauma Center revealed a 10 % incidence of cervical spine fractures that were intubated safely with direct laryngoscopy and inline stabilization [24]. However, this method is associated with a reduction in visualization of the larynx by at least one grade [25, 26]. Thus, in a patient with a marginal airway examination and suspected difficult visualization, it may not be the best option. Other methods of indirect visualization (video-laryngoscope or asleep fiberoptic intubation) after induction would also be acceptable [27–29]. However, in this case, a sedated fiberoptic intubation after topicalization was chosen. The advantage of this technique is that it allows for immediate neurologic evaluation after intubation. However, inadequate topical anesthesia of the larynx and trachea can result in significant patient discomfort with hypertension and tachycardia and placement of an endotracheal tube past a marginally anesthetized larynx and into the trachea can result in significant coughing with associated unacceptable cervical motion.

The second major consideration after intubation is obtaining baseline somatosensory- and motor-evoked potentials before and after surgical positioning. Even with an anterior surgical approach, significant surgical

positioning occurs after the induction of anesthesia due to the relaxation of paraspinous muscle spasms or “unlocking” of facet joints, which were “locked” in abnormal positions. This may also occur in patients positioned awake and tested clinically in the prone position. In a patient with an unstable cervical spine or significant stenosis, obtaining pre-position baseline evoked responses can be critical to the evaluation of cervical spine alignment after surgical positioning. Thus, the avoidance of long-acting neuromuscular blocking agents and volatile agents is helpful in obtaining and evaluating the baseline responses. In this case, the baseline responses were obtained after induction with the cervical spine position unchanged. However, after prone positioning, the loss of potentials prompted a critical alert to evaluate for potential causes of signal loss. Hemodynamic parameters and oxygenation were quickly reviewed. Until the validity of the information can be verified, the blood pressure was augmented to 20 % above the baseline response to ensure adequate spinal cord perfusion. Anesthetic administration was reviewed to insure that neuromuscular blockade and volatile anesthetics have not been administered. Frequently, neuromonitoring stimulating and recording electrodes are dislodged during prone positioning such that ensuring that stimulation impulses are delivered and recording electrodes are in place is essential at this time. At the same time, the surgeon needs to review and maximize cervical alignment based on the anatomy of the cervical pathology. In this case, the patient had intact anterior and posterior ligaments with bilateral unstable posterior bony elements with facet joint involvement. Despite the MRI finding of an intact posterior ligament, the mild anterior subluxation of C3 on C4 probably indicated some ligament laxity. Fluoroscopic evaluation of cervical spine alignment is helpful to review for an increase in subluxation or a rotational abnormality from the fracture at the C3–C4 facet joint. Evaluation in this case revealed slight increase in anterior subluxation with intact lordosis. After evaluation of positioning, it was determined that posterior translation of C3 with a slight reduction in lordosis could provide more anatomic alignment of the cervical spine in relation to the spinal cord. In this case, this resulted in rapid (<5 min) return of the motor responses and 15-min normalization of the sensory responses.

Questions

1. A 56-year-old male is involved in a motor vehicle accident and sustains

the neck injury. The patient's physical examination is consistent with a Brown-Sequard spinal cord injury. Which of the following likely represents the motor and sensory findings?

A. Bilateral upper extremity loss of motor function and unilateral lower extremity loss of pain and temperature sensation

B. Ipsilateral loss of pain and temperature sensation and contralateral loss of motor function

C. Ipsilateral loss of motor function and contralateral loss of pain and temperature sensation

D. Bilateral loss of pain and temperature sensation and unilateral loss of motor function

2. A 52-year-old female is undergoing a C2–7 posterior cervical fusion and a C5–6 posterior discectomy for spinal spondylosis, central disk herniation at C5–6 with an associated myleopathy. Immediately following prone positioning in a Mayfield head holder there is a 15 % decrease in the lower extremity somatosensory-evoked potentials (SSEPs) and 90 % loss in the motor-evoked potentials (tcMEPs) in the lower extremities. What is the next most appropriate step in management?

A. Proceed with procedure as planned.

B. Obtain lateral cervical C-arm images to optimize neck position

C. Observe for 15 min and then repeat motor and sensory neurophysiologic testing

D. Cancel the procedure and proceed with an emergency MRI

3. A 79-year old man falls, sustaining a hyperextension injury to his neck. An MRI shows the following. On motor examination, he has 2/5 strength in his deltoids, elbow and wrist flexors and extensors. He has 4/5 strength in his hip flexors, knee flexors, extensors, ankle dorsiflexors, and plantarflexors. Sensation is preserved in both his upper and lower extremities as well as his sacral segments. Injury to which of the following tracts contributes greatest to his motor function deficits?

   A. Dorsal columns

   B. Spinocerebellar tract

   C. Anterior corticospinal

   D. Lateral corticospinal

   E. Lateral spinothalamic

4. Which term **BEST** describes this spinal cord injury pattern in this 79-year-old man?

   A. Central cord syndrome

   B. Incomplete spinal cord injury

   C. Complete spinal cord injury

   D. Brown-Sequard syndrome

E. Posterior cord syndrome

Answers

1. A

2. B

3. B

4. A

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Footnotes

1 Key references marked with asterisk.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_33

33. Surgery for Scoliosis Correction

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Keywords Surgery – Scoliosis correction – Anesthetic – Intraoperative neuromonitoring – Chiari I malformation – Somatosensory-evoked potentials – SSEPs – Motor-evoked potentials – MEPs

Introduction

Idiopathic scoliosis is a common condition, with an incidence of 0.47–5.2 % in school-aged children [1]. In general, scoliosis is characterized by lateral and rotational derangements in the spine and vertebrae angles respectively. These deformities become progressively worse with time and may require

major corrective surgery to prevent deterioration of the spine angle and cardiopulmonary sequelae related to severe scoliosis [2]. These include restrictive lung disease, pulmonary hypertension, cor pulmonale, pain, and neurologic impairment, which, if left untreated, can be fatal by age 50 years. Corrective surgery often involves distraction and fusion of multiple levels of the thoracic and lumbar spine and is commonly associated with significant intraoperative problems including major blood loss, venous air embolism, and spinal cord injury (usually from spinal cord ischemia during de-rotation and straightening of the spine). A variety of surgical techniques and instrumentation have been reported. Posterior surgical approaches include (1) Harrington distraction with Wisconsin or Lugue segmental wiring, (2) combined distraction and wiring [Cotrel-Dubousset], and (3) mechanical fixation using pedicle screws. Techniques incorporating combined anterior release with either anterior or posterior instrumentation (Dwyer, Weiss springs) require a thoracotomy or a thoracoabdominal surgical approach (*see* Chap. 34, “Surgery on the Thoracic Spine”). The severity of the spinal deformity is graded by the degrees of angle of curvature (Cobb angle) and surgery is usually indicated when this angle exceeds 50°.

The majority of scoliosis (70–80 %) is idiopathic in nature and may have a genetic, multifactorial, and sex-linked association [1]. It is more common in girls than boys and is not typically associated with coexisting diseases, with the exception of cardiopulmonary derangements directly due to the severity of the Cobb angle. Non-idiopathic scoliosis comprises congenital, neuromuscular, and mesenchymal scoliosis. Congenital scoliosis is marked by malformed vertebrae and may be associated with coarctation of the aorta and cyanotic congenital heart disease. Neuromuscular scoliosis due to muscular dystrophy, cerebral palsy, spinal bifida, and spinal muscular atrophy is complicated by the chronic and debilitating nature of the primary disease. Furthermore, neuromuscular disorders are associated with increased risk of rhabdomyolysis, arrhythmias, myocardial dysfunction, and malignant hyperthermia leading to cardiac decompensation upon exposure to volatile anesthetics and succinylcholine. In advanced cases, cardiac failure occurs from cardiomyopathy, arrhythmias, and cor pulmonale. Mesenchymal disorders include Marfan syndrome, structural anomalies (myelodysplasia), primary or secondary malignancies of the spine, and trauma can be the cause of neuromuscular scoliosis. Thoracic surgery done in infancy is associated with iatrogenic scoliosis occurring during adolescence. Back pain in pediatric

patients suggests infection, tumor, trauma, or Scheuermann's kyphosis. Each of these diagnoses has implications for the anesthesiologist beyond the usual considerations for spinal surgery.

Hemodynamic stability and integrity of the spinal cord are the major challenges for the safe conduct of anesthesia during scoliosis surgery. Given the extensive surgical exposure, dissection, and vertebral distraction, sudden blood loss or venous air embolus can rapidly deteriorate to cardiovascular collapse. Therefore, normovolemia should be maintained throughout the procedure. Although the overall incidence of cardiac arrest in children undergoing surgical correction of spinal deformities is 0.4 %, patients with neuromuscular scoliosis are three times more likely to have intraoperative cardiac arrests when compared with patients with idiopathic scoliosis [3]. Factors that were associated with cardiac arrests were the number of vertebra levels fused and blood loss. The Scoliosis Research Society and the European Spinal Deformity Society have endorsed multimodal intraoperative neuromonitoring to assess spinal cord and rootlet integrity during scoliosis surgery. This report revealed a significant reduction in the rate of paralysis from an expected 4 to 0.55 % with the use of intraoperative neuromonitoring [4]. Given the dramatic reduction in neurologic morbidity, intraoperative neuromonitoring is an essential part of the intraoperative management of the child with scoliosis [5, 6]. Recent guidelines published by the American Clinical Neurophysiology Society (ACNS) provide an evidence-based assessment that intraoperative neuromonitoring detected changes associated with postoperative neurologic deficits [7]. The following case illustrates many of the intraoperative considerations in scoliosis surgery.

Case Report

A 13-year-old girl presented for posterior spinal fusion from T4–L4. She was first diagnosed with scoliosis at age 6 when her pediatrician noted a curvature to her back. This resulted in a referral to an orthopedic specialist who noted on physical examination that she had a 3° right upper thoracic and a 4° left lumbar paraspinal prominence. This translated into a thoracic curve measuring 11° convex to the right and a lumbar curve measuring 18° convex to the left by x-ray. A full spinal magnetic resonance imaging (MRI) scan did not detect other coexisting anatomical processes such as a Chiari I malformation and/or syrinx. Her mother and maternal aunt had mild stable

thoracic scoliosis. Given the history, physical and imaging procedures, the patient was diagnosed with mild juvenile idiopathic scoliosis.

She returned for follow-up every 6 months and by age 8 her lumbar curve had progressed to 30°. Initial conservative management with a Boston brace was unsuccessful due to noncompliance and her curvature became progressively worse in the ensuing 5 years.

At age 13 years, her thoracolumbar spine x-rays revealed a 50° right thoracic and a 70° left lumbar curve. She was postmenarchal for 9 months with a bone age of 15 years old. Bending x-rays demonstrated moderate flexibility. Her height and weight were 165 cm and 87 kg, respectively. The dramatic increase in her thoracic and lumbar curvature and her skeletal maturity necessitated the need for surgical stabilization of her spine.

The patient's preoperative evaluation revealed normal coagulation studies with a prothrombin time of 12.0 s, a partial thromboplastin time of 32 s, and platelet count of 325,000 and her hematocrit was 38 %. No other laboratory studies were obtained. Physical examination revealed an obese female. All other physical parameters were normal except for a noticeable thoracic hump. The baseline blood pressure was 110/62 mmHg. The patient was counseled by the anesthesiologist about the course of the anesthetic and prepared her for the possibility of an intraoperative wake-up test.

Anesthetic

Discussion

A multidisciplinary approach to the intraoperative management of an adolescent for scoliosis surgery mandates careful preoperative planning by the anesthesiologist, orthopedic surgeon, and the neurophysiologist. The neurophysiologist expressed a desire for "light" anesthesia to optimize intraoperative neuromonitoring . The surgeon requested that the mean blood pressure be maintained at 65 mmHg to ensure adequate spinal cord perfusion and to minimize blood loss during the procedure [8]. The anesthesiologist expressed concerns that an adequate level of anesthesia be administered in order to minimize the chance of intra-operative awareness [9].

A small bore intravenous line was inserted in the patient in the holding area. The patient then received midazolam for anxiolysis and perioperative amnesia because evidence has shown that patients receiving a light volatile anesthetic (up to 1 minimum alveolar concentration [MAC] of isoflurane and

nitrous oxide in combination) or a balanced anesthesia technique can have bispectral index (BIS) numbers in the high 60 to low 70 range during the anesthetic [9]. These high BIS levels can be a harbinger of potential intraoperative awareness. Given the concern for awareness during surgery, use of BIS was considered.

Discussion

BIS monitoring has been shown to decrease the incidence of intraoperative awareness in high-risk patients undergoing general anesthesia [10]. Standard motor-evoked potentials and somatosensory-evoked potentials can be performed while monitoring the BIS number without interference. However, the anesthesia team was planning on positioning the patient in the prone position with the face resting in a protective helmet system (ProneView, Dupaco, Oceanside, CA). The pressure points of the ProneView are the forehead and the chin and the anesthesia team was concerned that the BIS electrode might predispose the patient to a pressure sore on the forehead (*see* Fig. 33.1).

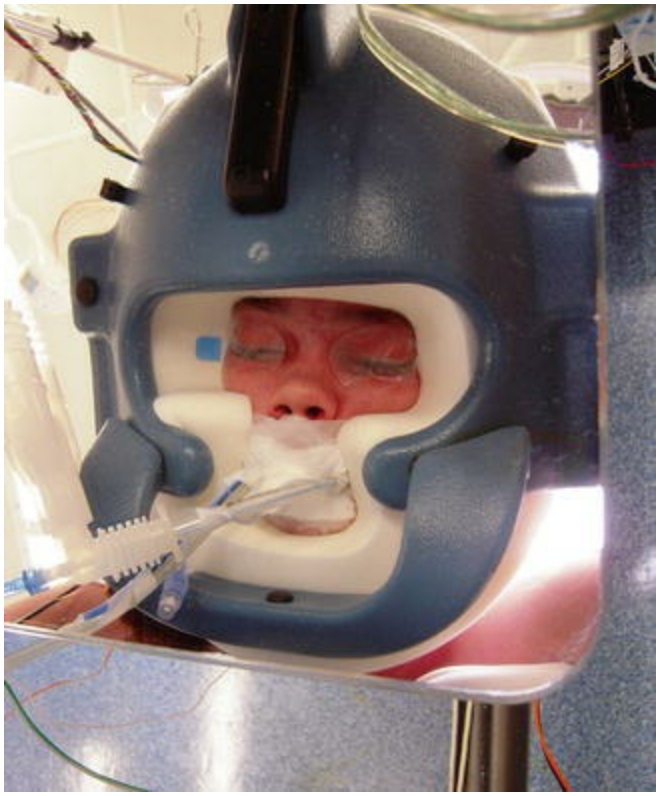

Fig. 33.1 Adolescent in the headrest (ProneView, Dupaco, Oceanside, CA). The potential pressure

points include the forehead and chin. It is important to make sure that the weight of the head is distributed between these pressure points

Anesthesia was induced with propofol and fentanyl and tracheal intubation was facilitated with low-dose rocuronium (0.5 mg/kg). Intubation was atraumatic and two bite blocks (made of soft gauze) were inserted into the mouth between the molars to protect the tongue from impingement during the MEPs [11]. Care was taken to tape the oral endotracheal tube securely because the patient would be prone for 4–6 h for this procedure. Several large-bore intravenous lines and a radial artery catheter were inserted.

Anesthesia was maintained with the administration of 0.6 % isoflurane and 70 % nitrous oxide. Several intravenous boluses of fentanyl (50–100 μg) were administered throughout the maintenance phase of the anesthesia in order to provide a constant level of analgesia.

The neurophysiologist was asked to acquire MEPs by stimulating at the C1 and C2 scalp electrode positions rather than using the C3 and C4 positions. SSEPs and electromyography (EMG) monitoring was also planned for this case.

Discussion

Although most intraoperative neuromonitoring groups prefer a total intravenous anesthesia (TIVA) technique and most centers if using volatile agents limit the total volatile plus nitrous oxide, there is evidence that using trains of 3–5 pulses (interstimulation interval, 2 ms) for MEPs will allow adequate neuromonitoring with a volatile gas technique as long as the total MAC is 1 or less for the majority of healthy patients with robust responses [12–14]. Other anesthetic drug combinations include a mixture of another volatile agent (desflurane or sevoflurane) with nitrous oxide up to 1 MAC (*see* Chap. 19, “General Anesthesia for Monitoring”) or a total intravenous anesthetic, which could consist of a narcotic, propofol, methohexital, ketamine, or dexmedetomidine with or without nitrous oxide. Our rationale for choosing for a volatile gas with nitrous oxide is that if neuromonitoring signals are lost or there is a surgical event that necessitated a “wake-up test,” rapid emergence from anesthesia can be easily achieved with the volatile anesthetics [15]. Monitoring the MEPs using the C1 and C2 scalp electrode position produces less activation of the masseter muscle than when the C3 and C4 electrode positions are used (Fig. 33.2).

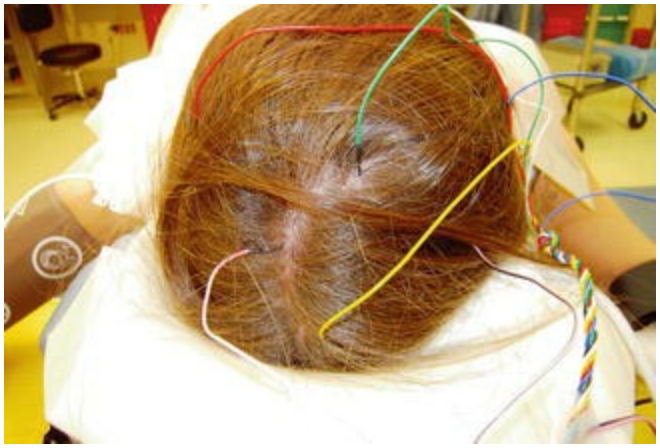

Fig. 33.2 View of neuromonitoring leads placed in a montage in the skin overlying the cortex

After induction of anesthesia, the patient's blood pressure was 88/50 mmHg. The isoflurane concentration was decreased to 0.2 %. The blood pressure improved to 95/55 mmHg and the inhaled anesthetics were maintained at the lower concentrations. The patient was carefully positioned prone on the Jackson table and all extremities were padded and a forced hot air warmer blanket (Bair Hugger; Arizant Inc., Eden Prairie, MN) was placed on the lower extremities. The neuromonitoring technician reported good SSEPs and MEPs in all four extremities. The surgeon made the incision, the blood pressure rose to 130/88 mmHg, and the anesthesiologist increased the inhaled anesthetic concentration (1 MAC) and administered an additional bolus fentanyl for a total peri-induction dose of 15 μg/kg. The blood pressure decreased to a mean of 66 mmHg. The neuromonitoring technician then reported that there was a decrease in amplitude and increase in latency in the potentials from three extremities and loss of signal in the right hand for the SSEPs . The patient's temperature at this time was recorded as 34.5 °C.

Discussion

The possible reasons for the decrements in the signal were identified and discussed. Although the initial plan of administering 1 MAC equivalent of isoflurane and nitrous oxide should have been compatible with neuromonitoring, it was determined that the baseline measurements were actually recorded when the patient was receiving 0.7 MAC. Volatile anesthetic drugs and nitrous oxide will decrease the amplitude and increase the latency of both the MEPs and the SSEPs. The MEPs are more sensitive to

the effects of volatile agents. In neurologically intact adolescents, administering 1 MAC equivalents of isoflurane and nitrous oxide should be compatible with adequate signals. But in this case, 1 MAC of gas represented an increase in anesthesia from baseline and thus would be expected to cause the observed changes in latency and in amplitude. Since the attenuation of the signals occurred during the skin incision, it was deemed unlikely that the changes could be attributed to surgical injury to the spinal cord and nerves.

The anesthesia team decreased the inhaled isoflurane and nitrous oxide concentrations and started a propofol infusion of 75 μg/kg/min. This maneuver maintained the patient's mean blood pressure between 65 and 70 mmHg. Since the modest increase in the inhaled isoflurane concentrations would not be sufficient to completely depress the SSEPs from the right hand, the technologist verified the placement of the electrodes and found them intact.

Within 5 min of decreasing the inhaled concentration of isoflurane and nitrous oxide , the SSEPs returned to their baseline values except for those on the right hand, which did not fully return and were only intermittent with prolonged latency and decreased amplitude. Coincidently, the pulse oximeter on the right index finger intermittently registered a weak signal.

Discussion

The different etiologies for the loss of SSEP signals from the right hand include loss of electrodes on the right hand, poor connection between electrode and skin of the right hand, injury to the spinal cord, and injury to the brachial plexus.

The technician checked the impedance of the electrodes on the patient's right hand and found it to be normal at 5 kΩ. The recording and stimulating leads on the patient's head, hand, arm, and shoulder were also intact. The arm position appeared to be normal. The anesthesia team informed the surgical team about the loss of signals and asked them whether there was any surgical manipulation of the lower cervical and upper thoracic spinal cord . The attending surgeon noted that surgical field included T4–L4 segments and did not include the high thoracic and low cervical area. The anesthesiologist peered under the drapes again and noticed that the right arm was abducted at the shoulder. At this point the orthopedic assistant surgeon admitted to "hip checking that arm out of the way" so they could better assist with the surgery. The anesthesiologist repositioned the arm so that the shoulder was not

abducted but in a neutral position and that the upper arms were positioned 90° in front of the patient's torso to limit traction on the brachial plexus. The anesthesiologist also established that the axilla was free from chest pads on the surgical table. The waveform on the pulse oximeter immediately normalized. Within 10 min, the SSEPs in the right hand returned to normal [16]. In this particular instance, both the pulse oximeter and the SSEP monitors revealed a positioning problem and possibly averted a postoperative neuropathy.

Decortication of the bone for the spinal fusion resulted in profuse venous bleeding and the surgeon requested that the anesthesiologist lower the mean blood pressure to 55 mmHg in order to stem the bleeding [17]. Although the anesthesia team had some concerns that the lower blood pressure might increase the risk of spinal cord and optic nerve ischemia, they concurred with the surgeon and lowered the blood pressure to a mean of 55 mmHg with labetolol [18]. Hypovolemia was rapidly treated by a 3:1 ratio of normal saline to blood loss fluid bolus. The patient's temperature at this time was 34.5 °C and the hematocrit was 26 % with normal arterial blood gas values. The anesthesiologist turned on the fluid warmer and applied a forced warm air blanket to the upper torso to help maintain the patient's temperature. Immediately, the neuromonitoring technician announced a deterioration in the monitoring signals. The anesthesiologist asked the neuromonitoring technician to characterize the recent change in signals and found that the amplitude and latency had not changed but that the signals became unreliable due to increased background electrical noise.

Discussion

Rapid fluid resuscitation with crystalloids can lead to excessive facial swelling, may interfere with organ function and can cause the patient to rapidly lose body heat in patients in the prone position. Both low body temperature and anemia are associated with increased latency and decreased amplitude in MEPs and SSEPs. However, electrical interference can lead to unreliable signals.

Electrical interference with the MEPs and SSEPs by other electrical devices commonly occurs in the operating room (Fig. 33.3). It is important to try to establish a temporal association between the addition of an electrical device such as a forced hot air warmer or a blood warmer with the onset of the electrical interference. The most efficient way to determine whether a

device is causing interference is to briefly turn the device off and see if the interference resolves. Once the likely culprit is identified, often moving the device to a location in the room away from the neuromonitoring wires will decrease the level of electrical interference (*see* Chap. 16, “IOM Instrumentation Layout and Electrical Interference”).

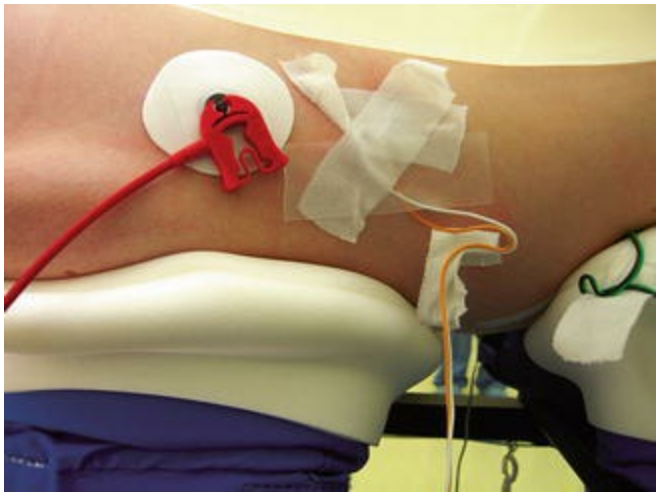

Fig. 33.3 Close proximity of the ECG lead and transversus abdominis neuromonitoring lead

The anesthesiologist turned off the blood warmer and forced air warmer and moved them to the contralateral side of the neuromonitoring wires. Although the electrical interference did not completely resolve, the signals were significantly improved [18, 19].

The surgeons inserted all their pedicle screws bilaterally. They then requested that the neuromonitoring technician help them do triggered EMG to ensure proper placement of the pedicle screws . The surgeons placed the stimulation probe on the pedicle screw and a needle electrode wire was inserted in the tissue above the surgical field to complete the circuit for the stimulation current (Fig. 33.4). The surgeon began to stimulate the first pedicle screw with 8 mA and gradually increased the current to 20 mA. No EMG signal was detected with stimulation.

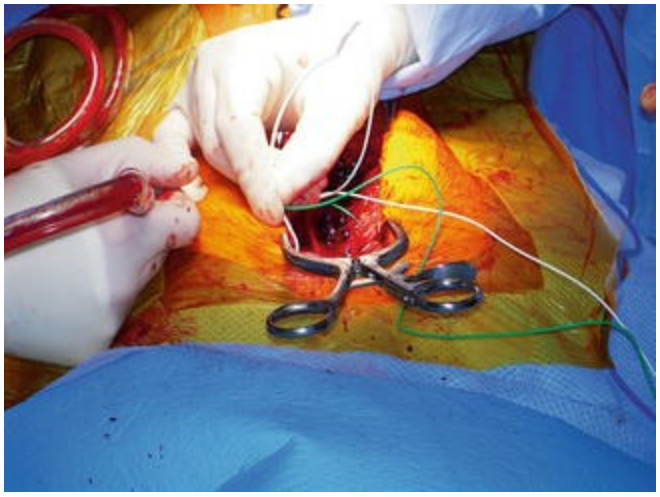

Fig. 33.4 Pedicle screw testing by the surgeon

Discussion

At this point it is important for the neuromonitoring team to confer with the surgical and anesthesia team. The causes for the lack of triggered EMG signal include excessive muscle relaxation, an unattached anode electrode wire, and/or a nonconductive pedicle screw. Some pedicle screws are made of hydroxyapatite and do not conduct electrical impulses. In this case, stimulation needs to be performed by inserting the probe into the screw pilot hole. In this particular case, the screws were made of an electroconductive material and the surgeon had neglected to plug in the anode needle electrode.

Once the anode electrode wire was inserted properly, the surgeon then began stimulating the pedicle screws in an orderly fashion starting on the right thorax and continuing to the final lumbar pedicle screw and then repeating the process on the left. All of the triggered EMG responses from stimulation of the pedicle screws from the T5 level to the L5 level were normal, indicating that there was no triggered EMG responses to less than 8 mA except for the right-sided T5 and T6 screws whose triggered thresholds were less than 6 mA, respectively.

Discussion

The triggered EMG is an appropriate test of pedicle screw placement because cortical bone is a good electrical insulator, which suggests that it should take a triggered electrical stimulus of greater than 6 mA to cause an EMG response [20]. A response at less than 6 mA can mean that the pedicle screw

has broken through the cortex and is lying close to the thoracic nerve roots. Since pooled blood can conduct an electrical current, it is possible to obtain a triggered EMG response at less than 8 mA when the operative field is not dry and if the current is shunted toward and excites the thoracic nerve roots. In general, lumbar pedicle screw testing is more reliable than thoracic pedicle screw testing [20]. It is also possible that current shunting can result in elevated screw thresholds [21].

The surgeons visually inspected and palpated the pedicle screw area and found no break in the cortex. So they felt it was unlikely that the pedicle screw had broken through the medial wall of the pedicle and was lying close to the spinal cord and nerve roots. However, both of these screws were submerged in blood. Despite meticulous suctioning of the retained blood from the operative field, stimulation of the screws at 6 mA did not evoke EMG responses in T5 and T6.

Once the patient's MAP reached 55 mmHg, there was a noticeable improvement in the surgical site with much less visible bleeding. The anesthesiologist was able to decrease the intraoperative replacement fluids and the surgeon found it much easier to continue. Despite active warming of the patient and intravenous infusions, the patient's core temperature continued to drift downward and reached 33.9 °C.

The surgeon placed the first rod and began to distract the spine. The neuromonitoring technician announced a loss of the lower limb MEPs and then shortly thereafter reported the loss of SSEPs to the lower limbs and that the MEP and SSEP signals to the upper arms showed significant decrease in amplitude and latency.

Discussion

The surgeon, anesthesiologist, and neuromonitoring technician conferred about the possible reasons for the poor signals [5]. The global decrement in both evoked potentials (poor signals in the upper extremities and loss of signals in the lower extremities) pointed toward a systemic nonsurgical reason for at least part of the decrease in signal quality. Factors associated with increased latency and decreased amplitude of signals include hypotension, hypovolemia, anemia, hypothermia, hypocapnia, and increased inspired concentrations of inhaled anesthetic agents. This particular patient had a normal $PaCO_2$, which dismissed hypocapnia as the sole contributing

factor. However, the patient was both hypothermic and hypotensive. In order to warm the patient, the room temperature was increased to 25 °C, the forced warm air blankets were increased to the warmest setting, and all intravenous fluids were warmed. They also rapidly elevated the blood pressure to preoperative levels. Although the patient's hypotension and hypothermia may diminish the SSEP and MEP signals for the lower limbs, it is likely that other factors may be involved. The operative etiologies for loss of signals include any surgical maneuver, which might interfere with the blood supply to the spinal cord in the thoracolumbar region. In attempts to control the bleeding, the surgeons may have inadvertently ligated a spinal artery. They also may have directly compressed a spinal artery or indirectly stretched or kinked a spinal artery during distraction of the spine leading to diminished blood flow and spinal cord ischemia. The surgeons inspected and loosened their retractors but did not see any pulsating vessels. They also removed the single rod to release any spinal cord distraction. The anesthesia team administered a phenylephrine infusion at this time to increase the patient's MAP to 10 % above baseline in an effort to improve spinal cord perfusion. After 10 min, the signals did not improve and the surgeon and anesthesiologist agreed to perform a wake-up test [21–23].

The volatile agent and the nitrous oxide were terminated. The nurse went under the drapes to watch the patient's feet during the wake-up test. It is essential that adequate help is available to prevent the patient from moving in an uncontrollable fashion and accidently extubating her trachea during the wake-up test. The anesthesiologist gently placed a hand over the top of the patient's head to prevent the patient from lifting their head during the test. He also placed a hand over the patient's right hand and had an assistant place their hand over the patient's left hand. These maneuvers were performed to prevent the patient from displacing the endotracheal tube or lifting their head out of the protective foam head holder. Once the end-tidal gases were at 0.2 MAC, the anesthesiologist requested that the patient squeeze his left hand to indicate she was able to respond to verbal commands. Once the patient did that, the anesthesiologist requested that the patient wiggle all their toes to examine spinal cord function. The patient wiggled all their toes on the second request and after reassuring that the patient had normal spinal cord function, the anesthesiologist re-anesthetized the patient with midazolam and propofol. The patient's SSEPs and MEPs returned to baseline values, which may have been the result of a blood pressure increase or reduction in anesthetic effect.

Discussion

The healthcare team conferred about the best way to proceed with this case. The decision was made to optimize parameters, which might interfere with adequate neuromonitoring. The room temperature was increased to 25 °C and the patient's core temperature rose to 36 °C. The anesthesia team chose to maintain the MAP at 65–70 mmHg, a hematocrit above 25 %, and electrolytes and arterial blood gases (ABGs) within normal limits [5]. Of note, a wake-up test is often associated with an increase in the blood pressure. Since high-dose opioids may delay emergence, the decision was made to reinstitute isoflurane and nitrous oxide in order to facilitate additional wake-up tests, if upon further distraction there was loss of signals.

The surgeons proceeded by carefully positioning their retractors and the first rod. Once the rod was placed, they gently distracted the spinal vertebrae in order to straighten the spine. This time there was no loss of signals and they placed the second rod with maintenance of both MEP and SSEP signals.

The surgeons closed and dressed the wound and the healthcare team positioned the patient in the supine position on the bed to facilitate the anesthetic emergence. At this time, it was noted that the sponge bite block that had originally been inserted between the left molars was now dislodged and was soaked with blood. Inspection of the tongue revealed a deep laceration on the left side with continued bleeding.

An otolaryngologist examined the patient and closed the laceration . The patient's trachea was successfully extubated and the patient was transferred to the postanesthesia care unit.

Discussion

The healthcare team discussed the factors that could have caused the tongue laceration . The patient biting down on their own tongue most likely occurred during the wake-up test or as a result of the MEPs. There are no reported episodes of tongue lacerations occurring during the wake-up test but numerous reports after MEP monitoring [11]. There is no absolute way to prevent this and tongue lacerations have occurred even when bite blocks were in place [24]. Most anesthesiologists make their own bite block by rolling up several pieces of gauze and taping them in place. It is important to adequately place them and then devise a method to ensure that the bite block is not displaced intraoperatively. Furthermore, the use of high voltage for MEPs

may amplify masseter muscle contraction and increase the chance for tongue injury. All bite blocks and sponges placed in the mouth must be accounted for at the cessation of the case.

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Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_34

34. Neurophysiological Monitoring in Thoracic Spine Surgery

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Keywords Neurophysiological monitoring – Thoracic spine surgery – Surgical approach – Neurological risk – Marfans syndrome – Osteogenesis imperfecta – Pathophysiology

Key Learning Points

- In the thoracic spine, the procedures may be approached anteriorly, posteriorly, or by a combined approach. Anterior surgery may involve thoracotomy or sternotomy, and may include division of the hemidiaphragm.
- The procedure with greatest risk utilized in deformity correction is a posterior vertebral column resection (osteotomy).
- Placement of pedicle screws in the thoracic spine is more challenging than in the lumbar spine since they are smaller, narrower, and have greater anatomical variability in diameter, shape, and have varying anteromedial and cephalad angulation. In addition to the risk to nerve roots, the spinal cord is also at risk for direct injury with a medially positioned screw. This is due to the spinal canal being smaller compared with the size of the spinal cord.
- Medial penetration of a thoracic pedicle screw can also produce a dural tear leading to a cerebrospinal fluid leak and intracranial hypotension. If it is associated with a nonreversible IOM change, it is always associated with a new-onset neurological deficit.
- Neurological risk is increased in some patients, especially with congenital kyphosis, neurofibromatosis, or skeletal dysplasia. It is also increased in patients with preoperative asymmetric neurological deficits, paresthesias, bowel or bladder dysfunction, or excessive neck or back pain.
- Although direct trauma to the spinal cord can produce injury, paralysis is thought to be most likely the result of an ischemic insult to the anterior and central portions of the spinal cord.
- Ligation of the segmental vessels to the spinal cord is routine during anterior thoracic surgery and has been generally considered safe if the ligation is unilateral, performed on the convexity of the curve and the ligation occurs at the mid-vertebral level.

Monitoring techniques for the prevention of blindness

in the prone position are not currently effective. It is thought to be related to ischemia of the posterior optic nerve.Introduction

Indications for spinal deformity surgery in the thoracic spine are similar to those in the cervical or lumbar spine. The major differences in the procedure include the special considerations needed to accommodate the anatomical variations in the orientation of the facet joints and pedicles, as well as the varying approaches to the spine, which may involve surgery through the chest cavity or extra-pleural from posterior with resection of the ribs.

Among the common indications is the correction of developmental, degenerative, congenital conditions, and iatrogenic causes leading to a spinal deformity (e.g., scoliosis and kyphosis) [1]. Idiopathic scoliosis is found in 2–3 % of all children but can also be associated with other conditions that have additional implications for anesthesia management [2]. These include Marfan syndrome and osteogenesis imperfecta [2]. Fewer than 10 % of children with scoliosis need surgery to prevent the consequences of curve progression, which include limitations of pulmonary function (girls have ten times the risk of boys, accounting for why surgery is more common in girls) [2]. Back pain is a complaint in 80 % of scoliotic patients [2]. Sagittal plane spinal deformity presents in a variety of forms, including congenital, Scheuermann's kyphosis, traumatic, oncologic, and iatrogenic. These cases often require prolonged anesthesia and increased blood loss, creating further difficulty with the provision of intraoperative neuromonitoring (IOM).

Spinal fusion has been the mainstay of surgical treatment of spinal deformity for nearly a century and often involves multilevel anterior discectomy with bone grafting combined with posterior pedicle screw constructs and fusion, which may extend above and below the thoracic region [3, 4]. The surgical indications for thoracic deformity correction include (1) idiopathic curve greater than 40°, (2) severe deformity with asymmetry in a growing adolescent, (3) a curve greater than 50° after skeletal maturity that has a high chance of progression, (4) thoracic lordosis with a high chance of progression to impair pulmonary function, (5) symptomatic Scheuermann's kyphosis with greater than 75° kyphosis, (6) thoracolumbar neuromuscular curves in patients with cerebral palsy, (7) spinal muscular atrophy, (8) myelomeningocele or poliomyelitis to prevent progression and pain, (9) adult patients with scoliosis with intractable pain, neurological dysfunction,

pulmonary dysfunction, or cosmetic issues, (10) adult patients with kyphosis due to trauma/tumor creating significant anterior sagittal imbalance, neurological dysfunction, or risk for progression, and (11) patients who have undergone previous spine surgery with progressive junctional level disease and kyphosis leading to intractable pain, neurological dysfunction, or risk for progression [1].

Congenital kyphosis occurs less commonly than scoliosis and is caused by developmental anomalies that impair longitudinal growth of the anterior or anterior–lateral portion of the spine. An abnormal vascular supply to the spinal cord has been postulated [5] as a cause for the condition. The apex of the deformity commonly occurs at the thoracolumbar junction. The most common form is associated with failure of the vertebral body to develop. Many of these patients have other anomalies such as hemifacial microsomia, Alagille, Jarcho-Levin, Klippel-Feil, Goldenhar, Joubert syndrome, and VACTERL, trisomy 18, and diabetic embryopathy [5]. The risk of neurological injury is high in these patients; monitoring is considered essential, especially in older children in whom the risk is higher than in those who are younger [5].

Scheurmann's kyphosis is associated with at least three levels of thoracic vertebral bodies with greater than 5° of anterior wedging, endplate irregularities (Schmorl's nodes), and increased kyphosis of the thoracic spine. This is generally identified in adolescents around puberty, when radiographic findings become easily identifiable. Surgical indications are similar to those described for other spine conditions, including intractable pain, neurological compromise, progressive deformity, cardiopulmonary compromise, and cosmesis.

Other indications for thoracic spine fusion include trauma, infection, tumor, and degenerative disk disease. Surgical indications in cases where infectious causes are suspected should include a bacteriological diagnosis and removal of spinal compression from an abscess [1]. Surgery for spinal tumors allows diagnosis, correction of a pathological fracture, treatment of intractable pain, and treatment for a primary cancer, solitary metastasis, or recurrence. Malignant etiologies have the highest perioperative mortality and infectious etiologies have the highest complication rate and length of stay [3]. Most cases of disk herniation are treated with discectomy (removal of the disk) and autograft or artificial cage replacement or by corpectomy (removal of the vertebral body) alone or with discectomy [3].

Surgical Approach

In the thoracic spine, the procedures may be approached anteriorly, posteriorly, or by a combined approach [1]. Each approach has advantages and disadvantages, and controversy exists about the added value of a combined anterior and posterior approach [6].

The anterior spine approach was initially used to treat Pott's disease in the early twentieth century [3]. More recently (since 1969), anterior instrumentation has been commonly used with trauma and tumors because it allows structural correction and spares the necessity of fusion of some distal levels [4, 7]. Surgery for spinal tumors appears to have improved results of assessing diagnosis, correction of a pathological fracture, treatment of intractable pain, and treatment for a primary cancer or solitary metastasis or recurrence [1]. The anterior approach has also been useful in adult scoliosis patients for curve improvement and has been suggested to be a requirement in the treatment of congenital spine deformities as well as trauma [7]. The anterior approach has also been found useful with spondylitis with involvement of the vertebral body by resection of the pathology and reconstruction of the spinal column [8].

The anterior approach to different areas of the spine is usually varied depending on the involved region of the spine. Three regions are usually identified (T1–5, T6–9, and T10–L1) [9]. For the cephalad region (down to T6), the approach usually involves a right thoracotomy, although very high approaches (C7–T2) may involve a sternotomy [3, 7]. Below T6, the approach involves a thoracotomy with the middle region (T6–12) usually approached by a left posterior–lateral thoracotomy.

In general, the thoracotomy is usually located about two interspaces above the target vertebral body or disk. For scoliosis, it is often on the convex side of the curve [3]. For T11–12 lesions, a thoracolumbar approach usually requires resection of the tenth rib and limited posterolateral division of the ipsilateral hemidiaphragm and its paravertebral interspace including the psoas musculature [3]. The caudal or thoracolumbar region (L1–2) is associated with a left-sided approach and minimal diaphragm mobilization (to avoid the liver) [7].

Anterior spine fusion is generally more advantageous than posterior fusion because it reduces the levels of fusion, prevents the crankshaft phenomenon (growth of the anterior portion of the spine when the posterior

spine is fused resulting in lordosis and bending of the fusion mass [10]), and is better at correcting hypokyphosis [1, 6, 11]. The anterior approach also provides excellent exposure to allow decompression of the spinal canal. This contributes to an improved neurological outcome with vertebral fractures [1, 7]. In addition, the anterior approach minimizes damage to the posterior ligamentous structures, spinal cord, and segmental nerve roots [3]. The anterior approach offers advantages of less blood loss, a kyphotic effect for a lordotic deformity, prevention of erector musculature denervation, and absence of prominent implants [6].

The anterior approach has higher morbidity rates than the posterior approach [7]. Pulmonary complications are quite common in up to 50 % of patients [3]. The most common problems are atelectasis, prolonged pleural air leakage, hemorrhage, infection, and post-thoracotomy pain [8]. In addition, with anterior spine surgery, the segmental vessels may be inadvertently or intentionally ligated, producing spinal cord ischemia or a relative ischemia that makes the spinal cord more sensitive to other adverse events [4]. The most feared complication is spinal cord ischemia from division of the artery of Adamkiewicz; especially in the regions where it is most commonly located (especially T9–12 on the left) [3]. The loss of critical anterior radicular arteries is particularly an issue in congenital conditions leading to spine deformity, because these patients appear to have abnormal vascularity [5].

However, any organ in the thorax can be injured. This includes the occurrence of chylothorax , especially when exposure occurs along the lower aspect of the thoracic spine during a right-sided approach [3]. Delayed rupture of the aorta due to a pseudo-aneurysm has also been reported [8, 9]. Of note, the death rate of patients with malignancy is higher such that some authors recommend reserving surgery for those patients who have preoperative neurological deficits [3].

Because some of the morbidity of the anterior approach is due to the necessity for a thoracotomy, newer techniques have been developed using thorascopic methods (video-assisted thorascopic surgery [VATS]). VATS has been successfully used in thoracic and thoracolumbar spine surgery. As with open thoracotomy, VATS requires a double lumen tube or bronchial blocker and lateral decubitus positioning; a right-sided approach is usually recommended [9].

All indications for surgery via a thoracotomy are also indications for VATS and include scoliosis, Scheuermanns’s disease, hemivertebrae,

crankshaft deformities, tumor resection, spinal decompression secondary to fractures, decompression of nerve roots secondary to spinal degeneration, and spinal correction of deformities. Contraindications are intolerance to one-lung ventilation, high airway pressures, emphysema, severe respiratory insufficiency, and previous thoracotomy [9].

VATS is comparable to open and posterior procedures in terms of curve correction and adequate exposure from T2–L1. It provides better cosmesis, reduced morbidity, lower blood loss, lower infection rates, better illumination and magnification of the spine (especially the dura and the origin of the nerve roots), less damage to adjacent tissues, pulmonary compromise, pain, blood loss, and muscle wall morbidity compared with standard thoracotomy. VATS increases operative time, intensive care unit time, the need for an iliac crest bone graft, and complication rates, but has shorter overall recovery time and hospitalization, with less pulmonary function impairment [9, 11].

The most common complications of VATS include pleural effusion, intercostal neuralgia, and ipsilateral pneumothorax [12]. It can be difficult to control bleeding with VATS so preservation of blood vessels is recommended [9]. Because of the higher death rates in patients with malignancy, the thorascopic approach may offer less risk in these patients [3].

There has also been a trend toward the use of a posterior approach to achieve similar surgical results as described for anterior surgery. In tumor and trauma, the vertebral body segment can be excised and anterior column support placed through a costotransversectomy. This surgical approach involves the resection of the ribs bilaterally, typically out to the level of the posterior angle, providing surgical access to the level. Again, the thoracic contents are at risk, although these procedures are done without breach of the pleural space. Similar to procedures done with a thoracotomy, anterior spinal cord blood supply may be at risk with these approaches.

Compared to the anterior approach, the posterior approach allows preservation of the thoracic wall musculature with decompression of neuroforamina and the central canal. It is better for patients who require fusions of multiple curves [6]. Advocates for the posterior approach indicate less morbidity and the reduced possibility of a kyphotic deformity from loss of alignment [1].

A second advantage of the posterior approach is that access to the posterior spinal elements allows an osteotomy. At least two osteotomies are used to treat sagittal plane deformity of the thoracic spine. The Smith-

Peterson osteotomy (SPO) was originally developed for the surgical correction of ankylosing spondylitis and is now used for other kyphotic deformities as well. This procedure involves removal of posterior column bone, facet joints, the inferior portion of the lamina of the rostral vertebrae, spinous process, and ligamentum flavum. This shortens the vertebral column, resulting in hyperextension at the level hinging around the disk space. Pedicle subtraction osteotomies (PSO) are also utilized when greater correction is needed. In this procedure, a wedge cut to the anterior third of the vertebral body (including the complete removal of the pedicles and posterior elements bilaterally) is undertaken. The procedure with greatest risk utilized in deformity correction is a posterior vertebral column resection (PVCR; removal of an entire vertebral segment), typically with the placement of anterior column support and angular correction. Neurological complications have been reported for each of these. A recent publication reported new neurological deficits in 3.7 % of patients. This risk increases incrementally with greater amounts of bone resection. PSOs resulted in nearly double (7 %) the risk for new neurological deficits. Complete cord injuries have been reported with PVCR procedures, and neurological changes are higher, although the rate is difficult to determine. Up to 22 % of patients have been reported to have intraoperative IOM changes [1].

It is thought that many of these complications are related to stretching and injury to the anteriorly located blood vessels [13]. If osteotomies are performed, the possibilities of residual fragments of bone, gel foam, or bone wax necessitate the examination of the spinal canal, especially if IOM indicates a possible problem [4]. If IOM changes occur with closure of the osteotomy, the correction is released and lesser correction or intraoperative changes to the surgical plan are made.

A debate exists about the best posterior instrumentation for the correction of scoliosis/kyphosis . Because of the access to the pedicles of the vertebrae, segmental instrumentation with pedicle screws can be used; these methods appear to produce the best three-column fixation with a more powerful correction of coronal plane deformities [14]. This is particularly useful in scoliosis when the curve exceeds 100° or a sagittal kyphosis of more than 120° is present [15].

The success of segmental instrumentation with pedicle screws has been well demonstrated in the lumbar-sacral spine, where the corrective forces are greater than hook and wire techniques. However, placement of pedicle screws

in the thoracic spine is more challenging than in the lumbar spine since they are smaller, narrower, have greater anatomical variability in diameter, shape, and have varying anteromedial and cephalad angulation [16–18]. One author has suggested that the pedicles from T4 to T8 may not be wide enough for pedicle screw insertion [19]. However, new techniques, including the use of computer-assisted navigation, have made it possible to instrument the thoracic spine, even in extremely difficult situations with greater success and decreased risk to patients.

The rates of thoracic pedicle screw malposition may exceed the reported rates for the lumbar spine, perhaps because the thoracic pedicles are smaller; especially in women where the pedicles are smaller than their male counterparts [20]. However, the complication rates of thoracic pedicle screws are similar to other methods of spinal instrumentation [21]. In addition to the risk of injury to nerve roots, the spinal cord is at risk with a medially positioned screw due to direct injury or spinal stenosis likely because the spinal canal is smaller compared with the size of the spinal cord [17]. This is particularly true on the concave side of the spine with scoliosis (especially at the apex), where the spinal cord may be in direct contact with the medial wall of the pedicle [16, 22–25].

With lateral malposition , the pedicle screw can irritate or injure the nerve roots as well as injuring major vessels (e.g., the aorta), pleura, spinal segmental arteries, and viscera. Because of the proximity to the roots, the identification of malpositioned screws has been attempted using stimulation of the screws to determine the thresholds for EMG activation of the muscles innervated by the corresponding nerve roots. This technique has been successfully utilized in the lumbar-sacral spine, but studies with this technique have had mixed results with pedicle screws placed in the thoracic spine cephalad to T10 [26]. Using this technique, malpositioned screws in the thoracic spine are more difficult to detect, likely because of less robust innervation of musculature (rectus abdominis and intercostal muscles) [27]. Attempts using the paraspinous muscles [28] and electrodes in the axilla [22] have had variable success.

The risk to the spinal cord by medial malposition appears to occur when the screw encroaches beyond 2 mm and compresses the spinal cord [22]. An alternate approach to identify medial malposition utilizes stimulation of the screw pilot hole with a four-pulse technique similar to that used transcranially for MEP [17, 20, 22]. This stimulation is thought to activate the corticospinal

tract in the spinal cord and is measured as triggered EMG in the leg muscles (anterior tibialis, medial gastrocnemius, abductor hallucis, and quadriceps). This technique appears to be successful, providing that the pilot hole is stimulated with a ball-tipped probe before the screw is placed (because the screws are made of titanium, which is a poor electrical conductor due to the oxide coating) [20]. It has been shown to significantly reduce the incidence of clinically relevant thoracic pedicle screw medial malpositioning [20].

Of note, medial penetration of a thoracic pedicle screw can also produce a dural tear, leading to a cerebrospinal fluid leak and intracranial hypotension [29]. Since a nonreversible IOM change with a tear is always associated with a new-onset neurological deficit, monitoring can guide whether repair of the leak is needed [30].

Neurological Risks of Thoracic Surgery

In general, the risks of neurological injury with surgery on the thoracic spine relate to the pathophysiology of the individual patient and the surgical procedure used. The reported risk of spinal cord injury in scoliosis varies between 0.3 and 1.4 % with the most recent data from the Scoliosis Research Society of 0.5 % (2006) when intraoperative monitoring has been used [4]. Neurological risk is increased in some patients, especially in those withcongenital kyphosis, neurofibromatosis, or skeletal dysplasia [4]. It is also increased in patients with asymmetric neurological deficits, preoperative paresthesias, bowel or bladder dysfunction, or excessive neck or back pain [4].

With respect to the surgical procedure, the proposed mechanisms of injury during spine surgery are direct cord trauma (hooks, wires, and pedicle screws), epidural hematoma, distraction, or compression of the spinal cord from correction by instrumentation, excessive tension on blood vessels leading to ischemia, spinal cord ischemia from relative hypotension, anemia, or ligation of anterior segmental vessels [4].

In general, surgical techniques have evolved to maximize the amount of correction and minimize the fusion levels. As such the instrumentation has evolved from Harrington distraction to rod-screw constructs [6]. These improvements now allow for segmental instrumentation and fusion through the use of multiple anchor points in the vertebrae. The ability to correct complex curves are significantly increased but the risk for neurological injury

is also increased with the addition of more fixation points [4]. Because metal instrumentation is stronger than bone, a screw or hook has the potential to cut through the bone if excessive force is applied [6]. As such, each step during instrumentation and correction has the potential to produce injury, making real-time continuous assessment or monitoring important for immediately identifying changes in neurological status. Adding osteotomies, corpectomy, and anterior fusion increases the risk of further neurological compromise as the vascular supply of the spinal cord can be disrupted due to direct ligation of segmental vessels [3]. Further, distraction or compression of the anterior blood supply can also lead to neurological changes.

Although direct trauma to the spinal cord can produce injury, paralysis is thought to be most likely the result of an ischemic insult to the anterior and central portions of the spinal cord. This makes blood pressure management very important [31]. In general, this means that early identification of the problem may allow correction of the offending element or adjustment of the physiology to improve blood flow and perfusion pressure, reducing the risk of permanent neurological injury. This will be most effective when the reduction in blood flow relates to the smaller vascular structures within the spinal cord and less when the major vasculature is compromised.

Major vascular injury during spine surgery depends on the level of surgery. For example, the internal carotid artery and vertebral artery are more commonly compromised with anterior cervical surgery and the vertebral artery is more commonly compromised during the posterior cervical approach [32]. In the anterior approach to thoracolumbar spine surgery, the aorta, inferior vena cava, and azygous and hemiazygous veins can be injured. Further, avulsion or sacrifice of the intercostal arteries can occur. The thorascopic approach is associated with less vascular injury [32]. Thoracic pedicle screws can injure the aorta (as can a K wire), and can lead to injury or a pseudoaneurysm [32].

Ligation of the segmental vessels to the spinal cord is routine during anterior thoracic surgery and has been generally considered safe if the ligation is unilateral, performed on the convexity of the curve, and the ligation occurs at the midvertebral level [32]. However, anterior spinal artery syndrome has been reported in patients who have had prior correction for kyphosis [32]. Compression of the superior mesenteric artery between the aorta and the duodenum has also been reported during spine straightening for scoliosis correction with nausea, vomiting, abdominal pain, and distention

occurring 1 week after surgery [32]. Anterior lumbar surgery has been associated with laceration of the iliac veins or (less commonly) the iliac artery; especially at the L4–5 level [32].

The risk of ischemic injury is increased due to the increasing complexity of instrumentation and the increasing complexity of the pathophysiology in patients presenting for surgery. This has raised a concern about optimal blood pressure management [33]. Although deliberate hypotension has been used successfully in some young healthy patients undergoing simple instrumentation, recommendations for a more physiologically normal blood pressure have emerged in older patients with increased neurological risk or increasingly complex procedures. For example, a mean blood pressure (BP) less than 55 mmHg increases neurological risk [4]. If it is desired to lower blood pressure to reduce bleeding, mild hypotension to a mean BP of 65 to 75 mmHg has been recommended prior to the corrective maneuver with a restoration of the mean BP to greater than 70 mmHg after spinal manipulation and correction [4]. Hence it has become common to increase the mean pressure, when appropriate, in patients exhibiting possible ischemia (such as when IOM indicates a possible neural compromise). A second suggestion is the use of intravenous lidocaine (2 mg/kg) to provide vasodilation in the ischemic spinal cord after segmental vessel ligation during anterior surgery [34].

Finally, if spinal cord injury is suspected, it has been suggested to keep the mean arterial pressure (MAP) greater than 80 mmHg postoperatively as well as to administer methyl prednisolone (although its effectiveness is debated) [35]. The optimal blood pressure in this circumstance should be individualized based on the patient's presurgical baseline and any vascular pathology. Ideally, clinical assessment or electrophysiological monitoring may help determine the minimally adequate pressure.

Monitoring in Thoracic Spinal Surgery

The Stagnara wake-up test was first described and is still used in some centers, but has largely been replaced by electrophysiology [36]. The somatosensory-evoked potential (SSEP) was introduced in 1977 by Nash and more recently transcranial motor-evoked potentials (MEPs) have been used since US Food and Drug Administration (FDA) approval in 1995 [37]. Of note, MEP changes have been reported with low blood pressure. As a result,

keeping the mean BP greater than 80 mmHg or 20 % above their normal baseline blood pressure has been recommended [4].

A variety of monitoring techniques have been used for thoracic spine surgery:

1. The Stagnara wake-up test has been used to assess motor function during the procedure [38]. Since the surgical procedure involves several possible mechanisms for spinal injury, there is not one clear time for a wake-up test to be helpful other than to confirm significant intraoperative electrophysiological changes.

2. Testing for clonus can be used on awakening, but as with the wake-up test, it will not allow a timely identification of a problem nor help identify a specific insult needing correction.

3. The spontaneous EMG of muscles innervated by the nerve roots in the operative field can be used as described above. However, in the thoracic region of the spine, this methodology may be less effective than for cervical or lumbar regions. Spontaneous EMG can also assess impending light anesthesia when background EMG activity is seen in multiple channels.

4. Cortical SSEPs can be used to assess transmission in the white matter of the dorsal columns through the operative field as well as to detect unfavorable circumstances in the arms, neck, brainstem, and cortex. When the cortical responses from the lower extremity change, the cortical response from the upper extremity can be used as a reference for global effects (e.g., anesthesia, whole body hypothermia) to differentiate these changes from problems in the operative field.

5. SSEPs recorded by an epidural electrode can also be used to assess spinal cord transmission, especially if there are not adequate cortical responses or those from the cervical spine. Optimally, this requires placing electrodes cephalad and caudal to the operative site. Techniques using the epidural or paraspinous electrodes for simulation and recording above and below the operative area have also been used.

6. MEPs recorded as compound muscle action potential responses (CMAPs) are useful for assessing transmission in the anterior white matter motor tracts. They are also a means for assessing the functional status of the gray matter of the lower extremities to the extent it is in the operative field (L4–S2 roots). As with the SSEP, the upper extremity responses serve as a reference.

7. MEPs recorded by an epidural electrode can also be used for this purpose, similar to the discussion of the epidural recordings for the SSEPs. However, with scoliosis, D wave changes have been observed due to the rotation of the spinal cord during spinal derotation [39].

8. The H-Reflex response can be used in conjunction with MEPs or as a replacement if conventional MEPs cannot be obtained. This response assesses the peripheral nerves, spinal gray matter reflex pathways, and will be sensitive to a cross-sectional spinal cord injury cephalad to the gray matter involved in the reflex (L4–S2 for posterior tibial nerve).

9. The electroencephalogram (processed or raw) can be used to assess the anesthetic effects on the cerebral cortex. For these surgeries, it is unlikely that cerebral ischemia would occur.

Unfortunately, one neurological complication of prone spine surgery is not detected by IOM. Postoperative visual loss is a rare but devastating complication of spine surgery in the prone position. The incidence ranges from 0.017 to 0.1 % and may be due to occipital lobe infarction, retinal infarction or, most commonly, posterior ischemic optic neuropathy. A case-controlled study revealed risk factors that include male gender, obesity, and head-down position (e.g., Wilson Frame), longer anesthesia duration, large blood loss, anemia, and crystalloid rather than colloid volume replacement [40, 41]. This is thought to be consistent with venous congestion as well as ischemia. Recommendations for reducing the risk have been published, but to date, monitoring of the full field, flash-induced electroretinogram, VEP, and intraocular pressure have not been systematically evaluated for their

effectiveness in the prevention of this condition [40–42] (see Chap. 4, “Visual Evoked Potentials,” for review of these techniques).

Case 1

A 33-year-old 70-kg woman with congenital scoliosis had an anterior T6–T8 interbody fusion with cages, lateral plate, and screws for degenerative thoracic disk disease. This resolved her symptoms but 3 years later she presented with chronic pain following a “pop” that started with back motion. CT and MRI studies were consistent with disease at the adjacent levels (T4–5 and T5–6) with probable nonunion of the original fusion (Fig. 34.1). She also had a history of depression. A pulmonary embolism occurred after her first spine fusion, which was thought to originate in her left arm. Her physical examination shows normal light touch, strength, and sensation in all extremities, but a tender spine sensitive to palpation over the region of the original fusion.

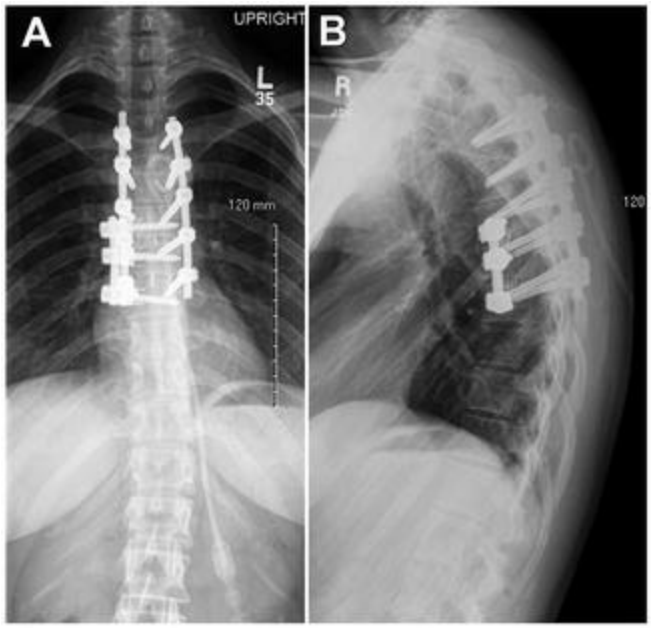

Fig. 34.1 Chest radiographs taken preoperatively of the patient in Case 1 showing the spine instrumentation

After failure of conservative therapy and facet joint injections, she was scheduled for posterior exploration of the original fusion T6–8 and posterior fusion T4–8 with segmental instrumentation using local autograft bone and

bone morphogenetic protein. Preoperative evaluation revealed no additional medical problems. General anesthesia was induced after sedation with midazolam (2 mg) using propofol (200 mg), lidocaine (40 mg), fentanyl (100 μg), rocuronium (50 mg), and vancomycin (1 g). General endotracheal anesthesia was maintained using a propofol infusion (160–170 μg/kg/min), sufentanil infusion (0.5–0.6 μg/kg/h), desflurane (2–3 % inspired), with no additional muscle relaxant. In addition, ketamine (50 mg) and decadron (4 mg) were given during the 5-h procedure. The patient was positioned prone with the head in a neutral position head holder and the arms were placed on arm boards with the shoulders abducted at 90°, elbows at 90°, and arms slightly forward from the plane of the chest.

In addition to the usual physiological monitors, processed EEG monitoring was used and blood pressure was monitored by an intra-arterial catheter (mean BP was maintained between 75 and 90 mmHg). Esophageal temperature was maintained between 35.9 and 37.2 °C. Intraoperative neurophysiological monitoring was conducted using SSEPs (median nerve and posterior tibial nerve), transcranial elicited MEPs recorded from the abductor pollicis brevis (APB) and abductor hallicus (AH) muscles, and free-run electromyography from the APB and T4–8 intercostal muscles. Pedicle screw testing was conducted and all responses were elicited at stimulation intensities greater than 20 mA.

The surgical procedure proceeded uneventfully. Pedicle screw placement was difficult owing to the narrow nature of the pedicles. Intraoperative CT scanning and computer-assisted navigation were used to enhance visible landmarks. Decortication of the spinous processes and placement of segmental instrumentation were accomplished and the wound was closed. The intraoperative monitoring was uneventful with no apparent changes due to surgical events. However, the amplitude of the cortical SSEPs from the left arm and the MEPs recorded from the left APB markedly decreased during the procedure. The arm position was adjusted and the blood pressure was raised resulting in resolution of the changes. The tracings are shown in Fig. 34.2. On awakening, the patient had no neurological changes and was discharged on postoperative day 3 with improved back symptoms and pain management. Her postoperative visits demonstrated continued improvement.

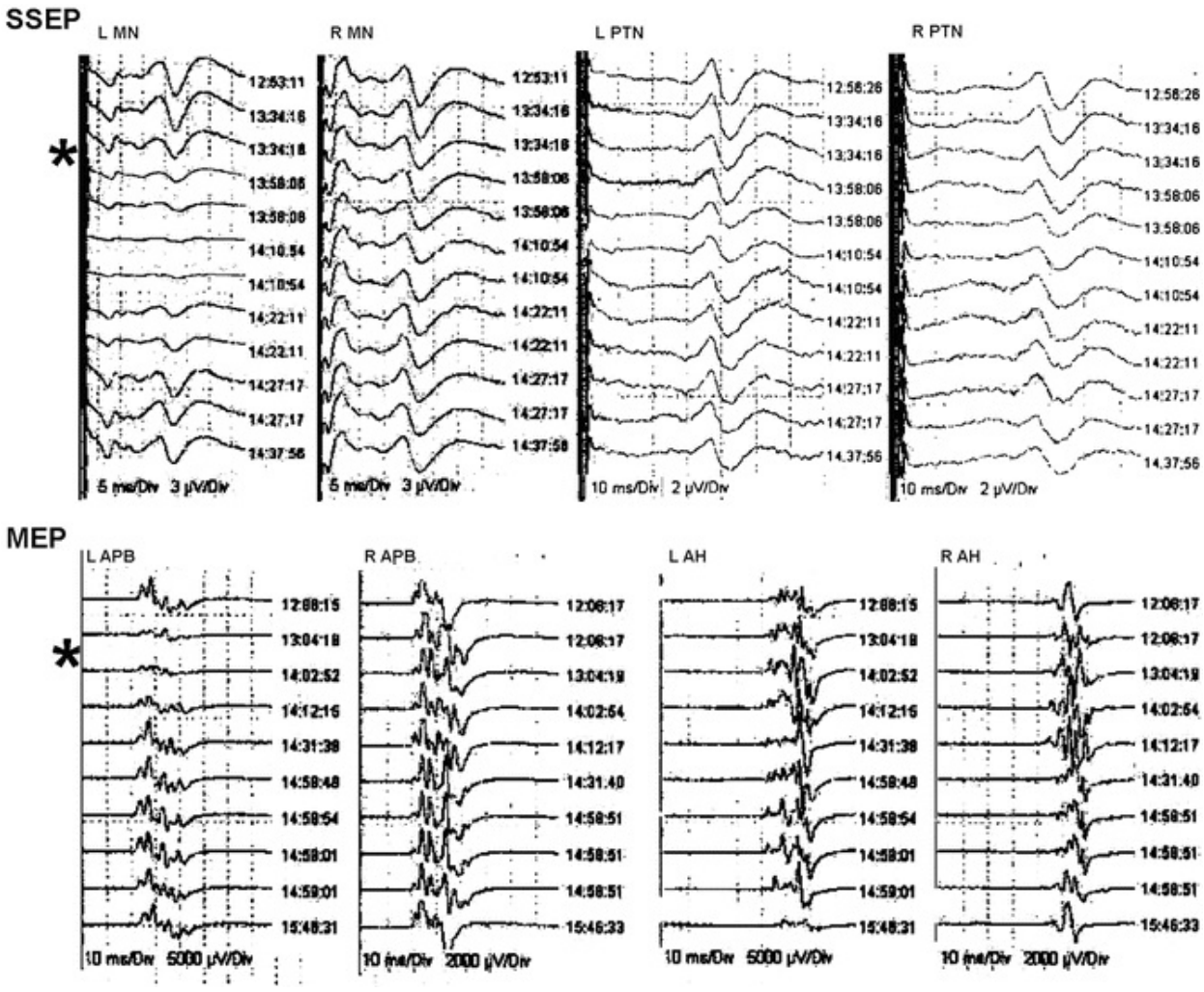

Fig. 34.2 Selected tracings during the surgery in Case 1. Cortical SSEP tracings are shown at various times from the left (*L*) and right (*R*) median (*MN*) and posterior tibial nerves (*PTN*). MEP tracings are shown at the bottom as recorded from the left and right abductor pollicis brevis (*APB*) and abductor hallicus (*AH*). The *asterisk* marks the onset of the loss of the SSEPs and MEPs recorded from the left arm

Discussion

For this case, the response changes can be assessed as the result of the four etiological categories: Surgical, anesthetic, technical, anatomic/positioning, and physiological. A surgical etiology was thought to be unlikely in this case primarily because the operative site was well below the neural tracts involved in the loss. When the surgeon was informed about the loss, they could not visualize how their procedure could account for this change.

Anesthetic effects would be an unlikely cause of the changes that were observed in this case, where two modalities in only one extremity were

affected. In general, anesthetic effects would most likely be bilateral and global (i.e., affecting all four extremities). On the other hand, the effects of anesthesia could result in a differential effect on modalities that are most sensitive to anesthetic agents (e.g., MEPs) as well as possibly a greater effect on lower extremity responses than upper extremity responses. Finally, if the amplitude of the responses is diminished and is near the background noise level, a greater anesthetic effect might be expected on very low amplitude responses as compared to larger amplitude, more robust responses.

Finally, if the arm that lost the responses had some sort of regional anesthetic effect, then anesthesia could have accounted for the loss. Aside from a regional blockade (such as brachial plexus block or Bier block), this would require that the anesthetic agent be selectively trapped in the arm and be of the kind to interfere with axonal conduction of the SSEPs and MEPs or generation of the MEPs. Because most intravenous anesthetic agents interfere with synaptic transmission, the only agent that might be involved would be muscle relaxants. However, this would not account for the SSEP loss. If, however, a local anesthetic (e.g., lidocaine) had been injected and was trapped (e.g., a tight blood pressure cuff), then anesthetic agents could potentially be involved.

A review of the anesthetic record and discussion with the anesthesiologist did not reveal any potential etiologies for the loss. A review of technical causes for the changes was conducted. Nothing in the programming of the machine used for acquiring the IOM modalities could account for the changes. The stimulators and recording amplifiers appeared to function properly. With respect to anatomy and positioning issues, these were thought to possibly be a cause. A cerebral stroke was thought to be unlikely since that would likely have altered at least one of the other extremities. The common nerve roots involved include C8 and T1 (median nerve C6–T1, APB C8–T1) and the patient reportedly had a bulging nucleus pulposus in the cervical spine. For this to have caused the problem, there would likely to have been adverse neck positioning. This late in the case, it was thought to be unlikely since there was no evidence of improper positioning initially and the neck position had not changed. The most likely anatomic/positioning issue was pressure or traction on the brachial plexus from unfavorable arm position. The arm was examined and it appeared to be in an acceptable position. It had not been moved by the surgeons leaning on it nor had it been moved by radiology equipment, but a combination of positioning with the factors noted

below was considered possible.

Examination of the forearm revealed a swollen tense arm that appeared to be caused by the infiltration of the intravenous line on that side and not due to a hematoma at the arterial line site. Temporary placement of the pulse oximeter on the fingers of that hand revealed a very poor tracing. In retrospect, the anesthesiologist noted some problems with the arterial line, which had been placed in the radial artery of that arm. Specific examination of the ground, stimulation and recording electrodes revealed marked swelling at the site of the SSEP median nerve stimulation and MEP recording needles. During SSEP stimulation, the hand motion was markedly different than it had been before the swelling. In addition, the blood pressure cuff appeared tighter than usual, perhaps due to the arm swelling.

The arm swelling could have both mechanical and physiological effects contributing to the signal loss. With respect to the SSEP stimulation electrodes, the swelling could have moved the needles away from the median nerve, decreasing the effectiveness of the stimulation and producing local ischemia in the hand impairing the recording of the MEP. Visual inspection of both sets of needles suggested that this might have been the case. With respect to the perfusion of the arm and physiological effects, the tense arm was suggestive of a developing compartment syndrome with resulting ischemia of the muscles and nerves involved in creation of the SSEPs and MEPs. In addition, the tense blood pressure cuff could also have been contributing to ischemia and the possibility of a vascular abnormality resulting in or from the DVT in that arm. Finally, the arm was cold from the infiltration of unwarmed fluids and this may also have contributed to the changes in the monitoring responses. Other physiological changes were also considered, but central changes such as relative hypotension, hypocarbia, and whole body hypothermia were thought to be unlikely since only one extremity was affected and the anesthesia monitors did not reveal these abnormalities.

In response to the change, the arm was repositioned to insure minimal problems at the brachial plexus and elbow. The mean BP was elevated by 10 mmHg. The noninvasive blood pressure cuff was moved to the other arm and the intravenous fluids in that arm were stopped. Warm pads were used to help with the arm temperature and absorption of the infiltrated fluids. The arm could not be elevated since this would increase the stress of the brachial plexus at the shoulder. The pulse in the arm, as assessed by the arterial line

and pulse oximeter was observed to insure that a compartment syndrome requiring fasciotomy was not needed. The change in the evoked potentials gradually resolved and the surgery was completed uneventfully. Fortunately, the loss of monitoring capability in the arm did not reduce the monitoring signals most needed for the surgical procedure. By the conclusion of the procedure, the swelling had markedly improved and no new neurological abnormality in the involved arm could be identified.

Case 2

A 35-year-old woman with posttraumatic/postinfectious kyphosis resulting in fusion of the T7 and T8 vertebral bodies presented with severe thoracic kyphosis measuring 137°. This patient was treated nonoperatively for several years, including physical therapy, medications, and alternative treatments without improvement. She endorsed worsening deformity with the inability to maintain forward gaze. After a complete medical evaluation, including preoperative evaluation with endocrine and anesthesia, a posterior PVCR of T7, and posterior instrumentation from T2–L2 was planned (Fig. 34.3).

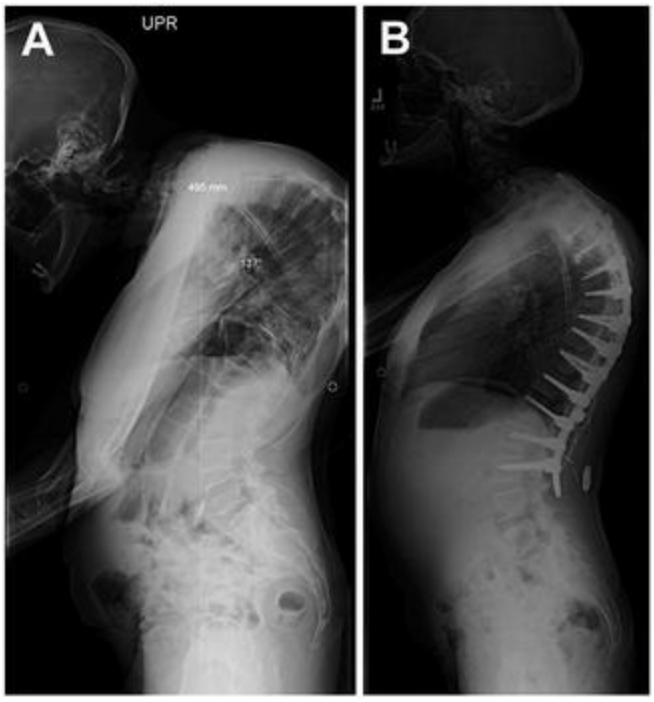

Fig. 34.3 Preoperative lateral radiograph of Case 2 showing the magnitude of thoracic deformity before (**a**) and after (**b**) surgery

General anesthesia was induced with propofol and maintained with total intravenous anesthesia. No volatile anesthetic was used at any time. Intravenous infusion of propofol, sufentanil, ketamine, and lidocaine were titrated for the remainder of the case. The patient was positioned prone with the head in a neutral position head holder and the arms were placed on arm boards with the shoulders abducted at 90°, elbows at 90°, and arms slightly forward from the plane of the chest.

In addition to the standard physiological monitors, processed EEG monitoring was used as well as an intra-arterial catheter to monitor blood pressure continuously. The mean arterial pressure was maintained between 85 and 110 mmHg for the case with intermittent use of vasoactive medications. Esophageal temperature was maintained between 35.9 and 37.2 °C. Intraoperative neurophysiological monitoring was conducted using SSEPs (median nerve and posterior tibial nerve), transcranial elicited MEPs recorded from the APB, tibialis anterior (TA) and abductor hallicus (AH) muscles, and free running electromyography from the bilateral rectus abdominus and iliopsoas muscles.

The surgical procedure proceeded uneventfully. During the exposure portion of the case, it was noted that the left lower extremity cortical SSEP signal amplitude attenuated to greater than 50 % of baseline values (Fig. 34.4) and the MEPs were maintained (Fig. 34.5). This was not observed in any other cortical signals for the remaining extremities. Importantly, the subcortical SSEP signals for the left lower extremity remained consistent with baseline values, thus an alert was not called. The left lower extremity cortical SSEP signals fluctuated above and below the 50 % threshold for the remainder of the procedure.

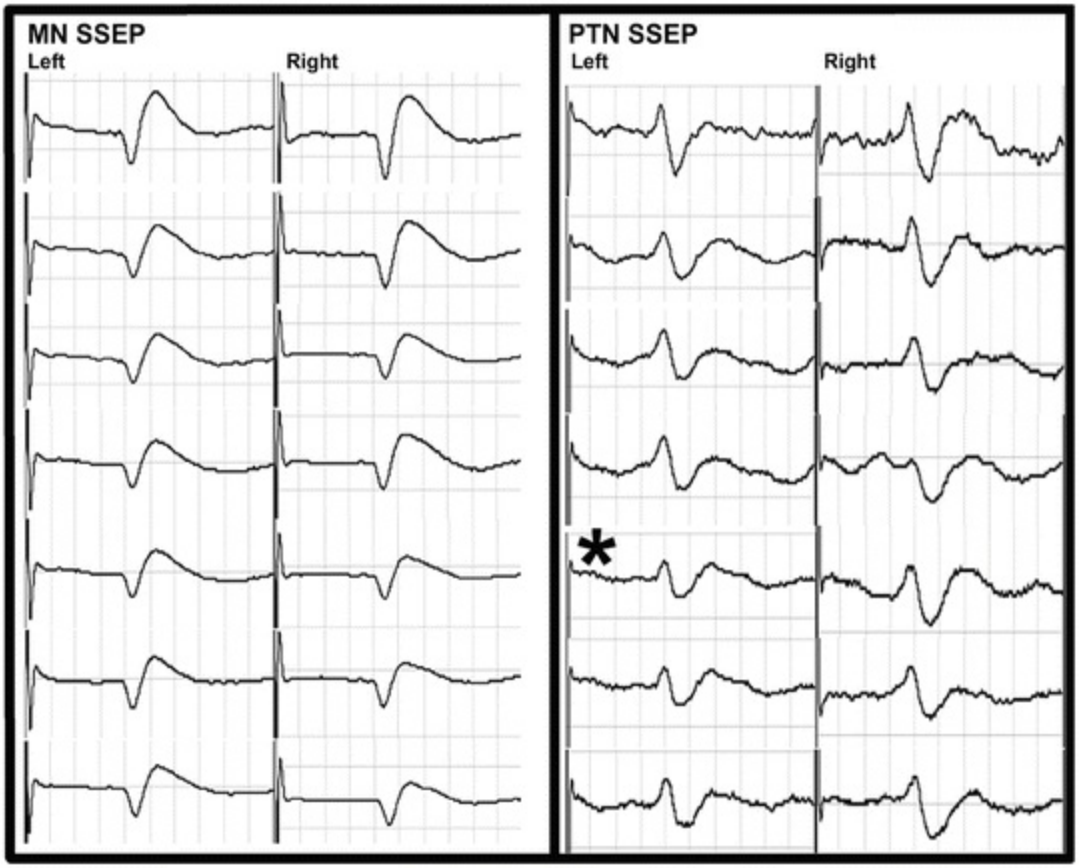

Fig. 34.4 Cortical SSEP tracings are shown at various times from the left (*L*) and right (*R*) median (*MN*) and posterior tibial nerves (*PTN*) for Case 2. The *asterisk* marks the onset of the loss of the SSEPs and MEPs recorded from the left arm

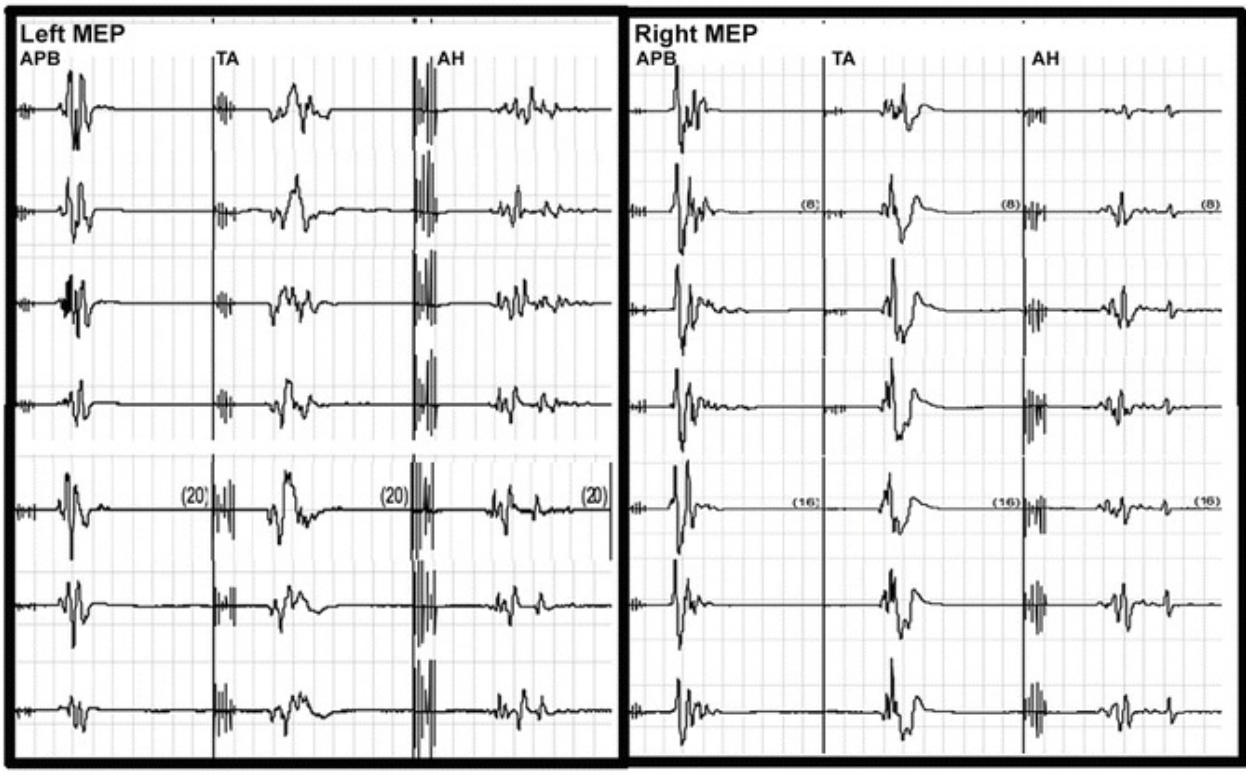

Fig. 34.5 Selected MEP tracings for Case 2 from the left and right abductor pollicis brevis (*APB*), tibialis anterior (*TA*), and abductor hallicus (*AH*). The tracings at the top were from the baseline and the bottom tracings were recorded at closing

Pedicle screw placement was difficult due to the narrow nature of the pedicles. Intraoperative CT scanning and computer-assisted navigation were used to enhance visible landmarks. No IOM perturbations were observed during this portion of the surgical procedure. Decortication of the spinous processes and a Smith-Peterson osteotomy (SPO) were then performed. During this segment of the procedure, acute blood loss and anemia prompted transfusion of two units of packed red blood cells. A decline in upper extremity amplitude was seen, but not to alert levels (>50 % decrease in amplitude). At this time, the surgeons requested a 10-mg dose of dexamethasone. The amplitude decrease resolved; no acute lower extremity amplitude changes or loss of MEPs were seen. Lastly, placement of segmental instrumentation and deformity correction was accomplished. During the osteotomy and spinal correction, MEPs were obtained frequently to ensure that vascular compromise and overcorrection was avoided. No further IOM perturbations were observed during this portion of the procedure. The wound was closed shortly thereafter and no new neurological

deficits were noted postoperatively.

Discussion

The change in SSEP amplitudes is better visualized when the amplitude values are plotted from the technical log of the case (Fig. 34.6). Looking at this graph, it is apparent that the amplitude of the upper extremity median SSEP responses (MN) increased their amplitude following baseline acquisition, perhaps due to an influence of residual anesthesia induction drugs at baseline that resolved during further recording. This “baseline drift” reduced the sensitivity of the monitoring for these tracings such that the values of the MN amplitudes did not reach alert thresholds during the SPO when the acute blood loss occurred. As such, monitoring should consider acute changes such as those seen during the osteotomy (C to D) as a basis for concern. For example, if the baseline had been reset to the higher values at the time of x rays prior to the surgery, the amplitudes would have fallen below the alert threshold of 50 % (i.e., the amplitudes would have fallen to 45–44 % [left, right] of the new baseline). Fortunately, correction of the anemia and volume loss corrected the likely cause of the amplitude decline. Because MEPs are more sensitive to spinal cord ischemia, it was good monitoring strategy to frequently follow the MEP values during this time to insure that the transfusion and physiological management were optimal.

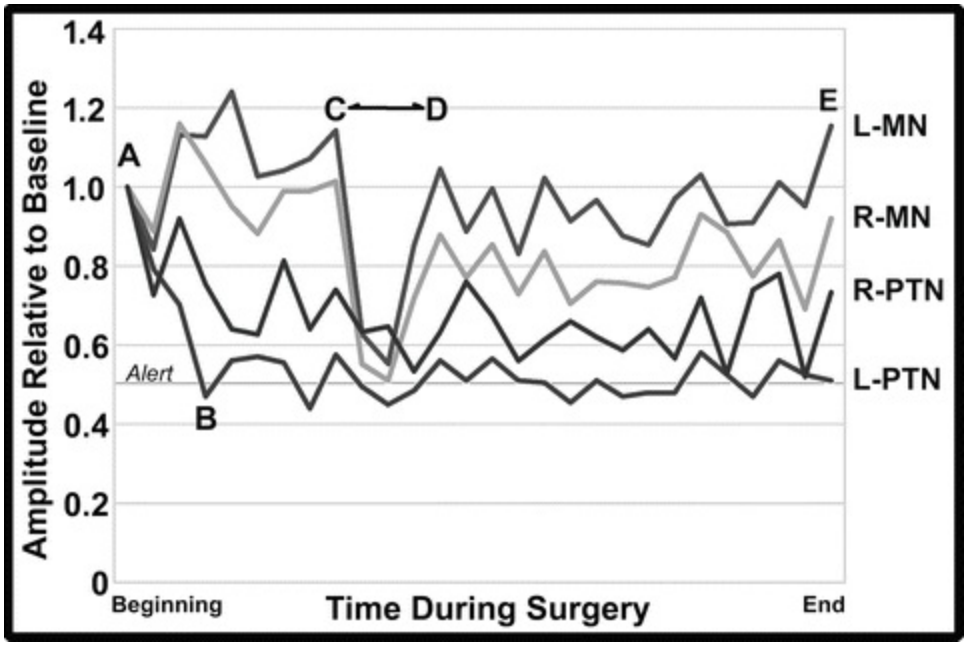

Fig. 34.6 Graph of selected tracings of the cortical SSEP amplitudes from the left (*L*) and right (*R*) median (*MN*) and posterior tibial nerves (*PTN*) as taken from the technical log of the case. Amplitudes are plotted as a fraction of the baseline values at the beginning of the monitoring (*A*) through closing (*E*, end). The amplitude of the left PTN response fell below the 50 % threshold alert criteria value at *B*. The amplitude of the left and right MN responses fell during the Smith-Peterson osteotomy (*C* to *D*) but did not reach the 50 % threshold alert criteria value

In contrast to the responses obtained from the upper extremity, the lower extremity amplitudes declined after the baseline recordings. Although not clear why, it was felt likely that a temperature decline in the lower extremity during positioning and skin preparation may have contributed to that change. A drop in esophageal temperature of 1.4 °C and a 6–7 % increase in latency were consistent with the reduced conduction velocity in the legs from a temperature decline. If the PTN baseline amplitude values had been reset to the amplitudes at the time of x rays prior to the surgery (i.e., 47–74 % [left, right] of the initial values), the amplitude values would have not have declined to less than 70 % of the new baselines. In this case, the team was reassured by the slow steady decline in amplitudes that preceded the surgical intervention and with the fact that MEPs remained present.

Such baseline drift has been seen in previous cases. The term “anesthetic fade” has been used for the increase in stimulation voltage needed to record MEPs as the surgery progresses [43]. In this case, declines and increases in SSEP amplitudes were both seen. Although an anesthetic-related factor may have been associated with the amplitude increase as noted above, it is unlikely that anesthesia contributed to the lower extremity SSEP amplitude decline since a global decrease would have been expected. As such, “anesthetic fade” might perhaps be better considered as “baseline drift” since multiple causes might contribute. As noted, tracking baseline drift so as to reset alert criteria and watching for acute amplitude declines are prudent practices to help optimize monitoring.

Conclusions

The use of intraoperative monitoring has become common place in the correction of spinal deformity. The initial demonstration of improved outcome was in the correction of scoliosis. The value in reducing preventable paralysis with scoliosis was shown by the Scoliosis Research Society (SRS) and European Spinal Deformities Society. They pooled the results of 173 surgeons who performed correction of spinal deformity in 51,263 cases

(scoliosis, kyphosis, fractures, and spondylolisthesis) [44]. The overall incidence of neurological injury with SSEP monitoring was 0.55 % (1 in 182 cases), well below the 0.7–4.0 % expected based on historical experience. In 1992, the SRS published a position paper that concluded that "neurophysiological monitoring can assist in the early detection of complications and possibly prevent post-operative morbidity in patients undergoing operations on the spine" [44]. This was echoed in the British literature, saying "it is standard practice to conduct some form of monitoring when performing any spinal operation that is associated with a high risk of neurological injury" [45]. This made the utilization of monitoring a virtual standard of care during axial skeletal and spinal cord procedures [46].

Recently the American Academy of Neurology with the American Clinical Neurophysiology Society published an evidence-based guideline update on spine monitoring with SSEPs and MEPs [47, 48]. They identified class I and class 2 evidence which showed that the detection of adverse IOM changes during monitoring allowed significant reduction in the occurrence of paraparesis, paraplegia, and quadriplegia. All patients with new-onset neurological changes had changes in IOM responses. This finding has been echoed by multiple studies, and the cost-effectiveness in scoliosis has been demonstrated [44, 46, 49–60].

Hence continuous IOM, in a real-time fashion utilizing MEPs as well as SSEPs, is crucial in preventing and minimizing neurological injury, which can be a direct result of the surgical intervention or an indirect result of factors unrelated to the surgical field. The complexity of modern-day spine surgery, the abnormal physiological position of the patient during surgery, and the length of the surgical procedures all put the patient at risk for neurological injury, which may vary from a simple peripheral nerve neuropraxia to a devastating complete spinal cord injury. Utilizing appropriate modalities of IOM can prevent and correct most of these complications through early detection.

Questions

1. Monitoring of the cortical SSEPs in thoracic spinal surgery

    A. Is unnecessary if MEPs are available

B. Monitors for the possibility of brachial plexus positioning injury

C. Has a better correlation with a motor injury than the H Reflex response

D. Monitors for anterior spinal artery ischemia

E. Monitors for loss of bowel or bladder function

2. Monitoring of spinal corrective surgery by MEPs with epidural electrodes

A. May give false-positive changes with spinal derotation

B. Allow detection of unilateral spinal injury

C. Are unnecessary when SSEPs are monitored

D. The I waves give an estimate of corticospinal fiber number

E. Is not useful because it requires muscle relaxation

3. Complications described with the anterior approach to the thoracic spine INCLUDE:

A. Diaphragm surgery

B. Pulmonary complications

C. Loss of segmental radicular artery supply to the spinal cord

D. Damage to the aorta

E. All of the above

4. The Peterson-Smith Osteotomy involves removal of

A. Posterior column bone

B. Facet joints and the spinous process

C. The inferior portion of the lamina of the rostral vertebrae

D. The ligamentum flavum

E. All of the above

5. Which of the following is not thought to be a primary mechanism of motor injury in spinal corrective surgery?

A. Direct trauma from instrumentation

B. Deliberate hypotension

C. Epidural hematoma

D. Dural tear

E. Ligation of the posterior spinal artery

6. Complications of thoracic pedicle screws include all of the following EXCEPT:

A. Direct spinal cord injury

B. Nerve root injury

C. Aorta injury

D. Pleural injury

E. Vertebral artery injury

7. Methods proposed to reduce the risk of postoperative blindness include all of the following EXCEPT:

A. Use of colloid solution rather than just crystalloid for volume resuscitation

B. Maintaining a head-down position to keep the eye perfused

C. Avoiding hypotension

D. Avoiding excessive anemia

E. Using a different positioning table than the Wilson frame when possible.

Answers

1. B

2. A

3. E

4. E

5. E

6. E

7. B

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Footnotes

1 Asterisk indicates key references.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_35

35. Intraoperative Neurophysiologic Monitoring for Lumbosacral Spine Procedures

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Keywords Scoliosis – Spinal stenosis – Degenerative disk disease – Herniated nucleus pulposis – Spondylysis – Spondylolisthesis – Spondylolysis – Cauda equina syndrome – Spinal cord tumor – Tethered cord – Traumatic lumbosacral fractures – Decompressive laminectomy – Foraminotomy – Anterior spinal fusion – Posterolateral lumbar fusion with or without instrumentation – Posterior lumbar interbody fusion – PLIF – Transforaminal lumbar interbody fusion – TLIF – Anterior lumbar interbody fusion – ALIF – Extreme lateral interbody fusion – ELIF – Lumbar

discectomy or microdiscectomy – Lumbar corpectomy – Tethered cord release – Rhizotomy – Disk arthroplasty

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Key Learning Points

- Multimodality monitoring (SSEP + Tc-MEPs + EMG) provides the surgeon with optimal information about the state of the nervous system. This helps to increase sensitivity and provide the surgeon with additional information on the specificity of any warnings issued.
- Many studies have demonstrated the value of pedicle screw EMG monitoring for the protection of nerve root and neural tissue during lumbar pedicle screw placement.
- Triggered EMG is an excellent technique for determining whether lumbar pedicle screws are properly placed; however, use of the technique for screws in other locations (thoracic, cervical) may be helpful although normative data are less clear.
- SSEP monitoring alone may not detect all iatrogenic nerve root injuries, particularly in surgeries involving lumbosacral levels. The combination of SSEPs with corresponding level EMG monitoring is most ideal for the detection and prevention of nerve tissue injury.
- The advantage of monitoring during lumbar discectomy procedures is not well defined.

Lumbar spine disorders are the most common causes of disability in persons under the age of 45, with annual direct and indirect costs of these disorders amounting to billions of dollars [1]. More than a half million lumbosacral spine surgical procedures are performed each year to treat these spine disorders. Disease states of the lumbosacral spine that may require surgical correction include: scoliosis, spinal stenosis, degenerative disk disease , herniated nucleus pulposis , spondylysis , spondylolisthesis , spondylolysis , cauda equina syndrome , spinal cord tumor , tethered cord , and traumatic lumbosacral fractures . Surgical procedures to treat these disorders include: decompressive laminectomy, foraminotomy , anterior spinal fusion , posterolateral lumbar fusion with or without instrumentation , posterior lumbar interbody fusion (PLIF), transforaminal lumbar interbody

fusion (TLIF), anterior lumbar interbody fusion (ALIF), extreme lateral interbody fusion (ELIF), lumbar discectomy or microdiscectomy, lumbar corpectomy , tethered cord release, rhizotomy , and disk arthroplasty .

It is essential to have a good understanding of lumbosacral spine and spinal cord anatomy, the patient's disease, and the corrective surgical procedure in order to determine which intraoperative neurophysiologic tests will detect iatrogenic spinal cord and nerve injury during surgery. The lumbosacral spine consists of five lumbar vertebrae and five sacral vertebrae. They are connected to each other and stabilized by the intervertebral disks, the posterior zygopophysial joints, and the supraspinous, interspinous, ligamentum flavum, posterior longitudinal, and anterior longitudinal ligaments. The five sacral vertebrae are fused to form the sacrum. In the adult, the normal spinal cord ends at the conus medullaris, which lies at approximately the L1–L2 level. The filum terminale is the extension of the pia mater that descends from the conus medullaris to the coccyx. The cauda equina consists of the bundle of lumbar and sacral nerve roots that exit off the spinal cord at the conus medullaris and travel in the spinal canal, until exiting from their respective foraminae.

Neurologic deficit is one of the most devastating iatrogenic complications that can occur following surgical correction of spine deformities. For lumbosacral spine procedures, preservation of nerve root neurologic function is the main priority, as only the thecal sac and nerve roots are located below the L1–L2 level. However, in the patient with a tethered spinal cord or other abnormality leading to the spinal cord being below L1–L2, the spinal cord may also be at risk.

The objective of intraoperative neurophysiologic cord monitoring is to immediately detect and alert the surgeon of any neurologic compromise during the surgical procedure, so that corrective action can be taken to reverse an injury before permanent damage occurs. During lumbosacral spine procedures, the intraoperative neurophysiologic monitoring tests used to preserve neurologic function and provide immediate feedback information regarding any iatrogenic injuries with potential neurologic deficit include somatosensory-evoked potentials (SSEPs) , transcranial motor-evoked potentials recorded as muscle responses (Tc-MEPs) or as direct spinal cord recordings (D waves) , continuous or spontaneous electromyography (EMG) , and triggered or stimulated EMG from nerve root or pedicle screw stimulation with resulting compound muscle action potential (CMAP)

recordings from corresponding myotomes. Refer to the chapters of this book relating to these tests for in-depth descriptions of these specific monitoring techniques. SSEPs are the most commonly used intraoperative neurophysiologic monitoring test during spine surgery. However, SSEP monitoring may not detect all iatrogenic nerve root injury [2–4]; particularly in surgeries involving lumbosacral levels. Because of this, EMG and MEP monitoring gained increased popularity. Several studies have shown that for lumbosacral spine surgery, the combination of SSEPs with corresponding level EMG monitoring is most ideal for the detection and prevention of nerve tissue injury [4, 5]. MEPs may also be useful for detecting spinal cord ischemia for those patients where the spinal cord extends below L1–L2.

Decompressive Laminectomy With or Without Fusion and Instrumentation

A decompressive laminectomy consists of the surgical removal of the vertebral laminae to create more space for compressed nerve tissue. The surgeon may perform a laminectomy with or without fusing vertebrae or removing part of the involved disk. Instrumentation of the unstable areas of the spine with rods, plates, screws, and wire devices may also be used if a posterior spinal fusion is performed. During decompressive laminectomy with or without fusion and instrumentation, the mechanism of iatrogenic neurologic injury has been attributed to direct injury to cord or nerve root during drilling or probing, during placement of hardware into the spine, or during the decompression or distraction of the spine. With the combination of SSEP, MEP, and EMG monitoring, immediate detection of injury is possible, and this real-time alert to the surgeon can allow for changes in the course of the procedure that may prevent permanent injury.

Although it has been reported that the medical literature does not support the hypothesis that intraoperative monitoring can improve patient outcomes in patients undergoing surgery with instrumentation for lumbar degenerative disease [2, 3], several studies have demonstrated the efficacy of using multimodal intraoperative monitoring (MIOM) during lumbosacral spine surgery [4–6]. Sutter et al. [5] prospectively studied 409 patients with lumbar stenosis undergoing lumbar decompression with or without instrumentation. All 409 patients were monitored with MIOM, which consisted of cortical and spinal SSEPs, MEPs, and continuous EMG. Of these, 390 had no MIOM

changes, and only two of these had false-negative monitoring results. Three hundred and eighty-eight patients had true negative findings, and only one patient had false-positive changes. Eighteen patients had true positive MIOM changes, which predicted a postoperative neurologic deficit. Of the 20 patients with postoperative deficits, 18 recovered function (12 recovered completely and 6 recovered partially). The sensitivity of MIOM for these procedures was 90 % and the specificity was 99.7 % for predicting a postoperative neurologic deficit. The authors speculate that in those cases with minor complications, the outcome would have been worse had the surgeon not been alerted.

Gunnarsson et al. [4] retrospectively analyzed 213 patients having thoracolumbar surgery with concurrent SSEP and continuous EMG monitoring in order to determine the sensitivity and specificity of each test for detecting new postoperative motor deficits. They found that SSEPs had a sensitivity of 28.6 % and a specificity of 94.7 %, whereas the sensitivity and specificity for EMG was 100 and 23.7 %, respectively. They concluded that the combined use of both modalities could be more powerful in identifying potential neural injury.

Voulgaris et al. [6] suggested that MEPs might have additional value for predicting postoperative outcomes. In a study of 23 patients who had lumbar decompressive laminectomies for spinal stenosis, 17/25 had greater than a 50 % increase in MEP amplitudes, while 6/17 had little increase or no change. In follow-up, the 17 patients with greater than a 50 % increase in MEP amplitude had the greatest decrease in visual analog pain scores.

Cole et al. [7] performed a retrospective propensity score-matched analysis on a national database of over 85,000 patients between 2006 and 2010, comparing rates of neurologic deficit following elective single-level spinal procedures (anterior cervical disk fusion [ACDF] , lumbar fusion, lumbar laminectomy and lumbar discectomy) with and without intraoperative neuromonitoring (IOM), as well as the associated payment differences. They found that in all single-level spine procedures with IOM, neurologic complications were significantly decreased only among lumbar laminectomies (0.0 % vs. 1.18 %; $P = 0.002$). No differences were observed with ACDF, lumbar fusions, or lumbar discectomies. There was a significant increase in total payments seen with all procedures with the addition of IOM: ACDF payments increased by 16.24 %, lumbar fusions 7.84 %, lumbar laminectomies 24.33 %, and lumbar discectomies by 22.54 %.

Pedicle screws are often used as a point of fixation. A hole is drilled into the pedicle wall of the vertebrae followed by the screw placement. Accidental breach of the pedicle wall exposes the adjacent nerve root, with possible nerve root irritation or injury during and following screw placement. The use of SSEPs alone, as demonstrated by Gundanna et al. [8] during lumbar surgery, does not always detect a malpositioned pedicle screw, which can lead to postoperative radiculopathy.

Current delivered from a monopolar stimulating electrode placed within a pedicle hole, or touching a pedicle screw, can elicit EMG CMAP responses from corresponding limb muscles, which can alert the surgeon to a pedicle wall breach before injury to an adjacent nerve root can occur (Fig. 35.1).

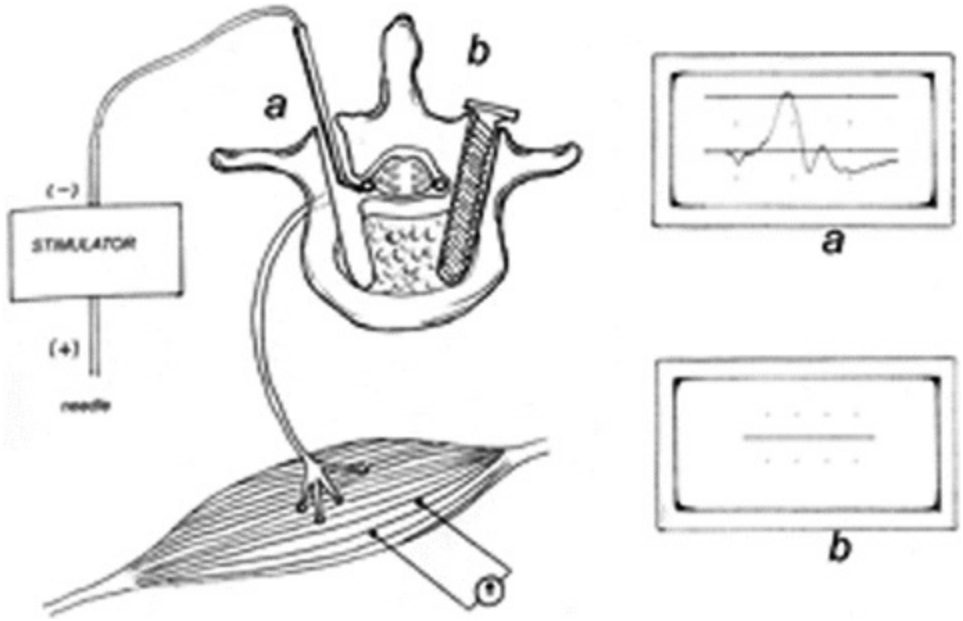


Fig. 35.1 Stimulus-triggered EMG for the detection of pedicle wall breach. Electrical stimulation of hole (**a**) with low current activates the adjacent nerve root, evoking a CMAP response, representing a pedicle wall breach. Stimulation of the screw at hole (**b**) demonstrates high impedance to current through a layer of cortical bone, as no evoked CMAP is produced. This represents correct screw position. Reproduced with permission from Husain [9]

Many studies have demonstrated the value of pedicle screw EMG monitoring for the protection of nerve root and neural tissue during lumbar pedicle screw placement [10–12]. Bindal et al. [13] acquired triggered EMG recordings by stimulating the pedicle access needle and pedicle tap during TLIF. Their findings altered the trajectory of the pedicle access needle in 76.2 % of the procedures, and they felt this had led to a safer pedicle cannulation.

Raynor et al. [14] reported on the use of triggered electromyogenic stimulation (TrgEMG) in 1078 spine procedures with lumbar (L2–S1) pedicle screw placement. An ascending method of constant current stimulation was applied to each screw in order to obtain a CMAP from lower extremity myotomes. They concluded that the probability of detection of a medial wall breach by a pedicle screw increases with decreasing EMG thresholds. The probability of detecting medial wall breach with a TrgEMG stimulation threshold of greater than 8 mA was 0.31 %. A threshold of 4.0–8.0 mA yielded a probability of 17.4 %, while less than 4.0 was 54.2 %. A TrgEMG threshold of 2.8 mA had a specificity of 100 % but a sensitivity of only 8.4 %. The authors concluded that TrgEMG is a useful adjunct during screw placement, but should always be used in conjunction with some other form of monitoring.

At the same time, numerous studies have suggested that evoked CMAPs from muscles innervated by lumbar nerve roots, with stimulus thresholds of less than 4–6 mA, are suggestive of a pedicle wall breach [15–17]. Parker et al. [18] concluded that using a 5-mA stimulus threshold TrgEMG had a very high specificity but low sensitivity. Sensitivity increased with increasing stimulation at the cost of a greatly lowered specificity. It should be noted that during monitoring, false-negative results could occur when stimulating only the mobile crown of a polyaxial-type screw [14]. Anderson et al. [17] stressed the importance of stimulating the screw either at the hexagonal port or directly at the screw shank to avoid these false-negatives.

Glassman et al. [19] demonstrated with postoperative CT that lumbar pedicle screw stimulations requiring more than 15 mA to obtain a CMAP were 98 % accurate in determining that the screw was located correctly in the pedicle.

Lumbar Interbody Fusion

Lumbar interbody fusion is a commonly utilized treatment for discogenic back pain (secondary to a degenerative, herniated, or inflamed disk) and spine instability. There are several different variations of the procedure, including posterior lumbar interbody fusion (PLIF), transforaminal lumbar interbody fusion (TLIF), anterior lumbar interbody fusion (ALIF), and extreme lateral interbody fusion (ELIF).

Posterior Lumbar Interbody Fusion (PLIF)

With this surgical technique, a midline posterior incision is made, the spinal muscles are separated and retracted, and the spine laminae and a small portion of the facet joints, which lay directly over the nerve roots, are removed. The affected disks are removed and a bone graft, allograft, or biomechanical spacer implant with cage is inserted into the disk space to promote fusion of the adjacent vertebrae. The spine is then stabilized with additional instruments (rods, screws, wires). Bose et al. [20] retrospectively analyzed 61 patients having PLIFs who were monitored with continuous EMG and triggered CMAP responses from muscles innervated by nerve roots adjacent to placed pedicle screws. Twenty-one percent of patients had sustained neurotonic activity or an evoked CMAP with a current intensity of less than 7 mA during pedicle screw stimulation prompting an alert and reposition of a pedicle screw. It was their opinion that MIOM minimized postoperative neural deficits.

Transforaminal Lumbar Interbody Fusion (TLIF)

During TLIF procedures , the spine is approached from the side of the spinal canal through a paramedian posterior incision. This modified posterior approach reduces the amount of surgical muscle dissection and minimizes nerve manipulation required to gain access to the vertebrae, disk, and nerves. Laminectomy, discectomy, facet fusion, and posterolateral spine fusion and instrumentation are typically performed. Disk material is removed from the spine through the right, left, or both sides of the spinal canal, and typically, a bone graft (bone block or cage implant) is inserted. Spinal strength and stability is then achieved with screws or rods. Nerve root retraction is often needed to place the interbody device. Real-time detection of neuropraxia can be achieved with a combination of continuous EMG recordings and evoked CMAP threshold responses following electrical stimulation from pedicle screws or screw holes [13]. Bindal et al. [13] reported the use of continuous electrical stimulation of the pedicle access needle with a 7-mA current during placement of 105 lumbar pedicle screws in minimally invasive TLIF procedures in order to assess safe screw placement. Current was held constant as the needle was placed percutaneously at the lateral portion of the determined transverse process, walked medially to the junction of the transverse process and the facet joint, and then inserted into the pedicle. At

this point, anteroposterior fluoroscopy was also used to confirm needle laterality. The 7-mA threshold resulted in 0 % incidence of EMG activation of the tap with a current of less than 15 mA. Detection of EMG at a current of 7 mA or less signaled close proximity of the medial nerve root resulting in lateral alteration of the needle trajectory in 76.2 % of their cases. (The author does state that there may have been false-positives. However, the 7-mA threshold was selected to yield a minimal false-negative rate.) With this method of percutaneous pedicle screw placement, they reported 0 % incidence of malpositioned hardware.

Anterior Lumbar Interbody Fusion (ALIF)

During ALIF , an incision is made in the lower abdominal area, and the abdominal muscles and vessels are retracted, allowing access to the front of the spine. When performing this procedure, particularly at the L4–L5 level, there is 5 % risk of both acute and delayed vascular insult secondary to tears and laceration of the aorta, common iliac and vena cava vessels, or retraction of the iliac arteries for adequate exposure of the disk space [21]. Venous injury occurs more frequently than arterial and is most commonly caused by retraction on the great vessels. Vascular injury is reported at a higher incidence in laparoscopic versus open ALIF [21]. Vascular tear or laceration is usually immediately recognized and repaired. However, ischemic injury due to retraction of vessels and possible thrombus occlusion may go undetected without continuous intraoperative monitoring. Undetected injury may result in a postoperative sensory or motor deficit, pain, and in some cases, mortality [22–26]. Monitoring techniques that can pick up lower extremity vascular occlusion include lower extremity vessel palpation, pulse oximetry, and spinal cord SSEP monitoring [24, 26, 27]. Nair et al. [28] report a case of iliac artery injury during an L3–S1 ALIF procedure that was detected with MIOM. On three different occasions during the procedure there were changes in tibial nerve SSEPs, abductor hallucis MEPs, or both, which corresponded with decreased pulses in the left leg following compression of the iliac artery with either a retractor or an L4–L5 spacer. Following notification to the surgeon, compression was released on all occasions, and blood flow was restored (Fig. 35.2). Similarly, Yaylani et al. [29] describe in a retrospective cohort study SSEP changes coinciding with retractor placement that subsequently resolved after surgeon notification and adjustment of the retractor during ALIF.

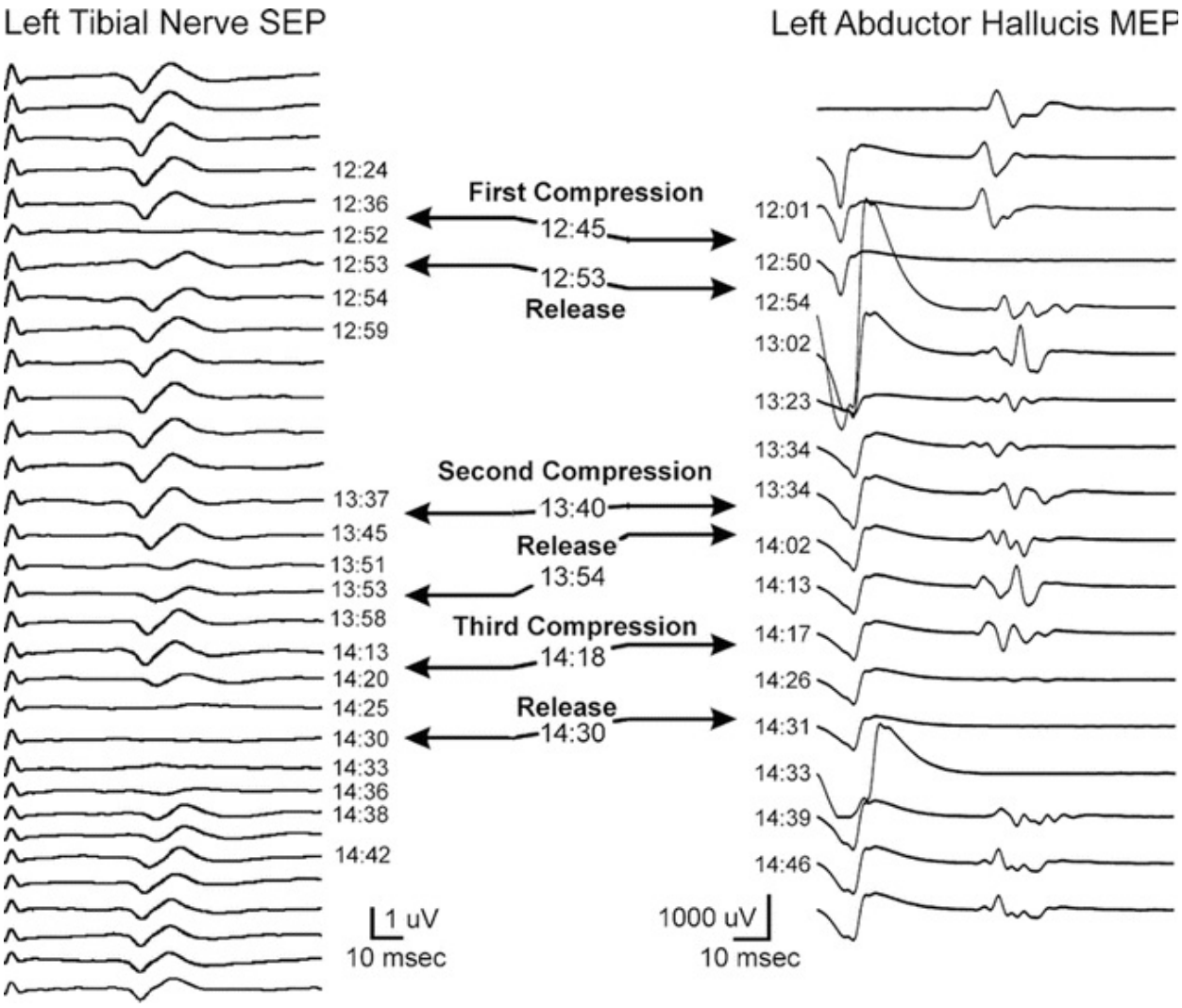
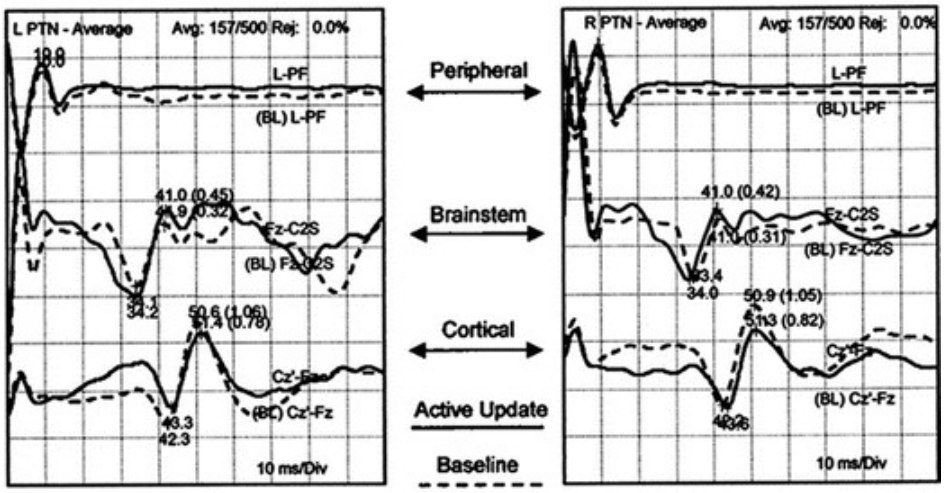


Fig. 35.2 Three compressive events during ALIF , with both SSEP and MEP signal decreases noted in the first and third compressions, and only SSEP decrease noted during the second compression. Reproduced with permission from Nair et al. [28]

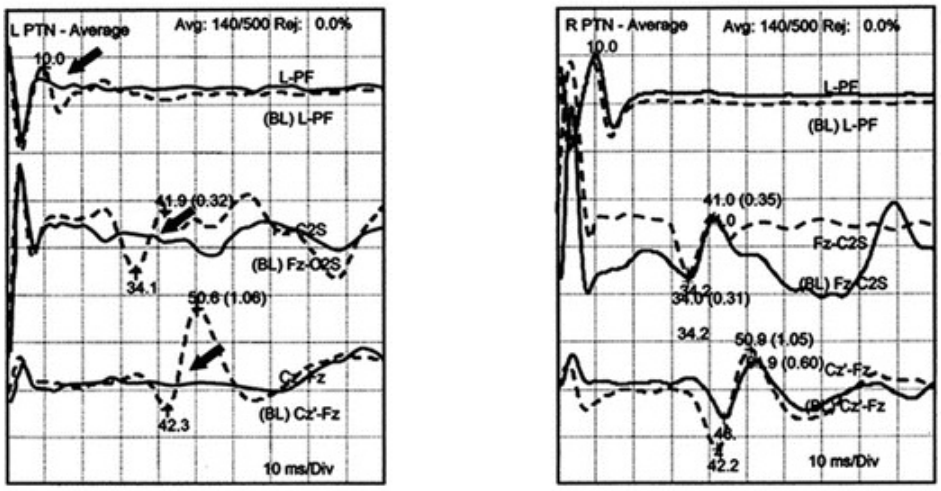
Isley et al. [22] depict another case of left common iliac occlusion after anterior interbody fusion that was detected with SSEP Intraoperative monitoring. No changes in SSEPs were noted during the ALIF, and no EMG discharges suggestive of nerve root irritation were noted during the discectomies, partial corpectomies, distraction, or instrumentation. However, during closure, there was a gradual decline and loss of the subcortical and cortical SSEP waveforms. Palpation and Doppler examination verified loss of pulses in the extremity. Following vascular consult, thrombectomy and patch angioplasty of the left common and external iliac arteries was performed, perfusion was restored, and SSEP waveforms recovered. This case

demonstrates the importance of continued monitoring until closure during this procedure (Fig. 35.3).

a POSTINDUCTION BASELINE



b CLOSURE OF ANTERIOR INCISON



c LEFT EXTERNAL AND INTERNAL ILIAC ARTERIAL THROMBECTOMIES AND PATCH ANGIOPLASTY

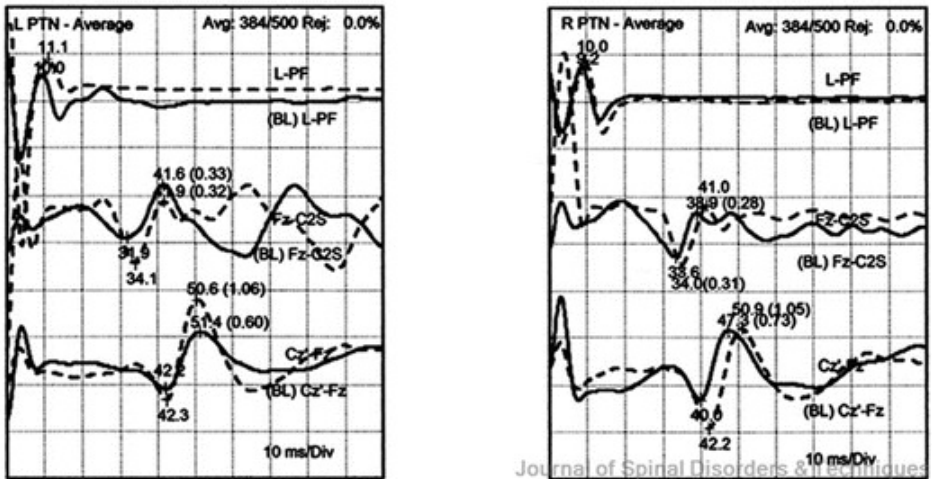


Fig. 35.3 Within each part figures are pairs of SSEP waveforms recorded at the popliteal fossa (*top traces*), brainstem (*middle traces*), and sensory cortex (*bottom traces*) for the left and right legs after stimulation of the PTN (labeled L PTN and R PTN, respectively) during three surgical events. Baselines are shown in (**a**). For the waveforms recorded to left PTN stimulation in (**b**), there was a loss of the dominant components at all recording sites due to thrombotic occlusion of the left common iliac arterial bifurcation. (**c**) Recovery of the SSEP waveforms after thrombectomies of the left common iliac arterial bifurcation. Reproduced with permission from Isley et al. [22]

Extreme Lateral Interbody Fusion (ELIF/XLIF)

The ELIF, also known as XLIF (Nuvasive, San Diego, CA) or DLIF (Medtronic, Minneapolis, MI), is a less invasive procedure with a smaller incision; however, a high incidence of lumbar plexus traction neuropraxia has been reported [23]. A flank incision is made with the patient in the lateral position, and the disk space is accessed by blunt dissection through the psoas muscle and traversing lumbar plexus. Once the disk space is entered, the disk is removed, and a new implant is inserted. During surgical dissection through the psoas muscle, traction on the lumbar plexus by the expandable cannulas used to perform the ELIF can cause a neuropraxia of the genitofemoral nerve with symptoms of thigh or groin numbness. The use of EMG monitoring using the EMG activity from muscles innervated by the lumbar nerve roots and plexus at risk during the surgery may decrease the incidence of nerve injury. The EMG-based Neurovision system (Nuvasive; San Diego, CA) incorporates a surgical dissection tool used by the surgeon that has a tiny stimulation electrode on the tip that provides the surgeon real-time continuous feedback on whether plexus structures are stimulated when dissecting through the psoas muscle.

Bendersky et al. [30] developed a new protocol for IOM during ELIF procedures, which included EMG and transpsoas stimulation. Monopolar needle electrodes were placed in the femoris and/or vastus medialis (for femoral nerve), grasilis muscle (obturator nerve), immediately below the anterior superficial iliac spine (lateral cutaneous femoral nerve), and in the cremaster muscle for men and the labium majus for women (genitofemoral nerve). Reproducible responses were obtained in 107 patients in these terminal branches of the lumbar plexus, which were well preserved during dissection. No patient (0 %) developed new motor postoperative deficits. Nineteen (17.75 %) patients had minor and transient sensory symptoms, lasting less than a month, and one patient (0.93 %) had longer duration of

sensory complaints (3 months). They concluded that detailed IOM of the lumbar plexus branches was beneficial in delineating the proximity of the intrapsoas nerves during ELIF procedures.

Paracoccygeal Transsacral Fixation

One additional minimally invasive fixation technique has been used for management of spinal instability at the L4–L5 and L5–S1 level. This approach involves placement of a guide pin through the paracoccygeal notch using fluoroscopic guidance with the patient in the prone position. The guide "walks" ventral to S2–S5, displacing the rectum until entering the spine at the junction of S1–S2 on a trajectory to L5. A trocar is threaded over the guide to L4–L5 or L5–S1. Working through the trocar, the disk can be removed and screws placed in the bone. Additional fixation can be placed using the anterior or posterior approach. This technique was introduced in 2004 as a method to minimize muscle dissection, nerve root retraction, and annular disruption. The biomechanical advantage of this procedure is the preservation of the supporting structures at the L5–S1 level [31]. EMG monitoring (including the pudendal nerve) is usually performed. Also possibly at risk are the sympathetic fibers of the hypogastric nerve (L2–L5) and the parasympathetic fibers from S2–S4. In addition, the rectum and vascular structures in the posterior pelvis and mesorectum (middle sacral artery and veins) are at risk.

Lumbar Microdiscectomy

Dimopoulos et al. [32] prospectively randomized 112 patients with extruded disk undergoing lumbar microdiscectomy with or without continuous intraoperative EMG monitoring of the muscles innervated by the nerve root at the operative site level. They concluded that there was no correlation found between intraoperative spontaneous or continuous EMG findings and immediate postoperative pain.

Two cases of postoperative cauda equina syndrome following single-level lumbar microdiscectomy have been reported. Both were initially detected by an abrupt decrease of intraoperative cortical and subcortical SSEP amplitudes [33]. Cole et al. [7], in a retrospective propensity score–matched analysis of a national database, found no significant decrease in neurologic complications when comparing lumbar microdiscectomy with and without IOM; however,

they did find that there was a significant increase in total payments for the procedure when using IOM. It is still to be determined if the benefits gained by monitoring during microdiscectomy are worth the time and cost of the test.

Questions

1. Which intraoperative neuromonitoring modality has been proven to be most beneficial in preventing injury during lumbar microdiscectomy?

    a. Somatosensory-evoked potential (SSEP)

    b. Triggered EMG

    c. Nerve action potential (NAP)

    d. None of the above

2. Lowering triggered EMG thresholds during pedicle screw placement has which of the following benefits?

    a. Better sensitivity and specificity

    b. Better sensitivity while sacrificing specificity

    c. Better specificity while sacrificing sensitivity

    d. Decreased incidence of medial wall breach

3. Which of the following statements is FALSE with regard to lumbosacral anatomy?

a. In adults, the filum terminale generally terminates at L1–L2

b. There are five lumbar and five sacral vertebrae in the lumbosacral spine

c. The cauda equine refers to bundles of nerve roots that exit off of the conus medullaris and travel in the spinal column until exiting at their respective foraminae

d. The sacral vertebrae are fused

Answers

1. D

2. C

3. A

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Footnotes

1 Asterisk indicates key reference.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_36

36. Intramedullary Spinal Cord Surgery

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Keywords Spinal cord tumor – Intramedullary – MEP – D-wave – Transient paraparesis

Key Learning Points

- Loss or deterioration of SSEPs during myelotomy is a common finding and NOT associated with motor deficits.
- Presence of muscle MEPs always correlates to the absence of significant motor deficits.
- Transient paraparesis is neurophysiologically characterized by loss of uni- or bilateral muscle MEPs and preservation of D-Wave.

Introduction

Intradural spinal tumorsare much less common than primary intracranial tumors, and overall represent 2–4 % of all primary tumors of the central nervous system (CNS). They may be intradural extramedullary tumors, that is, they are located inside the dural sac but outside the spinal cord, and thus exert external compression on the cord. This group comprises meningiomas and nerve sheath tumors (schwannomas, neurofibromas). They are more frequent in adults . The other, more delicate group are intramedullary tumors, also called intrinsic tumors, as they are located within the substance of the spinal cord. They are the predominant spinal tumor type in children. Histologically the most frequent intramedullary tumor is the ependymoma in adults, and the pilocytic astrocytoma in children. These and the great majority of all other tumor types are histologically benign, and graded 1 or 2 by the World Health Organization (WHO) system. Higher grade tumors are rare. Glioblastomas are extremely rare.

The typical presenting signs and symptoms of intradural tumors, and intramedullary tumors in particular, include pain, which is more pronounced in the reclining position. The typical patient has disturbed sleep because of pain in the neck, the shoulders, the arms and legs, uni- or bilaterally, often combined with mild sensory symptoms like numbness and paresthesias. Typically, this type of pain improves or resolves during the day. Neurologic dysfunction may occur in the form of deterioration of fine motor skills for the hands, gait and balance disturbance, or outright paresis. The great majority of patients have slow onset or slow progression of symptoms. Rapidly developing symptoms would indicate the rare case of higher grade tumor.

In recent years, due to the immense progress of clinical oncology, more and more patients with intramedullary metastasis have been presented and the occasional surgery to remove a metastatic lesion has been done.

Spinal cord tumors may also be vascular ; the hemangioblastoma being the most frequent type. This may occur with or without the genetic predisposition of von Hippel-Lindau disease . Cavernomas and arteriovenous malformations occur in the spinal cord, but particularly the latter are exceedingly rare.

The other genetic disorder associated with spinal cord tumors is neurofibromatosis . Type 1 frequently is associated with nerve sheath tumors; type 2 additionally with ependymomas.

A peculiar variant of ependymoma is also well known in the spinal canal: the myxopapillary ependymoma is called such because of its characteristic histologic appearance. It is usually located in or around the conus medullaris and the cauda equina. In fact, it may be located intra- and extramedullary at the same time, which makes resection treacherous. In terms of their internal structure, intramedullary tumors may be solid or cystic with various combinations of the two. The presence of cysts is a predisposition to cause spinal deformity, particularly scoliosis. Often, the presence of cysts facilitates the tumor removal as the cyst opening quickly provides space to directly access the tumor without going along the cord–tumor interface all along.

In terms of treatment , the widespread consensus, based on a lot of experience and some evidence, is that intramedullary tumors should be removed microsurgically. Because most tumors are benign, this mostly results in long survival. The rare malignant tumors have a poor prognosis. Adjuvant treatment, i.e., radiation and chemotherapy, is given only in exceptional circumstances of inoperability or persistent recurrence, or for the rare tumor which is higher grade (WHO 3 or 4).

The oncologic outcome is characterized by long survival. An intramedullary tumor very rarely changes the life expectancy. The neurologic outcome of surgery is characterized by a small motor morbidity. The rate of significant motor deficit may be under 5 %. However, the loss of some sensory function is surely much higher, probably above 50 %. This can result in ataxia, superficial sensory dysfunction or, most severely, loss of joint position sense.

Neurosurgical resection of spinal cord tumors greatly benefits from the use of intraoperative neurophysiologic monitoring. At this time, it is generally accepted that somatosensory-evoked potential (SSEP), D wave, and motor-evoked potential (MEP) data represent the functional integrity of the respective sensory and motor pathways in the spinal cord. There continues to be a debate about the evidence base as to whether or not the utilization of monitoring influences the overall outcome of spinal cord tumor resection.

The degree of resection, survival, and the neurologic outcome greatly depend on several crucial factors: well-delineated tumors where a “plane of dissection ” can be developed in surgery are more likely to be completely resectable and have an almost zero recurrence rate (ependymomas, hemangioblastomas). Astrocytomas may vary in their configuration and mostly have at least in part of their surface a diffuse interface to the normal

cord and thus are much less well resectable. The most important neurologic factor for postoperative neurologic outcome is the preoperative neurologic status: the patient with intact function and only minor symptoms has much less risk of surgery-induced deterioration than the patient with barely preserved function preoperatively. Consequently it is almost never possible to reverse a once-established neurologic deficit, meaning that a patient who comes to surgery already paraplegic usually cannot recover, even with complete tumor resection.

From the perspective of a neurosurgeon experienced in spinal cord surgery, the most important factors for successful resection include the expert application of intraoperative neurophysiologic techniques at all steps of the operation. Certainly, the surgical experience is an essential prerequisite anyway. But the interpretation of continuously acquired monitoring data in an environment of constant and easy communication between surgeon and monitoring team is indispensable.

It was not neurosurgeons but orthopedic surgeons who first implemented intraoperative monitoring with sensory-evoked potentials for the spinal cord in an effort to reduce neurologic morbidity of spinal surgeries [1]. The technology has vastly improved since these early times. In addition to the slow and unreliable [2] spinal monitoring with SSEPs , concepts for direct monitoring of the motor pathways were developed in the 1980s [3–9], implemented for practical use in the 1990s [10–14], and further refined and widely applied in the following decade [15].

Neurophysiology

Motor potentials are evoked with transcranial electrical motor cortex stimulation. The stimulus points are C3, C4, C1, C2, Cz, and a point 6 cm in front of Cz (International 10/20 EEG electrode system). Cork-screw electrodes are optimal for fixation to the scalp, but straight needle electrodes as well as surface electrodes are also in use.

Electrical stimulation with rectangular constant current impulses of 0.5 ms duration and intensities between 15 and 220 mA is used.

D waves [3] are elicited with single stimuli. This is therefore called the “single stimulus technique.” The D waves are recorded as traveling waves directly from the spinal cord with an electrode placed over the spinal cord usually in the spinal epidural space. Baseline recordings are obtained during

the surgical opening. The signal usually does not require averaging although recording quality often improves with a few averages. The stimulations are repeatable at a rate of 0.5–2 Hz. This provides practically “real-time” feedback. The relevant D wave parameter is its peak-to-peak amplitude. A decrease of more than 50 % of the baseline amplitude is considered critical and has been found to be associated with a motor deficit [12]. Latency changes of the D wave are mostly not due to surgery but to factors such as temperature [16]. Higher stimulation intensities are followed by shorter D wave latencies [8]. This is likely due to the corticospinal tract fiber activation occurring deeper in the white matter of the brain.

Muscle MEPs are elicited with transcranial electrical stimulation over the same electrodes as for the D wave. A train of five to seven stimuli with 4 ms interstimulus intervals [17, 18] is used. The technique is called “multipulse technique” [13] or “train stimulus technique” [9]. Compound muscle action potentials are recorded with needle electrodes from target muscles in all four extremities (thenar, anterior tibialis, abductor hallucis). Practically all muscles, including those innervated by cranial nerves and even the diaphragm and the external anal sphincter, can be used as recording sites. Muscle MEPs also do not require averaging and can be repeated at a rate of 0.5–2 Hz. With the focal anode as the stimulating electrode, a montage of C1/2 (anode at C1, cathode at C2) or C2/1 is tried first to elicit muscle MEPs in all four extremities. In individual cases, C3/4, C4/3, or Cz/6 are used as alternative stimulation points [19].

The principle of evoking muscle responses is understood in the context of the D wave concept: each individual electrical stimulus on the motor cortex, either on the exposed cortex or using transcranial stimulation [6], elicits a D wave in the corticospinal tract. A fast train of five stimuli at 250 Hz elicits five consecutive D waves, which then travel down the corticospinal tract 4 ms apart. The spinal alpha-motorneurons receive these five D waves and that increases their membrane potential up to firing threshold [4] even under the conditions of general anesthesia. The parameter monitored is the presence or absence of muscle MEPs in the target muscles within a stimulus intensity range of 15–220 mA. This all-or-none concept has been adopted because of the enormous variability of muscle MEP amplitudes [10, 20, 21] and because a motor deficit occurred only when the muscle responses were lost [7, 10, 14, 21].

With more and more MEP monitoring performed, worldwide safety

concerns have required further study into the biologic effects of electric neural stimulation. So far this growing use has not resulted in significant numbers of reported complications resulting from tissue damage [22, 23] or seizures. Nevertheless, this issue continues to be growing in importance [24].

Anesthesia for Neurophysiologic Monitoring

Total intravenous anesthesia with an as constant as possible infusion of propofol (100–150 μg/kg/min) and fentanyl (1 μg/kg/h) is ideal when MEP monitoring is utilized for an operation. Propofol for anesthesia with MEP monitoring has been reported with various stimulation techniques [25–30]. Bolus injections of both intravenous (IC) agents should be avoided because this appears to temporarily disrupt muscle MEP recording. This can be particularly problematic during the critical resection part of any spinal cord tumor surgery.

We found the addition of ketamine, 0.25 mg/kg/min, a particularly useful addition to the anesthetic management [31].

Halogenated anesthetics should not be used [23], even though low doses may be tolerable. They elevate muscle MEP stimulus thresholds and block muscle MEPs in a dose-dependent fashion [32]. Using them adds an uncontrollable variable without improving anesthesia.

Short-acting muscle relaxants are given for intubation only. Neurosurgeons and anesthesiologists may be somewhat uncomfortable with some patient movement during surgery, which results from the effects of transcranial motor cortex stimulation. “Partial” muscle relaxation [21] to improve on this problem continues to be debated. We doubt that it improves anesthesia management, but are convinced that it makes monitoring data less reliable. The proven specificity of muscle MEP data would likely suffer, and some patient movement from stimulation could still not be entirely avoided. Therefore, this would combine poor monitoring with poor relaxation.

Case 1

History, Clinical Assessment, and Imaging

This 55-year-old man had a several years’ history of subtle signs of neurologic dysfunction, such as nighttime back pain, slow deterioration of

endurance and stamina in sports, mild urinary dysfunction, and subtle reduction in sexual function. At diagnosis, the symptoms had escalated to a significant degree of gait dysfunctionand a walking distance reduced to about 100 m. Magnetic resonance imaging (Fig. 36.1) revealed a large mass in the lower thoracic spinal cord with extensive upper thoracic cord edema and venous engorgement around the conus. The tumor matrix appeared dark on T2, which indicates an above average degree of fibrous tissue. Urgent resection was recommended due to the presence of significant neurologic dysfunction and recent neurologic deterioration, as the degree of preoperative neurologic dysfunction correlates with the degree of perioperative deterioration [12, 33].

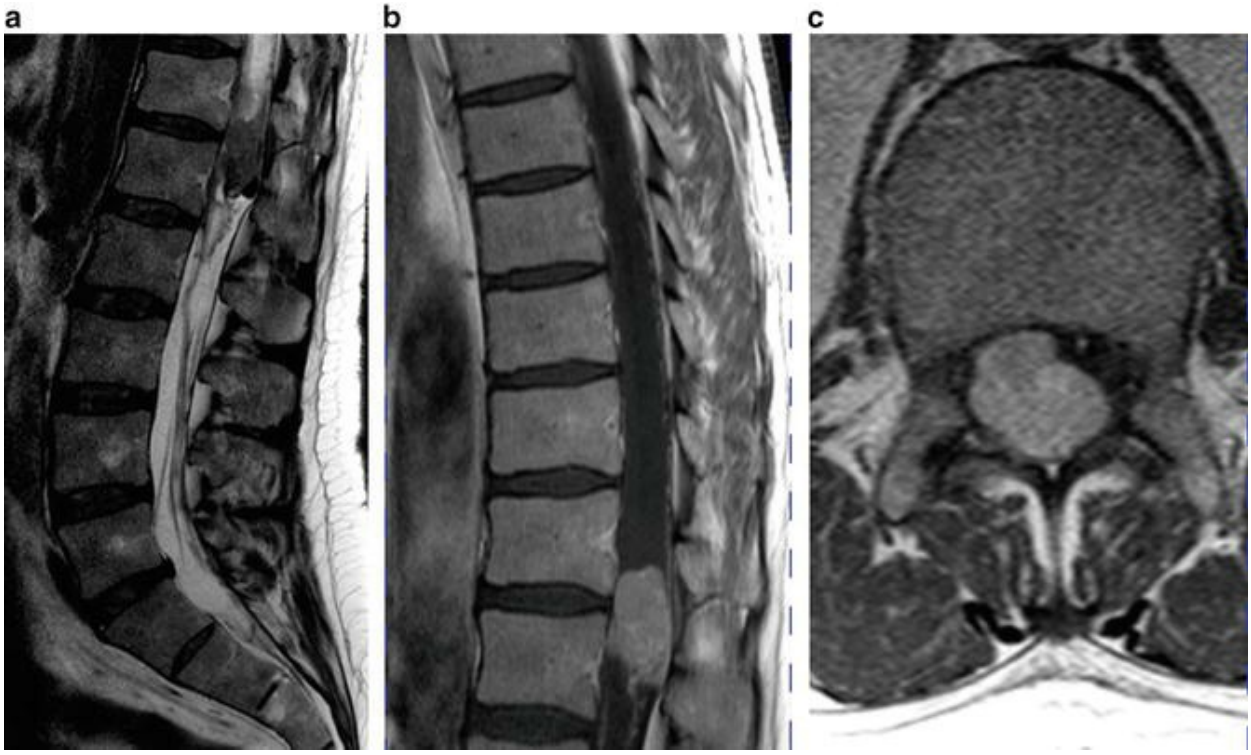


Fig. 36.1 Magnetic resonance images of an extensive intramedullary tumor in lower thoracic spinal cord with complete obstruction of the spinal canal (**a**), significant enhancement (**b**), and dark T2-signal indicating fibrous tissue (**c**). The large size on imaging does not even allow the differential diagnosis of an intramedullary versus an intradural-extramedullary tumor

Surgery and Intraoperative Monitoring

The monitoring routines for surgery of intramedullary spinal cord tumors include MEP and SSEP recordings from the upper and lower extremities.

Thenar, tibialis anterior, flexor hallucis brevis bilaterally were used. Cortical SSEP responses were recorded from median and tibial nerve stimulation. In thoracic tumors, the upper extremity recordings serve as controls for the surgically relevant lower extremity recordings. In addition, recordings of bulbocavernosus reflex, pudendal nerve SSEPs and anal MEPs can be attempted.

The patient was positioned prone with the head in a soft face padding mounted on a mirror plate. During the approach phase of the operation, a sudden drop in the cortical amplitude of the right median nerve was noted (Fig. 36.2). An immediate assessment of the situation showed that unchanged recordings from the left side excluded the possibility of a systemic effect such as a change in anesthesia regimen. The surgery was excluded because the relevant spinal level was low thoracic and therefore not corresponding to the median SSEP. Inspection of the electrodes and cables as well as the patient's positioning showed an insufficient padding and malposition of the right arm. This was corrected and the recordings normalized at the next set of recordings.

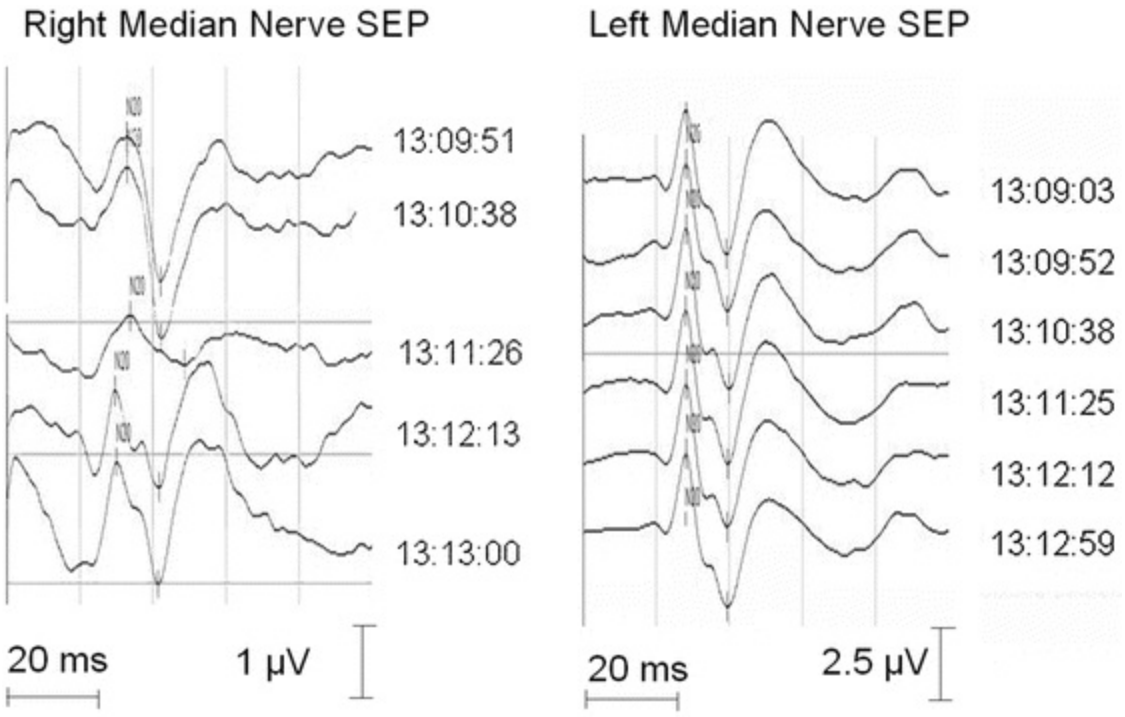


Fig. 36.2 A sudden drop in cortical signal amplitude from the right median nerve SEP prompted analysis and insufficient padding and suboptimal arm position was found and corrected. This resulted in rapid recovery of the response. The contralateral side showed no change at the same time, indicating

that it could not be caused by systemic factors

During resection of the spinal cord tumor, significant difficulty was encountered as the tumor was found to be very firm and thus could not be grabbed or easily decompressed. Internal decompression was achieved using a microsurgical laser [34]. This brought the size of the mass sufficiently down so that the remaining tumor mass could be dissected out of the edematous spinal cord in toto. There was no further significant change in either motor- or sensory-evoked potential recordings.

The patient awoke from anesthesia without significant motor deficits. Postoperative MRI showed complete tumor removal.

Case Summary Interpretation and Discussion

A 55-year-old man with progressive paraparesis underwent resection of an intramedullary tumor eventually diagnosed as a solitary fibrous tumor (Fig. 36.1) [35]. During surgery, a unilateral sudden decrease of median nerve SSEP was noted (Fig. 36.2) and found to be caused by less-than-optimal padding of the right forearm. Improved positioning rapidly improved the response. This was a mechanical problem unrelated to the operation per se, due to patient positioning which was identified and corrected immediately.

This case demonstrates that routinely recording evoked potentials from upper and lower extremities is useful even when the surgery takes place caudal to the level of the cervical spinal cord. Upper extremity recordings may serve as controls for difficult lower extremity recordings and as controls to systemic effects of core temperature change and the effects of anesthetic agents. Considering the possible influences of these factors, it became evident that the observed change must have been caused by a nonsurgical (far cranial to the surgery) influence and a nontechnical (no artifacts, correct electrode positions), nonsystemic (stable recordings contralaterally and on the lower extremities) problem. Positioning-related compressive neuropathy is not an infrequent occurrence in complex surgical positioning [36]. Early detection is possible with an evoked potential change such as the one shown here [37]. The case also provides evidence that even SEPs requiring averaging can provide fast information upon potential and correctable problems.

Case 2

History, Clinical Assessment, and Imaging

A 4-year-old boy with nighttime neck pain and progressive clumsiness of the right hand was diagnosed with a cervical intramedullary spinal cord tumor. On MRI, the lesion showed a marked heterogeneity and significant internal compression of the spinal cord by both solid tumor masses and cystic formations (Fig. 36.3). Tumor resection was recommended to obtain a histologic diagnosis and as optimal primary tumor treatment.

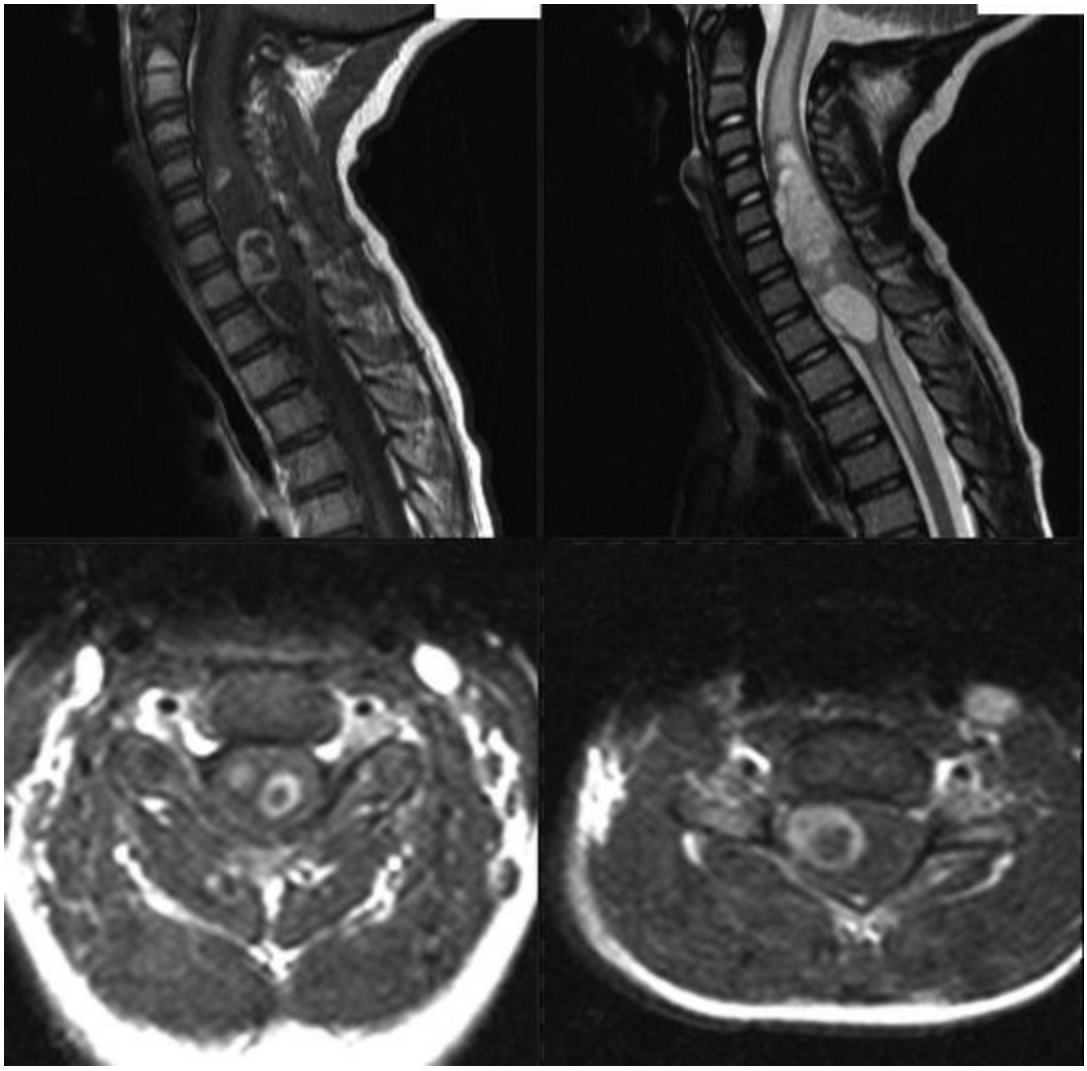


Fig. 36.3 Sagittal and axial MR images of the pilocytic astrocytoma in the cervical spinal cord

Surgery and Intraoperative Monitoring

Routine monitoring for cervical intramedullary spinal cord tumors includes MEP and SSEP recordings from the upper and lower extremities. Thenar, tibialis anterior, flexor hallucis brevis are used. In this context, cortical SSEP responses are recorded from ulnar and tibial nerves, respectively. If possible, an epidural electrode is inserted to record D waves.

The patient was positioned prone with the head fixed in neutral position in a four-pronged Sugita headholder. A laminotomy C3 to T3 was made for surgical exposure. After a dorsal myelotomy , the extensive tumor tissue was removed in piecemeal fashion using the Cavitron ultrasonic aspirator (CUSA), regular suction, and the microsurgical laser. MEP and SEP signals for the entire right side were permanently lost during resection on the right side (Fig. 36.4). Waiting, irrigation, induced hypertension, and additional steroid administration did not achieve recovery of the recordings. The resection remained subtotal. No attempt was made to remove tumor residuals adherent to the still-functioning left side of the cord. The patient awoke with a severe right-sided hemiparesis. Over the long run he recovered motor function of the left side, learned how to walk and run, but remained with a severely impaired right hand and an abnormal gait.

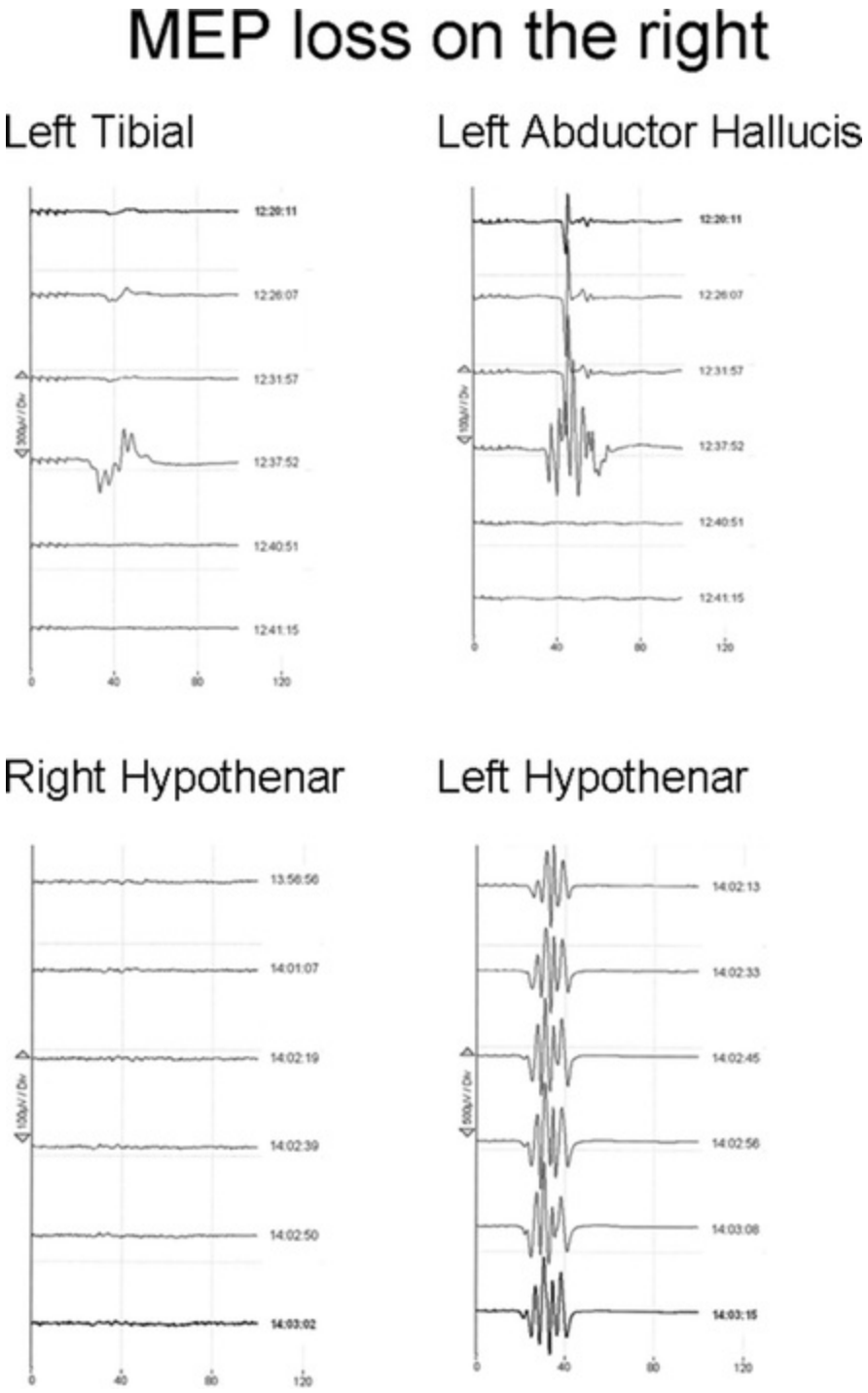


Fig. 36.4 MEP recordings from the right and left hypothenar (*bottom traces*) and the right tibialis anterior and abductor hallucis muscles, respectively (*top traces*). The lower extremity recordings disappear simultaneously at a well-defined point. The right hypothenar recordings disappeared gradually and remained stable on the left side

Case Summary Interpretation and Discussion

A 4-year-old boy underwent surgical resection of a cervical intramedullary spinal cord pilocytic astrocytoma . At a critical stage of the resection, a significant change of MEPs of both upper and lower extremities occurred on the right side. MEP and SSEP signals for the entire right side were permanently lost. The resection remained incomplete and the patient had a severe right-sided hemiparesis. The leg recovered partially, the upper extremity remained significantly impaired.

This case demonstrates both the immediate feedback provided by the loss of MEPs on one side and the significant neurologic consequences of a complete loss of both upper and lower extremity recordings. Usually the leg recovers faster and easier than the hand, and unilateral loss of lower extremity MEPs usually recovers completely [14]. However, the complete loss of both extremities on one side appears to have graver consequences. This young patient recovered gross motor function of the arm but not the motor skills adequate for the dominant hand. He developed left-handedness and his rehabilitation was aimed at achieving this goal. His walking improved rapidly to independence but his gait remained massively abnormal.

The preoperative anatomy allowed a preassessment that the right side was under significant risk and that the left side must be preserved at all cost. This concept unfolded during the operation in that indeed the right side suffered, but the left could be preserved and thus useful functioning and social independence was saved. Continuation of the surgery to achieve an anatomically complete resection even of the tumor components involving the left side of the cord would likely have resulted in a complete loss of motor function bilaterally.

Case 3

History, Clinical Assessment, and Imaging

A 54-year-old woman with a year-long progressive history of nighttime back pain presented with a sensory level below Th7 and MR imaging revealed an intradural-extramedullary tumor at the level of Th9 (Fig. 36.5).

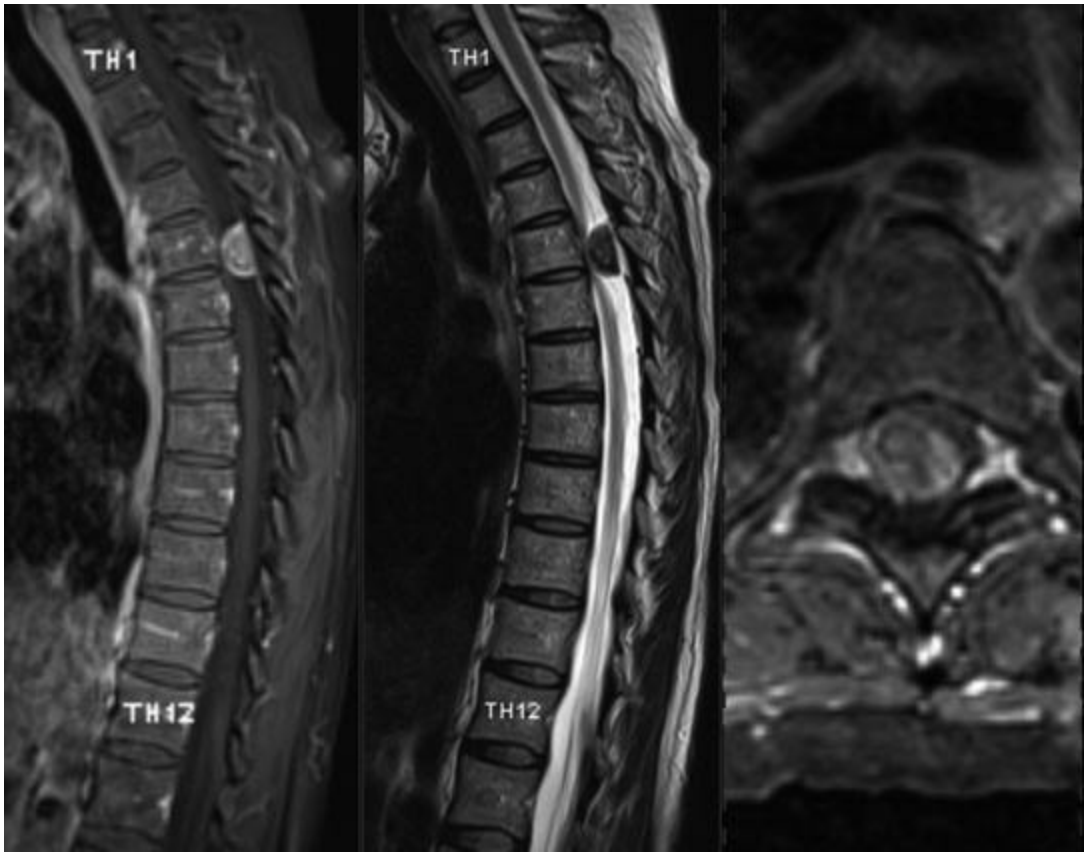
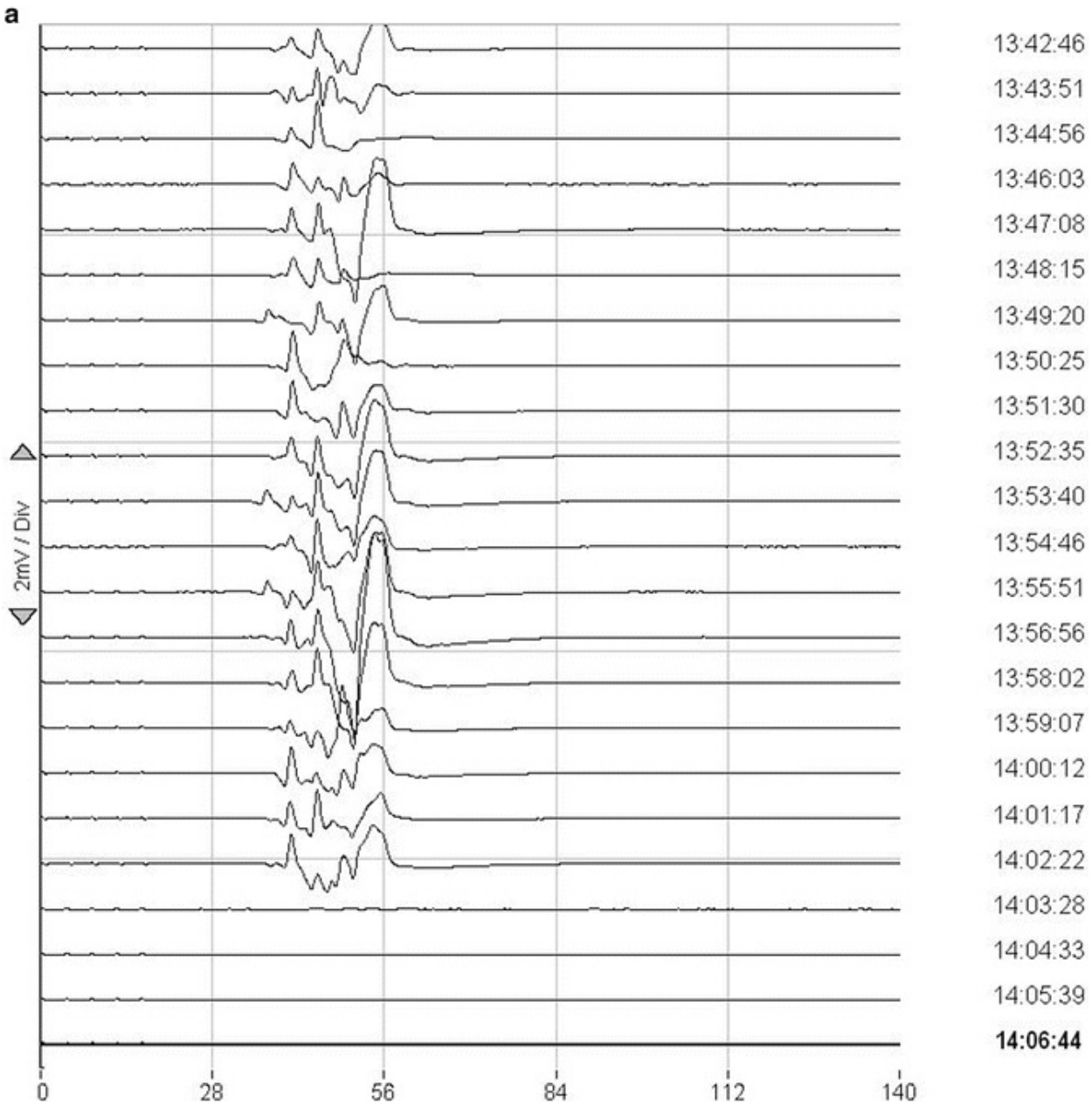


Fig. 36.5 Sagittal and axial MR images of what turned out to be a meningioma which was tightly adherent to the pial surface of the spinal cord

Surgery and Intraoperative Monitoring

The monitoring routines for surgery of intradural-extramedullary tumors and intramedullary spinal cord tumors are identical with MEP and SEP recordings from the upper and lower extremities. Thenar, tibialis anterior, flexor hallucis brevis bilaterally were used.

The patient was positioned prone. During the laminectomy, baseline recordings were obtained. Upon opening of the dura, significant hemorrhage occurred from around the tumor and epidurally. Adequate exposure and hemostasis required some time and some blood loss. Left tibialis anterior MEPs disappeared at that time. Blood loss was rapidly compensated with fluid replacement. There was no significant hypotension during that time. MEPs reappeared after about 40 min (Fig. 36.6).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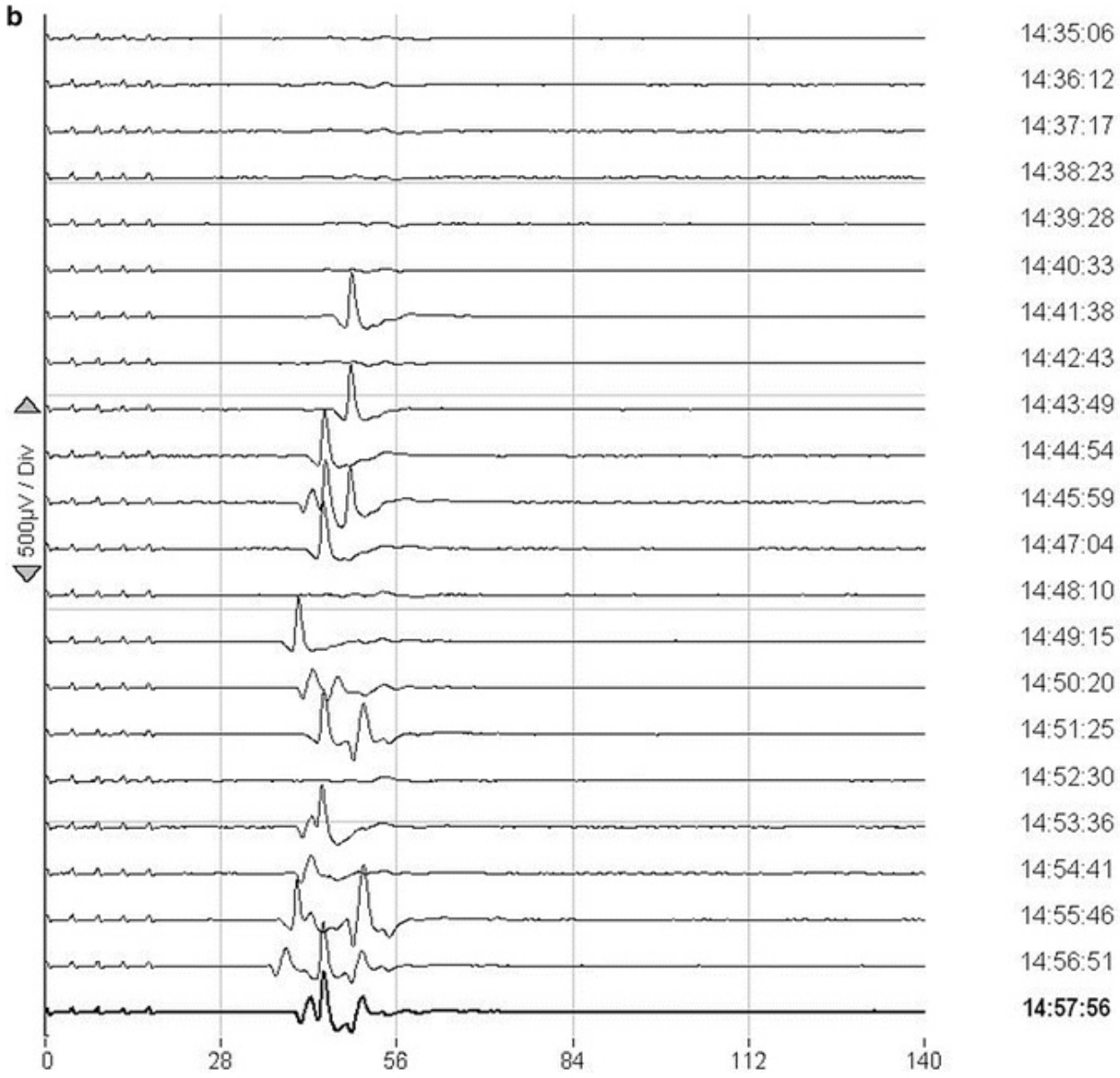

Fig. 36.6 Loss and reappearance of muscle MEPs in the lower extremity on one side during hemorrhage and tumor removal

Summary, Interpretation, and Discussion

A 54-year-old woman underwent laminectomy and resection of an intradural meningioma at T9. This case differs little from intramedullary tumor resections and is therefore presented in this context. After dural opening, a significant hemorrhage occurred. Rapid fluid replacement was considered important and started immediately. Thus, significant hypotension was avoided. Nevertheless, during this time a temporary loss of muscle MEPs

from the left tibialis anterior occurred. Both systemic and local factors could have contributed to these findings: local pressure on the tumor and subsequently to the spinal cord during hemostasis and initial tumor resection could have caused temporary MEP loss . In addition, the blood loss compensated through fluid replacement could have contributed to the MEP loss despite stable blood pressure in the situation of both local and systemic vulnerability of the corticospinal system originally due to tumor compression. We consider the proactive maintenance of stable circulatory parameters by the anesthesiologist essential to avoid lasting neurologic dysfunction. It would be an error to wait with fluid replacement until the blood pressure indeed decreases. Correction of the volume deficit at such a late time would be trailing events, carrying more risk for ischemic damage.

Discussion

The use of MEP data, both D wave and muscle MEPs, has found significant acceptance and implementation in the growing community of intraoperative monitoring specialists worldwide. Intramedullary and extramedullary tumors (like the one in Case 3) are basically monitored using the same techniques, practical setups, and interpretation criteria: preservation of muscle MEPs is always associated with preserved motor function, loss of muscle MEPs is highly likely to indicate temporary loss of motor function as long as the D wave is preserved. Loss of both muscle MEPs and D wave is indicating irreversible loss of motor function. There is a scenario of present muscle MEPs but absent or unrecordable D wave. This is interpreted as a desynchronization of the D wave and is sometimes observed in patients with intradural-extramedullary tumors as well as in patients who underwent prior radiation therapy.

The patient care essentially requires extensive integration of neurosurgery, neurophysiology, and neuroanesthesia. As the three case vignettes presented in this contribution show, an array of interpretation from all three specialties contribute to the integrated picture. The neuroanesthesiologist should not only be a passive “provider of anesthesia” for the operation but an active, and as Case 3 shows, even proactive partner in the entire effort to manage, control, influence and eventually maintain neurologic homeostasis and neurologic integrity of essential neural structures.

Questions

1. During a spinal cord tumor surgery in a 2-year-old child in prone position with the head turned rather sharply to the side and positioned in a ring, the muscle MEPs of the right upper and lower extremities first require higher stimulation intensity and soon disappear soon after baselines were obtained and BEFORE the surgeon even got to laminotomy.

   This is most likely due to:

   A. Hypothermia resulting from poor covering during anesthesia preparation and monitoring setup.

   B. Hypotension due to blood loss.

   C. Compression of the spinal cord at the level of the cervicothoracic junction.

   D. Poor positioning and position-induced transient spinal cord compression.

2. Upon resection of a T2 to T11 intramedullary ganglioglioma in a 14-year-old girl, a loss of muscle MEPs from the right tibialis anterior muscles occurs. The ipsilateral abductor hallucis has not been recordable even at baseline at maximum intensity settings. The D wave is down in amplitude about 30 % from baseline. Thenar MEPs are bilaterally intact and unchanged.

   What should you do next?

   A. Advise the surgeon of the change and recommend temporarily halting resection and start irrigation.

   B. Alert the anesthesiologist to a possible perfusion deficit.

   C. Ask the anesthesiologist if the anesthesia level may be too light.

D. Further increase the stimulus intensity and the number of pulses per train and repeat recordings.

3. A right-handed adult patient has an intramedullary astrocytoma with asymmetric configuration from C2 to C7. His symptoms are primarily nighttime pain in the ulnar left forearm. The surgical plan is to enter the cord on the left (i.e., symptomatic and nondominant) side.
   During this operation it is essential to preserve:

   A. SSEPs of the right leg, muscle MEPs of the left arm and the D wave.

   B. The D wave.

   C. SSEPs of the right arm and leg, D wave, bilateral upper extremity MEPs, and right lower extremity MEPs.

   D. Muscle MEPs of both tibialis anterior and abductor hallucis muscles.

4. A myxopapillary ependymoma of the conus and cauda equina extending from T11 to L5 is resected in a 5-year-old boy. What is the role of D-Wave recording in this surgery?

   A. The D wave must be recorded with priority over muscle MEPs and bulbocavernosus-reflex.

   B. The D wave cannot be recorded.

   C. The D wave must be recorded using a collision technique.

D. The D wave amplitude must remain above 50 % of baseline to ensure preserved sphincter function.

Answers

1. D

2. A

3. B

4. B

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Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_37

37. Intraoperative Monitoring in Tethered Cord Surgery

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Keywords IOM – Tethered cord surgery – Tethered cord syndrome (TCS) – Anesthetic management – Intraoperative neuromonitoring – Somatosensory-evoked potentials – Transcranial motor-evoked potentials – Electromyography, bladder pressure urometry – Bulbocavernosus reflex

Key Learning Points

- Derangements in this process of spinal cord will lead to various forms of spinal dysraphism, including the TCS. Although usually diagnosed in childhood, an adult form is well known. Developmental attachments and traction may remain subclinical and be aggravated over time by repeated traction of the conus medullaris during spine flexion, trauma, or degenerative stenosis of the spinal canal.
- Patients present with various sensorimotor changes in the lower limbs

and abdomen; these include pain (low back and leg), weakness, altered sensation, bowel and/or bladder dysfunction, and sexual dysfunction.

- Up to 90 % of all patients brought to surgery will experience either improvement or stabilization of their complaints.
- It is necessary to identify and protect the multiple nerve roots in the cauda prior to surgical resection of the filum terminale or any other fibrous adhesions causing the tethering phenomenon, as well as protection of the motor and sensory tracts. Mapping techniques are useful in identifying and sparing functional neural structures. They are also helpful in identifying nonfunctional neural tissue to allow for complete untethering.
- A multimodality approach to monitoring the neural structures at risk is warranted. Neurophysiologic monitoring is needed not only to predict but also to prevent nerve injury. Therefore, monitoring modalities available to achieve this include posterior tibial and median nerve somatosensory-evoked potentials (SSEP), pudendal and individual spinal nerve root sensory-evoked potentials, transcranial motor-evoked potentials (MEP), spontaneous and evoked electromyography (EMG) of musculature in the myotomes from L2 to S4, the bulbocavernosus reflex (BCR), and pressure urometry.
- Regarding the efficacy of multimodality monitoring, EMG had a sensitivity of 100 % and SSEP had a specificity of up to 100 % in several studies.
- Intraoperative motor-evoked potential improvement has been reported after complete and successful untethering. This was associated with clinical improvement in the immediate postoperative period.
- Several authors support the use of evoked EMG of the anal sphincter as adequate to monitor pudendal nerve function and to preserve both fecal and urinary continence.
- Relaxation is mediated by sympathetic preganglionic fibers from T11–L2, which synapse with the postganglionic nerves in the mesenteric and sacral plexuses; finally traveling to the bladder via the hypogastric nerve. A method of monitoring the detrusor contraction through the use of vesical pressure has been used successfully in at least two case study

series. Stimulation of the autonomic fibers of S2–4 will then yield an increase in bladder pressure.

- The BCR aids in the assessment of three anatomical structures/pathways at spinal levels S2–4. The afferent path is formed by the sensory fibers of the pudendal nerve, and the efferent limb travels over the motor fibers of the pudendal nerve to the muscles of the pelvic floor including the external anal sphincter. The pudendal nerve can be electrically stimulated over the dorsum of the penis or the clitoris with the motor response captured with needle electrodes inserted into the anal sphincter. Whether or not the BCR correlates with preservation of sphincter control or sexual function postoperatively is controversial.

Introduction

The tethered cord syndrome (TCS) is a constellation of symptoms resulting from an abnormal fixation and restricted movement of the spinal cord. The immobility of the spinal cord is caused by attachment of neural tissue to inelastic structures such as a thickened filum terminale, adhesions (developmental or postsurgical), lipomeningomyelocele , intradural lipomas, or arachnoiditis [1]. It is interesting to note that the embryological origins of the spinal cord are twofold: the proximal segment is formed when the ectoderm overlying the notochord forms the neural plate, involutes, and then closes to form the neural tube with cranial and caudal neuropores; distal to the caudal neuropore is the caudal cell mass, which differentiates into the distal neural tube, the end of which is the ventriculus terminalis. The caudal cell mass forms the conus medullaris, filum terminale, and cauda equina. During gestation the conus ascends in relation to the vertebral bodies, and tissue caudal to the ventriculus terminalis forms the filum. The vertebral column grows at a rate disproportional to the neural structures resulting in elongation of the filum and ascension of the conus until, at about 3 months' postnatal age, it rests at the L1–2 level [2]. Derangements in this process will lead to various forms of spinal dysraphism including the TCS. Although usually diagnosed in childhood, an adult form of this condition is well known that can also be caused by trauma or previous surgery to the spine. Developmental attachments and traction may remain subclinical and be aggravated over time by repeated traction of the conus medullaris during spine flexion, trauma, or degenerative stenosis of the spinal canal. Animal

models have shown that continuous traction produces histopathological changes in white and grey matter that are proportional to the tension applied to the cord and the length of exposure. Neurophysiologic changes in both somatosensory-evoked potentials and motor-evoked potentials correlate with histopathological findings [3]. Patients present with various sensorimotor changes in the lower limbs and abdomen, which include pain (low back and leg), weakness, altered sensation, bowel and/or bladder dysfunction, and sexual dysfunction, as seen in Table 37.1 [4]. In a recent series of 24 adult patients with TCS, scoliosis and congenital talipes equinovarus were found in 45.8 and 12.5 % of patients, respectively [5]. While pain is the most common manifestation in adults, children present more often with a motor weakness and alteration in tone and reflexes [6]. It is possible that this occurs due to the inability of the young children to communicate sensory changes or changes in urinary function like urgency or incomplete voiding.

Table 37.1 Presenting complaints in patients with TCS

Clinical feature	**Patients, *n* (%)**
Muscular weakness	46 (78)
Back pain	43 (73)
Bladder dysfunction	42 (71)
Altered sensation	40 (68)
Leg pain or sciatica	33 (56)
Cutaneous stigmata	15 (25)
Foot deformities	13 (22)
Muscular atrophy	13 (22)
Leg length discrepancy	5 (8)
Spinal deformity	5 (8)
Fecal incontinence	4 (7)
Sexual dysfunction	2 (3)

Adapted from Lee et al. [4]

As a result of the mechanical tethering of the spinal cord, there is a reduction in blood flow to the lower segments of the spinal cord, particularly in the conus. This leads to a derangement of oxidative metabolism in the grey matter of the cord with an impaired reduction/oxidation state in the cytochrome a, a3 system. Energy metabolism is therefore impaired.

Spectrophotometry and Doppler flowmetry studies in humans and in experimental animal models show that this process can be reversed by surgical release of the cord resulting in improved blood flow and return to a more normal redox state [5, 7]. Neurologic improvement then parallels these changes. Surgical intervention is usually recommended for symptomatic patients, but it is still controversial whether to intervene on asymptomatic patients with evidence of tethered cord [5, 6]. Surgical treatment is aimed at the most complete untethering and release of the spinal cord as is possible utilizing microsurgical techniques. The goal is to relieve or stabilize symptoms and avoid further deterioration of neurologic function. Data show that the symptom most responsive to treatment is pain of the back or legs (up to 83 % improvement), followed by weakness (up to 69 %). Patients with a back and radicular pain history shorter that 1 year had better pain relief after untethering compared to those presenting with symptoms of longer duration [8].

Several studies have shown that up to 90 % of all patients brought to surgery will experience either improvement or stabilization of their complaints (Table 37.1) [4].

Case Presentation

A 47-year-old man presented to the neurosurgeon with a history of nonradiating pain in the midthoracic region of his back. In addition, he complained of dull, aching pain in the posterior aspect of the left thigh and in the left buttock. He had noticed progressive weakness in his left leg and foot along with numbness and tingling in the left leg. When asked, he also admitted to intermittent difficulty voiding his bladder. His medical history consisted of essential hypertension, social alcohol consumption, and a 4–5 MET (metabolic equivalent of task) exercise tolerance. He was taking lisinopril for his blood pressure with good control. Physical examination revealed a decrease in sensation to touch in the left leg along the anterolateral aspect including the dorsum of the foot and great toe. His muscle strength was 5/5 in the arms and right leg, but was 3–4/5 in the left foot dorsi- and plantar flexion. Radiographic studies consisted of X-rays of the thoracic and lumbosacral spine as well as full spine MRI. The MRI showed a cystic lesion in the thoracic spine at the T6–7 level, and the appearance of a short and thickened filum terminale (Fig. 37.1). He was scheduled for a thoracic

laminectomy and cyst removal and a lumbar exploration and untethering of the spinal cord.

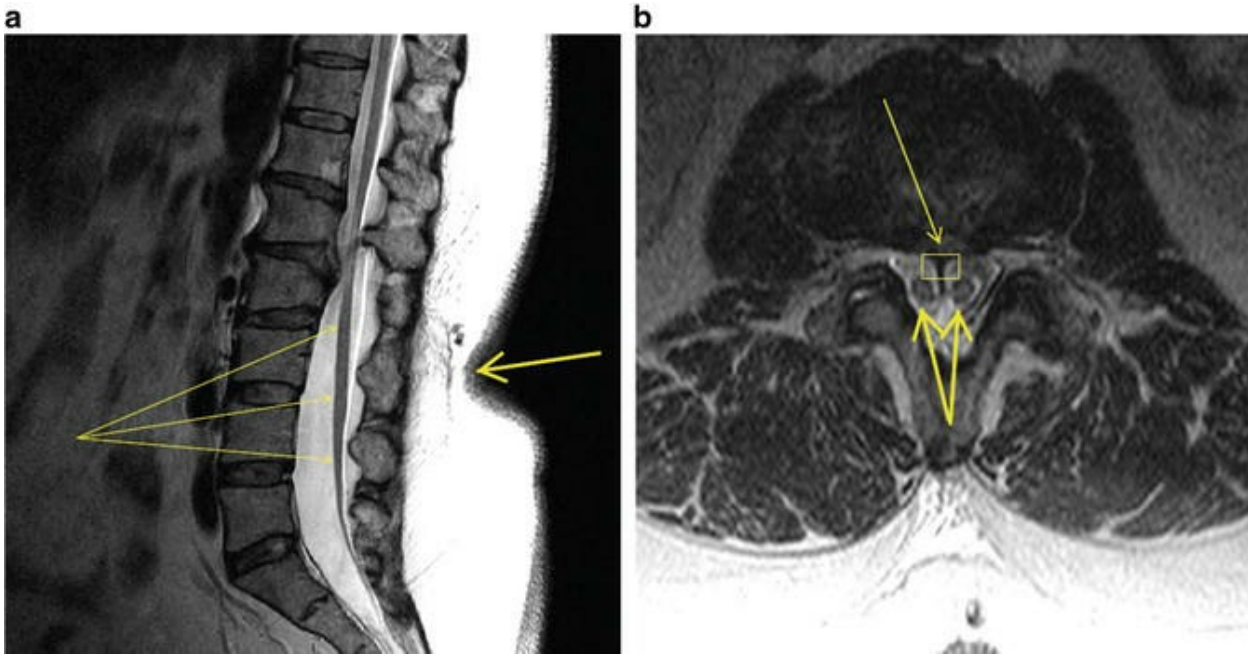

Fig. 37.1 MRI of lumbosacral spine. (**a**) Sagittal view. Note thickened filum terminale indistinguishable from low-lying conus medullaris (*fine arrows*) and adherent to posterior elements in caudal canal. Also note skin indentation on back with hair growth (*thick arrow*), which is pathognomonic of spinal dysraphism. (**b**) Transverse view. Note septum (*fine arrow and rectangle*) bifurcating the conus medullaris (*thick arrows*)

Monitoring Modalities

Given the location of the spinal cyst and the proposed untethering procedure, neurologic structures at risk include the thoracic spinal cord (both corticospinal tracts and posterior columns) and the nerves of the cauda equina. These structures may be injured through various mechanisms including vascular compromise (surgical interruption, vasospasm, arterial hypotension, anemia, hypoxemia), compression from surgical retractors, overheating from electrocautery, or traction from improper positioning or surgical manipulation [9]. Paramount during surgery is the need to preserve motor and sensory function of the lower extremities as well as bowel, bladder, and sexual function. This necessitates the identification and protection of multiple nerve roots in the cauda prior to surgical resection of the filum terminale or any other fibrous adhesions causing the tethering phenomenon, as well as protection of the motor and sensory tracts. Mapping

techniques are useful in identifying and sparing functional neural structures. They are also helpful for identifying nonfunctional neural tissue to allow for complete untethering. Due to distorted anatomy in some patients, identification of neural structures based on anatomy and visual appearance only could be challenging. On the other hand, some patients have lost function of neural structures that can only be identified as nonfunctional with intraoperative neurophysiologic studies. Intraoperative neurophysiologic monitoring has also been used in a recent study by Jackson et al. [10] to confirm functional level in patients 18 months to 5 years old presenting for untethering after having fetal repair of myelomeningocele .

During the procedure, two modalities will be used to meet the objectives. First, mapping will identify and separate functional neural elements from nonfunctional fibrous bands and the filum. Second, monitoring will continuously assess the functional integrity of neural tracts. In addition, the surgeon will benefit from immediate warning of impending damage when contacting any neural structures in the surgical field with the expectation that changes can then be made to minimize or avoid permanent injury. Neurophysiologic monitoring is needed not only to predict but also to prevent nerve injury. Therefore, monitoring modalities available to achieve this include posterior tibial and median nerve somatosensory-evoked potentials (SSEPs), pudendal and individual spinal nerve root sensory-evoked potentials, transcranial motor-evoked potentials (MEPs), spontaneous and evoked electromyography (EMG) of musculature in the myotomes from L2 to S4, the bulbocavernosus reflex (BCR), and pressure urometry.

Anesthetic Management

To optimize outcome, the anesthetic technique was tailored to minimize deleterious effects on the monitoring modalities employed (SSEPs, MEPs, EMG), allowing the best feedback to the surgeon regarding impending neurologic injury. A total intravenous anesthesia (TIVA) technique was employed with judicious use of neuromuscular blockade. The patient was premedicated with 2 mg intravenous (IV) midazolam. Electrocardiogram, noninvasive blood pressure, bispectral index analysis (EEG, BIS), and pulse oximeter probes were attached, and the patient was preoxygenated with 10 L O_2 by mask for 3 min. Anesthesia was induced with 1.5–2.0 mg/kg propofol and 15 μg sufentanil IV. After confirmation of the ability to provide

ventilation by face mask, 50 mg rocuronium was given IV. When adequate muscle relaxation was confirmed, the trachea was intubated with a 8.0-mm ID endotracheal tube and secured at 23 cm depth. No additional neuromuscular blocking agents were administered for the duration of the case. Ketamine , 1 mg/kg, was given intravenously. For maintenance of anesthesia, an intravenous infusion was begun using a mixture consisting of 10 mg propofol and 0.5 mg ketamine per cc for hypnosis and infused at a rate between 100 and 300 μg/kg/min of the propofol. Sufentanil was used for analgesia. An additional 45 μg was given IV bolus (titrated) to achieve a loading dose of 1 μg/kg as tolerated while maintaining mean arterial blood pressure (MABP) of greater than 70 mmHg, and a continuous infusion was begun at a rate of 0.3 μg/kg/h. The propofol/ketamine and sufentanil infusions were adjusted during the case to maintain the bispectral index at 40–60 and the MABP between 70 and 90 mmHg. A radial artery cannula was placed to continuously monitor blood pressure and the patient was placed in the prone position with both arms tucked to the sides for surgery after placement of the intraoperative neuromonitoring (IONM) needles, grounding pad, and protective pads.

Intraoperative Neuromonitoring

Pursuant to the goals of mapping, monitoring, and warning, as stated above, several authors have advocated a multimodality approach to monitoring the neural structures at risk [11–21]. In particular, Krassioukov et al. [14] studied a group of 61 patients undergoing complex lumbosacral procedures; among them were 15 cases of tethered cord. All patients were monitored with a combination of evoked and spontaneous EMG and posterior tibial nerve SSEPs . Of the three patients who awoke with new neurologic deficits, only one had a significant change in SSEPs. The presence or absence of responses during stimulated EMG resulted in the alteration of the course of the surgical procedure in 24 cases (42 %). Regarding the efficacy of multimodality monitoring, Gunnarsson et al. [15] performed a retrospective analysis of 213 cases of thoracolumbar surgery, three of which were for tethered cord, using a combination of EMG and SSEPs . In their series, 14 patients had new neurologic deficits all of which had significant EMG activation, but only four had a change in SSEPs considered significant. In their study, EMG had a sensitivity of 100 %, and SSEPs had a specificity of 94.5 %. This reinforced the use of more than one monitoring technique. In a series of 44 adult patients

undergoing surgery for tethered cord, Paradiso et al. [16] found that the combined use of SSEPs and EMG limited neurologic morbidity. They had one patient with a transient and one patient with a permanent neurologic deficit postoperatively. In one patient, a significant change in SSEP monitoring resulted in a change in surgical strategy. Their calculated measures of efficacy showed a sensitivity of EMG of 100 % and a specificity of SSEPs of 100 %—very similar to the Gunnarsson study. Beyazova et al. [22] recommended the inclusion of direct stimulation of nerve roots since it produced a positive response that differentiated neural tissue from nonfunctional connective tissue in three of ten patients while SSEPs or MEPs had not changed throughout the procedure. Sala et al. [23] recently confirmed that multimodal intraoperative neuromonitoring techniques, particularly the use of MEPs that includes anal sphincter and BCR, reduced morbidity in a series of 47 patients. This study found that 12 % of patients presented unexpected muscle responses when tissue considered as nonfunctional was stimulated [19]. Garg et al. [5] retrospectively studied 24 adult patients who presented for tethered cord procedures. Neurophysiological monitoring was not conducted since it was not available. In one patient, weakness increased due to the accidental section of a functional neural structure. This situation could have been prevented by the use of intraoperative neuromonitoring, as it has been prevented in other series of patients. Sala et al. [23] (64 patients) and Valentini et al. [21] (149 patients) reported the use of multimodal neuromonitoring approach in their institutions for complex spinal cord untethering and occult spinal dysraphism, respectively. Both concluded that the combination of mapping and other monitoring techniques such as EMG, MEPs, and BCR improved the level of untethering while decreasing morbidity [20, 21]. For rare dysraphic malformations like retained medullary cord, a form of severe tethering lesion, the use of mapping was considered indispensable since anatomical appearance alone will not be sufficient to resect the retained cord safely [23].

In this patient, the modalities employed were SSEPs , MEPs, stimulated and spontaneous EMG, the bulbocavernosus reflex, and pressure urometry. Posterior tibial and median nerve SSEPs were chosen to assess the functional integrity of the posterior columns below the level of surgery and to use the arms as a control above the level of surgery as well as to monitor for positioning injury. To monitor the stimulated and spontaneous EMG, specific muscles were chosen to cover the myotomes from L2 to S4 as inclusively as

possible given the amount of channels available. Also, bladder pressure urometry, through the use of a urinary catheter attached to a pressure transducer system, allowed monitoring of the bladder detrusor muscle function.

Somatosensory-Evoked Potentials

Posterior tibial nerve SSEP monitoring allows continual functional assessment of the posterior columns with sensory input from the dermatomes of L4 through S1 with the primary contribution from L5 and S1. Given the dual surgical approaches in the thoracic spine and the lumbosacral spine, posterior tibial SSEPs provided essential information about injury to dorsal spinal cord structures, especially in the thoracic region, and sensory nerves in the lower levels. In this situation, electrodes were placed in the popliteal fossa to record nerve action potentials (thus insuring adequacy of stimulus), over the cervical spine to record subcortical responses, and in the scalp to record cortical responses. Subcortical cervical responses help to differentiate whether changes in the cortical response are due to anesthetic effects or from other causes since, as mentioned in an earlier chapter, these are resistant to the effects of anesthetic drugs.

The median nerve is formed from fibers from the roots of C6–T1 with occasional contributions from C5. Median nerve SSEPs therefore monitor the functional integrity of the posterior columns above the thoracic level of this patient’s cyst. Electrodes are placed over the brachial plexus, cervical spine, and scalp for the same reasons as mentioned previously for posterior tibial nerve SSEPs. These will not be affected by any surgical maneuvers in the thoracic or lumbosacral spine and can therefore aid in the differential diagnosis of changes, being used as a control compared with the posterior tibial responses. They can also be used to detect and prevent impending positional injury to the brachial plexus or median nerve—an issue when the patient is prone.

While posterior tibial SSEPs will provide information from the L4 to S1 level, the entire cauda is at risk during untethering. To enhance input to the surgical team, somatosensory-evoked potentials (SSEPs) from the levels S2 to S4 can be obtained from stimulation of the pudendal nerve. This is accomplished by stimulating the nerve on the dorsum of the penis or the clitoris. However, since the responses obtained are of low amplitude and require a high number of repetitions to generate repeatable responses, thus

making reliable acquisition difficult, the utility of this technique has been questioned and was not used on this patient [13, 17, 18, 24].

Transcranial Motor-Evoked Potentials

The surgical approach to the thoracic spine cyst places the corticospinal tracts at risk for injury from multiple factors including physiologic derangements such as hypotension. SSEP monitoring alone will not suffice to monitor for this injury as SSEPs are not a measure of motor tract function and are mediated by anatomical structures with a separate vascular supply. Therefore, MEP monitoring is essential. Monitoring the functional integrity of the motor tracts in tethered cord surgery is important because the presence of the muscle response at closure correlates with preserved muscle control and the absence of postoperative motor deficits [18]. Intraoperative motor-evoked potential improvement has been reported after complete and successful untethering. This was associated with clinical improvement in the immediate postoperative period [25]. Responses were monitored in the upper and lower extremities for the same reasons as stated for SSEPs: to be used as control responses and to monitor for positional injuries. Motor-evoked potentials were monitored using transcranial electrical stimulation of the motor cortex and recording the compound muscle action potential (CMAP) generated from the abductor pollucis brevis (APB) , abductor hallucis (AH), and tibialis anterior (TA) muscles. For the lumbar approach to the untethering of the spinal cord, D wave monitoring of the MEPs would not be helpful since these are not recordable below the level of the conus medullaris. Electrodes placed in the external anal sphincter will provide feedback on the motor elements of the pudendal nerve (S2–S4).

Electromyography

Both evoked and spontaneous EMG were employed in this patient for two reasons. The first is to allow the surgeon to identify discrete nerve roots (mapping) and differentiate them from nonfunctional tissue such as fibrous bands and the filum. When using evoked EMG to isolate the functional neural tissue from the inert filum and to determine where to make the release cut, it has been suggested by Quinones-Hinojosa et al. [26] that a filum to motor root stimulation threshold ratio of 100:1 is adequate to insure that the sectioned tissue contains no neural elements [26]. The second reason is to

provide the surgeon with immediate feedback of impending injury when making contact with nerves thereby allowing him or her to modify the surgical technique and avoid permanent damage. Some authors believe that this is the most important modality employed during tethered cord surgery [19, 20, 23] and can provide prognostic value [27]. In this study, the investigators stimulated the caudal end of the spinal cord and recorded the threshold necessary to elicit motor responses in muscles of the leg and perineum. Patients with a higher stimulation threshold after untethering experience further neurologic deterioration postoperatively. Leg and pelvic muscles that are useful in covering the myotomes from L2 to S4 are listed in Table 37.2, with the level providing the primary contribution being underlined.

Table 37.2 Myotomes used for monitoring the tethered cord

Vastus medialis (Quadriceps femoris)—L2, L3, L4 (femoral nerve)
Tibialis anterior—L4, L5 (deep peroneal nerve)
Extensor hallucis longus—L4, L5 (deep peroneal nerve)
Abductor hallucis—L5, S1, S2 (medial plantar branch, tibial nerve)
Gluteus maximus—L5, S1, S2 (inferior gluteal nerve)
Lateral Gastrocnemius—L5, S1, S2 (tibial nerve)
Medial Gastrocnemius—S1, S2 (tibial nerve)
Soleus—S2 (Tibial nerve)
External anal sphincter—S2, S3, S4 (inferior rectal branch, pudendal nerve)
Urethral (vesical) sphincter—S2, S3, S4 (deep branch, perineal nerve)

While it is controversial whether there is sufficient variation in the primary motor nerve root supply to the anal and urethral sphincters to warrant monitoring of each muscle separately, it is difficult both to obtain electrodes suitable for use on a urinary catheter and to reliably place them within the vicinity of the urethral sphincter. Several authors support the use of evoked EMG of the anal sphincter as adequate to monitor pudendal nerve function and to preserve both fecal and urinary continence. In this patient, electrodes were placed in the vastus medialis (quadriceps femoris), tibialis anterior, lateral gastrocnemius, abductor hallucis, and external anal sphincter muscles. Bipolar stimulating forceps were used to minimize current spread to adjacent structures.

Sensory-Evoked Potentials

On occasion, a structure may be stimulated in the surgical field and yield no corresponding motor response in monitored muscles. The structure may be the dorsal sensory root of a spinal nerve. To insure that this is not the case, prior to surgical release, a sensory-evoked potential may be performed. The structure can be stimulated with a handheld hook electrode using the SSEP stimulation and recording parameters already in use with the posterior tibial nerve, and subcortical and cortical responses can be acquired. The cortical response of a nerve root that is stimulated in this fashion will appear with an initial positive deflection at approximately 20 ms (P20) [13, 17].

Bladder Pressure Urometry

Proper bladder function consists of two separate components: storage, which is regulated by the external sphincter (dysfunction of which is manifested as urinary incontinence), and emptying, which is initiated by contraction of the bladder detrusor muscles. While the external sphincter is innervated by the motor branches of the pudendal nerve, the detrusor contraction is under autonomic control. Detrusor contraction is innervated by parasympathetic fibers from spinal segments S2–4 via the pelvic nerve, which synapses with postganglionic fibers near the bladder wall. Relaxation is mediated by sympathetic preganglionic fibers from T11–L2, which synapse with the postganglionic nerves in the mesenteric and sacral plexuses, finally traveling to the bladder via the hypogastric nerve. Acquiring direct EMG activity from the detrusor muscle fibers is technically difficult and risks bladder wall puncture. Therefore, a method of monitoring the detrusor contraction through the use of vesical pressure has been used successfully in at least two case study series [28, 29]. The technique involves placing a urinary catheter, filling the bladder with 250 cm^3 of normal saline solution, and attaching the catheter to a standard pressure monitoring transducer with the pressure waveform displayed on the vital sign monitor (Fig. 37.2). Stimulation of the autonomic fibers of S2–4 will then yield an increase in bladder pressure (usually 35–70 cm H_2O). The latency between stimulation and contraction is approximately 2–10 s. Stimulation intensity is 4–5 mA and must be continuous over 10–20 s [16, 28, 29].

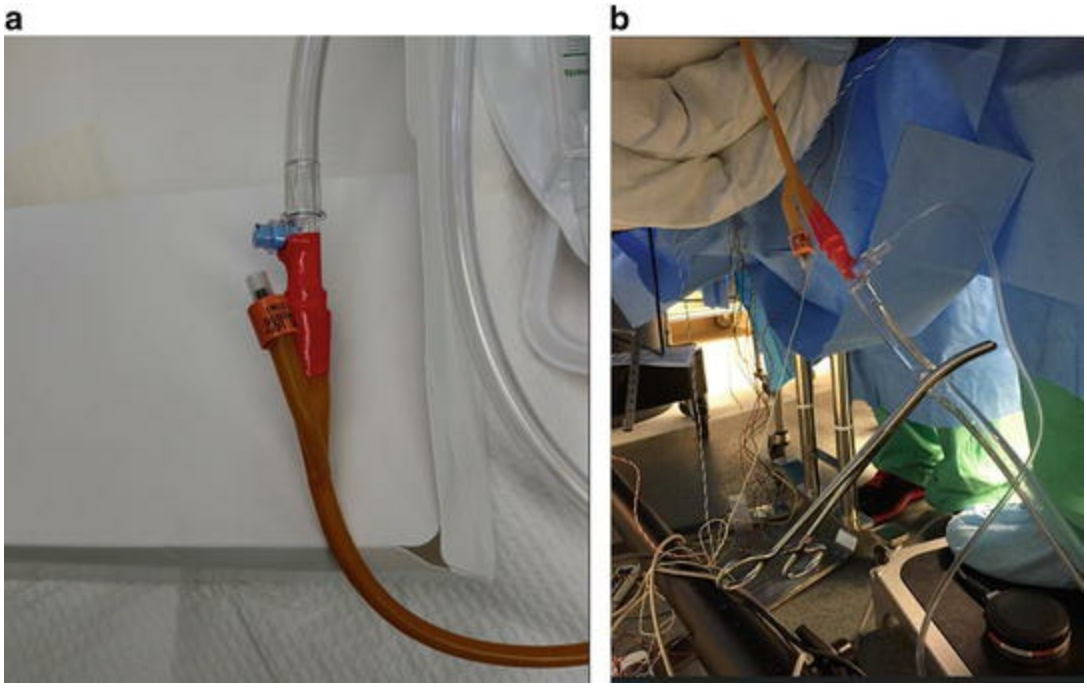

Fig. 37.2 Bladder pressure monitoring. This technique requires the placement of a urinary catheter (**a**). Note that the catheter has a port to connect the transducer. After placing the catheter, filling the bladder with 250 cm^3 of normal saline solution and clamping the catheter to avoid emptying of the bladder is needed. A standard pressure monitor transducer is attached to the catheter (**b**). The pressure waveform is displayed on the vital sign monitor

Bulbocavernosus Reflex

The BCR aids in the assessment of three anatomical structures/pathways: sensory, motor, and the grey matter of the spinal cord, at spinal levels S2–4. The afferent path is formed by the sensory fibers of the pudendal nerve. These neurons synapse in the grey matter of the spinal cord at the spinal segments S2–4 and the efferent limb travels over the motor fibers of the pudendal nerve to the muscles of the pelvic floor including the external anal sphincter. The pudendal nerve can be electrically stimulated over the dorsum of the penis or the clitoris with the motor response captured with needle electrodes inserted into the anal sphincter. Another method of obtaining this response is to stimulate the dorsal roots of S2–4 and record the CMAP from the anal sphincter [18]. Although this reflex tests a complete reflex arc, because the reflex is polysynaptic, it is sensitive to the effects of volatile anesthetics. This makes the response difficult to maintain during surgery [17, 20]. Also, whether or not the BCR correlates with preservation of sphincter control or sexual function postoperatively is controversial [12, 18]. (For more

information, see Chap. 8, “The Use of Reflex Responses for IOM”).

Intraoperative Course

At the outset of surgery, the patient’s anesthetic was maintained as described above with the blood pressure targeted to be within 10 % of the preoperative baseline as measured in the preoperative holding area on the morning of surgery. The patient had a preoperative systolic blood pressure of 100 mmHg. Monitoring modalities employed included (1) posterior tibial and median nerve SSEPs with recording electrodes placed at the C3′, C4′, FZ, Cs5 (cervical spine at the C5 level) positions (International 10–20 System); (2) MEPs with responses monitored in the left and right APB, AH, and TA muscles; (3) evoked and continuous EMG of the left and right vastus medialis (quadriceps femoris), TA, AH, gastrocnemius , and external anal sphincter muscles; (4) bladder pressure urometry; and (5) BCR testing. The first stage of his operation was to remove the thoracic cyst. Baseline SSEP tracings were obtained and showed reduced amplitude of the responses from the left leg compared with those from the arms and right leg. Monitoring modalities were stable throughout the cyst excision. Once the thoracic cyst was resected, the lumbosacral spine was surgically exposed in preparation for release of the tethered cord. Posterior tibial and median nerve SSEPs were monitored continually and remained stable. MEPs were obtained from the TA and AH muscles bilaterally, confirming functional integrity of the spinal segments L4–S2. Interestingly, no response to transcranial electric stimulation was noted in the bladder pressure although there was a response in the anal sphincter.

While the SSEPs and MEPs give the surgeon information about the function of the motor and sensory tracts, they neither provide an early warning for injury nor identify neural elements contained within the thickened filum. For those reasons, the evoked and spontaneous EMG are more valuable and provide a mapping technique.

During dissection of the cauda equina and after placement of a retractor, it was noted from the spontaneous EMG that there was low frequency, asynchronous motor unit firing in the anal sphincter electrodes (Fig. 37.3). From the absence of firing in any of the leg muscle leads, it was determined that the left or right lower sacral (S3–4) roots were being compressed. The surgeon inquired whether this was a warning of a potential injury. The IONM team assessment was that this represented only contact activation. Neurotonic

discharges, or A-trains, as they are sometimes referred to, differ from these contact potentials because they appear as high-frequency rhythmic discharges and are indicators of neurologic injury. These contact potentials resolved upon repositioning of the retractor.

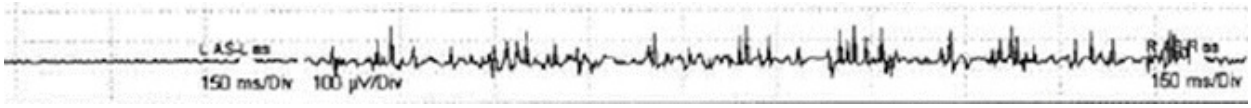

Fig. 37.3 Contact discharges from the right anal sphincter leads. Shown is low frequency, asynchronous motor unit firing in the right anal sphincter electrodes, which occurred during dissection of the cauda equina and after placement of a retractor

To map the nerve roots, the surgeon used bipolar stimulating forceps, which delivered 5-mA, 1-Hz stimulation pulses. Responses were noted in all of the monitored muscles. Particular attention was paid to identification of the anal sphincter responses in isolation from the leg muscle responses in order to delineate the S2–4 nerve roots (Fig. 37.4).

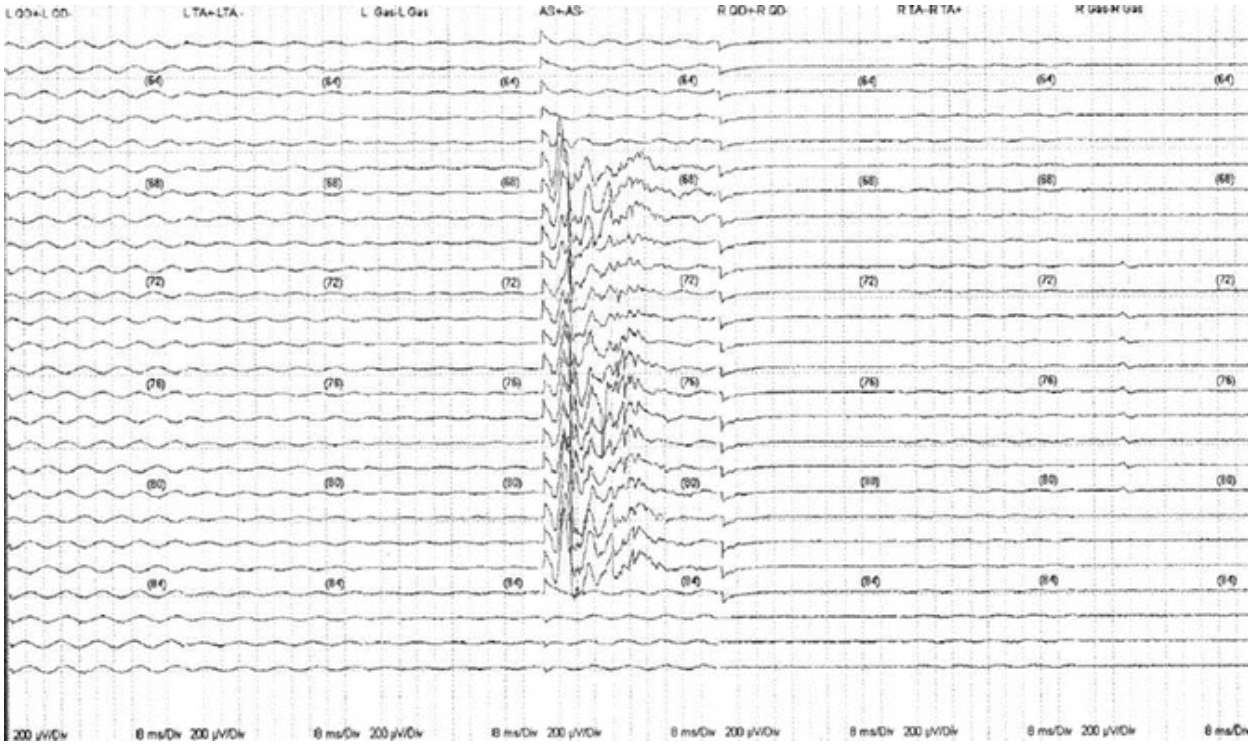

Fig. 37.4 Stimulated EMG of the anal sphincter during cauda equina mapping. Shown are the responses from muscles during mapping of the cauda equina to locate S2–S4. Of note is that these tracings reveal EMG activity in the anal sphincter muscle (but not the other muscles) during stimulation of the nerve roots using a bipolar stimulating forceps. Shown are a series of recordings (stack) with

each successive recording stacked on top of the other tracings

At those levels THAT elicited a response in the anal sphincter, the stimulation was repeated with a train of pulses delivered at a rate of 4.6/s for approximately 10 s or until an increase in bladder pressure was noted. In the event of a change, the pressure was allowed to return to baseline after cessation of stimulation prior to proceeding to the next root. Once the visible nerve roots were mapped, the filum terminale was again stimulated with particular attention paid to the anal sphincter response . At one point, the filum was stimulated at an intensity of 5 mA, and a low amplitude response was obtained from the anal sphincter muscles with an increase of approximately 15 mmHg in the bladder pressure. Since the surgeon reported that his visual assessment would have been that this was inert tissue, further dissection was carried out in tissue layers in order to locate functional neural fibers. After several layers were separated, tested, and removed, the continuous high-frequency stimulation technique was again employed. This resulted in an increase in bladder pressure of greater than 50 mmHg, indicating the presence of nerve fibers contributing to detrusor function as well as high-amplitude firing in the anal sphincter (Fig. 37.5).

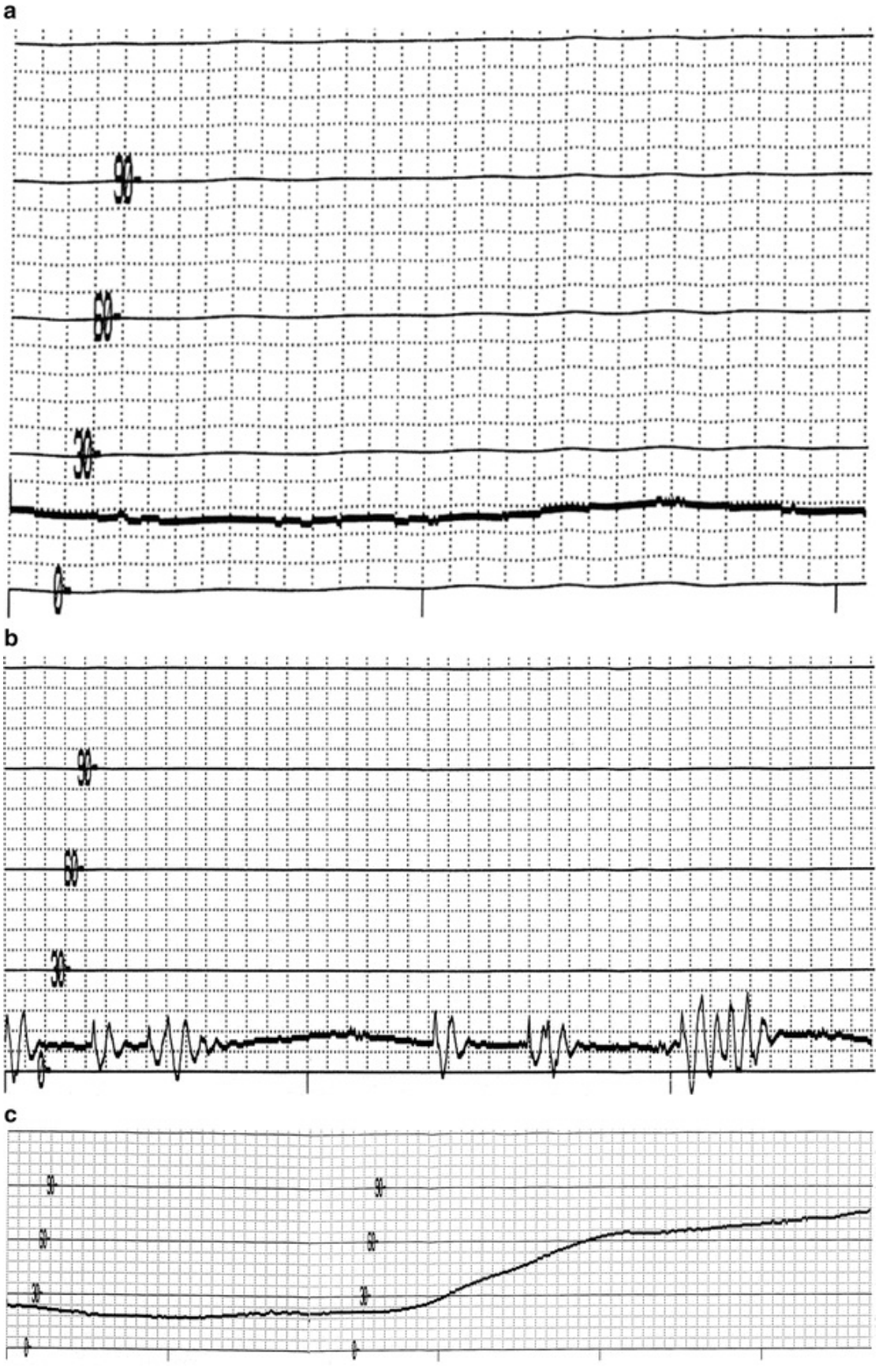
a
90
60
30
0
b
90
60
30
0
c
90
60
30
0

Fig. 37.5 Response of bladder pressure to stimulation. (**a**) Baseline pressure (~17 mmHg). Note respiratory variation in the bladder pressure. (**b**) Baseline tracing with artifact caused by increase in intra-abdominal pressure from surgeon's manipulations. (**c**) Response of bladder pressure to continuous stimulation of nerve bundle buried in filum terminale. Note increase from baseline of 17 mmHg to greater than 65 mmHg. Note that the baseline pressure varies among the tracings depending on the volume of urine in the bladder

As a result, surgical dissection was discontinued to preserve the neural bundle. It was decided that all inactive tissue had been safely detached at that point. Preservation of the lower sacral roots was confirmed by the continued presence of an anal sphincter muscle response when MEPs were elicited. In addition, elicitation of the BCR was accomplished after the filum was cut (Fig. 37.6).

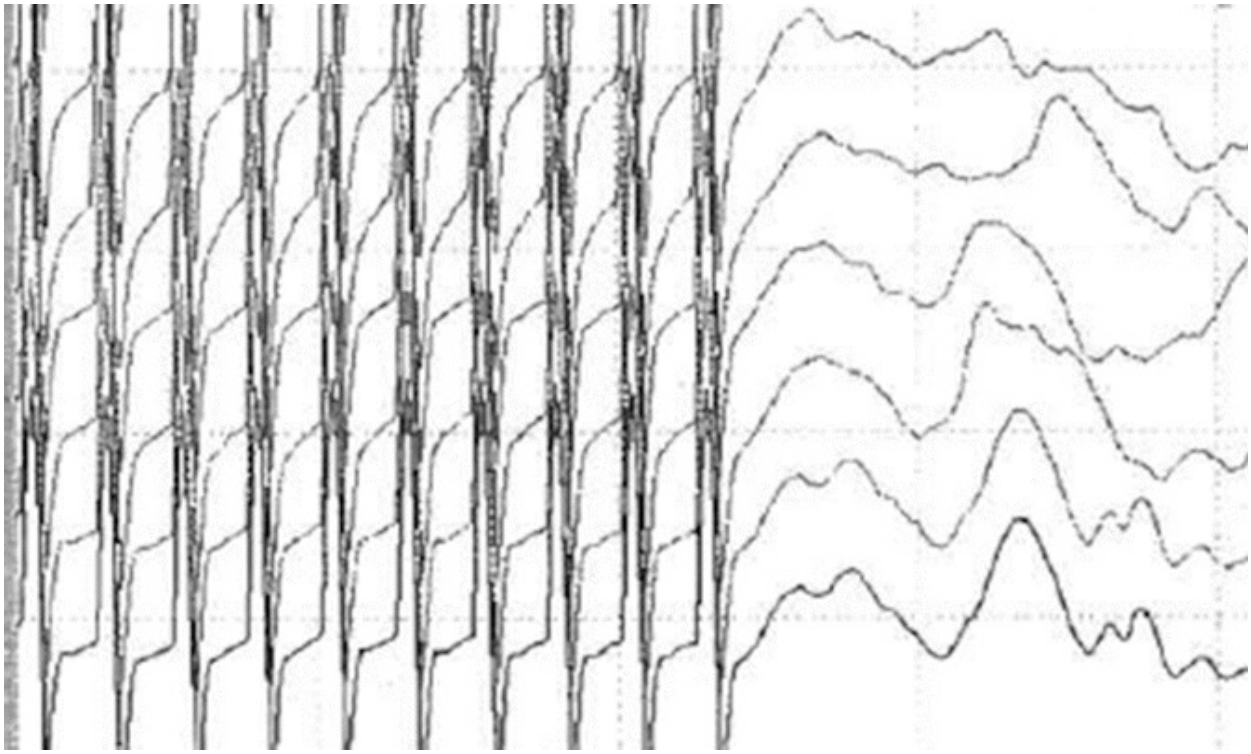

Fig. 37.6 Presence of bulbocavernosus reflex documented after cutting of filum terminale. Shown are EMG responses from the anal musculature recorded during the testing of the bulbocavernosus reflex after cutting of the filum terminale to verify the integrity of the S2–S4 nerve roots. The summation method was used with a train of ten stimuli and recording of anal sphincter EMG response at the 35- to 55-ms interval

Postoperative Outcome

In the postanesthesia care unit (PACU) , the patient was responding to commands and moving all four extremities. Because the patient's state was influenced by the residual effects of anesthesia, it was difficult to ascertain if there was a change in his muscle strength. Gross examination did not reveal any changes from the baseline sensory examination. Over the first 2 weeks following the operation, the patient had significant progressive resolution of his back pain as well as his leg pain. Leg weakness persisted initially and was treated with physical therapy. The patient did report subjective improvement in his urinary bladder voiding function. There was no deterioration in his anal sphincter function.

Questions

1. In tethered cord surgery, the most common mechanisms of injury are vascular compromise, compression, overheating, and traction.

   A. True

   B. False

2. The main objective of neuromonitoring in tethered cord surgery is to preserve motor and sensory function of the lower extremities as well as bowel, bladder, and sexual function.

   A. True

   B. False

3. To accomplish the goals of neuromonitoring in tethered cord surgery, the use of SSEP monitoring as a single technique identifies all neurological structures at risk.

A. True

B. False

4. Mapping techniques are not necessary since visual identification of relevant neurological structures is usually possible.

   A. True

   B. False

5. Multimodal neuromonitoring techniques including somatosensory-evoked potential (SSEP), transcranial motor-evoked potentials (MEP), spontaneous and evoked electromyography (EMG), the bulbocavernosus reflex (BCR), and pressure urometry are the most recommended techniques for intraoperative neuromonitoring in tethered cord surgery.

   A. True

   B. False

6. Bladder pressure urometry could be used as a surrogate of EMG direct monitoring of the detrusor muscle since direct monitoring is difficult and could cause complications.

   A. True

   B. False

Answers

1. A

2. A

3. B

4. B

5. A

6. B

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Footnotes

1 Asterisk indicates key references.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_38

38. Surgery in the Peripheral Nervous System

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Keywords Surgery – Peripheral nervous system – Application of operative recordings – Somatosensory-evoked potential – Brachial plexus – Peripheral nerve recordings – Operative diagnosis of nerve

Key Learning Points

- Operative nerve recordings are easy and provide valuable information that facilitates decision-making
- Nerve recordings have few anesthetic constraints
- The information obtained can be diagnostic
- Using operative recordings can improve outcomes

Objectives

There are many reasons to record from peripheral nerve in an operating room setting. These include “monitoring” functions for the purpose of providing an

ongoing evaluation of peripheral nerve function during procedures that place the nerve at risk. Examples of such procedures would be hip replacement surgery, thyroid/parathyroid surgery, and any procedures that would place peripheral nerves at exaggerated risk for positioning palsies. These recordings will have much in common with recordings made for the purpose of facilitating diagnosis of a nerve lesion . Early efforts to repair injured peripheral nerve surgically were often performed with a minimum of relevant information [1]. Having such information is perhaps a more significant reason to record from peripheral nerve; to provide diagnostic information relating to nerve injury. The purpose of this chapter is to provide emphasis on this subject. In this case, recordings obtained during surgery can provide definitive information that allows the surgeon to make informed decisions. An accurate diagnosis of a peripheral nerve problem at the time of surgery allows the surgeon to provide the optimal method to deal with the pathology.

The vast majority of peripheral nerve injuries leave the nerve in some degree of continuity [2, 3]. A particular nerve lesion in continuity may create a spectrum of damage within the nerve itself and this often precludes an accurate diagnosis with conventional EMG testing [4–6]. The best method to deal with such an injury is thus difficult to determine, but nevertheless is a prime determinant of outcome. Human peripheral nerve is capable of significant regeneration following an injury, if conditions are optimal, but the efficacy is much less than the regeneration seen in lower mammals [7, 8]. Intuitive decisions by the surgeon are not likely to provide the optimal conditions for regeneration [6, 9]. Deciding between a relatively simple neurolysis and a more complex section, removal of lesion, and suture repair will greatly affect outcome [10]. To elucidate, a neurolysis involves splitting the outer sheath of the nerve, the epineurium (see Fig. 38.1), to expose the fascicles within and then removing the buildup of connective tissue between them. The method of electrically stimulating nerve and recording the compound nerve action potential (CNAP) across the lesion in continuity can provide definitive information on the status of the fiber population within the nerve. Thus, axonotmetic and mild neurotmetic pathology, seen in Fig. 38.1, can be given sufficient time to allow for spontaneous regeneration. With this information in hand, the surgeon can then accurately choose the best method of repair. Furthermore, if a protocol is established that allows some opportunity for spontaneous regeneration to occur following a nerve injury, regeneration can be assessed using this same methodology [11]. Use of this

method, then, prevents the surgeon from further damaging nerve that is already in the process of regeneration. A recommended protocol would be to postpone surgery on an acute injury by an interval of 3–5 months. During this time, spontaneous regeneration will begin if conditions permit. Then, at surgery, a determination can be made whether such regeneration is in progress or not [2]. A more severe neurotmetic injury rarely regenerates spontaneously and would require complete section of the nerve and removal of the scar that blocks the regrowth of axons and then reconnecting the proximal and distal ends.

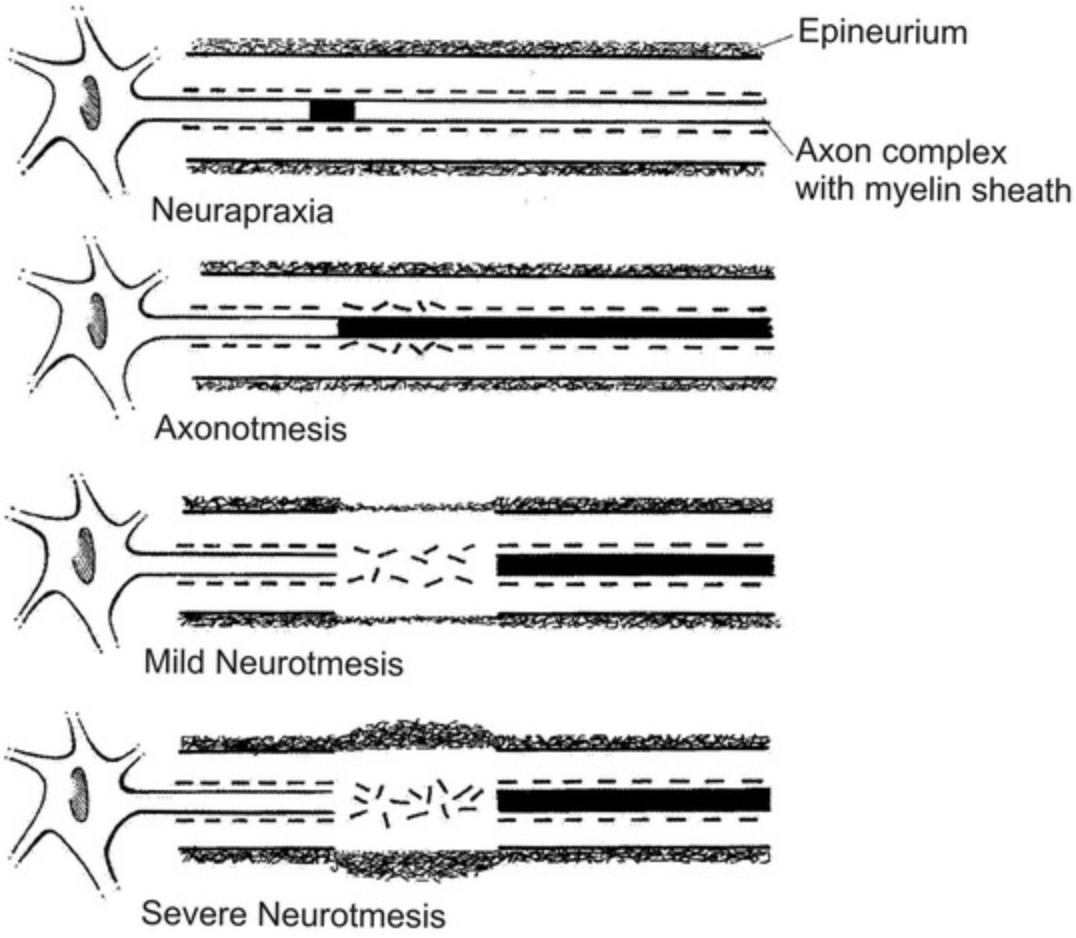


Fig. 38.1 Degrees of nerve injury that leave the nerve in continuity . The mildest injury is neurapraxic, which represents a loss of electrical function with little, if any, anatomic change. More severe is an axonotmetic injury with disruption of the axonal membrane but minimal disturbance to connective tissue. Wallerian degeneration of the axon occurs. Progressively more severe is the mild neurotmetic injury (mild connective tissue damage) and then severe neurotmetic injury (severe connective tissue damage and severe scarring). The latter will usually require a complete surgical repair

The anesthetic considerations associated with operative recording from peripheral nerve are minimal. General anesthetics do not affect peripheral nerve directly and the CNAP is minimally affected by halogenated agents, nitrous oxide, and intravenous anesthetics . If the patient becomes significantly hypothermic, there may be a mild to moderate decrease in nerve conduction velocity, but the amplitude of the CNAP would not be significantly affected. In the protocol described here, the stimulating electrodes and the recording electrodes are both placed on peripheral nerve. Therefore, neuromuscular junction blockade would not affect the CNAP. In some instances, though, it is reassuring to see evoked movement when stimulating peripheral nerve. It is not advisable to use evoked movement instead of a CNAP to evaluate nerve function. The reason for this is described elsewhere in this chapter.

The method of stimulating and recording CNAPs is straightforward and requires little experience to become proficient [12]. Since the size of the CNAP is considerably larger than the brain potentials recorded in operative monitoring, the process of signal averaging is not required. The necessary instrumentation is commonly available. Either equipment used for operative monitoring or EMG instrumentation can be used successfully. There are very few anesthetic considerations that would affect peripheral nerve recordings. Perhaps the most important would be the use of a tourniquet on the limb from which recordings will be made. If a tourniquet is used, the tourniquet should be released at least 20 min prior to any recordings. This would provide ample opportunity for perfusion to restore normal function prior to any recordings.

Stimulation of nerve through electrodes in direct contact is safe and effective. Stimulation parameters vary somewhat depending upon the size of the nerve being studied. For example, the normal, healthy ulnar nerve at the elbow requires an intensity of approximately 4–6 mA (8–10 V) when pulse duration is very short (<0.1 ms). We use these very-short-duration stimulus pulses to determine the presence of larger, myelinated fibers that can mediate motor function. Very small, unmyelinated fibers will not respond to these short-duration pulses [14]. However, nerve that has been chronically compressed or nerve that is highly scarred may require very high levels of stimulation at this pulse duration [11, 13]. In this case, it may be necessary to use intensities as high as 30–40 mA (60–80 V) at very short pulse durations (0.02 ms) to insure stimulation of fibers embedded in scar [14]. It should be noted that very-short-duration stimulus pulses (on the order of 0.02 ms)

preferentially activate larger, myelinated fibers that will mediate motor function. While there may be some concern for possible damage to nerve stimulated directly at these intensities, it should be pointed out that even with these high intensity levels there is little risk of damage to the nerve itself. Long periods of stimulation may induce a variety of factors that damage nerve. However, damage produced by short-term stimulation results primarily from the heat due to electrical currents or from electrolysis, the "plating" effect of salt deposition. Both of these processes require significant electrical p ower. One can easily see that the average electrical power, expressed in watt-seconds, conveyed by 30 mA of current flowing for 0.1 ms and a repetition rate of 5 pulses/s is very small and very little heat is produced. (Power = $I^2 RT$ = (current)^2 × resistance × time. Assuming current = 30 mA, resistance = 2000 Ω, and 5 pulses at 0.1 ms, P = 0.032 × 2000 × 0.0005 = 0.0009 W-S of average power delivered under these conditions). There is also very little electrolysis over the short term (several seconds of stimulation) because of a small amount of power. Kline and Hackett [11] histologically examined peripheral nerves from primates used in nerve research and have never found evidence of damage with stimulation well beyond these intensities. Further, in operative studies on human subjects, there have been no reports of postoperative nerve dysfunction as a result of this stimulation [11]. Under the conditions described here, electrical stimulation remains a safe mechanism for the evaluation of peripheral nerve.

Recording the CNAP from normal peripheral nerve is also very easy since the response is large in size (0.2–1 mV). Since the response is large in size, it does not require averaging to enhance the response. In fact, averaging is to be discouraged since it could lead to a deceptive large appearance of a response when, in reality, the response is extremely small. In the absence of averaging, it has been determined that a minimum of 4000 fibers of adequate size must be present in order to produce a clear CNAP [15]. This number of fibers has the potential to mediate significant function and therefore the appearance of a clear CNAP is a good prognostic indicator.

Figure 38.2 illustrates the type of electrodes that I have successfully used to stimulate and record from peripheral nerve. Stainless steel electrodes represent a good cost-effective means of providing stimulation.

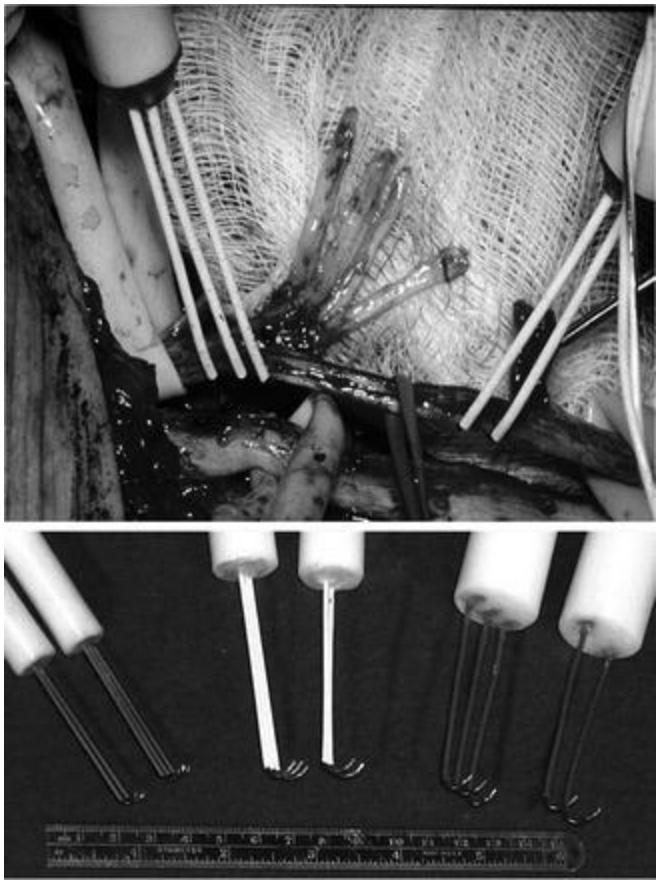


Fig. 38.2 Electrodes used for the stimulation and recording of peripheral nerve CNAPs. (*Top*) Electrodes applied directly to nerve. The stimulating electrode is a tripolar electrode and the recording electrode is bipolar (see text). Note that the electrodes can be used over just a few centimeters of nerve length. (*Bottom*) Selection of different size electrodes to be applied to various size peripheral nerves. The gap between contacts can be varied with the size of the nerve to be studied

Of great importance, however, is that silver electrodes not be used to provide stimulation. When silver electrodes are used, there is the possibility that silver salts could be deposited and these are very toxic. The stimulation of an intact nerve in situ presents an unusual set of circumstances [10]. The application of a potential difference with electrodes along the length of a nerve creates two current paths. First, there is a current in the gap between the two electrodes; second, there is a current flowing away from the electrodes, through the nerve, through the tissues of the body, and back to the other electrode. The latter current path is problematic as a current along the length of the nerve will be recorded together with the CNAP. This produces excessive stimulus artifact and, when the distance between stimulating and recording electrodes is short, may obscure the action potential. A solution to

this problem is to use a tripolar electrode with the outermost terminals connected together. In this arrangement, the application of a potential difference between the inner and outer electrodes still produces two currents; neither involves the whole nerve. The reduction in stimulus artifact achieved in this way permits even very small action potentials in injured or regenerating nerves to be seen. The use of a tripolar electrode also serves to limit the spread of stimulating current longitudinally along the length of nerve [10]. The latter is undesirable as misleading observations are made when sufficient current spreads several centimeters away from the stimulating point. While there may be no viable axons at the point of stimulation, the spread of current may excite distant viable axons, leading to the production of a CNAP. This phenomenon could lead to the false inference of excitable axons at the point of stimulation. A further exposition of this problem has been published previously [10].

For recording, a bipolar pair of electrodes is used. The configuration of the recording electrodes is also important to the successful evaluation of the electrical characteristics of peripheral nerve. Two stainless steel wire electrodes along the length of the nerve with a separation of at least 3–5 mm work well. If these electrodes are moved too close together, the amplitude of the recorded action potential will be reduced; thus, a larger distance of 5 mm is recommended, particularly for larger nerves. Further description of the features of recording electrodes has also been published previously [10].

Figure 38.3 demonstrates the appearance of the normal CNAP and to contrast this with the appearance of a very abnormal CNAP. The normal CNAP shows relatively large amplitude and a very short duration. The short duration indicates that the conduction velocities of the numerous fibers within the nerve are very similar. By contrast, the low amplitude seen in the abnormal CNAP indicates fewer fibers present and these show extensive temporal dispersion due to wide variations in conduction velocities [16]. These findings will be referred to in the practical illustrations.

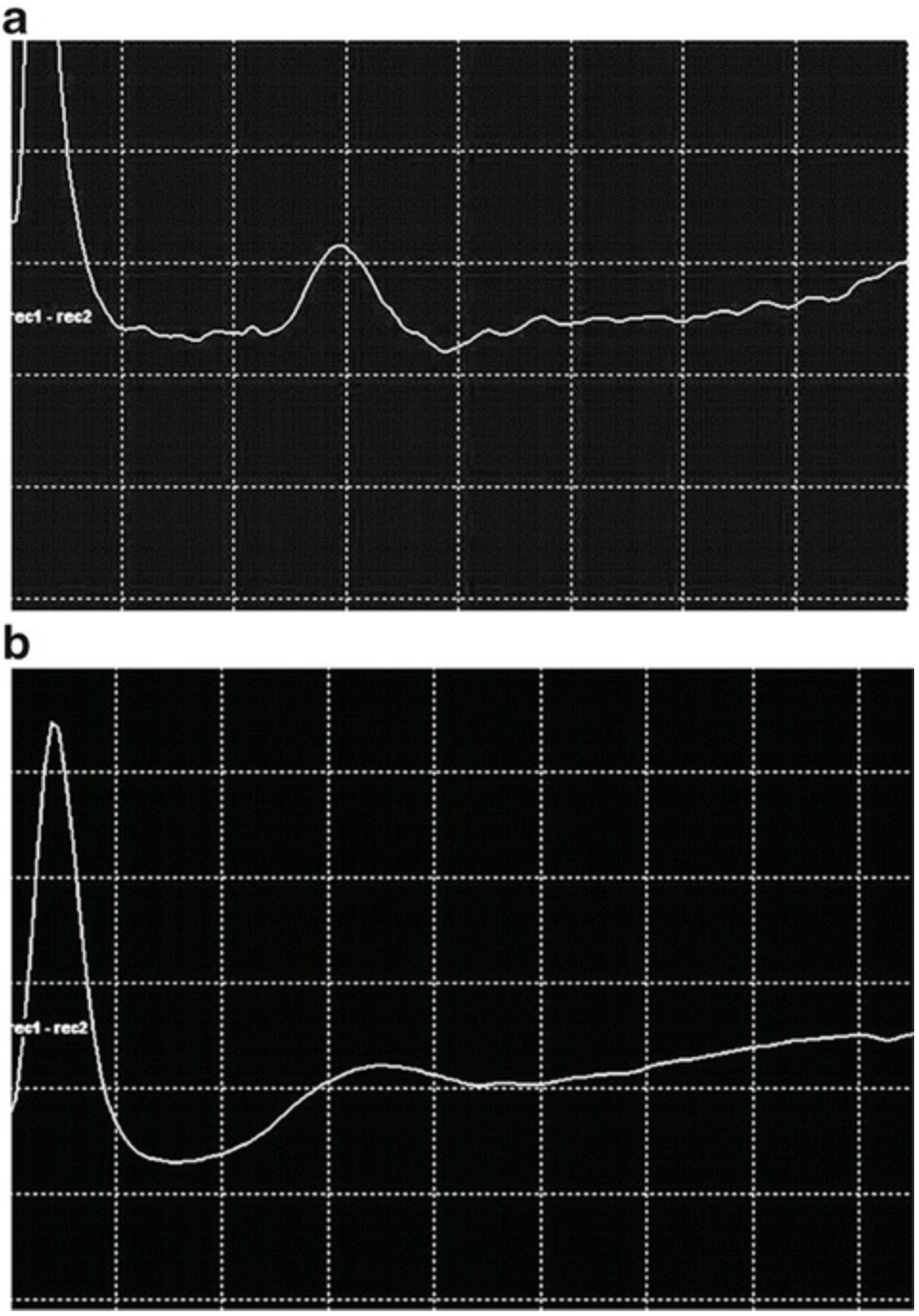


Fig. 38.3 Normal CNAP (**a**) recorded over a length of 15 cm through the brachial plexus. Note the shorter duration of the CNAP when compared to the abnormal response below. Calibration: 200 μV/div, 1 ms/div. Abnormal CNAP (**b**) recorded over a length of 7 cm through the brachial plexus. The lower amplitude is a reflection of fewer fibers and the broad base indicates dispersion of conduction velocities. Calibration 200 μV/div, 1 ms/div

It is very important to note that the patient's history should be placed into context with the operative peripheral nerve recordings. An example of this

relevance would be the case of a stretch injury to the brachial plexus. When the more proximal elements are stretched, there is the possibility of an avulsive injury to the nerve roots. In a severe avulsion, the nerve roots are torn loose from the spinal cord in such a way that the dorsal root ganglia are separated from the spinal cord leaving them connected to the sensory fibers of peripheral nerve. In this case, the sensory fibers of peripheral nerve will remain normal, but are disconnected from the spinal cord. The motor fibers of the same root are separated from their cell body in the anterior horn of the spinal cord and these fibers will undergo Wallerian degeneration. With operative stimulation and recording during brachial plexus exploration, a large CNAP such as that seen in Fig. 38.5 becomes the indicator of a poor prognosis. It shows normal sensory fiber activity in the clinical situation with no motor activity. These are the characteristics of an avulsive injury. In this case, a repair would not be effective.

Practical Illustrations of the Application of Operative Recordings

I would like to provide illustrative examples of two specific cases that will emphasize important points. These cases have been selected as good examples of general principles.

Case 1

The first case is that of a 34-year-old man who first noticed a swelling in the bicipital groove of his left arm about 8 months previously. There was no history of trauma. The lump grew rapidly and was associated with a progressive loss of function in the median and ulnar distributions of his left arm. EMG studies performed 3 weeks prior to surgery indicated extensive denervation potentials in both the median and ulnar nerve distributions. An MRI study was performed and is shown in Fig. 38.4a. The presence of a nerve tumor is clearly demonstrated.

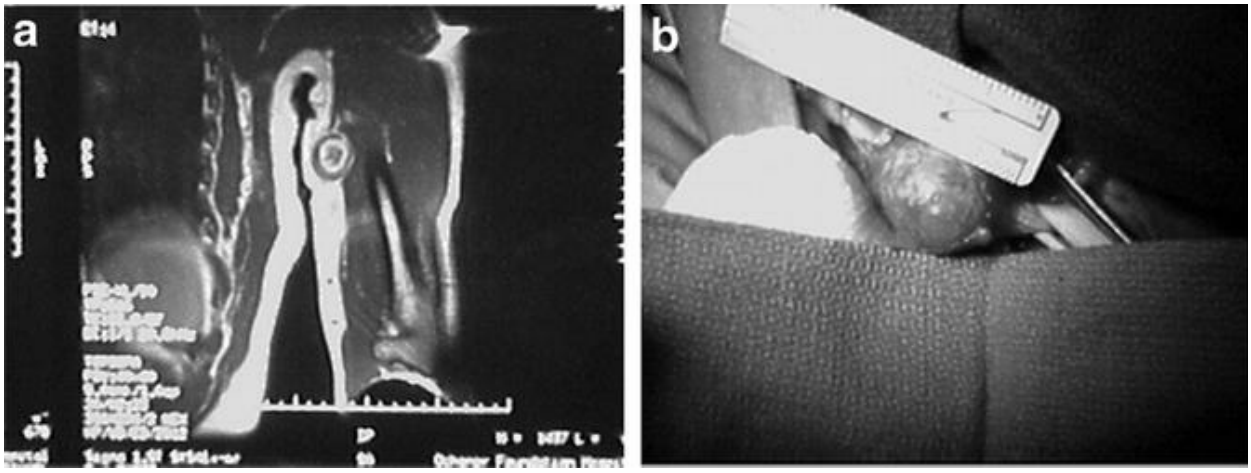


Fig. 38.4 MRI of the left upper arm of a patient with a large, rapidly growing tumor in the left bicipital groove (**a**). Exposed tumor attached to the median and ulnar nerves in the bicipital groove (**b**)

The patient was taken to surgery and the median and ulnar nerves were exposed over a length of approximately 12 cm in the bicipital groove revealing a large tumor, seen in Fig. 38.4b. In the absence of operative neurophysiology, the appearance of this large tumor together with the preoperative EMG studies would have clearly indicated the necessity to resect this lesion and repair the median and ulnar nerves by suturing the proximal and distal ends of the severed nerves. This kind of repair would have meant that all of the fibers of both the median and ulnar nerves would have to regenerate through the distal reaches of the arm. This process would have required years to accomplish. The function restored by such a repair would be considerably less than that achieved if a more conservative repair could be applied. Therefore, a precise diagnosis at the time of surgery could greatly affect outcome.

Stimulating and recording electrodes were both applied proximal to the tumor. The stimulating electrodes were placed proximal to the recording electrodes. This is routinely done to insure that stimulation activates all of the fibers within the nerve. If stimulation is performed distally and recordings made proximally, those fibers that are added to the nerve proximal to the stimulating electrodes would not be stimulated. This means that some of the fibers beneath the recording electrodes would not be active and would not contribute to the size of the CNAP. In this case, with both stimulating and recording electrodes proximal to the tumor, a large normal CNAP was recorded. This is illustrated in Fig. 38.5.

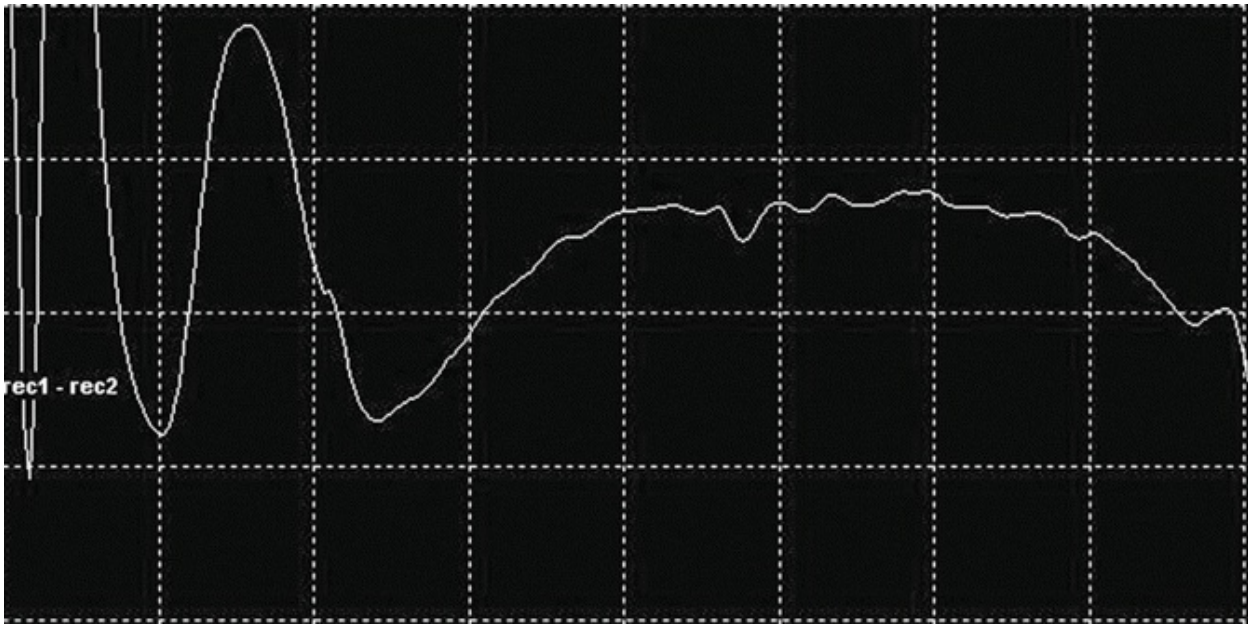


Fig. 38.5 Large, normal CNAP recorded with both stimulation and recording proximal to the tumor. The very short latency between stimulus artifact and CNAP reflects a very short distance between stimulating and recording electrodes

Subsequently, the recording electrodes were shifted distal to the tumor and stimulation and recording were once again performed. The recordings revealed an unusual “double” CNAP as seen in Fig . 38.6.

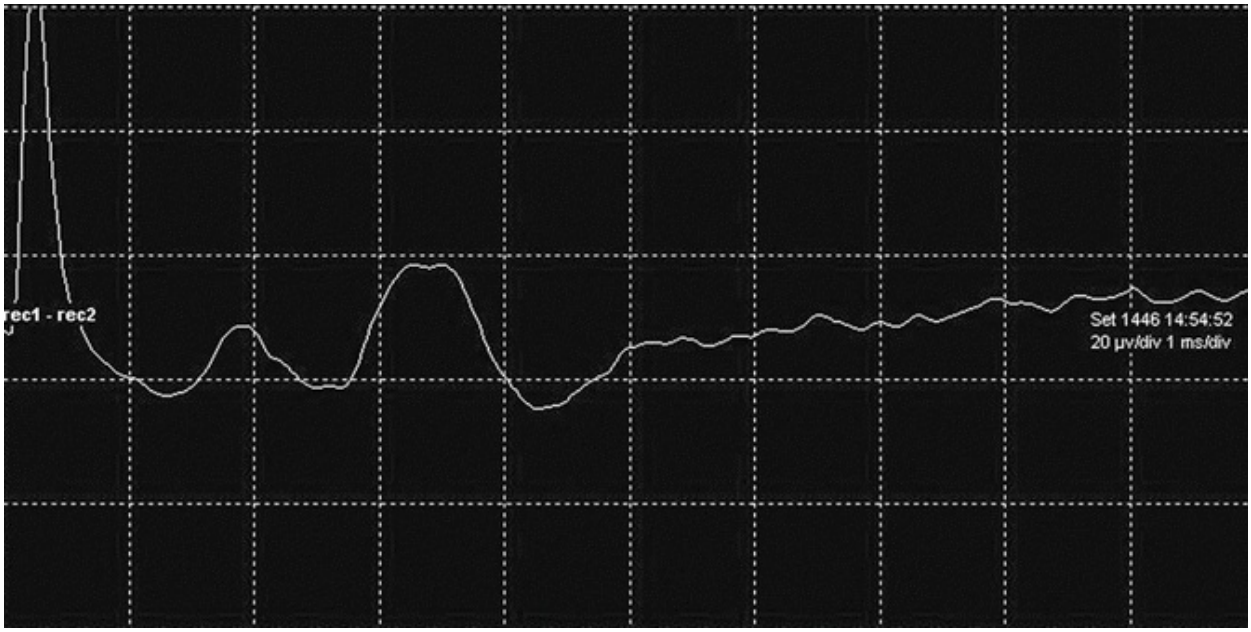


Fig. 38.6 Complex “double” CNAP recorded with stimulation proximal to the tumor and recording electrodes positioned distal to the tumor. This indicates two distinctly different populations of axons in

the median and ulnar nerves. The majority of fibers (the larger potential) show a markedly delayed conduction velocity due to demyelination from chronic compression

The first component of this “double” response was produced by a small population of relatively normal fibers. These fibers likely mediated those functions in median and ulnar nerve distributions that still remained. The second component of the “double” response represented function in fibers that were severely affected by the tumor. These fibers did not produce significant function since they appeared to be severely demyelinated. Voluntary function requires a train of impulses be conducted through the nerve. However, one of the characteristics of severe demyelination is a rate-dependent conduction block that suppresses volleys of action potentials [17]. The stimulating and recording process produces only a single conducted action potential and thus can demonstrate functional connection when voluntary effort cannot. Undoubtedly, many of the fibers of the median and ulnar nerves were interrupted by the tumor and the loss of these fibers was manifest in the preoperative EMG studies. These lesioned fibers made no contribution to the CNAP that was observed. This CNAP demonstrated the presence of large numbers of functional fibers through the region of the tumor. This clearly contraindicated complete resection of the median and ulnar nerves to remove this tumor. Therefore, a more conservative neurolysis was performed and a biopsy specimen was sent for frozen section. Surprisingly, the pathology report indicated that this tumor was not even a nerve tumor. Indeed, it proved to be a myosarcoma that had invaded the nerve from adjacent muscle. With this information in hand, a complete removal of the tumor was accomplished and the continuity of the median and ulnar nerves was preserved.

A postoperative follow-up of this patient at 8 weeks indicated a pronounced return of function in the median and ulnar nerve distributions. Over this short time period, the reason for the return of function was likely due to remyelination of fibers in the median and ulnar nerves that had been compressed by the tumor. It is clear in this case that the use of operative neurophysiology produced a far better outcome than a visual inspection that would have led to complete resection of the tumor.

Case 2

The second case is that of a 5-year-old boy with a flail right arm from birth.

Radiographic studies gave no indication of meningoceles that might suggest an avulsive injury with the roots being ripped out from the spinal cord. Repeated EMG studies showed profound denervation of all muscles in the right arm, indicating an extensive loss of motor axons. It was decided to perform an exploratory procedure on his right brachial plexus in an effort to confirm that this represented the level of his lesion and also to perform a repair if that was indeed the case.

At surgery, the brachial plexus was extensively exposed and stimulation and recording electrodes applied at the trunk and cord levels. Recordings made from upper middle and lower trunk failed to reveal any CNAP. However, when the upper trunk was stimulated, it was noted that the patient exhibited evoked movement in hand intrinsic muscles. Recordings from the medial and lateral cords also failed to reveal any CNAP at all. While the hand movements suggested the existence of some axonal regrowth, the absence of CNAP s gave no indication of regeneration.

The explanation for these findings lies in the patient's age and the mechanism of regeneration . In the 5 years following his brachial plexus injury, this patient did have the regrowth of a very small number of axons, perhaps eight or ten, that regrew spontaneously. However, these axons did not mature to a size that would permit them to mediate voluntary movement. Therefore, the patient had no voluntary ability to produce visible contractions. When the stimulating electrodes were applied, the stimulus pulses synchronized action potentials in the 8–10 fine fibers that had regrown the length of the arm [18]. When all of these tiny motor units contracted simultaneously, they could then produce visible contraction, creating the impression of significant innervation. Given that these fibers had a window of 5 years to mature and had not done so, it was unlikely that they would ever develop the capacity to mediate voluntary movement. This observation illustrates the point that motor activity is a poor measure of the integrity of peripheral nerve. The presence of motor activity can be misleading.

Visible scarring could be seen in the upper middle and lower trunk levels, though, more proximally, the roots had a more normal appearance. Since there was not adequate length of these elements at the root level to perform both stimulation and recording, it was decided to stimulate the proximal roots and record the somatosensory-evoked potential from the contralateral sensory cortex. When this was done, the C5–C8, and T1 roots all produced large somatosensory-evoked potentials. This indicated functional nerve at the

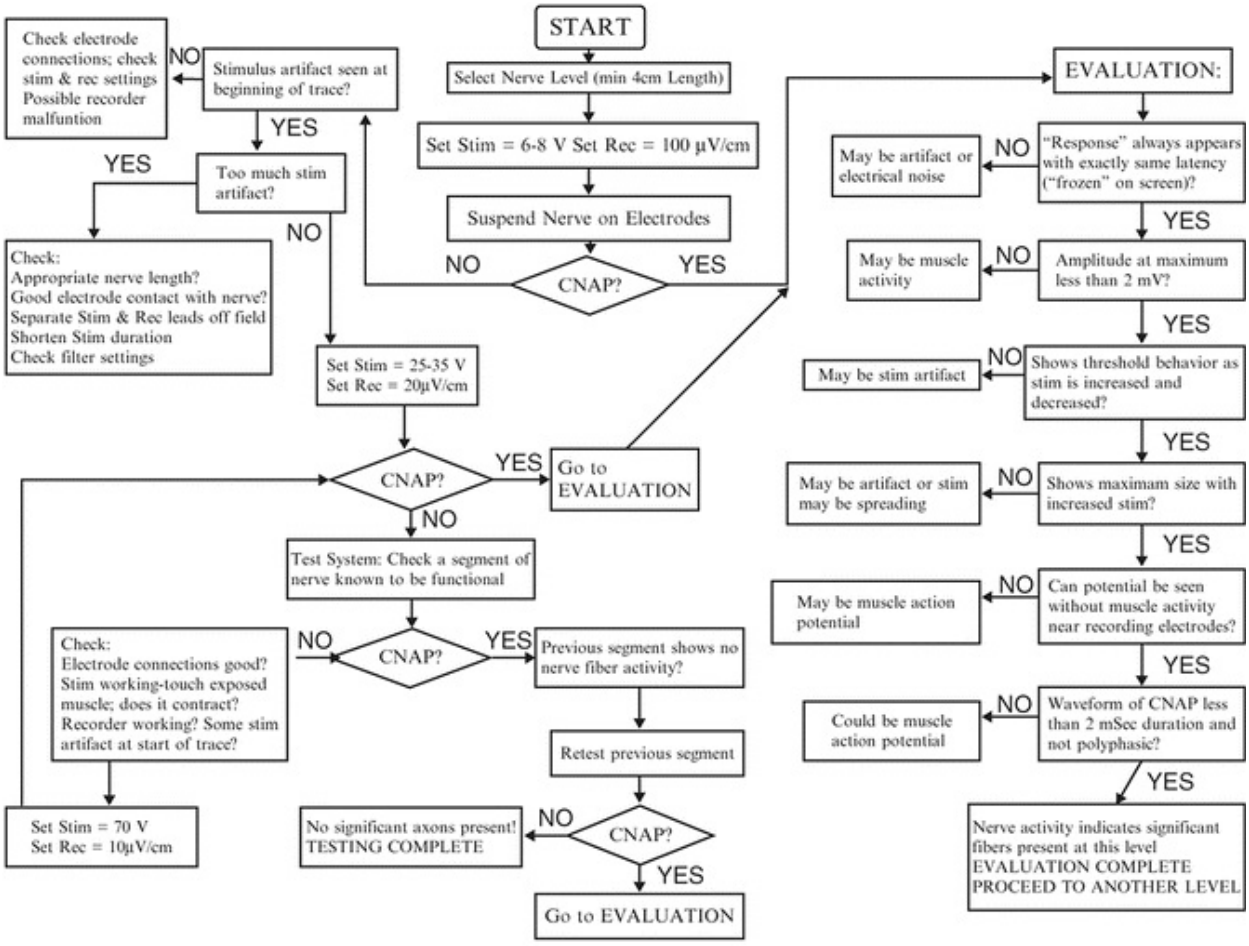
proximal root level. This illustrates that it is not always necessary for both stimulation and recording to be performed within the operative site. As necessity dictates, the stimulation or the recording site can be shifted outside of the surgical site. With the knowledge that the proximal roots were all viable, it was decided to place sural nerve grafts in the upper, middle, and lower trunks.

Two years postoperatively, this patient had regained some voluntary control of deltoid, biceps, and triceps muscle. While this does not restore his right arm to complete functional use, it does present much greater rehabilitative potential. He now has the opportunity to oppose his normal left arm with a prosthetic device on the right.

In summary, this case demonstrates that the regenerative potential of a juvenile is far greater than that of an adult. At 5 years post-injury, an adult would not possess as much regenerative potential. This case also demonstrates that improvisation in the method of stimulating and recording from peripheral nerve can be very effective in providing useful information. This case provided good localization of the level of viable nerve tissue as a grafting point and served to produce an outcome that was far superior to methods that would rely on intuitive decisions by the surgeon.

Summary

Operative recordings of peripheral nerve activity provide definitive diagnostic information that significantly improves clinical outcomes of nerve repair. Many of the factors considered in the cases presented here could also be applied to “monitoring” activities as well. Thoughtful application of these principles can easily lead to the development of new and better means of evaluating and monitoring peripheral nerve activity. In an effort to encourage the use of these techniques, I have included a flow chart that is intended to facilitate this procedure (Fig. 38.7). This flow chart includes technical issues as well as the neurophysiology of peripheral nerve and serves as a practical aid to operative recordings. With the acquisition of reliable data from peripheral nerve recordings, intuitive decision-making on the part of the surgeon becomes unnecessary.



Flow Chart For Operative Peripheral Nerve Stimulation And Recording

Fig. 38.7 Flow chart used intraoperatively to facilitate diagnostic testing of peripheral nerve injuries

Questions

1. The presence of a clear CNAP in a section of peripheral nerve indicates;

    a. that the patient's symptoms are due to a neurapraxic injury

    b. that electrical stimulation is more effective than voluntary effort

    c. the presence of at least 4000 functional, large axons in that section

    d. at least unmyelinated axons are working

e. there should also be evoked movement present

2. The effects of anesthesia on the CNAP:

   a. are most prominent for nitrous oxide

   b. are most prominent for halogenated agents

   c. can completely block the CNAP

   d. selectively decrease conduction velocity

   e. are minimal when stimulating and recording from nerve

3. A very long duration CNAP with low amplitude indicates

   a. a wide distribution of fiber types within that nerve

   b. that only sensory fibers are being recorded

   c. that only motor fibers are being recorded

   d. that resection and repair is necessary

   e. stimulus intensity is too high

Answers

1. c

2. e

3. a

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Footnotes

1 Asterisk indicates key reference.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_39

39. Surgery of the Aortic Arch

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Keywords Surgery – Aortic arch – Hypothermia – Cerebral protection – Circulatory arrest – Temperature monitoring – Neuroelectrophysiological monitoring – Acid base management – Cerebral oximetry – Transcranial Doppler – Aortic dissection

Key Learning Points

- Hypothermia is the main therapeutic preventative approach for minimizing neurological deficits during circulatory arrest.
- Hypothermia protects the brain by suppressing electrical activity and by

depressing presynaptic release of excitatory amino acid transmitters

- Extended periods of circulatory arrest have been associated with apoptotic histologic changes in the central nervous system neurons and may be responsible for one of the pathological processes involved with delayed neurological deficits following hypothermic circulatory arrest.
- Circulatory arrest durations >35–45 min with insufficient patient cooling leads to postoperative neurological deficits.
- Surrogate temperature data tend to lag behind true brain temperatures during rapid temperature changes; because of variability across patients and surrogate temperature sites, the best surrogate temperature site for accurately predicting brain temperature is not currently available.

Case Presentation

A 62-year-old chairman of a well-known investment firm is seen in the emergency room of a tertiary hospital. He complains of severe chest pain , which is “tearing” in nature and localizes to the anterior chest. His past medical history is remarkable for hypertension, hypercholesterolemia, coronary artery disease, and an aortic arch aneurysm. His aneurysm is 5.5 cm in diameter and he was scheduled to undergo an elective surgical repair 7 days from his present emergency room visit. He had a left carotid endarterectomy in the past, which required placement of a shunt following carotid cross clamp application. On examination, his blood pressure is equal, bilaterally, in both the arms. Auscultation reveals a regular rhythm without a murmur. His EKG is unchanged from his most recent EKG performed for his scheduled, elective aneurysm repair, 2 weeks ago. His medications include atorvastatin, metoprolol, aspirin (81 mg), and lisonopril. The chest X-ray shows a widened mediastinum. After his blood pressure and chest pain were stabilized with a short-acting beta-blocker, narcotics, and sedatives, a CT angiogram was obtained. This revealed an aortic dissection with a tear located in the aortic arch. The dissection extends proximally to the sinus of Valsalva and distally down the descending aorta. The patient and his family are concerned that his neurological function after surgery will impair his ability to function at a high level at his job.

Introduction

A dissection of the aorta, which involves the ascending aorta, is referred to as a Stanford Type A dissection [1]. Type A aortic dissections are true surgical emergencies with the mortality rate increasing 1–2 % per hour after the onset of symptoms [2]. The mortality rate for medical management is 56 %, whereas the mortality rate for a surgical repair ranges from 6.3 to 30 % [2].

Because the patient has a dissection starting from the sinus of Valsalva and extending beyond the arch to the descending aorta, the surgeon elects to replace the entire aorta from the sinus of Valsalva to the proximal descending aorta. The surgical approach will require cardiopulmonary bypass with hypothermic circulatory arrest and selective antegrade cerebral perfusion [2, 3]. This chapter reviews pertinent issues regarding the intraoperative management of this patient.

Circulatory arrest with durations greater than 35–45 min and insufficient patient cooling lead to postoperative neurological deficits. Neurological deficits can be classified as transient neurological deficits (TNDs) , fixed deficits, and delayed deficits. TNDs include a disease spectrum of coma, delirium, confusion, psychosis requiring pharmacologic treatment, seizures, and transient Parkinsonian symptoms [4–13]. These patients have normal CT and/or MRI scans and they typically recover during the postoperative period prior to discharge. Ergin et al., however, have shown that these patients, when properly tested, are found to have cognitive deficits weeks to months after their hospitalization [12, 13]. These results suggest that TNDs are markers for subtle brain damage that occur during circulatory arrest. TNDs increase in incidence as a function of increasing age, duration of circulatory arrest, and temperature achieved prior to circulatory arrest. TND has been reported to have an incidence as high as 63 % with deep hyperthermic circulatory arrest (DHCA) at core temperature of 10–15 °C for 40–80 min [4–13]. More recent reports cite an incidence of 4 %, using newer selective antegrade cerebral perfusion techniques [5, 14, 15].

In contrast, patients with fixed deficits have abnormal CT and/or MRI scans [1–7]. This deficit is usually considered to result from embolic phenomenon. Increased age, atherosclerotic load of the aorta and arch vessels, thrombi within the aorta, unstable vital signs, and neurological deficit prior to surgical repair have all been described as risk factors for fixed postoperative neurological deficits [2, 3, 7, 14–18]. Recent permanent stroke

rates have been reported at 6.5 % for DHCA, 9.8 % for DHCA plus direct cannulation of the carotid arteries, and 1.1 % for DHCA with right subclavian artery antegrade cerebral perfusion [14, 15].

Lastly, a delayed deficit that appears hours to days following the surgical procedure is caused by either embolic phenomenon or apoptosis [19, 20]. The apoptotic process is considered to occur after episodes of milder ischemic stress (i.e., shorter period of circulatory arrest or cooler body temperature) compared to ischemic episodes giving rise to deficits occurring intraoperatively [19, 21, 22].

Hypothermia and Cerebral Protection During Circulatory Arrest

As mentioned previously, surgical correction of an aortic dissection of the aortic arch will require a period of circulatory arrest. The main therapeutic preventative approach for minimizing neurological deficits during circulatory arrest is hypothermia [23–28]. The normothermic brain uses up to 20 % of total body oxygen consumption . Approximately, 60 % is used to support electrical and synaptic activities of the central nervous system, while the remaining 40 % is used to maintain normal transmembrane electrochemical gradients [29–38].

Cerebral blood flow (CBF) in the adult averages 50–60 mL/min/100 g of brain tissue [29, 30, 32, 37]. Because there is little capacity for storage in the brain of glucose and oxygen beyond what is immediately used for ongoing metabolism, the metabolic rate of the brain can be calculated from glucose and/or oxygen uptake [34]. A consequence of the lack of energy substrate storage within the brain results in limited tolerance for the normothermic brain to short periods of absent blood flow (i.e., 3–5 min at 37 °C) before experiencing ischemia.

In the normal individual, CBF and metabolism are coupled so that an increase in metabolic demand is met with an increase in CBF [29, 30, 37–39]. CBF also demonstrates pressure autoregulation, where for a given level of metabolic demand, CBF remains constant over a range of perfusion pressures (50–150 Torr) [29, 30, 37–39]. This pressure autoregulation relationship shifts to a higher pressure baseline in hypertensive patients [30, 37].

As the brain is cooled, the metabolic rates for both glucose and oxygen decrease [30, 32, 35]. Experimental animal studies have shown that the

cerebral metabolic rate for oxygen decreases by 50 % at 27 °C and will decrease further as the brain temperature decreases to 18 °C [31, 32, 35, 37]. Human studies have demonstrated comparable results [34]. With cooling, because of metabolic coupling, CBF will decrease.

However, as brain temperatures fall below 20 °C, the ability to control CBF by cerebral metabolic rate is attenuated [37, 39]. While cooling . leads to an exponential decrease in metabolic rate, cerebral blood flow decreases in a linear fashion. At 18 °C, the ratio of blood flow to metabolic rate is 70:1, whereas at 37 °C it is 20:1. Thus, cooling of the brain leads to a state of luxury perfusion [29, 30, 37–39].

Hypothermia protects the brain by several mechanisms. First, electrical activity of the brain is typically suppressed at temperatures below 17 °C [40–42]. This consequently reduces metabolic demand by 50–60 % [29, 31, 34, 36]. Hypothermia also decreases the utilization of intracellular high energy phosphorus compounds (i.e., increases the phosphocreatine:ATP ratio) required for the maintenance of normothermic membrane structure [31]. The Q_{10} temperature coefficient describes the ratio of two cerebral metabolic oxygen consumption ($CMR0_2$) measurements at temperatures separated by 10° [34, 38]. The Q_{10} determined for swine, dogs, and humans was 2.46, 2.2, and 2.3, respectively [34, 37, 38]. Using this information and assuming a 5-min central nervous system tolerance during circulatory arrest at 37 °C, McCullough et al. [34] calculated a safe duration of hypothermic circulatory arrest as a function of several target temperatures (Table 39.1). These calculated safe arrest durations are, in general, consistent with the outcome studies. In studies with experimental animals, circulatory arrest durations greater than 30 min led to increased histological evidence of ischemic necrosis of brain tissue [33]. In addition, clinical, neurological, and behavioral scores deteriorate in animals experiencing prolonged circulatory arrest duration [31–33, 43]. Reich et al. demonstrated an increased incidence of postoperative cognitive dysfunction in patients undergoing circulatory arrest at 13 °C for durations greater than 29 min [12]. Therapeutic effects of hypothermia have, likewise, been demonstrated in patients experiencing cardiopulmonary arrest at 37 °C who were cooled immediately following restoration of spontaneous circulation [26–28].

Table 39.1 Calculated safe duration during hypothermia circulatory arrest

Temperature (°C)	Cerebral metabolic rate (% of baseline)	Safe duration of HCA (min)

37	100	5
30	56 (53–60)	9 (8–10)
25	37 (33–42)	14 (12–15)
20	24 (21–29)	21 (17–24)
15	16 (13–20)	32 (25–38)
10	11 (8–14)	45 (36–62)

Calculations based on assumption that there is a 5-min tolerance for circulatory arrest at 37 °C. Values in parentheses are 95 % confidence intervals. Printed with permission from McCullough et al. [34]
HCA hypothermic circulatory arrest

A second mechanism for the protective effect of hypothermia is through depression of presynaptic release of excitatory amino acid transmitters (e.g., glutamate and aspartate). This leads to a decrease in excitotoxicity and a subsequent decrease in the extent of neuronal damage after circulatory arrest [32, 44, 45].

Finally, in a study where swine were cooled to 19 °C and placed in circulatory arrest for 90 min and histologically examined at various times from 1 h to 1 week after circulatory arrest, neuronal damage was most significant in the animals that were histologically examined 8–72 h after circulatory arrest. They noted that caspace-3 and -8, indicators of apoptosis, were elevated. Caspace-3 remained elevated for 72 h [19]. Increased activity was also seen in cytosolic cytochrome c . and fos-protein. Apoptotic histological changes were observed in central nervous system neurons. The authors concluded that apoptosis is one of the pathological processes involved with delayed neurological deficits following hypothermic circulatory arrest.

With few exceptions, pharmacological protective strategies have not been found to protect the human central nervous system from ischemic damage during cardiopulmonary procedures [46–61] (Table 39.2). Hence, we depend on deep hypothermia as one of our primary techniques for brain protection.

Table 39.2 Randomized, placebo-controlled trials of pharmacologic neuroprotection for adults undergoing cardiac surgery

Drug	Proposed primary mechanism	References	*n*	Type of surgery	Main findings
Thiopental	↓ $CMRO_2$	Nussmeier	182	Valvular	Thiopental ↓ cognitive complications

		et al. [46]			10 days after surgery
		Zaidan et al. [47]	300		No difference in neurologic outcomes thiopental versus placebo
Propofol	↓ $CMRO_2$	Roach et al. [48]	300	CABG	No difference in cognitive complications 5–7 days or 50–70 days after surgery propofol vs. controls
Nimodipine	Ca^{++}channel blocker	Legault et al. [49]	225	Valvular	Study terminated early due to higher mortality in treated vs control group; no evidence of benefit with nimodipine on cognitive outcomes
Prostacyclin	↓ platelet aggregation, ↓ inflammation	Fish et al. [50]	150	Valvular	No difference in cognitive outcomes 2 weeks after surgery between treated and control patients
Aprotinin	Mechanism(s) unknown; may be due to ↓↓ pericardial aspirate	Levy et al. [54]	287	CABG	No strokes in “high” and “low” dose aprotinin groups vs controls (n = 5) and “pump” prime only (n = 1) groups (P = 0.01) inflammation
		Harmon et al. [55]	36	CABG	Cognitive deficits 2 weeks after surgery lower in aprotinin vs placebo group (23 vs. 55 %, P<0.05)
Lidocaine	Na + channel blockade; membrane stabilization/↓ EAA release	Mitchell et al. [56]	55	Valvular	Neurocognitive outcome better 10 days and 10 weeks after surgery in lidocaine vs placebo group but not at 6 months
		Wang et al. [57]	42	CABG	Improved neurocognitive function 9 days after surgery with lidocaine vs. placebo
Clomethiazole	GABA receptor agonist	Kong et al. [58]	219	CABG	No difference in neurocognitive function 4–7 weeks after surgery in clomethiazone vs placebo groups
Pexelizumab	↓ C5a and C5b-9	Mathew et al. [59]	800	CABG	Pexelizumab had no effect on global cognition but did lower decline in the visuo-spatial domain compared with placebo

Modified with permission, Hogue et al. [128]
CMRO $_2$ cerebral metabolic rate for oxygen, *CABG* coronary artery bypass grafts, *EAA* excitatory amino acid, *NMDA* *N*-methyl-D-aspartate, *GABA* gamma aminobutyric acid

The protection offered by deep hypothermia, however, is limited to relatively short periods of time (see Table 39.1) [34]. Hence, selective

antegrade cerebral perfusion is often administered as an adjunct protective scheme during the surgical procedure [62–75].

During the rewarming phase following circulatory arrest, $CMR0_2$ increases along with an increase in cerebral blood flow. Typically, in the absence of selective antegrade cerebral perfusion, there is an initial cerebral blood flow hyperemia, which is caused by an oxygen debt accumulated during the arrest phase [29, 30, 35, 37, 38]. This reflects residual metabolic activity present even at profound hypothermic brain temperatures. After a short hyperemic phase, cerebral blood flow decreases inappropriately for the increased metabolic demand present during and after rewarming. Thus, cerebral blood flow again becomes uncoupled from metabolic demand [29, 30, 37–39]. There is evidence of increased production (i.e., up regulation) of endothelial adhesion molecules, which tend to trap “clusters” of leukocytes in the small cerebral blood vessels. This leads to leukocyte activation with subsequent blocking of cerebral blood vessels and an increase in the postoperative inflammatory process [29, 30, 35, 37]. Webster et al. [76] recently demonstrated that, during global cerebral ischemia, hypothermia decreased the activation of DNA-bound NF-Kappa B. NF-Kappa B . is a major transcription factor regulating genes associated with inflammatory mediators. Inhibition of this transcription factor attenuates inflammation.

Another occasional consequence of circulatory arrest is increased intracranial pressure caused by cerebral edema [77]. This develops after cardiopulmonary bypass is reinstituted. It can be detected by observing bulging fontanelles in neonates or infants. If a transcranial Doppler is available, a decrease or reversal of diastolic cerebral blood flow velocity is detected [78]. The increased intracranial pressure can be reversed by 10–15 min of cold perfusion after cardiopulmonary bypass is resumed following a period of circulatory arrest [77].

Temperature Monitoring

Because of the importance of profound hypothermia for protecting the central nervous system, many surgeons rely on body temperature to decide when an appropriate decreased target brain temperature has been reached prior to beginning circulatory arrest. Direct brain temperature is usually not available during routine cardiac procedures. Clinicians must rely on extracerebral temperature monitoring for determining a safe temperature for initiating

circulatory arrest. Stone et al. [79] were the first to compare the accuracy of several surrogate temperature monitoring sites to temperatures acquired directly from the brain. Their patients were undergoing open craniotomies for clipping of giant aneurysms, which required periods of circulatory arrest. Temperature probes were placed 4 cm within the depth of the cerebral cortex and were compared to temperature data recorded from the bladder, rectum, pulmonary artery, tympanic membrane, nasopharynx, esophagus, and skin of the axilla and lower limbs. Comparisons were made during cooling to 16 °C and during rewarming to 37 °C after a period of circulatory arrest. Prior to cooling, with the exception of the sole of the foot, temperatures from all recording sites were equal. During rapid cooling in preparation for circulatory arrest, none of the surrogate monitoring sites tracked the brain's temperature well (Fig. 39.1). All temperatures lagged behind the brain temperature. The nasopharyngeal and esophageal temperature probes showed the smallest difference in comparison to direct brain temperatures. Just prior to initiating circulatory arrest, the difference between the temperatures at the surrogate sites and the actual brain temperature was ± 2.8 °C. During rewarming, the same phenomenon was noted. Here, nasopharyngeal and esophageal temperature probes recorded temperatures that were closest to the brain temperature. Of concern, when the nasopharyngeal temperature reached 37 °C, the brain was typically 1–2 °C higher. As hyperthermia is known to increase the degree of ischemia-induced brain damage, these results were concerning [80–85]. The variability across patients, as well as across temperature-monitoring sites, precluded choosing one site as the best surrogate temperature for predicting brain temperatures during rapid temperature changes. Stone et al. [79] also studied patients undergoing excision of brain tumors during normothermic conditions. Temperatures recorded at cortical depths of 1 cm were typically cooler by 0.5–3 °C compared to temperature probes placed at cortical depths of 4 cm. In addition, the superficial cortical temperature recordings showed greater variability, particularly when cold irrigation fluids were used. They reasoned that the variability of the superficial temperature recordings was caused by the effects of ambient temperature and cool irrigation fluids.

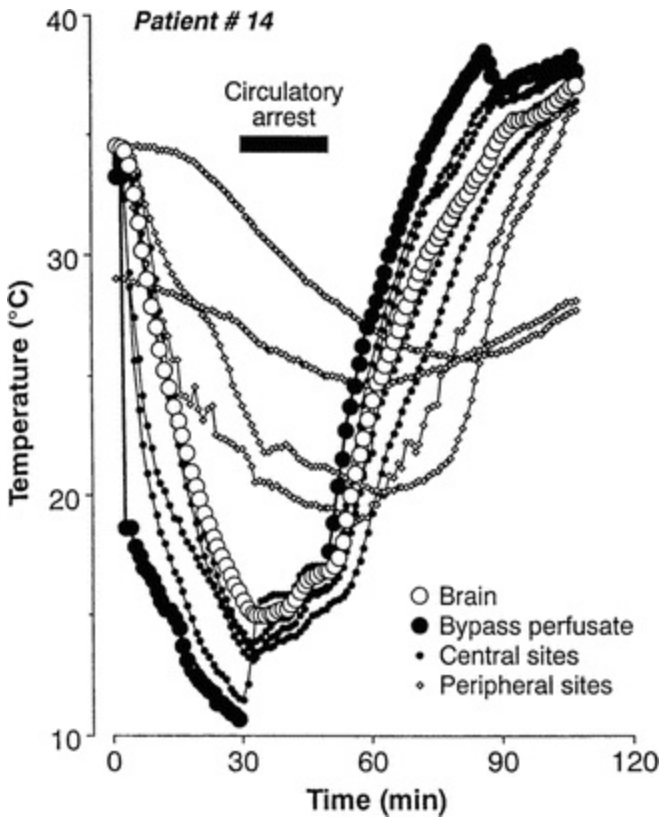

Fig. 39.1 Plots of temperature changes during rapid cooling and rewarming of patients on cardiopulmonary bypass (CPB) . Temperatures acquired from the brain, CPB arterial inflow (bypass perfusate), central sites (i.e., pulmonary artery, nasopharynx, esophagus, tympanic membrane), and peripheral sites (bladder, rectum, axilla, sole of foot). With the exception of the sole of the foot, all temperatures were equal prior to cooling. Sites which tracked the brain temperatures the closest were the nasopharynx and esophagus. Reprinted with permission from Stone et al. [79]

Crowder et al. [86] subsequently studied the correlation of brain temperature to tympanic membrane, esophagus, bladder, pulmonary artery, and the jugular bulb temperature. The jugular bulb was considered to be an excellent monitoring site as it drained 60–66 % of venous blood flow from the homologous cortex, with 1 % contamination from extracranial sources [86–88]. Brain temperatures were monitored with temperature probes placed in the subdural space distant to the craniotomy site (i.e., under the intact cranium , so as to minimize the effects of ambient room temperature on the subdural temperature recordings). Moderate hypothermia was induced with the lowest reported brain surface temperature reaching 32.3 °C. Their results confirmed Stone's study and showed that large fluctuations of the brain surface temperature (i.e., subdural temperature) caused by irrigation fluid and ambient temperature made the comparison of jugular bulb and true

parenchymal brain temperature unreliable. Additionally, jugular bulb temperatures tended to be higher than all other monitoring sites during rewarming. Nevertheless, studies following Crowder et al.'s report have assumed that the jugular bulb can be used to track brain temperature during rapid temperature changes. Grocott et al. [87] showed that nasopharyngeal temperatures were lower than jugular bulb temperatures, but, in general, they tracked jugular bulb changes accurately during rapid cooling. At rewarming, however, jugular bulb temperatures were consistently 1–2 °C higher (implying that brain temperature may be higher than nasopharyngeal temperature). Similar results have been reported by other investigators [88].

In summary, all investigations have demonstrated that surrogate temperature data tend to lag behind true brain temperatures during rapid temperature changes. The greatest bias is found during rewarming and can lead to brain temperature reaching 1–3 °C higher than recorded from surrogate temperature sites [79]. A second conclusion derived from all investigations is that the variability across patients, as well as the data from surrogate temperature sites, precludes choosing one best site for accurately predicting brain temperatures during rapid cooling and rewarming.

Neuroelectrophysiological Monitoring

The appropriate temperature for initiating circulatory arrest should be cold enough for reducing adverse neurological outcomes through the mechanisms discussed in the section on "Temperature Monitoring." On the other hand, excessive cooling may lead to adverse outcomes secondary to intraneuronal ice crystal formation with subsequent injury (e.g., usually expected at temperatures below 10 °C) [40]. Secondly, longer bypass time is required in order to achieve these low temperatures as well as increased time for rewarming. Hence, several investigators have studied the use of temperature-related changes of the electroencephalogram (EEG) and somatosensory-evoked potentials (SSEPs) for determining the appropriate temperature for initiating circulatory arrest [40, 41].

Stecker et al. studied typical changes seen in the EEG during cooling prior to circulatory arrest (Fig. 39.2). Four EEG patterns were noted (please see Chap. 10 for review of EEG monitoring). The order of appearance with decreasing body temperatures is as follows: pre-cooling EEG (Fig. 39.2d), appearance of periodic complexes (Fig. 39.2e), burst suppression (Fig. 39.2f),

and electrocerebral silence (Fig. 39.2g). The distribution of patients demonstrating each of the characteristic EEG patterns as a function of temperature is shown in Fig. 39.2a–c. The importance of these results is that there is a range of temperatures rather than a single best temperature for which each of the sequential EEG patterns occurs during cooling on bypass. The mean nasopharyngeal temperature where periodic EEG complexes are noted was 29.6 ± 3 °C. Burst suppression occurred at 24.4 ± 4 °C and electrocerebral silence at 17.8 ± 4 °C. Therefore, typically the patients will be cooled at 2 °C below the temperature at which suppressed EEG is achieved prior to initiating circulatory arrest.

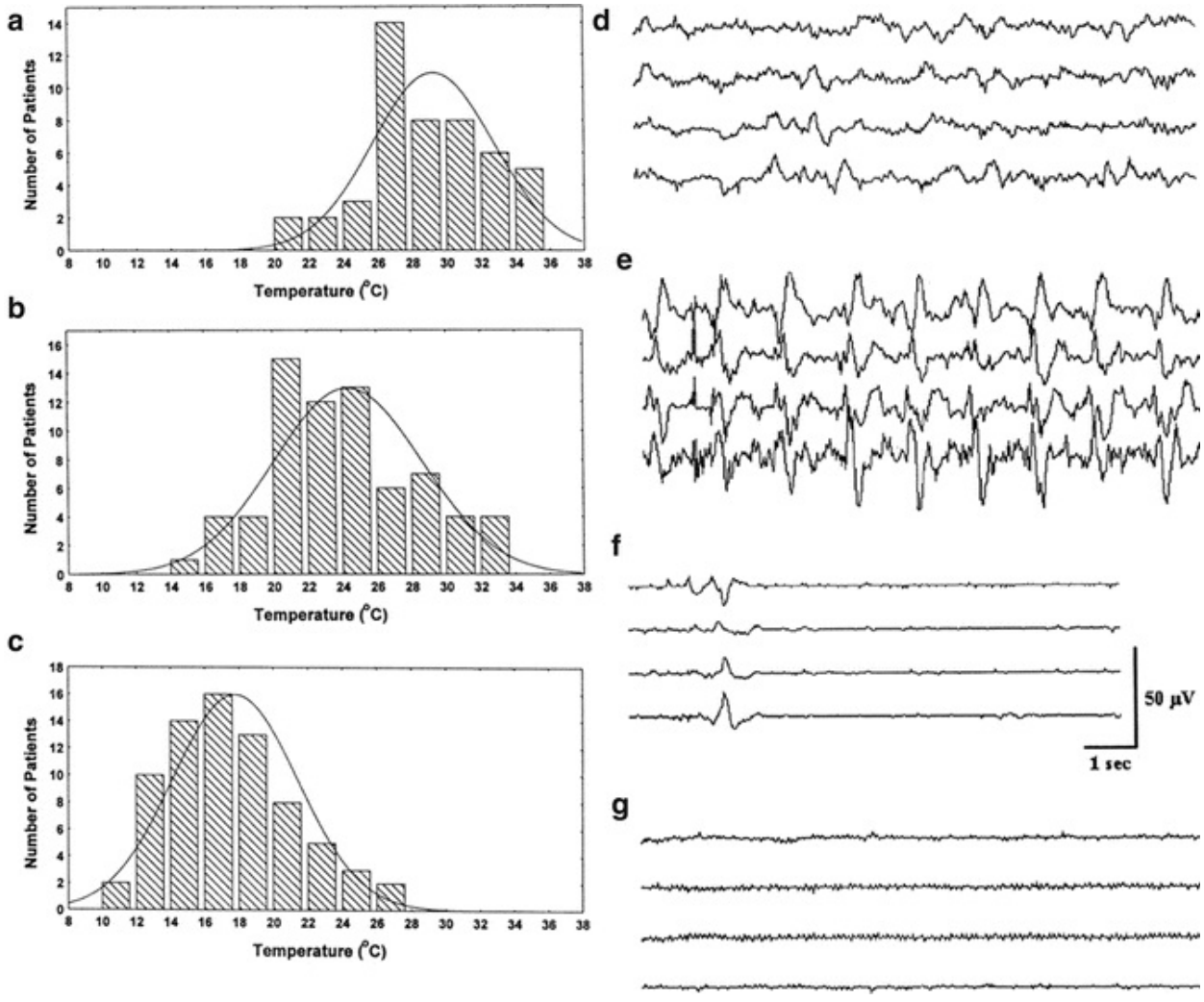

Fig. 39.2 The distribution of nasopharyngeal temperatures for patients developing (**a**) periodic EEG samples, (**b**) burst suppression, and (**c**) electrocerebral silence during rapid cooling prior to circulatory arrest. Examples of typical EEG patterns prior to cooling are shown in (**d**): Periodic complexes and burst suppression are shown in (**e**) and (**f**), respectively. (**g**) shows an example of EEG suppression.

Reprinted with permission from Stecker [93]

Please refer to Chap. 1 for an in-depth review of SSEP responses. Figure 39.3 demonstrates the relationship between the cortical (N20), spinal cord (N13), and Erb's point (i.e., brachial plexus) response latencies with temperature [88]. Note that latency increases at each recording site as body temperature decreases. This temperature effect on latency is due, in part, to the effect of temperature on conduction velocity along axons such that, at 2.7 and 7.2 °C, conduction blocks occur in unmyelinated and myelinated axons, respectively [88]. These effects are in turn due to the effects of hypothermia on the rate of change of sodium channels within axonal membranes [89, 90]. Stecker demonstrated an increase in SSEP refractory periods as body temperature decreases, suggesting that a slower stimulation frequency and increased stimulation intensity are required for acquiring SSEP responses at colder temperatures [40, 90, 91].

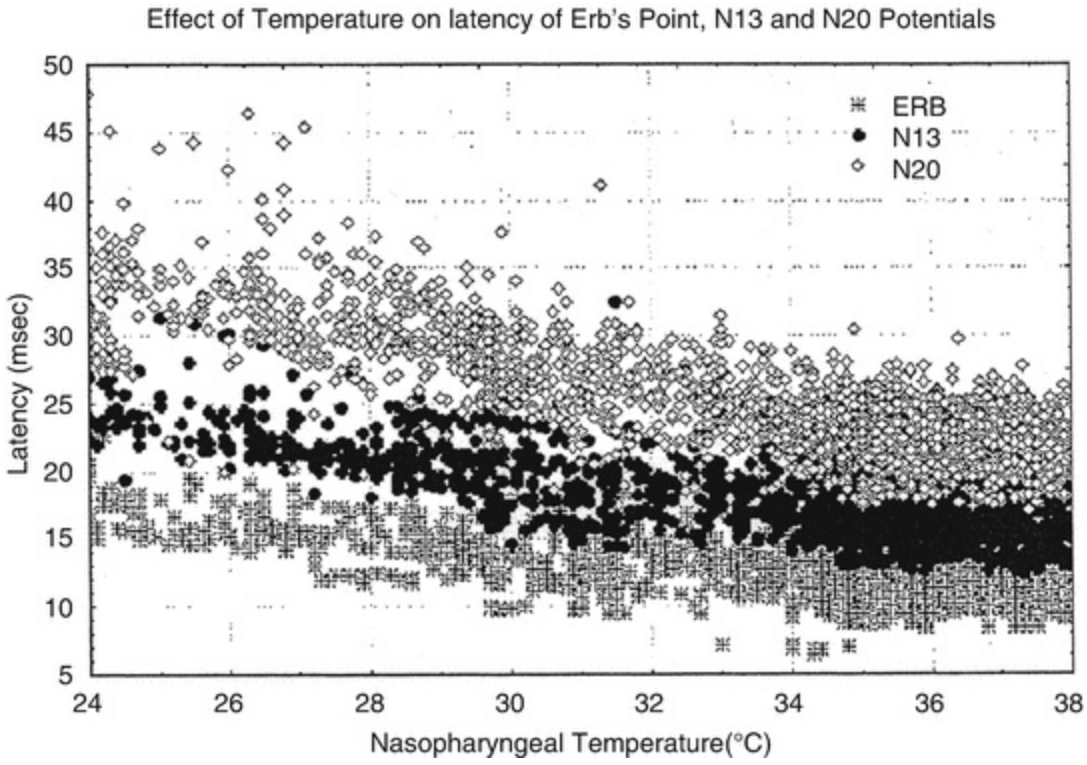

Fig. 39.3 This figure shows the differential sensitivity to cooling of the latencies for the N20 (sensory cortex response), N_{13} (spinal cord dorsal column responses near the brainstem), and ERB (brachial plexus activation). Note the limited change in latency of the brachial plexus responses with increasing prolongation of the spinal cord dorsal columns and sensory cortex latencies with colder temperatures. Reprinted with permission from Stecker [91]

Figure 39.4 demonstrates that at sufficiently low body temperatures, SSEPs are lost. This phenomenon offers a second physiological parameter, in addition to EEG changes, for determining an appropriate target temperature for suppressing electrical activity in the brain. Figure 39.5 demonstrates the orderly disappearance of the thalamocortical (C) , followed by the suppression of the cervicomedullary responses (D, E) as colder nasopharyngeal temperatures are reached. Figure 39.5a, b shows the distribution of nasopharyngeal temperatures for loss of the cortical and cervicomedullary responses. The N20-P22 complex acquired from thalamic and cortical generators disappears with body cooling to a nasopharyngeal temperature of 21.4 ± 4 °C and the cervical medullary responses (N13) are lost at 17.8 ± 4 °C. These SSEP values are consistent with the results acquired by Ghariani et al. [92]. As was the case for EEG changes during cooling, a single targeted temperature is inadequate for accurately predicting the individual brain and spinal cord electrical suppression during induced hypothermia. EEG, cortical, and subcortical SSEP responses (for determining subcortical depression) were monitored during the cooling phase of our case. The results were used for determining the appropriate nasopharyngeal temperature for initiating circulatory arrest.

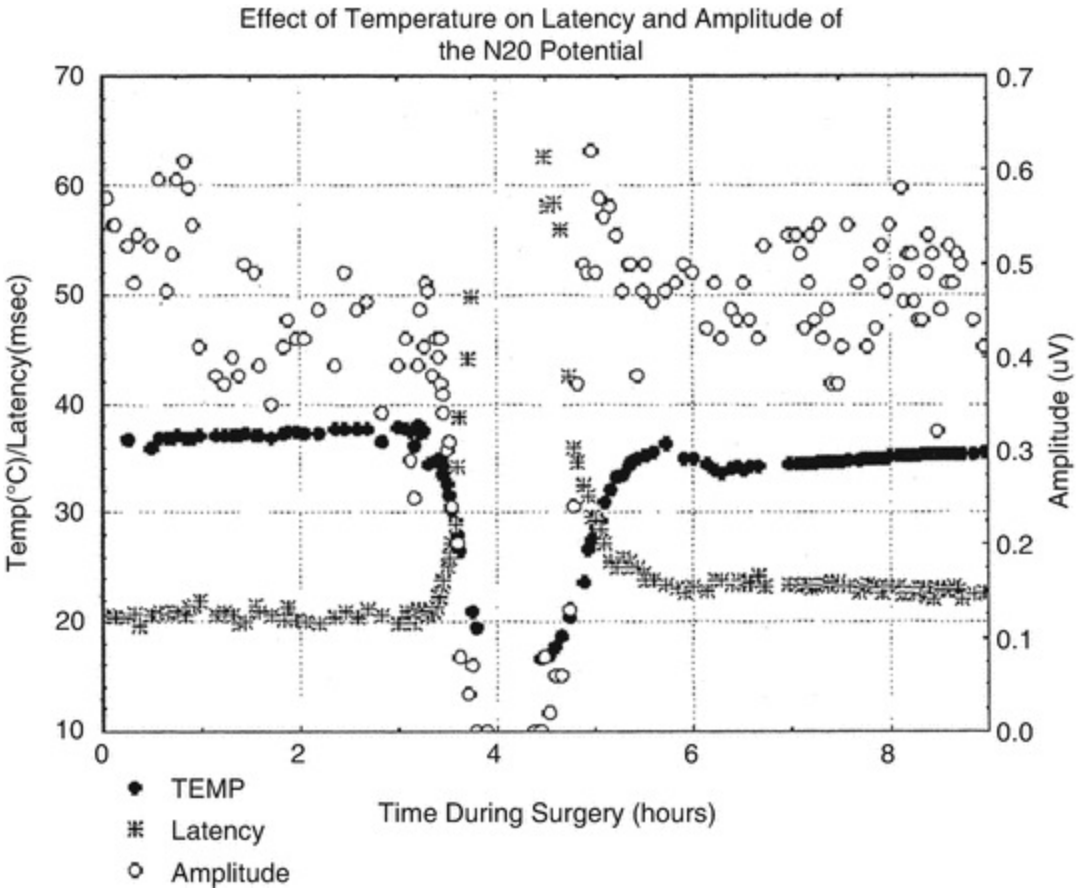

Fig. 39.4 The effect of cooling and rewarming of the somatosensory cortex N20 latency and amplitude. The variability of the N20 amplitude is greater than the latency. The N20 latency is probably a better N20 parameter for monitoring the effect of temperature on the cortex. Reprinted with permission from Stecker et al. [91]

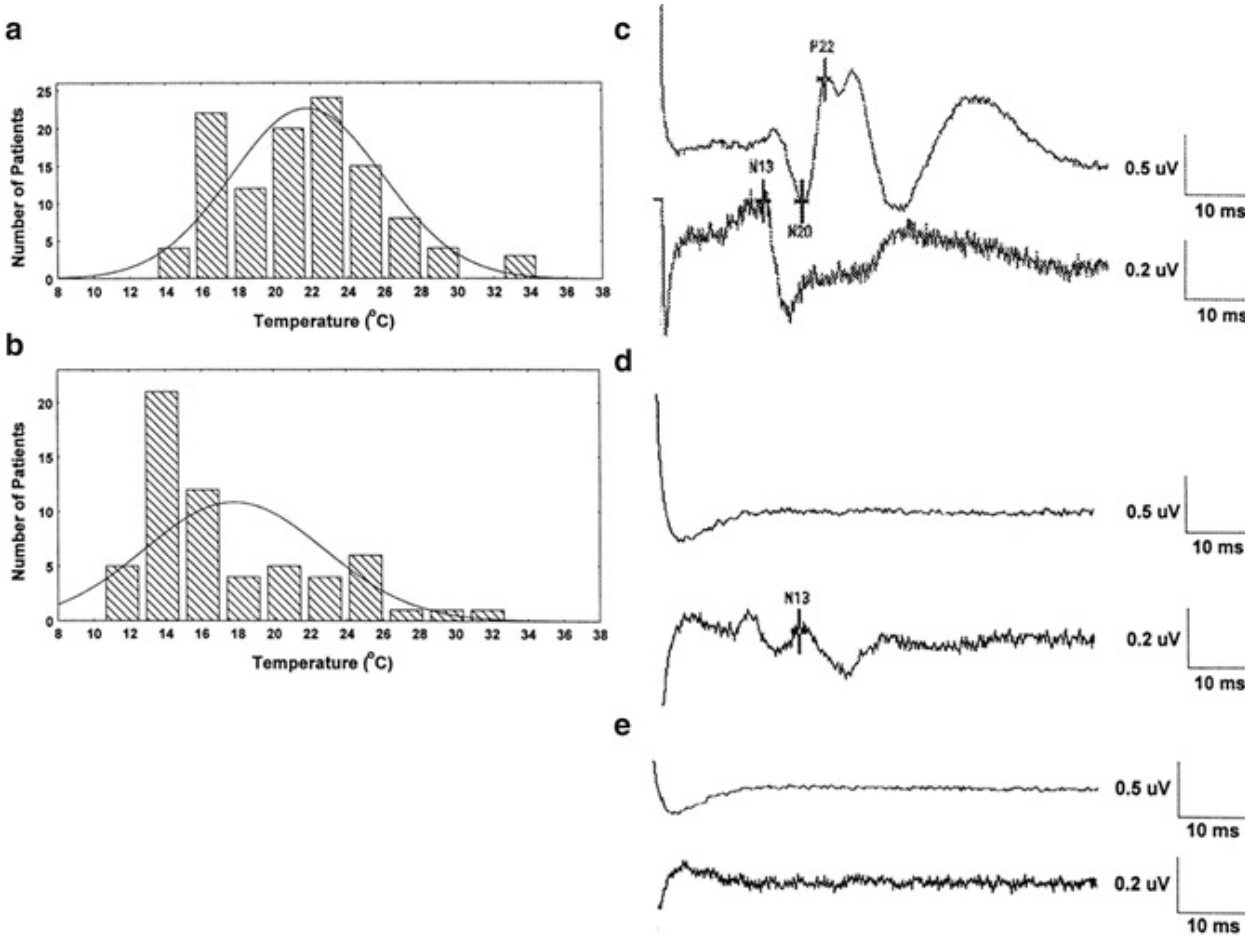

Fig. 39.5 The distribution of nasopharyngeal temperatures for loss of the N20-P22 cortical SSEP complex (**a**) and spinal cord N13 responses (**b**) in patients undergoing rapid cooling prior to circulatory arrest. Examples of typical SSEPs during rapid cooling prior to cooling (**c**), after loss of the cortical SSEP responses with prolongation of the N13 (**d**) and loss of the N13 spinal cord response. Reprinted with permission from Stecker et al. [93]

After the portion of the surgical repair of the patient's dissection is carried out during circulatory arrest and selective antegrade cerebral perfusion, the patient is rewarmed. Electrophysiologic modalities for tracking the rewarming process have also been studied [93]. During this phase of the procedure, the EEG and SSEP responses take on an additional significance beyond merely tracking the rewarming effects on the central nervous system. In this case, they can also predict the occurrence of new neurological deficits occurring during the circulatory arrest phase of the procedure.

Stecker demonstrated the pattern of EEG and SSEP responses observed during rewarming prior to separation from bypass. In neurologically normal patients, the order of reappearance of SSEP and EEG activity was consistent

across the patients studied. The N13 SSEP waveform reappeared first after rewarming followed by the thalamocortical SSEP responses (i.e., N20-P22). EEG burst suppression activity appeared next followed by continuous EEG activity, which occurs on average 28.1 min later. The rewarming rate on average was 0.42 ± 0.19 °C per minute from a circulatory arrest nasopharyngeal temperature of 14.4 ± 2 °C. In general, the time of recovery of the N20-P22 SSEP responses during rewarming increased by 0.3–1.0 min for each minute of circulatory arrest. Of importance, the time as well as the nasopharyngeal temperature for reappearance of continuous EEG and the thalamocortical SSEP (i.e., N20-P22) responses were significantly longer and higher, respectively, in patients who developed new postoperative neurological deficits compared with patients with normal postoperative neurological outcomes (Tables 39.3 and 39.4). Based on these results, a multivariable analysis allowed calculation of the relative risk of new postoperative deficits occurring during the circulatory arrest and initial rewarming phases of the operation by determining the product of 1.56 and 1.27 and the temperature for the reappearance of continuous EEG and N20-P22 SSEP responses, respectively (see Table 39.5). This approach accurately predicted new postoperative neurological deficits 89 % of the time. Ghariani et al. [92] found similar delays in recovery of central nervous system (i.e., CNS) electrical activity in patients with new postoperative neurological deficits [92].

Table 39.3 Summary of times and temperature for events during rewarming in patients neurologically intact postoperatively[a]

Description	Factor	*n*	Mean (SD)	Factor	Mean, SD	Factor	Mean (SD)
Reappearance of burst suppression	T^{R}_{as}	48	19.0 (9)	NT^{R}_{as}	21.2 (5)	CT^{R}_{as}	20.6 (3)
Reappearance of continuous EEG	T^{R}_{Cont}	47	47.1 (26)	NT^{R}_{Cont}	30.1 (5)	CT^{R}_{Cont}	26.8 (4)
Reappearance of N_20-P_{22}	$T^{R}_{N_20}$	66	14/2 (7)	$NT^{R}_{N_20}$	18.6 (3)	$CT^{R}_{N_20}$	20.0 (3)
Reappearance of N_{13}	TRN_{13}	37	12.6 (6)	$NT^{R}_{N_{13}}$	17.2 (2)	$CT^{R}_{N_{13}}$	19.2 (2)

Reprinted with permission from Stecker et al. [40]
Shows the times and temperatures for the reappearance of EEG burst suppression, continuous EEG, the upper limb N20-P22, and subcortical N13 SSEP responses during rewarming. All data were acquired from patients

without either permanent transient neurological deficits. The fourth column shows the individual time factors and mean and standard deviation for the times in minutes for EEG and SSEP responses listed in the first column. The sixth and eighth columns show the mean and standard deviation for the nasopharyngeal temperature (i.e., NT) and central temperatures (i.e., CT, bladder and rectal temperature sites) for return of each EEG and SSEP factor listed in the first column. The third column lists the number of patients whose data was used for calculating each mean and standard deviation
EEG encephalogram, *SSEP* somatosensory-evoked potential
[a]Includes only patients without either preoperative, intraoperative strokes, or postoperative confusion

Table 39.4 Summary of times and temperature for events during rewarming in patients with neurological deficits [a]

Description	Factor	No.	Mean (SD)	*P* [b]	Factor	Mean (SD)	*P*	Factor	Mean (SD)	*P*
Reappearance of burst suppression	T^{R}_{as}	9	26.2	0.02	NT^{R}_{as}	24.8 (6)	0.07	CT^{R}_{as}	22.5 (5)	0.23
Reappearance of continuous EEG	T^{R}_{Cont}	9	80.5 (28)	0.0008	NT^{R}_{Cont}	36.2 (0.8)	0.0007	CT^{R}_{Cont}	32.8 (4)	0.0006
Reappearance of N_20-P_{22}	$T^{R}N_20$	16	20.3 (9)	0.0004	$NT^{R}N_20$	22.3 (4)	0.0002	$CT^{R}N_20$	20.0 (2)	0.95
Reappearance of N_{13}	$T^{R}N_{13}$	10	16.5 (9)	0.12	$NT^{R}N_{13}$	18.8 (2)	0.07	$CT^{R}N_{13}$	19.7 (3)	0.45

Reprinted with permission from Stecker et al. [40]
Shows the times and temperatures for the reappearance of EEG burst suppression, continuous EEG, the upper limb N_20-P^{22}, and subcortical N_{13} responses. The data for this table are calculated and reformatted, the same as for Table 39.3. The data were acquired from patients with new permanent or transient neurological deficits. Note the longer times and higher nasopharyngeal and central temperatures for the reappearance of each factor listed in the first column compared to patients with normal neurological outcomes
[a]Includes only patients with intraoperative strokes or postoperative confusion
[b]Probability that corresponding factors in the neurologically normal and postoperative neurologic impairment groups are the same by Student's test

Table 39.5 Multivariable analysis of factors associated with either intraoperative stroke or postoperative confusion by stepwise logistic regression[a]

Factor	Relative risk (per °C)	95 % CI	*P* value
$NT^{R}Cont$	1.56	1.1–2.2	<0.001
$NT^{R}N_{20}$	1.27	1.02–1.56	0.015

Reprinted with permission from Stecker et al. [40]
Relative risk factors calculated for the nasopharyngeal temperature at which continuous EEG or the N20 cortical SSEP responses reappear during rewarming is shown. The relative risks are listed in the second column and the 95 % confidence intervals (CI) in the third column. The level or significance for the results is found in the fourth column. The relative risk for new neurological intraoperative strokes or postoperative TNDs can be calculated by multiplying the relative risk and the nasopharyngeal temperature at which continuous EEG or the N20 cortical responses reappear
[a]All patients

Finally, other investigators demonstrated that loss of SSEP responses prior to cooling or following circulatory arrest during aortic surgery correlated with new deficits [92, 94, 95]. Cheung et al. [94], however, demonstrated a large degree of variance for cortical SSEP amplitudes acquired from patients with normal outcomes following bypass procedures. In order to predict new focal deficits, a 21-fold left–right amplitude asymmetry of the N20-P22 (i.e., thalamocortical) response was required [94].

Acid Base Management on Bypass

Hypothermia has profound effects on neutral pH of water. During cooling, CO_2 solubility increases, shifting the equilibrium of the following equation to the right.

$$H^+ + HCO_3^- \leftrightarrow H_2CO_2 \leftrightarrow H_2O + CO_2$$

This shift results in an increase in pH during cooling.

There are two management approaches for dealing with these arterial blood gas results. The first is referred to as the pH stat management scheme where the pH is kept constant. In this case, the perfusionist will either add CO_2 to the patient's blood or reduce the gas flow entering the oxygenator.

This is done to correct the hypothermic blood pH to 7.4, at the expense of an increased load of CO_2. Increased CO_2 leads to vasodilatation of the cerebral arterioles [29, 35, 96–99]. This uncouples autoregulation prior to 21–22 °C (i.e., where it is lost during alpha stat management). Cerebral blood flow increases in the cerebral cortex, as well as the brainstem, leading to a decrease in temperature gradients. Temperature gradients might exist when pH stat management is not used during rapid cooling.

The second management scheme is the alpha stat management where the state of intracellular charges is kept constant. In this case, blood gas pH is not corrected for temperature. Thus, the perfusionist does not add CO_2 to the blood. Autoregulation is maintained for a longer period of time during cooling, with the expected decrease in cerebral blood. It is interesting to note in this regard that functioning poikilotherms use the alpha stat blood gas management. On the other hand, hibernating animals use pH stat [29, 30, 37]. Perhaps the reason for these preferences lies in the fact that pH stat management leads to a more uniform hypothermic body temperature and perhaps improved protection during hibernation.

Neonates, when cooled using alpha stat management for circulatory arrest, had an elevated incidence of choreoathetosis [96, 98, 100]. The incidence of this postoperative deficit decreased when pH stat management was used. This suggested improved and uniform hypothermic protection of the brainstem due to increased vasodilation. Animal studies showed an increased tolerance to circulatory arrest when pH stat management was used [100]. Furthermore, the alkalotic pH obtained with alpha stat management in conjunction with hypothermia shifts the oxyhemoglobin saturation curve to the left. This reflects increased affinity of hemoglobin for oxygen during conditions of high pH and low temperature [96–100]. Thus, high venous oxygen saturations with alpha stat management during cooling may not be caused by a cold brain extracting less oxygen from hemoglobin , but because hemoglobin will not release oxygen under cold, alpha stat management [96, 100]. With pH stat, on the other hand, left shift of the oxyhemoglobin saturation will decrease due to the increased acidity in the hypothermic patient’s blood [100]. This implies that more oxygen will be available to brain cells during hypothermic circulatory arrest than with alpha stat management. However, oxygen supplies to the hypothermic brain during circulatory arrest may be principally met by dissolved oxygen in the stagnant cerebral blood volume during circulatory arrest [33, 35, 38]. In any event,

caution should be exercised when interpreting increased venous oxygen saturations during hypothermia as a reflection of decreased oxygen extraction due to cold-induced reductions in metabolic oxygen demand when alpha stat management is used [98, 100].

Alpha stat management with the attendant cerebral blood flow decrease during hypothermia has been viewed as a benefit for patients undergoing cardiopulmonary bypass without circulatory arrest as enzymes tend to function more efficiently with alpha stat management in the cooled patient [29, 30, 37, 100]. A second benefit of alpha stat management in the adult patient is that decreased blood flow delivers fewer emboli to the brain as demonstrated in experimental animals [17, 18, 29, 30, 35, 37].

In summary, in neonates in whom embolic injury is less common, pH stat may be the preferred blood gas management scheme for cooling prior to circulatory arrest . This is due to the increased blood flow, which leads to a more uniform cooling of the brain compared with alpha stat management. Alpha stat management may be preferred during rewarming where the expected improvement in enzyme function and decreased delivery of emboli may lead to improved neurological function in the rewarmed patient. However, in adults in whom the risk of embolic neurological injury is greater, current clinical practice is to use alpha stat management for both cooling and rewarming.

Cerebral Oximetry

Cerebral oximetry offers several benefits both as an adjunct monitor during normothermic bypass and during hypothermic circulatory arrest and selective antegrade cerebral perfusion. As discussed in Chap. 14, cerebral oximetry is thought to measure cerebral venous blood oxygen saturation. Some authors have suggested that a 20 % decrease from an anesthetized baseline value represents a significant decrease, suggesting cerebral increased oxygen extraction during ischemic stress [36, 101]. Others suggest that oximetry values less than 50 % represent a state of relative ischemia, leading to excessive extraction [101, 102]. When bilateral oximetry is monitored, others have correlated a 10–15 % asymmetry in venous oxygen saturation as an indirect indication of unilateral ischemia of the brain (Fig. 39.6). Venous oxygen saturation changes may then serve as an adjunct for EEG and evoked potential detection of cerebral cortical ischemia. Some investigators have

predicted new neurological deficits based on asymmetries in the bilateral cerebral oximetry data [103].

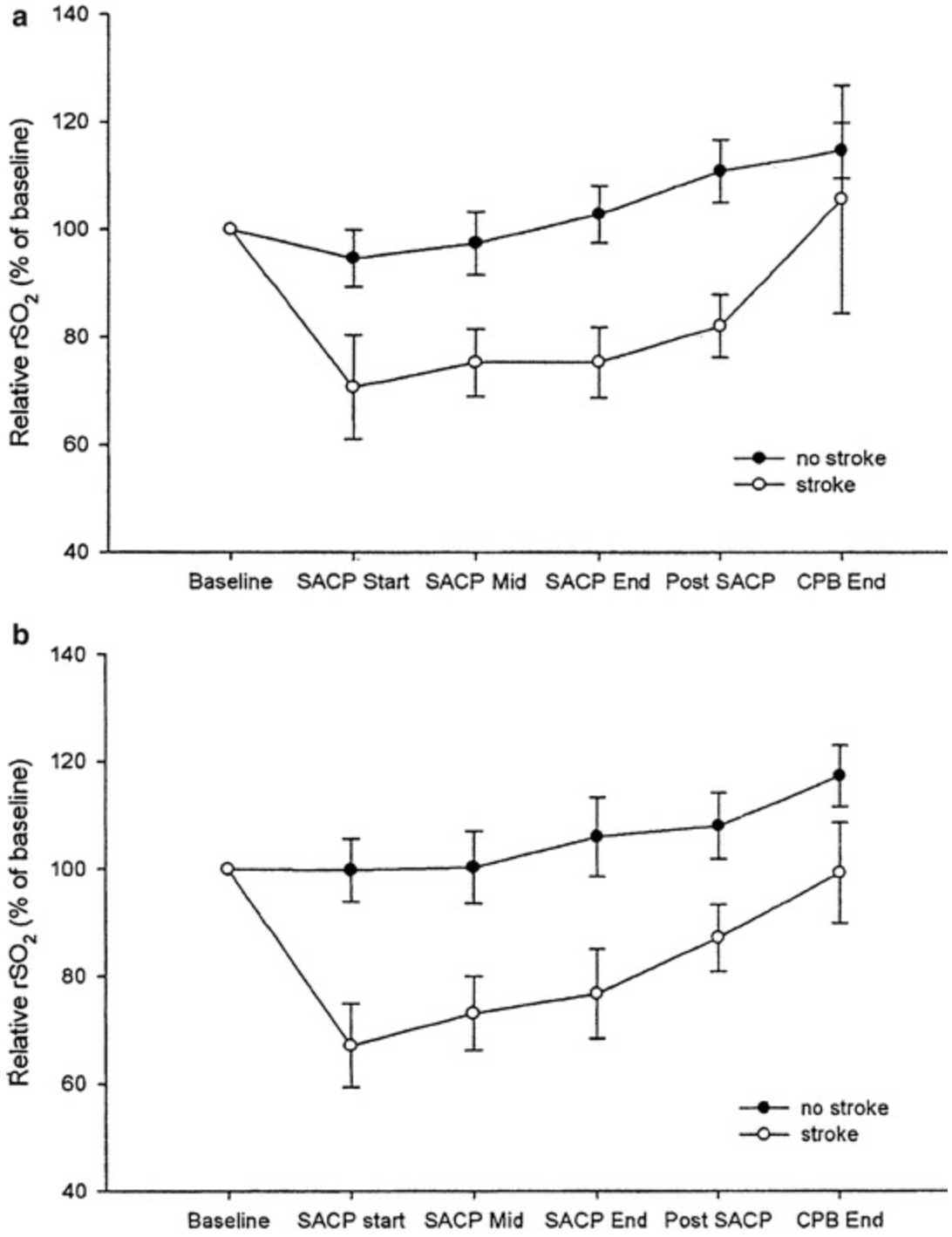

Fig. 39.6 The cerebral regional oxygen saturation values relative to baseline (100 %) for the left (**a**) and right (**b**) hemispheres in patients with (n = 6) and without (n = 40) postoperative permanent deficits. Data are plotted as means ± SEM. Reprinted with permission from Olsson et al. [103] SACP,

selective antegrade cerebral perfusion; CPB, cardiopulmonary bypass; rSO_2, cerebral regional oxygen saturation; SEM, standard error of mean

During profound hypothermia and circulatory arrest, cerebral venous oxygen saturation is the only monitor available for warning when the safe duration of circulatory arrest has been reached [104]. Despite cooling the patient to profound hypothermic temperatures, cerebral metabolism, although profoundly reduced, still persists during circulatory arrest [105–107]. This is demonstrated by the steady decrease in venous oxygen saturation, which varies from 1.2 to 0.81 % decrease per minute observed in patients during circulatory arrest [105, 106, 108]. Investigators have demonstrated that after the initial decline in venous saturation, venous saturation values tend to level out to a plateau [104]. If the plateau value is 50 % or better, some clinicians assume that it is safe to continue the circulatory arrest duration [102].

Other investigators suggest, however, that when the plateau is reached, it is time to institute selective antegrade cerebral perfusion, as the plateau represents a state at which maximum oxygen extraction has already occurred (Fig. 39.7) [104]. An increased duration of circulatory arrest once the plateau has been reached may lead to an increase of neurological deficits [104, 107, 108]. The same investigators have demonstrated in neonates that increased hematocrits tend to increase the tolerance for circulatory arrest. An increased tolerance for circulatory arrest is shown by an increased time from the initiation of circulatory arrest to the plateau phase of the cerebral oxygen saturation curve [108]. This has not been duplicated in an adult study, which showed an increase in cerebral oxygen desaturation with higher hematocrits during the initial phase of circulatory arrest [106]. On the other hand, outcome studies for neonates and adults show improved outcomes when extreme hemodilution is not used during bypass and circulatory arrest [109–111].

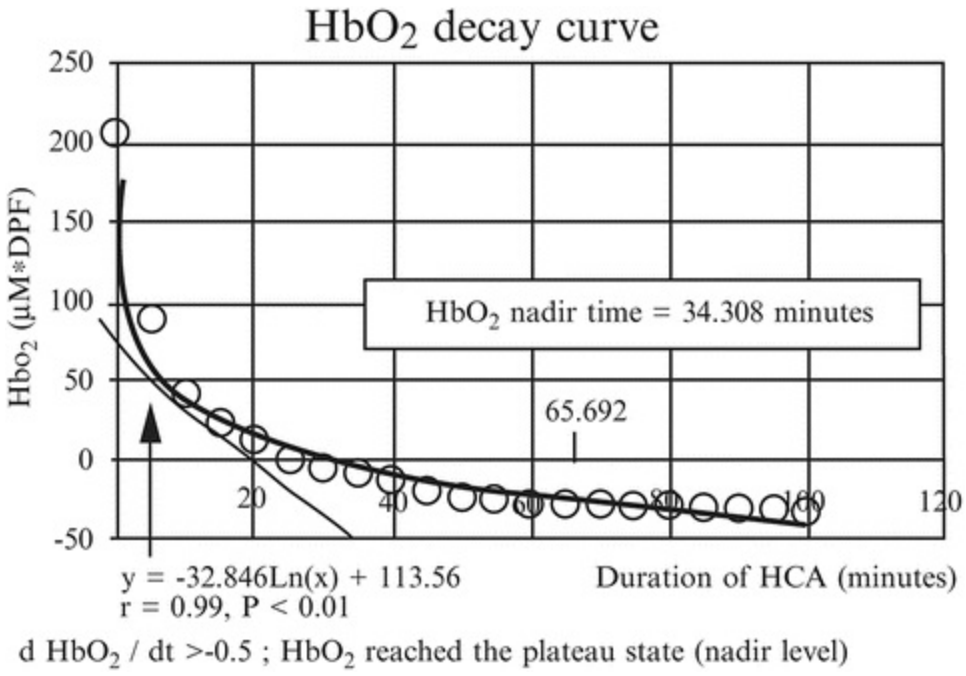

Fig. 39.7 The time course of the decrease in regional cerebral venous oxygen saturation as recorded from a cerebral oximeter in piglets after the initiation of deep hypothermic circulatory arrest. The decrease in oxygen saturation is plotted as saturated hemoglobin in μmol/L. A nadir value is defined as the point along the curve where saturated hemoglobin reaches a plateau state. This, in turn, is derived as the time when the rate of change (i.e., the slope) of hemoglobin saturation curve becomes more than −0.5. Reprinted with permission from Sakamoto et al. [104] HCA, hypothermic circulatory arrest; HbO_2, oxygenated hemoglobin

The importance of cerebral oximetry as a central nervous system monitor takes on added significance when it is realized that it is the only monitor available during circulatory arrest [112, 113]. Not all investigators, however, agree on its efficacy [114].

Transcranial Doppler

There are several reasons for employing transcranial Doppler (TCD) during the repairs of an aortic arch aneurysm or dissection. (Please refer to Chap. 13 for an in-depth review of the TCD technique.) The first is to serve as an adjunct to SSEP and EEG monitoring. Prior to initiation of cardiopulmonary bypass, sudden elevations in systolic pressure during surgical exposure may extend the dissection flap to involve the arch vessels, and thus, compromise flow to the upper extremities and/or brain. Monitoring bilateral middle cerebral artery blood flow velocities will help detect compromised flow to the

brain.

After a safe period of circulatory arrest has been reached as determined by cerebral oximetry (see previous section), the surgeon will employ selective antegrade perfusion [62–75]. During the initiation of selective antegrade cerebral perfusion, the perfusion pressure required to initiate flow may be higher than anticipated in order to overcome the critical closing pressure of the cerebral arterial vasculature. The appearance of middle cerebral artery blood flow velocity will assure that adequate perfusion pressures are being used as well as detecting any problems in the placement of the selective antegrade catheter [115, 116].

Cardiopulmonary bypass and selective antegrade cerebral perfusion both have risks for cerebral embolization [16–18]. Transcranial Doppler is an excellent monitor for detecting cerebral embolization [115–117]. The passage of air or particulate embolic debris through the cerebral arteries produces a characteristic ultrasound signature referred to as a high-intensity transient (HITS). Of interest, the larger the transient high-intensity signal recorded by the TCD, the greater the chance that the events represent an air embolus, due to the large differences in refractory index between air and blood [117]. Dexter and Hindman [118] calculated the absorption time of emboli as a function of emboli size and partial pressure of nitrogen in the emboli and blood.

Blood flow obstruction, caused by air emboli ranging in size from 25 to 100 μm in diameter, is reversed due to the absorption of the air emboli within 4 min (i.e., in the absence of nitrogen tension in the emboli and blood). Larger bubbles, with volumes of 0.1 mL or greater, may obstruct blood flow for up to 12 h. Theoretically, air emboli of sufficient size may lead to new central nervous system ischemic injury. If cerebral emboli are detected, the surgeon may elect to use a short period of retrograde cerebral perfusion in an attempt to “flush out” air and solid embolic debris prior to rewarming and/or separation from cardiopulmonary bypass [119]. Retrograde cerebral perfusion is a method used to protect the brain during circulatory arrest by perfusing the brain in a retrograde manner via the superior vena cava [120]. TCD can assure that retrograde perfusion is actually perfusing the cerebral circulation successfully [116, 121].

Finally, following separation from cardiopulmonary bypass and return of pulsatile flow, the TCD may be useful for detecting reduced blood flow typical of patients who have undergone a period of circulatory arrest.

Increased cerebral vascular resistance is detected as an increase in the pulsatility and can progress to an absence of diastolic blood flow velocity. One cause of loss of diastolic blood flow velocity is an increase in intracranial pressure caused by cerebral edema [78].

Combination of Cerebral Oximetry and Transcranial Doppler

A recent pilot study showed that cardiopulmonary bypass pump flows significantly correlated with cerebral oximetry and that flow of antegrade cerebral perfusion correlated with the middle cerebral artery (MCA) mean velocity and they defined a critical threshold level at which MCA blood flow ceased [122]. They found that maintaining antegrade cerebral perfusion flow rate at approximately 10 mL/kg/min resulted in cerebral oximetry values of 45 % or greater. Thus, it is possible that a combination of monitoring techniques can provide individualized parameters to follow during DHCA.

Conduct of the Surgical Repair of the Aortic Dissection

The surgeon plans to use the right axillary artery for the arterial cannulation site for bypass. There are several reasons for his choice [63, 69, 71, 75]. First, the right axillary artery is relatively free of atherosclerosis and calcification compared with the ascending aorta, aortic arch, and descending aorta. Thus, manipulating this vessel has a lower risk of dislodging atherosclerotic debris into the circulation, which could lead to stroke or embolic damage of the other organs. Secondly, it eliminates the need for femoral artery cannulation used for retrograde arterial perfusion, which can also lead to a dislodged atherosclerotic plaque from the descending aorta and the possibility of cannulating the false lumen of the aorta. Finally, the right axillary artery can be used for both systemic as well as selective anterior cerebral perfusion [3] (Fig. 39.8).

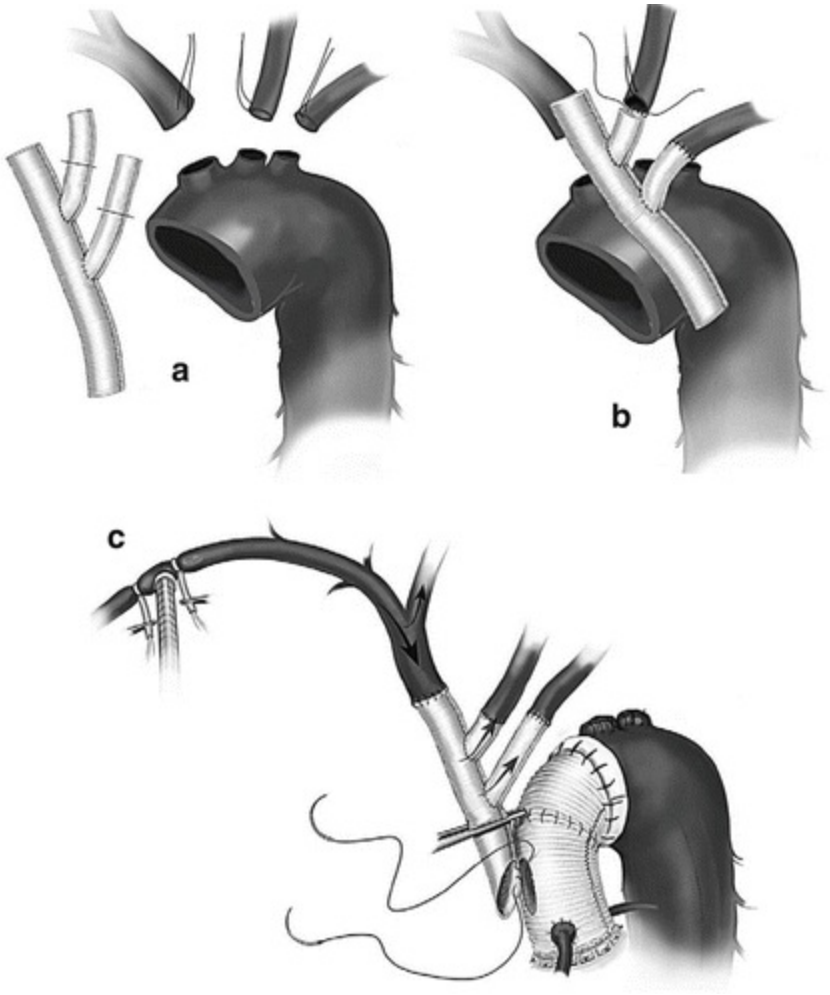

Fig. 39.8 (**a**) During deep hypothermic circulatory arrest , the brachiocephalic vessels are divided approximately 1 cm distal to their origin, where they are generally free of disease, and a trifurcated graft is appropriately trimmed. (**b**) The braciocephalic anastomoses are completed. (**c**) With the main limb of the trifurcated graft clamped, antegrade selective cerebral perfusion is initiated through the axillary artery. During selective cerebral perfusion, the elephant trunk technique is used to reconstruct the arch and that graft is anastomosed to the proximal repair. The trifurcated graft is then anastomosed to the reconstructed aorta. Reprinted with permission from Spielvogel et al. [3]

Prior to anesthetic induction , the right radial artery and left radial or femoral arteries are cannulated for monitoring blood pressure. Left radial artery or femoral artery pressure lines allow monitoring of systemic perfusion. The right-sided arterial pressure line is used for monitoring cerebral perfusion pressure when the axillary artery is used for selective antegrade cerebral perfusion. Two large bore intravenous lines are placed for volume infusion. A BIS (bispectral index) EEG monitor and bilateral regional cerebral oximeter monitors are placed before induction. Finally, recording

and electrical stimulation electrodes are placed for recording EEG, as well as upper and lower limb SSEP responses.

Rapid sequence induction is performed using propofol , fentanyl, and succinylcholine for intubation. Esmolol infusion and nitroglycerin are available in order to minimize any pressure increases during tracheal intubation. Isoflurane is used as the main maintenance agent. A nasopharyngeal temperature probe and bilateral transcranial Doppler transducers are also placed. A transesophageal echo probe (TEE) is placed in order to verify the extent of the dissection and also to verify the presence of pericardial fluid or blood and aortic insufficiency. A central line is then placed in the right internal jugular vein under ultrasound guidance.

After the right axillary artery is cannulated, a median sternotomy followed by bicaval venous cannulation is completed. The patient is then placed on bypass and cooling is initiated by perfusing cold (10 °C) oxygenated blood though the right axillary arterial cannula. The pH stat blood gas management scheme is used during cooling. The surgeon will cool beyond a nasopharyngeal temperature sufficient for suppression of all EEG, as well as upper and lower limb cortical and brainstem SSEP activity. Circulatory arrest will be initiated at 2 °C below the nasopharyngeal temperature where EEG and SSEPs are lost.

As bypass is initiated, the right and left TCD show absent flow in the middle cerebral arteries, although normal flow velocity was demonstrated prior to beginning bypass. The operative team speculated that the absent flow velocity may be due to elevated critical closing pressure and thus increased the perfusion pressure as recorded by the right axillary artery. An increase of 5 Torr is required for middle cerebral artery flow velocity to appear.

During cooling, the head is packed in ice in order to minimize rewarming of the brain during circulatory arrest . As the patient is cooled, the ascending aorta and arch vessels are surgically exposed. A trifurcated graft is prepared for anastomoses to the arch vessels (see Fig. 39.8). Prior to circulatory arrest, manipulation of the aorta is kept to a minimum in order to reduce the incidence of embolic dislodgement. Finally, although not immediately obvious, the use of the right axillary artery perfusion technique in conjunction with the use of the trifurcated graft for replacing the arch vessels eliminates the concern of a possible absence of perfusion of the left cerebral circulation during selective anterior cerebral perfusion. Right axillary artery perfusion can be a problem if the patient is missing both an anterior and

posterior cerebral communicating arteries. Recall that this patient had a previous left carotid endarterectomy requiring a shunt using EEG changes as criteria for placing the shunt [123–126]. Approximately, 17 % of the patients are missing both communicating arteries [124]. However, this operating plan allows for perfusion of both the right and left carotid arteries, regardless of the Circle of Willis abnormalities.

Sixty milligrams of potassium chloride is added to the cardiopulmonary bypass perfusate in order to elicit a diastolic cardiac arrest. At 16 °C, the EEG, cortical, and subcortical SSEP responses are suppressed. Left and right cerebral oximetry values have increased from 60 % and 64 to 85 % and 90 %, respectively. Using pH stat blood gas management, the elevated cerebral oximetry values are considered a reflection of the increased venous oxygen saturation due to decreased oxygen extraction; a result of depression and subsequent loss of cerebral and subcortical electrical activities. During cooling, the perfusionist ensures that the hematocrit is between 25 and 30 and blood glucose values are less than 130 mg per deciliter.

The patient is then placed in Trendelenburg position to prevent air trapping, and circulatory arrest is initiated. During circulatory arrest, a clamp is placed on the proximal end of the trifurcated graft. The innominate artery is transected distal to its origin at the aortic arch where atherosclerosis is expected to be minimal. The large limb of the trifurcated graft is anastomosed to the distal end of the innominate artery in an end-to-end fashion. The left carotid artery is subsequently anastomosed similarly to the second of the remaining side grafts.

During the initial portion of circulatory arrest, as expected, transcranial Doppler (TCD) flow velocities disappear. The cerebral oximeter demonstrates a bilateral decrease in venous oxygen saturation reflecting reduced but still present brain metabolic activity. The values decrease bilaterally and approach a plateau at 40 and 42 % as monitored from the right and left side of the forehead. The surgeon is warned that the values are below 50 % and the plateau suggests that maximum oxygen extraction may have occurred. Rather than completing the anastomoses of the left subclavian artery to the third limb of the graft, the surgeon elects to place a cross clamp across the proximal left subclavian graft and initiates selective antegrade cerebral perfusion through the right axillary artery. The perfusate is oxygenated blood at 16 °C. Selective antegrade perfusion is accomplished by blood flowing from the right axillary artery to the right subclavian artery,

through the innominate artery, as well as into the graft and up the left cerebral artery (see Fig. 39.8). As antegrade cerebral blood flow is resumed, the TCD demonstrates that bilateral middle cerebral artery (MCA) flow velocities and the cerebral oximeter values increase to above 80 % bilaterally. The surgeon then completes the anastomoses of the third branch of the trifurcated graft to the left subclavian artery.

Although the brain, right upper limb, and part of the spinal cord are perfused, the rest of the body is still in circulatory arrest. The surgeon now directs his attention to the distal aortic arch. The distal arch is excised and an elephant trunk is constructed by inverting a tubular graft and placing both lumens in the descending aorta. An anastomosis is created with the edge of the inverted graft and the descending aorta. The inner portion of the graft is then everted and will form the proximal portion of the aortic arch. The distal portion of the elephant trunk is left free within the descending aorta. If the patient survives this operation, he will have the option of a second operation for repair of the descending aorta where the free end of the elephant trunk will be used for the proximal descending aortic anastomoses. As the aortic valve is normal, the surgeon then constructs a second tubular graft from the aortic valve annulus for replacing the ascending aorta. The right and left coronary arteries are then anastomosed to the proximal graft above the native aortic valve. The ascending aortic graft is then anastomosed to the proximal portion of the elephant trunk. The proximal portion of the trifurcated graft is subsequently attached to the newly formed aortic graft.

After all anastomoses are completed, a hole is made in the arch for flushing out any atherosclerotic, calcified, and/or air emboli in order to minimize cerebral or systemic embolization . The patient is then rewarmed. Total circulatory arrest lasts for 28 min and selective anterior cerebral perfusion lasts for 80 min. After selective anterior cerebral perfusion, the patient is placed back on full cardiopulmonary pulmonary bypass. When the temperature reaches 24 °C, the EEG and upper limb cortical and subcortical SSEP responses have returned. However, lower limb cortical, subcortical, and popliteal SSEP responses fail to recover. Bilateral TCD traces show antegrade bilateral MCA flow velocity with <5 high intensity transients (i.e., HITS) over 30 min, suggesting an absence of significant cerebral embolization. Bilateral cerebral oximetry values have decreased from the low 80 % range to 62 % and 64 %, respectively, for right- and left-sided cerebral oxygen saturation, as the patient reaches a nasopharyngeal temperature of 36

°C. The patient is maintained at 36 °C in order to avoid cerebral hyperthermia . These results suggest to the operative team that the lower limbs have become ischemic; either from an extension of the dissection distally, down the descending aorta or embolization from the ascending aorta and/or arch during the reinstitution of systemic cardiopulmonary bypass [126].

Examination of the TEE shows no evidence of an extension of the dissection in the upper thoracic aorta. Doppler examination of the bilateral femoral and popliteal arteries, however, fails to register blood flow. A vascular surgeon is consulted who performs bilateral embolization of the lower limb vessels. Flow returns and the patient is weaned from bypass successfully with minimal ionotropic support. TCD shows bilateral pulsatile middle cerebral blood flow velocity with normal diastolic flow velocities. The lower limb popliteal and cortical SSEP responses return within 5 min after the patient has been separated from bypass. The axillary artery and right atrial venous cannulas are removed. The patient's anticoagulation is reversed. After surgical bleeding is controlled, the patient's surgical wounds are closed. The patient is transferred to the cardiac intensive care unit. The following day, the patient is extubated with a normal postoperative neurological clinical examination. No delayed neurological deficits are observed over the subsequent 48 h. The patient was discharged to a rehabilitation facility on the seventh postoperative day.

Conclusion

Knowledge is power. We have demonstrated several instances during aortic surgery where neurophysiological, chemical, and hemodynamic information can be helpful for guiding the management of the surgical procedure. Perhaps the importance of these data is that it can detect deleterious changes occurring during the procedure that would not otherwise be known until the patient recovers from anesthesia in the postoperative period (e.g., initial absence of select anterior cerebral perfusion, determination of the safe duration of circulatory arrest, and lower limb embolization in this case). Detection, and an appreciation of these changes, can lead to early proactive treatments that may decrease the incidence of new postoperative deficits. In the future, a better understanding of the use of these data may allow early postoperative noninvasive intervention, such as intracranial vascular emboli extraction, angioplasty, stent placements, localized thrombolysis, or the use of several

pharmacological agents [note: there is little evidence at present to support the use of most pharmacologic agents felt to have a useful protection or treatment effect for patients undergoing circulatory arrest] within a window of opportunity where they might make a difference in patient outcome. Experience with these monitoring modalities will hopefully further the efficacy of their use [127].

There is a range of temperatures rather than a single best temperature for which each of the sequential EEG patterns occurs during cooling on bypass.

Questions

1. Which of the following is true regarding hypothermia during deep hypothermic circulatory arrest during aortic arch surgery?

    a. The main therapeutic preventative approach for minimizing neurological deficits during circulatory arrest is hypothermia.

    b. All patients can tolerate circulatory arrest durations >60 min safely.

    c. Protection offered by deep hypothermia allows prolonged periods of circulatory arrest and adjuncts such as selective antegrade cerebral perfusion and is rarely necessary.

    d. Target temperature for hypothermia should be <10 °C to allow optimal cerebral protection.

2. Which of the following neuromonitoring techniques provides useful continuous data during circulatory arrest in patients undergoing aortic arch surgery?

    a. somatosensory-evoked potentials

    b. bispectral index

    c. transcranial Doppler

d. cerebral oximetry

e. jugular bulb saturations

f. EEG

3. Which of the following statements is true?

   a. The appropriate temperature for initiating circulatory arrest is best determined by observing a 50 % decrease in cerebral saturation from baseline.

   b. Transcranial Doppler is an excellent monitor for preventing cerebral embolization.

   c. The longer it takes for the reappearance of continuous EEG and thalamocortical SSEPs after discontinuation of circulatory arrest as well as the higher the nasopharyngeal temperature is at the time EEG and SSEPs appear, the risk of developing new postoperative neurologic deficits is greater.

   d. Cooling occurs uniformly and thus the site of temperature monitoring is not as important as the actual temperature attained.

Answers

1. a The main therapeutic preventative approach for minimizing neurological deficits during circulatory arrest is hypothermia. Because the brain lacks energy substrate storage within the brain, the normothermic brain can tolerate only short periods of absent blood flow before experiencing ischemia (i.e., 3–5 min at 37 °C). Circulatory arrest

durations greater than 35–45 min with insufficient patient cooling lead to postoperative neurological deficits. Brain protection offered by deep hypothermia is limited to relatively short periods of time (see Table 39.1). Thus, selective antegrade cerebral perfusion is often administered as an adjunct protective scheme during the surgical procedure. Although hypothermia is neuroprotective, excessive cooling may lead to adverse outcomes secondary to intraneuronal ice crystal formation with subsequent injury (e.g., usually expected at temperatures below 10 °C).

2. d All of the monitors listed can be utilized in patients undergoing aortic arch surgery. However, during circulatory arrest where there is no blood flow, cerebral oximetry is the only monitor that will provide meaningful data. EEG and SSEPs will be lost with progressive hypothermia.

3. c In neurologically normal patients, the order of reappearance of SSEP and EEG activity was consistent across the patients studied. The N13 SSEP waveform reappeared first after rewarming followed by the thalamocortical SSEP responses (i.e., N20–P22). Of importance, the time as well as the nasopharyngeal temperature for reappearance of continuous EEG and the thalamocortical SSEP (i.e., N20–P22) responses were significantly longer and higher, respectively, in patients who developed new postoperative neurological deficits compared to patients with normal postoperative neurological outcomes. Transcranial Doppler is an excellent monitor for detecting cerebral embolization but cannot prevent cerebral embolization.

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Footnotes

1 Key references marked with asterisk.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_40

40. Electrophysiological Monitoring During Thoracic Aortic Aneurysm Surgery

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Keywords Electrophysiological monitoring – Thoracic aortic aneurysm surgery – Monitoring strategy – Thoracic aortic aneurysm surgery – Spinal cord blood supply – Intraoperative monitoring – Somatosensory-evoked potentials (SSEPs) – Motor-evoked potentials (MEPs)

Key Learning Objectives

- The role of IOM has been to identify spinal cord ischemia to allow

changes in management that could improve spinal cord function and reduce permanent spinal cord injury.

- The chance of neurological injury is directly related to the time of ischemia and inversely related to the amount of residual blood flow.
- The motor tracts are perfused by the anterior spinal artery while the SSEP is perfused by the posterior spinal artery.
- The anterior spinal artery is perfused from the vertebral arteries, 2–8 radicular arteries from the aorta (the largest of which is referred to as the artery of Adamkiewicz), and lumbar arteries.
- The blood supply to the spinal cord is critically dependent on a mesh work of blood vessels supplied cephalad from the vertebral arteries, at the caudal end from sacral and iliac arteries, and from radicular perforators from intercostal arteries.
- Elevated CSF pressure reduces spinal cord perfusion
- Open surgical procedure allows complete repair but has higher surgical morbidity (especially thoracotomy). The endovascular technique has lower morbidity but may not allow optimal organ perfusion (especially visceral organs). The long-term risk of paralysis may be the same.

Introduction

Intraoperative monitoring (IOM) of the central nervous system during surgery to repair aneurysms of the thoracoabdominal aorta (TAA) is an area of significant inquiry due to the substantial incidence of neurological injury with surgery. In particular, there is an interest in reducing the reported incidence of paralysis, which varies from 0.5 % with aortic coarctation repairs (where the procedure is short and the patient usually has well-developed collateral circulation) to nearly 48 % with emergency repairs of extensive thoracoabdominal degenerative lesions [1, 2]. It is clear that the risk of perioperative paralysis varies due to a substantial number of factors including the vascularity affected by the surgery, the specific patient anatomy and disease, and the procedure.

A thoracoabdominal aneurysm is defined when dissection of the aorta results in an arterial diameter exceeding 50 % of the normal diameter [3]. The

causative factors include those that cause degeneration of the medial vascular wall with loss of elastic fibers and vascular smooth muscle cells and with proteoglycan deposition. Conditions associated with medial degeneration include increases in wall stress from hypertension, pheochromocytoma, cocaine use, and coarctation [3]. Physical trauma from weight lifting, deceleration injury in motor vehicle accidents, or falls can increase wall stress and cause dissection. Smoking increases dissection risk [3]. Inherited disorders can also result in dissection and include Marfan syndrome , Loeys–Dietz syndrome , the vascular form of Ehlers–Danlos syndrome , inflammatory diseases of the aorta, Turner syndrome, bicuspid aortic valve, and familial thoracic aortic aneurysm and dissection syndrome.

The role of IOM has been to identify spinal cord ischemia so as to allow changes in management that could improve spinal cord function and reduce permanent spinal cord injury. Paraplegia results from a variety of mechanisms that can cause reduced spinal cord perfusion including generalized ischemia, inadequate distal perfusion pressure, and the loss of critical radicular arteries, including the arteria radicularis magna. In addition, raised spinal cord cerebrospinal fluid pressure can reduce the effective arterial perfusion pressure to the spinal cord. IOM can detect the onset of ischemia and monitor the effectiveness of the treatment used to reduce the ischemia and extend the safe time needed for the surgical procedure.

IOM, Time, and Neurological Injury

Because the procedure involves repair of the aorta, there is an inevitable reduction in spinal cord blood flow; in addition, the procedure requires that the surgeon work as quickly as possible such that ischemia does not produce irreversible neurological damage. Thus, procedures that extend the ischemic period must be balanced with the potential benefit. It is in this respect that IOM is used to identify when additional time needs to be used to improve ischemia (i.e. reimplanting of a critical artery), or when this additional time is not needed such that the overall ischemic time is kept to a minimum.

This situation is similar to carotid endarterectomy (*see* Chap. 30, “Carotid Surgery”). Shown in Fig. 40.1 is the relationship of cerebral blood flow (plotted along the horizontal axis), IOM cortical electrical activity, and the presence of irreversible injury to the brain. Although the data for the spinal cord are not as well known as that depicted for the brain, the relationship of

these variables is thought to be the same.

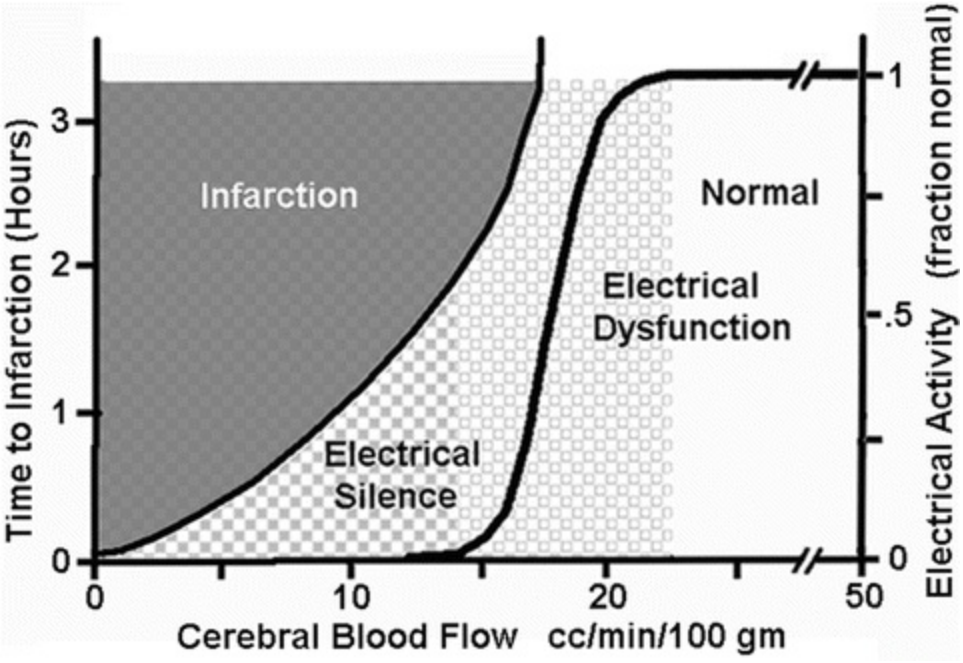

Fig. 40.1 Depiction of electrical activity and the occurrence of irreversible cell death (infarction) as cerebral blood flow is reduced from normal (50 cm^3/min/100 g). As shown, the EEG becomes abnormal below 22 cm^3/min/100 g and absent when blood flow reaches 15 cm^3/min/100 g. Infarction occurs at 17–18 cm^3/min/100 g after 3–4 h and progressively shorter periods with blood flow below this level

As shown, cortical electrical activity becomes abnormal below the threshold of adequate blood flow, which is estimated to be about 22 cm^3/min/100 g of brain weight and absent below 15 cm^3/min/100 g (ischemic threshold) [4]. This ischemia can eventually lead to cellular death given sufficient time, with the time being related to the degree of hypoperfusion. Increasing severity of neural injury is inversely proportional to blood flow, increased severity with decreased flow, and directly proportional to time. Increased severity is seen with increased duration of ischemia. Hence, the fall in electrical activity signals a reduction in blood flow and the need to improve flow to increase the allowable operative time until irreversible injury occurs.

As described below, during TAA repair , improvement in flow may involve increasing blood pressure or reimplantation of blood vessels important for spinal cord perfusion or reducing the cerebrospinal fluid

pressure to improve the net perfusion pressure. These maneuvers usually require additional operative time (e.g., reimplanting intercostal arteries), which risks increasing the ischemic time such that IOM can help determine if it is necessary and if it is effective.

Spinal Cord Blood Supply

Because of the role of spinal cord blood flow, it is useful to review the blood supply of the spinal cord. The spinal cord is supplied by the anterior spinal artery (AntSA) , which perfuses the anterior two-thirds to four-fifths of the spinal cord , including the white matter motor tracts and the grey matter containing the anterior horn cells. The AntSA is key to the perfusion of the motor tracts and the MEP. Two posterior spinal arteries (PostSAs) supply the remaining portions of the cord, including the white matter dorsal columns and a small part of the posterior funiculi. The PostSAs are keys to the perfusion of the pathway of the SSEP. The PostSA and to some degree the AntSA run the length of the spinal cord; however, the AntSA is not continuous, especially in the midcervical, upper thoracic, and a narrowed region just cephalad to the lumbar enlargement. An anastomotic vascular ring surrounds the spinal cord and provides some shared blood flow between the anterior and posterior spinal arteries.

The spinal cord blood flow is autoregulated similar to the brain [5]. As such, the normal spinal cord will attempt to maintain spinal cord blood flow over a wide perfusion pressure. In some individuals, autoregulation extends from approximately 50–150 mmHg above the normal cerebrospinal fluid pressure (CSFP) . However, similar to the brain , a wide variation exists, with some individuals having a lower limit of autoregulation that is substantially higher than for most individuals [6]. If the perfusion pressure falls below this lower limit of autoregulation, the spinal cord blood flow becomes directly dependent on perfusion pressure, which inevitably leads to ischemia.

The anterior and posterior spinal arteries are fed by arterial vessels from the aorta along the spinal column. In the cephalad region, they are fed by the vertebral arteries, and as they descend along the spinal cord they receive radicular perforators from the aorta. The paired PostSAs are fed by small radicular arteries at nearly every vertebral body. The AntSA receives blood flow from only two to eight radicular arteries that originate from the aorta [7]. In the cervical region, two or three segmental arteries arise from the cervical

or subclavian arteries. The thoracic cord usually has only one to three anterior segmental arteries arising from the aorta, making it particularly susceptible to ischemia; blood flow to the spinal cord is compromised by reductions in pressure due to the long distances between major vessels. The region between T4 and T7 is thought to be the least well-supplied region of the spinal cord, and it is particularly vulnerable to ischemia. This explains the higher risk of paralysis in patients with disease of the thoracic segment of the aorta.

One anterior segmental artery is larger than the others and supplies about 75 % of the blood flow to the AntSA. This artery is referred to as the “arteria radicularis magna ” (ARM or Artery of Adamkiewicz) and supplies the lumbar enlargement of the spinal cord. The location of the ARM is variable, with the artery arising in 75 % of patients from mostly left-sided intercostal arteries at T9–T12.

The vascular anatomy in patients with TAA is highly variable and patients may develop collateral circulation around arteries occluded by mural thrombi or arterial plaques. A meshwork of collateral blood vessels develops with the lumbar arteries (L3–L5) and the pelvic circulation becoming the main blood supply to the spinal cord in almost a quarter of the patients [8, 9]. This meshwork may explain why loss of some radicular arteries may not have the same consequences as in a normal patient. This also explains why the distal perfusion of the aorta is critically important during aorta cross-clamping.

In some patients, the radicular perforators from the PostSAs are critically important to spinal perfusion because of wide spacing between AntSA vessels, creating watershed regions of interrupted and poor perfusion. These critical arteries are most commonly seen between T8 and L4 [7, 8, 10]. In patients who are dependent on these vessels, critical intercostals need to be identified and reimplanted in order to reduce the incidence of operative paraplegia. With the ARM supplying 75 % of blood flow, it is extremely important to reimplant the ARM in patients deemed at risk for loss of other critical vessels [8, 11–13]. Further, when critical radicular arteries are disconnected from the aorta during surgery and not reconnected, retrograde flow may cause a redistribution of blood from the AntSA [14].

In summary, the blood supply to the spinal cord is critically dependent on a meshwork of blood vessels supplied cephalad from the vertebral arteries, at the caudal end from sacral and iliac arteries, and from radicular perforators from intercostal arteries (which include the ARM). No consistent vascular

pattern is seen in all patients, and spinal cord dependency on specific vascular regions varies. For example, in some patients, the supply from the cephalad vessels is sufficient such that the entire aorta can be excluded (without reimplantation of intercostals vessels) with no postoperative paraplegia occurring. In others, the key role of the pelvic circulation requires atrial-femoral or femoral venoatrial bypass to provide retrograde distal perfusion. Some patients are critically dependent on specific intercostal vessels. Unfortunately, these vessels cannot be identified using arteriograms. The role of IOM is to assist in identifying the specific ischemic risk factors in each patient and guide the necessary corrective measures to reduce neurological risk.

Open Surgical TAA Repair

Because of the risk from spinal cord, visceral, and limb ischemia, together with renal and respiratory failure, an open surgical repair of a TAA contributes to early mortality and morbidity. The recent American College of Cardiology/American Heart Association Guidelines for the Diagnosis and Management of Patients with Thoracic Aortic Disease gave recommendations for intervention based on the size of the thoracic aorta [15]. Based on these guidelines, open surgery is recommended for patients with TAAs larger than 6 cm (Class I, Level of Evidence: B) and for smaller sized aneurysms in patients with connective tissue disorders (Class I, Level of Evidence: C) [16]. Surgical repair is also recommended when there is end-organ ischemia or significant celiac, superior mesenteric, or renal artery atherosclerosis (Class I, Level of Evidence: B) [3]. Acute dissection involving the ascending aorta needs swift open surgical repair, although in some cases, hybrid approaches or endovascular interventions can be used [3, 17]. Finally, symptomatic aneurysms should be resected regardless of size [18].

Monitoring Strategy During Open TAA Surgery

To understand the role of IOM , it is useful to consider the surgical procedure in stages and consider the strategy for use of IOM so as to reduce the risk of paralysis [19]. Initially, proximal cross-clamping of the aorta is done. At this point, all spinal cord perfusion comes from the vertebral arteries. This cross-clamp also causes a critical elevation of blood pressure proximal to the clamp

with accompanying elevations in cerebrospinal fluid (CSF) pressure in the brain and spinal cord. This increased CSF pressure can further reduce spinal cord perfusion pressure (SCPP) [SCPP = spinal arterial pressure − spinal CSF pressure] compounding the reduction of spinal cord blood flow [2]. In order to minimize hypoperfusion, many surgeons try to limit the aortic cross-clamp to no more than 30–40 min.

Since perfusion is often not adequate, a surgeon may place a shunt or bypass pump between the proximal and distal aorta to extend the safe operative time. This bypass reduces the proximal hypertension and the associated increased CSFP . It provides better distal spinal cord perfusion for patients who are dependent on the caudal vessels [8]. Although a bypass perfusion pressure of 60–70 mmHg is generally accepted as adequate, the pressure necessary to effectively perfuse critical vessels is not known in any given patient without functional testing provided by IOM. Adequate pressure where IOM studies maintain pre-cross-clamp amplitude and latency is as high as 90–110 mmHg [20, 21]. Use of these distal perfusion techniques has been reported to reduce the risk of paralysis to about 10 % from the risk of 30–50 % with cross-clamping alone [14].

In some patients, distal perfusion alone is adequate to provide spinal cord perfusion. In other patients, perfusion from the critical radicular arteries is also required to prevent paraplegia. In more than half of the patients with aneurysms, a rich collateral network surrounding the spinal cord prevents ischemia, even when otherwise critical intercostal arteries are sacrificed [22]. But a group of patients with inadequate collateral networks may exist, in which reimplantation of intercostal arteries may be crucial for maintaining adequate spinal cord blood flow. These patients can be identified using IOM testing during segmental cross-clamping of the aorta.

Several methods are available to provide reperfusion of critical arteries once they are identified. One approach is to preserve the back wall of the aneurysm where the intercostal arteries arise and use it in the aortic reconstruction thus restoring critical perfusion [2]. Since this technique may not be feasible, other techniques have been developed to identify and implant the arteries in the repaired aorta segment. Because of its importance, some surgeons attempt to identify the ARM preoperatively to ensure that it is reimplanted into the aortic graft. Simply reimplanting the ARM further reduces the risk of paralysis from 10 % with distal perfusion to 5–6 % [14, 23]. If it cannot be identified, some surgeons reimplant all intercostals in the

T8–T12 range [2].

Intraoperative monitoring can also be useful to help assess if other techniques employed to reduce the risk of spinal cord ischemia are useful. Of particular note is the use of CSF drainage to maintain a low CSFP and improve the net perfusion pressure (CSFPP). Intraoperative monitoring can assist in identifying the critical CSFP that improves perfusion [24, 25].

In short, the goal of the surgical technique is to optimize the perfusion and reduce the overall ischemic time of the spinal cord. Hence, the surgeon must work expeditiously during the cross-clamp time. The value of IOM is to promptly identify spinal cord regions that are ischemic while the insult is reversible and then guide the interventions to correct the ischemia and reduce the risk. IOM has been applied successfully to these surgeries and has reduced the risk of intraoperative paralysis.

Attempts to increase the allowable ischemic time in TAA repair by using hypothermia have not been universally applied because it can lead to adverse systemic effects of prolonged cardiopulmonary bypass and profound hypothermia (e.g., coagulopathy, endothelial dysfunction, systemic inflammation) when applied systemically [26]. However, since deep hypothermia (14.1–20.0 °C) can reliably protect the spinal cord from ischemic damage, techniques using regional hypothermia are being explored. The results in early reports of TAA repair under regional spinal cord hypothermia using a custom-designed epidural catheter were excellent [26, 27]. Unfortunately, an ideal agent for pharmacologic neuroprotection has yet to be found [27].

Application of Intraoperative Monitoring to TAA Surgery

Since SSEP monitoring has been available since the 1980s, the most extensive clinical experience has been with SSEP monitoring. During aortic surgery, use of this technique can identify ischemia of the neural tract including peripheral nerve, white matter tracts of the dorsal columns, and ischemia in the brainstem or cerebral cortex.

A *slow* onset of cortical SSEP change (>15 min) usually indicates peripheral nerve ischemia. Isolated events, such as the femoral artery bypass cannula occluding flow to the leg, is one of the most frequent causes of peripheral nerve ischemia and *unilateral* loss of SSEP. If a bilateral change

occurs *within* 15 min, it has been assumed to be of spinal cord origin, either from inadequate distal aorta perfusion or loss of critical intercostals. Thus, clinicians have used the SSEP to determine if bypass was necessary, if the pressure of bypass was adequate, and if it was safe to exclude a specific radicular artery.

One of the earliest human studies using the SSEP was done by Cunningham and Laschinger et al. [28]. They observed four patterns of change in the SSEP depending on the mechanism of ischemia. A type I pattern was where the SSEP was altered in 3–4 min following proximal cross-clamping of the aorta with complete loss in 8–9 min. This pattern was thought to be indicative of inadequate perfusion of the spinal cord from the distal arterial supply. This emphasized the value of bypass perfusion [29]. A type II pattern was where the SSEP did not change after aortic cross-clamping, suggesting adequate spinal perfusion was present from cephalad vessels.

A type III pattern was where the patient was critically dependent on a radicular artery and changes in the SSEP were noted when it was occluded. This points out the use of the SSEP to locate the critical intercostals during aortic cross-clamping. The SSEP was shown to be restored when the critical intercostal was reimplanted or unclamped. Other studies report similar changes; rapid reperfusion of critical intercostal vessels restores the cortical SSEP and appears to reduce the risk of paraplegia [28, 30, 31]. A type IV pattern, where a gradual “fade out” reduction in amplitude but not latency of the SSEP over 30–50 min, is considered characteristic of lower extremity hypoperfusion [32]. This may signal the need to reorient the bypass cannula.

Use of the SSEP has not been completely reliable for always being able to predict paralysis since it does not monitor the motor tracts and instead monitors proprioception and vibration pathways in the posterior spinal cord [20]. In some cases, an SSEP loss has been correlated with motor injury. This is seen most often when an SSEP loss occurred rapidly after cross-clamping (within 3–5 min) or when the duration of an SSEP loss was prolonged (40–60 min) [29, 33–35].

With the advent of reliable motor-evoked potential monitoring, clinical inquiry turned toward the use of transcranial motor-evoked potential (MEP) monitoring. This form of monitoring differs from SSEP monitoring in that the responses can detect ischemia in the anterolateral white matter tracts, the spinal grey matter, and the peripheral nerve and muscles. The use of MEPs is

of particular interest since aortic occlusion in dogs demonstrated that the predominant injury from spinal cord ischemia is grey matter necrosis [36, 37].

Although false negatives with MEP monitoring have occurred (i.e., immediate postoperative paralysis with preserved intraoperative MEP), most studies show an excellent correlation of outcome with MEP findings [8, 13, 20, 21, 25, 32, 38]. All studies, both clinical and experimental, have reported a rapid change in MEP, within 2–4 min, to ischemic conditions where the ischemia includes the spinal grey matter serving the muscles monitored. This rapid response provides more useful feedback in the intraoperative environment where time is critical in determining outcome. These clinical studies suggest that MEP monitoring is more sensitive to ischemia than SSEP monitoring and provides significant additional reductions in paraplegia.

Comparison of SSEP and MEP in Aorta Surgery

Clinical studies have found that when comparing SSEP and MEP findings, there is a relatively long delay (7–30 min) between the onset of ischemia and the disappearance of SSEP, whereas the MEP generally changes comparatively quickly within 2–5 min [21, 32, 39–41]. The most important finding was that SSEP changes were not always associated with MEP changes.

Clearly, the effectiveness of the monitoring and some of the differences between the SSEP, MEP, and epidural recorded responses relate to the specific neural tracts being monitored and their susceptibility to ischemia. Based on the available data, the time to electrical failure of various neural tissues is shown in Table 40.1. The cerebral cortex is the most sensitive to ischemia, with a loss of electroencephalographic (EEG) activity within 20 s after inadequate perfusion. In the spinal cord, the grey matter is most sensitive to ischemia, with a loss of synaptic activity within 1–2 min. Conduction in sensory and motor white matter tracts (axons) demonstrates alterations in activity within 3–6 min (SSEP tract) or 11 min (motor tract) and a loss of conduction at between 7 and 18 min (SSEP) or 11 and 17 min (MEP). Hence, the white matter tracts of the sensory and motor systems are about equal to each other in terms of sensitivity to ischemia [20, 32, 42, 43]. Isolated peripheral nerve ischemia results in the loss of SSEP and MEP conduction after 20–30 min.

Table 40.1 Time to electrical failure in selected spinal neural tissues

Tissue	Time to electrical failure
Cerebral cortex	20 s
Spinal grey matter	1–2 min
White matter (sensory)	7–18 min
White matter (motor)	11–17 min
Peripheral nerve	20–45 min

Data from collected sources [2, 20, 24, 28, 39, 43, 59, 60]

The second issue comparing SSEP to MEP pertains to the prediction of outcome. When focusing on motor outcome, the MEP has the greater predictive power because it actually measures function in the cortical-spinal tract (CST). However, since only 5 % of the CST fibers are involved in the response, the correlation is not exact [44]. Further, a variety of other descending tracts are needed for coordinated motor function, so losses in associated tracts may hamper motor function despite maintenance of adequate motor cell function in the CST [44]. Use of SSEPs also has the drawback that ischemia in the anterior spinal region that supplies the motor tracts may not be reflected in the posteriorly located SSEP tracts. Thus, the differences in arterial blood supply, AntSA versus PostSAs, produce a differential vulnerability to ischemia. Hence, the loss of the SSEP and MEP acts as a surrogate for the entire functional aspect of the spinal cord.

The progression of spinal cord ischemia after TAA interventions can frequently be identified by IOM and arrested before irreversible infarction results [27]. This spinal cord rescue depends on the early detection and immediate multimodal intervention to maximize spinal cord oxygen supply. The routine application of IOM in TAA repair remains controversial, although many operative teams have successfully integrated it into their practice [15]. Some studies show a significant role of MEPs during TAA repair and the subsequent surgical strategies necessary to maintain or regain spinal cord function, leading to significantly reduced paraplegia rates [45]. The recent American College of Cardiology/American Heart Association Guidelines for the Diagnosis and Management of Patients with Thoracic Aortic Disease indicate that motor- or somatosensory-evoked potential monitoring can be useful when the data will help to guide therapy (CLASS IIa, *Level of Evidence: B*) [16]. Protocols to guide therapy include those

mentioned above (e.g., CSF drainage, increase in mean arterial and distal aortic pressure, reattachment of intercostal arteries) [45].

Endovascular Stent Placement

Although open surgical repair is the superior technique, thoracic endovascular aneurysm repair (TEVAR) avoids subjecting patients whose comorbid conditions predispose them to significant morbidity or mortality to the open procedure (especially a thoracotomy) [46]. Endovascular grafting may be of particular value in patients with significant comorbid conditions (older age, substantial cardiac, pulmonary, and renal dysfunction) who would be considered poor or unacceptable candidates for open surgery [16]. Recommendations from the American College of Cardiology/American Heart Association Guidelines for the Diagnosis and Management of Patients with Thoracic Aortic Disease are that in patients with degenerative or traumatic aneurysms of the descending thoracic aorta exceeding 5.5 cm, saccular aneurysms, or postoperative pseudoaneurysms, endovascular stent grafting should be strongly considered when feasible (CLASS I, *Level of Evidence: B*) [3, 16].

The potential advantages of endovascular grafting include the absence of a thoracotomy incision and the need for partial or total extracorporeal circulatory support and clamping of the aorta. This procedure also has the advantage of a shorter ischemic time for distal tissues. In addition, several factors increase the blood flow reserve of the spinal cord during the perioperative period. These include (1) an increased cardiac output, (2) increased blood pressure, (3) avoidance of hypoxemia and anemia, (4) preservation of the critical intercostal arteries, and (5) reduced CSF pressure [21, 47].

The clinical advantages of endovascular stent placement have been stated to include shorter intensive care unit and hospital stay, lower 30-day mortality, fewer pulmonary complications, reduced pain, and reduced transfusion requirements [46, 48]. For example, 50 % of patients have chronic obstructive pulmonary disease, and the reduced pulmonary complications associated with stent placement improve the likelihood of hospital discharge [46].

However, endovascular treatment of TAAs is significantly more complex due to the need to incorporate visceral arteries in the repair at the same time that the aneurysm is excluded. One major problem with the endovascular

techniques is the limited ability to provide vascular supply to blood vessels originating from the aorta in the region of the stent. This has led to stents with branches or fenestrations to provide a means to supply vessels such as the renal or mesenteric arteries [46]. The stents have not, however, been well developed for providing flow to the ARM or critical radicular arteries, such that spinal cord ischemia could occur if these vessels are compromised and are essential. These stents may require 4–6 weeks of manufacturing time, making them less useful in an emergency or for an urgent repair [15].

Several factors may limit the ability to use TEVAR in an individual patient. These include the absence of suitable “landing zones” above and below the aneurysm (usually 2–3 cm of normal diameter aorta without circumferential thrombus for the stent to attach), an aortic width at the landing zones that exceeds the recommended width for the largest available endovascular grafts (generally 10–15 % larger than the width of the aorta), a lack of vascular access sites, and severe aortic atherosclerosis [3, 16].

The disadvantages of TEVAR include late complications, which are uncommon with the open technique (graft migration, stent fracture, endovascular leaks, and stent failure necessitating surgical correction) [48]. In addition, TEVAR is associated with increased risk of atheroembolic stroke and retrograde type A dissection (especially in patients with fragile aortic wall) [49].

Although the complications of the open portion of the procedure are reduced, there is evidence that endovascular treatment of TAAs, similarly to open repair, carries the same risks of paraplegia, renal failure, stroke, and death [15]. High-risk factors of spinal cord injury during endovascular aortic repair are (1) coverage of the left subclavian artery, (2) extensive coverage of long segments of the thoracic aorta, (3) prior downstream aortic repair, (4) compromising important intercostal (T8–L1), vertebral, pelvic, and hypogastric collaterals, and (5) an aorta prone to give off atheromatous emboli [47].

The literature on the endovascular technique appears to report a lower than expected incidence of paraplegia when compared with open procedures [50–52]. Although patient selection may account for this, several other reasons may explain a lower risk of paraplegia, including the absence of opening or cross-clamping of the aorta, greater hemodynamic stability, and a “backwash” through the false lumen to the critical radicular arteries from the distal end of the stent. These events can contribute to increased obstruction of

the relevant vessels during and after the procedure [50, 52].

With deployment of a stent, the problem of ischemic injury is made more difficult because it is difficult to evaluate for critical radicular arteries and impossible to reimplant these arteries. Consequently, paraplegia has been described as a complication of endovascular stent placement [53]. Test occlusion prior to permanent stenting can be a valuable method for changing the management approach [54, 55]. Hence, sacrificing the critical intercostal arteries is inevitable with TEVAR. Therefore, many cases in spinal cord injury have an incomplete and delayed appearance as compared with open aortic surgery [47, 56].

Including the delayed spinal cord injury, the incidence of spinal cord injury averages 3–5 % with TEVAR [47]. There are no data that conclusively demonstrate that the prevalence of spinal cord injury is less for endovascular approaches than for open surgical repair [16]. Studies of IOM in endovascular procedures have shown that neurophysiological monitoring has been viewed as an effective method to detect spinal cord ischemia [40].

Hence, the major advantage of TEVAR relates to medical issues and the surgical risk of the open procedure [48]. Unfortunately, recent evaluations have suggested that endovascular therapy may not be effective [18]. Further, one fundamental concern remains to be evaluated with endovascular procedures [18]. This is that stents normally are designed to prevent the walls of the vessels and atheroma from collapsing into and occluding the vessel. However, with vessel dissection and aneurysm formation, the potential problem is that the stent is inside the vessel and may not effectively prevent the vessel walls from expanding. The impact of this may take some time to be fully evaluated. Clearly, more studies and long-term follow-up are needed.

Hybrid Techniques

As mentioned previously, one major problem with endovascular procedures is providing adequate vascular blood supply to organs below the diaphragm. In an effort to avoid some of the disadvantages of the open procedure and take advantage of the endovascular approach, hybrid procedures have been developed with an open procedure followed by endovascular stenting. Depending on aneurysm morphology, the hybrid repair consists of three steps: an optional infrarenal repair, extra-anatomic debranching of renovisceral vessels, and deployment of stent grafts [57].

Although this removes the need for thoracotomy and high aortic cross-

clamping with its significant morbidity, the morbidity of the open stage of the procedure remains high, so it is reserved for high-risk open surgical candidates [15, 57, 58]. To date, insufficient data are available to comment on the risk of neurological injury.

IOM Techniques During Thoracic Aortic Aneurysm Surgery

A variety of monitoring techniques have been used for thoracic aortic aneurysm repair :

1. Cortical SSEPs can be used to assess transmission in the white matter of the dorsal columns to detect spinal cord ischemia. They can also detect cortical ischemia and unfavorable circumstances in the arms and legs relating to positioning (arms) and perfusion of the legs (if occluded by a distal bypass).

2. MEPs recorded as muscle responses (CMAPs) are desirable to assess the transmission in the anterior white matter motor tracts. Their use will also assess the grey matter. They may also detect peripheral ischemia in the legs secondary to the distal bypass

3. Use of the H Reflex can be used in conjunction with MEPs (or as a replacement if conventional MEPs cannot be obtained). Its use assesses the peripheral nerves, spinal grey matter reflex pathways, and will be sensitive to a cross-sectional spinal cord injury cephalad to the grey matter involved in the reflex.

4. Electroencephalogram (processed or raw) can be used to assess the anesthetic effects on the cerebral cortex and detect ischemia in the brain.

Presentation of Case 1

The patient is a 67-year-old woman who presents for endovascular stenting of her thoracic aorta. She is obese (120 kg) and has a history of smoking (40

pack-years) and hypertension. She takes metoprolol and amlodipine. She has limited exercise tolerance (cannot climb a flight of stairs due to shortness of breath). She is allergic to intravenous radiographic contrast agents. She presented with a lower thoracic stabbing pain that was associated with a distal penetrating ulcer in the lower thoracic aorta. In addition, a more proximal region of the aorta was dilated to 5 cm.

She was brought to the interventional suite and general anesthesia was induced with propofol (200 mg), fentanyl (200 μg), and succinylcholine (100 μg). After the trachea was intubated using a double-lumen endotracheal tube, anesthesia was maintained using a propofol infusion (150–175 μg/kg/min) and sufentanil infusion (0.3–0.8 μg/kg/min).

Mean blood pressure was maintained between 75 and 80 mmHg using phenylephrine, hydralazine, nitroglycerine, and adjustments to the anesthetic infusions. Heart rate was maintained at 50–55 beats per minute. Neurophysiological monitoring included processed EEG, cortical somatosensory-evoked responses from median nerve and posterior tibial nerve stimulation, and transcranial motor-evoked potentials recorded from muscles in the hand (adductor pollicis brevis) and lower extremities (anterior tibialis and abductor hallucis).

An initial pelvic angiogram revealed that her femoral artery was only 7 mm in diameter, which was too small for the percutaneous placement of the 9 mm stent, so a surgical cut down was done in the left common iliac artery. To facilitate this exposure, muscle relaxation was instituted (vecuronium, 10 mg). At this time, the MEPs in all extremities were lost and the SSEPs were unchanged (Fig. 40.2a). The MEP responses returned but at a lower amplitude as the muscle relaxation decreased. Following placement of the sheath into the iliac artery, the pulse and the MEPs from the left leg were lost. The SSEPs from the left leg were markedly diminished over the next 20 min (Fig. 40.2b). Two endovascular stents were placed through the iliac artery to the aorta to cover the dilated aorta and the ulcerated region. The mean blood pressure was decreased to 64 mmHg to determine if the stent would stay dilated against the aortic wall. Two small doses of muscle relaxant (two additional 2-mg doses of vecuronium) were given to facilitate closure of the iliac artery access site. The procedure completed uneventfully with return of adequate pulses and the SSEPs and MEPs from the left leg after repair of the arteriotomy. She awakened from anesthesia without neurological deficit and was discharged to home on the fifth postoperative day.

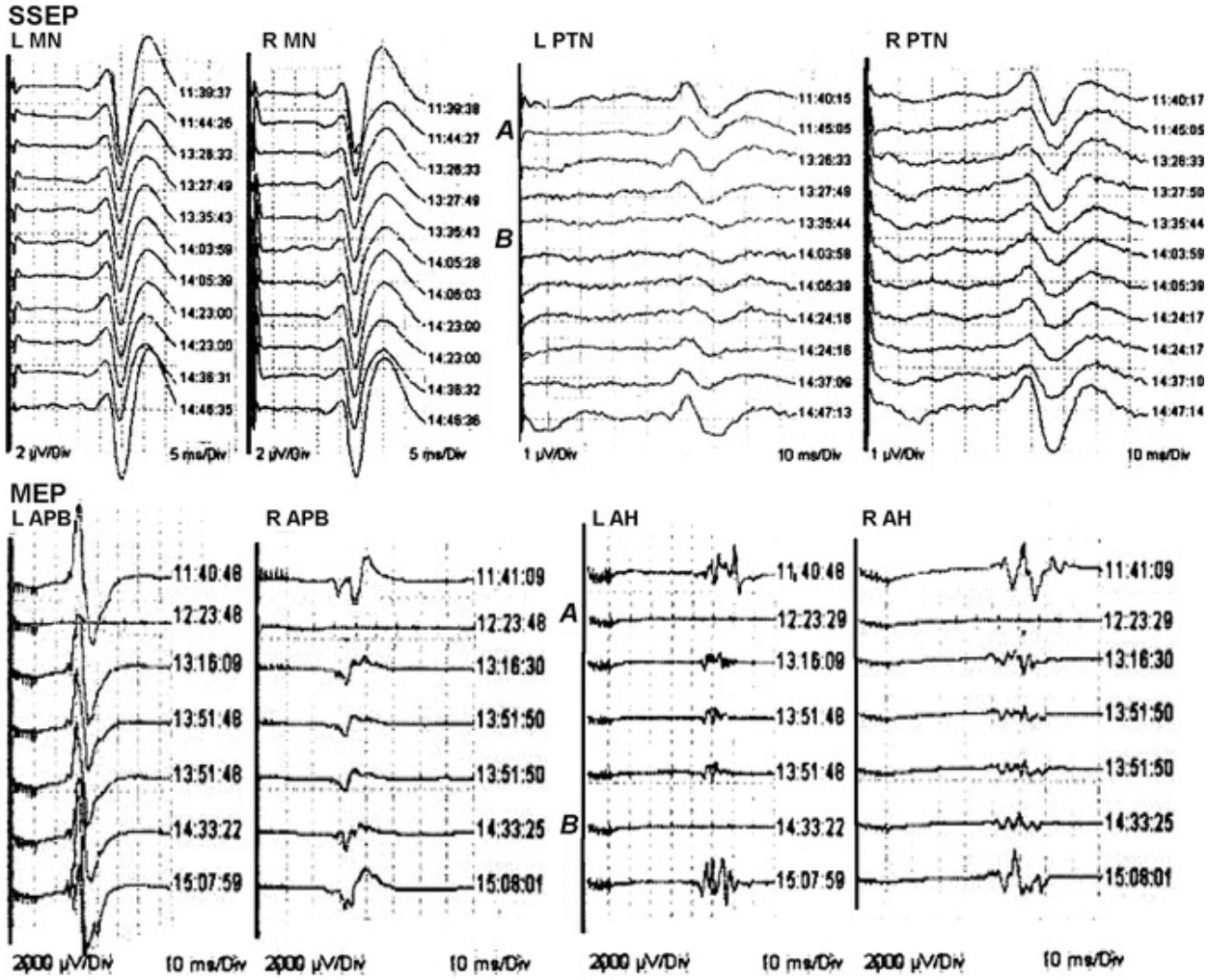

Fig. 40.2 Shown are the SSEP (*upper panel*) and MEP (*lower panel*) tracings for Case 1. Selected SSEP recordings (*upper panel*) are shown at various times as recorded from stimulation of the *left* (*L*) and *right* (*R*) median (MN) and posterior tibial (PTN) nerves. The lower panel shows selected MEP tracings at various times as recorded after transcranial stimulation from the *left* (*L*) and *right* (*R*) adductor pollicis brevis muscles in the hand (APB) and the abductor hallucis muscles (AH) in the lower extremity. (**a**) Indicates recordings shortly after neuromuscular paralysis was instituted. (**b**) Indicates the time when blood flow to the left leg was occluded during the procedure

Discussion

For the global loss of the MEPs during exposure of the iliac artery, the loss is most likely due to the delivery of muscle relaxants by the anesthesia team. Certainly, this loss could be caused by the delivery of additional anesthetic agents (e.g., inhalational agents or a large dose of propofol), but these were not given. At this time, the anesthesia was being delivered by constant infusions, which had not changed. A global loss of MEPs could be caused by

technical issues such as a loss of stimulation, loss of a stimulating electrode, or stimulator failure. However, maintenance of the stimulation artifact in the responses and examination of the machine and scalp suggested that these were not the explanation. The physiology of the patient such as temperature and blood pressure also had not changed, suggesting that this was not the cause. Finally, the surgery had not begun at this time, suggesting that it was unlikely that the interventional maneuvers were the cause of the change unless anaphylaxis to the intravenous contrast had ensued (at which time the SSEP would likely have been lost as well). Hence, the loss was ascribed to the muscle relaxant, and the responses returned as the muscle relaxant effect was diminished by time or the use of neuromuscular block reversal agents (neostigmine or Sugammadex). It is important to note that the train-of-four (TOF) responses measured in the hand or face may not reflect the degree of muscle relaxation in the leg. This is because different muscle groups can be affected differently by the same dose of muscle relaxant, and, in this case, the change in blood flow to the leg could alter the pharmacokinetics in that leg. Hence, the monitoring team should be monitoring a TOF from the monitored muscles. Of note, the MEPs were not lost at closing when additional small doses of muscle relaxant were given. This is consistent with the ability to acquire MEPs under partial paralysis when the responses are robust, but it does reduce the sensitivity to ischemia (which would have been less likely at this time since the stent had already been deployed for some time).

The loss of the SSEPs and MEPs from the left leg that happened during the placement of the sheath in the iliac artery was most likely due to the decrease in blood flow to the leg consistent with the loss of activity in the pulse oximeter in the toe and loss of pulses in that extremity. Anesthesia changes would be unlikely since anesthesia effects would most likely be global and MEPs would more likely be affected than SSEPs. Because numerous electrodes are involved in stimulation and the recording of both the SSEP and MEP (two muscles) responses, it is unlikely that a technical cause was the reason for their loss. With respect to surgery, the only surgical procedure at this time was the sheath placement in the femoral artery such that other surgical causes would be unlikely. Finally, other physiological changes, such as hypothermia in the one leg, would be unlikely to have had such an abrupt onset. Since the responses returned when the flow was restored to the leg, this confirms that the occlusion of the iliac artery by the sheath was the cause. Unfortunately, this loss of responses prevented the

SSEPs and MEPs from this leg from being used as a monitoring tool during the stent deployment and only the right leg was available.

Presentation of Case 2

The patient is a 56-year-old woman who presents for TEVAR . She has a history of hypertension and dyslipidemia and has a BMI of 20. She underwent a repair of an aortic coarctation at age 19. The patient developed acute heart failure and inadequate distal perfusion 2 weeks prior to the current events. Imaging revealed pseudoaneurysm of aortic graft and pseudoaneurysm of the thyrocervical trunk. A carotid-subclavian bypass was performed 3 days before in preparation for TEVAR. On the day of surgery, the patient is alert and oriented. She has limited exercise tolerance. Motor strength and sensation are preserved in the upper and lower extremities.

She was brought to the interventional suite. General anesthesia was induced with propofol (120 mg), fentanyl (200 μg), and rocuronium (30 mg). After intubation, propofol infusion (125–150 μg/kg/min) and sufentanil infusion (0.2–0.6 μg/kg/h) were started for maintenance of anesthesia. Anesthetic agents and vasoactive medications were adjusted to obtain a mean blood pressure between 70 and 80 mmHg and a heart rate between 50 and 60 bpm. Neurophysiological monitoring was planned and consisted of processed EEG, cortical SSEPs elicited by median nerve and posterior tibial nerve stimulation, and transcranial MEPs recorded from muscles in the hands (adductor pollicis brevis), legs (anterior tibialis), and feet (abductor hallucis). The procedure started with appropriate neurophysiological monitoring responses. During deployment of the endovascular graft, there was a sudden rupture of the proximal segment of the pseudoaneurysm. Within a few minutes, the patient arrested. Surgery was converted into an open thoracoabdominal procedure. During arrest, the EEG became silent and the SSEP and MEP signals rapidly disappeared. After aggressive resuscitation and surgical repair, the patient was stabilized and the neurophysiological signals started returning (Fig. 40.3a, b). A week later, the patient's neurological exam was normal. No sensory or motor deficits were detected.

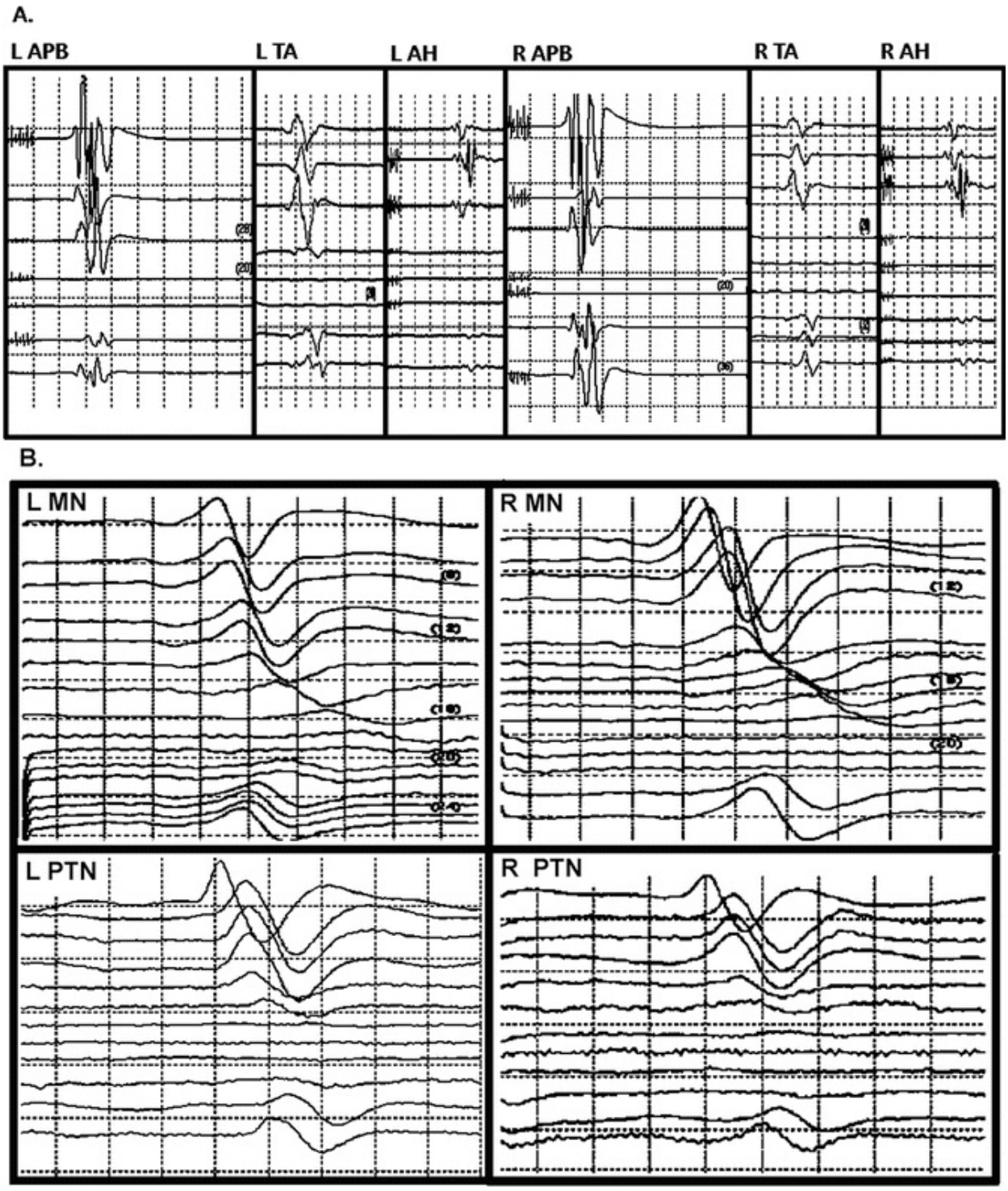

Fig. 40.3 Shown are the MEP and SSEP tracings for Case 2. (**a**) Motor-evoked potential tracings recorded after transcranial stimulation of *left* (*L*) and *right* (*R*) adductor pollicis brevis (APB) muscle in the arm, tibialis anterior (TA) muscle in the leg and abductor hallicus muscle in the foot. Signals in *red* show traces at baseline. From top to bottom, tracing shows progression of the case from adequate neurophysiological responses to absence of responses during cardiac arrest and returning of signals after surgical repair and stabilization. (**b**) Somatosensory-evoked potential tracings detected after

stimulation of the *left* (*L*) and *right* (*R*) median nerve (MN) for the upper extremities and posterior tibialis nerve (PTN) for the lower extremities. Traces showed adequate neurophysiological signals at baseline (traces in *red* at the top) and progression to the absence of signals during cardiac arrest. At the bottom of each image, returning of signals can be seen

Discussion

In this patient with an intact neurological exam before surgery, it was expected that the somatosensory- and motor-evoked potential signals would be adequate at baseline. If appropriate responses are not obtained when they are expected, a judicious approach should be done to identify the reason for the unexpected responses. For example, the use of neuromuscular blockers to facilitate placement of the endotracheal tube eliminates or decreases motor-evoked potentials. A TOF could help understand this situation. The use of inhalational agents by the anesthesia team and physiologic changes like hypotension could also affect both the somatosensory- and motor-evoked responses with the motor-evoked potentials being more susceptible. Technical problems like stimulator failure or the accidental loss of the stimulation electrode during positioning and preparation are also possible.

After the proximal segment of the aneurysm ruptured in this case, the rapid decline of neurophysiological responses was witnessed until a complete loss was recorded after cardiocirculatory arrest. The complete absence of neurophysiologic signals correlated with the lack of perfusion in different organs during arrest, including the brain and spinal cord. The fact that the EEG, somatosensory-, and motor-evoked potential signals declined rapidly and disappeared simultaneously indicates what was also evident clinically; it was not due to changes in the anesthetic regimen or temperature—it was directly related directly to the surgical emergency. Note that the MEPs declined more rapidly than the SSEP. The return of signals was reassuring that the resuscitation was effective.

In open and endovascular procedures, the role of IOM is to identify spinal cord regions that are ischemic before the damage to the tissues is irreversible. It also helps guide the effect of the different interventions to correct the ischemia. In this particular situation, IOM was helpful in detecting the integrity of the neurological system before intervention and providing information about the return of perfusion to the different organs by detecting the return of the somatosensory- and motor-evoked potentials and also brain activity when the patient was becoming stable. Symmetry in the responses was considered when analyzing the signals as they returned since asymmetric

responses (e.g., no somatosensory and/or motor responses obtained from one side of the body, or an asymmetric EEG) suggest a residual ischemic event in the brain.

Questions

1. Paraplegia results from a variety of mechanisms that include

    A. High CSF pressure

    B. Generalized ischemia

    C. Inadequate distal perfusion pressure

    D. Loss of critical radicular arteries

    E. All of the above

2. The blood supply of the aorta is thought to be a meshwork of vascular collaterals. Which of the following is not a critical component?

    A. Vertebral artery

    B. Subclavian artery

    C. Segmental arteries from the aorta

    D. Artery of Adamkiewicz

    E. Lumbar Arteries

3. When MEPs deteriorate, all of the following maneuvers may be helpful EXCEPT:

A. Raise the proximal mean blood pressure

B. Raise the distal mean pressure from the bypass bump

C. Reimplant a critical radicular artery

D. Lower the CSF pressure

E. High-dose methylprednisolone

4. Various methods of surgery have been utilized to repair TAA. The lowest risk of paralysis is with:

A. Open surgical repair

B. Endovascular repair

C. Hybrid techniques

D. All are about the same

5. Time to electrical failure with spinal cord ischemia is shortest with:

A. EEG

B. Cortical SSEP

C. Spinally recorded SSEP

D. The MEP D wave

E. Muscle-recorded MEPs

Answers

1. E

2. B

3. E

4. D

5. E

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Footnotes

1 Asterisk indicates key reference.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_41

41. Monitoring During Cardiopulmonary Bypass

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Keywords Multimodality neuromonitoring – Cardiopulmonary bypass – Neuroprotection – Surgical – Neurologic injury

Key Learning Points

- Since brain injury during cardiopulmonary bypass is multifactorial, optimal neuroprotection is best achieved with multimodality neuromonitoring .
- Multimodality neuromonitoring permits patient management to be individualized rather than guided by recipe.
- Perfusion cannulae misadventures may result in neurologic injury via hypoperfusion, hyperperfusion, or embolization.
- The nonphysiologic characteristics of extracorporeal circulation including hemodilution, nonpulsatile perfusion, cooling, and rewarming also represent sources of neurologic injury.

Introduction

Despite the dramatic advances in myocardial preservation during cardiac surgery, brain injury remains a common and serious complication [1]. Although myocardial revascularization may be achieved on a beating heart, the majority of these surgeries, as well as all open-heart surgery, require the use of cardiopulmonary bypass (CPB) . The brain injury may be either diffuse or regional, with sequelae ranging from encephalopathy or stroke to subtle cognitive decline or disruptive personality changes [1]. Injury mechanisms include embolization, hypoperfusion, hyperperfusion, systemic inflammatory response, and hyperthermia [1]. Furthermore, two or more of these mechanisms may coexist. For example, hypoperfusion can exacerbate particulate or gaseous embolic injury by reducing the clearance of particulates or gas bubbles from the cerebral microcirculation [2].

Temporary removal of the heart and lungs from the systemic circulation and the processes of extracorporeal circulation and oxygenation create many opportunities for a surgical misadventure. Traditionally, management of perfusion and oxygenation has been based on systemic measures, normative values, and standardized patient management protocols. Since systemic physiologic monitors reflect average values obtained from a patient total vascular bed length that may exceed 50,000 miles [3], it is not surprising that brain-specific hypoperfusion or dysoxygenation may be undetected. The following case report exemplifies this phenomenon. The report also illustrates the benefits of multimodality neuromonitoring in promptly detecting cerebral hypoperfusion and guiding its successful correction.

Causes of Injury During CPB and Neural Structures at Risk

The possibility of central nervous system injury begins before CPB initiation. Extracorporeal circulation is achieved via perfusion cannulae placed in major arterial and venous access points. Before or after CPB, cannula malposition may critically obstruct blood flow to or from the brain, spinal cord, and/or peripheral nerve, depending on the site of cannula placement [4]. In addition, during CPB, a malpositioned inflow cannula may direct the flow jet away from cerebral vessels and lead to regional or global brain ischemic injury [5].

Alternatively, the flow jet may be directed into the opening of a single cerebral artery with the risk of hemorrhagic hyperperfusion.

The perfusion cannulae and cardiac vents also pose a risk of embolic injury. Cannula introduction into a diseased aorta may dislodge atheromatous material into the cerebral circulation. During high-flow CPB, intra-aortic negative pressure is created at the aortotomy site. Consequently, an imperfect purse string suture around the cannula may permit air introduction into the cerebral circulation. Vent suction, negative venous pressures, and perfusionist administration of drugs and fluids may also introduce air into the extracorporeal perfusion circuit [6].

The circuit priming solution may be either blood based or a clear crystalloid solution. Particularly in the case of a bloodless prime and small patient, significant hemodilution may occur that can compromise adequate O_2 delivery to the brain while systemic oxygenation remains within an acceptable range. If a hematogenous prime solution utilizes stored whole blood or red cells, brain O_2 debt may still develop despite near-normal hematocrit and hemoglobin concentration. The debt is the result of storage-induced erythrocyte dysfunction [7].

Nonpulsatile perfusion poses a potential risk to the cerebral cortical watershed areas and midbrain structures nourished by long, tiny lenticulostriate perforating arteries [8]. Injury risk is further heightened because blood is a non-Newtonian liquid with the flow characteristics of a Bingham fluid (i.e., viscosity is inversely related to flow velocity) [9]. Thus, with unchanged systemic mean perfusion pressure, the peak blood flow velocity reduction that typically accompanies nonpulsatile perfusion may compromise oxygen delivery in these vulnerable brain regions. Functional magnetic resonance imaging (MRI) has allowed visualization of this CPB-induced multifocal brain hypoxia [10].

In the absence of multimodality neuromonitoring , anesthesia providers and perfusionists have traditionally relied on systemic perfusion pressure as a guide to the adequacy of brain perfusion. This reliance spawned the pervasive concept of “brain-safe” perfusion pressure . It is based on the widely held assumptions that (1) the lower autoregulatory limit is 50 mmHg and (2) nearly all patients maintain cerebral pressure autoregulation during CPB. It should be recognized that evidence of intact autoregulation assures only that cerebral perfusion and oxygenation are pressure independent. No assurance is given regarding the adequacy of perfusion to prevent brain O_2 debt. Thus,

moderate hypocapnia may sustain autoregulated cerebral blood flow at a low level insufficient to meet the local brain O_2 needs [11].

Pharmacologic considerations also influence the role of suboptimal blood pressure management in the genesis of iatrogenic brain injury during CPB. The relationship between systemic pressure and cerebral perfusion is unpredictable. Thus, in the absence of neuromonitoring, brain perfusion and oxygenation in response to administration of vasoactive agents is undefined [12].

Variable brain response to blood pressure change should be expected. Blood pressure increases within a patient's individualized autoregulatory range typically result in an unchanged brain O_2 saturation [13]. In contrast, when baseline pressure is lower than the individual's autoregulatory lower limit, brain O_2 saturation becomes pressure dependent [13]. Should cerebral vascular resistance increase more than systemic resistance, blood pressure increase will be accompanied by a brain saturation decrease. Only appropriate neuromonitoring can distinguish among these possibilities for a given patient [13].

Iatrogenic brain injury during CPB may also result from suboptimal cooling for deep hypothermic neuroprotection. The large interpatient variation in brain response to cooling is exemplified by the extraordinarily wide 10 °C range of cranial temperatures associated with the onset of hypothermic electrocerebral silence [14]. In patients with CO_2 $^-$ reactive cerebral arteries, cooling with alpha-stat acid–base management may result in incomplete and nonuniform brain cooling and brain O_2 debt [11]. Alternatively, the higher blood flow achieved with pH-stat management leads to uniform cooling and cerebral hyperoxia [15]. A randomized clinical trial has demonstrated the superiority of pH-stat management for deep cooling [16]. Although many cardiac centers shift to alpha-stat during rewarming to hopefully expedite the return of autoregulation, this approach currently is without the support of randomized clinical evidence (*see* Chap. 39, "Surgery of the Aortic Arch").

Case Description

This 3-year-old, 15-kg ASA Class 3 patient underwent surgical repair of both a cardiac ventricular septal defect and subaortic stenosis via a median

sternotomy. Anesthesia was induced with sevoflurane and maintained with isoflurane and fentanyl/midazolam supplements. Near-normothermic nonpulsatile CPB was achieved with an inflow cannula placed in the ascending aorta and outflow cannulae in both the ascending and descending venae cavae. A blood prime was used to limit hemodilution.

The surgery was uneventful during the prebypass and bypass phases. However, immediately after discontinuation of CPB, sudden suppression of all neuromonitoring modalities suggested development of a major brain insult, despite unchanged respiratory gas and volatile anesthetic concentrations, systemic perfusion pressures, arterial and mixed venous oxygenation, and cranial temperature as well as an acceptable hemoglobin concentration. Nevertheless, neuromonitoring guided prompt identification and correction of the injury source, which resulted in an immediate restoration of cerebral cortical perfusion, oxygenation, and synaptic function.

Available Physiologic Monitors

Systemic arterial blood pressure was monitored continuously via the right radial artery. A 5-Fr. triple-lumen catheter inserted into the right internal jugular vein continuously monitored central venous and pulmonary artery pressures as well as cardiac output intermittently. During periods of pulsatile perfusion, systemic arterial oxygen saturation was measured continuously by pulse oximetry with a sensor on the right foot. In the presence of mechanical ventilation, inspired and end-tidal O_2, CO_2, and volatile anesthetic concentrations were monitored continuously. With nonpulsatile CPB, intermittent blood samples were obtained for determination of hemoglobin, hematocrit, arterial, and mixed venous blood gases.

Cerebral neuromonitoring consisted of (1) four-channel electroencephalography (EEG) (FP1-T7, FP2-T8, C3-O1, C4-O2) with bilateral frontal Bispectral Index (BIS®) trend (A-1000, Medtronic-Covidien, Boulder, CO) via gold cup electrodes; (2) bilateral frontal regional O_2 saturation (rSO_2) using the INVOS™ 4100 cerebral oximeter (Medtronic-Covidien, Boulder, CO) with pediatric sensors; and (3) right middle cerebral artery blood flow velocity with the TCD ultrasonography (NeuroGuard®, Medasonics, Fremont, CA). Cranial temperature was monitored with a thermocouple placed in the nasopharynx.

Monitor Noteworthy Changes

Approximately 2 min after CPB discontinuation, the EEG waveforms suddenly became totally suppressed (i.e., flat line). The density spectral array EEG trend display (Fig. 41.1 at 11:10) showed an abrupt diffuse loss of all high-frequency EEG activity and a drop in the total power amplitude measure. In addition, bilateral BIS values began a rapid fall from 65 to 30 scale units (Fig. 41.2, *upper traces*).

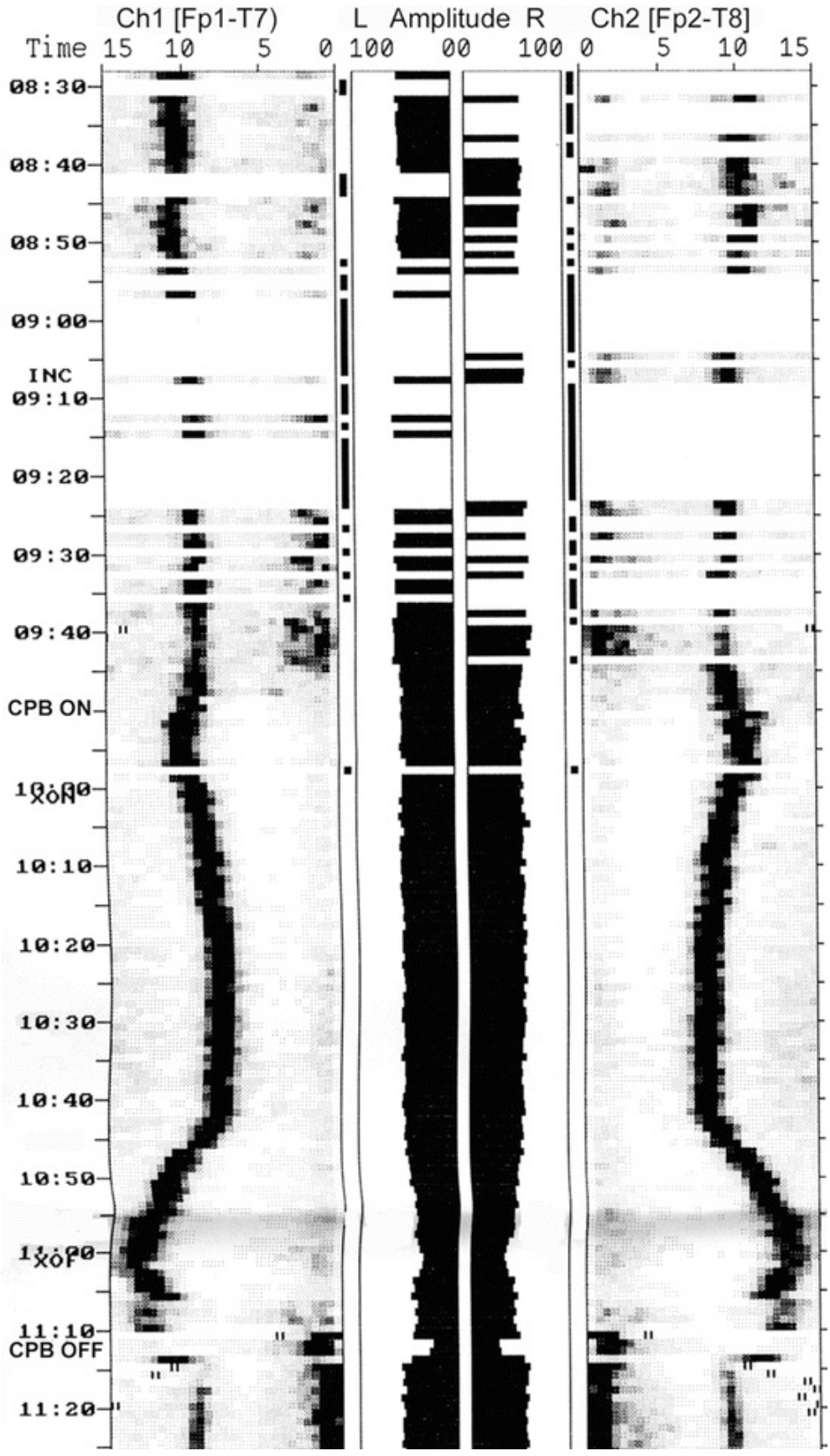
Ch1 [Fp1-T7)
L Amplitude R
Ch2 [Fp2-T8]
Time 15 10 5 0 100 00 100 0 5 10 15
08:30
08:40
08:50
09:00
INC
09:10
09:20
09:30
09:40
CPB ON
10:00
XON
10:10
10:20
10:30
10:40
10:50
11:00
XOFF
11:10
CPB OFF
11:20

Fig. 41.1 This EEG recording represents *left* (channel 1) and *right* (channel 2) frontotemporal trends of density spectral array (DSA) frequency and total power amplitude trends. Recording began following anesthesia induction and continued until 15 min after discontinuation of CPB. Signal loss from 8:55 to 9:25 was the result of electrocautery interference. Note the sudden bilateral loss of all high frequency EEG activity and total power decline at 11:10, immediately after CPB discontinuation. Also observe the rapid return of these measures following successful identification and correction of a potentially injurious physiologic imbalance

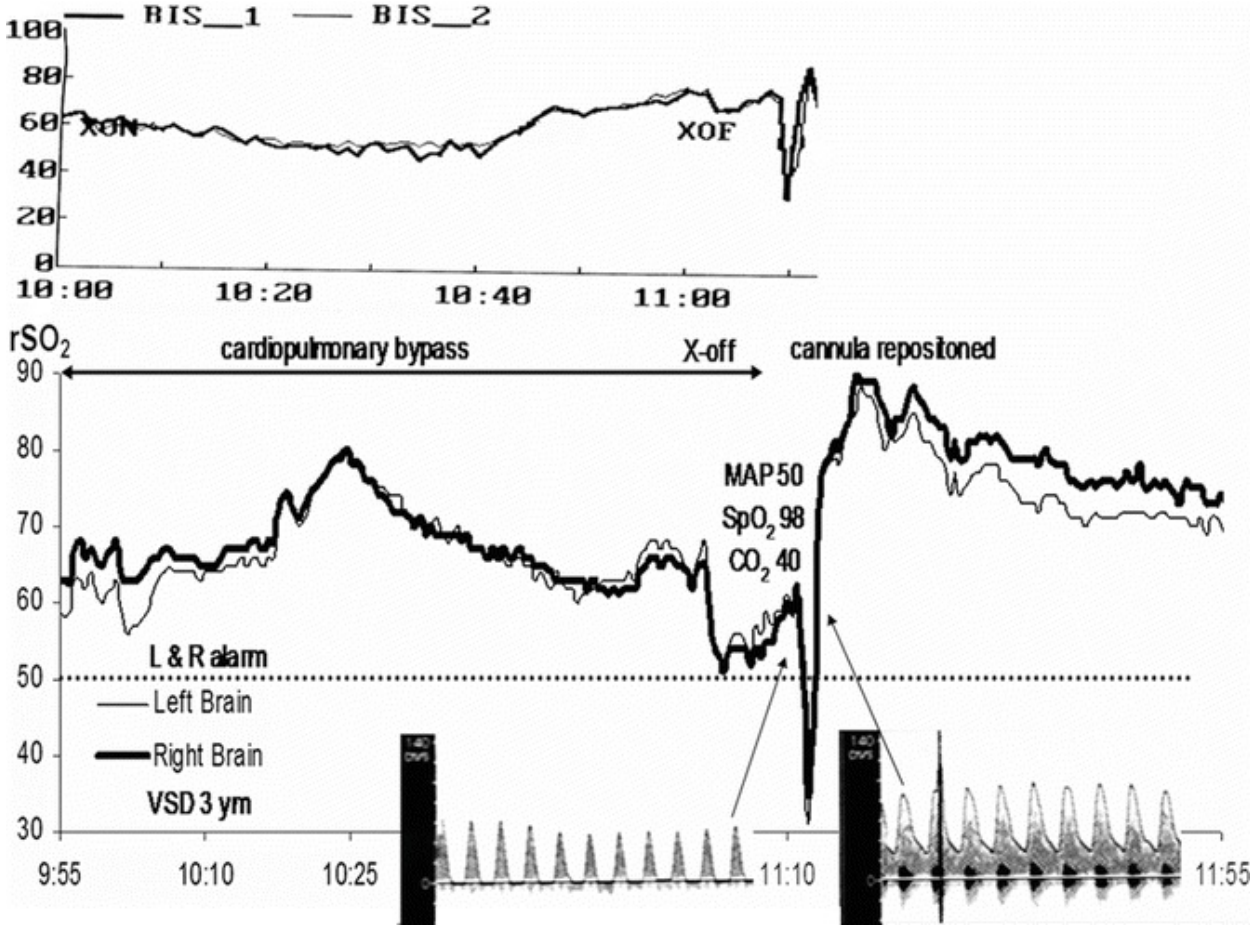

Fig. 41.2 Displayed are the multimodality neuromonitoring changes associated with developing physiologic imbalance and its prompt correction. The upper traces depicting a precipitous bilateral EEG Bispectral Index (BIS) suppression signify diffuse major cerebrocortical synaptic suppression of uncertain origin. Profound bilateral brain regional O_2 saturation (rSO_2) decline suggests developing brain O_2 debt as contributing to the EEG suppression. The suppressed TCD waveform in the *lower left panel* identifies the cause of the O_2 debt as an arterial inflow compromise. Repositioning of the aortic cannula resulted in an immediate recovery of all these measures

This major cortical synaptic suppression was accompanied by growing oxygen debt within the microcirculation of the same cortical regions. The

debt was manifested by a precipitous bilateral decrease in rSO_2 (Fig. 41.2, *middle traces*).

Lastly, TCD systolic and diastolic velocities fell from 100/40 to 50/0 cm/s (Fig. 41.2, bottom left waveform). Once the cause of the neuromonitoring changes was identified and corrected, all measures rapidly returned to their pre-insult appearance (Fig. 41.2).

Differential Diagnosis

Technical

The most important advantage of multimodality neuromonitoring is that it minimizes the possibility of misinterpreting a technical recording problem as a sign of nervous system injury. Thus, it is extraordinarily unlikely that a single technical problem would simultaneously produce apparent EEG suppression, brain oxygen desaturation, and diminished blood flow velocity. For example, EEG and TCD signals may be altered or suppressed by electrocautery and other sources of radiofrequency energy (Fig. 41.1). In contrast, because rSO_2 is based on near-infrared spectroscopy, it is typically immune to this interference. TCD is susceptible to environmental acoustic influences and both TCD and EEG may be altered by patient movement, but rSO_2 remains unaffected. Intense electromechanical radiation within the visible or near-infrared frequency spectra may disrupt rSO_2 monitoring but have no effect on the other modalities. Technical problems sufficient to affect all three modalities (i.e., electrical power fluctuations) would almost certainly also disrupt other monitoring and patient support devices.

Physiologic

EEG suppression unequivocally indicates a reduction in cortical synaptic activity, but the cause is often initially undefined. Suppression may reflect a relatively benign process, like excess hypnosis or hypothermia, or a malignant one such as hypoxia or ischemia. Because of this uncertainty, it was imperative that the cause of sudden EEG suppression be promptly identified.

In support of this notion, our group earlier examined the consequences of major EEG suppression in a cohort of 600 adult cardiac surgery patients managed with CPB [14]. EEG suppression was defined as a greater than 50

% decline in total power in at least 1 of 19 channels that persisted for longer than 10 min and was unrelated to either cooling or increased hypnosis. Twenty of the 22 patients awakening with new neurologic deficits experienced noteworthy intraoperative EEG suppression. There also were ten patients with comparable EEG changes but no postoperative neurodeficit. The odds ratio that a neurodeficit would be preceded by EEG suppression was 568:1 ($P < 0.001$). All the deficit-related EEG changes were widespread, involving frontotemporal cortex in at least one hemisphere. This experience also suggested that the vast majority of ischemia-related EEG changes could be identified using a simplified two- or four-channel electrode montage.

The sudden large decline in rSO_2 indicated developing brain O_2 debt, but neither its cause nor functional significance could be defined without additional information. In both adult [17] and pediatric [18] patients, low brain rSO_2 has been associated with signs of brain injury. However, in the absence of cooling or hypnotic increase, the combination of rSO_2 decline with EEG suppression reliably identifies a potentially injurious functionally significant brain O_2 imbalance [19].

TCD measures blood flow velocity, not flow [20]. Altered rheology (i.e., hemodilution, hemoconcentration, hypothermia) may thus affect velocity, while total erythrocytic flow remains unaltered. In addition, an abrupt reduction in both systolic and diastolic middle cerebral artery flow velocity may be due to either an actual blood flow decrease or an unrecognized subtle shift in ultrasound probe position. Nevertheless, in the absence of ultrasound probe movement, sudden velocity declines are highly correlated with hypoperfusion [20]. As with rSO_2 changes, the functional significance of a velocity decrease requires information on cortical synaptic activity (i.e., EEG).

TCD is very helpful for the causal determination of coupled EEG and rSO_2 declines. Ultrasound provides the only means to unambiguously detect a cerebral particulate or gaseous embolic shower [21]. In the present case, a lack of emboliform high-intensity transient ultrasonic signals and an unchanged TCD velocity trend suggested that neither embolization nor hypoperfusion was involved. Attention was then focused on impaired oxygen delivery.

During pre- and postbypass pulsatile perfusion, with stable systemic perfusion pressure and cardiac output, the nature of TCD waveform changes

permits discrimination between impaired cerebral arterial inflow and venous outflow. In the former case, both systolic and diastolic velocities fall [22], while in the latter only diastolic velocity decreases and the waveform becomes hyperpulsatile [23]. Sudden onset hyperpulsatility is suggestive of a venous cannula malposition, whereas a progressive onset is characteristic of expanding cerebral edema and intracranial hypertension [22].

Marked cerebral arteriolar constriction resulting from severe hypocapnia could produce all the neuromonitoring changes observed in this case. This explanation was discarded because hypocapnia also would have been manifested by low end-tidal CO_2 values.

Pharmacologic

Only severe cerebral vasoconstriction could conceivably lead to total EEG suppression, cerebral hypoperfusion, and oxygen debt. However, vasoconstrictor agents, typically used during cardiac surgery, act on both the systemic and cerebral circulations. Consequently, doses sufficiently high to constrict cerebral arterioles would also result in systemic hypertension. Thus, a pharmacologic etiology for the selective cerebral hypoperfusion and dysoxygenation appeared to be very unlikely.

Surgical

The sudden appearance of severe diffuse cerebral ischemia without systemic manifestations of hypoperfusion immediately directed attention to possible disruption of arterial inflow or venous outflow. In our experience, perfusion cannula malposition is an uncommon cause of cerebral ischemia during adult CPB [24]. However, the probability of its occurrence appears to be inversely related to patient size [14]. We have observed that nearly one-quarter of noteworthy neuromonitoring changes occurring during pediatric CPB are related to malposition of a perfusion cannula, vascular clamp, ligature, or vent [25].

Patient Management and Outcome

Since the diminished TCD waveform was most consistent with a cerebral inflow restriction, the malpositioned aortic cannula was repositioned. A seemingly small cannula reorientation immediately resulted in a normal TCD

waveform, rSO_2 increase, and EEG recovery. The remainder of the surgery and postoperative recovery was uneventful.

Conclusion

Clinical studies now have demonstrated that multimodality neuromonitoring may be associated with improved outcome and associated lower costs [26]. Thoughtful integration of the information provided by each modality helps to overcome the limitations of each independent modality.

Questions

With each of the following questions, indicate whether the statement is true or false.

1. During cardiac surgery, cerebral injury mechanisms may include embolization, hypoperfusion, hyperperfusion, systemic inflammatory response, and hyperthermia.

    a. True

    b. False

2. A malpositioned aortic perfusion cannula may result in potentially injurious cerebral hypo- or hyperperfusion.

    a. True

    b. False

3. Maintenance of mean arterial blood pressure within normal limits ensures adequate subcortical perfusion.

    a. True

b. False

4. Cooling the brain to less than 20 °C ensures maximal neuroprotection during planned circulatory arrest.

   a. True

   b. False

Answers

1. a
2. a
3. b
4. b

Disclosure

The author is a member of the Medtronic-Covidien Speakers' Bureau.

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Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_42

42. Interventional Neuroradiology

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Keywords Intraoperative neurophysiological monitoring – Neuroendovascular surgery – Neuromonitoring plan – Neuromonitoring – Anesthetic management – Motor-evoked potentials – Somatosensory-evoked potentials

Key Learning Points

- Intraoperative angiography affords repeated assessment of blood vessel patency during neuroendovascular surgery, but does not provide information about the functional integrity of neural structures fed by those vessels.
- There are limits to the resolution of angiographic imaging and unknown or varying neural tolerances for partial vessel occlusion.
- Intraoperative neurophysiological monitoring (IONM) complements

angiographic imaging by providing real-time functional information about at-risk neural structures, early warning of evolving iatrogenic neurologic compromise, and opportunity for timely intervention to avoid or mitigate new-onset postoperative deficits.

- A multimodality IONM strategy extends anatomic coverage for detection of isolated ischemic change and provides neurophysiologic monitoring redundancy in the context of common at-risk vascular supplies.

Introduction

Since the first reports describing endovascular treatment of cerebral arteriovenous malformations over 50 years ago [1], neuroendovascular technologies have continued to develop, advancing diagnosis of vascular abnormalities within the central nervous system, providing opportunities for treatment of previously inoperable brain and spinal cord lesions, and making possible minimally invasive alternatives for a variety of open neurosurgical therapies [2–4].

While neuroendovascular surgery arguably has improved the margin of safety over many open neurosurgical procedures, it is not without inherent risk. Introduction of arterial catheters within the brain; deployment of balloons, stents, or coils; and therapeutic embolization all have the potential for unintended compromise of vital blood supplies, which can result in temporary or permanent neurologic deficit. While the risk of neural injury secondary to hemorrhage or vascular occlusion remains low, the consequences of neurologic deficit are both broad based and significant.

Although intraoperative angiography affords repeated assessment of blood vessel patency during the course of neuroendovascular surgery, it does not provide information about the functional integrity of neural structures fed by those vessels. Moreover, there are limits to the resolution of this imaging technology, as well as unknown or varying neural tolerances for partial vessel occlusion that may be identified angiographically, and could impact negatively on neurologic outcome. Intraoperative neurophysiological monitoring (IONM) complements angiographic imaging by providing real-time functional information about at-risk neural structures. As such, it can add an additional margin of safety during neuroendovascular surgery by detecting evolving neural compromise and prompting timely intervention to

reverse or limit the extent of an untoward neurologic complication.

Neurophysiological monitoring during neuroendovascular procedures is a natural extension of neuromonitoring principles and methods developed for open surgical treatment of vascular lesions affecting the central nervous system [4–12]. In addition to early detection of evolving iatrogenic neural injury, IONM can play an important role during provocative testing of critical blood supplies using techniques such as temporary vessel occlusion or injection of amobarbital sodium or lidocaine [4].

As in traditional open surgical approaches, the neuromonitoring plan for neuroendovascular surgery must be based on careful preoperative assessment of potential risk to neural structures, consistent with that described for monitoring spinal cord and nerve root function [13]. The selection of appropriate monitoring modalities follows from this assessment, and successful implementation is highly dependent both on tailored anesthetic management and skilled, real-time interpretation of test results.

Neuromonitoring Plan

Assessment of risk begins with evaluation of the patient's pathophysiology and review of the treatment plan. A partial list of diseases amenable to endovascular therapy includes cerebral aneurysms; arteriovenous malformations within the brain, spinal cord, and dura; carotid artery stenosis; cerebral vasospasm; central nervous system tumors; intractable epistaxis; and thromboembolic stroke [14]. Injury to central neural structures during interventions such as coiling, embolization, angioplasty, stenting, and thrombolysis can occur from interrupted delivery of oxygen and nutrients to these tissues secondary to embolic occlusion of vessels, hypotension, vasospasm, and/or hemorrhage. Because this interruption may be restricted to particular anatomic regions, it is important to understand the regional specificity and sensitivity of each available neuromonitoring modality and to provide complementary cross-coverage using a multimodality monitoring approach. For example, multichannel electroencephalography (EEG) has proven to be highly sensitive to evolving cortical ischemia secondary to occlusion of the carotid artery, but is largely insensitive to subcortical ischemia [10, 15]. Complementing EEG are motor- and sensory-evoked potentials, which, respectively, reflect functional conduction along the length of specific descending and ascending pathways within the nervous system,

thereby extending neuromonitoring surveillance below the cortex.

Specifically, transcranial electric motor-evoked potentials (tceMEPs) , mediated by the corticospinal tracts [16, 17], allow for functional monitoring of descending motor fibers within the internal capsule, brainstem, and spinal cord, as well as associated spinal cord interneurons, alpha motor neurons, and peripheral motor nerves (*see* Chap. 2, “Transcranial Motor-Evoked Potentials”).

Likewise, somatosensory-evoked potentials (SSEPs) , mediated by ascending long tract fibers, can be used to monitor function of peripheral somatic nerve fibers, nuclei within the dorsal column-medial lemniscus pathway, somatic relay nuclei within the thalamus, ascending fibers within the internal capsule, as well as neurons within primary somatosensory cortex [18] (*see* Chap. 1, “Somatosensory-Evoked Potentials”). Brain stem auditory-evoked potentials, mediated by the auditory nerve, cochlear nucleus, superior olivary complex, and lateral lemniscus, allow for specific monitoring of brain stem structures when the posterior circulation of the brain is at risk [19] (*see* Chap. 3, “Auditory-Evoked Potentials”).

Adoption of a multimodality assessment strategy, therefore, not only extends anatomic coverage for detection of isolated ischemic change during neuroendovascular surgery but also can provide neurophysiologic monitoring redundancy in the context of common at-risk vascular supplies.

In addition to detecting evolving central nervous system deficit, IONM plays an important tangential role in protecting the patient from peripheral nerve injury and limb ischemia. In particular, positioning of the patient’s arms may place the ulnar nerve at risk of injury from compression and/or stretch. Ulnar nerve SSEPs and upper extremity tceMEPs have proven sensitivity for identifying such evolving injury during spine surgery [20, 21] and are an important monitoring adjunct during neuroendovascular procedures. Similarly, lower extremity tceMEPs and SSEPs are sensitive to lower limb peripheral nerve compression as well as ischemia from vascular occlusion related to the femoral artery sheath [22, 23] (*see* Chap. 41, “Monitoring During Cardiopulmonary Bypass”).

Anesthetic Management

The critical importance of proper anesthetic technique for effective neuromonitoring is often underappreciated. Use of volatile agents and nitrous

oxide can significantly depress amplitudes and increase variability of tceMEPs and cortical SSEPs, resulting in unreliable responses or even the inability to record viable signals [24–26]. In these situations, suboptimal anesthetic technique may call the value of IONM inappropriately into question.

Alternatively, a total intravenous infusion technique of propofol in combination with an opioid (e.g., remifentanil), supplemented by intermittent, low dose (1–2 mg) bolus of a benzodiazepine (e.g., midazolam), has been shown to provide an optimized anesthetic base for neurophysiological monitoring [24]. Alternative agents such as ketamine and etomidate are viable intravenous adjuncts that may be administered in place of or in combination with propofol, when the latter is either contraindicated or in short supply [27, 28].

Each of these total intravenous anesthetic protocols can be used to achieve and maintain desired anesthesia endpoints, including akinesis, without use of additional neuromuscular blockade beyond the preintubation dose. It is important to emphasize that use of partial neuromuscular blockade during neuroendovascular surgery will compromise monitoring of the corticospinal tracts both by reducing tceMEP amplitudes and introducing significant variability [29] (*see* Chap. 19, “General Anesthesia for Monitoring”).

Interpretation of Data

Effective neuromonitoring requires accurate and timely interpretation of recorded neurophysiological signals within the context of ongoing surgical manipulations as well as the patient’s global physiologic/anesthetic state. Functional neurologic changes can occur within seconds of vascular occlusion, which must be detected and communicated immediately to the surgeon and anesthesiologist in an effort to facilitate prompt intervention. For these reasons, the authors believe that it is imperative that an interpreting neurophysiologist be present in the operating room during neuroendovascular procedures, rather than exclusively at a remote site with only network access to the recorded data. In the event of a functional neurophysiological change, physical presence within the operating room allows for effective communication about the severity of evolving injury, discussion of possible proximate causes, and implementation of rescue intervention .

Case Studies

We reviewed 135 neuroendovascular procedures monitored by a single professional surgical neurophysiology practice over a 56-month period to assess incidence and type of neuromonitoring alerts and to evaluate efficacy of monitoring. Seventy-four percent of the procedures involved coiling of anterior circulation aneurysms and 16 % posterior circulation aneurysms. The majority of the remaining procedures addressed repair of arteriovenous fistulae or other classifications of vascular malformation.

Neuromonitoring alerts occurred in eight (5.9 %) of 135 procedures. Alerts were associated with iatrogenic vascular compromise in four (50 %) of eight cases. There were two cases of acute aneurysm rupture during catheter positioning, resulting in unilateral loss of tceMEPs in one and bilateral loss of both SSEPs and tceMEPs in the other. In both cases, anesthetic level was deepened rapidly with propofol bolus, using EEG burst suppression as a therapeutic target in an effort to reduce cerebral metabolic demand during emergent treatment to achieve hemostasis.

In a third case involving embolization of a carotid artery fistula , balloon occlusion of the right internal carotid artery produced unilateral loss of cortical SSEPs to stimulation of the left ulnar and left posterior tibial nerves, as well as attenuation of tceMEPs from bilateral lower extremities, as shown in Fig. 42.1. Here, the balloon was deflated immediately and mean arterial pressure elevated from 78 to 102 mmHg in an effort to restore adequate cerebral perfusion. All neuromonitoring changes resolved within several minutes of these interventions, and the procedure continued uneventfully.

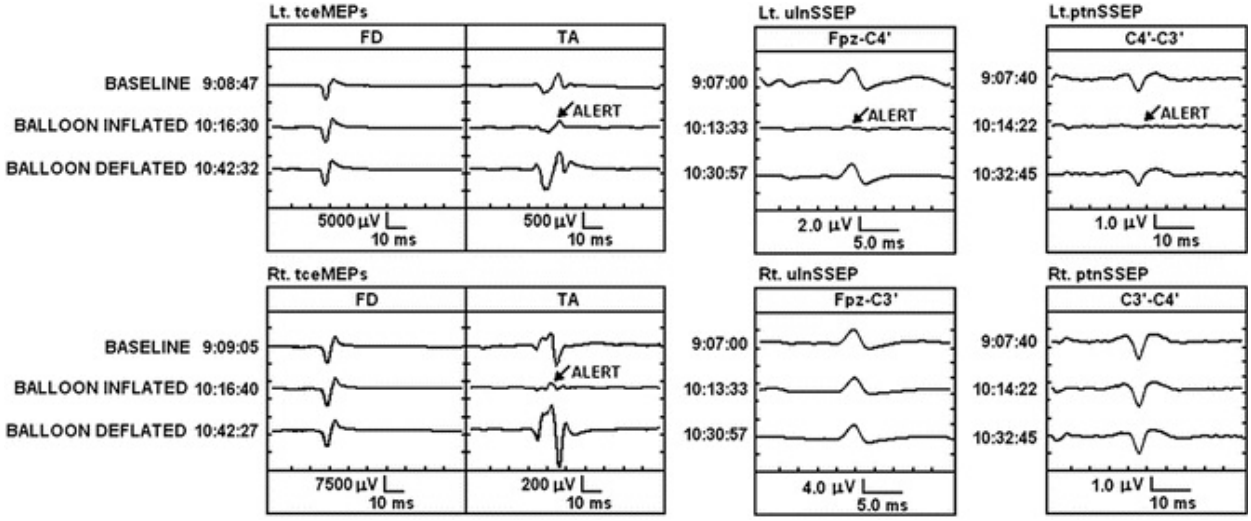

Fig. 42.1 Representative transcranial electric motor-evoked potentials , ulnar nerve somatosensory-evoked potentials (SSEPs) , and posterior tibial nerve SSEPs recorded during neuroendovascular surgery for embolization of carotid artery fistula. The *top* set of traces in each panel shows baseline-evoked potentials recorded during the early stages of the procedure. The *middle* set of traces shows evoked potentials during balloon occlusion of the right internal carotid artery. *Arrows* indicate significant amplitude attenuation of tceMEPs from left and right tibialis anterior muscles, as well as disappearance of cortical SSEPs to stimulation of the left ulnar and posterior tibial nerves. The *lower* set of traces in each panel shows full recovery of previously attenuated potentials following deflation of the balloon. *uln* ulnar nerve; *ptn* posterior tibial nerve; *FD* first dorsal interosseous muscle; *TA* tibialis anterior muscle; *Fpz*, *C3′*, *C4′* international 10–20 system designations for scalp recording electrode positions

The fourth instance of vascular compromise occurred during coiling of an anterior communicating artery aneurysm. Following placement of several coils, there was abrupt loss of tceMEPs from the right upper and lower extremities, as shown in Fig. 42.2. Responses from the left upper and lower extremities were unchanged from baseline, as were cortical SSEPs to interleaved stimulation of the left and right ulnar nerves, respectively. Cortical SSEPs to stimulation of the right posterior tibial nerve showed only a nominal, clinically insignificant 25 % attenuation from baseline, while those to stimulation on the left side were unchanged. Placement of additional coils was halted temporarily and an arteriogram performed. The arteriogram showed no embolic occlusion or evidence of obvious vasospasm at that time; however, it is not implausible that this acute right upper and lower myotomal tceMEP loss represented an early functional manifestation of developing vasospasm not yet appreciated on angiography. Following a brief surgical pause, tceMEPs on the right side reappeared and response amplitudes returned to baseline range. Placement of coils subsequently was resumed and completed successfully with no additional episodes of tceMEP amplitude attenuation.

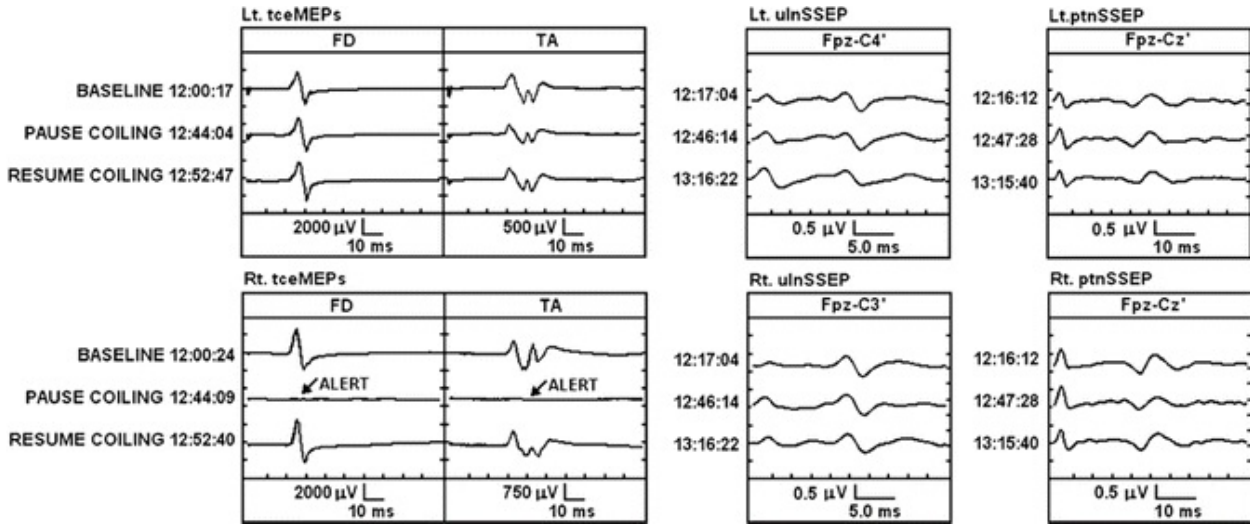

Fig. 42.2 Representative tceMEPs, ulnar nerve SSEPs, and posterior tibial nerve SSEPs recorded during neuroendovascular surgery for coiling of anterior communicating artery aneurysm. The *top* set of traces in each panel shows baseline-evoked potentials recorded during the early stages of the procedure. The *middle* set of traces shows evoked potentials following placement of several coils. *Arrows* indicate disappearance of tceMEPs from right first dorsal interosseous and tibialis anterior muscles at this time. The *lower* set of traces in each panel shows full recovery of previously attenuated potentials following a surgical pause and angiography to rule out vascular occlusion

Upper extremity positioning alerts occurred in five (3.7 %) of 135 procedures and typically involved compression of the ulnar nerve. In each case, repositioning of the affected arm resulted in prompt resolution of neurophysiologic changes, as shown in Fig. 42.3. During the early stages of the procedure, tceMEPs from left first dorsal interosseous (FD) muscle and cortical SSEPs to stimulation of the left ulnar nerve decreased in amplitude by greater than 60 % from baseline. At this time, there were no concomitant changes in any of the other tceMEPs, including those from left extensor carpi radialis muscle, which unlike the FD muscle is innervated by the radial and not the ulnar nerve.

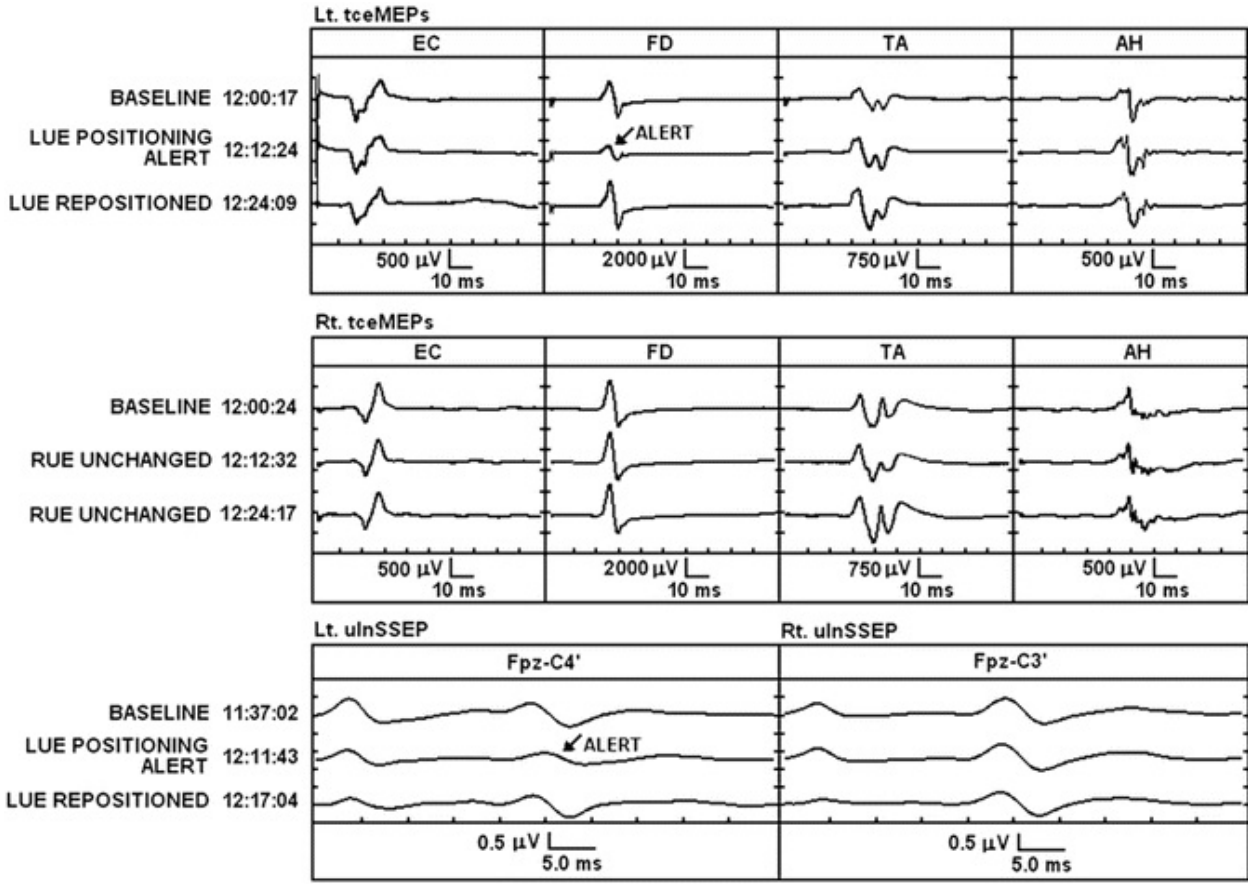

Fig. 42.3 Representative tceMEPs, ulnar nerve SSEPs, and posterior tibial nerve SSEPs recorded during the early stages of neuroendovascular surgery for coiling of anterior communicating artery aneurysm. The *top* set of traces in each panel shows baseline-evoked potentials. The *middle* set of traces shows evoked potential changes secondary to positioning of the left upper extremity. *Arrows* indicate attenuation of the tceMEPs from left first dorsal interosseous muscle and the cortical SSEP to stimulation of the left ulnar nerve. The *lower* set of traces in each panel shows full recovery of previously attenuated potentials following repositioning of the left upper extremity. *LUE* left upper extremity, *RUE* right upper extremity

In light of motor and sensory signal changes that appeared restricted to the left ulnar nerve, attention was directed to inspection of the left upper extremity. Following repositioning of the left arm, both the SSEPs and tceMEPs recovered to baseline amplitude.

Conclusions

Neurophysiological monitoring is effective in detecting evolving neural compromise and prompting timely intervention during neuroendovascular surgery. In the reported series, incidences of cerebrovascular and positioning-

related neurophysiological changes were 3 % and 3.7 %, respectively. These results suggest that while the primary focus of neuromonitoring during neuroendovascular procedures is detection and reversal of developing iatrogenic injury secondary to vascular compromise, its role in identification of reversible positioning-related peripheral nerve compression should be neither overlooked nor underestimated. Finally, the high specificity of neuromonitoring during cerebrovascular surgery [6] is of value in confirming adequacy of collateral cerebral perfusion when there is a question of partial vessel occlusion during neuroendovascular therapy.

Success of monitoring during neuroendovascular surgery depends not only on the skill of the neuromonitoring team in detecting significant neurophysiologic change but also on close cooperation between the surgical neurophysiologist, anesthesiologist, and endovascular specialist in identifying the cause of change and initiating appropriate treatment.

Questions

1. Somatosensory-evoked potentials are sensitive to ischemic insult of

   (a) Afferent fibers within the internal capsule

   (b) Efferent fibers within the internal capsule

   (c) Cortical neurons of the post-central gyrus

   (d) (a) and (c)

   (e) (a), (b) and (c)

2. Multichannel EEG is most sensitive to ischemic injury of

   (a) Basal Ganglia
   (b) Internal Capsule

(c) Thalamus

(d) Cerebral Cortex

(e) Cerebellum

3. Brain stem auditory-evoked potentials facilitate functional assessment of structures fed by the

(a) Basilar artery

(b) Carotid artery

(c) Anterior Cerebral Artery

(d) Middle Cerebral Artery

(e) All of the above

4. Transcranial electric motor-evoked potentials

(a) Are unaffected by the presence of neuromuscular blockade

(b) Can identify ulnar nerve compression

(c) Cannot be monitored during endovascular procedures because of excessive patient movement

(d) Always change in concert with somatosensory-evoked potentials

(e) Always change in concert with brainstem auditory-evoked potentials

5. Ischemic insult to the lateral lemniscal pathway is best detected using

   (a) Somatosensory-evoked potentials

   (b) Motor-evoked potentials

   (c) Brain stem auditory-evoked potentials

   (d) EEG

   (e) (a) and (b)

6. Ischemic insult to the internal capsule is best detected using

   (a) Somatosensory-evoked potentials

   (b) Motor-evoked potentials

   (c) Brain stem auditory-evoked potentials

   (d) EEG

   (e) (a) and (b)

Answer Key for

Key for Test Questions

1. d
2. d
3. a
4. b
5. c
6. e

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Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_43

43. Intraoperative Neuromonitoring in Pediatric Surgery

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Keywords Intraoperative neurophysiologic monitoring – Somatosensory evoked potentials – Motor evoked potentials – Electromyography – Auditory brainstem evoked response

Key Learning Points

- Developmental factors have profound influences on the neurophysiology of young children; consequently, obtaining evoked potentials may require special techniques
- The intraoperative use of volatile anesthetic agents in young children can make obtaining meaningful IONM data impossible.
- Motor evoked potentials may be more easily obtained in very young children than SSEPs as a consequence of developmental factors if permissive anesthetic techniques are used during surgery.
- Care must be exercised when placing needles in the infant scalp due to the presence of open fontanels and sutures.

Introduction

The monitoring modalities most commonly used in adults are also commonly used during pediatric surgical procedures, including electromyography (EMG), somatosensory evoked potentials (SSEPs), transcranial motor evoked potentials (TcMEPs), electroencephalography (EEG), brainstem auditory evoked responses (BAERs), and other specific cranial nerve (VII, IX, X, XII) EMG monitoring . Monitoring the bulbocavernosus reflex during complex tethered cord releases and resections of spinal cord lipomas can provide useful information, as this modality is one of the few that provides information on the integrity of both afferent and efferent pathways simultaneously. The potentials obtained from young children and infants may require special techniques to elicit them because the nervous system of young children is still in development. Some of the major developmental processes are summarized in Table 43.1.

Table 43.1 Monitoring modalities and developmental factors

Modality	Age affected	Factors	Manifestation	Adaptive strategy
MN, UN SSEPs	Birth—2 years	Central myelination	Broad, low-amplitude delayed cortical potentials	Decrease stimulus rate; increase pulse length
PTN SSEPs	Birth—4–6 years	Dorsal column myelination	As earlier	As earlier
TcMEPs	Birth—2 years	a	Exquisite sensitivity to volatile agents	Temporal facilitation techniques, high frequency stimulation for CN, UE
D-wave	Birth—2 years	CST myelination	Impossible to record	None known; rely on TcMEPs
EMG	Birth—2 years	b	Low signal amplitude, short duration potentials	Avoid surface pads for intraoperative recording, needle electrodes
BAERs	Birth—1 year	Central myelination	Sensitivity of wave V to volatile agents	TIVA technique
BCR	All	Polysynaptic reflex	Sensitivity to volatile agents	TIVA technique, pulse-train stimulation —double tap or double train with long ITI

[a]Factors include reduced monosynaptic connections from CST to α-motor neurons (αMNs), altered αMN biophysical properties, immature target muscle, and dispersion of D waves and I waves on CST due to relatively high variance in conduction velocities

[b]Factors include reduced muscle fiber diameter, reduced compound actional potential duration, and relatively large subcutaneous tissue layer

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Anesthetic Management of Pediatric Surgical Procedures That Require Intraoperative Neurophysiological Monitoring

The anesthesiologist must balance the condition of the patient , the surgical procedure, and the monitoring modalities to be used when selecting an anesthetic technique. Rare metabolic diseases such as mitochondrial myopathies may limit the choice of anesthetic agents that can be safely used. In these cases, the anesthesia team, surgeon, and neurophysiology team must formulate a plan that will provide as much information as possible to guide the procedure while protecting the patient from exposure to potentially hazardous anesthetic agents.

TIVA is the preferred anesthetic technique if TcMEPs are to be elicted. If TIVA is not a feasible option, 0.5 MAC of inhalation agent (desflurane) supplemented with remifentanil can be used in the absence of significant neurological compromise. Higher stimulation intensities may be required to elicit TcMEPs due to volatile agent effects at the level of the alpha motor neurons (αMNs) [1]. Increased stimulus intensities have attendant risks of excessive patient movement and increased risk of bite injuries such as tongue lacerations. The use of volatile agents is also associated with an increased rate of false-positive alerts compared with TIVA [2].

It is generally accepted that healthy young adults, with no pathology involving the pathways involved in IONM, can be anesthetized with either a TIVA or 0.5 MAC desflurane-based anesthetic during monitored (IONM) procedures. This is not the case for young children. The presence of low residual concentrations of sevoflurane, following an inhalation induction, may significantly impair the generation of TcMEPs in the lower extremities. Currently, unpublished data from the author’s institution indicates that volatile agent added over a TIVA, as is sometimes done to suppress patient movement, can dramatically reduce TcMEP amplitudes in the lower extremity muscles of young healthy adolescents. TIVA , with propofol and remifentanil, is the recommended primary anesthetic regimen when IONM is required in pediatric patients. The addition of ketamine (5–20 μg/kg/min) to

the anesthetic may help provide improved hemodynamic stability, but care must be taken to terminate a ketamine infusion in a timely manner due to the pharmacokinetic properties of ketamine. Ketamine, propofol, and isoflurane have been shown to cause neurodegeneration in the brains of subhuman primates when used in high doses over a period of time [3]; however, the effects in humans are an area of controversy as these agents may protect from damage due to nociceptive inputs [4]. Some propofol sparing may also be achieved by using dexmedetomidine , but dexmedetomidine must be used judiciously as blood levels greater than 0.6 ng/mL depress the MEPs [1]. A low-dose infusion (0.2 μg/kg/h) without a loading bolus keeps the blood levels below the threshold. If electromyography (EMG) or TcMEPs are used as one of the monitoring modalities, the neuromuscular blocking agents (NMBs) should be avoided if possible. If used for intubation, the use of short-acting agents is preferred as baseline potentials may be acquired within 10–20 min of intubation in some cases. NMBs should be completely avoided, or completely reversed if cranial nerve EMG and/or cranial nerve TcMEPs are to be acquired in young children.

Concern about the ability to assess anesthetic depth with TIVA is cited as a primary reason for not using this technique. Recently published data define the EEG patterns associated with the initial loss of consciousness and maintenance of such loss in healthy volunteers receiving propofol infusions [5, 6], sevoflurane [7], and dexmedetomidine [8]. EEG patterns associated with surgical anesthesia conditions in infants from age 0 to 6 months using sevoflurane have also been published [9]. Similar patterns are also found when using fast-Fourier analysis (FFA) of frontal montage EEG in patients in the same age groups receiving TIVA anesthetics (Fig. 43.1a–d). Although EEG data can be informative regarding cortical activity, it is not completely reliable as a predictor of movement. The successful use of TIVA relies on the suppression of nociceptive stimuli with sufficient narcotic dosing, as propofol has limited ability to prevent movement in dose ranges compatible with eliciting reliable TcMEPs in the lower extremities of young children. Using a combination of bilateral frontal montage EEG with fast Fourier transform, and EMG, it is possible to monitor both the cortical response to anesthetic dosing and EMG signs of incipient movement. Spontaneous EMG used to monitor the facial and lower cranial nerves has been found to be predictive of incipient patient movement during emergence from anesthesia [10, 11]. We have also found that spontaneous EMG activity in the small muscles of the

hands can signify incipient movement as well.

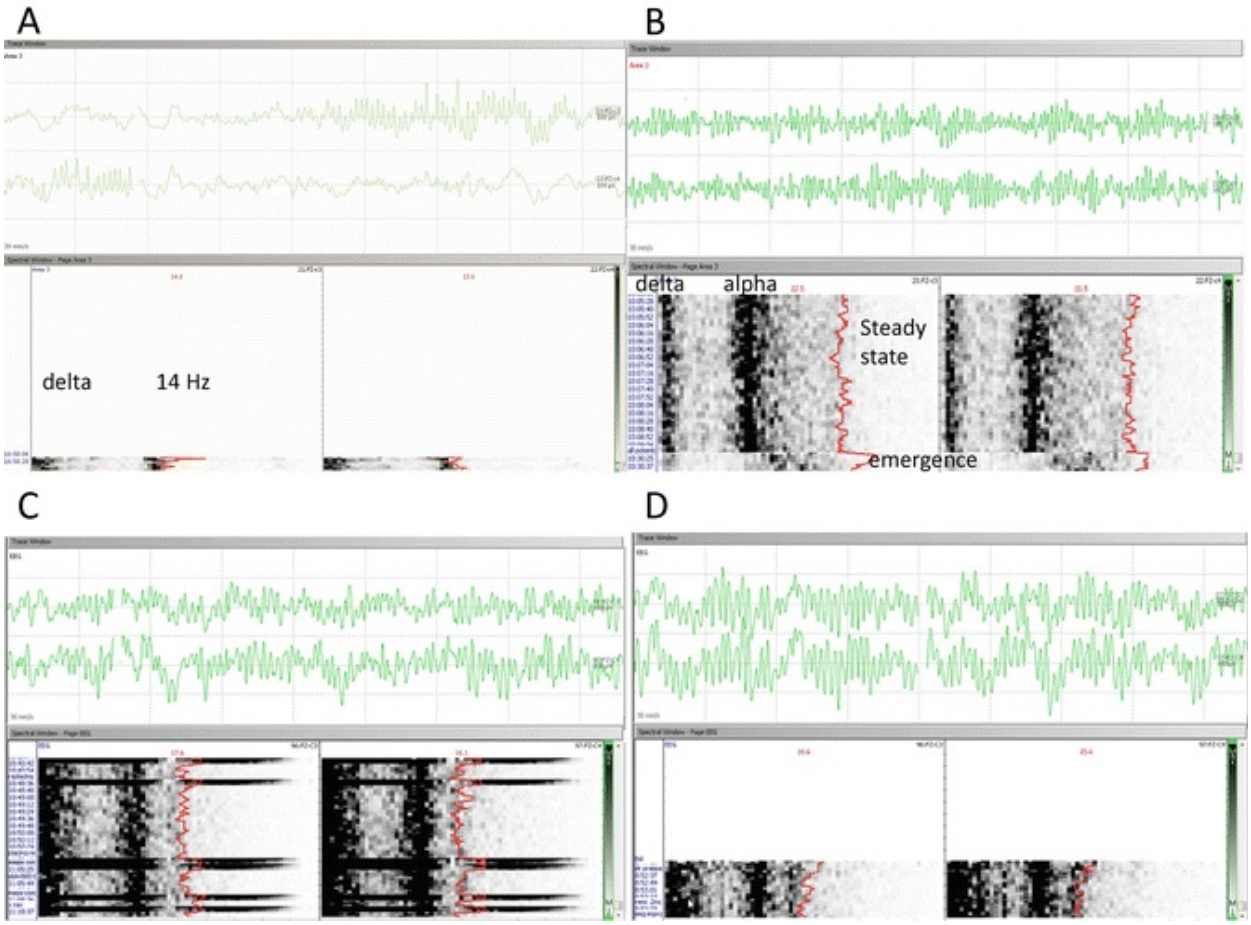

Fig. 43.1 Two-montage frontal EEG/DSA during TIVA anesthesia in children of different ages. (**a**–**d**) Real-time raw EEG and time-stacked density spectral array (DSA) acquired during TIVA anesthetics for children of ages 4 months, 14 months, 5 years, and 15 years, respectively. (**a**) At 4 months of age, the presence of a high-power delta band is associated with a surgical plane of anesthesia. There is also a 14-Hz beta frequency band present in this sample. (**b**) Dense delta and alpha bands are associated with a surgical plane of anesthesia at this age. The raw EEG from the 14-month-old child was recorded during emergence; the DSA shows a transition from a surgical plane (steady state) to a pattern suggestive of emergence. The EEG and DSA patterns for the 5-year-old child (**c**) and the 15-year-old child (**d**) are very similar

Monitoring Modalities and Development

Somatosensory Evoked Potentials

Somatosensory evoked potentials (SSEPs) constitute a set of signals generated by action potentials of nuclei in the CNS and primary sensory cortical neurons in response to stimulation of peripheral nerves; most

commonly the median or ulnar nerves for the upper extremities and the posterior tibial nerves for the lower extremities . These signals travel ipsilaterally from the site of the initial peripheral nerve stimulus and then ascend via the dorsal columns, conveying vibration and proprioceptive sensation to either the cuneate (upper extremities) or gracile (lower extremities and trunk) nuclei in the medulla. From there, the response crosses over to the contralateral side in the arcuate fibers and travels to the ventral-posterior lateral tiers of the thalamus via the medial lemniscus. Then the response travels to the cortex through the posterior limb of the internal capsule. Therefore, monitoring SSEPs provides information concerning the integrity of the vibration and proprioceptive sensory tract from the periphery to the primary sensory cortex [12–14]. The basics of SSEPS are covered in more detail in Chap. 1.

The challenge posed by pediatric patients, especially the very young, is that the different parts of the pathways involved in the formation of SSEPs mature at different rates. Myelination of the central pathways is generally complete by 2 years of age, but the myelination of the dorsal columns is not complete until about 8 years of age [15]. The medial lemniscus is usually fully myelinated by 12 months and the thalamocortical projections by 12–18 months of age [16]. As a consequence of the delayed myelination of the dorsal columns, there tends to be greater dispersion of signals traveling up the dorsal columns of a 2-year-old child than an adult, thus resulting in a lower likelihood of generating a useable PTN cortical SSEP in the 2-year-old child. Failure to obtain cortical PTN SSEPs in children younger than 2 years is not uncommon; the rate of failure increases in the face of pathology within the spinal cord and with anesthesia/sedation [17]. We have found that TcMEPs are obtained more frequently than PTN SSEPs when monitoring thoracic and lumbar spinal cord function in children younger than 6 years of age, when using a TIVA technique [18].

The median nerve peripheral responses and cervical potentials have very short latencies in infants and children younger than age 2. Although conduction velocities in the peripheral nerves do not reach adult values until 5 years of age [19], due to the shorter distance between stimulus and recording electrodes, the latencies are much shorter than in an adult. Once the signals reach the medullary nuclei (gracile and cuneate), slower synaptic transmission and slower central conduction times, due to incomplete myelination, result in prolonged peripheral to cortical interpeak latencies and

near-adult-value cortical latencies.

Infant cortical SSEPs and cortically dependent neurophysiological signals will, in general, be more sensitive to anesthetic effects than will cortical SSEPs in a school-age child or an adolescent [20]. Recording cortical potentials in this group of children is challenging and is very dependent on the anesthesia team providing a permissive anesthetic and managing it carefully.

When attempting to record SSEPS from an infant or child under 2, the technologist can increase the chance of recording potentials by reducing the stimulus rate and increasing the stimulus pulse width compared to the rate and pulse widths typically used to record SSEPs in adults. Additionally, the waveforms will have altered morphologies; the cortical potentials will have lower amplitudes and longer durations due to the “smearing” effects of conduction velocity dispersion. For many clinical applications, cortical potentials are not essential. For example, when monitoring a tethered cord release, high-quality cervical potentials recorded by using an Fz-C5s montage will provide the essential information concerning the integrity of the sacral roots that comprise the PTN (L4–S3). It is often possible to obtain adequate cervical PTN potentials in the same patient as poorly reproducible PTN cortical potentials ; failure to include the Fz-C5s montage due to “insufficient” channels may obviate any chance of monitoring PTN potentials in young children.

There is one important technical concern when performing SSEPs in infants under 18 months of age, and that relates to the fontanelles . The anterior and posterior fontanelles are midline openings in the skull that, in conjunction with open sutures, permit rapid brain growth during infancy. The anterior fontanelle may initially enlarge after birth but then decrease in size after 6 months of age. It is typically closed to palpation between 9 and 18 months of age. The anterior fontanelle should be located in young infants as it is proximate to the Fz site. Needle placement at or close to the anterior fontanelle should be avoided. Some infants have a palpable wide metopic suture in the frontal midline. If found, needles should be placed off the midline. The posterior fontanelle is typically closed to palpation by 4 months of age.

Transcranial Motor Evoked Potentials

Within 10 years of the adoption of SSEPs as a means to monitor scoliosis

surgery, it was noted that postoperative deficits could occur despite unchanged SSEPs [21]. In response, MEPs were introduced, allowing assessment of the integrity of the large diameter corticospinal tract (CST) axons and the αMNs.

The basic neurophysiology of motor evoked potentials is discussed in Chap. 2, “Transcranial Motor Evoked Potentials.” The introduction of MEPs into pediatric clinical practice was motivated by the observation that intra- and postoperative motor deficits can occur without a sensory deficit as monitored by SSEPs. Therefore, it is necessary to monitor the functional integrity of the motor tracts of the spinal cord apart from the sensory tracts. MEPs serve this purpose. MEPs are usually elicited by applying a high voltage, short duration stimulus to the scalp overlying the primary motor cortex. This electrical stimulus depolarizes the axons of the pyramidal neurons (D waves) and the interneurons (I waves) [22]. The D and I waves are conducted along the CST to activate the spinal αMNs [23]. The MEP, recorded from a pair of needle electrodes placed in the muscle groups of interest, represents the compound muscle action potential (CMAP) initiated by the D and I waves. The amplitude, latency, and morphology of the CMAP are the criteria to assess the integrity of the motor pathways. Criteria have been developed for issuing an alert to the surgical team due to changes in the MEPs [24–26]. There are no published large series examining the application of these criteria for alerting the surgical team to changes in children under age 6; however, clinical experience and data from a small series study [27] indicate these criteria are applicable in this age group with the caveats discussed in Macdonald et al. [24].

The D waves are insensitive to anesthetic agents and can be generated even in the presence of greater than 1 MAC of volatile agent [28]. While the amplitude of the D wave may not be affected, the exact latency of the D-wave may be sensitive to volatile agents. The I waves are highly sensitive to anesthetics [28] as well as to ischemia. Cortical ischemia produces an abrupt decrease in MEP amplitude of about 50–75 % due to loss of late I waves [29]. Cortical inhibitory circuits are immature in the infant and may lag excitatory circuits [30]; this may contribute to a reduction in I wave production with transcranial stimulation. The sensitivity of MEPs to anesthetic agents is due largely to the sensitivity of the αMNs. All anesthetics decrease the resting membrane potential of the αMNs; thus, a greater change in membrane potential is required to achieve depolarization [31]. The

neuromodulatory influence of serotonin and noradrenaline has a significant effect on αMN excitability by regulating channel open-state time and resting membrane potential [32]. Volatile agents reduce serotoninergic output while ketamine may potentiate it [33, 34]. All of the adverse effects of anesthetic agents on MEP generation are more prominent in young children due to immaturity of the motor system. Although direct corticospinal tract to αMN connections are present in the MNs innervating muscles of the hand [35], there are both anatomic and molecular changes in the properties of the αMNs associated with maturation [36–38].

As a consequence of these factors, special techniques such as temporal or spatial facilitation may be required to elicit MEPs in very young children. The temporal facilitation technique, also called double-train stimulation, can be very effective for obtaining TcMEPs from young children [39, 40]. Spatial facilitation is technically more difficult and is limited to the homonymous muscle in a single (or two, upper or lower) limb(s), whereas temporal facilitation has no such limits. The stimulation parameters found to be effective in over 60 % of cases are shown in Table 43.2. The interstimulus interval is defined as the time between pulses in a train of pulses and has units of milliseconds. Some equipment manufacturers do not specify interstimulus interval per se, but rather specify rate in pulses per second. A rate of 1000 pulses per second yields an interstimulus interval of 1 ms. The intertrain interval is the time between trains. It is defined in the literature as the time between the start of the first train and the start of the second train. However, on some commercially available equipment, the definition is the time between the *end* of the first train and the start of the second train—the distinction is critical. The intertrain interval (ITI) and interstimulus interval (ISI) may require optimization depending on the target muscle group and any underlying pathology. The degree of facilitation is sensitive to the intertrain interval [39]; the maximum amplitudes of TcMEPs obtained from upper versus lower extremity muscles will generally occur at different interstimulus intervals, with longer ISIs favoring lower extremities [41].

Table 43.2 Parameters for use of temporal facilitation TcMEPs

Parameter	Value	Range	Comments
Voltage	Start 125/125	As needed	Achieve MEP amplitude variance of < 20 % of mean
Pulse length	75 μs	50–100	100 μs optimal but considered slow charge in US
Pulses in train	4/4	3/3–4/6	Longer trains may elicit LE MEPs

Interpulse interval[a]	1–1.33 ms	1–3 ms	Short IP(S)I favors UE and CN, longer favors LE
Intertrain interval[b]	12 ms	9–15 ms	Equipment-specific definition

[a]Interpulse interval or interstimulus interval (ISI) is the reciprocal of pulse frequency (p/s); p/s of 500 is equivalent to an ISI of 2 ms
[b]The definition of ITI varies between users of the term. Journee et al. define ITI as the time between *start* of the first train and start of the second train. Some equipment manufacturers define ITI as the time between the *end* of the first train and the start of the second train. The difference is the length of the first train. Use of the correct definition is important to avoid inhibition occurring as a result of a longer, or shorter, than desired ITI

Electromyography

The basic principles of electromyography have been discussed in Chap. 7. The application of the technique to infants and children under anesthesia does not require the use of special techniques such as those required to elicit TcMEPs. The muscle mass of infants and young children is reduced compared to adults; at birth, the diameter of individual fibers is about one-fourth that of an adult. Fiber diameter increases in size through puberty [42]. Additionally, the mean duration of motor unit action potentials is significantly shorter in infancy and early childhood than at 20 years of age. Thus, EMG responses will have a different appearance and may have lower than expected amplitude, especially if subdermal needles are used. Positioning the needle electrodes intramuscularly will enhance the value of EMG monitoring [43].

Electroencephalography

The EEG waveform represents the fluctuating influence of excitatory postsynaptic potentials (EPSPs) and inhibitory postsynaptic potentials (IPSPs) on the dendrites of cortical neurons in part generated by the interaction of cortical and thalamo-cortical relay neurons. The frequencies observable from these recordings are limited by the skull, galea, and scalp as these structures form an effective low-pass filter. The EEG can be recorded and analyzed by direct inspection of waveform patterns and by means of the density spectral array (DSA). The EEG exhibits certain characteristics that

are age and anesthetic agent dependent [44]. In general, there is a progression of the EEG frequency content from posterior to anterior—the fastest frequencies occurring in the frontal recording montages. The normal EEG displays symmetry between hemispheres and shows synchronization across montages. Sharp wave and spikes may suggest an underlying seizure disorder. Abnormally slow EEG suggests diffuse metabolic abnormalities. The anesthetic depth is determined by the proportion of alpha activity (8–15 Hz), beta activity (15–25 Hz), theta activity (4–7 Hz), and delta activity (1–3 Hz) recorded on the EEG tracing. Spectral edge frequency has been used as a marker of anesthetic depth although the correlation between sedation scores and SEF95 remain imperfect as is true for bispectral index (BIS) [45]. Children younger than 2 years of age, especially those younger than 12 months, display higher SEF95 values for similar sedation scores than older children; the same is true for BIS values [46].

For many procedures, a simple two-montage EEG such as Fp1-C3, Fp2-C4 may be sufficient. Procedures involving the cerebral vasculature may require use of more extensive EEG monitoring, using montages that cover the at-risk vascular territories and the watershed areas associated with the cerebral vasculature in question. As noted previously, much of the frontal EEG spectral power in a young child under anesthesia is in the delta frequency band. However, significant alpha frequency power may also present in children over 6 months of age. Loss of the alpha frequency power and generalized EEG amplitude reduction during vascular procedures or mass lesion resections near major vessels, unless associated with an abrupt change in anesthetic “depth,” or level, is cause for alerting the surgeon, analogous to similar changes during a carotid endarterectomy (see Chap. 20, “Monitoring Applications and Evaluating Changes”).

Brain Stem Auditory Evoked Responses

The neurophysiology of brainstem auditory evoked responses and the techniques for acquiring them are discussed in Chap. 3, “Auditory Evoked Potentials .” Auditory evoked responses are typically divided into short, middle, and long latency responses. During surgery, only the short latency responses are resistant to the effects of anesthetic agents and are useful for assessing the integrity of the eighth cranial nerve and the ascending auditory pathways to the level of the inferior colliculus. The “resistance” of short-

latency BAERs to anesthesia is age dependent; clinical experience indicates that identification of wave V in infants younger than 6 months who have been anesthetized with sevoflurane is much more difficult, due to low amplitude signals, than in infants anesthetized with propofol (Unpublished data). In the nonanesthetized state, BAERs can be recorded from infants at 25 to 27 weeks' gestation. Term infants will have wave I latencies similar to those of adults; wave III and V latencies reach adult values by 18–36 months of age [47].

Bulbocavernosus Reflex

Monitoring the bulbocavernosus reflex has been proposed by Skinner as a means of preserving lower sacral nerve function during intradural and extradural surgeries at the level of the conus medullaris, cauda equina, sacral plexus, and the pudendal nerve [48] (see Chap. 8, "The Use of Reflex Responses for Intraoperative Monitoring" for details). Acquisition of the reflex requires use of a multipulse technique applied as a double train with a long intertrain interval. Alternatively, a double-tap technique can be used. In either case, the acquisition time must be sufficiently long to capture the response (200 ms window). The reflex is also sensitive to anesthetic technique in young children and infants; TIVA is the preferred anesthetic technique for acquisition of this reflex. Recording electrodes are placed on opposite sides of the anal sphincter. These same electrodes can be used to record TcMEPs from the anal sphincter. Loss of the BCR but not the anal sphincter TcMEP suggests damage to the efferent pathways in the reflex arc. We record BCRs during complex tethered cord releases, lipoma resections, and similar procedures. The presence of a preexisting major urodynamic abnormality usually makes recording the BCR impossible, whereas mild abnormalities are not incompatible with recording the BCR (Fig. 43.2).

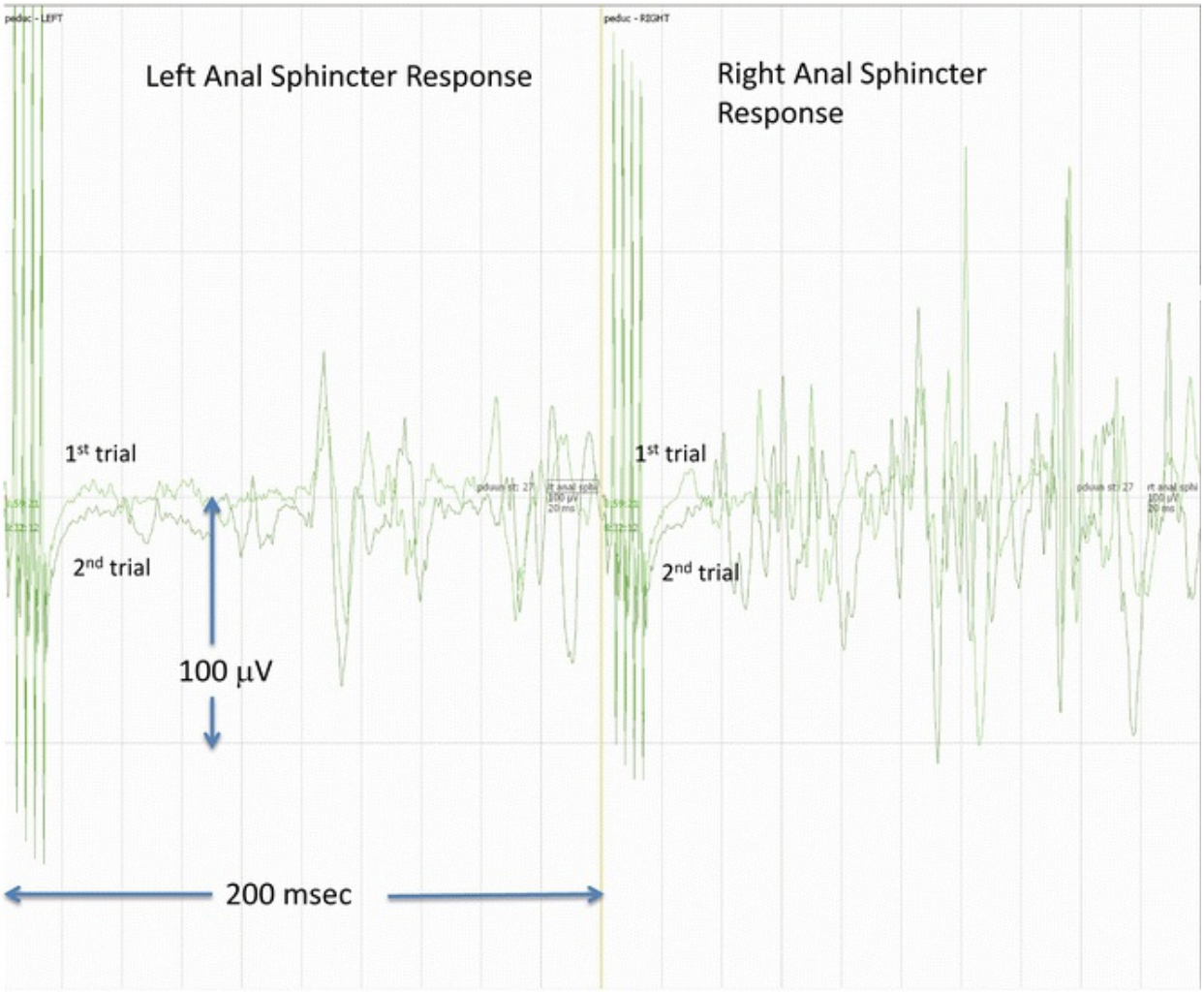

Fig. 43.2 Bulbocavernosus reflex (BCR) . The BCR was elicited from an 11-month-old girl undergoing repair of complex tethered cord and spinal cord lipoma resection. The stimulating cathode was placed at the clitoris and the anode slightly laterally and caudad. Correct positioning of the anal sphincter recording electrodes is also important (see Skinner reference for details). Two trials of right side stimulation are shown. In this case, a bilateral response is obtained. Note the complexity and duration of the response. The right side response appears to have two parts; loss of either the early or the late response may be significant and should be reported to the surgeon

Common Pediatric Surgical Procedures Utilizing IONM

A summary of common pediatric surgical procedures and the IONM modalities utilized during these procedures is presented in Table 43.3. A detailed discussion of some of the listed procedures follows.

Table 43.3 Common pediatric surgical procedures and IONM modalities

Procedure	Modalities	Comments
Posterior spinal fusion	UN & PTN SSEPs, TcMEPs EMG, trig-EMG	
Spinal cord tumor resection	UN & PTN SSEPs, Dorsal column mapping, D wave, TcMEPs, EMG	D wave may not be obtained if child < 22 months. old or lesion below T10
Tethered cord and variants	EMG, trig-EMG, BCR, +/− UN & PTN SSEPs, TcMEPs	Inclusion of sphincters in TcMEP montages when possible
Selective dorsal rhizotomy	EMG, trig-EMG	Trig-EMG acquired using single pulse and 50-Hz pulse train
Chiari (with syrinx) decompression	MN & PTN SSEPs, TcMEPs, +/− CN XI EMG	Significant bradycardia may be seen during coagulation of cerebellar tonsils
Resection of supratentorial mass lesions	MN & PTN SSEPs, TcMEPs, +/− DCS[a], SCM[b]	Use near-threshold techniques for TcMEPs
Resection of infratentorial mass lesions CPA region/lateral	MN & PTN SSEPs, TcMEPs, BAERs, CN VII-EMG +/− CN V, VI, IX, X -EMG, CN VII TcMEP	Use near-threshold techniques for TcMEPs
		Hemispheric stimulation suggested for CN TcMEPs
Resection of infratentorial mass lesions fourth ventricle/midline	MN & PTN SSEPs, TcMEPs, BAERs, CN VII-EMG +/− CN V, VI, IX–XII -EMG, CN VII, X, XII TcMEP	Use near-threshold techniques for TcMEPs
		Hemispheric stimulation suggested for CN TcMEPs

[a]Direct cortical stimulation (DCS) parameters are different than those for TcMEPS. Anode stimulation keeping delivered current below 25 mA with remote cathode (e.g., Fz). Typical: 4-pulse train, 500 μs pulses with 2–4 ms ISI

[b]Subcortical mapping (SCM) is useful for estimating distance between resection point and CST. Multiple studies have concluded that the distance in millimeters between the stimulus point and the CST is equal to the number of mA needed to elicit a motor response. The techniques described by Seidel et al. [58] have worked well in children

Posterior Spinal Fusion

Perhaps the most common surgical procedure performed in children and

adolescents utilizing IONM is posterior spinal fusion for scoliosis. Scoliosis may result from congenital abnormalities, neuromuscular disorders, or may be idiopathic. Prior to the availability of IONM, the “wake-up” test was used to assess the integrity of the motor system during surgery. The problem with this approach is that the wake up is a snapshot at one point in time. The time between insult and the discovery of a loss of movement may be too long to take meaningful steps to mitigate the damage. The combined use of EMG, SSEPs, and MEPs is advocated for spine surgery to correct scoliosis and kyphosis [49, 50]. Significant changes in MEPs may be associated with technical factors, physiological factors (hypotension), positioning, anesthetic effects, or surgical causes [51].

Permanent or transient neurologic injury can occur during pedicle screw placement. Pedicle screws provide a rigid mechanism to connect each vertebral segment with the rods that straighten the spine. A correctly placed pedicle screw should be completely surrounded by bone; a misplaced screw may breach the spinal canal medially and can directly traumatize the spinal cord, which may result in instantaneous or delayed loss of MEPs and SSEPs. A medial breach with trauma to the spinal cord may be associated with EMG discharges several segments below the level of screw placement [52]. Evaluation of TcMEPs after large discharges of this type is suggested, as these discharges have been associated with acute loss of TcMEPs [52]. Boney tissue has greater impedance to electric current than nerve tissue. Direct application of electrical current to each pedicle screw and the monitoring of EMG activity from muscles that receive their innervation from spinal nerves associated with screw locations can detect a breach of the pedicle wall and potentially avoid injury to nerve roots or to the spinal cord caused by malpositioned or misdirected pedicle screws. Pedicle screw thresholds below 4 mA are associated with a high rate of medial breach for screws placed in the lumbar–sacral region. In practice, a threshold of 6 mA is typically used for thoracic screws [53]. The introduction of titanium pedicle screws has led some authors to develop alternative techniques for pedicle screw testing. Probing the tap hole while using a ball-tip probe using a multipulse technique with constant current has been proposed as an alternative to conventional pedicle screw testing [54].

There is debate over the appropriate criteria to use for issuing an “alert” or “alarm” based on MEP changes [25]. There is no debate about the implications of sudden loss of both MEPs and SSEPs following placement of

a pedicle screw or a sublaminar wire. It is important that all parties are in agreement as to the specific criteria to be used before a case is started and the course of action to be followed in the event of an alarm. If baselines show a large amount of variability, then total loss may be the best criteria, as false positives are avoided and there is time for recovery from ischemic events if corrective measures are taken within 30 min [55]. One caveat to this approach is that ischemia in the high thoracic region may go undetected for many minutes due to the fact that white matter is more resistant to ischemia than motor neurons [56]. This scenario is much less common than direct trauma to the cord, but one must be vigilant, as treating the root cause may prevent a long-term or permanent loss of motor function.

Anesthetic Management During Spine Surgery

In the past, posterior fusions were performed with controlled hypotension. This technique is no longer recommended. Intraoperative blood pressure management is dependent on the severity of the curve, the type of spinal deformity (kyphosis vs scoliosis), and existing comorbidities. Severe kyphosis should receive special attention, as the incidence of neurological injury with reduction of kyphosis is significantly higher than that for scoliosis [57]. Osteotomies may be performed if a curve is rigid or for sagittal imbalance or other complex deformities. Pedicle subtraction and three-column osteotomies are associated with greater risk of neurological injury [57].

Acute, complete loss of SSEPs and/or MEPs during a spinal deformity correction procedure poses a significant challenge to the operating team. Spinal cord injury can occur from direct injury, from a vascular injury related to an implant, or from vascular compromise not directly related to the implant (ischemia secondary to hypoperfusion). Once SSEP or MEP loss is detected, previously established protocols designed to cover this contingency should be executed. Checklist approaches for the management of loss of neurophysiological potentials have been published [58]. Frequently, mean arterial blood pressure (MAP) is elevated to some predetermined target range to increase the spinal cord perfusion pressure. This can be accomplished by reducing the dose of anesthetic agent, increasing intravascular volume through colloid or blood transfusion, or by infusion of a vasoconstrictor (phenylephrine) or an inotrope (dopamine). The hematocrit and arterial blood gases should be optimized. At the same time, the surgeon will evaluate the

field to judge if there is reversible intervention or other evidence of direct injury.

Dorsal Rhizotomy

Selective dorsal rhizotomies are done to decrease spasticity in children with cerebral palsy, spinal cord injury, or traumatic brain injury. The spasticity results from abnormal regulation of the gamma motor neurons and abnormal connections between 1A afferents and αMNs. The combination results in the classic cog-wheel behavior seen with passive movement of a joint. Excitatory influences dominate at the alpha motor neurons, leading to spasticity and contractures.

Surgically, afferent (sensory) dorsal nerve roots from L1 to S1 are divided into rootlets and the rootlets are selectively cut to reduce the spasticity. Each rootlet is sequentially tested, initially with a 1- to 2-Hz constant current pulse to determine the threshold current needed to elicit a stable EMG response. The threshold current is then applied for 1 s at 50 Hz and the response noted [59]. The response is graded by the number of muscles exhibiting EMG activity, and the intensity and duration of the activity (see Fig. 43.3a, b). Responses involving muscles contralateral to the stimulated root are always pathological. Direct palpation of muscle responses by an experienced physiatrist augments the neurophysiological data and can be very helpful in selecting rootlets to cut versus rootlets to save. Sacral roots below S1 are generally not interrogated during these procedures as these roots contain fibers important to preservation of urogenital function. If S2 plays a significant role in the spasticity, attention is paid to the sphincter activity elicited when individual rootlets are stimulated, as significant sphincter activation may be grounds for sparing the rootlet.

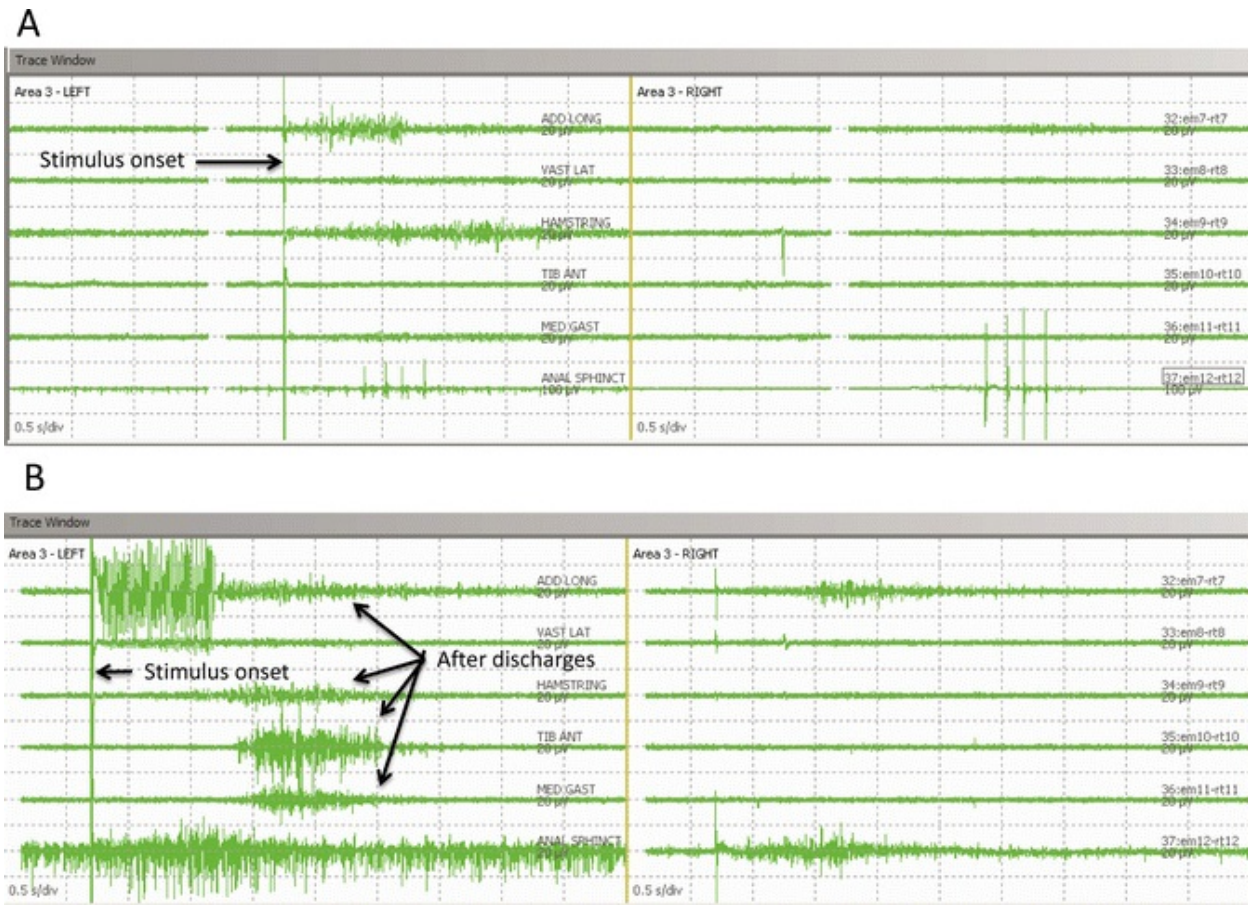

Fig. 43.3 Triggered EMG Responses to a 50-Hz stimulus during selective dorsal rhizotomy (SDR) . The response to a 1-s-long 50 Hz stimulus of a dorsal L5 rootlet during a SDR is shown in both panels. A minimally pathological response is shown in (**a**); this was the best rootlet among all tested from the L5 root. A very pathological response is shown in (**b**). There is EMG activity after the end of the stimulus (after discharges) from multiple muscles ipsilateral to the stimulus and from the adductor longus on the contralateral side. The patient's main gate impediment was scissoring

In general, 50–65 % of all rootlets are sectioned but at least one rootlet from each root is spared to preserve normal sensation in the distribution of the root in question. Muscle relaxants must be avoided and excessive depth is undesirable as the technique relies on αMNs responding to input from homonymous 1A afferents. Preservation of the clonus response helps assure that EMG responses can be elicited using reasonable stimulating currents. Therefore, the goal of IONM is to help the surgeon to restore the balance between the inhibitory and excitatory motor influences, while preserving as much sensory innervation as possible. Postoperatively, this procedure results in improved muscle tone, mobility, and balance.

Tethered Cord Release

Tethered cords occur because the conus medullaris is prevented from migrating cephalad as the child grows. Tethered cord can be diagnosed clinically or radiographically. The most common signs and symptoms are leg muscle weakness and sensory loss, bowel or bladder dysfunction, back or leg pain, and disturbed gait. MRI may reveal a displaced cord, scar, lipoma, or tight filum. Pathophysiologically, there is a mechanical deterioration that distorts the cord and neuronal components. A growth spurt can cause increased tension on the distal portion of the cord, leading to impaired blood flow and cord ischemia, which usually improves after surgery. Most often the anomalous tissue preventing the natural migration also contains nerve tissue as well. Similar to dorsal rhizotomies, direct-stimulation EMG allows the surgeon to differentiate the nerve tissue from the anomalous tissue prior to cutting to allow the cord release. Monitoring bowel and bladder function via anal sphincter and detrusor muscle EMG and monitoring BCR helps to maximize the probability of preservation of function.

Craniotomy for Tumor/Mass Lesion Resection

Multiple structures are at risk during resection of intracranial mass lesions depending on the location of the lesion. Multiple IONM modalities may be employed to help assure the surgeon of the integrity of the nervous system. During resection of supratentorial tumors, the CST may be close to the resection margins. The location of the incision may prevent optimal placement of the stimulation electrodes for eliciting TcMEPs. In some cases, sterile stimulation electrodes may be placed in the field on the motor cortex. The motor strip must first be identified using phase reversal of the median nerve SSEP N20 peak prior to direct cortical stimulation (see Fig. 43.4). Subcortical mapping, using cathodal stimulation, is useful to determine this distance between the resection margin and the CST and to estimate the likelihood of residual deficits associated with the subcortical resection [60].

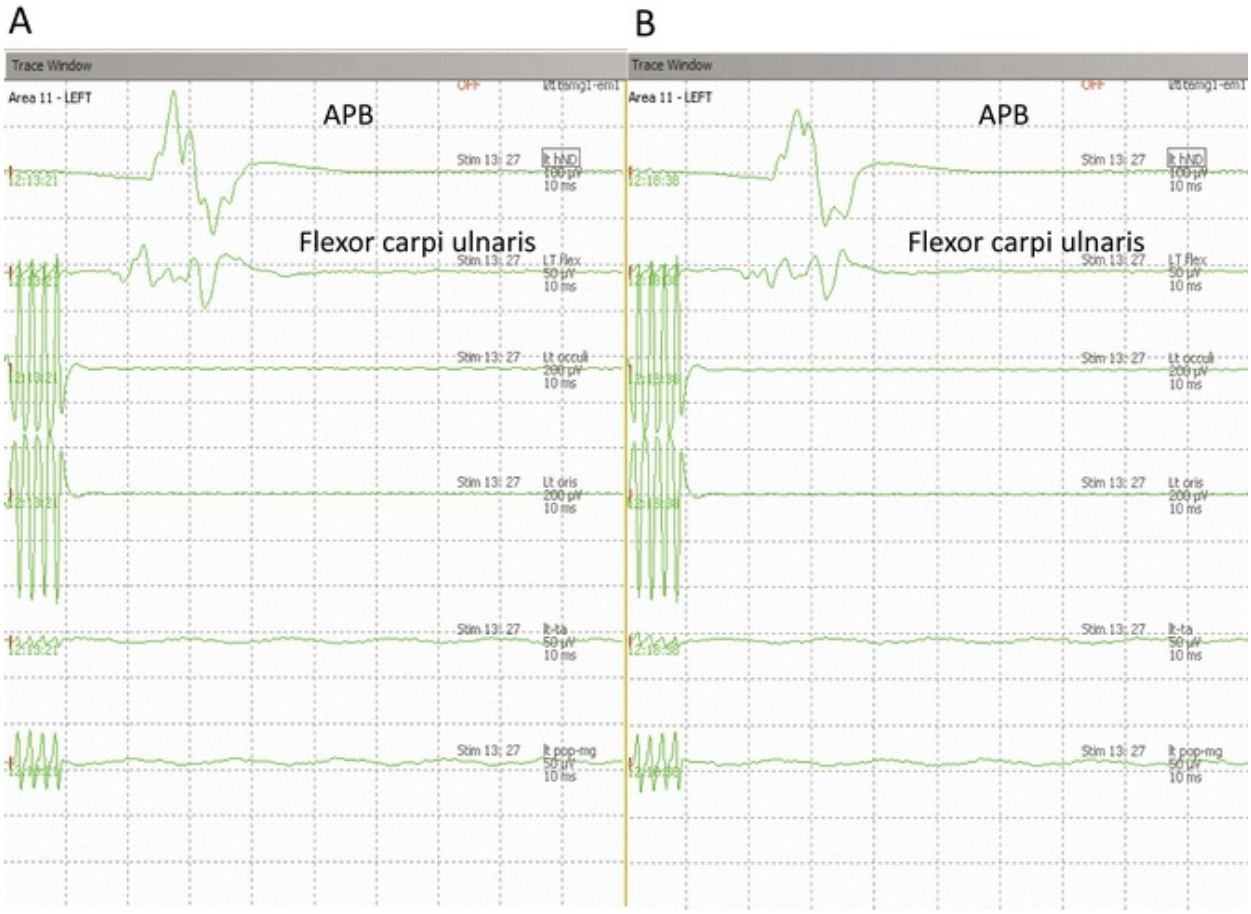

Fig. 43.4 Direct cortical stimulation (DCS) during supratentorial tumor resection . Two consecutive trials of direct cortical stimulation over hand motor area using a 1 × 4 grid (#3 location) are shown in (**a**, **b**), respectively. The stimulation parameters were four pulses, 500-ms pulse length, 4 ms ISI, 25 mA. Note there is minimal variability in the amplitude as long as the grid remains stationary

Monitoring cranial nerve function is frequently done during resection of infratentorial lesions (see Fig. 43.5). Individual cranial nerves may be monitored by use of cranial nerve (CN) EMG (Fig. 43.6b). EMG from specific cranial nerves is very sensitive to the effects of NMBs; consequently, these drugs should be avoided if CN EMG is employed. Special techniques have been described to elicit EMG responses from CN VII, X, and XII [61, 62]. Cranial nerve EMG displays specific patterns predictive of later dysfunction, especially so for the facial nerve [63, 64]. EMG responses to direct stimulation of the floor of the fourth ventricle (rhomboid fossa) may be used to map the location of cranial nerves and their nuclei in order to find a safe entry point for tumor resection [65]. The location of critical structures in the rhomboid fossa may be significantly distorted depending on the location of a brainstem lesion [66]. While much attention is paid to the location of the

facial colliculus, it is important to remember that the hypoglossal nucleus and the motor nucleus of CN X are in close proximity to the floor of the fourth ventricle in the caudal segment of the rhomboid fossa and the nucleus of CN VI lies near the facial colliculus. These mapping techniques cannot guarantee the integrity of the corticobulbar tracts. However, these should be monitored by either direct cortical stimulation or by transcranial techniques [62, 65, 67]. Hemispheric stimulation is the technique of choice for eliciting cranial nerve TcMEPs in children in order to minimize the probability of direct stimulation of the facial nerve on the side of interest. Correct placement of the anode over the face motor area is key to successful acquisition of CN VII and XII TcMEPs. High-frequency pulses (1 ms ISI) appear to work well with 75 μs pulses. The actual latency of the facial nerve TcMEP may be normal or significantly prolonged at baseline depending on the size, location, and secondary effects of the mass lesion (see Fig. 43.5c, d).

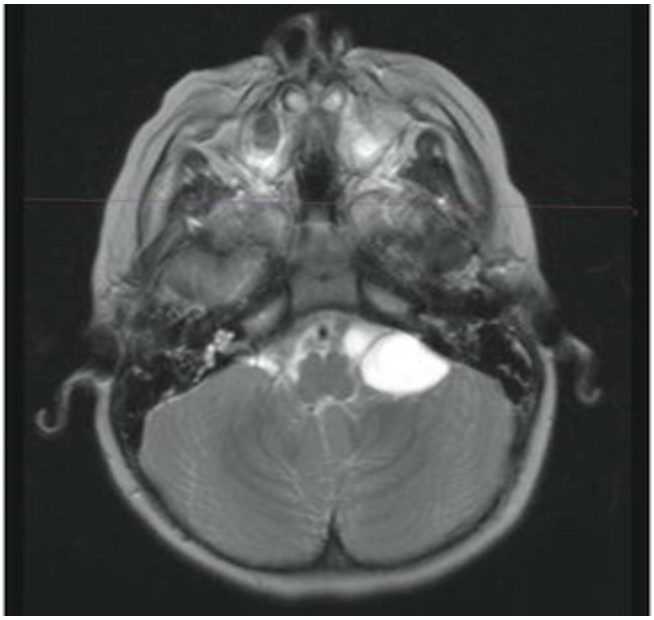

Fig. 43.5 Brainstem cavernoma . The MRI shows the location of a brainstem cavernoma in a 15-month-old child who developed acute onset of right-sided weakness and a right lower facial droop. Both the CST and corticobulbar tracts were involved. CN VII EMG was used during the resection but CN VII TcMEPs could not be obtained at baseline on the right, consistent with the presenting physical findings

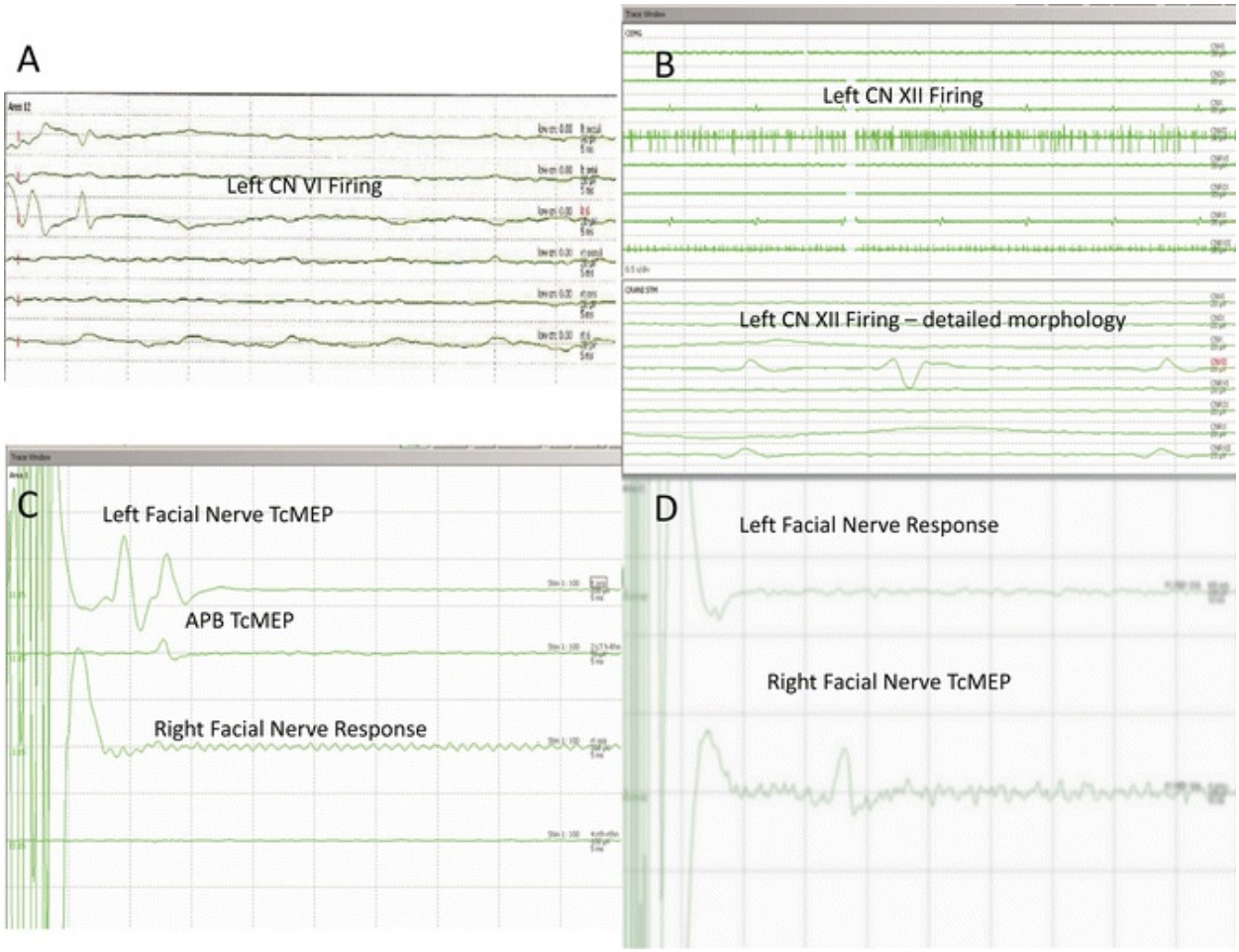

Fig. 43.6 CN EMG and CN VII TcMEPS during posterior fossa tumor resections . (**a**) An example of CN VI firing briefly during the resection of a posterior fossa tumor lying high in the rhomboid fossa (CN VI and VII monitored). (**b**) Demonstrates a train from CN XII on the left. The detailed morphologies of the CMAPs are shown in the bottom half of the panel. The lower cranial nerves were at risk during the resection of the tumor monitored using CN VII—XII EMG bilaterally. Two facial nerve TcMEPs are shown in (**c**, **d**). (**c**) Illustrates a left facial nerve TcMEP with a normal latency; a small APB MEP is present at a longer latency. The right facial nerve response is shown to be sure that the left TcMEP is a real MEP and not the result of direct stimulation of the facial nerve. The facial nerve TcMEP in (**d**) has a delayed latency. The tumor in this case was much larger than that of case in (**c**) and distorted the brainstem at the level of the facial colliculus

The only afferent pathway that can be monitored is the auditory pathway. The BAER provides information concerning the integrity of the auditory nerve, cochlear nucleus, and lateral lemniscus. Sudden significant changes in heart rate and/or blood pressure may be the only indications of irritation of CN IX/X afferent pathways and should prompt immediate notification of the surgeon by the anesthesia team.

Monitoring of tumor resections in the posterior fossa requires a highly

skilled IONM team and careful attention to the anesthetic management. The techniques used to elicit TcMEPs for intracranial surgery are different than those used during spine surgery. The region of the CST depolarized on the anode side must be as close to the axon hillock as possible to avoid depolarization of the CST beyond the region at risk. In most cases, acquisition of TcMEPs from the intrinsic muscles of the hand and digital flexors is sufficient to provide information regarding the integrity of the motor pathways. Exceptions to this generalization include lesions near the lateral part of the crus cerebri, as the CST fibers projecting the αMN innervating lower extremity muscles are in close proximity. Excessive anesthetic depth, producing burst suppression, or use of volatile agents in young children may prevent eliciting lower extremity TcMEPs when appropriate stimulating conditions for intracranial surgery are utilized. Further, smaller changes in the amplitude of the MEPs are needed to achieve alarm criteria during intracranial surgery than for spine surgery and the time window for corrective action is shorter during intracranial surgery than for spine surgery [68, 69]. The influence of anesthetic agents can confound the interpretation of changes if the anesthetic is not well managed or communication between the IONM team, the anesthesia team, and the surgical team is less than ideal.

Conclusion

A close working relationship between the anesthesiologist, the surgeon, and the neuromonitoring team yields optimal patient care during these specialized surgical procedures. The anesthesiologist must have an in-depth understanding of the surgical procedure, as well as a general knowledge of the different IONM modalities available, to help insure an anesthetic plan tailored to the successful interpretation of IONM data and optimal patient outcome.

Questions

1. At what age is the anterior fontanelle typically closed to palpation?

2. True or False: The inability to obtain D-waves in an 18-month-old child precludes obtaining motor evoked potentials.

3. What is the EEG “signature” for loss of consciousness with propofol?

4. What technique is especially helpful when trying to elicit motor evoked potentials from young children?

Answers

1. 9–18 months of age

2. False; although D waves cannot be recorded with current techniques in an 18-month-old child, MEPs can be recorded in a very high percentage of cases if TIVA is used for the anesthetic.

3. The presence of high power in the delta and alpha frequency bands, in frontal montages, has been shown to be associated with loss of consciousness with propofol.

4. Double-train stimulation as described by Journee and coworkers facilitates obtaining MEPs in young children. The optimization of stimulating parameters is frequently required to obtain optimal results.

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Section IV
Intensive Care

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_44

44. Monitoring in the Intensive Care Unit

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Keywords Monitoring – Intensive care unit – Cerebral oxygenation – Blood pressure monitoring – Spinal cord injury – Hypotension – Traumatic brain injury – Subarachnoid hemorrhage

Key Learning Objectives

- Balance multimodal monitoring for optimization of cerebral perfusion and oxygenation
- Consider the risks and benefits of noninvasive versus invasive hemodynamic monitoring in neurocritical care
- Describe the challenges of static central venous pressures as an estimate of preload
- Present the benefits of dynamic monitors of preload responsiveness.

Introduction

Neurologic illness is complex and often complicated by adverse effects on

the cardiopulmonary system. Studies have shown improved outcomes for patients treated in a dedicated neurologic intensive care unit (NICU) likely secondary to specialized nursing care, neurointensivist teams, and protocolized management of complex neurologic illness [1]. The common types of hemodynamic monitors within any intensive care unit (ICU) include temperature monitoring, continuous blood pressure measurements, electrocardiography, respiratory and ventilatory parameters, as well as static and dynamic measurements of volume status and cardiac output [2, 3]. Neuromonitoring within the NICU is often conducted with transcranial Dopplers, intracranial pressure (ICP) monitors, cerebral oxygen monitors, microdialysis catheters, and electroencephalograms; all of which are described in detail elsewhere in this text [4]. This discussion is presented in the context of a few case descriptions to exemplify the complexities of monitoring and managing patients with severe neurologic disease.

Case 1: Traumatic Brain Injury

A 42-year-old man presents to the emergency room after a gunshot wound to the left temporal region, with alcohol and cocaine in his initial toxicology screen. Upon admission, he demonstrated signs of high ICP with loss of consciousness and Cushing's response, which includes hypertension, bradycardia, and an abnormal respiratory pattern [5]. His initial Glascow Coma Scale score was seven, which is consistent with severe traumatic brain injury (TBI) . The patient's trachea was immediately intubated and he was admitted to the NICU for management of intracranial hypertension (ICH) and severe TBI. A full discussion of ICP monitors can be found in Chap. 15, "Monitoring Intracranial Pressure"; however, the basic concepts for treating ICH and physiologic monitors appropriate for the management of TBI shall be discussed in this section.

After intubation and transfer to the NICU, the patient was empirically treated for ICH with hyperventilation in an effort to decrease the partial pressure of carbon dioxide (PaCO2) in the blood, thereby increasing the pH of the cerebral spinal fluid (CSF) . Alkalinizing the CSF stimulates chemoreceptors and results in vasoconstriction of the cerebral vasculature [6]. Vasoconstriction decreases the cerebral blood flow and ICP within minutes. However, hyperventilation is only a temporary treatment for ICH because over the course of 8–12 h, the CSF will equilibrate the pH and reverse the

vasoconstriction. If hyperventilation is continued, the patient is at risk of rebound vasodilation and increased ICP or ischemia secondary to profound vasoconstriction. Consequently, it is important to frequently sample arterial blood gases and correlate the $PaCO_2$ with dynamic ICP measures while instituting other methods for treating ICH [6]. Alternatively, one can use capnography, the measure of expired or end-tidal carbon dioxide ($ETCO_2$) as a surrogate for $PaCO_2$ and thus a continuous monitor of ventilation. However, frequent calibration with blood–gas analysis is required as there are many factors that can alter the alveolar-arterial gradient for carbon dioxide, including low cardiac output and increases in anatomic or physiologic dead space ventilation [7].

During the acute phase of resuscitation for his severe TBI, the patient underwent placement of an external ventriculostomy drain for monitoring and management of ICH. Over the course of a few hours, the patient's ICP rose over 20 mmHg, which is generally considered the threshold for initiating pharmacologic therapy knowing that sustained ICP has been associated with poor outcomes and mortality [8–10]. Pharmacologic therapy for ICH includes diuresis with osmolar or loop diuretics, hyperosmolar therapy with hypertonic saline or mannitol, sedation, and finally burst suppression or barbiturate-induced coma and paralysis [8, 11, 12]. Furthermore, simple maneuvers to improve ICP should be instituted such as elevating the head of the bed, keeping the neck neutral to allow for unobstructed venous drainage, minimizing respiratory dyssynchrony and intrathoracic pressure associated with positive pressure ventilation, and avoiding painful procedures or stimuli without adequate sedation and analgesia that would increase blood pressure and or cerebral blood flow.

The early goals of treatment in TBI focus on the prevention of secondary injury. Primary injury involves the regions of the brain damaged with the initial insult. Secondary injury occurs with the systemic and regional alterations in pathophysiology that commonly result from neurologic insults and lead to decreased oxygen delivery to the surrounding parenchyma such as seizures, focal cerebral swelling, or increased ICP causing decreased cerebral perfusion. Systemic causes of secondary injury include hypotension, hypoxemia, anemia, hypo- or hypercapnia, hyperglycemia, and hyperthermia [12]. Preventing the systemic causes of secondary injury is at the forefront of critical care management in the NICU. There are several monitors available to measure brain tissue oxygenation including cerebral oximetry, jugular bulb

saturation (see Chap. 14, “Monitoring of Jugular Venous Oxygen Saturation”), and tissue oxygenation monitors [13]. Furthermore, microdialysis catheters can be inserted into the parenchyma and used to monitor the metabolic stress levels of brain tissue with continuous measures of glucose, pyruvate, and lactate [14]. Clinically, these monitors provide a guide for managing cerebral perfusion pressure, which depends on mean arterial pressure and intracerebral pressure and should be balanced with cerebral metabolic rate and oxygen utilization.

Cerebral Oxygenation

In light of refractory intracerebral hypertension , our patient received a jugular venous oxygen saturation monitor to measure the oxygen delivery to the brain. On day 2 of admission, the saturation fell below 50 %, which is a common threshold signifying risk of ischemia and secondary injury. Assuming the decreased measurement is not secondary to systemic causes such as anemia, hypoxemia, hypocapnia, or hypotension , cerebral causes including increased ICP and elevated metabolic rate must be diagnosed and treated. The patient was hemodynamically stable, normothermic, sedated, and paralyzed at the time. Accordingly, electroencephalography was initiated to rule out seizure and nonconvulsive status epilepticus. These clinical findings associated with the acute phase of TBI are often responsible for significant increases in cerebral metabolism and oxygen demand [15, 16].

After 5 days of maximal medical therapy for refractory ICH including hyperosmolar treatment with mannitol, diuresis with furosemide, and an induced barbiturate coma, the patient’s ICP normalized, but he developed significant metabolic alkalosis consistent with loop diuretic treatment and refractory hypokalemia and hypomagnesemia. The ECG demonstrated frequent premature ventricular contractions consistent with hypokalemia. These findings often precipitate malignant arrhythmias such as torsades de pointes, ventricular tachycardia, and ventricular fibrillation [13]. The diuretic treatment should be held until the potassium and magnesium for this patient are replete and the metabolic alkalosis resolves.

This is just one example of numerous possible metabolic derangements diagnosed with continuous electrocardiography. The ECG changes associated with central nervous system injury were first recognized over 50 years ago by Burch and colleagues [17]. Most often found after subarachnoid hemorrhage, these changes include peaked T waves, prolonged QT intervals , and U

waves. The pathophysiology of neurogenic myocardial dysfunction is not clear because several pathology case series from that time demonstrated normal hearts at autopsy [18].

Temperature Monitoring

On day 4 of admission, the patient was still intubated for altered mental status. While receiving cefazolin for prophylaxis with an external ventriculostomy drain, phenytoin for seizure prophylaxis, and haloperidol for agitation, the patient developed a fever of 38.3 °C. The differential diagnosis for hyperthermia in this patient ranges from infection to alcohol withdrawal, adverse effects of antibiotics, anticonvulsants, and antipsychotic medications, or central fever secondary to thalamic injury.

Hyperthermia increases the oxygen requirements of the brain and the metabolic rate of the body and is associated with worse prognosis, especially after neurologic injury [19]. Accurate monitoring of the core body temperature is necessary as peripheral measurements of temperature may be inaccurate for patients with hypoperfusion from low cardiac output, vasopressor therapy, or induced hypothermia. The role of therapeutic hypothermia after traumatic brain injury remains controversial. Several animal models and a few clinical trials of induced moderate hypothermia to core body temperatures of 32–33 °C have shown significantly reduced cerebral metabolic rate and promise for improved behavioral outcomes, but large multicenter clinical trials have yet to show conclusive evidence of improved long-term outcomes [20]. Furthermore, hypothermia has several adverse effects including shivering, increased risks of infection, arrhythmias, and coagulopathy [21].

The patient was ruled out for acute infection. His fever was controlled with an active cooling blanket until the antiepileptics and antipsychotic medications could be discontinued. He continued to recover from the ICP crisis and eventually was weaned from mechanical ventilatory support and transferred to acute rehabilitation.

Case 2: Subarachnoid Hemorrhage

A 37-year-old previously healthy woman presents with sudden and severe headache. Diagnostic imaging confirms a diffuse aneurysmal subarachnoid

hemorrhage (SAH) secondary to a ruptured anterior communicating artery aneurysm. The patient was admitted to the NICU for monitoring of her hemodynamics, ICP, and neurologic status while awaiting the availability of surgical treatment to secure her aneurysm.

Aneurysmal subarachnoid hemorrhage is associated with multiple neurologic and systemic complications [22, 23]. Several grading scales have been developed to standardize prognosis and treatment recommendations. The most common grading scales are the Hunt and Hess grade, the World Federation of Neurosurgical Surgeons (WFNS) Scale , and the Fisher Scale . The Hunt and Hess grading scale ranges from zero to five depending on the patient's level of consciousness, symptoms of headache or visual changes, and their neurologic examination; it was originally described to predict surgical risk during aneurysm clipping. Similarly, the WFNS scale is also a clinical assessment scale ranging from zero to five depending on Glascow Coma Score and the presence or absence of motor deficits; it is primarily used to predict clinical outcomes. The Fisher scale differs from the former two in that it involves radiographic severity of SAH via CT scan and ranges from one, for no evidence of blood, to four for diffuse SAH or intracerebral and intraventricular blood clots. The Fisher scale correlates with the risk of vasospasm, which may lead to delayed cerebral ischemia (DCI) and poor neurologic outcome [24].

Rebleeding after cerebral aneurysm rupture constitutes the most significant morbidity and mortality risk. Blood pressure control is vital until the aneurysm is secured with a surgical clip or endovascular coils. Delayed cerebral ischemia secondary to arterial narrowing, classically referred to as vasospasm , occurs 3–14 days after subarachnoid hemorrhage. DCI secondary to vasospasm remains the most common and preventable neurologic complication of aneurysmal subarachnoid hemorrhage leading to poorer prognosis and higher rates of long-term disability [23]. The pathophysiology involves cerebral vascular reactivity and arterial intimal narrowing that can progress to cerebral ischemia, infarction, and permanent neurologic dysfunction.

The incidence of vasospasm is often monitored with transcranial doppler ultrasonography (TCDs) , serial neurologic exams, and cerebral angiograms. TCD ultrasonography is simple, conducted at the bedside, noninvasive, repeatable, and therefore the most frequent screening tool for cerebral vasospasm outside of serial neurologic exams [25, 26]. A full description of

TCD ultrasonography and its clinical applications is discussed earlier in Chap. 13 (“Transcranial Doppler”); although briefly, TCDs measure velocity of flow in cerebral arteries assuming that higher velocities correspond to a narrower arterial lumen and therefore indicate vasospasm. The value of TCD ultrasonography rests in the individual trends for each patient [26]. For example, if our patient routinely demonstrated TCDs ranging in the low 100 cm/s but suddenly showed an increased velocity more than 200 cm/s in the anterior cerebral artery window, clinical correlation for vasospasm and diagnostic angiogram would be indicated.

Although TCDs often correlate with angiographic evidence of vasospasm, their sensitivity is limited for DCI at about 70–80 % most likely because they provide only one snapshot of clinical assessment without continuous monitoring [25]. Brain tissue oxygen monitors offer continuous monitoring of areas at risk for ischemia or infarction. However, they are invasive and fail to provide a global assessment of cerebral perfusion [23]. Comparative studies evaluating the correlation of continuous monitors of cerebral perfusion based on flow, pressure, or oxygen indices including tissue partial pressure oxygen monitors, thermal dilution cerebral blood flow measures, and ICP measures have yet to demonstrate reliable associations with clinical outcome but many of these studies are small and differ in patient selection and methodology [25, 27].

Blood Pressure Monitoring

Common management protocols for the prevention of rebleeding and treatment of cerebral vasospasm after aneurysmal SAH include specific parameters for blood pressure control and careful monitoring of the patient’s fluid status, myocardial function, and respiratory physiology [22, 23].

Noninvasive blood pressure techniques typically measure distal pulsations with external compression of arterial flow. This method can only be used intermittently long term and is therefore limited in the intensive care unit where the risk of circulatory instability is high and recognition of fluctuations in systolic and diastolic pressures is vital. Intra-arterial pressure monitoring provides a continuous and direct measure of systolic and mean blood pressure with a displayed waveform throughout the cardiac cycle. It is indicated when rapid swings in blood pressure or fluid shifts are anticipated, specific narrow range of blood pressure control necessary, and when noninvasive measurements are inaccurate.

Continuous blood pressure monitoring with periodic correlation to noninvasive cuff pressures ensures the most accurate estimate of systemic blood pressure. Furthermore, the arterial pulsations and waveforms can be used to estimate cardiac output and preload mechanics.

Any patient with a subarachnoid hemorrhage is at risk of significant medical and neurologic complications, including cardiogenic and neurogenic pulmonary edema causing respiratory failure, as well as common disturbances in sodium balance (Table 44.1) [28, 29]. Invasive hemodynamic monitors also provide access for frequent monitoring of arterial blood gases to ensure adequate oxygenation, ventilation, and correct metabolic derangements or electrolyte imbalance.

Table 44.1 Sodium diathesis

Criteria	SIADH	CSW	DI
Serum sodium mmol/L	<135	<135	>145
Serum osmolarity mOsm/kg	<285	<285	>290
Urine osmolarity mOsm/kg	>200	>200	>200
Urine sodium mmol/L	>25	>25	–
Fluid balance	↑	↓	↑

SIADH syndrome of inappropriate antidiuretic hormone, *CSW* cerebral salt wasting, *DI* diabetes insipidus

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Case 3: Spinal Cord Injury

A 22-year-old male suffered a complete spinal cord injury at C6 after diving into a shallow pool. The patient presents to the emergency room hypotensive and bradycardic. Other diagnostic studies are negative for further injury. Neurologically, the patient is insensate below C5 and quadriplegic corresponding to American Spinal Injury Association (ASIA) class A injury [30, 31]. However, he remains alert and oriented, maintaining spontaneous ventilation and appropriate oxygen saturation. Of note, all patients suffering traumatic insult severe enough to cause spinal cord injury and hypotension should be evaluated for other injuries; particularly those presenting an immediate threat to life such as intracerebral hemorrhage, tamponade from aortic dissection, pneumothorax, and intra-abdominal injury [30].

Management of acute spinal cord injury aims to prevent secondary injury

from neuronal hypoperfusion with associated progression of neurologic deficits. Accordingly, the maintenance of adequate cardiac output and systemic blood pressure for optimal spinal cord perfusion is paramount to the critical care goals for patients with spinal cord injuries [32]. Neurogenic shock often complicates high thoracic and cervical spinal cord injuries. It is a form of distributive shock characterized by autonomic dysfunction with a sympathectomy causing low systemic vascular resistance, decreased venous return, and hypotension [30, 32]. Fluid administration to restore and maintain euvolemia is the primary goal of early resuscitation of distributive shock and often guided by central venous pressures (Fig. 44.1), but clinical evaluation of the patient's intravascular volume status remains difficult [26].

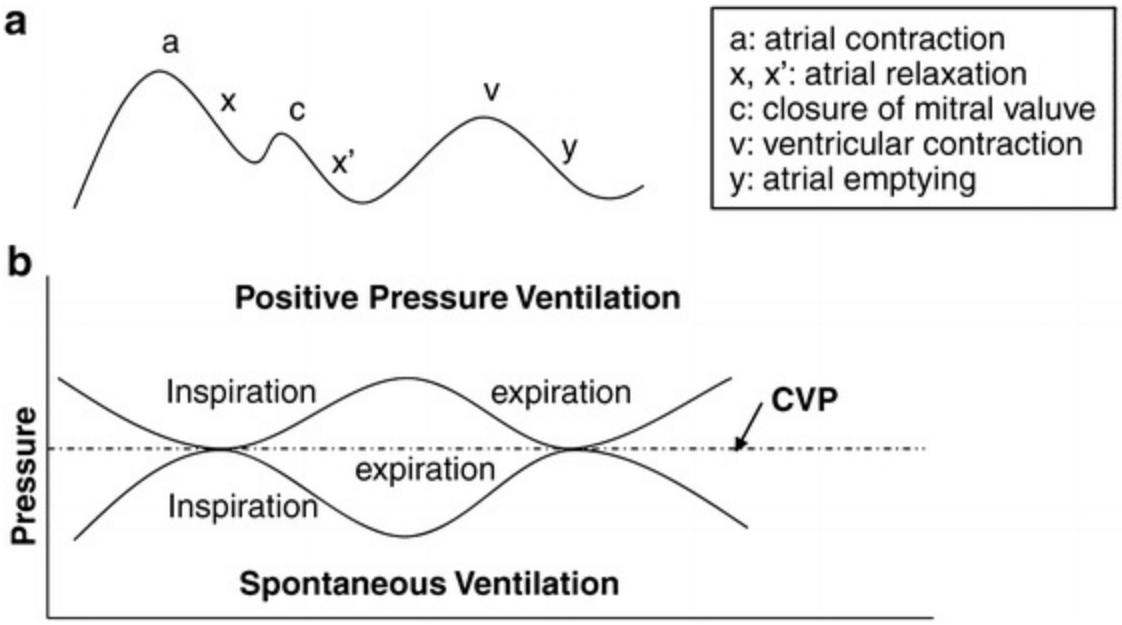

Fig. 44.1 Central venous pressure waveform (**a**). Variations in central venous pressure (CVP) with positive pressure ventilation versus spontaneous ventilation (**b**). The true value of CVP should be measured at end-expiration

Monitoring Fluid Status and Cardiac Output

The assessment of fluid status depends on the assimilation of multiple signs, symptoms, monitors, and laboratory values . This patient was managed with volume expansion and blood pressure augmentation to maintain a mean arterial pressure greater than 85 mmHg. Given the need for accurate assessment of intravascular volume and vasopressors to support the blood pressure, the patient had multiple indications for a central venous catheter.

The typical CVP waveform is depicted and described in Fig. 44.1a. In order for the CVP to accurately estimate preload, intrathoracic pressure must equal atmospheric pressure, which occurs only at the end of expiration [33]. The CVP waveform varies with the cyclic changes in intrathoracic pressure during spontaneous and positive pressure ventilation [33, 34]. Figure 44.1b depicts the point along the CVP waveform where pressure should be recorded for clinical determination of transmural venous pressure.

Pulmonary Artery Catheters

Central venous pressure estimates preload by assuming a normal compliance within the left and right ventricles and pressure measurements that correlate with the left ventricular end diastolic volume or preload. The CVP misrepresents left ventricular filling pressures when ventricular or pulmonary artery compliance decreases or in the case of valvular disease or dysfunction. A pulmonary artery catheter (PAC) “wedged” with balloon occlusion to stop flow measures the pulmonary artery occlusion pressure (PAOP) which estimates left ventricular end-diastolic pressure through the static column of fluid in equilibrium with the left atrium. The PAOP is a better surrogate for preload as it is independent of right ventricular compliance and pulmonary hypertension or mitral stenosis [33, 35]. PACs also provide measures of cardiac output, mixed venous oxygen saturation, and estimates of systemic vascular resistance.

Returning to our patient with acute cervical spinal cord injury and hypotension , should he be refractory to volume resuscitation with progressive end-organ hypoperfusion and tissue hypoxia, he meets the definition of shock. Given traumatic injury in this patient, he could be suffering from hypovolemic, distributive, cardiogenic or obstructive shock secondary to hemorrhage, spinal cord injury, tamponade, or pneumothorax. Table 44.2 uses the common variables obtained from a PAC to describe the various hemodynamic features that differentiate shock states and allows for the appropriate treatment with fluids, blood products, inotropic support, or vasopressors.

Table 44.2 Four types of shock

Type of shock	**Clinical example**	**CVP**	**SVR**	**PAOP**	**CO**	**SVO_2**
Hypovolemic	Acute hemorrhage	↓	↑	↓	↓	↓

Cardiogenic	Myocardial infarction, congestive heart failure	↑	↑	↑	↓	↓
Obstructive	Pulmonary embolism, tamponade, tension, pneumothorax	↑	↓	↓	↓	↓
Distributive	Sepsis, neurogenic shock, anaphylaxis	↓	↓	↓	↑	↑↓

CVP central venous pressure, *SVR* systemic vascular resistance, *PAOP* pulmonary artery occlusion pressure, *CO* cardiac output, SVO_2 mixed venous oxygen saturation

Preload Responsiveness

The first priority for resuscitation of distributive shock with spinal cord injury is volume expansion to increase preload and restore euvolemia. However, the value of CVP or PAOP adequate for optimal spinal cord perfusion varies with each patient and does not always correlate with fluid responsiveness [33]. The Frank Starling Curve describes the relationship that increases in stroke volume result from increased preload but only to a point beyond which inotropic or vasopressor support is necessary to augment blood pressure. Preload responsiveness is traditionally evaluated with a fluid challenge and observation of the resultant change in blood pressure or cardiac index. However, fluid boluses increase the risk of iatrogenic pulmonary edema, total body volume overload, and hyperchloremic metabolic acidosis. In the case of a patient with an indwelling arterial catheter receiving positive pressure ventilation, preload responsiveness can be assessed by observing the variation in pulse pressure or systolic blood pressure [34, 36].

Conclusion

Neurologic intensive care units staffed with nurses and physicians skilled and experienced in caring for patients with neurologic illness improve outcomes. The sophistication of neuromonitoring modalities in conjunction with hemodynamic monitors optimizes the management of critically ill patients and allows the intensive care team to monitor end organ perfusion continuously. In the NICU, the central nervous system is the tissue most at risk of ischemia. As mentioned earlier and in other chapters of this text, there are several monitors of cerebral perfusion and cerebral function available for continuous assessment during critical illness. Each type of monitor has advantages and disadvantages, complications and indications specific to

different types of patients, and different classes of hemodynamic shock (Table 44.2). Outcomes literature supporting the use of continuous hemodynamic monitoring is lacking but often the risks are small and the patient morbidities high. This chapter reviewed the clinical role of several measures of cerebral perfusion and function as well as invasive and noninvasive hemodynamic monitors for patients in the ICU after neurologic injury.

Questions

1. A 55-year-old man is in the neurologic intensive care for therapeutic hypothermia after sudden cardiac arrest. The patient is hemodynamically unstable on vasopressor support. Which of the following temperature sources is not appropriate for monitoring this patient:

    a. Skin temperature probe

    b. Bladder catheter

    c. Rectal temperature probe

    d. Pulmonary artery catheter

2. A 22-year-old man suffers an acute traumatic cervical spinal cord injury with subsequent neurogenic shock. He requires full mechanical ventilatory support and is hypotensive on phenylephrine to maintain blood pressure goals. Which of the following parameters is the best indication that the patient would have a positive blood pressure response to a fluid bolus?

    a. Central venous pressure of 9 cm H_2O

    b. Pulse pressure variation of less than 15 %

c. Systolic blood pressure variation of greater than 10 mmHg

d. Stroke volume variation of less than 15 %

3. A 74-year-old woman presents to the neurologic intensive care with an acute ischemic stroke of the right middle cerebral artery with associated cerebral edema, significant midline shift, and impending herniation. She is intubated, mechanically ventilated, and sedated. Her elevated intracranial pressure is treated immediately with mannitol and burst suppression as she is prepared for decompressive craniectomy. Which of the following is the most appropriate monitor of alveolar ventilation with the goal of acute hyperventilation?

   a. End tidal CO_2

   b. Arterial $PaCO_2$

   c. Minute ventilation

   d. Oxygen saturation

Answers

1. A

2. C

3. B

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Footnotes

1 Asterisk indicates key reference.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_45

45. Epilepsy and Seizures: OR and ICU Applications of EEG

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Keywords Monitoring – Electroencephalography – Electrocorticography – Seizure activity – Penfield technique – Direct cortical stimulation – Intensive care unit – Awake craniotomy – Anesthesia

Key Learning Points

- Epilepsy is present in 0.5–1 % of the population and 20–40 % of the patients have seizures that cannot be controlled with antiepileptic drugs. Approximately 50 % of these patients are surgical candidates, of which 30–60 % of patients will become seizure free.

- Before surgery, patients are evaluated using continuous EEG with video monitoring and a variety of functional studies of their cortical activity such as functional MRI.
- A preoperative Wada test is used to determine the dominant hemisphere where speech and language eloquent cortex is located.
- Some patients have an initial craniotomy to place grid and depth electrodes so that EEG and video monitoring can be performed before a second craniotomy to resect the epileptogenic zone where the seizure initiates.
- The motor cortex can be identified by stimulation of the cortex and the patient identifying motion if awake or by muscle activity response from MEP if under general anesthesia .
- The eloquent cortex can be identified in the awake patient by errors in speech and language tasks during cortical stimulation.
- General anesthesia for craniotomies where ECoG recording is done requires minimal inhalational agents and may require total intravenous anesthesia if muscle responses from direct cortical stimulation with motor evoked potential methods are used.
- EEG is useful in the ICU for the detection of nonconvulsive seizures, the detection of cortical ischemia, and titration of metabolic-suppressing drugs.

Introduction

The electroencephalogram (EEG) is useful for several types of monitoring in the operating room and in the intensive care unit (ICU) . As presented in Chap. 10 (“EEG Monitoring”), the EEG is the product of the electrical activity in synapses of cortical pyramidal cells. As such, its measurement on the scalp or from electrodes applied directly on the surface of the brain allows insight into the synaptic activity. EEG may be recorded using a variety of montages and reported both as EEG waveforms, quantitative data, and as processed variables (Chaps. 10 and 11, “Clinical Application of Raw and Processed EEG”). In particular, the ability to detect the electrical activity of seizures is a unique aspect specific to EEG that is useful during surgery and

in the ICU.

With recent advances in EEG electrode technologies, the ability to record real-time continuous EEG (cEEG) with video for hours, days, and weeks without having to remove electrodes for computerized tomography (CT) and/or magnetic resonance imaging (MRI), has increased its overall use in the ICU. EEG is used in a variety of clinical settings, with the largest majority being used for the detection and evaluation of seizures in the comatose or altered mental status patient and impending ischemia [1]. These applications will be reviewed here.

Epilepsy

Epilepsy is one of the most common neurological disorders , affecting 0.5–1 % of the population [2, 3]. A seizure, i.e., a single occurrence, is a change in neuronal activity that presents as an abnormal EEG pattern associated with a variety of clinical symptoms (Fig. 45.1). These range from starting with impairment of consciousness to focal or generalized tonic clonic movements (termed *convulsive*). Nonconvulsive seizures also occur (and may go undetected) in the patient with altered mental status or coma. Epilepsy can have both genetic and acquired causes , with interaction of these factors in many cases. Genetic defects , likely effecting ion channels, are thought to be commonly involved. When the cause of a seizure is known (e.g., associated with a brain tumor) the condition is not usually referred to as epilepsy. The terms seizure and epilepsy are often used interchangeably. However, epilepsy should only be used to describe a clinical diagnosis when seizures are unprovoked and recurrent.

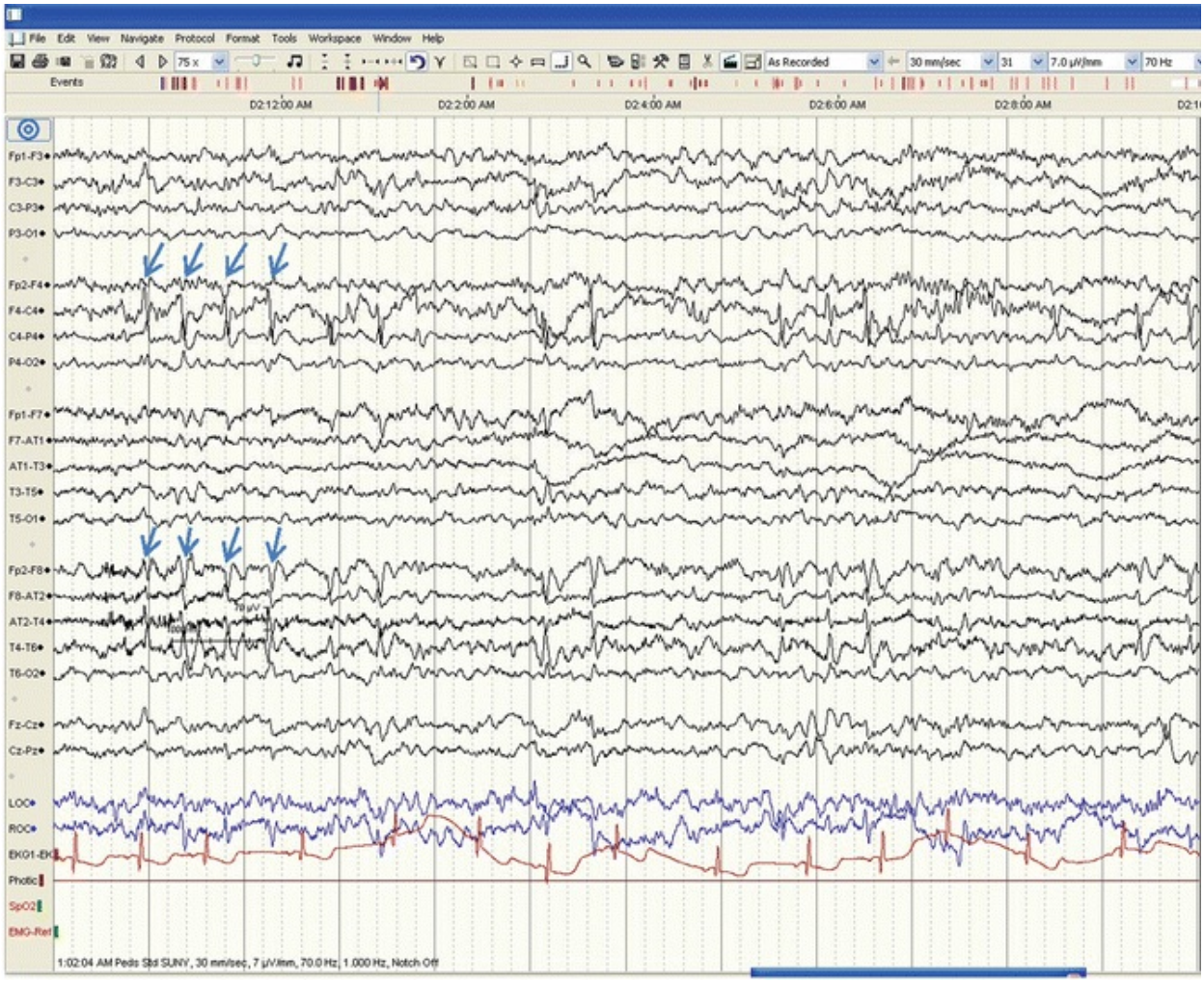


Fig. 45.1 Classic scalp recorded spike and waves in the right central-temporal head regions at *arrows* (*south west arrow*)

Currently, over 20 antiepileptic drugs (AEDs) are available but 20–40 % of patients cannot be successfully controlled on one or more drugs either due to ineffectiveness or unacceptable side effects [2, 3]. A lack of understanding of the generation of seizures inhibits the development of effective drugs . Mortality in drug-resistant patients is four times that in patients who are responsive to medication, prompting the desire for treatment to stop seizure activity to improve the quality of life and life expectancy. About 50 % of drug-resistant patients are candidates for surgery. Surgery to help the patient achieve a seizure-free state involves removing the neural tissue of the “epileptogenic zone” and is successful in 30–60 % of patients in terms of long-term freedom from seizures [2]. This region is often referred to as the epileptogenic zone : the region where ictal discharges originate is called the

“irritative” zone and the region that produces symptoms is referred to as the “symptomatogenic” zone .

Whether seizures are focal or generalized determines the type of surgical procedure . Some seizures are partial (starting in one hemisphere and affecting only part of the central nervous system) while some are generalized (starting in both hemispheres). Partial seizures may be preceded by an aura. Seizures are thought to originate in one or more localized zones thought to be the result of central nervous system (CNS) insults, which are usually never identified. Complete resection of the epileptogenic zone leads to the best results with freedom from seizures. In some patients the epileptogenic zone is impossible to resect because it cannot be identified, exists in multiple hemispheres, or because it overlaps with important eloquent cortex (e.g., motor or speech areas). These patients may be candidates for nonresective procedures such as disconnection of pathways that propagate the seizure (e.g., corpus callosotomy) or stimulation/modulation techniques (deep brain stimulation, vagal nerve stimulation, trigeminal nerve stimulation, responsive neurostimulation) [4].

When being evaluated for surgery, patients undergo simultaneous video and standard scalp 24-h EEG monitoring from 32 or more channels to characterize their clinical manifestations and associated electrographic patterns. Termed Phase I, video EEG monitoring (vEEG) can take days to a week depending on the successfulness of recording seizures. These patients are admitted into a dedicated epilepsy monitoring unit (EMU) generally with simultaneous withdrawal of AEDs. This facilitates the ability to record multiple seizures or nonepileptic events not requiring surgery within a short period of time. The patient or present family member participates in their seizure identification by actively pressing a portable alarm system. This alerts caregivers of the need to ensure patient safety during the ictal phase of the seizure, test the patient’s postictal clinical condition, and review the simultaneously captured vEEG .

During the admission, standard activation procedures such as hyperventilation and sleep deprivation are used to enhance seizure capture. There may be multiple triggers for seizures. Therefore, it is important to use provocative techniques based on patient history to maximize the effectiveness of the patient admission. Video EEG is considered the standard in distinguishing seizures from other nonseizures such as parasomnias , syncopal episodes , and events with a psychogenic origin [5]. It is important

to characterize the clinical context of the semiology of the patient's event to further help localize the region of seizure onset (epileptogenic zone). The recent advances of EEG-triggered functional MRI (fMRI) allow vEEG to be recorded simultaneously while performing fMRI during ictal and interictal periods. The premise being that since seizure activity causes increased cerebral hemodynamic changes, these can be correlated with fMRI blood oxygen level-dependent technique alongside the vEEG to closer pinpoint the epileptogenic zone [6]. Due to its practical limitations (recording during ictal events) its practice, while compelling, is limited.

Functional MRI , however, can play a useful role preoperatively in the identification of critical anatomical locations and their functions. Using rapid echo planar imaging while the patient performs multiple motor tasks such as tongue movements , fist clenching , toe or finger taps and a multiple language task such as the verb generation task or the semantic decision-making task, detects small changes in signal intensity related to changes in cerebral blood flow. Computerized image processing can then define the areas of cortex activated by the specific task. Simultaneous three-dimensional rendering of cerebral topography gives a unique display of critical relational anatomy, creating both a structural and functional brain model. The ability to localize different body representations in the primary motor and somatosensory cortex, as well as for localizing and lateralizing language function prior to surgery, is a complementary presurgical evaluation with the Gold Standard Wada test (intracarotid amobarbital testing) for language hemispheric dominance and for guidance with intraoperative cortical stimulation [7].

Because scalp vEEG recording is a considerable distance away from where a seizure may originate, scalp electrodes are only capable of detecting a seizure discharge after it has spread considerably. While scalp vEEG is good at giving an overview of the electrical activity of the brain and suggests where the seizures are originating, if surgical ablation of an epileptogenic zone is being considered, further patient assessment is needed during Phase II and/or Phase III monitoring. Phase II monitoring involves a craniotomy , where placement of multiple-sized subdural grids and strip electrodes are placed bilaterally depending on the presumed epileptogenic zone (Fig. 45.2). If further hemispheric localization is needed, Phase III monitoring involves a unilateral craniotomy with electrode recordings from up to 128 contact points and may involve the addition of depth electrodes (stereoelectroencephalography) in the hippocampal head regions. Surgical

EEG recordings during these phases assure evidence of proper electrode contact with the cortical surface, creation of the preliminary maps identifying where the placement of the grids and electrode strips are located, and the ability to create the intracranial recording montage in the OR. Anesthesia management for this surgery is similar to others where electrocorticography is being recorded.

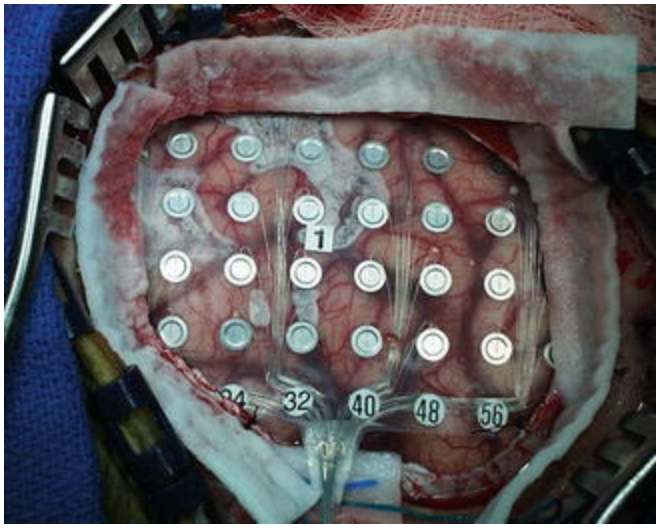


Fig. 45.2 Craniotomy showing 64-channel electrode grid placement on the cortical surface

Following surgical recovery, the patient is again monitored in an EMU where attempts are made to further lateralize the epileptogenic zone by recording from the implanted electrodes and additionally analyzing the seizures using computerized techniques such as three-dimensional imaging . Using cortical electrodes, recorded seizures from the epileptogenic zone usually have high-frequency oscillations or evolving “rapid discharges ” as compared to the standard spike and wave architecture seen from scalp leads [4] (Fig. 45.3). Phase II or III recording can last up to 2 weeks in the attempt to record multiple seizures with the same clinical manifestations (seizure signature) and localize them to their epileptogenic zone.

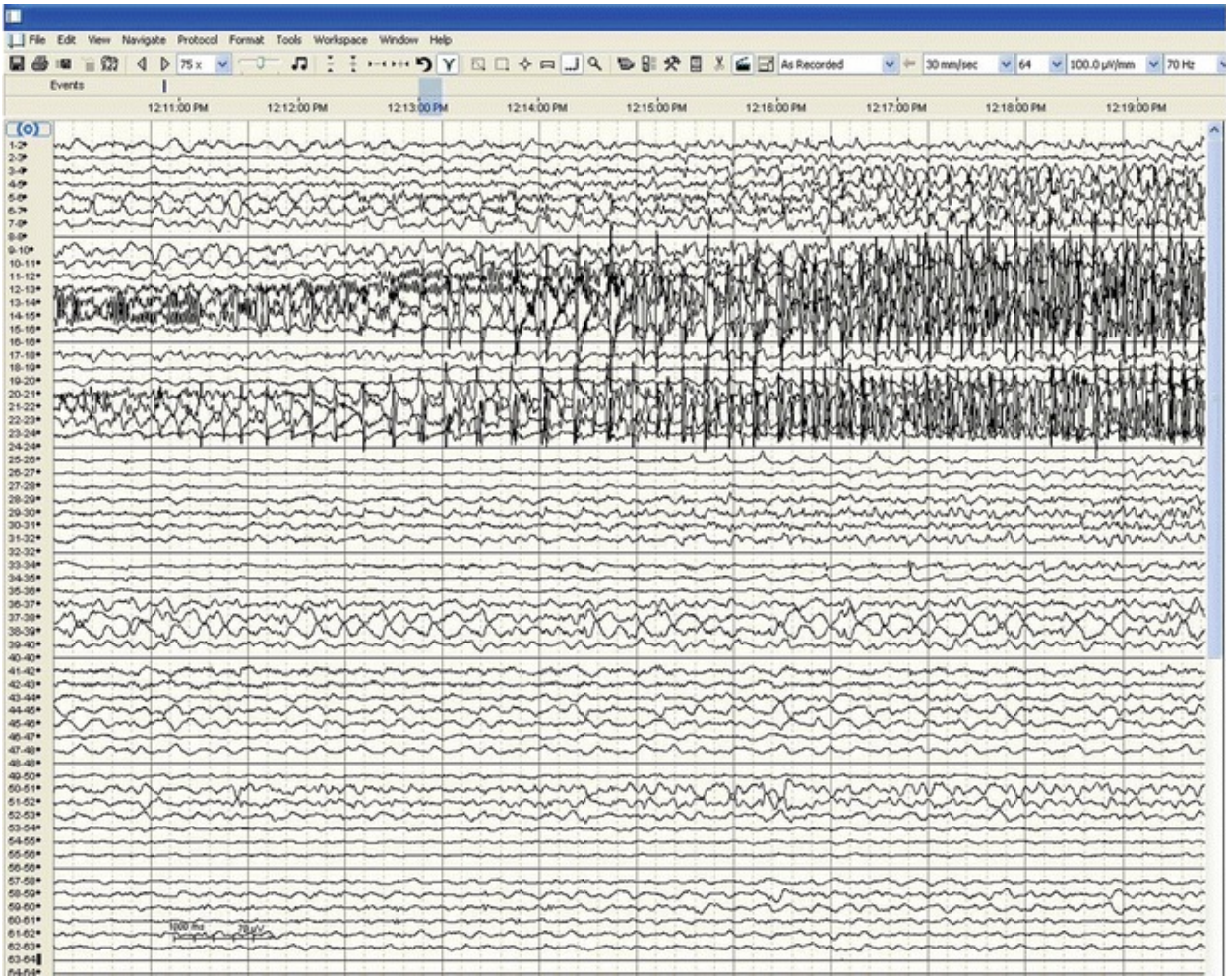
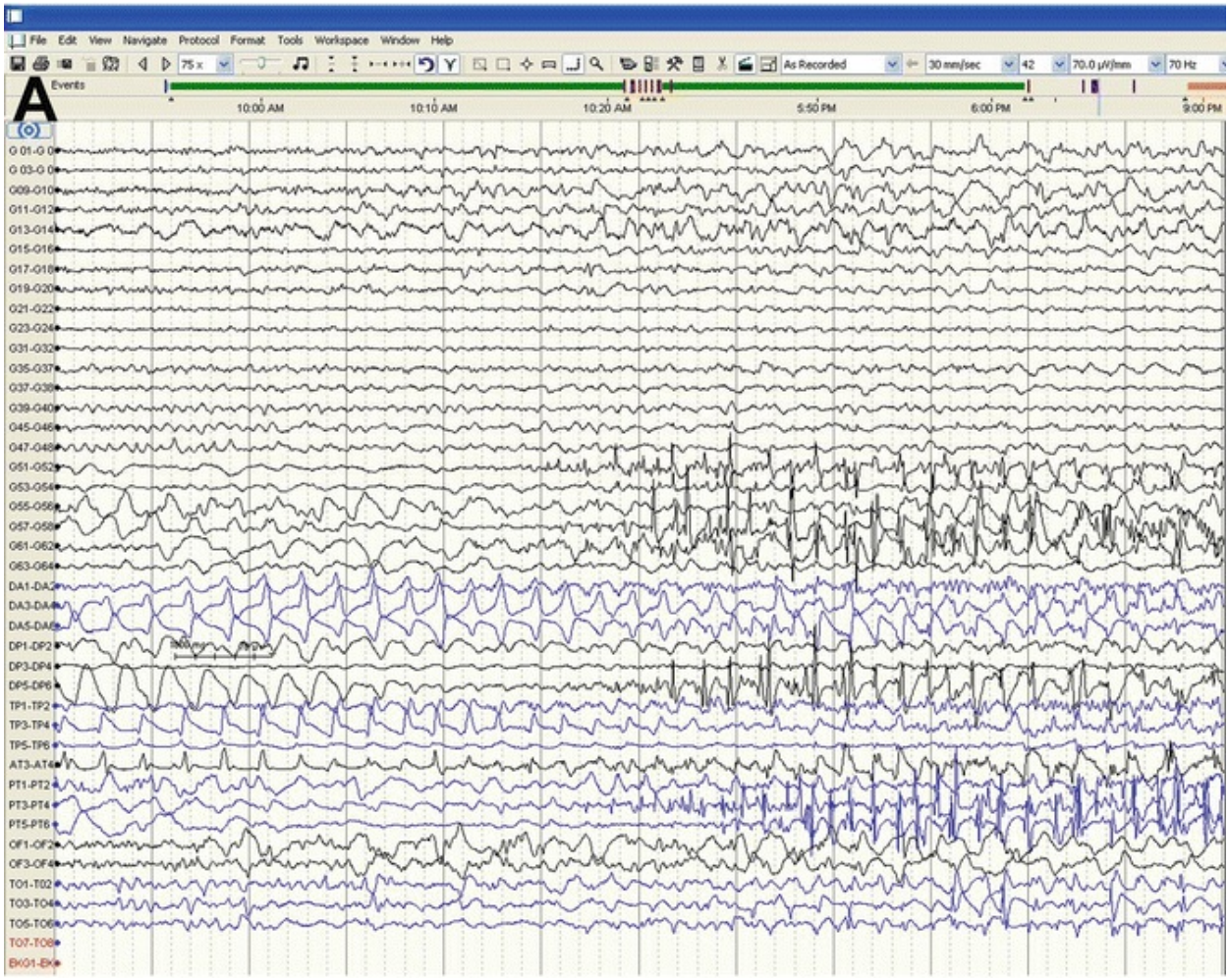


Fig. 45.3 Seizure activity consisting of high-frequency oscillations beginning in electrode contact point 14 followed by spread of the seizure to adjacent areas

The patient then returns for another craniotomy to remove the electrodes, determine the cortical tissue to be removed, map functional tissue to be avoided, and resect the epileptogenic zone. In the operating room, recording of EEG directly from the cortical surface (ECoG) is valuable in the identification and localization of epileptic activity in preparation for pathological tissue resection as a means to control intractable epilepsy (Fig. 45.4a–c). Depending on the patient cooperativeness and the site of the epileptogenic zone, the approach to the surgery can either be done with the patient awake for the key portions (awake craniotomy) or done under general anesthesia . The choice of anesthesia agents greatly affects the ECoG .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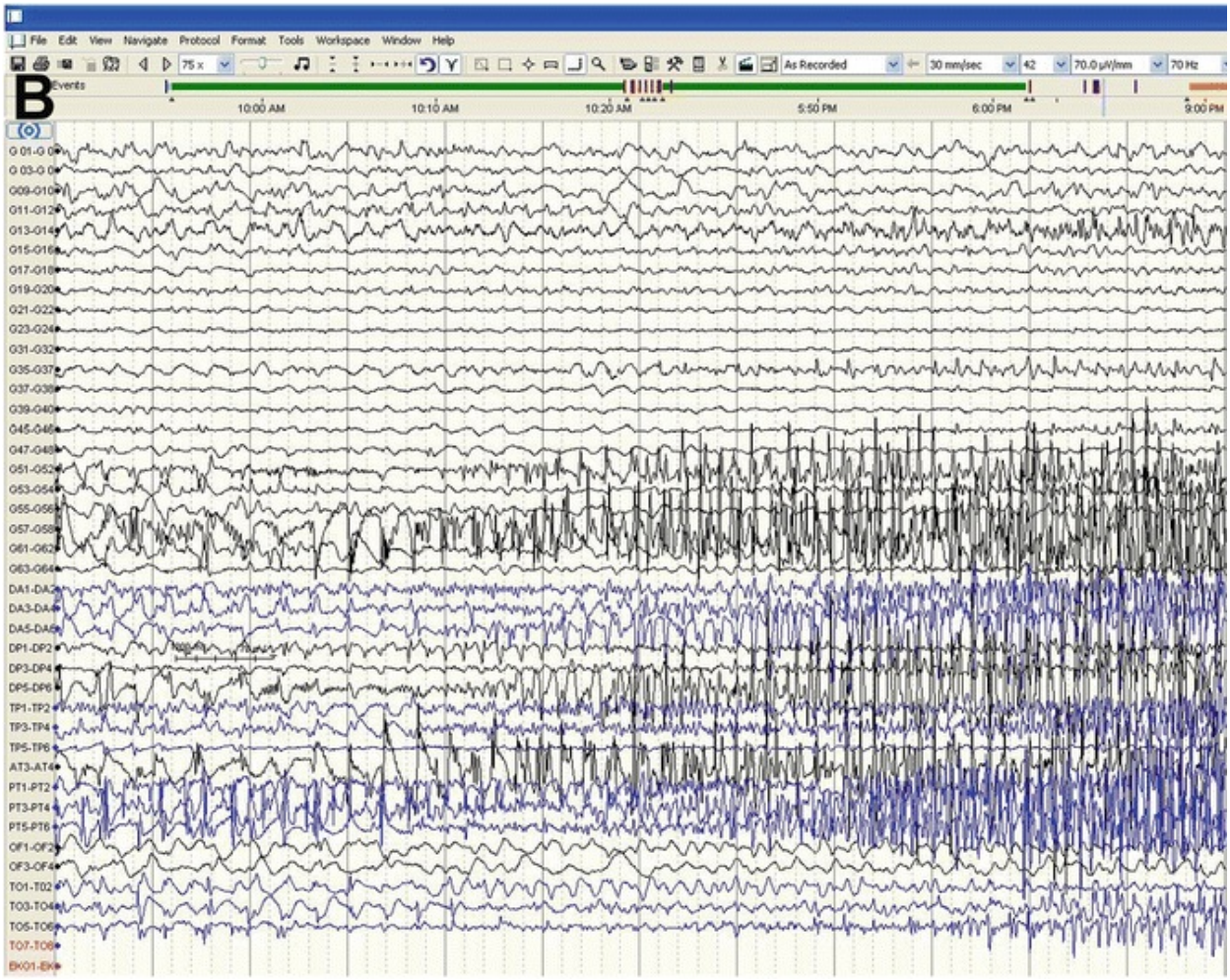
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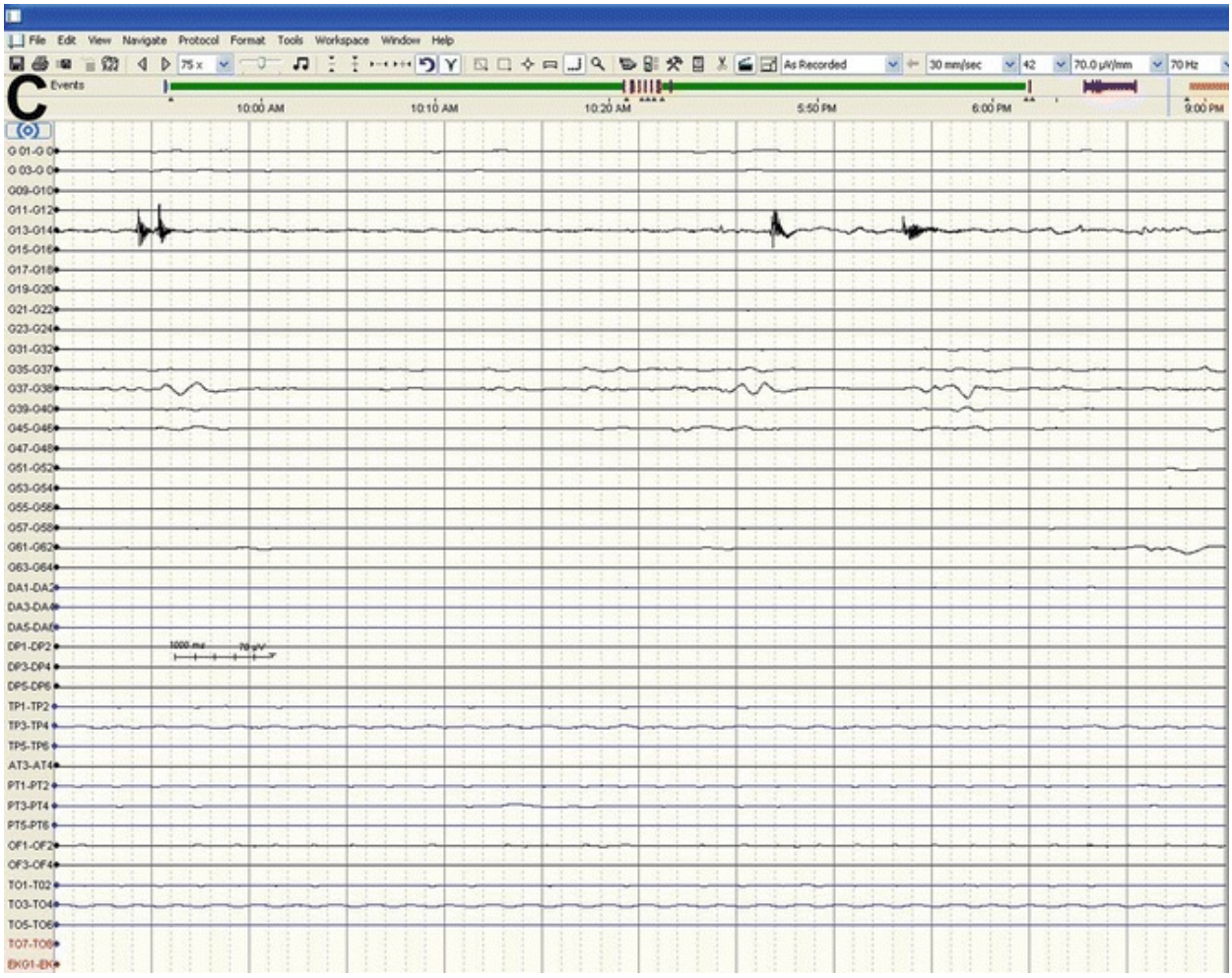


Fig. 45.4 (**a**) Start of Focal Seizure during ECoG beginning in the depth electrodes DA4/DA5 and anterior temporal grid strips. (**b**) Seizure spreads to adjacent cortical grids and strips. (**c**) Seizure stopped with saline applied directly to cortical surface—followed by cortical depression

Because of the patient's ability to participate in identification of eloquent regions, awake craniotomy is the preferred technique when these must be identified in the dominant hemisphere. This also minimizes the impact of anesthesia agents. For anesthesia considerations for an awake craniotomy , *see* Chap. 18 ("Anesthesia for Awake Neurosurgery "). In general, local anesthesia is used for the placement of stereotactic frames and head fixation devices (e.g., Mayfield) and topical anesthetics for discomfort of a urinary catheter. Infusions of propofol or dexmedetomidine with opioids (e.g., remifentanil) can assist during positioning and sedation until the craniotomy has been completed and the surgeons are ready for the procedure (at which time the infusions of the sedative and opioid are stopped).

However, general anesthesia will be needed in some patients who will be

unable to cooperate or if an attempt at an awake procedure fails. If general anesthesia is used, it is important to maintain a stable light anesthetic during the ECoG recording using agents that minimize the depression of the ECoG signatures necessary for foci location. Opioids, with either propofol or dexmedetomidine, have been used. If halogenated agents are needed, very low doses of isoflurane or desflurane have been used [8]. Sevoflurane and nitrous oxide are not recommended.

During the craniotomy , electrophysiological monitoring is used for several components. First, ECoG is used to confirm or identify the epileptogenic zone to be ablated. If the epileptic activity is not sufficiently active, medications that have been used to activate it are shown in Table 45.1 [8]. Of note, some of these medications may activate seizure activity nonspecifically (i.e., from areas other than the epileptogenic zone, may induce seizures, and some have doses that may not be appropriate in the awake patient [notably opioids]). Ketamine is one of these nonspecific neurostimulants. Use of methohexital and alfentanil appears to have the largest experience. Activation may be particularly important if general anesthesia is used. Hyperventilation appears to increase the nonspecific activation [8].

Table 45.1 Intravenous medications which may activate epileptogenic foci

Drug	Dose
Methohexital[a]	25–100 mg
Etomidate	0.2 mg/kg
Propofol	50–175 mg
Fentanyl[a]	17–35 μg/kg
Remifentanil	1–2.5 μg/kg
Alfentanil	20–100 kg

Data from Chui et al. [8]
[a]Denotes drugs that can activate nonspecifically

When the abnormal foci is located near the eloquent cortex (speech or motor cortex), an awake craniotomy combined with ECoG allows for identification and localization of these regions near the epileptogenic zone. Defining the margin between abnormal and functional cortex allows normal brain preservation, complete epileptogenic zone resection, and a reasonable

possibility of permanent seizure free state. Stimulation of the cortex is used to identify the functional tissue to be preserved.

Optimally, the identification of functional tissue to be spared is done during an awake craniotomy with preoperative identification of such areas using imaging techniques (e.g., single-positron emission tomography [SPECT], PET for metabolically active areas with tasks, Wada testing to determine the dominant hemisphere, fMRI to create structural and functional brain models) or by use of the implanted electrodes at the bedside. In the operating room, mapping of these regions is done using different means of stimulation (handheld stimulators versus electrode grid strips) (Penfield technique versus direct cortical stimulation with motor evoked potentials; dcMEPs) and recording techniques are used to locate the eloquent cortex from the abnormal tissue [9] (*see* Chap. 9, "Brain and Spinal Cord Mapping").

For motor cortex mapping (*see* Chap. 9), focal electrical stimulation of the cortex combined with a clinical response in the awake patient locates the motor cortex by causing nonvoluntary motor activity. When awake, the patient is asked to identify movement (often a "tug") in response to stimulation. This patient participation can be continued if desired until the resection is complete or when the resection is halted as encroachment on the region is identified clinically. Occasionally the anesthesia team may identify associated movement. In the awake patient, the Penfield/Ojemann technique is typically used for stimulation.

For mapping of the speech-related areas, the brain is stimulated during a language-related task. For example, the patient may be shown a series of pictures of common objects and asked to name them (Boston Naming Test). The eloquent cortex is identified when the task is interrupted (speech arrest/pause or word errors) [10].

Second, ECoG is used to identify undesirable after discharges or elicited seizure activity caused by the stimulation. The Penfield/Ojemann stimulation technique is associated with a moderate incidence of seizures so ECoG monitoring is important for seizure identification for this technique [11]. This activity may confound the identification of the initial epileptogenic foci by activating tissue adjacent to the epileptogenic zone and may pose a threat to the overall patient management (e.g., loss of airway in the wake patient). The EEG has characteristic waveforms after cortical stimulation and can be used to identify activity that is associated with preictal (precedes seizure) EEG,

spreading seizure-like EEG, or an electrographic seizure. All of these EEG changes are usually stopped by cold saline applied directly on the exposed cortex. These can be followed by an appropriate (short acting) bolus of antiepileptic drugs (AED) such as propofol or methohexital should saline not terminate the seizure. Stimulation-induced seizures are frequent occurrences ranging from about 10 to 20 % of patients when a 50- to 60-Hz monopolar stimulator device is used (Penfield/Ojemann technique) [10, 12].

If general anesthesia is required or chosen, the motor cortex may be identified using direct stimulation of the cortex and recording of muscle responses using the motor evoked potential technique of direct cortex stimulation (dcMEP) and muscle recordings , as detailed in Chap. 2 ("Transcranial Motor Evoked Potentials"). For this stimulation, the high-frequency train technique for eliciting motor evoked potentials is more effective in overcoming the inhibitory effect of general anesthesia than the Penfield/Ojemann technique. As detailed in Chaps. 2 and 21 ("Intraoperative Neurophysiological Monitoring for Intracranial Aneurysm Surgery"), the stimulation parameters of the dcMEP technique are critical such that the motor cortex is stimulated rather than stimulation deeper in the subcortex, as would occur with a stronger stimulus.

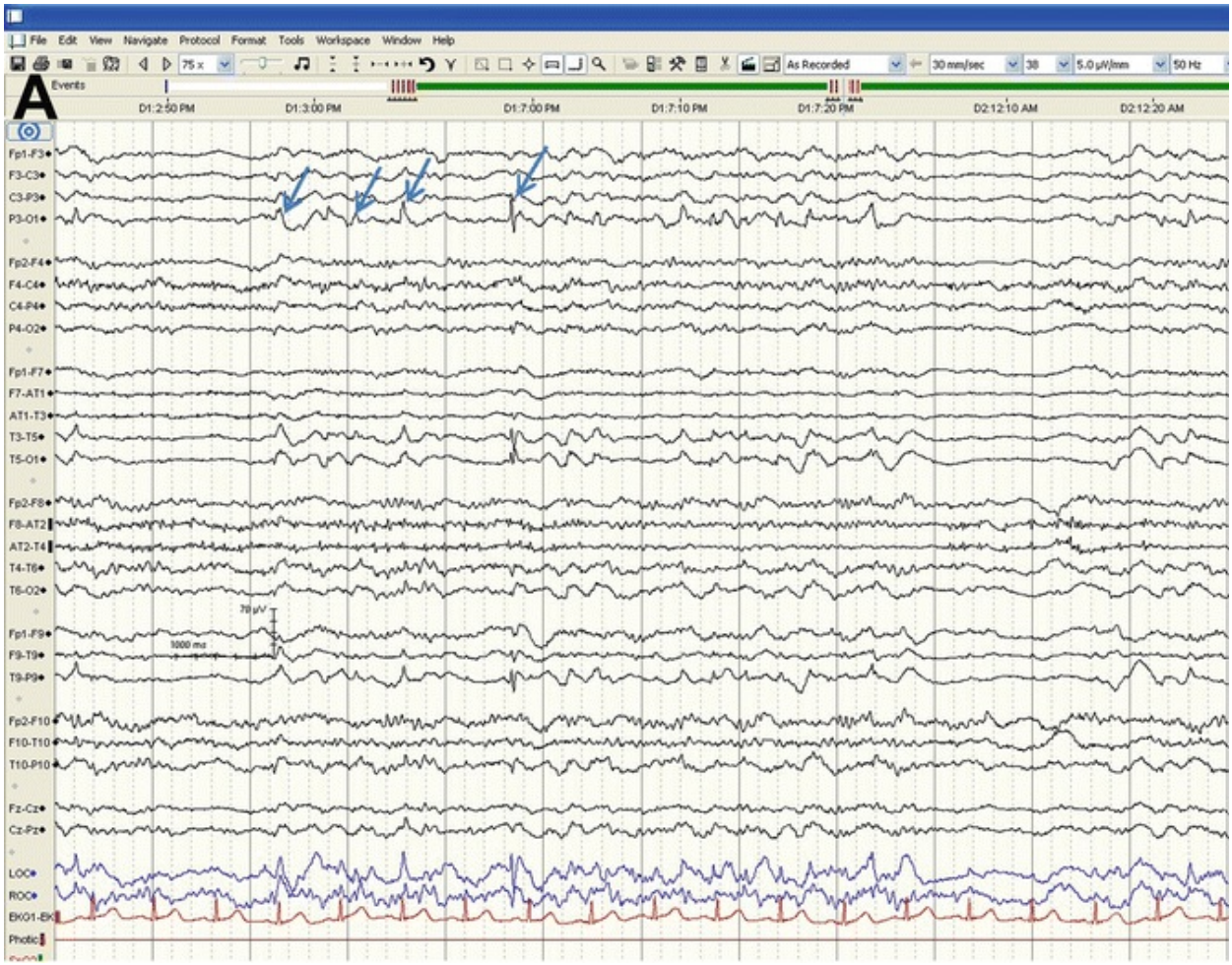
If the direct cortical MEP stimulation technique is used, total intravenous anesthesia is required (*see* Chap. 19, "Anesthesia Management and Intraoperative Electrophysiological Monitoring "). Muscle relaxants should also be avoided during this monitoring and train-of-four monitoring should be used to confirm resolution of any relaxants administered earlier in the procedure. As with the awake technique, monitoring can be continued during the resection. Fortunately, the incidence of stimulation-associated seizures is lower with the dcMEP technique (1–2 %) due to the reduction in voltage needed to produce the same outcome (*see* Chap. 9, "Brain and Spinal Cord Mapping ") [10, 12, 13]. Identification of the speech areas under general anesthesia is not currently possible. Neuronavigation techniques may be helpful inferring the location of the eloquent cortex from preoperative imaging studies (as earlier). Some preliminary studies suggest direct cortical stimulation may be helpful as cortical stimulation of some speech-related regions may activate regions of the motor cortex related to speech [14, 15]. If during the Phase II or Phase III monitoring, vEEG in conjunction with high-resolution MRI identifies mesial temporal sclerosis in which seizures originate from focal areas of the hippocampus, a less invasive craniotomy is

performed with the use of MRI-guided laser technology. Unlike traditional lobectomy, the use of a laser-tipped probe is directed through a burr hole in the back of the skull toward the hippocampus to ablate the epileptic foci. This minimally invasive surgery is performed under general anesthesia with hospital stays being reduced typically to overnight [16].

Intensive Care EEG Monitoring

In a present-day critical care setting, it is no longer unusual to use multiple channel [16–32] continuous EEG or continuous EEG with video (cEEG) for making patient management decisions. Unlike a traditional bedside 20- to 30-min EEG, which is one point in time and interpreted hours to days after the recording, cEEG , continuous EEG in the critical care environment (CCEEG) (or neurotelemetry as it is termed when continuous recording and analysis for interpretation is provided), allows for uninterrupted assessment that triggers immediate treatment. If there is an unexplained neurological exam change with no corresponding image findings, a secondary cause of altered mental status or coma must be explored. cEEG demonstrates aspects of brain physiology that are not reflected in structural neuroimaging (CT or MRI). While functional neuroimaging techniques , such as PET , single-photon emission computed tomography (SPECT) , and functional MRI (fMRI) can exhibit physiologic changes, they do not deliver the millisecond range of temporal resolution of CCEEG [17].

Continuous EEG is useful for seizure detection in the ICU , particularly when patients are pharmacologically paralyzed. It has been reported that more than half of the seizures in an ICU are associated with no or only subtle signs of clinical convulsive activity making diagnosis delayed or nonexistent. With the incidence of nonconvulsive status epilepticus (NCSE) in the critically ill of up to 37 %, the use of CCEEG identifies and allows for quantification of seizure activity [9] (Fig. 45.5). Specifically, in the traumatic brain-injured (TBI) patients, the estimate of NCSE occurring is 4–14 % [9].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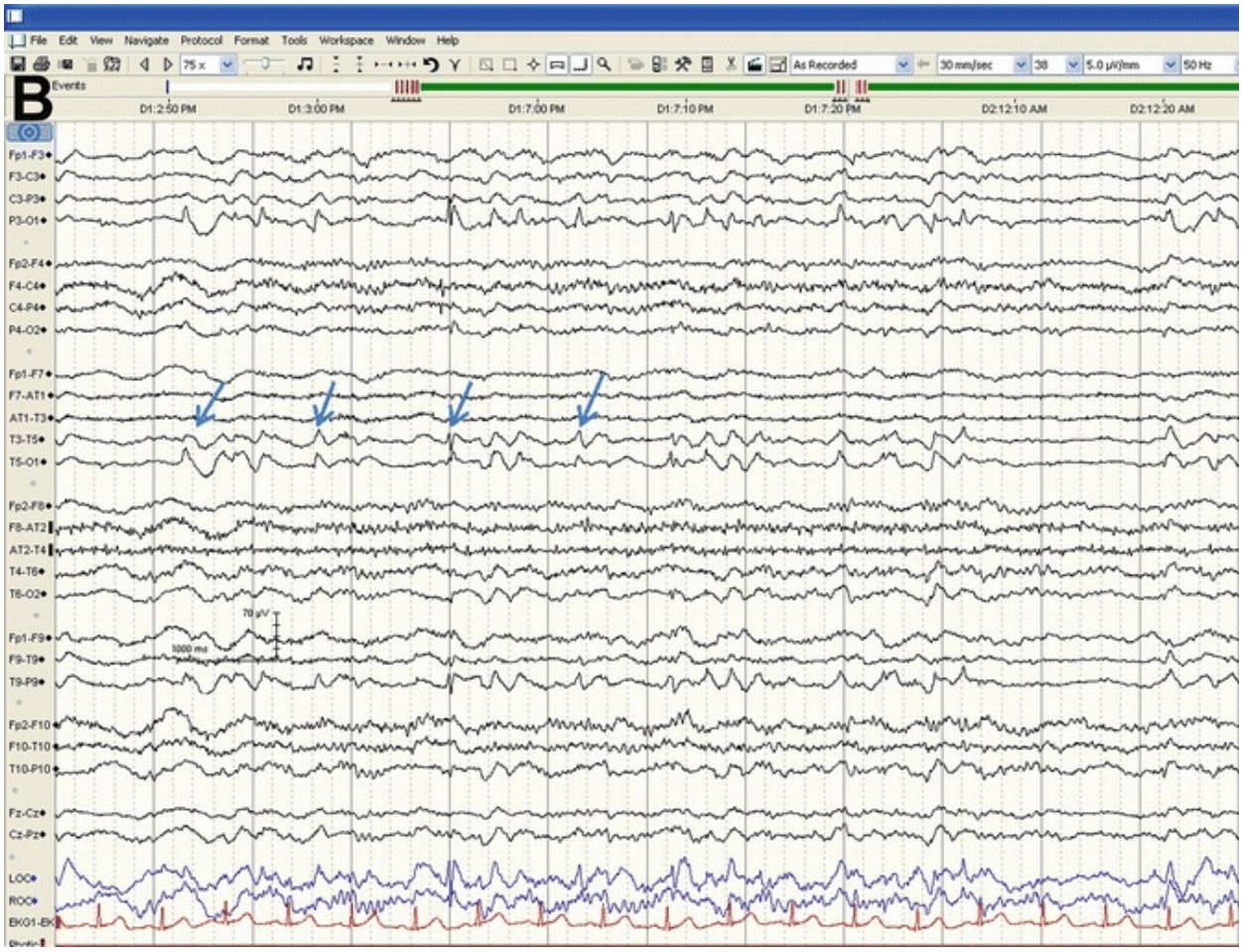


Fig. 45.5 (**a**) Nonconvulsive seizures in ICU patient admitted for h/o alcohol abuse found unconscious and unresponsive. Abundant to continuous focal left occipital (O1/T5) sharps, spike, and waves in runs of 7–9 Hz (*south west arrow*). (**b**) Field extends more anteriorly (T3 electrode) with periods of relative attenuation lasting 1–1.5 s between episodes (*south west arrow*)

Evidence has suggested that the initial 30 min of using cEEG recording can predict the likelihood of seizures given the presence of certain EEG patterns of periodic lateralized discharges (LPDs) or generalized discharges (GPDs) as compared to generalized slowing. While periodic patterns are seen from a wide variety of clinical etiologies, the discharges themselves are highly correlated with nonconvulsive seizures and may represent an ictal (seizure) pattern in some patients with continuous to abundant activity [18] (Fig. 45.6).

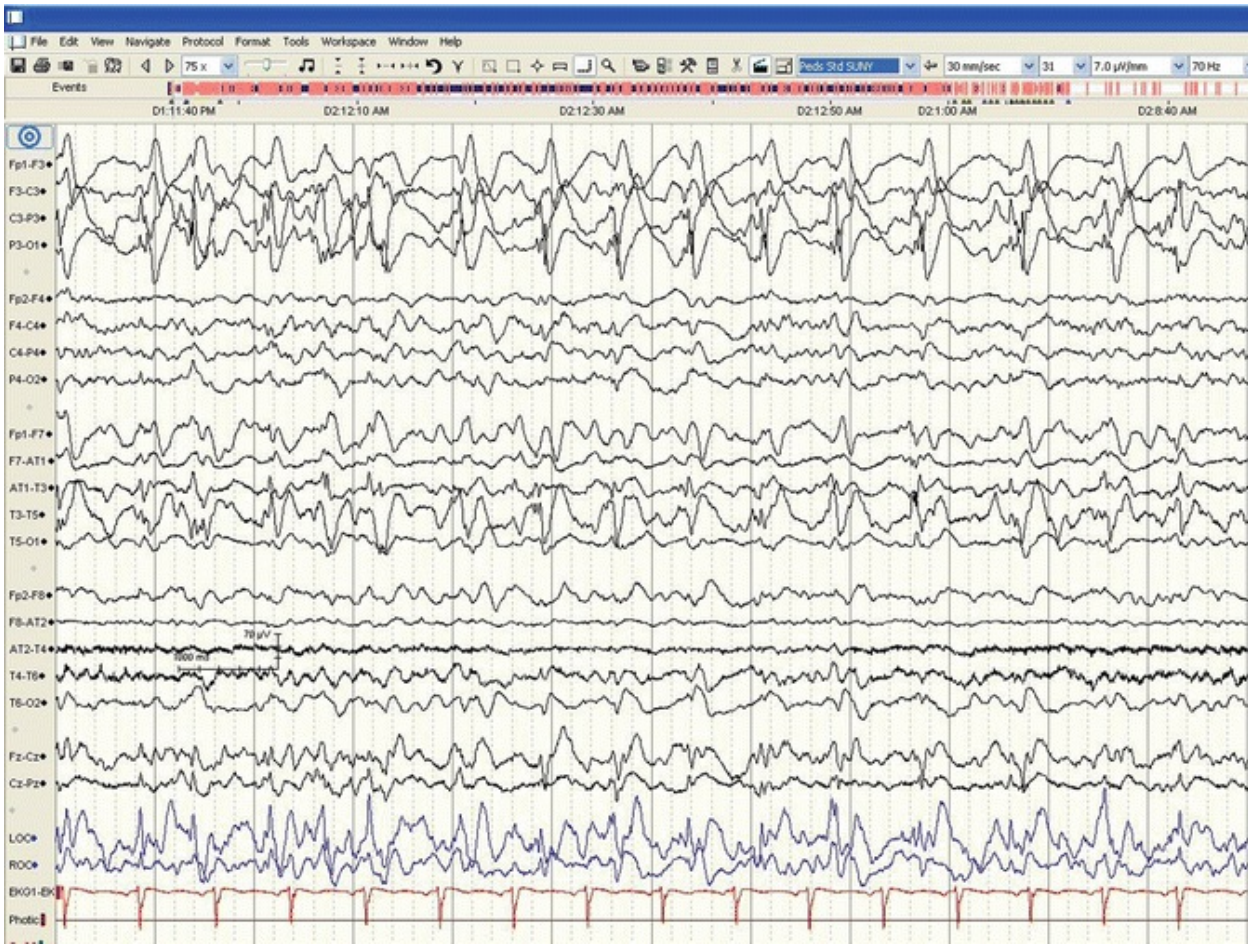
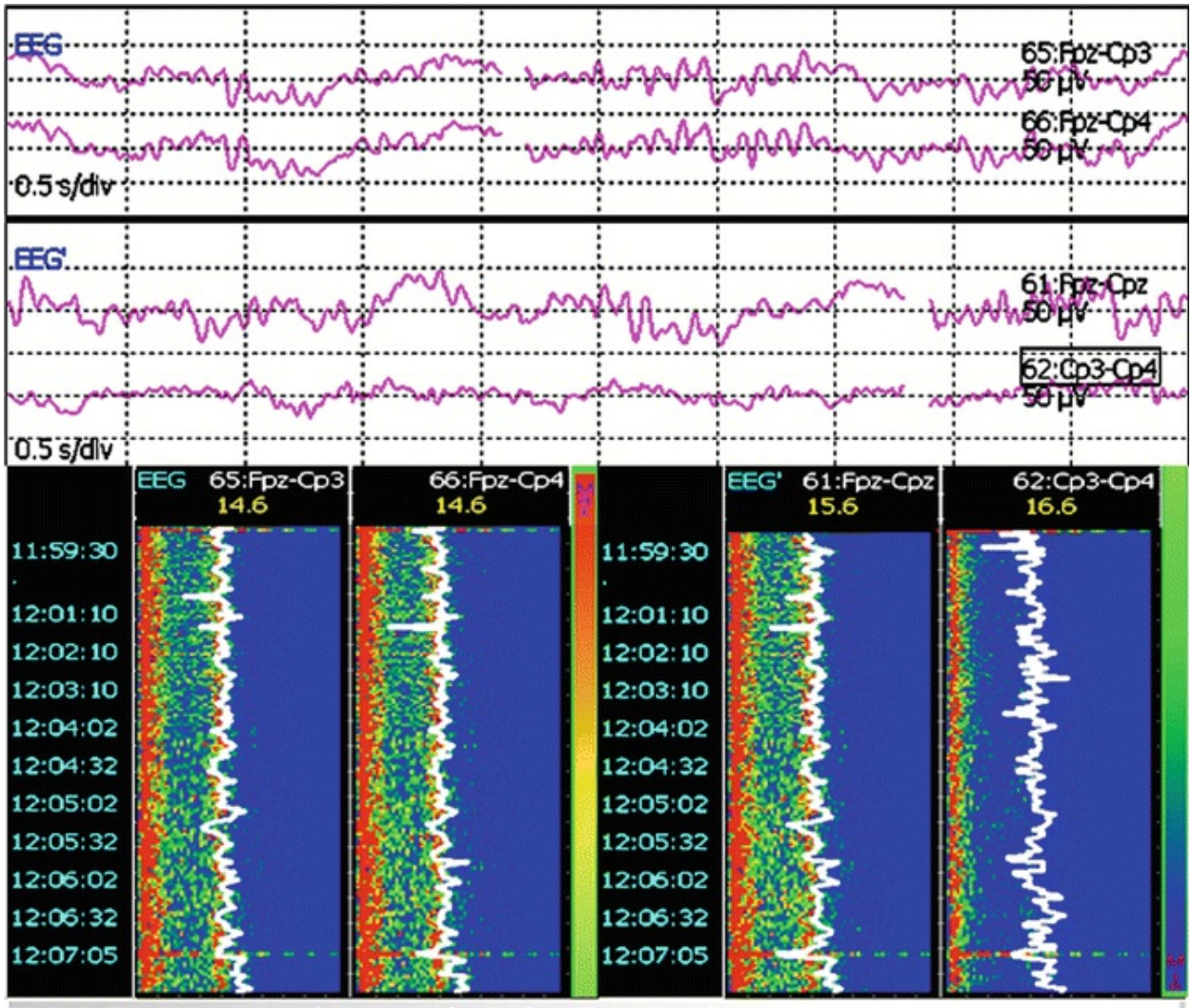


Fig. 45.6 Left periodic lateralized discharges (*PEDs*) in ICU patient admitted for altered mental status

In other patients, periodic discharges (PDs) persist despite the absence of seizures or after seizures have been controlled by AEDs. Presence of these should be carefully investigated clinically for evidence of toxic-metabolic, intracranial lesions, and/or infectious diseases [18]. Conversely, if the initial cEEG pattern is only one of generalized slowing, the patient is unlikely to develop seizures on subsequent cEEG monitoring [18]. In the ICU, the goal of cEEG is seizure identification and immediate treatment to prevent secondary injury and subsequent neurological deterioration caused from seizures since they are associated with a very high cellular metabolic rate. High metabolic demand causes an unfavorable supply-to-demand relationship and ultimately to cellular injury and then death. This is true in the traumatic brain injury, subarachnoid hemorrhage, acute ischemic stroke, and intracranial hemorrhage patients. Therefore, seizure control is essential for positive patient outcomes.

Continuous EEG in the critical care environment can be used to monitor central nervous system drug effects such as the use of antiepileptics for seizure control and to guide patient care management for additional pharmacological support if seizures are refractory (refractory status epilepticus [RSE]). RSE carries a poor patient outcome with mortality rates reported to be 23–61 % [19]. Should additional pharmacological support of two or even a third AED not control RSE , continuous drips of midazolam, propofol, or pentobarbital are used for seizure control. The use of EEG to manage the drug delivery is recommended in the guidelines of the European Federation of Neurological Societies (EFNS) [20]. Titration of these medications reduces the side effects, notably hypotension and delayed return of consciousness. Further, residual drug level from higher than needed doses may delay EEG diagnosis of brain death.

While standard cEEG is generally multichannel raw data, the use of trending parameters in parallel to raw EEG is a valuable quantification tool in determining quickly the number of periodic patterns in a 24-h period (Daily Pattern Duration) and daily seizure burden or the duration of seizures in a 24-h period (Daily Seizure Duration) [21]. When compared daily, these can help determine the effectiveness of treatment. In today's ICU equipment, multiple quantitative measures are generally derived from the fast Fourier transform (FFT) digitally displayed as density spectral arrays to color spectrograms and/or quantitative parameters such as spectral edge frequencies (SEF) , asymmetry indexes , and frequency ratios as a few examples [22] (Fig. 45.7). While CCEEG has been poorly studied for the most appropriate trending choices, it is intuitive to choose quantitative measures and digital displays that demonstrate ratios of amplitude and frequencies. These may be different from seizure identification and seizure burden versus impending ischemia and metabolic suppression. Due to lack of centers providing CCEEG , the choice of quantitative EEG (qEEG) parameters is still a matter of debate and opinion. What is not in debate is the ability to always look at the raw cEEG display to allow assessment of the signal for quality, low voltage focal abnormalities easily missed by qEEG , and for contamination by artifact (Fig. 45.8).



Numeric EEG - Measurement: Abs.Power, Mode: Absolute Value

Trace	95%		Total	Delta	Theta	Alpha	Beta1	Beta2
Name	SEF	BSR	0.0 - 32.0	0.5 - 3.5	3.5 - 7.5	7.5 - 13.0	13.0 - 21.5	21.5 - 32.0
	Hz	[%]	[µV²]	[µV²]	[µV²]	[µV²]	[µV²]	[µV²]
61:Fpz-Cpz	11.7	0.00	459	336	27.0	44.1	12.6	2.0
62:Cp3-Cp4	9.3	0.00	161	102	7.5	7.0	4.4	1.3
65:Fpz-Cp3	11.7	0.00	348	224	17.5	41.5	10.6	1.7
66:Fpz-Cp4	11.7	0.00	590	469	24.2	45.5	12.7	1.8

Fig. 45.7 Raw EEG with color density spectral array (*CDSA*). Note the spectral edge Frequency (*SEF*) line indication at 95 % in white on the CDSA. An additional table of numerical values provides multiple resources to analyze the raw EEG

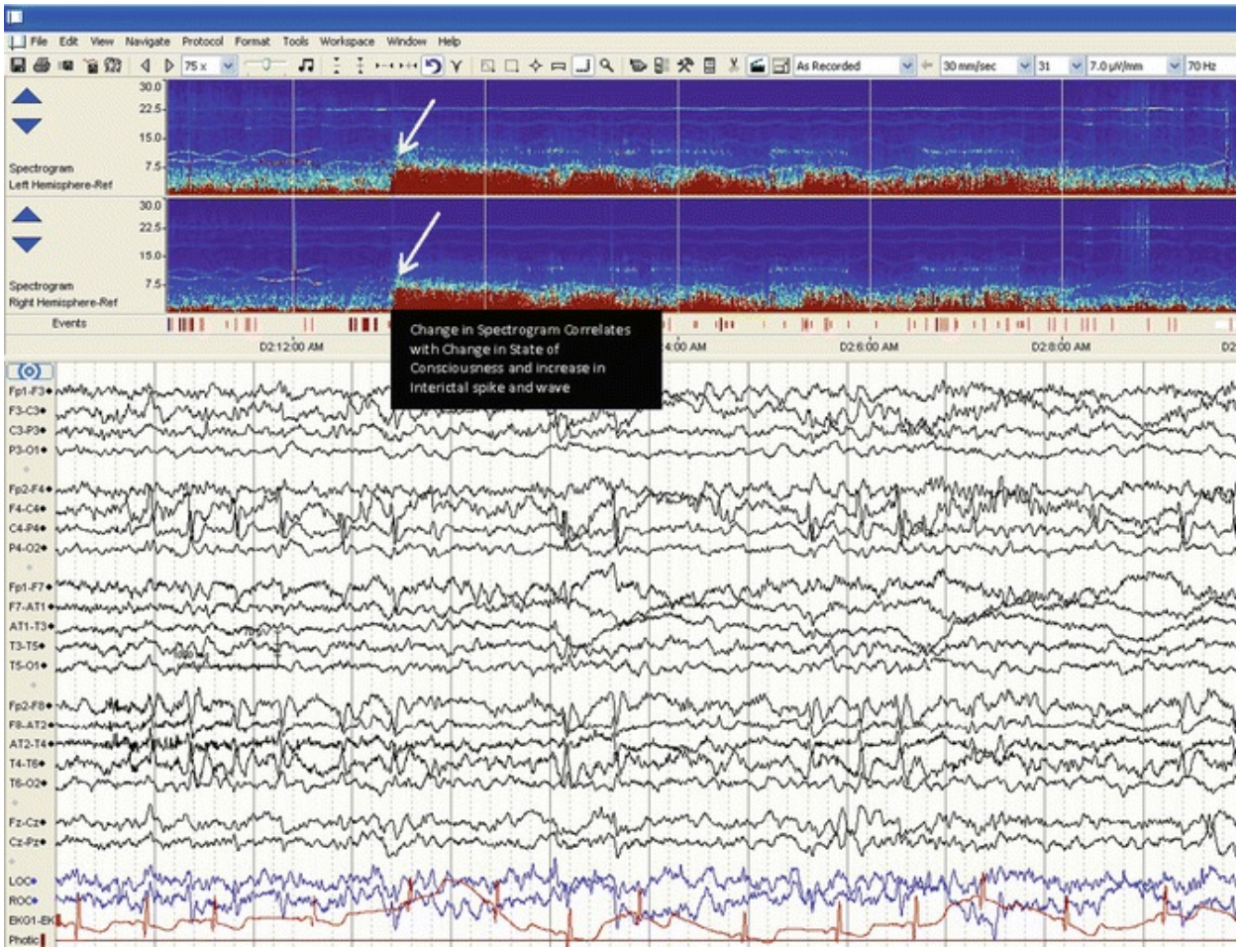


Fig. 45.8 EEG with trend spectrogram of left and right hemispheres derived from FFT shows change in state of consciousness of patient and increase in interictal spike and wave. While a change is noted (*south west arrow*), only raw EEG reveals the significance of the change

In ICU patients, cEEG will also warn of other systemic abnormalities affecting the brain such as hypoxia, hypotension, and acidosis [9]. Correlation with advanced hemodynamics such as partial pressure of brain tissue oxygen ($PbtO_2$) , cerebral metabolic rate of oxygen consumption ($CMRO_2$) , or microdialysis (MD) , and changing cardiopulmonary physiology provides a comprehensive multimodality approach to patient assessment (Fig. 45.9).

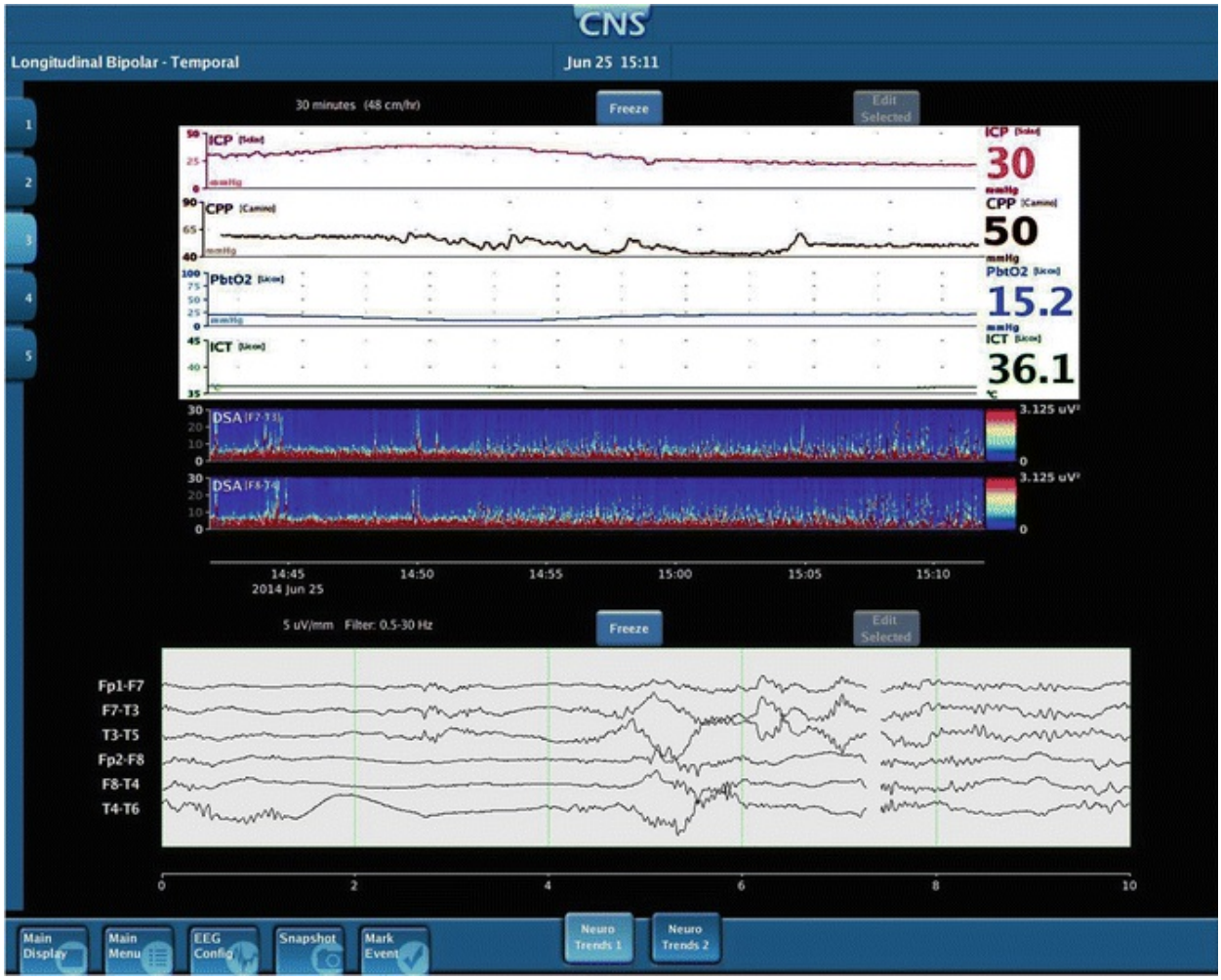


Fig. 45.9 Multimodality monitoring with hemodynamics of intracranial pressure (*ICP*), intracranial temperature (*ICT*), cerebral perfusion pressure (*CPP*), partial pressure of oxygen in brain tissue (*PbtO2*), 2-channel density spectral array (*DSA*), and raw EEG from six channels (three from the left and three from the right hemisphere) correlated in time. Courtesy Dick Moberg

In addition, cEEG monitors the benefit or harm of other clinical interventions such as sedation management during treatment of high intracranial pressure or management of neuromuscular block during therapeutic hypothermia. Increased electromyography (EMG) in the EEG is evidence of inadequate sedation and neuromuscular block allowing for notification to the care team of the need for pharmacologic intervention. This will occur long before the patient is fully conscious or moves. Further, an absence of cEEG activity with the absence of medications that could suppress neuronal and cortical activity is helpful in the management of end-of-life decision making.

Other EEG Applications in the ICU

The EEG has been used in several other ways in the ICU. These include processed EEG to quantify sedation (*see* Chap. 11, "Clinical Application of Raw and Processed EEG") and the detection of unexpected cerebral ischemia. The latter is similar to the use of the EEG during carotid endarterectomy (*see* Chap. 30, "Carotid Surgery"). The ability to detect ischemia early allows management changes to improve blood flow so that the probability of irreversible damage is reduced.

Decreasing electrical activity in the EEG is an early finding when an adverse metabolic environment is present and can be used to detect neuronal ischemia. The most common causes of ischemia are hypoperfusion (restricted flow), hypotension (inadequate net perfusion pressure to provide adequate cerebral blood flow), and inadequate oxygen-carrying capacity (severe anemia). Similar to its use in the operating room during carotid endarterectomy (*see* Chap. 30), multichannel cEEG over the entire cortex can be used to determine if vessel compromise is associated with regional hypoperfusion or when relative ischemia occurs as a result of metabolic demand exceeding supply. Since anatomic variations in the circle of Willis and inadequate flow in major arteries can occur, compensation for loss of blood flow may not occur. The multichannel cEEG has the advantage of being applied over the entire cortex and can therefore detect ischemia in all vascular territories perfusing the cortical surface.

When blood flow in a vessel is reduced, cEEG can signal poor collateral flow such as during intracranial vascular surgery. This change can suggest that medical interventions such as induced hypertension must be performed to improve collateral flow. Continuous EEG monitoring during these interventions can assist in determining their effectiveness in restoring blood flow. Without an improvement in EEG activity, administration of medications to suppress metabolic activity and extend cellular tolerance to hypoperfusion may be selected (see later). Unfortunately, drug metabolic suppression eliminates the effectiveness of cEEG to detect ischemia because the EEG amplitude and frequencies are suppressed.

The power of cEEG monitoring for ischemia is that the EEG abnormalities appear rapidly; the cEEG usually fails in 20 s following complete cessation of blood flow. The cEEG becomes abnormal below the threshold of adequate blood flow, which is estimated to be 22 cm^3/min/100 g

and absent below 15 cm^3/min/100 g (ischemic threshold) (*see* Chap. 40, “Electrophysiological Monitoring During Thoracic Aortic Aneurysm Surgery ,” Fig. 40.1) [23]. This ischemia can eventually lead to cellular death; cell death is also a function of the duration of hypoperfusion. For example, cell death may take 3–4 h when the cerebral blood flow is just below the threshold where the cEEG becomes abnormal. Infarction occurs after a shorter period of time when the blood flow is lower than this level. Recovery of cellular function as perfusion improves is rapidly detected with the return of cEEG activity. Medical intervention such as induced hypertension subsequently increases perfusion reversing ischemic change; this response has been documented during cEEG monitoring in surgical patients. The EEG is often considered the “gold standard” for this purpose when the patient is anesthetized.

In the ICU, cEEG has been used in efforts to detect vasospasm and delayed cerebral ischemia(DCI) in high-grade subarachnoid hemorrhage (SAH) patients. In this patient population, a reported 20–40 % of patients are at risk [24]. In the early literature, the use of alpha variability as a derived quantitative measure of cEEG trended over time had a high positive predictive value in identifying vasospam when the alpha reactivity was poor or nonreactive [25]. Delayed cerebral ischemia, however, in the ICU may occur slowly over time (hours to days) in this population. This is difficult generally to appreciate with traditional surface cEEG . Therefore, new approaches have emerged to record impending ischemia.

One of these is the recording of cortical spreading depolarization waves (CSD) . CSDs are large transitory neuronal depolarizations that slowly propagate, 1–3 min, through cerebral cortex from brain-injured tissue. CSD waves are cortically associated with isoelectricity, periodic discharges, and prolonged depression of spontaneous EEG activity. Cerebral perfusion pressure decreases usually precede the appearance of CSD. The increases in cellular metabolism needed for cellular repolarization may be more than the energy supply available in the ICU patient [26]. This can be damaging to the compromised ICU patient. Recording of CSD requires implantation of invasive grid strip electrodes placed closely over the regional area of brain injury to record ECoG. This, however, can be accomplished during the craniotomy for evacuation of the hemorrhage. Evidence of CSD in the acute brain disorder will likely require the development of new clinical protocols to manage preservation of cerebral blood flow to improve recovery for the SAH

patient [27].

Finally, the EEG has been used to monitor intentionally induced metabolic suppression so as to favorably alter the nutrient supply and energy demand relationship of neural cells. As detailed in Chap. 19, about 50 % of the metabolic activity of neural cells is used by normal synaptic activity. The agents used for metabolic suppression vary as some drugs have additional desirable qualities (e.g., free radical scavenging with barbiturates) and undesirable qualities (e.g., slow kinetics with thiopental, adrenal suppression with etomidate).

This technique has been referred to as “barbiturate coma ” when produced by barbiturates and has also been used during surgeries such as carotid endarterectomy (*see* Chap. 30) and intracranial vascular surgery (*see* Chap. 21). Drugs are often titrated by assessing their effect on the EEG. The gradual depression in EEG mirrors the depression in synaptic activity until maximum metabolic suppression occurs. This coincides with cessation of electrical activity (i.e., a flat EEG). When maximum suppression is required, the treatment end-point most often used is burst suppression (near maximal suppression) where the EEG shows periods of electrical activity that are interspersed with periods of electrical silence (Fig. 45.10). It is important to note that these drugs have a maximal metabolic depression of about 50 % of normal metabolism.

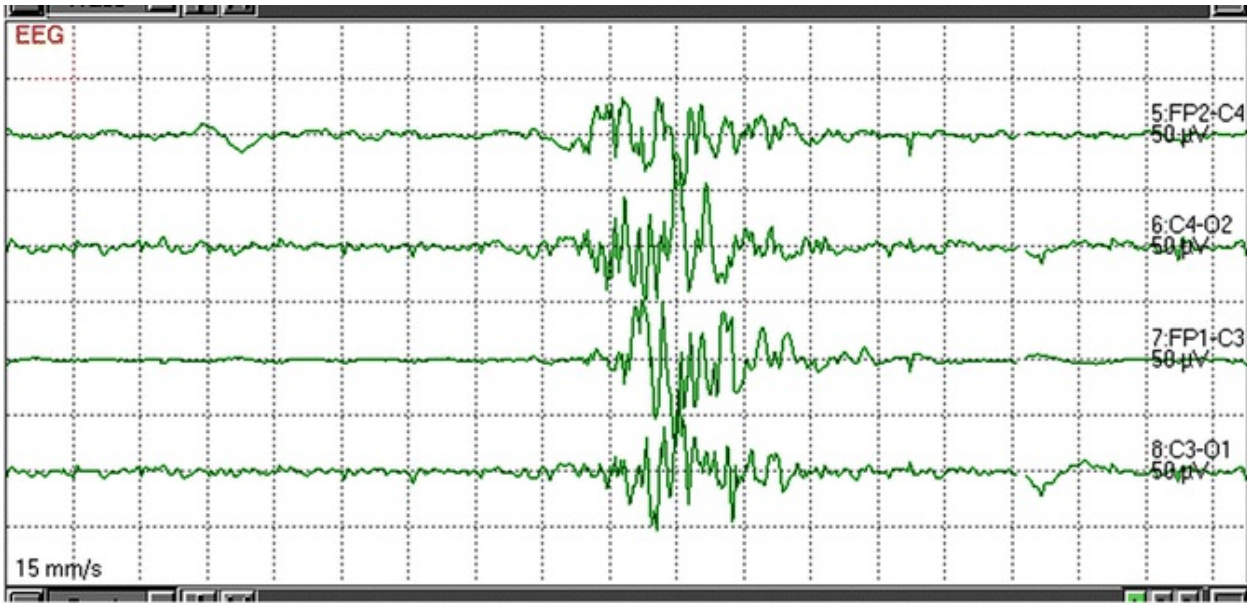


Fig. 45.10 Induced burst suppression EEG. Long interelectrode distance recording showing brief bursts followed by suppression. Optimal burst suppression is generally considered four bursts per

minute

Current data in animal models suggest that prolonged periods of burst suppression may not be necessary to get potential neuroprotective effects [28]. Modest EEG suppression, similar to that seen with routine general anesthesia , has equivalent neuroprotective effects to burst suppression in animals. Hypothermia is most commonly used to augment reductions in cerebral metabolism since reductions in temperature can reduce nonsynaptic metabolic activity. Because electrical seizure activity increases metabolic demand, the use of EEG to identify and suppress seizures is also helpful in reducing the circumstances of excess demand.

Conclusion

Recent advances in EEG recording technology and the ability to “see” the synaptic activity of cortical neurons allow the EEG to be a powerful tool in the operating room and ICU. In particular, the unique ability to detect the electrical activity of seizures makes it an extremely valuable tool in the operative management of epilepsy and in the care of patients in the intensive care unit.

Questions

1. Surgical candidates for resection of epileptogenic zones:

    a. Have discrete epileptogenic zones located in one hemisphere

    b. Only have epileptogenic zones in the nondominant hemisphere

    c. Always have epileptogenic zones near the speech areas

    d. Never have epileptogenic zones near the motor cortex

    e. None of the above

2. Patients who are not candidates for resection of the epileptogenic zone by surgery may still come to surgery for

    a. Placement of a vagal nerve stimulator

    b. Placement of a trigeminal nerve stimulator

    c. Placement of deep brain stimulation electrodes

    d. Corpus callosotomy

    e. All of the above

3. To aid in identifying the Motor Cortex in surgery the following is(are) used

    a. The patient reporting tugging when the area is stimulated by the Penfield/Ojemann technique

    b. EMG in muscles when the area is stimulated by direct cortical MEP techniques

    c. By phase reversal of the SSEP

    d. All of the above

4. When electrical activity from the cortical surface does not reveal ictal activity, which of the following medications have been used to activate the seizure activity :

    a. Etomidate

b. Methohexital

c. Alfentanil

d. Propofol

e. All of the above

5. EEG monitoring in the ICU

a. Is not useful in patients who are pharmacologically paralyzed

b. Can detect seizure activity in patients who do not have tonic–clonic activity

c. Is useful when high doses of medications are used to depress neuronal metabolic activity

d. Always predicts brain infarction when the EEG activity ceases

e. All of the above are true

Answers

1. a

2. e

3. d

4. e

5. b

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Footnotes

1 Key references marked with asterisks.

Antoun Koht, Tod B. Sloan and J. Richard Toleikis (eds.), Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals, DOI 10.1007/978-3-319-46542-5_46

46. Monitoring Cerebral Blood Flow

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Keywords Cerebral autoregulation – Cerebral blood flow (CBF) – Cerebrovascular reserve

Physiology

Mechanisms of Cerebral Blood Flow Regulation

The flow of blood to the brain is finely regulated to provide substrates according to the needs of neural tissue . This coupling occurs via several mechanisms. These include neurogenic, humoral, and myogenic processes [1–3].

The cerebral vasculature is extensively innervated with a wide variety of

neurotransmitter-containing nerves that appear to work in close concert with the endothelium and neural metabolism. A wide variety of nerve types innervate the cerebral vasculature to confer vasoconstriction or vasodilation on the cerebral vasculature. The neurons innervating the cerebral vessels arise from numerous areas. These anatomic loci include intracranial ganglia [4, 5], the spinal cord [6], other extra cranial nerves [7], or intracerebral nuclei [8].

Neural metabolic factors also clearly have an important role in the fine tuning of local CBF. Products of metabolism such as lactate and $PaCO_2$ act to decrease pH so as to cause vasodilation, with nitric oxide, and other factors contributing to this aspect of autoregulation [2, 9–12]. Such a notion is reinforced by observations of coupled variations in CBF with extremity movements or thought processes [2, 10]. It is thought that nitric oxide is an important component of this neural metabolic fine tuning of local CBF [9, 11, 12]. Indeed, it has been suggested that hypercapnea-mediated increased CBF occurs by way of nitric oxide [9].

In addition to innervation and neural metabolic control of cerebral circulation, influences are exerted by way of blood pressure and humorally mediated influences. Blood pressure has long been known to have an impact on the cerebral circulation. Alterations in blood pressure result in changes in cerebral vascular resistance to maintain CBF constant within the range of physiologic blood pressures. This has been observed in a dynamic manner by correlation with transcranial Doppler blood flow velocity measurements [13]. At the extremes, however, blood pressure changes result in a linear pressure-dependent change in flow. This relationship is altered by chronic hypertension shifting the relationship to higher pressures.

CBF is exquisitely sensitive to changes of $PaCO_2$ with a linear change in CBF reported to occur with changes in $PaCO_2$ [14–18]. This sensitivity of CBF to $PaCO_2$ is the underlying physiological factor supporting the use of CO_2 changes to provocatively alter CBF through inhibition of carbonic anhydrase with acetazolamide [19–22] or through induced alterations in minute ventilation or inspired CO_2 to change $PaCO_2$ [23].

Oxygen level is an essential aspect for the maintenance of CBF. Ordinarily, the CBF remains relatively constant with variations in PaO_2 as long as arterial oxygen saturation is greater than 95 %. However, with decrements in PaO_2, the CBF increases substantially in a compensatory manner to maintain oxygen supply [24]. Conversely, hyperoxia is a cerebral

vasoconstricto r [25].

Autoregulation

Numerous reports document the shift of the lower limit of pressure autoregulation with chronic hypertension [26]. The anatomic basis for this is thought to be vascular hypertrophy and the remodeling of the microcirculation [26]. CO_2 reactivity is reportedly maintained with chronic hypertension [17]. However, responses to humoral effectors are altered during chronic hypertension due to decreased endothelial responses [27, 28]. Because of the shift of the autoregulation curve to higher pressures, there is always concern that decreasing blood pressure will result in ischemia [29].

It should be noted that traditional notions of cerebral autoregulation, with CBF constant over a CPP range of approximately 50–150 mmHg, have not gone without a challenge [30]. Drummond [30] argues that this common notion is derived from a figure in a review article by Lassen [31], which itself was an estimate based on data from pregnant volunteers undergoing blood pressure alteration with hydralazine and veratrum viride published by McCall [32] in 1953. Despite the use of potentially cerebral vasoactive drugs, these observations remained unconfirmed in humans. Drummond suggests that most human data published since 1953 support a lower limit of autoregulation (LLA) of 70 mmHg, with one investigator suggesting the onset of cerebral ischemia symptoms in normal humans to arise at an MAP of 55 mmHg [33]. Moreover, his closer review of published data suggests large interindividual variation in the LLA . Drummond suggests that the only safe approach to an individual patient is to assume that no less than 75 % of his or her resting MAP should be assumed to be the LLA . Symptoms of cerebral hypoperfusion tend to arise when MAP falls to about 50 % of the resting value. These assertions of the need to individualize are increasingly being supported in the context of head injury with recent studies of the use of dynamic autoregulation assessment to determine optimal blood pressure for a given patient [34–37].

It is also of interest that the LLA , based on CPP (MAP-ICP), may vary with ICP and with jugular venous pressure. McPherson et al. [38] in a canine model noted that the LLA was higher with elevated jugular venous pressure. This may, however, actually reflect the lack of knowledge regarding the proper definition for CPP and that it may vary depending on the influence of

the venous starling resistor [38, 39]. Brady et al. [40], in an atraumatic immature piglet model of intracranial hypertension, found that the LLA had a positive correlation with ICP. That is, LLA CPP was higher with higher levels of ICP. They suggest the possibility that compensating for an increase in ICP with an equivalent increase in arterial blood pressure (ABP) may not be sufficient to prevent a decrement in CBF and cerebral ischemia. Further studies in adults will be needed. Nonetheless, Brady et al. [40] point out that Cremer et al. [41] observed a LLA elevation in adult trauma patients with intracranial hypertension.

The overall suggestion is that there is a need for an individualized dynamic autoregulation assessment to determine each patient's optimal CPP [34–37]. Indeed, this may be only one component of a battery of multimodal monitoring, so-called integrative neuromonitoring, that is increasingly being advocated [42]. Autoregulation assessment methods are presented later in this chapter.

Cerebrovascular Reserve

Occlusive cerebral vascular disease produces decrements in CBF such that aerobic metabolism may not be supported, with a consequent decrement in neuronal function and a risk of neuronal injury or death. However, a subtler manifestation of occlusive cerebral vascular disease is a decrease in *cerebrovascular reserve*. That is, a compromise in vascular in-flow results in compensatory vasodilatation such that, at the microcirculatory level and at a given systemic blood pressure, there will be a greater degree of vasodilatation than there would be otherwise, resulting in normal blood flow. The functional consequence of this is that ordinary perturbations, which are otherwise well tolerated through physiologic vasodilation, will not be tolerated if further vasodilation cannot be achieved. Thus, decreases in blood pressure or oxygen supply may not be tolerated such that a stroke may arise. The abnormality of CO_2 reactivity in occlusive cerebral vascular disease has been documented in a number of reports [23, 43–46]. The newer methods of continuous autoregulation assessment may provide insight regarding the status of a given patient's level of cerebrovascular reserve, as a loss of reserve should translate to an increased correlation of ABP and CBF or a shift of the CPP optimum described later.

Another approach to characterizing cerebral autoregulation has been

espoused by Dewey et al. [47], Early et al. [48], and Burton et al. [49]. Using observations in pacemaker-dependent dogs and a beat-to-beat measure of brain blood flow, they observed that abrupt cessation of cardiac activity produced zero cerebral blood flow well above zero pressure. Indeed, they reported that this critical closing pressure varied with the resting MAP , generally being about 40–50 mmHg below MAP. They concluded that the normal cerebral circulation assumes a tonic state of contraction that varies with MAP and ICP ; more tone at higher blood pressure or lower ICP, less at lower blood pressure or higher ICP, such that the true dynamic cerebral perfusion pressure is MAP-CCP, with CBF = (MAP-CCP)/CVR. Burton's model can be used to describe critical closing pressure (CCP) as CCP = ICP + tension of arterial walls [47]. The CCP is presumed to be altered by various drugs and disease states to thereby produce variations in CBF despite otherwise unchanged traditional CPP (MAP-ICP). Thus, the true definition and measurement of CPP may be a good deal more dynamic and complex than is commonly understood at this time.

More recently, further studies of CCP were done in humans with traumatic brain injury by Czosnyka et al. [50]. If autoregulation is relatively intact, CCP-ICP remains high, but with injury sufficient to produce dysautoregulation, CCP-ICP decreases indicating decreased tension in arterial walls. Transcranial Doppler waveform analysis is suggested by several authors as a potential means to measure and monitor CCP in huma ns [51–53].

Cerebral Blood Flow Measurement and Clinical Applications of Specific Techniques Perioperatively

A number of measurement technologies have evolved over the years to evaluate CBF. Generally, the methods entail assessment of washin and/or washout of a tracer substance or bulk flow measurement. Methods which have been described include stable xenon CT CBF [54–56], technetium-labeled RBC techniques [57], thermodilution techniques [58], ^{133}xenon methods [59, 60], ultrasonic volume flow [61], positron emission tomography (PET) [62, 63], single-photon emission computed tomography (SPECT) [15, 64–67], AVO_2 difference assessment [68, 69], radioisotope measurement of brain–blood turnover [70], forehead thermography [71], thermal diffusion

flowmetry [72], planar gamma camera images cerebral blood flow (CBF)/cerebral blood volume (CBV) determination [73], laser Doppler flowmetry [74], ultrafast CT with iodinated contrast [75], and arterial spin labeling perfusion fMRI [76]. Recent studies increasingly indicate a role for continuous autoregulation assessment using transcranial Doppler (TCD) [77], ICP [35–37], near-infrared spectroscopy [78, 79], or brain pO_2 [80].

The methods most commonly used are as follows (with descriptions of some uses):

Stable Xenon CTCBF

With this technique, the subject inhales 26–33 % stable xenon. The xenon is rapidly taken up into the blood, transported to, and taken up into the brain. End-tidal xenon is recorded continuously and assumed to be arterial. Xenon is radiopaque such that changes in radiodensity with serial CT scanning can be used to calculate CBF throughout the brain. The method computes solubility (λ) throughout the brain and then uses the adjusted λ for all CBF calculations. This results in more valuable data in patients with disease states where λ may not be uniform throughout the brain. The technique has been criticized because of pharmacological effects of xenon. Xenon inhalation effects reportedly include decreasing CO_2 and augmenting CBF [81].

However, using multiple early images and weighting calculations to do the early portion of the wash-in curve has eliminated the effect of flow activation on CBF calculation [54–56, 82]. In addition, in the evaluation of CBF in normals, the flow values that are obtained with stable xenon CTCBF (XeCT CBF) are clearly consistent with those obtained with other methods, suggesting that potential bias induced by xenon inhalation is not a significant factor. Many of the patients who are undergoing CBF assessment are having it done to assess areas of low blood flow. Thus, regardless of concerns about potential CBF increasing effects, XeCT CBF has been shown to be a versatile and useful tool, especially in the evaluation of low blood flow conditions. Moreover, because studies can be repeated at 20-min intervals, reactivity challenge testing of therapies can be performed dynamically. The fact that a reactivity challenge can be readily done while a patient is in the CT scanner is a major advantage as it can be done in the course of obtaining structural information during routine CT scanning. Because of the capability to do repeat studies in a single CT scan visit, dynamic studies to evaluate therapy

or cerebrovascular reserve assessment can also be done with Xe CTCBF technology. The advent of portable CT scanning now makes feasible the notion of doing intraoperative XeCT CBF studies [83].

Xe^{133} CBF

Radioactive xenon methods that have been widely used include either inhalation, intravenous injection, or intra-arterial injection [59, 60, 84, 85]. All such methods eliminate considerations about xenon effects on CBF as only trace amounts of xenon are administered. However, the CBF values are obtained from gamma counters located at specific loci on the scalp that record CBF in only one dimension. In conditions of low flow, this technology can be problematic, missing low flow deep in the brain or conversely missing low flow on the cortex because of persistent flow in deeper structures (look-through phenomenon) [86]. An important advantage of this technique is that it can be done at the bedside. Nonetheless, it requires availability of a clinical CBF laboratory with this capability. It has been demonstrated to be quite suitable for intraoperative use [87–93].

Jugular Bulb AVO_2 Difference

AVO_2 difference measurement is based upon the "Fick" equation using a jugular bulb catheter. Given a stable cerebral metabolic rate, changes in AVO_2 difference of oxygen will represent changes in CBF. Thus, it cannot be used to provide quantitative nor regional CBF and it does depend on accurate insertion of a catheter into the jugular bulb. However, it can be used at the bedside with continuous oxygen saturation monitoring to provide information regarding adequacy of CBF relative to cerebral metabolic rate (CMR) [68, 69] and to infer changes in CBF over time. The primary problem with data acquired with AVO_2 difference techniques arises in situations of heterogeneous CBF or metabolic rate. It is a global measure and its information can be misleading when hyperemic areas overshadow focally ischemic areas of the brain (*see* Chap. 14, "Monitoring of Jugular Venous Oxygen Saturation").

Thermodilution rCBF

Thermodilution rCBF uses continuous thermodilution techniques in a probe

placed directly into brain parenchyma. It has been validated against microspheres in animals and XeCT CBF in humans [94] to thus provide continuous second-to-second information regarding CBF in the area insonated. By its nature, it provides only regional information. It has been used clinically to assess effects of papaverine [95] and nimodipine [96] given for vasospasm, assess CO_2 reactivity [97], titrate blood pressure during vasospasm [98], and evaluate the effects of intraoperative arterial occlusi on on rCBF [99].

Transcranial Doppler

Transcranial Doppler (TCD) ultrasonography uses reflected ultrasound from basal cerebral arteries and the Doppler principle to determine the velocity of blood (cm/s) in a given insonated artery (*see* Chap. 11, "Clinical Application of Raw and Processed EEG"). It provides real-time dynamic information regarding blood flow velocity (BFV) , providing continuous waveform similar to that obtained with intra-arterial blood pressure monitoring. An example of this capability was published by Kofke et al. [100–103] and Eng et al. [104] reporting TCD recordings during the dynamic state associated with anesthetic induction and endotracheal intubation. Insonated arteries include the proximal arteries of the circle of Willis.

Training is required to acquire and identify a signal from a cerebral artery. Moreover, once acquired, maintaining acquisition of a good signal for monitoring purposes can be quite challenging. Minor changes in the angle of insonation can result in loss or degradation of the signal. Thus, well-trained and motivated nurses and technicians are needed to use TCD successfully as a monitor in the neuro-intensive care unit (neuro-ICU) or operating room (OR). In the OR it is best used with the aid of a strap system, which can hold the TCD probe in a constant position during the procedure.

The reproducibility of TCD recordings depends on a constant angle of the transducer insonating a given vessel. This is an important operator-dependent factor . This factor is minimized as the insonation angle becomes more parallel to the vessel being examined. Another important factor in interpreting BFV measurements is the vessel diameter. Decreases in vessel caliber can increase BFV (suggesting hyperemia) in the face of decreasing CBF. In addition, hematocrit, $PaCO_2$, and blood pressure can also influence BFV, although this may actually be a reflection of changes in CBF [105,

106].

It is important to note that TCD is not a quantitative flow monitor in mL/100 g/min. Rather it provides information, which can be useful, regarding the presence and character of flow. There are some situations where TCD changes may reflect changes in CBF , particularly in situations of abrupt changes in arterial inflow [107]. It has several uses in the ICU and OR . These uses include assessment of vasospasm, vascular reactivity, increased intracranial pressure, brain death (screening) [108], arterial patency, flow direction, emboli, and hyperemia [109]. Eng et al. [104], using TCD as a monitor during induction of anesthesia, demonstrated its potential value as a monitor as the TCD demonstrated the effects of aneurysmal rupture as it guided their therapy for this emergency situation (Fig. 46.1) [104]. Examination of this figure shows a period of intracranial circulatory arrest, which is the waveform seen with brain death. Also in this figure is an example of increased pulsatility, or a “spiky” waveform appearance associated with intracranial hypertension.

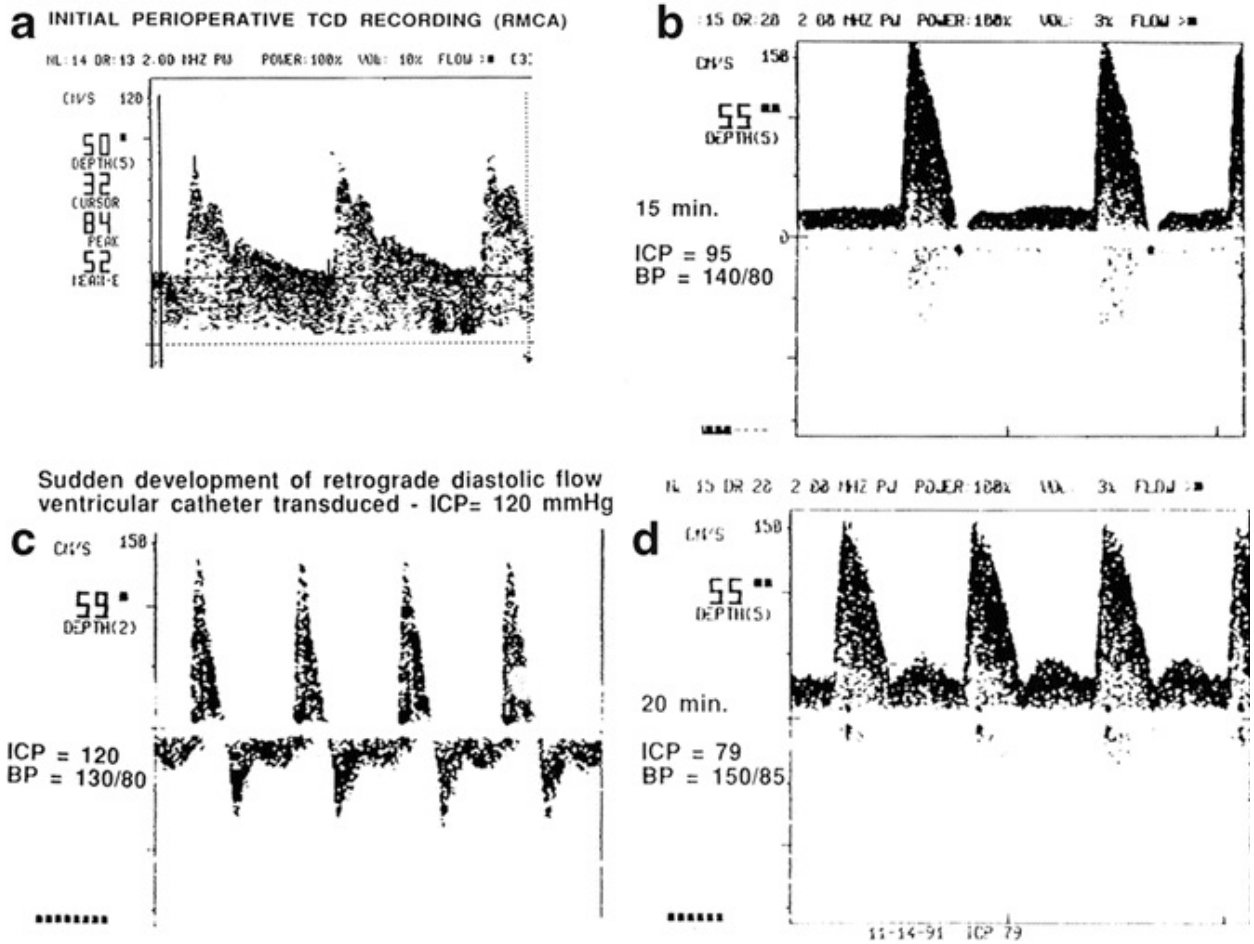

Fig. 46.1 Blood flow velocity measured by TCD during carotid endarterectomy. Preinduction (**a**). Internal and external carotid arteries clamped (**b**). Significant decrease in BFV occurs with loss of pulsatility. With unclamping (**c**), significant emboli are observed in the middle cerebral artery. Postischemic hyperemia (**d**) is detected (From Eng et al. [104]; with permission)

Vasospasm

TCD has been reported to be an early indicator of the presence of vasospasm prior to the onset of a clinically evident ischemic deficit. These observations are based on the physical principle that, with narrowing of a basal cerebral artery, blood flow velocity would increase, even as flow decreased. Thus, TCD has found a routine place in many neuro-ICUs as a noninvasive screening tool for the occurrence of vasospasm [110–113]. However, subsequent studies, perhaps related to increased use of nimodipine, have shown that increased velocity in subarachnoid hemorrhage (SAH) patients is associated with hyperemia more often than it is associated with vasospasm [114]. In addition, TCD can miss distal spasm. Thus, TCD, although still possibly of value as a rough screening tool, has insufficient sensitivity and specificity to be the sole criterion to make important therapeutic decisions in SAH . It still may be used as a trend once it is established that a patient clearly is in vasospasm or is hyperemic. Alternatively, it may be used to assess the extent of vasodilatory cerebrovascular reserve, and thus provide indirect information regarding how close a vasospastic condition is to producing clinically evident symptoms [115–117]. It is unclear whether this approach can differentiate hyperemia versus vasospasm .

Cerebrovascular Reserve

Analogous to similar measures with XeCT CBF , determination of the extent of vascular reserve can also be done with TCD and provides a semiquantitative indicator of the severity of injury to a given vascular bed. Reactivity assessment is done by manipulation of either perfusion pressure or carbon dioxide. For a given change in mean arterial pressure, within the normal autoregulatory range, there should be no change in blood flow velocity. A change in flow velocity indicates abnormal autoregulation. Moreover, this has been further developed such that the degree to which changes in blood flow velocity match changes in blood pressure has been developed into a TCD-based autoregulation index, Mx[77].

Carbon dioxide reactivity can be assessed by increasing inspired CO_2 or

by increasing tissue CO_2 via administration of acetazolamide. Blood flow velocity normally should increase 3–4 % per mm Hg increase in $PaCO_2$. Failure of brain to do so implies lack of cerebrovascular reserve such that the brain may not tolerate minor perturbations in O_2 delivery. A CO_2 reactivity index can be defined with CO_2 inhalation [118]:

$$CO_2 \text{reactivity index} = (V2 - V1) / (\Delta \text{end-tidal} CO_2)$$

Normal CO_2 reactivity index is 1.78 ± 0.48 (SD). In patients with cerebrovascular disease, this index was found to vary from 0.15 to 2.6 [119]. Failure of the brain to demonstrate a normal increase in blood flow velocity with a CO_2 increase implies the presence of maximal vasodilation.

Intracranial Pressure

Increases in intracranial pressure into the 20- to 30-mm Hg range, although of epidemiological significance, have not been shown to have substantial physiologic significance in terms of a dangerous decrement in CBF (although there may be important negative effects due to semiocclusive narrowing of bridging veins) [39, 120, 121]. As ICP increases, cerebral vasodilation occurs in a compensatory fashion and the actual CBF tends to not be in the ischemic range at lower ICPs [122]. However, with further ICP increases approaching diastolic arterial pressure [123] and infringing on the critical closing pressure of the cerebral microvasculature [47, 48], flow, which ordinarily is continuous throughout the cardiac cycle, becomes discontinuous, decreasing to zero during diastole. This is consistent with the theoretical conclusions of Giulioni et al. [122] wherein they suggest, based on considerations of intracranial elastance and vasomotor tone, that systolic increase and diastolic decrease in BFV should occur when ICP reaches the “breakpoint” value. They suggest that the Gosling Pulsatility Index should be a useful indicator of high ICP. ICP in such situations of zero diastolic flow theoretically should be in the 40- to 60-mmHg range [47, 48]. Indeed, an ICP of 48 mmHg is the average level at which patients progressing to brain death have been observed initially to sustain a high ICP and a systolic spike pattern with the oscillating pattern developing at 62.5 mmHg [124]. Hassler et al. [123] clearly showed the relationship between ICP and phasic blood pressure and how TCD waveform can reflect ICP encroachment on diastolic flow when ICP exceeds diastolic pressure. This pattern is shown in Fig. 46.1b.

As intracranial pressure increases or cerebral perfusion pressure decreases, the character of the TCD waveform thus changes, becoming more "spiky" in appearance with increased pulsatility [122, 123] (Fig. 46.1). This is the basis for the definition of the pulsatility index ([systolic flow velocity-end-diastolic velocity]/[mean diastolic velocity]) [125]. As diastolic perfusion is increasingly compromised, the cerebral circulation takes on more characteristics of the higher resistance peripheral circulation with lower diastolic flow velocity. Ultimately, diastolic flow velocity is zero as cerebral perfusion becomes discontinuous. Based on observations such as this, TCD may be useful to make general inferences about cerebral perfusion pressure and, specifically, to know if ICP exceeds diastolic blood pressure [126, 127].

ICP assessment with TCD is based predominantly on retrospective reports, having not yet been assessed prospectively in a large number of patients to determine whether TCD could be used to reliably and noninvasively determine the CPP in a given patient. Nonetheless, using TCD to make inferences about ICP is gaining attention in cases where invasive ICP monitoring is contraindicated due to coagulopathy [128, 129]. Given the difficulty making direct ICP measurements, TCD waveform analysis should also be of value in cases of posterior fossa hypertension, although this remains unvalidated .

Brain Death

As cerebral perfusion pressure progressively decreases to sustained levels associated with no CBF (Fig. 46.1), brain death ensues. With TCD this manifests as diastolic reversal of flow presumably due to blood "bouncing" backward off an edematous brain as demonstrated by Hassler et al. [123]. Thus, TCD may be useful as a screening tool for brain death. However, it is important to consider the diastolic blood pressure when making such assessments. A strikingly similar TCD waveform can be generated in a totally sentient patient with aortic insufficiency and diastolic pressure low enough to be in the range of normal intracranial pressure. Notably, a normal TCD waveform should be a good way to rule out brain death. This can be remarkably useful in some operative circumstances.

Vessel Patency

Occasionally, a patient may be admitted to the neuro-ICU after having had a

procedure to the middle cerebral or internal carotid arteries. In such cases, TCD has been used during or after surgery to confirm continued patency of the blood vessel [130]. As clinical symptoms may not occur until the vessel is completely occluded or may not occur at all, especially with confounding effects of an anesthetic, TCD may be used to indicate when flow in the monitored vessel is changed in an unwanted manner.

Emboli

Emboli can be readily detected with TCD. This is most commonly a relevant question during cardiac or carotid surgery (Fig. 46.2) [131]. In the ICU, TCD can help determine the adequacy of anticoagulation in patients with artificial cardiac valves or patients with tenuous proximal vascular patency [132, 133]. However, it has been observed that emboli are very common in some situations, without obvious neurological sequelae. Thus, determination that a given frequency of emboli in a given patient warrants major changes in therapy is presently a matter of clinical judgment.

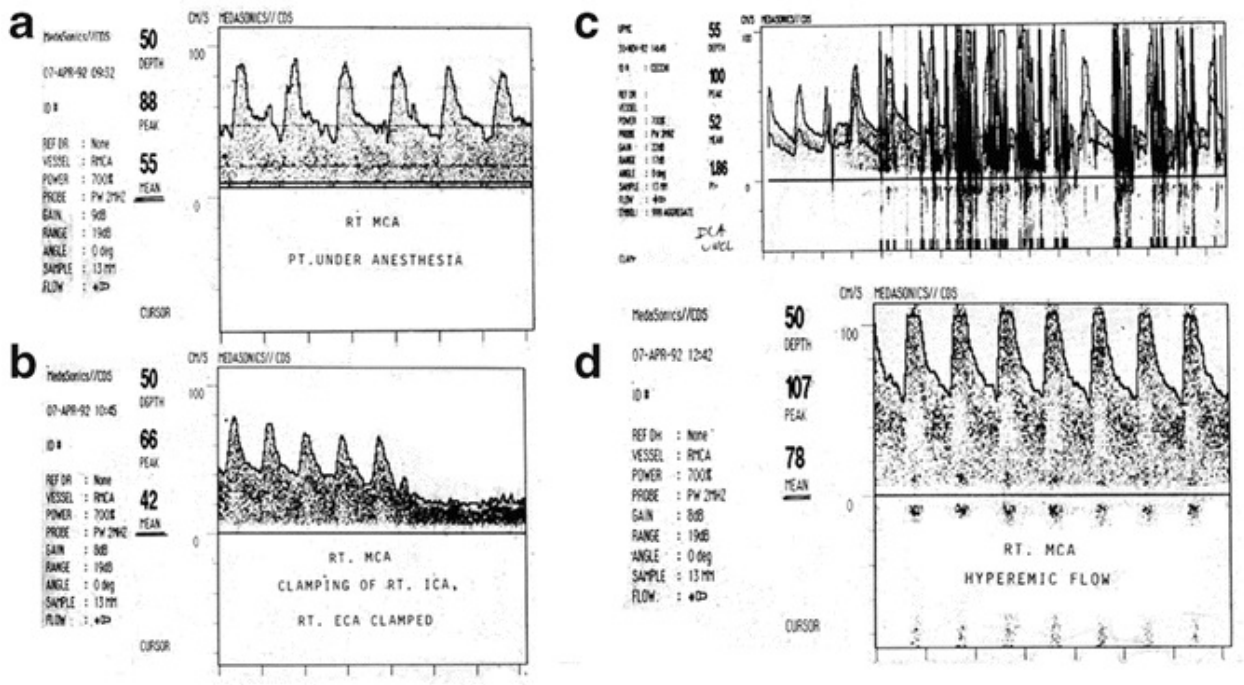

Fig. 46.2 Blood flow velocity measured by TCD during carotid endarterectomy. Preinduction (**a**). Internal and external carotid arteries clamped (**b**). Significant decrease in BFV occurs with loss of pulsatility (**c**). With unclamping significant emboli are observed in the middle cerebral artery. Postischemic hyperemia (**d**) is detected (From Kofke [165]; with permission)

Hyperemia

Hyperemia can be a major problem in some clinical conditions, as after AVM resection, after carotid endarterectomy (Fig. 46.2), with hepatic failure, and systemic hypertension. Given a baseline value or calibration of a TCD value with a CBF determination, TCD can be used to ascertain the presence of a cerebral hyperfusion syndrome. This has been reported after carotid endarterectomy by Steiger et al. [134, 135] and Lindegaard et al. [135]. Such syndromes risk the occurrence of so-called normal perfusion pressure breakthrough, wherein cerebral edema and/or hemorrhage can occur, despite the presence of normal blood pressure. After carotid endarterectomy, cerebral hyperemia is thought to predispose to postoperative cerebral hemorrhage, presumably as a consequence of impaired cerebral autoregulation [136]. Thus, TCD might be useful to judge the cerebral risk and titrate the need for aggressive prevention and/or treatment of systemic hypertension.

N ear-Infrared Spectroscopy Based Monitors of CBF

Recent reports indicate that noninvasive quantitative assessment of rCBF using near-infrared spectroscopy (NIRS) should soon be available to clinicians for use in the operating room and ICU.

Kim et al. [137] recently described a NIRS-based system incorporating real-time assessment of diffuse correlation spectroscopy (DCS) , a complex measure of erythrocyte motion, to derive a noninvasive, continuous quantitative index of rCBF . They validated it in animal studies with microspheres [138] and in preliminary studies of patients undergoing sequential XeCT CBF studies under various physiologic conditions associated with changes in CBF [137]. Blood flow under the patches measured by DCS correlated well with rCBFs assessed by the XeCT method. This group has, moreover, in animal [139] and human [140] studies, demonstrated the feasibility of using their technology to concurrently continuously measure $CMRO_2$.

Concurrent with the earlier developments based on diffuse correlation spectroscopy, a group in Israel (Ornim, Inc.) is developing another system using NIRS plus ultrasound to derive a noninvasive continuous measure of rCBF and brain oxygen saturation. Proprietary data made available to the author suggest a correlation between the Ornim CerOx unit and thermodilution CBFs in humans undergoing hyperventilation. More peer-

reviewed information will be needed and if supportive, this may indicate availability of another noninvasive quantitative regional CBF monitor.

These two lines of investigation suggest a realistic expectation that continuous CBF monitoring will soon be clinically available. Moreover, coupling this with continuous regional brain O_2 saturation (RSO_2) and oxygen extraction fraction (OEF) information should permit concomitant $CMRO_2$ monitoring, which will provide bedside information on whether the rCBF is properly coupled to metabolism. Finally, these monitors should also eventually provide continuous regional information on the presence of intact autoregulation. This will be an improvement on the below-described newly developed global monitors of autoregulation (for more information, *see* Chap. 12, “Near-Infrared Spectroscopy”) .

A rterial Spin Labeling

Defined as perfusion per unit of tissue, CBF is optimally measured with a diffusible tracer that can exchange between the blood and the brain. The currently established CBF imaging modalities include single-photon emission computed tomography (SPECT) , positron emission tomography (PET) , and XeCT CBF , all of which use radioactive diffusible tracers. Because none of these techniques can be applied routinely due to logistic or financial constraints, newly developed technologies, such as CT perfusion (CTP) and arterial spin labeling (ASL) MRI, are becoming alternative standard imaging modalities for CBF evaluation and monitoring.

Applying a magnetic label as the diffusible tracer to blood water molecules, produced by saturating or inverting the longitudinal component of the MRI signal, ASL MRI provides quantitative CBF data and can be performed routinely and repeatedly without contrast administration or ionizing radiation. As labeling and imaging strategies evolve to improve the intrinsic limitations on signal-to-noise ratio per unit time and reduce several potential systemic measurement errors, ASL technique will likely become a standard MR sequence for CBF evaluation and monitoring [141].

Computed Tomography Perfusion

Computed tomography perfusion uses a nondiffusible contrast agent that is administered as a rapid intravenous bolus. Through sequential imaging to simultaneously record changes in the contrast agent concentration as a

function of time, CTP generates data sets that principally include CBV, mean transit time (MTT) , CBF, and time to peak (TTP) [142, 143]. CTP can be rapidly obtained with simultaneous evaluation of cerebral arteries through CT angiography and does not require any particularly costly equipment, making it the imaging modality of choice for acute stroke evaluation. The extent of vertical brain coverage depends primarily on scanner detector configuration and the currently available 320 detector row scanners offer 16 cm slab of parenchyma. Because of the mathematical modeling employed and its use of a nondiffusible contrast agent, CTP -CBF data are currently regarded as qualitative rather than quantitative; however, relative perfusion values generated from contralateral reference parenchyma have demonstrated practical clinical utility, particularly in acute stroke imaging [144]. Active CTP research efforts are ongoing to reduce the innate radiation exposure and enhance its quantitative capacity [144, 145].

Intraoperative Cerebral Blood Flow Monitoring

Conventional methods for intraoperative assessment of blood vessel patency include digital subtraction angiography (DSA) and Doppler ultrasound and flowmetry . Although established as the gold standard for intraoperative vascular imaging, DSA requires substantial resources, additional operative time, and staff with a specific set of expertise to perform the procedure. Doppler ultrasound and flowmetry do not have high accuracy as an assessment tool for vessel lumen compromise [146]. Established noninvasive CBF imaging modalities such as PET are currently impractical for intraoperative uses due to logistical and financial constraints.

Presently, there is not yet a well-validated noninvasive intraoperative technology to not only visualize but also quantitatively measure cortical microcirculatory perfusion in sufficiently high temporospatial resolution. Using various intrinsic and extrinsic contrast agents, optical imaging modalities have emerged as the most promising intraoperative CBF monitoring techniques. Among such developing technologies, indocyanine green videoangiography (ICG-VA) represents the most widely practiced intraoperative blood flow imaging tool.

Indocyanine Green Videoangiography

Introduced for neurovascular procedures more than 30 years ago [147, 148], fluorescence angiography has evolved to become a relatively mature and routinely applicable tool for simple, reliable, fast, and noninvasive intraoperative evaluation of blood flow. Indocyanine green (ICG) is a dye that gets injected into the bloodstream, subsequently excited with an infrared light source, and ultimately imaged with a camera that detects the fluorescence intensity. Because most modern surgical microscope systems have integrated ICG measurement capacities, this technology requires no additional intraoperative equipment but the actual ICG fluorescent dye for intravenous injection. It is commonly used during brain aneurysm clipping, intracranial–extracranial bypass, carotid endarterectomy, and resection of arteriovenous malformation and dural arteriovenous fistula [149].

ICG-VA uses fluorescence intensity as the principal contrast mechanism for imaging blood flow; therefore, this technology provides primarily qualitative information about blood flow, i.e., the presence or absence of blood flow in a vessel, and lacks quantitative measurement. FLOW 800 (Carl Zeiss, Oberkochen, Germany) was recently introduced as a microscope-integrated software tool that analyzes fluorescence intensity in a more detailed fashion [150, 151]. This software visually presents additional information on blood flow dynamics as a color-map and ICG intensity–time curve to identify direction of blood flow and relative timing of entry of ICG into exposed regions of brain. Although other optical imaging technologies such as laser speckle contrast imaging (LSCI) provide more quantitative information about blood flow, they are not yet practical and easily available for intraoperative uses [152, 153].

The current ICG-VA technology displays fluorescence intensity as a white signal on a black background that makes the operative field not visible on the monitor. This represents another significant limitation of the technology. New techniques such as fluorescence angiography with augmented microscopy enhancement (FAAME) are being developed to overlay the ICG signal onto the operative field so that an integrated presentation of real-time imaging of blood flow dynamics in an anatomically realistic background can be directly visible through the microscope oculars [154].

Monitors of Autoregulation

When cerebral autoregulation is intact, small changes in blood pressure will

typically produce no changes in CBF, blood flow velocity, ICP , or brain oxygenation. These properties have been put to advantage in creating a number of approaches to continuously monitor the state of cerebral autoregulation by continuously calculating and monitoring the degree of mathematical correlation between ABP and these brain parameters. Dynamic time domain analysis of cerebrovascular autoregulation using TCD, ICP, PbO_2, or NIRS-based regional oxygen saturation is a current topic of investigation with promising reports of potential efficacious and valid bedside use [35, 77, 78, 155, 156].

TCD-Based Autoregulation (Mx)

Recent advances in transcranial Doppler ultrasonograpy have allowed insights into dynamic, nearly instantaneous, assessment of cerebral autoregulation in critically ill patients. This approach determines the correlation coefficient between blood flow velocity (middle cerebral artery) and arterial blood pressure in real time at the bedside to make inferences regarding autoregulation. A high correlation of blood flow velocity with blood pressure suggests poor autoregulation, whereas no correlation is normal. Czosnyka et al. [34] observed in TBI patients a U-shaped curvilinear relationship in flow velocity versus ABP , with worse autoregulation (i.e., high correlation) with ABP less than 75 mmHg and ABP greater than 125 mmHg (Fig. 46.3). In another context, Joshi et al. [77], using TCD-based autoregulation assessment (Mx) in cardiac surgery patients reported an association of disturbed Mx with postoperative stroke [78, 79].

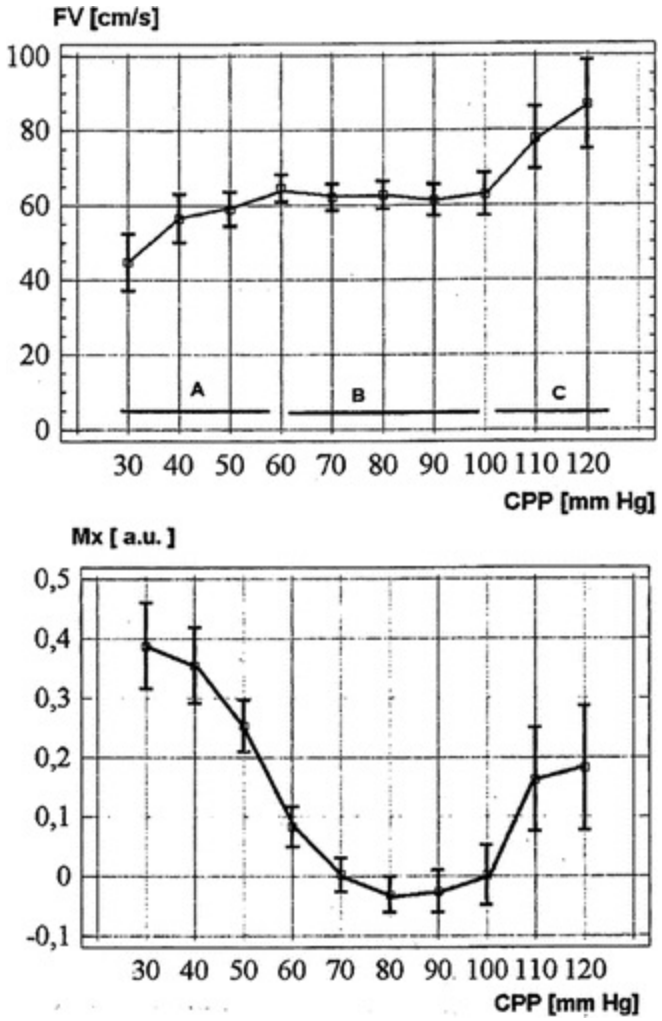

Fig. 46.3 Graphs demonstrating results of empirical regression of mean flow velocity by TCD (*upper*) and the Mx (a correlation coefficient) (*lower*) as they relate to CPP. Three distinctive zones of CPP—Zone A lying below the lower limit, Zone B lying within the range, and Zone C lying above the upper limit of autoregulation are marked. Vertical lines represent standard errors within CPP bins. *a.u.* arbitrary units, *s* second (From Czosnyka et al. [34]; with permission)

ICP -Based Autoregulation (Prx)

Intracranial pressure ordinarily does not vary with changes in blood pressure within the normal autoregulatory range. However, with injury-induced cerebral dysautoregulation, ICP will vary with ABP such that information on the state of cerebral autoregulation can be inferred. The ICP pressure-reactivity index (PRx) is a described quantitation of the aforementioned description of abnormal dynamic correlation of ICP changes with ABP changes and is another means to dynamically evaluate autoregulation [35–37, 157], with reports indicating that Prx correlates well with other

autoregulation indices [36, 37, 158, 159]. Steiner et al. [35] reported on the use of Prx monitoring in TBI patients to determine the optimal CPP. Patients with better autoregulation in this optimal range as defined by Prx had better outcomes. Moreover, patients with dysautoregulation related to higher ABP with corresponding ICP elevation also had worse outcomes, suggesting that autoregulation monitoring, to ensure adherence to an individual's optimal CPP, may be an outcome-altering ICU measure. Zweifel et al. [36] report congruent observations. Notably, Prx, as with TCD-based autoregulation studies, also appears to undergo a U-shaped curvilinear relationship with variations in CPP, with it being abnormally high (i.e., ICP varies with ABP) at low (ischemic) and high (hyperemic) CPP in TBI patients. Moreover, further complementing this are observations of abnormally high OEF and low OEF at these respective ABP extremes. This is underscored by reports of a significant ischemic burden in TBI patients [160–163], suggesting a delicate balance between hypotension-associated hypoperfusion and hypertension-associated edema/ICP exacerbation, both of which will worsen regional ischemia. Taken together, these autoregulation studies introduce the notion that there is an individualized ABP optimum in TBI patients [36] that should be a therapeutic goal .

COx

Autoregulation monitoring is also being reported using brain near infrared spectroscopy (COx), suggesting that noninvasive autoregulation assessment will be a feasible bedside modality that can be used to deliver the optimal CPP. Joshi et al. [77] reported, in cardiac surgery patients, an association of disturbed Mx with postoperative stroke with good agreement between Mx and Cox, thus demonstrating feasibility of COx assessed with NIRS [78, 79]. Finally, brain PbO_2 has been reported to also be amenable to use as a regional autoregulation monitor (ORx) [80].

All of these autoregulation indices appear to be feasible to use to monitor and individualize CBF in the operating room. Initial studies in the cardiac surgery [77, 79], and sitting orthopedics [164] contexts support a potential role for brain autoregulation monitoring in neurosurgery and other operative settings, which may help guide blood pressure management.

Conclusion

In summary, many different technologies are now available to provide monitoring information regarding cerebral blood flow in critically ill patients during and after surgery. The available techniques provide a range of options in terms of quantitation, anatomic resolution, portability, and speed of information availability. Unfortunately, no perfect monitor is yet available that provides all of the needed attributes and makes the data easily available at the bedside in the ICU or OR. Nonetheless, the available methods have provided for significant advances in our approach to thinking about and managing cerebral blood flow in the critically ill.

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Afterword to First Edition

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Future of Monitoring the Nervous System

As far as can be traced back, the first time the words “monitoring” and “spinal cord” were mentioned together in the title of an article was in 1972. At that time it was a revolutionary idea, much better appreciated if one remembers that diagnostics in neurosurgery consisted of pneumoencephalography, oily myelograms and mostly direct carotid angiograms. Computerized tomographic (CAT) scans did not exist in clinical practice, let alone magnetic resonance imaging (MRI). Although, the first evoked potentials (EP) had been recorded by Dawson in 1947, the typical averaging technique was not developed until 1951. In a 1972 book on “Evoked Potentials in Psychology, Sensoriphysiology, and Clinical Medicine,” only one of five chapters was devoted to clinical applications. The clinical applications of EP were mostly the possibilities of testing the integrity of sensory pathways and of locating brain lesions (D. Regan) [1]. One of the concluding sentences was: “…..it follows that future EP methods for objectively testing…..sensoripathways might prove to be clinically useful. There is encouraging evidence that such exciting developments are possible…”. That was the time when Tamaki et al (1972) [2] and Croft et al (1972) [3] first published on the concept of monitoring spinal cord function by using EP. Parallel to that Kurokawa (1972) [4], Shimoji (1971) [6] and Ertekin (1978) [7] had started to record spinal cord action potentials and measure conduction velocities in the spinal cord. The neurosurgeon J. Brodkey had also collaborated with the orthopaedic surgeon C. Nash who organised the first workshop on “Clinical application of spinal cord monitoring for operative treatment of spinal diseases” in September 1977 in Cleveland [8]. That meeting was already attended by neurophysiologists, neurosurgeons and orthopaedic surgeons. In his review of the development of

intraoperative spinal cord monitoring, Tamaki in 2007 mentioned, that [9] "…..the first surgeon to mention the need for developing this technology was Dr. Jacquelin Perry then working at Rancho Los Amigos Hospital…..". Before that somatosensory evoked potentials (SSEPs) had already been used in the diagnosis of myelopathy by Halliday in 1963, for spinal cord injury by Donaghy in 1969, Eidelberg in 1971 and Perot in 1972. Visual EP had been applied for the diagnosis of multiple sclerosis by Halliday in 1972. One of the first books to appear on intraoperative monitoring was in 1984 by Saikon Publishing, edited by Homma and Tamaki [10]. Soon brainstem auditory evoked potentials (ABRs) were also monitored for posterior fossa surgery.

These early developments underline two observations that have been associated with intraoperative neurophysiological monitoring throughout its existence: it was always a multidisciplinary approach, usually initiated by operative specialties or by anaesthetists, and there were always different technologies used. In the early days direct recordings of non-averaged potentials were acquired directly from the spinal cord instead of non-invasively acquiring averaged recordings of EP. I was initiated to EP recording in late 1974 by Takanori Fukushima who was then a researcher at Berlin Free University, Department of Neurosurgery. The signal averager I inherited from him was the size of two man-sized cupboards with dozens of knobs and dials, all of which unfortunately could be set incorrectly. Artefact suppression was of poor quality, averages took a long time and had to be documented on Polaroid. Measuring of latencies was done by hand. In the second half of the 1970s, the first commercial monitoring machines became available and applications expanded, both, in the operating room (OR) and outside. Another spinal cord monitoring workshop was organised in St. Louis in January 1979 and the proceedings already contained the first clinical papers on the application of these methods in the OR [11].

At that time, everything was new and many things needed to be defined: "What was more important, a diminution of amplitude or a delay in latency?" How to define the range of normal fluctuation in amplitudes, which latency delay is considered significant, what are the effects of the various anaesthetics? Many important questions needed to be answered and problems needed to be solved. In Japan a Society of Spinal Cord Electrodiagnosis was founded and it should be stressed that the Japanese orthopaedic surgeons and anaesthesiologists have been instrumental in developing a large experience with patients. The tenth issue of the *Journal of Electrodiagnosis of the Spinal*

Cord in 1987 already contains clinical studies on the corticospinal D-responses, on brachial plexus injury, on conus medullaris lesions, on the effect of spinal cord destruction on spinal cord blood flow and on monitoring during surgery of carotid aneurysms, scoliosis and spinal cord tumour surgery.

Numerous books have appeared in the meantime, published by quite a diverse group of specialists from anaesthesiology, neurophysiology, neurology, neurosurgery and orthopaedic surgeons. The Handbook of Clinical Neurophysiology has devoted its volume 8 to “Intraoperative Monitoring of Neural Function” [12]. A total of 56 chapters are devoted to compound nerve action potential techniques, motor EP, ABRs, electromyographic, reflex and nerve conduction monitoring and a host of lesions: epilepsy surgery, cerebral tumours, movement disorders, brain stem lesions, skull base surgery, microvascular decompression, middle ear surgery, lower cranial nerve surgery, spinal tumours, scoliosis and the list goes on and on, covering also peripheral nerve surgery, vascular surgery and even intensive care monitoring. This not only reflects the development of the wide spectrum in the past but may be an indication of further developments.

After the first ABRs were recorded in 1971 the first series of intracranial nerve monitoring was published by Levine et al (1978) [13]. The 1980s was the period of rapid expansion and new applications for various kinds of intraoperative neurophysiologic monitoring. The growing clinical applications made it more and more important to define what is a “false positive” and what is a “false negative” monitoring event. What should be the criteria to warn the surgeon or intervene with the surgery? All this is closely related to the definition of normal variability and to what is a clearly abnormal EP. In those pioneering days various proposals for warning criteria were made and these were more or less based on observing many cases and a certain gut feeling of what is considered too much of a change.

Considering future developments, it is well known that predictions are always difficult and predicting the future is particularly difficult. I discovered one of our own old slides from 1992 in which future developments were discussed, some of which became true (motor tract monitoring, improved averages with digital filtering) and others proved that some things are not so important (automated peak detection, frequency analyses, analyses of refractoriness). On the other hand, there were a lot of totally unexpected discoveries. It was observed that you could lose your ABR from positioning

or from the dura opening or cerebellar retraction alone. Also it was noted that a potential loss may occur while applying retraction when opening the sylvian fissure or inducing vasospasm by the oozing blood from a tumour. Many developments that were popular at one time such as dermatomal SEPs, which were primarily used for topographic diagnosis of spinal cord diseases lost their value with the introduction of MRI imaging. The same occurred to single pulse transcranial motor cortex stimulation which was later replaced by transcranial multiple pulse stimulation. Soon it could be demonstrated that monitoring did indeed improve surgical results. Hearing loss associated with microvascular decompression went down from 4.8 to 1.7% in Pittsburgh and from 7.7 to 2.3% in Lyon. Other authors found that monitoring was effective in preventing new deficits in 5.2% of cases [14].

It turned out that intraoperative neurophysiological monitoring soon became a didactic tool. It gave the surgeon feedback and taught about phenomena which was not clear before the use of monitoring (e.g. loss of ABR and hearing after coagulation of a capsular artery on the dorsal surface of an acoustic neurinoma 2.5 cm away from the acoustic nerve on the ventral side of the tumour). Thus, surgical technique was modified in many ways for each individual surgeon while using these techniques for a number of years. Monitoring does influence surgical strategy not only acutely during the case of today but also in changing the daily practice of surgery. Neuromonitoring has changed surgery into functionally guided surgery. Peter Jannetta put it in the following words: "…Thus, surgeons are, in a way practicing preventive surgery when they perform operations ….. with intraoperative monitoring of evoked potentials…".

What are the thoughts on the future? I do remember that a few years after the enigma of how to monitor the motor tracts was solved by the introduction of transcranial multipulse stimulation by our group, by the establishment of the D-wave technique by the Japanese colleagues and by Deletis' group in New York, I thought most of what could possibly be done in the field of intraoperative neurophysiologic monitoring had been achieved. Thankfully I never said that too loud in public, as the developments in the last 10 years have demonstrated the magnitude of the growth in the application of intraoperative neurophysiologic tools. As new people come into the field and are confronted with clinical problems, there is no doubt that new ideas will come up and new applications of electrophysiological tools in the OR will be developed. If no questions are asked, no answers will be given. If questions

are asked, the next generation will start looking for answers. As the clinical field expands, new challenges will arise and this will lead to new applications. A wonderful example is the surgery of brain stem cavernomas which only developed in the last 15 years. The challenge was to define a safe way to enter into the brainstem and this led to the application of neurophysiology for mapping cranial nerve nuclei at the floor of the fourth ventricle, soon to be combined with monitoring of the motor function of those cranial nerves. Another more recent example is the purely intracerebral tract monitoring during glioma surgery which opened new perspectives for monitoring tumour surgery and brain research.

I had the privilege to be involved with and to be a witness of the development of intraoperative neurophysiologic monitoring. Now, I see a future for intraoperative neurophysiologic monitoring in more than one field of surgery.

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