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Foreword

For a neuroophthalmologist, perimetry and visual fields are "basic food." Without it, he/she will not be able to survive. My teacher, Elfriede Aulhorn (1921–1991), developed the famous Tübingen perimeter and established modern clinical perimetry. For her, it was most important to correlate visual field defects with the underlying lesion. In the 1980s, she developed her first automated perimeter. In contrast to other devices, the grid of this instrument was designed to provide exact information about the shape of the visual field defect. As a result, it became possible to localize the underlying lesion anatomically. At the same time, neuroimaging became popular and we learned how to predict the site of the lesion, and gained a still better understanding of the visual field and visual pathways.

Many years have passed since then and perimetry has changed. Today, clinicians are mainly interested in summarizing all results into one number: the mean defect. The availability of neuroimaging seemed to make exact perimetry needless and old fashioned. Knowledge about the correlation of visual field and brain anatomy has been lost. Diagnostic errors are a consequence when, for example, a visual field defect is attributed to a harmless arachnoid cyst, while the actual cause, a small tumor, has been overlooked.

This alone justifies a book about homonymous hemianopias. They play a very important role in the neurologic and ophthalmologic clinic. Losing one half or one quarter of our visual field is more devastating than to lose visual acuity in one eye. Reading, driving a car, and orienting in difficult environments may become difficult or impossible. Strange add-on symptoms like palinopsia or neglect may occur and visual hallucinations may frighten the patient. Knowledge about homonymous hemianopias may help to understand our patients' symptoms and may guide us to offer them help. Help does not mean restoration training, a reduced visual field cannot usually be restored, but orientation training is a help to cope with the defect.

Karolina Skorkovska has put together an important book. It closes the gap after Kölmel's book from 1988, which came out before MRI became available as a routine diagnostic tool and before automated perimetry began to replace Goldmann perimetry. This emphasizes the importance of Karolina Skorkovska and her coauthors' work. It is an interdisciplinary

cooperation between ophthalmologists, neurologists, neuropsychologists, and basic scientists. For me, as a neuroophthalmologist, I would call it the "book of the year." It is high time, after almost 30 years, to have a new book about homonymous hemianopias.

Tübingen, Germany
March 2017

Helmut Wilhelm

Preface

Homonymous hemianopia is a well-known technical term used by different medical experts. However, does an ophthalmologist know all possible causes of the visual field defect he has just diagnosed? Can a neurologist advise the patient about rehabilitation? Is a psychologist aware of the central visual disorders that can be connected with homonymous visual field defects and are no indication that the patient has gone mad? How is the life of these patients affected, and can they drive a car?

To be correctly managed, patients with homonymous hemianopia require a proper interdisciplinary approach. This book is designed for medical subspecialists who may be dealing with this condition for the first time, as well as for experienced clinicians who want to update their knowledge. The most recent book on this topic was written in 1988 (http://www.springer.com/de/book/9783540189749).

The international team of authors consists of acknowledged experts in this field as well as young, enthusiastic researchers who explored this topic in their postgraduate studies and have subsequently pursued it. The book begins with anatomy and pathophysiology of the visual pathway, explains stroke as the most common cause of the disease, and continues with diagnostic procedures and findings in the practice of an ophthalmologist, neurologist, or neuroradiologist. A separate chapter is devoted to driving with homonymous hemianopia and the possibilities of rehabilitation in these patients.

I would like to thank Professors Barbara and Helmut Wilhelm who were my mentors during my postgraduate study in Tübingen, Germany, and who have also advised me on this book. My special thanks go to the authors who agreed to devote their time to the project. Many thanks to Springer for their confidence in the project and particularly to the developmental editor Katherine Kreilkamp who helped us through the editing process.

Brno, Czech Republic — Karolína Skorkovská

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Anatomy of the Human Visual Pathway

1

Marek Joukal

Abstract

Vision is the primary sense in humans. There are approximately one million axons in the optic nerve, constituting almost 40% of the total number of axons in all cranial nerves. The primary sensors for sight are the 130 million rods and seven million cones found in the retina. With the release of glutamate, they transform electromagnetic waves of light with a wavelength between 400 and 700 nm to graded changes of the membrane potential. The signal from photoreceptors continues to the bipolar cells and then to the retinal ganglion cells. Their axons pass through the optic nerve, the optic chiasm, form the optic tract, and reach the lateral geniculate body of the thalamus. The axons coming from the nasal hemiretina are crossed in the optic chiasm, while axons from the temporal hemiretina stay uncrossed. Neurons of the lateral geniculate body send their axons to the optic radiation and terminate in the primary visual cortex – the striate area in the ipsilateral occipital lobe where the first analysis of visual information is performed. Further processing takes place in extrastriate visual areas in the occipital, parietal, and temporal lobes. The visual pathway shows a precise retinotopical organization at all levels that gives the anatomical background for symptoms when some part of optic pathway is damaged.

Keywords

Visual pathway • Vascularization • Pathophysiology • Retina • Optic nerve • Optic chiasm • Optic tract • Lateral geniculate • Optic radiation • Striate cortex • Extrastriate cortex

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1.1 Introduction

The visual pathway is composed of four neuronal elements. Photoreceptors, bipolar cells, and retinal ganglion cells are found in the retina. Axons of ganglion cells pass through the optic nerve, optic chiasm, and optic tract. The fourth neuronal elements are found in the lateral geniculate body; their axons form the optic radiation and terminate in the primary visual cortex (Fig. 1.1).

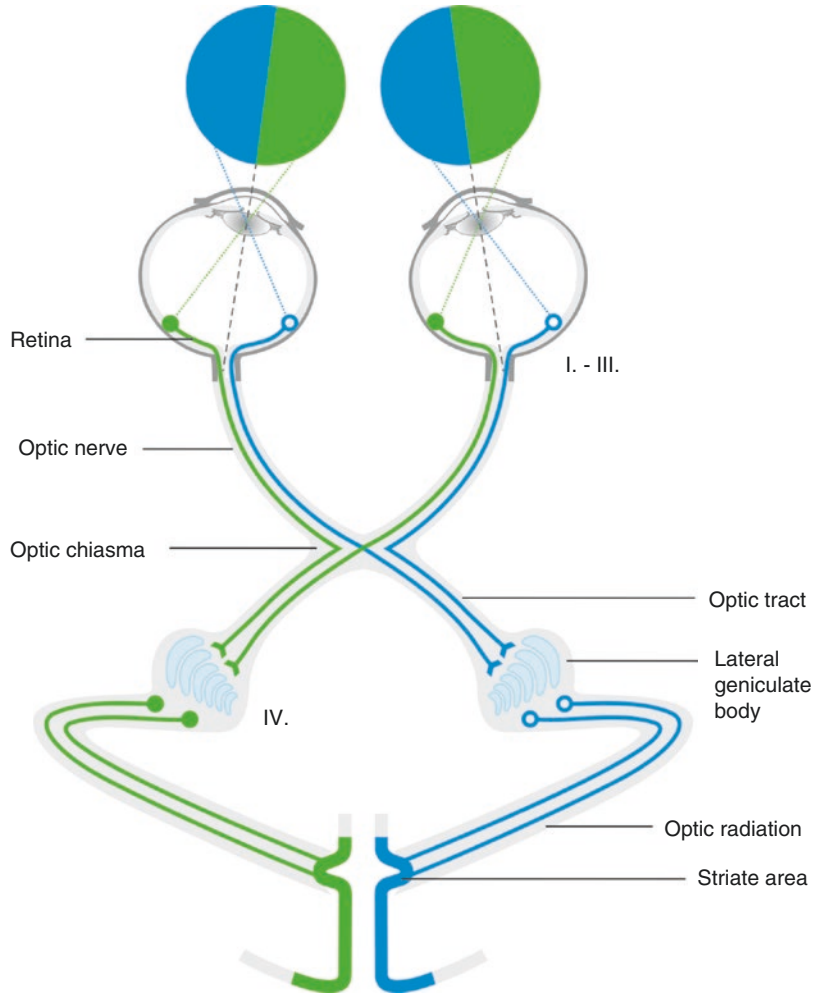

Fig. 1.1 Schematic drawing of the visual pathway and its neuronal composition

1.2 The Retina

The retina is the innermost thin layer of tissue covering the back of the eye. It develops from the optic vesicles of the hindbrain. Each optic vesicle "caves in" to form the optic cup, which consists of two layers and is connected to the developing brain by the optic stalk. The outer layer of the optic cup becomes the pigment epithelium of the retina, and the inner layer differentiates into the complex neural layer of the retina. The optic stalk becomes the optic nerve.

The retina is functionally divided into small spots called receptive fields, composed of the circular receptive field centre and the peripheral area (Fig. 1.2). The neurons that are excited by light hitting the centre and inhibited by light hitting the peripheral area are called ON-neurons. Neurons that have the opposite reaction to the light are known as OFF-neurons.

1.2.1 The First Neuron: Rods and Cones

The outer part of the retina adjacent to the choroid is pigment epithelium composed of cuboidal cells with pigmented granules in their cytoplasm. Internal to this layer is a layer of photoreceptors. There are two types of photoreceptors in the retina, the rods and cones, which represent the first neuron of the optic

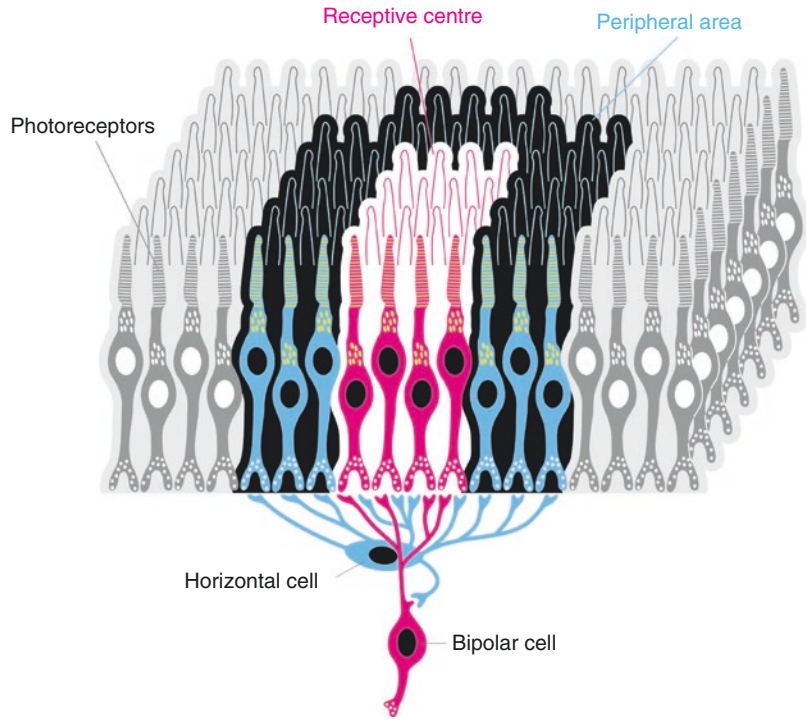

Fig. 1.2 The receptive field centre provides a direct connection among the photoreceptors and bipolar cells, while the signal from the photoreceptors in the peripheral area passes through horizontal cells to the bipolar cells (Adapted from Dubový and Klusáková [2], with permission)

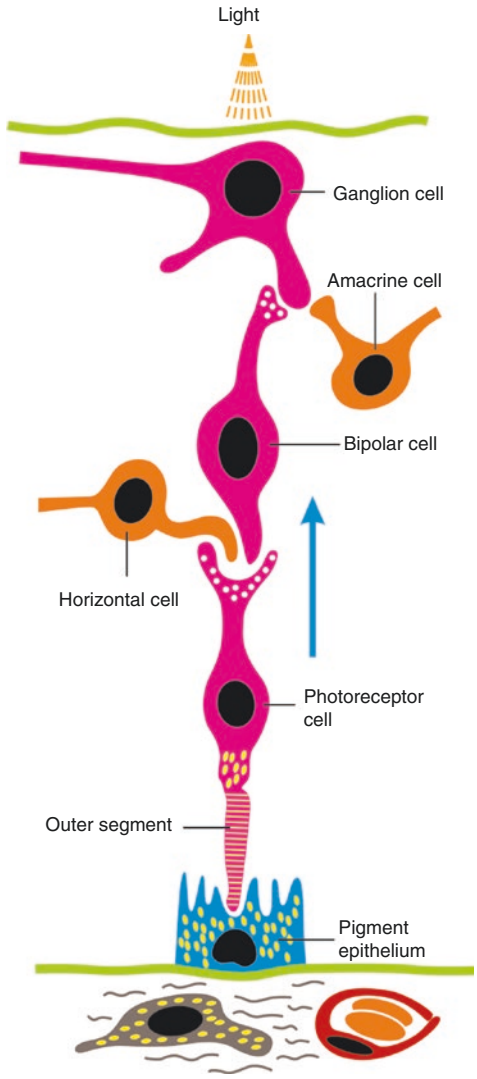

Fig. 1.3 A highly simplified picture of cellular connections in the retina (Adapted from Brodal [1] by permission of Oxford University Press, USA)

pathway (Fig. 1.3). The retina contains 130 million rods, which are much more sensitive than the cones and react to extremely small amounts of light. They are responsible for vision when the light is dim – scotopic vision. Rods contain the photopigment rhodopsin – composed of a protein part, opsin – and retinal, which is an aldehyde of the vitamin A molecule. Seven million cones are found in the central fovea of the retina. They are responsible for vision in strong light (photopic vision) and perception of shape and color. The photopigment of cones differs slightly from rhodopsin in the structure of the opsin molecules. There are three types of cone opsin and thus three kinds of cones absorbing light of different wavelengths. One kind of cone responds best to light in the blue part of the spectrum (maximum wavelength 420 nm), another in the green part (maximum wavelength 530 nm), and the third in the red part (maximum wavelength 560 nm). Each photopigment is bleached not only by light with wavelengths to which it is maximally sensitive but also by stronger light with shorter and longer wavelengths; thus, one kind of cone alone cannot inform about color [1–4].

In addition to rods and cones there is a third type of photosensitive cell in the retina – retinal ganglion cells expressing the photopigment melanopsin. They give rise to the retinohypothalamic tract and were identified only recently. These cells convey the general level of environmental illumination to the suprachiasmatic nucleus of the hypothalamus where the primary circadian pacemaker is localized. They are also connected with the pretectal area of the midbrain and are involved in the pupillary light response [5, 6].

1.2.2 Second Neuron: Bipolar Cells

The bodies of bipolar cells form the inner nuclear layer of the retina. Their dendrites are in contact with the base of the rods and cones. In cones there are two kinds of bipolar cell: ON bipolar cells are excited when light hits the photoreceptor and are inhibited in the dark. The second type of bipolar cell is excited in the dark and inhibited in light; therefore, they are called OFF bipolar cells. In rods all bipolar cells are hyperpolarized when the light hits the rods (Fig. 1.4).

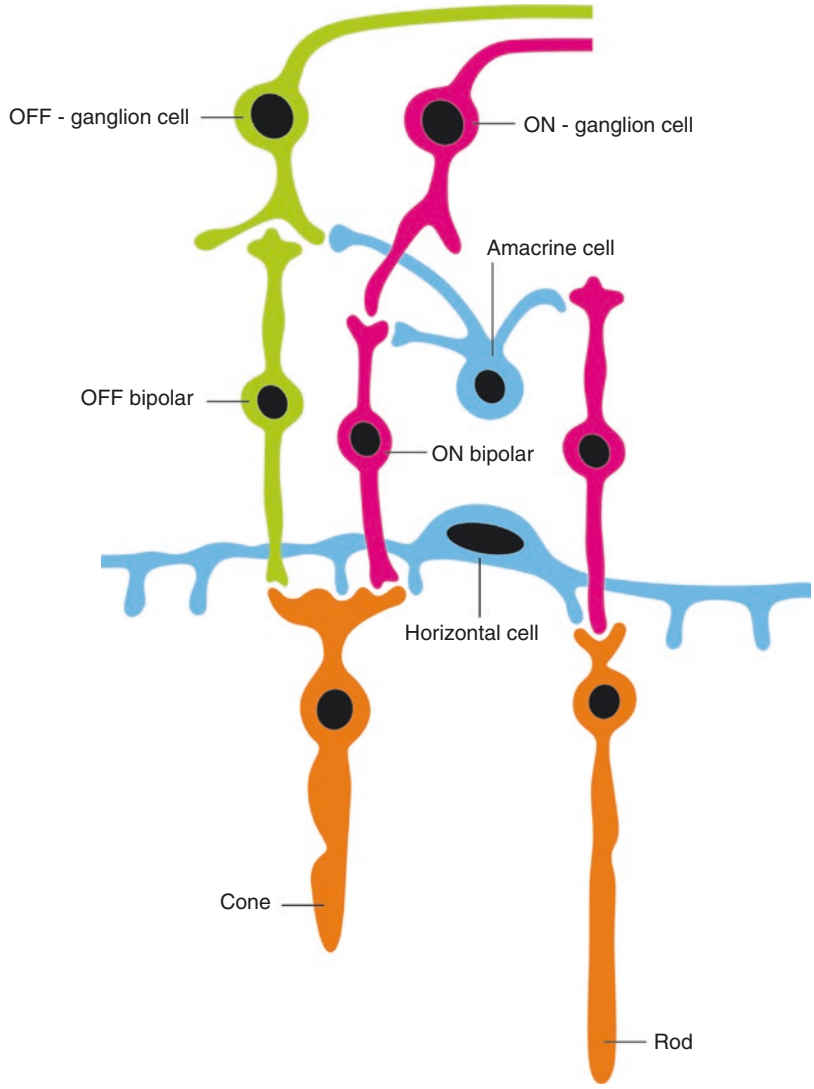

Fig. 1.4 Schematic drawing of two types of bipolar cells and their connection with the ganglion cells of the retina (Adapted from Brodal [1] by permission of Oxford University Press, USA)

1.2.3 The Third Neuron: Retinal Ganglion Cells

The dendrites of ganglion cells are in contact with ON or OFF synaptic centers via axons of bipolar cells. The ON ganglion cells are excited when the light hits the centre of the receptive field and inhibited by light on the periphery of the receptive field. This inhibition is processed via horizontal cells [1–4]. Apart from the division of ganglion cells to ON and OFF, anatomic studies of the monkey found that these cells differ greatly in size. Therefore, we can distinguish the M-cells (magnocellular) and P-cells (parvocellular). The P-cells have smaller cell bodies, a less extensive dendritic tree, and

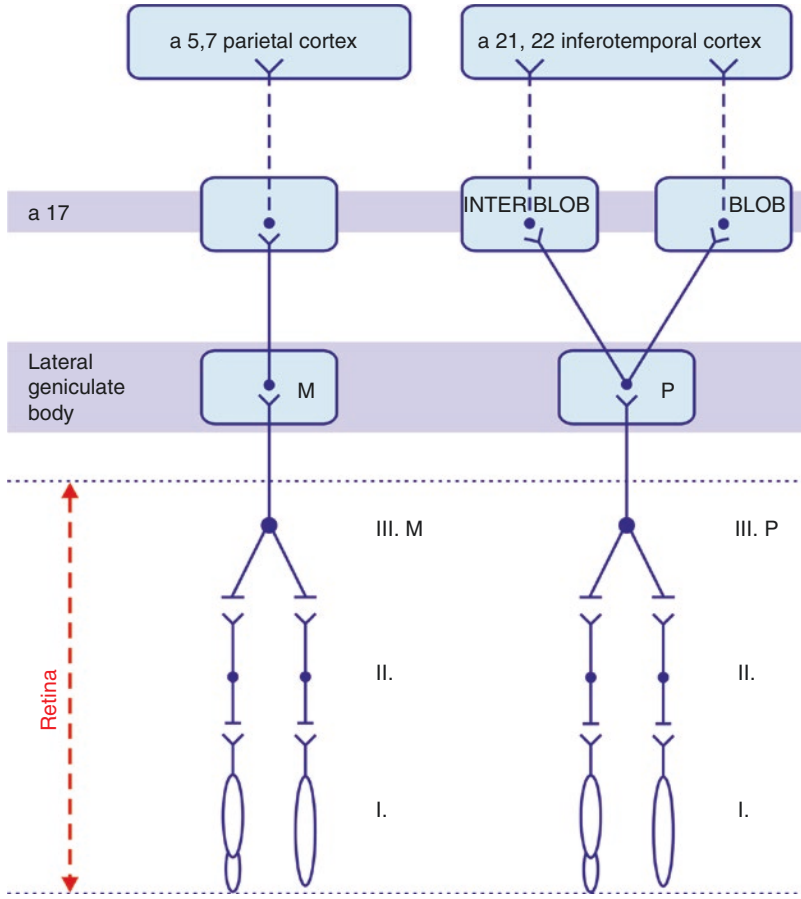

Fig. 1.5 Schematic diagram of the magnocellular (*M*) and parvocellular (*P*) retinal ganglion cells projection through the lateral geniculate body to the visual cortex

a thinner axon than M-cells. The P-cells are most numerous; they constitute about 80% of all ganglion cells in the retina. A major difference in comparison to M-cells is that the P-cells respond preferentially to light with a particular wavelength. This means that P-cells are color-specific, whereas M-cells do not have such specificity. Axons of M- and P-cells terminate on M- and P-neurons of the lateral geniculate body, respectively (Fig. 1.5) [7].

1.2.4 Interneurons of the Retina

There are two kinds of interneurons in the retina that are responsible for visual information processing based on modulation of bipolar and ganglion cells activity – amacrine cells and horizontal cells. Amacrine cells are intercalated between bipolar cells and ganglion cells within the inner nuclear layer. They are in contact with the axons of the bipolar cells and dendrites of the ganglion cells. Many bipolar cells of rods exert their effect on ganglion cells only or mainly via amacrine cells. Amacrine cells are responsible for interaction between ON and OFF synaptic centers, which is important for the increase of contrast and the detection of motion. The horizontal cell processes establish contact with the inner segments of the photoreceptors and with the dendrites of bipolar cells. Therefore, they serve for regulation of transmission from the photoreceptors to the bipolar cells. Horizontal cells are responsible for the typical receptive fields of the bipolar cells and ganglion cells with central excitation and lateral inhibition.

There are two parallel signal pathways from the cones. The ON ganglion cells increase the impulse frequency when the light hits the cones to which they are connected. The OFF ganglion cells are stimulated in darkness. This organization increases the range of light intensities more than if there were only one channel. The functional connection of neurons in the retina comes from photoreceptors to bipolar cells and then to ganglion cells. The axons of ganglion cells form the optic nerve. Comparison of the number of photoreceptors (more than 100 million) and ganglion cells (one million) shows that there is a large convergence of signals in the retina. In addition to the direct connection of neurons, the signal is also conducted via interneurons [1–4].

1.2.5 Blood Supply of the Retina

The retina is supplied by the central artery that is a branch of the ophthalmic artery. The central retinal artery arises inferiorly to the optic nerve and runs within the nerve to the eyeball. It emerges at the optic disc where it divides into the terminal branches for each quadrant of the retina. The retina can also be supplied by variant cilio-retinal arteries that are branches of ciliary arteries. This variant is found in approximately 20% of the population (Fig. 1.6) [3, 8, 9].

Each segment of the capillary network is drained by retinal venules that continue into progressively larger vessels. These venules constitute the central retinal vein that exits the eyeball. Latent collaterals between the central retinal vein and the choroidal venous drainage can be located at the border between the optic nerve and the retina [10].

1.2.6 Lesions of the Retina

The symptoms of partial damage or interruption in any part of the optic pathway correspond to anatomical arrangement of cells and fibers. Lesions of the retina or optic nerve prevent the transduction of signals from the eye to higher

1. Internal carotid artery
2. Anterior cerebral artery
3. Anterior communicating artery
4. Posterior communicating artery
5. Basilary artery
6. Posterior cerebral artery
7. Posterior choroidal artery
8. Calcarine artery
9. Middle cerebral artery
10. Anterior choroidal artery
11. Superior hypophyseal artery
12. Ophthalmic artery
13. Central retinal artery
14. Cilio-retinal arteries

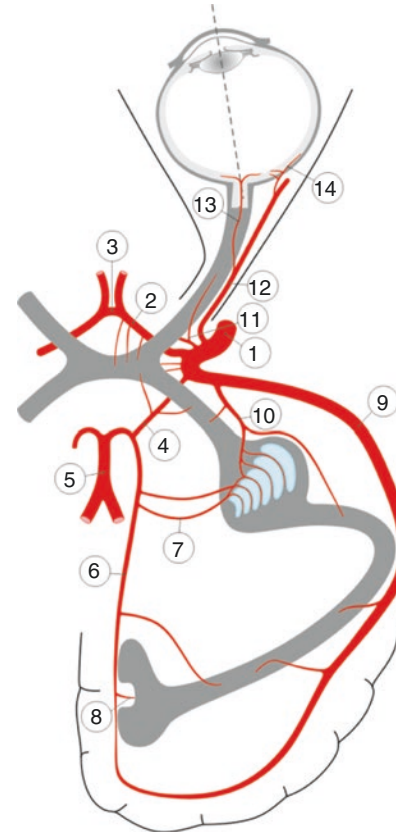

Fig. 1.6 A simplified schematic drawing of visual pathway vascularization

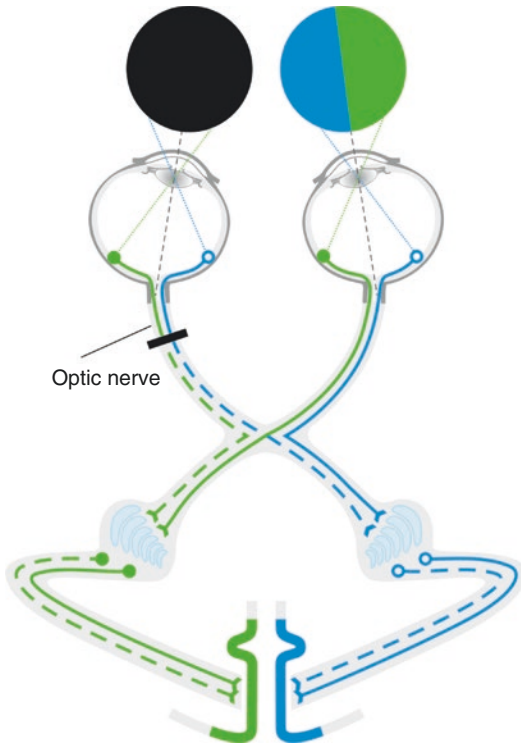

Fig. 1.7 Lesion of the optic nerve or retina causes monocular blindness

levels of the optic pathway; therefore, it induces monocular blindness (Fig. 1.7) [1, 3, 11].

1.3 Optic Nerve

The axons of the retinal ganglion cells run toward the posterior pole of the eye and pass through the wall of the eyeball at the optic papilla. The axons then constitute the optic nerve that is in fact a protrusion of the hindbrain. The optic nerve is covered by extensions of the cranial meninges and subarachnoid space filled with cerebrospinal fluid. The nerve passes posteromedial in the orbit toward the optic canal. The optic nerve emerges in the middle cranial fossa after exiting the optic canal [1–4].

1.3.1 Blood Supply of the Optic Nerve

According to the topography of the optic nerve it can be divided into proximal (intracranial), middle (intracanalicular), and distal (intraorbital) parts. The blood supply of these parts is provided by different arteries (see Fig. 1.6). The intracranial as well as intracanalicular parts of the optic nerve are supplied by the superior hypophyseal artery, a branch of the internal carotid artery. The contributions of the ophthalmic artery to this part of the nerve are negligible. The intracanalicular part is mainly supplied by the intrinsic capillary network from the superior hypophyseal artery. This supply may be easily interrupted by compression on or swelling of the optic nerve in the very narrow optic canal. The most distal part (intraorbital) part is supplied by the ophthalmic artery [12].

1.4 Optic Chiasm and Optic Tract

The optic nerves of both sides meet in the optic chiasm, where the fibers of the nasal hemiretinae cross to the contralateral optic tract, while the axons of the temporal hemiretinae stay uncrossed. There is a slight preponderance of crossed to uncrossed fibers (53:47) [13, 14]. The main portion of all axons (90%) forms the lateral root of the optic tract and continues to the lateral geniculate body. The remaining 10% of axons constitute the medial root of the optic tract. These axons terminate in the tectum of the mesencephalon (retinotectal tract), especially in the superior colliculus and the pretectal nuclei. These fibers are important for optic reflexes, such as pupillary reflex or vestibulo-ocular reflex. Some fibers of the optic tract terminate in the hypothalamus (retinothalamic tract) where they contribute to regulation of circadian rhythms [1, 4, 15, 16].

1.4.1 Blood Supply of the Optic Chiasm

The optic chiasm is highly vascularized. The main blood supply is provided by the branches of the internal carotid artery, anterior communicating artery, and anterior cerebral artery (see Fig. 1.6). Some small branches supplying the chiasm come from the middle cerebral artery, posterior communicating artery, and anterior choroidal artery [10, 17, 18].

1.4.2 Lesions of the Optic Chiasm

In a contrast to lesions of the optic nerve, where monocular blindness occurs, lesions in the optic chiasm produce various visual symptoms according to their localization. These lesions can be divided into those that affect the anterior angle, the body, and the posterior angle of the optic chiasm [19]. The anterior angle lesions, where the fibers from the nasal hemiretina are localized, induce varying degrees of temporal defect in the ipsilateral eye. The specific visual field defect is called "junctional scotoma" and affects the contralateral superior temporal field. In case of extensive lesion in the anterior angle of the optic chiasm monocular blindness can also occur [11, 20]. Bitemporal hemianopia is a specific symptom of lesions located in the body of the optic chiasm where the crossed fibers from the nasal hemiretinae of both eyes are affected (Fig. 1.8) [1, 19]. Posterior angle lesions in the optic chiasm are expressed by bitemporal hemianopic scotomas.

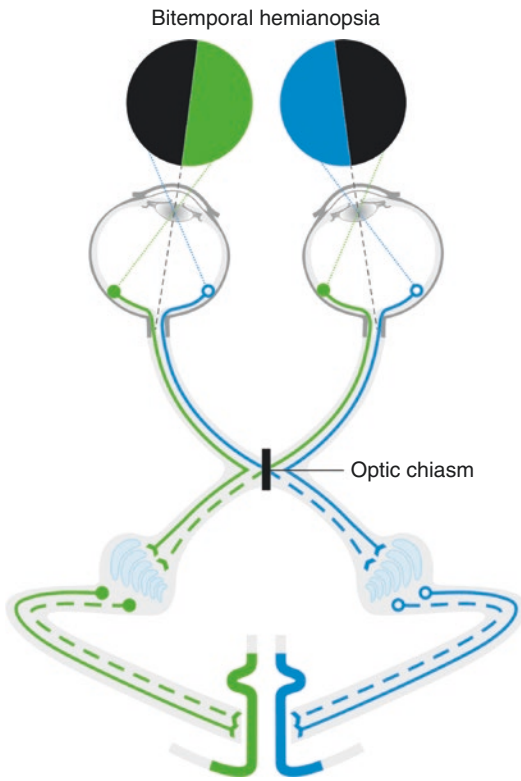

Fig. 1.8 Bitemporal hemianapia is caused by lesion in the optic chiasm

Such defects may be mistaken for cecocentral scotomas and attributed to a toxic, metabolic, or even hereditary process rather than to a tumor; however, in true bitemporal hemianopic scotomas color perception and visual acuity are spared, in contrast to that in central scotomas [19].

1.4.3 Blood Supply of the Optic Tract

The optic tract is mainly supplied by the anterior choroidal artery (branch of the internal carotid artery) and by the posterior communicating artery (see Fig. 1.6). The anterior half is supplied by both arteries, while the posterior half is supplied only by the anterior choroidal artery. The collaterals of the anterior choroidal artery are found on the temporal side of the optic tract, while on the nasal side they come from the posterior communicating artery. Within the optic tract a very rich microvascularization provides possible collateral blood circulation [21]. The superior part of the optic chiasm and the optic nerve is drained to the venous plexus that is opened to the anterior cerebral veins. The inferior part is drained by the venous plexus that empties into the basal vein [10].

1.4.4 Lesions of the Optic Tract

Homonymous visual field defects occur when the optic pathway is damaged posteriorly to the optic chiasm. Lesions in the optic tract prevent transduction of the signal from the ipsilateral temporal and contralateral nasal hemiretina, i.e., if the lesion is found in the right optic tract, the patient is blind in the left half of the visual field (Fig. 1.9) [1, 11]. This finding, known as homonymous hemianopia, is rare in the optic tract and, together with lesions of the lateral geniculate nucleus, represent only 5–11% of total cases [11, 22, 23].

1.5 Lateral Geniculate Body

The lateral geniculate body is part of the hindbrain and contains bodies of fourth neurons of the optic pathway. It is composed of six cellular layers (1–6 in

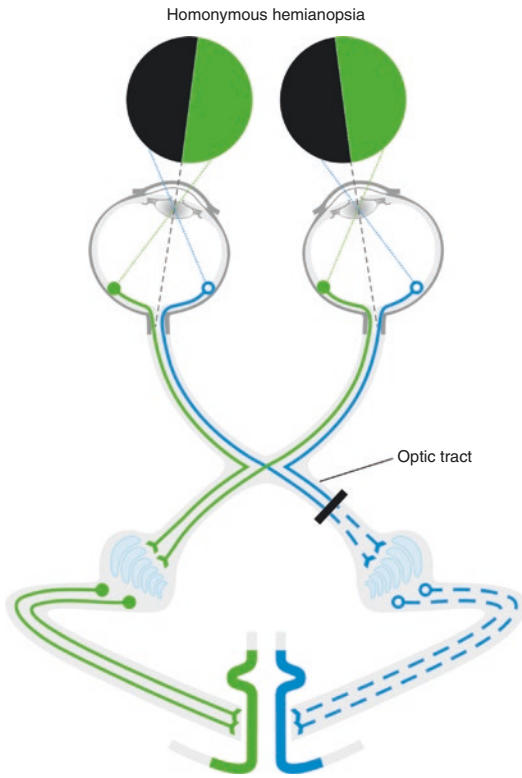

Fig. 1.9 Lesion of the visual pathway behind the chiasm produces homonymous hemianopia

ventrodorsal direction) separated by axons and dendrites. The two anterior layers are formed by bodies of large neurons and are therefore called magnocellular layers. The posterior four layers are composed of small cells and are called parvocellular layers. Large retinal ganglion cells (M-cells) send their axons to the magnocellular layers of the lateral geniculate body, whereas the small retinal ganglion cells (P-cells) send their axons to the parvocellular layers. Three layers receive the crossed axons while the other three layers receive the uncrossed axons. The bodies of neurons in layer 2, 3, and 5 receive the information from the ipsilateral temporal hemiretina, while layers 1, 4, and 6 receive information from the contralateral nasal hemiretina (Fig. 1.10).

1.5.1 Blood Supply of the Lateral Geniculate Body

The lateral geniculate body has dual bloody supply: from the anterior choroidal artery (branch of the internal carotid artery) and two or three posterior choroidal arteries that are branches of the P2 segment of the posterior cerebral artery (see Fig. 1.6) [24]. These arteries form a network on the surface of the lateral geniculate body and can provide collateral blood circulation in case of occlusion of one artery. The superficial capillary network gives off small arterioles that directly supply the lateral geniculate body [21]. Each six layers of the lateral geniculate body contain an individual capillary network connected by anastomoses.

The lateral and medial horn of the lateral geniculate body is supplied by the anterior choroidal artery, whereas the hilum by the posterior choroidal artery (branch of the posterior cerebral artery). In more than 48% of individuals the lateral geniculate body receives blood also from other branches of the posterior cerebral artery such as the hippocampal, anterior temporal, posterior temporal, and parietooccipital artery, and the middle posterior choroidal artery [25].

1.5.2 Lesions of the Lateral Geniculate Body

Lesions of the lateral geniculate nucleus are found less frequently than those of the optic tract, and most frequently are caused by infarction of the anterior or lateral choroidal arteries [24]. The lateral and medial portions of the lateral geniculate nucleus represent the superior and inferior hemifields, respectively. These portions are supplied mainly by the anterior choroidal artery; therefore, its occlusion causes a quadruple sectoranopia that is an incomplete wedge-shaped homonymous hemianopia [26, 27]. The hilum of the LATERAL GENICULATE nucleus is supplied by the lateral choroidal artery; its occlusion induces homonymous horizontal sectoranopia [11, 28, 29].

1.6 Optic Radiation

Neurons of the lateral geniculate body send their axons to the cortex. These axons form the optic radiation as a part of the posterior limb of the

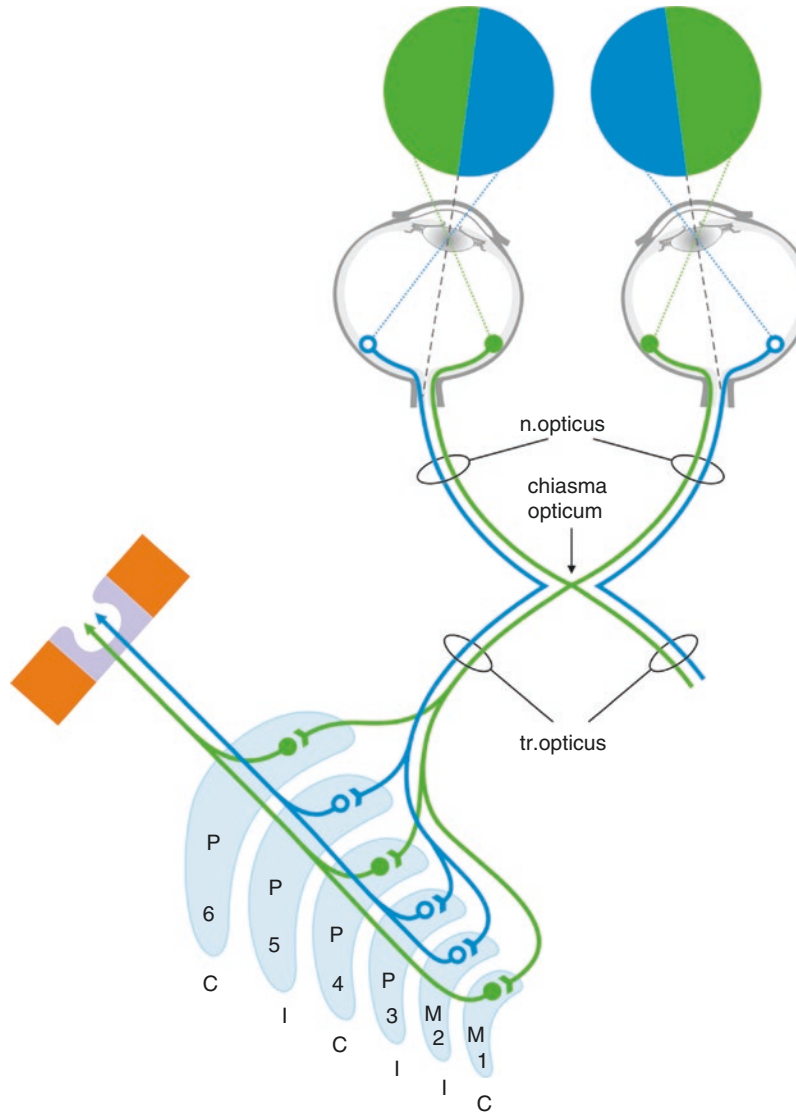

Fig. 1.10 Schematic drawing of the lateral geniculate body organization. Six cellular layers (1–6) formed by magnocellular (*M*) and parvocellular (*P*) cells connect with the ipsilateral (*I*) temporal hemiretina and contralateral (*C*) nasal hemiretina

internal capsule. The inferior fibers contain information about the superior visual field and initially pass anteriorly as the Meyer loop. The Meyer loop passes lateral to the anterior portion of the temporal horn of the lateral ventricle, then courses through the temporal lobe to terminate in the primary visual cortex below the calcarine fissure in the medial surface of the occipital lobe. The superior tracts contain information regarding the inferior visual field, travel through the parietal lobe, and terminate in the superior part of the primary visual cortex above the calcarine fissure [11, 16, 30].

1.6.1 Blood Supply of Optic Radiation

The optic radiation is supplied by three main arteries: anterior choroidal artery, middle cerebral artery, and posterior cerebral artery (see Fig. 1.6). The anterior segment of the optic radiation receives branches from the anterior choroidal artery, middle cerebral artery, thalamogeniculate arteries, and posterior and lateral choroidal arteries. The middle segment of the optic radiation is supplied by arterial branches from the middle cerebral artery, parietooccipital

artery, and anterior and middle temporal arteries. Lastly, the posterior segment of the optic radiation receives branches from the middle cerebral artery and the posterior cerebral artery. All these branches penetrate directly through the optic fibers [31].

1.6.2 Lesions of the Optic Radiation

The fibers of the optic radiation have retinotopic organization, thus even small structural lesions produce circumscribed, sharply marginated, absolute, congruent homonymous contralateral visual field defects (Fig. 1.11) [32]. The superior fibers carry information from the inferior visual field, and the inferior fibers inform about the superior visual field. Lesions in the inferior temporal components of the optic radiation result in a contralateral superior quadrantanopia or wedge-shaped defect ("pie-in-the-sky"). Damage to the superior parietal fibers of the optic radiation induces contralateral inferior quadrantanopia or lower homonymous field defect [19]. Homonymous hemianopia with macular splitting can occur in the case of large lesions of the optic radiation, often caused by infarction [22].

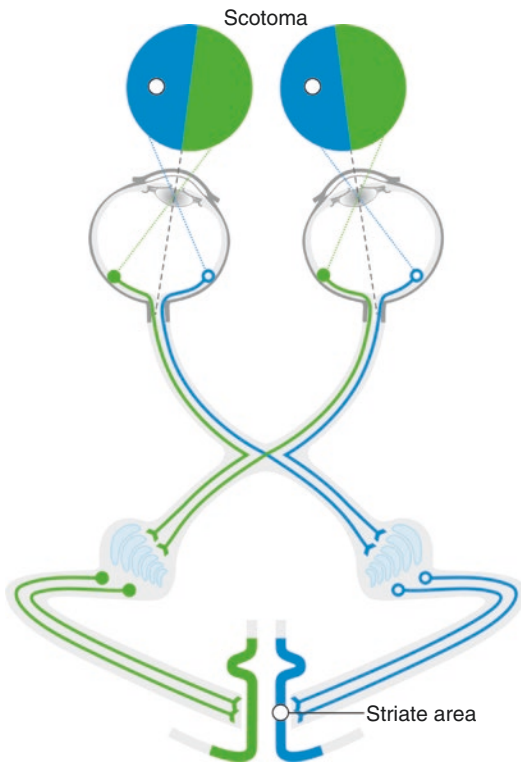

Fig. 1.11 Lesion in the optic radiation or striate area causes circumscribed, congruent, contralateral, homonymous visual field defects (*scotomas*)

1.7 The Visual Cortex

1.7.1 Primary Visual Cortex

The primary visual cortex or striate area (also known as V1 or visual area 1) is localized alongside the calcarine sulcus on the medial side of the occipital lobe. The striate area has been named according to the white stripe of myelinated axons that runs parallel to the cortical surface. The striate area contains the retinotopic map of the visual field and approximately 50% of that area represents only the central 5° of the visual field (Fig. 1.12) [32]. The primary visual cortex is formed by six layers of neurons (laminae I-VI) as part of the neocortex and forms the area 17 of Brodmann. The axons of the lateral geniculate body terminate mainly on the lamina IV where the information is transmitted to the other cortical centers. The cells of the striate area with similar orientation selectivity are organized to columns perpendicular to the surface of the cortex. The striate area can be divided into three basic systems responsible for processing particular modalities of vision. The first system is formed by three cortical columns that are specific for perception from the left and right eyes. This organization is important for binocular vision and basic for depth perception. The second system is composed of cells that receive information from identical retinal positions and have the same axes of orientation; this provides the perception of movement. The third system is organized into

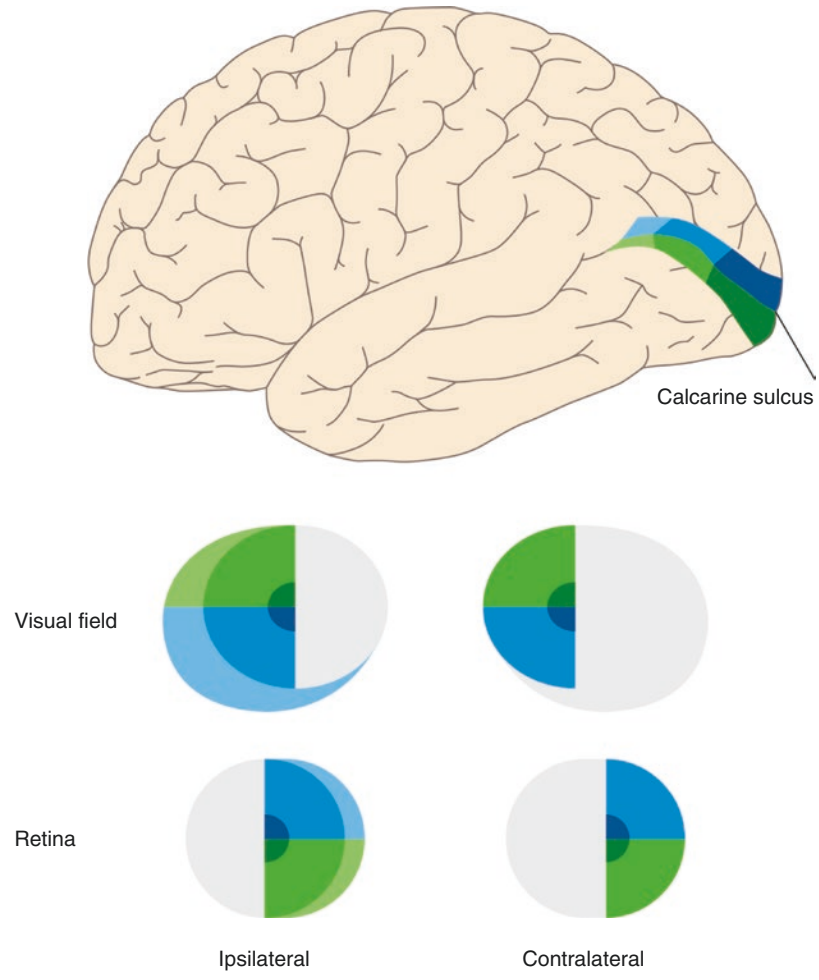

Fig. 1.12 The cortical localization of the visual pathways and visual field showing the highly magnified foveal representation in the cortex, which covers approximately half of the visual cortex

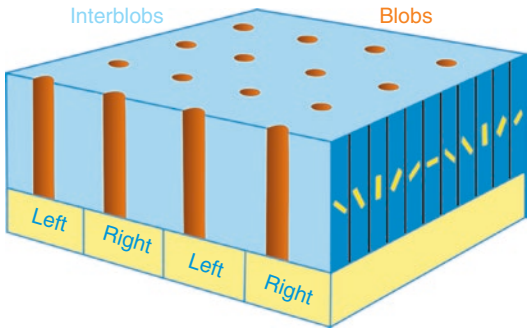

Fig. 1.13 Schematic picture of the columnar organization in the striate cortex (Adapted from Dubový and Klusáková [2], with permission)

columns that form the irregular spots on the transverse sections called "blobs". They are responsible for perception of color. Between the areas of blobs are localized neurons that are called "interblobs" specific for the perception of shape (Fig. 1.13) [1–3, 33, 34].

1.7.2 Extrastriate Visual Cortex

Information from the primary visual area is sent to the associated cortical centers called extrastriate visual areas where the final processing of vision takes place. As mentioned previously, the

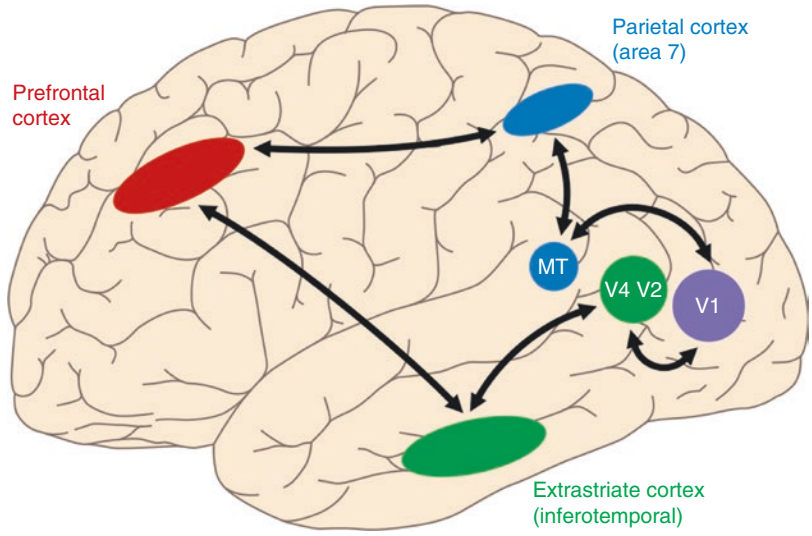

Fig. 1.14 Ventral and dorsal pathways from the striate to the extrastriate cortex. The ventral stream is important for object identification, and the dorsal stream for perception of movement and space (Adapted from Brodal [1] by permission of Oxford University Press, USA)

primary visual cortex is also known as V1; the parts of the extrastriate visual cortex are called V2–V5. They are composed of Brodmann areas 18 and 19 with several subdivisions [10].

Information from the primary visual cortex reaches the extrastriate areas via the ventral and dorsal stream (Fig. 1.14). The ventral stream passes downward from the occipital lobe to the temporal lobe and carries information about object identification including shape, contrast, and color, also called the "what" pathway. Information about spatial features and movement, called the "where" pathway, runs in the dorsal stream upward from the occipital lobe to the parietal lobe [1–3, 33].

1.7.3 Blood Supply of the Visual Cortex

The occipital lobe of the forebrain is supplied by cortical branches of the posterior cerebral artery (see Fig. 1.6). The calcarine artery and the parietooccipital artery arise from the distal part (P3) of the posterior cerebral artery. The visual cortex that is localized alongside the calcarine sulcus is mostly supplied by the calcarine artery. This artery originates directly from the posterior cerebral artery in 78% of individuals, from the parietooccipital artery in 16%, and from the posterior temporal artery in 6%. The calcarine artery in 75% of cases does not follow the calcarine sulcus. It can be localized at the floor of the calcarine fissure, on the medial surface of the occipital lobe paralleling the fissure, or upward and posterior to the calcarine sulcus. Sometimes the artery splits into inferior and superior branches that accompany the superior and inferior margin of the calcarine sulcus, respectively [35].

The calcarine artery is supplemented by the parietooccipital artery and/or the posterior temporal artery that are direct branches of the posterior cerebral artery. Furthermore, there are many possible anastomoses between the cortical branches (intratree anastomoses) of the posterior cerebral artery and between the posterior cerebral artery and middle cerebral artery [10] supplying, in particular, the macular visual cortex.

The inferior surface of the occipital lobe is drained via inferior occipital veins to the occipitobasal vein, which opens to the lateral tentorial sinus. The blood drainage of the lateral surface of the occipital lobe is provided by superficial cortical veins that open to the occipital vein. The occipital vein faces anteriorly and often opens to the superior sagittal sinus.

1.7.4 Lesions of the Primary Visual Cortex

Lesions of the occipital lobe produce almost 40% of homonymous hemianopias, and 70% of them are arterial infarctions [23]. Lesions of the occipital pole are responsible for contralateral homonymous scotomas that are extremely congruous. Lesions that are localized more anteriorly involve the peripheral vision; in particular, lesions of the most anterior edge of the striate cortex can produce monocular peripheral temporal defects, the so-called temporal crescent. The lesions that affect the area above and below the calcarine sulcus cause the inferior and superior quadrantanopias, respectively [11, 22]. Bilateral lesions of the occipital lobe simultaneously, or more usually sequentially, can induce any combination of bilateral homonymous hemianopia with or without macular sparing and various degrees of congruency [11, 19]. When the striate cortex is totally damaged, mostly from the cerebrovascular lesions, cortical blindness occurs [36].

The macular area of the visual cortex is localized in a "watershed area" on the boundary between the areas perfused by the posterior and the middle cerebral arteries (see Fig. 1.6). The visual cortex subserving midperipheral and peripheral fields is supplied only by the posterior cerebral artery. Therefore, during times of blockage of one of the arteries that supply the watershed area, such as in atherosclerosis, the ipsilateral macular cortex may be spared from ischemia by virtue of its dual supply. This may be an explanation for the phenomenon of macular sparing. On the other hand, when there is generalized hypoperfusion state (e.g. in heart failure or intraoperative hypotension), the first area of the visual cortex to be affected is that supplied by terminal branches, the macular visual cortex, resulting in a central homonymous hemianopia.

1.7.5 Lesions of the Extrastriate Cortex

Lesions of the temporal extrastriate visual cortex cause various changes in the ability to recognize visual objects. Symptoms differ according to localization of the lesion in the ventral or dorsal stream. Lesions in the ventral stream are expressed by cerebral achromatopsia when the patient reports seeing in shades of grey. This could be combined with prosopagnosia, superior quadrantanopia, or topographagnosia, when the patient is lost in familiar surroundings. The destruction of bilateral lingual and fusiform gyri by infarction of the posterior cerebral artery results in prosopagnosia, when the patient is unable to identify and recognize familiar faces. Infarction in the left posterior cerebral artery territory destroys the inferior occipitotemporal region, resulting in acquired alexia, which is expressed by loss of the ability to read in previously literate subjects with normal visual acuity [1, 11, 37].

Lesions of the dorsal stream produce Bálint syndrome, which was originally described in patients with bilateral parietal lobe lesions but also in patients with bifrontal lesions. This syndrome is a combination of optic apraxia, the inability to shift the gaze voluntarily; simultanagnosia, the inability to comprehend the totality of the picture or scene; and optic ataxia that is expressed by the impairment of visually guided grasping or reaching, despite adequate strength and coordination [11, 38, 39].

Conclusion

Organization of the visual pathway shows a precise retinotopical organization at all levels. Homonymous visual field defects arise due to the damage of the optic pathway behind the optic chiasm by various pathological processes. Knowledge of the visual pathway anatomy and its peculiarities enables good correlation with clinical symptoms of visual pathway damage and provides the background for appropriate diagnostic and therapeutic procedures.

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Pathological Physiology of the Visual Pathway

2

Petr Marsalek, Marek Hajný, and Martin Vokurka

Abstract

Homonymous hemianopia is a visual defect caused by various pathological processes of the central nervous system, particularly if located beyond the optic chiasm. In the first part of this chapter, we describe the physiological principles of cortical visual processing. In the second part, we discuss the pathological physiology and etiopathogenesis of the disorders.

Causes of homonymous defects include cerebral stroke (primarily), as well as neurodegeneration, demyelinization, hypoxia, trauma, tumors, and carbon monoxide intoxication.

Keywords

Carbon monoxide poisoning • Cerebral achromatopsia • Cerebral stroke • Hemorrhagic stroke • Homonymous hemianopia • Ischemic stroke • Pathological physiology • Pathophysiology • Visual field defect

Abbreviations/Index Entries

3D	Three-dimensional, stereoscopic
BA	Brodmann area
CNS	Central nervous system
CO	Carbon monoxide
Color vision	Codes in applied color science: R, red; G, green; B, blue; M, magenta; Y, yellow; C, cyan; W, white; K, black
Color Vision	Cone types: LW, long wavelength, also red; MW, medium wavelength, also green; SW, short wavelength, also blue
deg	(angular) degrees, (°)
FMRI	Functional (nuclear) magnetic resonance imaging
HH	Homonymous hemianopia, sometimes also called hemianopsia
LGN	Lateral geniculate nucleus
M, P	Magnocellular, parvocellular

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rad	Radians
sq deg	Square degrees, square degrees, deg^2, $(^o)^2$
sq rad	Square radians, steradians, sr, rad^2
V1, V2, V3, V4, V5	Primary (and secondary) visual areas
V5	is also denoted as MT, medio-temporal

2.1 Normal Function

2.1.1 Introduction

In the first part, we address several concepts and controversies in visual physiology. We delineate differences between early and advanced visual processing. We discuss several physiological aspects in the hierarchy of cortical visual processing and various dichotomies in visual perception, which include: the disparity of images in the left and right eye; the dichotomies between color and black-and-white vision, between magnocellular and parvocellular pathways, between "what" and "where" streams of advanced vision; and other features of central (cortical) vision. When a part of the pathway is disordered, the crossing of pathways in the central nervous system (CNS) can be advantageous. A small fraction of uncrossed fibers play a role in both spatial and stereoscopic vision. For proper fusion of both retinal images, focusing and vergence at the geometrical place called horopter are necessary (Fig. 2.1).

2.1.2 Normal Visual Field

One-dimensional angle is typically used in perimeter description. Normal binocular vision spans more than 180 deg (angular degrees) horizontally with the highest visual acuity in the fovea. The binocular visual field extends to about 135 deg vertically; its horizontal scope is 115 deg of binocular fusion and 60–70 deg of monocular flanks on both sides (Fig. 2.2). This yields approximately one half of the total visual field to binocular vision. As the occipital cortex is divided vertically into two hemispheres and horizontally by the calcarine sulcus, the visual field is divided into four quadrants. From the geometrical point of view, square sizes of these parts can be expressed more precisely in square degrees (sq deg, also deg^2) or square radians (rad^2), also called steradians (sr). For the schematic subjective visual field with the anopia in the top right quadrant see Fig. 2.3. While (one-dimensional) angles are expressed in degrees and radians, square angles are expressed in square versions of these units. The whole sphere surface spans 4π sr, which is circa $4 \times 3.14 = 12.57$ sq deg. This is 41,253 sq deg, i.e., 40,000 sq deg. The binocular field covers about one tenth of the whole sphere, 4000 sq deg. Most literature uses the horizontal angular measures as shown at the beginning of this text.

There are (subjectively unnoticed) gaps of blind spots in both eyes. The physiological blind spot corresponds to the optic nerve head. However, visual cortices are endowed by a powerful filling-in process, so that we are

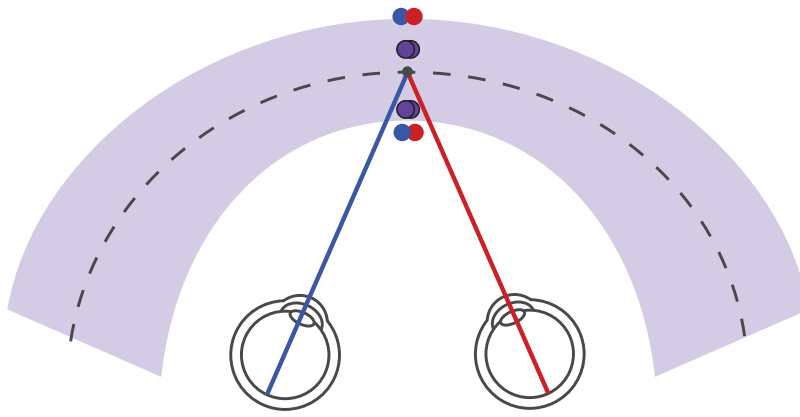

Fig. 2.1 Binocular visual field, horopter. For proper binocular fusion, proper accommodation and vergence are necessary. Circular–hyperbolic curve of sharpest binocular fusion is called horopter. Its surrounding region is a place of optimum binocular depth

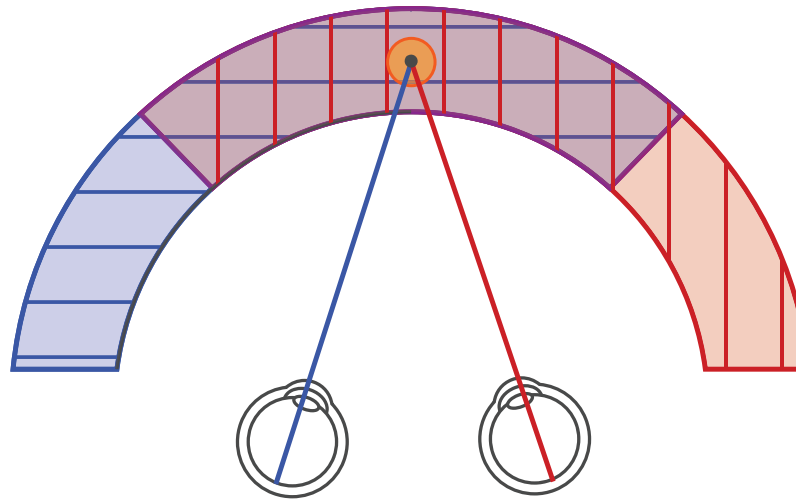

Fig. 2.2 Binocular visual field, top view. The top view of the binocular visual field is a simplification bridging the subjective aspect of the binocular field and the geometrical properties of horopter, which is related to the physical optical properties of eye and geometrical constraints

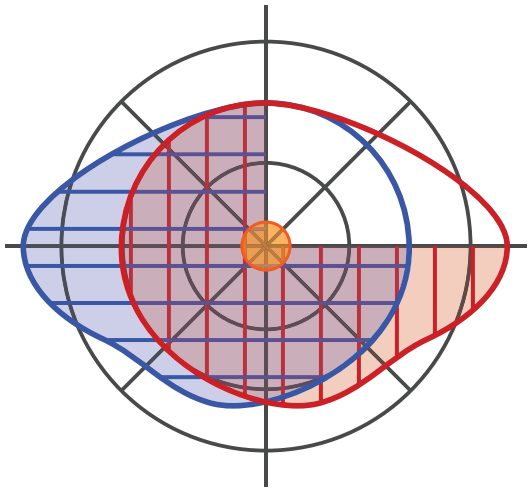

Fig. 2.3 Binocular visual field, subjective view. The binocular visual field spans 40,000 deg ^{2}. The homonymous visual defect typically affects one quadrant (here top right) while the region of best visual acuity (fovea) is spared, due to the overlap of left and right optic radiation

Table 2.1 Simplified classification of visual impairment. Left column lists four categories of this simplified classification, based either on the impaired visual acuity or on the size of the remaining visual field, which is also expressed in per cent of the normal square visual angle

Visual impairment	Visual acuity	Spatial vision	Remaining visual field (in percentage of spatial angle)
Normal vision	6/6	4000 sq deg	100%
Low vision	6/18	1000–3000 sq deg	Between 25 and 75%
Blindness	3/60–6/60	100–400 sq deg	Less than 4%
Amblyopia	N/A	300 sq deg	Circa 75%

unaware not only of the physiological blind spots, but of any smaller visual field defects due to the homonymous and other central defects including also retinal defects.

Normal vision has a wide angle. Its highest visual acuity resides in the fixation point. The extent of visual impairment is determined by the size of the visual field together with the best corrected visual acuity in the better eye (Table 2.1). The simplest classification of vision levels can be designated as normal, low vision, and practical blindness, or amblyopia. In Europe, practical blindness is defined as a visual field of less than 100 sq deg, which is 0.25% (per cent) of the normal field. In the United States, visual field is reduced to 400 sq deg, which is 1% of the normal field. The regulations in the US are more strict due to the higher percentage of practically blind subjects applying for driving licences.

As visual impairment interferes mostly with spatial navigation, including driving, reading, and face and object recognition, we attempt to abstract from the technical details how these higher level faculties arise from elementary cortical processing. We will therefore discuss the cortical hierarchy of secondary visual analyzers from this phenomenological point of view.

2.1.3 Cortical Imagery Is Crossed

In normal and pathological physiology, there have been tendencies to search for both utility and economy in a particular functional system. Such a search for efficiency and teleology raises the following questions, "Why are all the pathways in the central nervous system in man crossed? Does it bring a functional advantage?" It might be that an injury or any disorder affecting the receptor organ does not affect its neural center, given that it is on the other side of the body. This is on one hand an advantage, on the other hand, crossed pathways have longer distances for signal to travel and the crossings are particularly vulnerable.

Retinal output, which comprises one million neural fibers, is located within the cerebral cortex on the side of the head opposite to the location of the eye. The crossing is a point reflection, in a sense. The left visual hemifield projects into the right cortical hemisphere, lower visual hemifield above the calcarine sulcus and vice versa.

2.1.4 The Uncrossed Part of the Visual Pathway Serves Spatial and Stereoscopic Vision

Approximately less than half (47%, see Chap. 1, Anatomy of the Human Visual Pathway) of the central visual pathway is uncrossed. This has an obvious functional importance. Uncrossed fibers carry the information about spatial relations from the corresponding parts of the two retinas. This information is utilized in the dorsal group of secondary visual analyzers (associative visual areas). This dorsal pathway is called the "where" stream of the visual pathway, as it serves to locate, where the visual objects are and where they are moving to. The ventral, "what" stream serves object recognition (see also 2.1.7). Any visual system capable of sensing motion and space (e.g., vision of insects and flies in particular), must use and process spatial frequency information. Spatial frequency changes occur on any static surface, where high and low contrast stripes are alternating. Like slowly moving ripples on the surface of water, spatial and temporal frequencies can similarly be composed in one percept. Spatial frequency and temporal frequency are two elementary visual characteristics used by movement detectors in all visual systems, including vision in vertebrates and invertebrate animals [1, 2] and artificial vision in robots. These detectors are realized in man by the uncrossed fibers.

2.1.5 Stereo Vision: Only One of Many Consequences of Viewing with Two Eyes

For the proper fusion of two images of both eyes, coordinated eye movements and proper focusing are required. Such motor actions of eye convergence and divergence, accommodation, and adaptation involve subcortical centers. However, even when the two conditions of correct vergence and focus are met, the central image processing might misinterpret information due to occlusions, conflicts between the left and right retina, and other discrepancies in the visual scene. All these conflicts are resolved by ocular dominance, but foremost by alternating the inputs from the left and right eye at the rate of 1 per second [3]. Either the domination or the alternation results in a unified top level percept generated by higher cortical areas. The remaining unconflicting content contributes to stereo vision. This *true* stereo vision starts at near point (punctum proximum) and does not reach farther than 3 m [4]. The rest of our spatial vision is typically due to monocular modalities such as perspective, parallax, image fading, and color changes with distance. In all modalities (e.g., space, motion, color, shading, and more), visual space is multidimensional, recreated by our vision as a mosaic of facets in several dimensions. In contrast, these more general properties of vision in its multidimensionality—stereo vision—give us geometrical dimensionality in the narrow sense of the term, the three-dimensional space perception, as described by Julesz [4], Grossberg et al. [5], and others.

Therefore, the inner image of the outer world, though endowing a firm illusion of constancy and stability, is continuously and quickly recreated by our visual processes. In accord with the

phenomenological approach we adopt in this text, we can divide the visual processes into early vision (the early 150 ms of cortical processing) and advanced (high level, late) vision, which includes all cortical processing beyond this rather arbitrary time limit. Clearly, the above-mentioned alternating of inner image due to the conflicts of left and right eye images falls into the advanced vision category.

These observations have proffered different opinions of contemporary visual physiology. As the primary visual cortices (Brodmann area 17) contain a raw material from the point of view of proper binocular fusion, some authors argue that these cortices are not accessible to our conscious perception. Some of these concepts regarding the attended and unattended parts of the cortical visual processing are still subject to discussion within the visual science community [6].

Another controversial issue related to homonymous visual field defects is the existence of the "blindsight" phenomenon [7]. With the advent of functional imaging methods, the blindsight has been demonstrated reproducibly in a defined small group of patients [8]. Subjects with blindsight are capable of a restricted set of visual discriminations of orientation and motion in their blind (hemi)-field. Their cortical blindness does not bring them a conscious percept, as they deny seeing anything. Yet they are able to track fast-moving stimuli with their hand and possess visual-motor coordination in similar conditions [9]. They are unable to report these skills or use them outside of experimental conditions, given that they are not aware of them. Apparently, in blindsight, the visual information bypasses some of the pathways necessary for conscious perception and according to some authors may be driven by subcortical centers [10].

Also, there is debate as to whether or not face recognition and object recognition are the same modality, with one cortical processing site (fusiform gyrus, face fusiform area), or include more processing units and, therefore, more modalities. Wilson et al. [11] systematically map the dimensionality of the human face attributes, like concave or convex noses (see Fig. 2.4 top

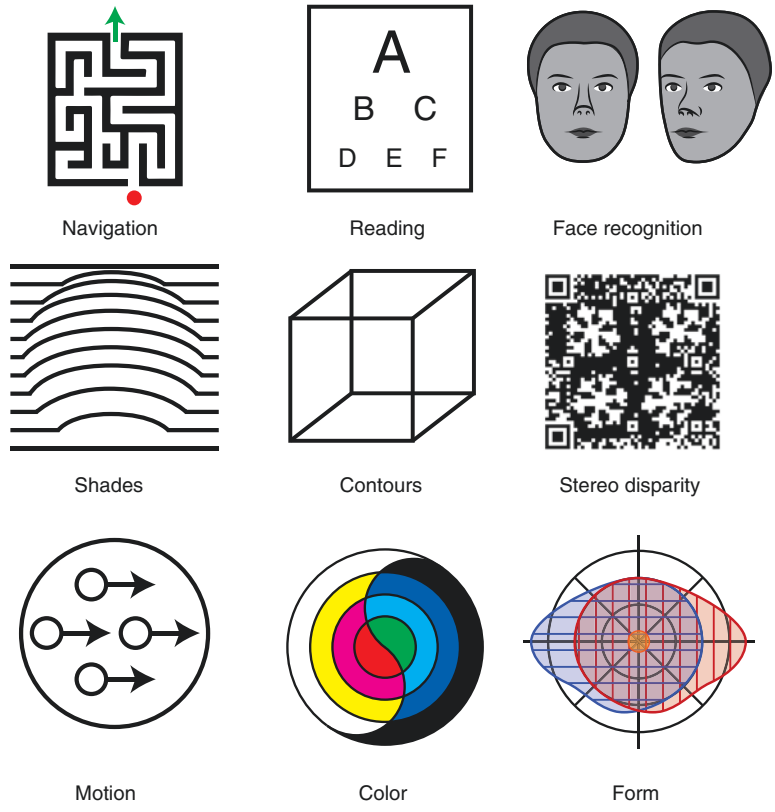

Fig. 2.4 Iconic depiction of different visual processes. Examples of visual faculties are ordered from elementary at the *bottom* to complex at the *top*. From *top left* to *bottom right* they are: spatial navigation, reading, face and object recognition, this is adapted from Wilson [11]; three-dimensional (3D) structure from shading, 3D structure from contours and perspective 3D perception from binocular disparity (Adapted from Van Essen and De Yoe [12], see also Julesz [4]; motion perception; color and luminance perception, form and location perception. The elementary visual processes are these at the bottom. The purpose of such simplification is only to remind us that many more abstract concepts are guided by visual schemes. Sometimes the visual depictions can be misleading)

right) [12], male or female face, and many other attributes. Other visual modalities from both ventral "what" and dorsal "where" streams are multidimensional.

2.1.6 Color Vision Is Three-Dimensional (Trichromatic) Under Most Photopic and Perceptual Situations

Even though only one of the two groups of photoreceptors (cones and rods) work, while the other group is either not activated (black-and-white, night, scotopic, rod vision) or saturated (color, daylight, photopic, cone vision), we are not aware of the color or black-and-white dichotomy unless shown in a specific experimental situation. The signal from the retina via the optic nerve also distinguishes these two components, regardless of the ambient light condition. The magnocellular output is characteristically fast, motion perceiving, and color-blind, while the parvocellular is colorful, slower, and static (Figs 2.5 and 2.6). Other similar dichotomies can be exemplified like black versus white contrast and other

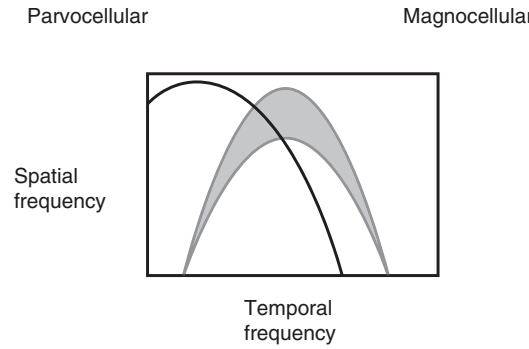

Fig. 2.5 Spatial and temporal tuning of parvocellular and magnocellular pathways. The two tuning curves show the spatial and temporal sensitivity of the parvocellular (*left curve*) and the magnocellular (*right set of curves, in gray*) pathways. *X*-axis shows temporal frequency and *Y*-axis shows spatial frequency

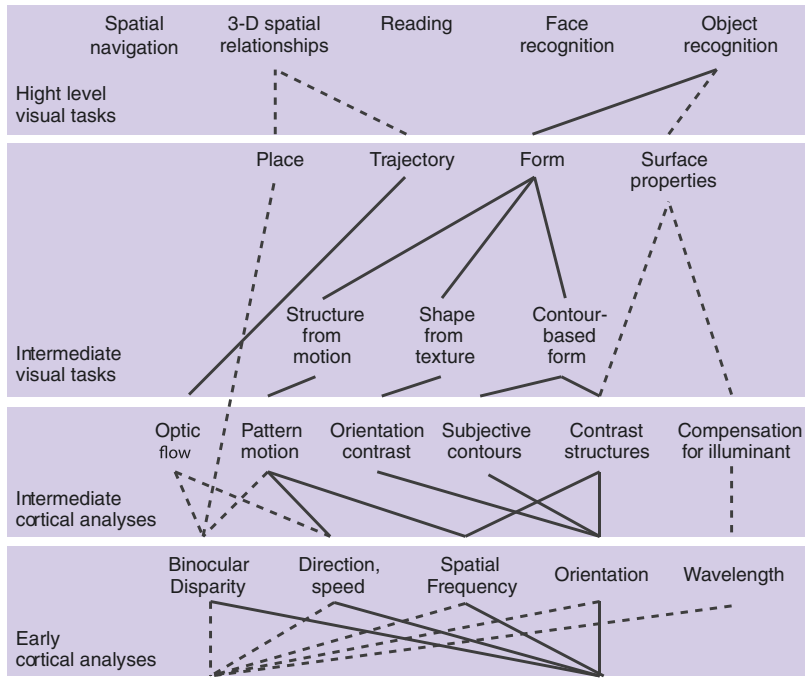

Fig. 2.6 Parallel and sequential processing in the visual cortex. This figure corresponds to Table 2.2. Figure shows relations of early vision processes (*bottom*) to late vision (and high level visual tasks, *top*). This schema is simplification of the information flow, while Table 2.2 lists the categories of the individual visual processes (From Van Essen and DeYoe [12], with permission) (Gazzaniga MS, editor. The cognitive neurosciences. Figure 24.7, page 394,© 1994 Massachusetts Institute of Technology, by permission of The MIT Press)

contrasts due to a color opponent system such as red versus green or yellow versus blue.

The sensitivity of rods and cones to different wavelengths is expressed in the notation. Color vision types of cones are LW (long wavelength, red color), MW (medium wavelength, green color), and SW (short wavelength, blue color). Under photopic conditions, rods are saturated and do not contribute to color sensation (Fig. 2.7). Genetic variations in color vision can be found in retinal mosaicism in women, who in one of their two X-chromosomes carry the deficient gene for some of the color vision anomalies. Even though this retinal mosaicism has been demonstrated by methods of molecular biology, these women stay trichromatic due to the properties of the central visual pathways [13].

It might seem superfluous to discuss color vision and other modalities with regard to homonymous visual field defects. Yet we will see in the second part of this chapter that some homonymous visual defects, in particular carbon monoxide (CO) poisoning, have distinct modalities affected in one quadrant or hemifield. Therefore, we must discuss all the modalities involved.

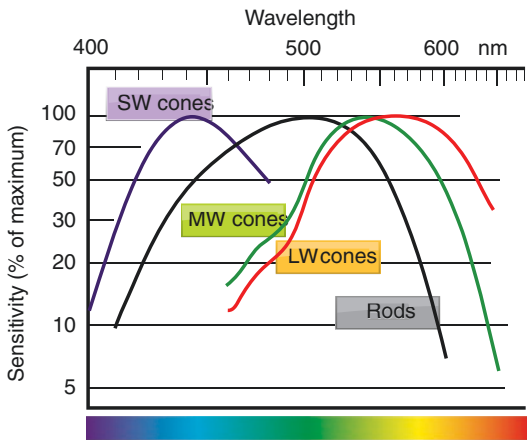

Fig. 2.7 Physiological trichromacy arises from three types of cones working in scotopic light conditions. However, color vision defects in HH are due to central defects. While color deficits like protanopia and deuteranopia arise from retinal defects, color blindness in rare types of homonymous disorders arise from the defects in central color opponent-processing. Cortical color opponent systems are illustrated in the bottom middle cell of Fig. 2.4

2.1.7 The Hierarchy of Cortical Visual Perception

Visual cortex is divided into hierarchy of many distinct anatomical and functional units. To simplify this issue, we discuss mostly functional features of visual processing. Parallelism of visual cortex enables the division of labor among secondary cortical areas. Individually processed features are called modalities in accordance with the psychophysical terminology. Most visual modalities can be interpreted as stages of geometrical processing. They are functionally interconnected. Some are processed in parallel. Feed-forward connections are complemented by feed-back. Even purely geometrical description of vision can uncover necessary existence of visual illusions. Imagine for example the Necker cube illusion. It can be demonstrated that the processing must contain (signal processing) filters, elementary geometrical operations, and hierarchy of stages in any natural or artificial visual system. Some of the neural circuits are more vulnerable and we will focus on those, which can be affected in central visual disorders.

Modalities that are involved in both the perception of motion, faces, and with (electrophysiologically) defined *best response* are localized each in corresponding secondary visual areas. Other modalities, such as stereo disparity [14], ocular dominance, color information, and those related to *constancy of perception,* are not located within one area but are processed throughout the visual association cortices. They are often in specific neocortical layers, parts of cortical columnar organization, blobs and interblobs, and regions distinguished by histological dyes [15, 16] (Table 2.2 and Fig. 2.6).

Since not all the modalities are localized, in Table 2.2 and Fig. 2.6 we review only the high level, phenomenological aspect of the visual cortical hierarchy. Figure 2.6 illustrates that in perceptual qualities of object, one modality is, or can be, recreated from the other, such as the structure from motion, shape from texture, form within contours, David Marr's two and half dimensional (2.5D) sketch from the *primal* sketch [17]. There are many other correspondences between the source and the target computational processes. The necessity of hierarchy in the vision was documented by

Table 2.2 Perceived visual scene and object consist of individual modalities

Processing levels	Modality						Anatomic structures
Visual streams	Where	(Ventral)	Infero-temporal	What	Postero-parietal	(Dorsal)	Dorsal and ventral streams
High level tasks	Visual navigation	3D spatial relationship	Car driving	Face recall	Object recall	Reading	Associative areas
Intermediate visual tasks	Place	Trajectory	Visual – Motor	2.5 D	Surface properties	Form	Associative areas
Intermediate visual tasks	Motion from shading	Structure from motion	Shape from texture	Contour based form	Shape from shading	Shape from disparity	Associative areas
Intermediate analysis	Optic flow MSTD	Pattern motion, MT	Orientation contrast, V1	Illusory contours, V1, V2, [16]	Complex shapes and patterns V2, V4	Correction for illumination V4	Brodmann areas 18, 19
Early cortical analysis	Binocular disparity MD, ID	Direction, speed, MD	Spatial frequency, MD, ID, BD	Orientation, ID, MD	Color	Unified photopic and scotopic processes	Brodmann area 17
Pathways	Magnocellular	Magnocellular	Magnocellular	Parvocellular	Parvocellular	Parvocellular	Retina, chiasm, LGN

Adapted from Van Essen and DeYoe [12] and Van Essen and Gallant [15]. From the bottom to the top are individual stages of visual processing from the retina to the highest visual cortices. The direction of information flow is also from the bottom to the top, however, multiple parallel and collateral processing is involved. The condition described as *illusory contours* is that described in Von der Heydt et al. [16]

Abbreviations: *3D* three-dimensional, *2.5 D* 3D environment of the observer projected onto the 2D planes of the retinas, allowing for some depth perception, *MD* magnocellular dominated, *ID* interblob dominated, *BD* blob dominated, *MSTD* dominated by processing in the area MST, *V1, V2, V3, V4, V5 (MT)* primary (and secondary) visual areas, V5 is also denoted as MT, *MT* medio-temporal, *LGN* lateral geniculate nucleus

the pioneering work of Marr. This work does not contain many descriptions of processes realized by neurons serving vision, because they were not so described at that time. However, the theory presented there can be successfully applied to both biological and robotic vision. It contains a clear physical, geometrical, and algebraic account on computation involved in vision. This account is definitive regarding the abstract processes of vision and successfully stands the test of time.

Despite the anatomical discontinuities in the cerebral cortex, normal visual function gives us seamless perception and subjective representation of the outer world. The creation and recreation of the outer world by powerful cortical processes gives us an illusion of constant and consistent perception with smooth transitions. This includes true optical illusions. Illusory contours demonstrated to arise in the processing of the V2 area are one of the classical examples of these cortical phenomena [16]. Discontinuities related to homonymous defects follow the division of the visual field into four quadrants.

We must be aware of many additional dichotomies of the secondary visual cortices, which originate in the division between the parvocellular versus the magnocellular pathways. They divide the mosaic of cortical modalities into two groups, called the "what" and "where" visual streams. The first is involved in object and face recognition, while the second serves object location and movement detection.

The "what" (*ventral*) stream function is the visual object recognition. It originates from the parvocellular pathway, which has slower conduction velocity than the magnocellular and transmits also color information. Relaying connections of the "what" stream can be summarized as: from the V1 to V2, to V3, to V4, then to IT (inferior temporal cortex) and to BA 7a (Brodmann area 7a, frontal eye field; some of the feed forward connections run in parallel).

The "where" (*dorsal*) stream function is location and determining the movement of the salient points within the visual field. It detects and compares angular velocity within the visual field. It originates from the magnocellular, faster pathway, transmitting information in the shades of gray. Its connections run from the V1 to V2 and then to V4, MT (medio temporal cortex, denoted also as V5) and medial superior temporal area (MST, BA 5a).

Particularly high level faculties are required for the reading of either phonetic alphabets (such as Arabic, Bengali, Cyrillic, Greek, Hebrew, Latin, Japanese Kana, Korean, and so on) or iconic (such as Chinese, denoted Kanji by Japanese, ancient hieroglyphic, and others) characters. We mention here only the simplest division of alphabets into these two categories. This is because these two faculties quite probably involve two different cortical analyzers, as it is described by functional magnetic resonance imaging. Reading disabilities— alexia and dyslexia in one of these two alphabets, or in both—may accompany homonymous disorders.

Perception of stereo disparities (between left and right eye) contributes to stereo vision, among other modalities making up spatial vision. Some of perceptual phenomena related to these modalities are out of the scope of this review and in homonymous defects remain largely intact. An important exception is the defect in the cortical processing of color, which has been described as central color blindness, also termed cerebral achromatopsia, in one hemisphere or quadrant.

Primary visual area V1 does not contribute to a conscious perception of the outer scene. This has a functional cause, as the primary visual cortex includes perceptual conflicts due to the conflicting information entering both eyes. Higher visual areas are needed to resolve these conflicts. Therefore, the conscious and attentional processing is located in higher areas and not in the primary visual cortex [6].

Most dichotomies in visual perception arise from the division of labor between the magnocellular and parvocellular pathways. Magnocellular neurons are fast and sensitive to high temporal frequency. Consequently, they are sensitive to motion and are color blind. Parvocellular pathways are slower, sensitive to higher spatial frequency, and bring more details requisite for fine recognition and color vision. A third category of koniocellular neurons have distinct anatomic locations between the two and are not numerous. The dichotomies in cortical processing can be described in both detailed anatomical structure

and also in higher level cortical processing. The propagation of visual action potentials to higher cortical areas has unique time synchronization properties. Synchrony of action potentials and local field potentials in human and other primates is related to movement, continuity, and coherence of visual objects [18]. This is documented also by both native electroencephalogram recording and event-related potentials [19]. The timing of action potentials is important. Their detailed studies bring a new understanding of the binding problem, bistable percepts, and effects of signal convergence among other phenomena [20].

To understand how visual objects and percepts are encoded into action potentials remains one of the major challenges of visual electrophysiology. Encoding can be classified as both explicit and implicit [6]. Explicit code has a straightforward relation to some stimulus qualities (modalities, see, for example, the best stimuli for simple and complex cells). In implicit code this relation is not known.

Higher cortical processing detects the location of a target within the visual field; serves object recognition, spatial navigation, and reading; and enables movement detection and tracking. Oculomotor programs and eye movement coordination are executed in subcortical centers, yet the signal that determines eye position is also present in the cortex.

2.2 Pathological Physiology and Etiology of Homonymous Visual Field Defects

2.2.1 Homonymous Defects Arise in the Optic Tract and Beyond

The second part of this chapter deals with the etiopathogenesis of homonymous disorders. Congenital homonymous hemianopia is an uncommon entity and is associated with specific features. Acquired homonymous visual field defects may arise from hypoxia, vascular problems such as hemorrhage or ischemia, trauma, and tumors. This list continues with infectious causes, including tuberculosis, which still makes its way into the population between temporary retreats. Rarer causes are atrophy or surgical removal of some visual areas due to virtually all other causes cited here. Multiple sclerosis also causes homonymous hemianopia (HH). Parkinson disease and Alzheimer disease are sometimes included. However, these two diseases are not addressed in detail, given the complex effect of these nosological units on the cerebral cortex.

Congenital occipital hemianopia is due to prenatal or perinatal posterior brain damage, including porencephaly, cerebral ischemia, occipital lobe dysplasia, congenital ganglioglioma, vascular malformations associated with Sturge-Weber syndrome (occurring with or without facial port-wine stains) or occipital arteriovenous malformations, prenatal injury to the periventricular white matter, etc. Most cases of congenital HH are due to unilateral or asymmetric cerebral lesions, but congenital optic tract syndromes or damage to the LGN can rarely occur. Congenital hemianopia is usually discovered as an incidental finding in early adulthood, with the patient having no prior knowledge of a visual field defect. Pediatric specialists recognize it often only when it is coupled with other neurological abnormalities (e.g., hemiplegia, epileptic seizures, Sturge-Weber syndrome, or complications of arteriovenous malformations, etc.). Visual field defects in congenital hemianopia are invariably absolute in density, complete, and splitting the macula. With the possible exception of incongruity in partial hemianopias, there are no known perimetric features that distinguish congenital occipital hemianopia from acquired homonymous hemianopia. However, what distinguishes an occipital hemianopia as congenital is the classic ophthalmoscopic finding called homonymous hemianopic atrophy, and the presence of a relative afferent pupillary defect, both of which are assigned to the transsynaptic retrograde degeneration of the retinogeniculate striate pathways (see also Chap. 4).

Cerebral stroke is the leading cause of homonymous visual field defects. It can be ischemic and/or hemorrhagic and can be due to different pathologies of the circulatory system. Hypoxia of

the mammalian central nervous system is not tolerated for long. Irreversible damage starts between 7 and 10 min from the onset of hypoxia. Hypoxia is better tolerated in newborns and in cooled tissue when metabolic demands are not high. The lowered temperature also occurs in cold water drowning or during surgery with extracorporal circulation. Given that gray matter possesses nucleated neurons and a corresponding transcription system, gray matter is more sensitive to hypoxia than white matter, which consists of axonal fibers, myelin, and glia.

Multiple sclerosis is caused by antibodies that attack the myelin sheath. This condition may cause homonymous disorders and is frequently recurrent. The myelin sheath is either destroyed by the direct action of the immune system or is insufficiently produced by the myelin-producing cells. Multiple sclerosis is partly reversible, as the neuronal bodies with nuclei are not affected and the myelin sheath is repaired by glial activity. Proposed causes of multiple sclerosis include both genetic and environmental factors such as infections. It is more frequent in women and is the most common autoimmune disorder of the human central nervous system.

Migraine and epilepsy are seizures that can be restricted to visual cortices and give rise to the phenomenology of homonymous defects. They manifest as both a scotoma and HH and are restricted to a given region of the visual cortex. Epileptic seizures can occur locally in the visual cortices and then spread to a confined region of cerebral cortex. This is also known as Jacksonian epilepsy.

A migraine starts as a relatively small discrete scotoma. Then it travels at slow constant speed with phosphenes, flickers, checkers, scintillations, and other similar phenomena in front of the scotoma and moves across one of the quadrants [21]. As the subjects are fully conscious of these phenomena, they can check the central origin of the scotoma by closing one eye followed by the other, which will not alter their perceptions. Some subjects can even drive a car with a migraine-related scotoma. Experiments in motor vehicle driving simulators show what visual skills are required for driving. Classical description of visual migraine hints that it is located in primary visual areas and the higher visual processing is not affected. In laboratory conditions the defects in particular modalities associated with migraine were classified [22]. From that we can conclude that driving with a visual migraine is possible, yet not advisable.

We shall treat carbon CO poisoning as a separate cause although very rare. The reason is that CO poisoning is a hypoxic insult that selectively affects different groups of neurons. Transport hypoxia in CO poisoning frequently damages the visual cortex, because visual areas are more sensitive to this type of hypoxia than other brain regions. Quite variable deficits are due to different exposition times and different CO concentrations, resulting in oxygen content differences in the blood. This hypoxia results in various central, therefore mostly homonymous, visual defects. Patients with CO poisoning may have diverse symptoms, whose explanation requires understanding the mechanisms of central visual processing. Some cases manifest a homonymous color blindness (also called cerebral achromatopsia), motion blindness (also called stroboscopic vision), or blindsight (discussed above); in short, virtually all homonymous defects can result from CO poisoning. In most cases with good residual vision, affected patients are astonished when they are shown the results of their examination, as they were not aware that they were afflicted with color blindness or other defects in the homonymous hemifield.

Most head injuries causing homonymous disorders are located in multiple sites of the cerebral cortex, and therefore do not occur as the clear cut cases of HH of other origin. The defects cross anatomic and perfusion boundaries. The cause of head injury is typically due to some form of violent trauma, where patients are usually males under the age of 30. To attempt to restore the visual function in patients with traumatic HH, no special rehabilitation or approach is used. However, more detailed diagnostics can reveal some additional defects, as both the subjective and instrumental measurements of visual defects are more difficult in comparison to other sensory and motor subsystems due to the anosognosia characteristic of visual disorders.

Tumors in general can be classified according to their invasiveness as benign or malignant, and according to their original tissue as primary and secondary, also called metastases. If affecting the postchiasmal visual pathway, they can cause HVFD. Expanding brain tumors cause intracranial hypertension, which leads to the corresponding symptoms: headache, nausea, vomiting, and other symptoms from vegetative, circulatory, and respiratory centers; squinting, blurred vision, and papilledema. Progression of intracranial hypertension leads to the loss of consciousness and coma and can cause death by suppression of these vital centers. Based on diagnosis, treatment options include conservative methods like radiation and chemotherapy, stereotactic surgery, or gamma radiation surgery. These choices influence the prognosis and resulting functional defects of the affected part of the cortex. Intraoperative stimulation is used to functionally map the borders between the Brodmann areas and subregions. While areas associated with speech and language must be spared and locations in hemispheres dominant for language are treated differently than the nondominant, visual areas are not considered exclusive in this regard. Therefore, brain tumors causing homonymous disorders can be indicated for surgical extirpation based on the pathological diagnosis. While these tumors exhibit variable symptoms, their surgical removal leads to a complete loss of function.

Homonymous disorders are not associated with the Alzheimer disease in general. Current theories on the pathogenesis of Alzheimer disease include actions of more than ten genes, accumulation of tau protein, amyloid protein, and decrease of nonspecific cholinergic activation of cerebral cortex. Alzheimer disease is a type of dementia and manifests as cognitive and memory deficit. Dementias in general include more etiopathogenetical nosological categories. In dementias, higher cognitive functions, as language and orientation are affected, but visual processing is not specifically affected. In general, patients with dementia recognize visual objects to the extent permitted by their declining cognition. Therefore higher visual functions, but not these related to perimeter or contrast sensitivity, are affected. Contrast sensitivity declines with the order of 10% when compared with the age matched group [23].

Conclusion

Clearly, cortical defects as a result of HH, hemifield scotomas, hemifield color blindness, other homonymous defects, and blindsight can manifest in many different visual disabilities. Typically, patients are not aware of the defects, nor the extent and exact quality of the defects, even though they realize that something is wrong. Less noticed defects are in the nondominant (typically, the right) hemisphere. Specifically, in the parietal lobe, where the outer body scheme is represented, defects are manifested as hemineglect, as a specific instance of an anosognosia. Consequently, patients are not aware of the damage. Most HH patients are indifferent to their symptoms.

Even though the defect persists after a stroke (which is the most frequent cause of HH), patients may report subjective improvement. After rehabilitation and spontaneous restitution, they feel better and some are able to resume their daily tasks and routine [24]. Rehabilitation can be demonstrated in some visual tasks, but not as restoring vision in the deficient region of the visual field. Despite having lost the ability to read, patients can regain their reading abilities by training. They accomplish this by targeting the text out of their scotoma, while bringing more input to the intact parts of the brain. They learn to use prismatic glasses and other compensatory aids for the same purpose of subjectively widening the visual field. The patients subjectively note improvements, even though visual field widening cannot be demonstrated objectively [24, 25]. Therefore, the prognosis of HH is modest, yet positive.

Further, when axons from the retina cannot supply their signal to the major target, the lateral geniculate nucleus or LGN, the ganglion cells, the LGN cells, and the pyramidal cells of the fourth layer of the visual cortex undergo an involution and reorganization within the possible plasticity of the adult cortex.

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Ischemic Stroke and Homonymous Visual Field Defects

3

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Abstract

Cerebrovascular diseases are major causes of morbidity and mortality in developed and developing countries. The major burden of cerebrovascular diseases is due to long-term disability and economy losses. In this chapter, we describe basic epidemiology, etiology, management, treatment (intravenous thrombolysis and mechanical thrombectomy), and secondary prevention of ischemic stroke. Special emphasis is put on ischemic strokes in the territory of posterior cerebral artery, which represent 5–10% of all ischemic strokes. Over 90% of the patients have visual field defects. The most frequent type of visual field defect is represented by homonymous hemianopsia occurring in about three-quarters of the patients with occlusions of posterior cerebral artery.

Keywords

Ischemic stroke • Posterior cerebral artery • Intravenous thrombolysis • Mechanical thrombectomy

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3.1 Introduction

Stroke represents a major cause of disability and is the second leading cause of death worldwide (after coronary artery disease), with an incidence of about 17 million per year. It affects the elderly and the young (in 2010, 31% of strokes affected adults under 65; more than 83,000 children and youths under 20 have had strokes). Improvements in primary prevention and lifestyle changes have led to a decreased incidence of age-adjusted stroke. Nevertheless, the overall number of strokes has been increasing and is expected to accelerate over the coming decades because of the aging population. It is predicted that stroke will account for 6.2% of the total burden of illness in developed countries by 2020 [1, 2].

3.2 Etiology of Ischemic Stroke

Ischemic strokes represent 85% of all strokes, 15% are hemorrhages. Ischemic strokes can be either a cerebral infarction or a transient ischemic attack (TIA).

Cerebral ischemia represents a consequence of arterial or arteriolar occlusion leading to blood flow reduction. TIA is defined as a transient (< 24 h) episode of focal neurologic dysfunction caused by a cerebral, retinal, or spinal cord ischemia without infarction (the majority of TIA last only few minutes). Symptoms are similar to those of cerebral infarction; the only difference is the duration of symptoms and negative MRI excluding acute ischemic changes. Possible ischemic stroke mechanisms include atherothrombotic (30%), lacunar (20%), or cardioembolic origin (30%); of other known etiology, e.g., arterial dissection, vasculitis, hemodynamic infarctions, thrombophilia, cortical vein, or dural sinus thrombosis (5–10%); and 5–10% are cryptogenic (strokes of unknown cause) [2, 3].

3.3 Pathophysiology of Ischemic Stroke

Acute occlusion of cerebral artery or arteriole leads to an immediate decrease in arterial blood flow in the particular vessel territory. Large vessel occlusions are associated with more severe neurologic deficits than occlusions of more distal and smaller arteries. Immediately after the acute occlusion, cerebrovascular and systemic compensatory mechanisms are activated: acute stress reaction, blood pressure increase, and recruitment of collateral circulation in order to maintain sufficient perfusion. If the blood flow is above 20 ml/100 g per min (40% of a normal flow), cerebrovascular autoregulatory mechanisms lead to increased oxygen extraction. Below this level, the neurotransmission will cease, and neurologic symptoms occur. Nerve cells are able to survive without oxygen for a few minutes, but if sufficient blood flow is not restored they die at an average of 1.9 million nerve cells per minute. Processes of ischemic and apoptotic changes are dynamic and occur within the next few hours and days. If the vessel is not opened and brain perfusion restored, failure of these compensatory mechanisms and critical decrease in arterial perfusion will lead to severe hypoxia progressing into ischemia, neuronal death, and infarct evolving and growth [4, 5].

3.4 Management of Acute Ischemic Stroke

Patients with suspected acute stroke must be transported to hospital with the highest priority and urgently need to be evaluated by a stroke neurologist or experienced physician. Brain computed tomography (CT) or magnetic resonance imaging (MRI) with angiography must be performed immediately. The urgent priority in the

treatment of acute ischemic stroke is reopening the occluded artery because early recanalization improves short-term and long-term outcomes. To date, intravenous thrombolysis using recombinant tissue plasminogen activator and endovascular treatment (mechanical thrombectomy) are recommended as proven treatment strategies.

3.4.1 Reperfusion Strategies

Intravenous Thrombolysis in Acute Ischemic Stroke If a diagnosis of ischemic stroke is confirmed based on neuroimaging and no contraindications are found, thrombolysis must be initiated without any time delay. Additional diagnostic procedures, which do not influence the decision to treat, may be performed after the initiation of thrombolysis (e.g., treatment may be initiated even before the lab test reports are complete, if there are no specific disorders based on the patient's personal history).

The current recommended strategy is an intravenous infusion of tPA (0.9 mg/kg over 1 h, with 10% of a total dose given as an initial bolus; maximum dose is 90 mg regardless of patient weight). The benefit of intravenous thrombolysis is proven within 4.5 h after stroke onset. Even within the 4.5-h time window, the earlier the patients receive the treatment, the better: e.g., if the treatment is initiated within the first hour after the symptom onset, then a full recovery after 3 months might be expected; of the patients treated within 90 min, every third patient can expect a good clinical outcome; and of the patients treated within 3 h, every seventh can expect a good clinical outcome. In comparison, of the patients treated within 3–4.5 h, there is only one fully recovered patient out of 14 patients [6]. To conclude, if there is no contraindication, intravenous thrombolysis with tPA must be given as soon as possible.

Endovascular Treatment in Acute Cerebral Artery Occlusion Complete recanalization of occluded artery is achieved only in 20–30% of cases treated with intravenous thrombolysis. Consequently, about half of the patients who are treated with intravenous thrombolysis will still have unfavorable outcomes. One of the most important predictors of poor outcome is the lack of recanalization.

Modern mechanical thrombectomy devices (e.g., stent-retrievers) can recanalize occluded artery quite quickly (Fig. 3.1). This therapeutical approach can be used in combination with intravenous thrombolysis (e.g., "bridging concept" – intravenous thrombolysis should not delay the endovascular treatment initiation) or alone in specific situations, where thrombolysis is contraindicated. These situations include, e.g., recent surgery, use of anticoagulants, or initiation of stroke treatment behind the time window for intravenous thrombolysis (after 4.5 h). It has been proven that endovascular treatment is safe and significantly reduces morbidity and mortality. Positive endovascular trials published in 2015 have resulted in indisputable evidence of the clinical effectiveness of mechanical recanalization in acute occlusion in anterior cerebral circulation (internal carotid artery/middle cerebral artery). The number needed to treat to result in one patient with a good functional outcome is staggeringly low – only 3–7 patients, and thus mechanical thrombectomy represents one of the most effective treatment strategies in medicine [7–14].

The current recommendations for endovascular treatment according to European Consensus [15] and American Heart and Stroke Associations (AHA/ASA) [16] are the following:

1. Age $\geq$ 18 years (in some specific situations it is possible to intervene even in younger patients).
2. Time window up to 6 h from symptom onset in patients with salvageable brain tissue according to brain imaging.

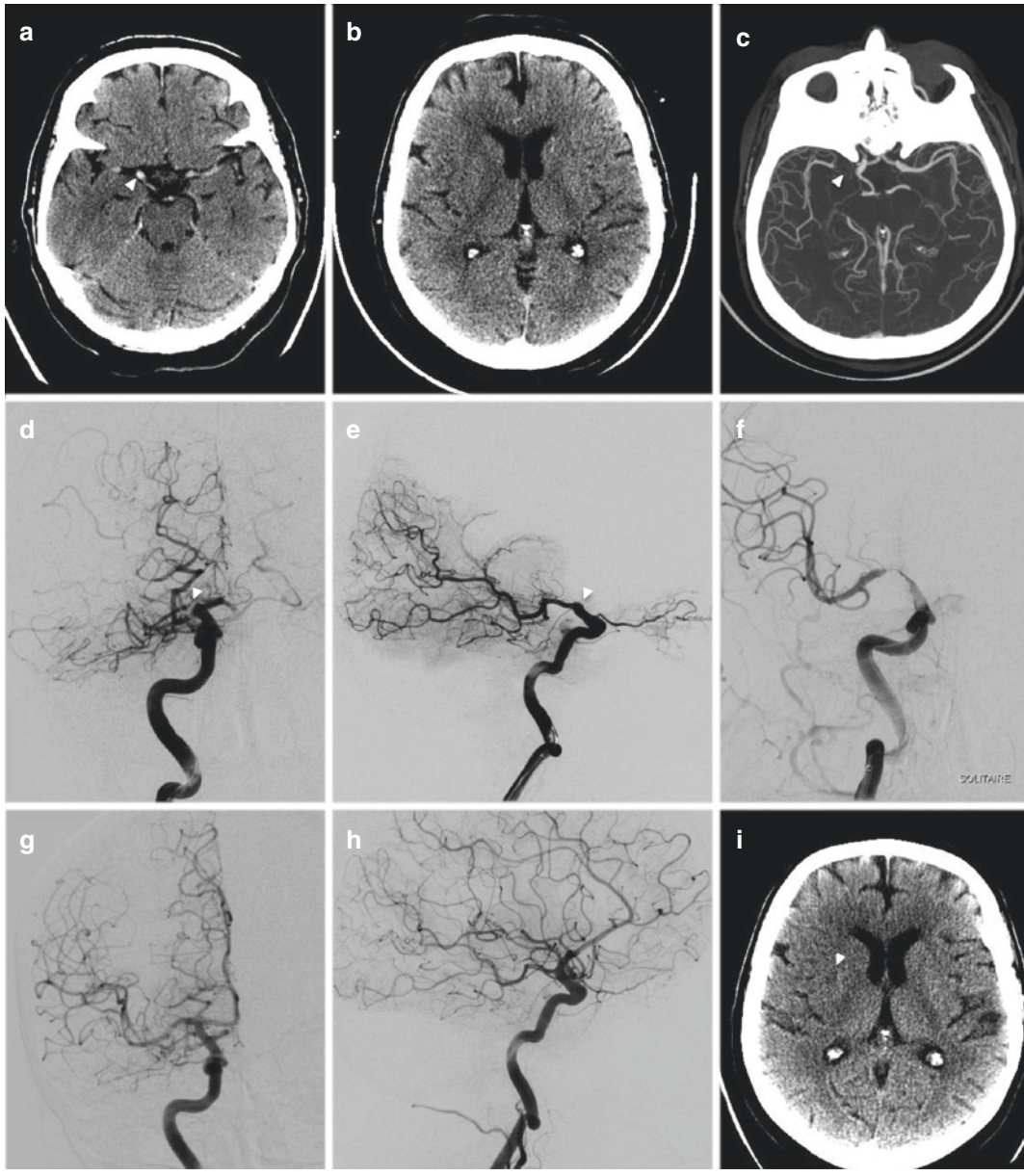


Fig. 3.1 Mechanical thrombectomy of acute occlusion of right middle cerebral artery using stent-retrievers. A 62-year-old woman presented with left-sided hemiparesis, central facial palsy, and aphasia (National Institutes of Health Stroke Scale 14). Admission noncontrast computed tomography (CT) scan (**a**) showed a dense middle cerebral artery sign (*arrow head*); there was no evidence of early ischemic changes evaluated by the Alberta Stroke Program Early CT Score (**b**). CT angiography confirmed acute occlusion of the right terminal internal and proximal middle cerebral artery (**c**). The patient received intravenous thrombolysis and underwent mechanical thrombectomy (**d**–**h**). A 24-h follow-up noncontrast CT (**i**) showed only a hypodensity within the right lentiform nucleus (*arrow head*). (**d**, **e**) Anteroposterior and lateral angiogram show no flow in the middle cerebral artery territory (*arrow heads show clot localization*); (**f**) immediate flow restoration after the stent-retriever placement; (**g**, **h**) complete recanalization after the stent retrieval

3. Neurological deficit evaluated by National Institutes of Health Stroke Scale (NIHSS) ≥ 6.
4. Early ischemic changes of brain parenchyma evaluated by the Alberta Stroke Program early CT score (ASPECTS) ≥ 6 [17].
5. Internal carotid artery and/or M1 segment of middle cerebral artery occlusion(s) detected on CT angiography/MR angiography. (Benefits of endovascular treatment for occlusions in M2 and M3 segments of the middle cerebral artery, anterior cerebral artery, vertebral artery, basilar artery, or posterior cerebral artery are uncertain, but the use of endovascular therapy with stent retrievers may be reasonable for carefully selected patients.)

3.5 Secondary Stroke Prevention

The aim of secondary prevention is to reduce the risk of early stroke and late stroke recurrence by including antiplatelet therapy or anticoagulation, statin use, and blood pressure control and periodic monitoring. Other modifiable risk factors, such as diabetes mellitus, coronary artery disease, alcohol consumption, smoking, obesity, and sleep apnea must be reduced as well. In clinical practice, unless anticoagulants are indicated, patients with acute ischemic stroke are treated with antiplatelets. The most commonly used antiplatelet therapy is aspirin or clopidogrel. If the cardioembolic origin of stroke is proven, then antiplatelets are replaced with vitamin K antagonist (warfarin) or new oral anticoagulants (NOAC)—dabigatran, rivaroxaban, and apixaban. In patients using warfarin, a target INR of 2.5 is recommended (range 2.0–3.0). Treatment with NOACs is associated with a significantly lower risk of intracranial bleeding. The selection of the most suitable anticoagulant should be individualized with consideration for the risk factors, patient's preference, cost, interactions, etc. [18–20].

3.6 Stroke in the Territory of the Posterior Cerebral Artery

The posterior cerebral artery (PCA) provides blood supply to the occipital lobe, the inferior part of the temporal lobe, and various deep structures, including the thalamus and the posterior limb of the internal capsule. Transferred to the visual pathway, it provides blood supply to the visual cortex, optic radiation, and in part to the lateral geniculate body.

Clinical manifestation of PCA ischemic strokes may be diverse, depending on the affected portion of the PCA territory. Patients may suffer from visual field defects, motor and sensory deficits, and neuropsychiatric disturbances. Visual field defects occur in over 90% of patients with cortical PCA strokes (Figs. 3.2 and 3.3) [21–23]. The most frequent type of a visual field defect is homonymous hemianopia affecting up to 75% of patients with PCA occlusions [23]. Pattern and severity of visual field defects may vary according to the lesion location and its extension [24]. Patients may have a macular sparing, isolated central hemianopia, or the visual field defects may be limited to quadrantanopia only [25–27]. More frequent *superior quadrantanopia* will be caused by lesions involving the lower bank of the striate cortex or inferior optic radiation. *Inferior quadrantanopia* is due to lesions in the upper calcarine bank or involvement of the upper optic radiation in the parietal lobe.

Patients with PCA strokes may report problems such as grayness, spots, voids, and focusing difficulties [28]. Elderly with PCA strokes may also complain of dizziness [29]. In addition,

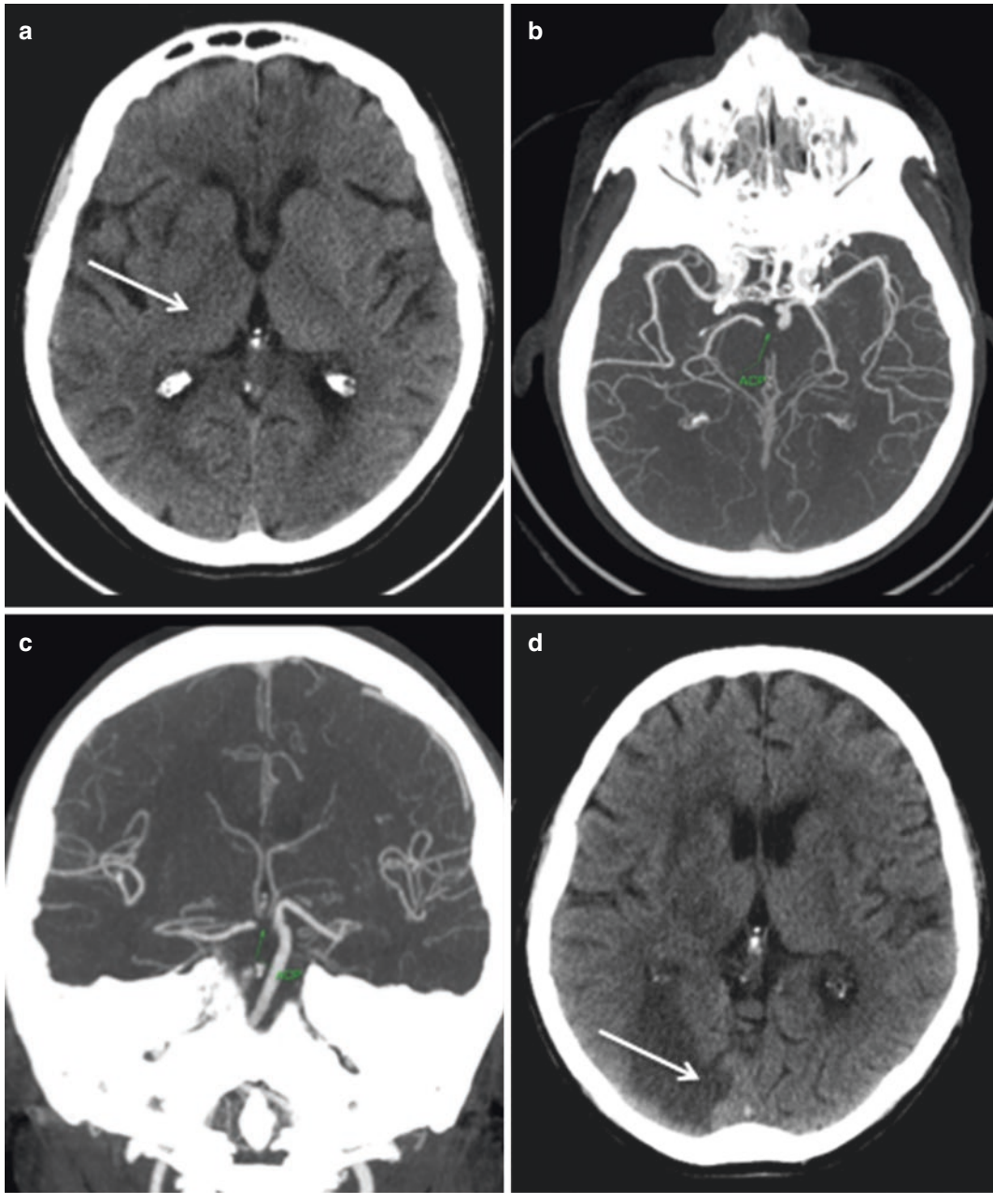


Fig. 3.2 Ischemic stroke of the right posterior cerebral artery. (**a**) Admission noncontrast computed tomography (CT), very discrete early ischemic changes in the right thalamus (slightly hypodense area in the deep structures) (*white arrow*). (**b**, **c**) Axial and coronal CT angiography scans of intracranial arteries showing an occlusion of the right proximal segment of the posterior cerebral artery (PCA) (*green arrow*), clinically causing the left homonymous hemianopsia. (**d**) Control CT (after 24 h) demonstrating a demarcation of infarcted area in the right PCA territory

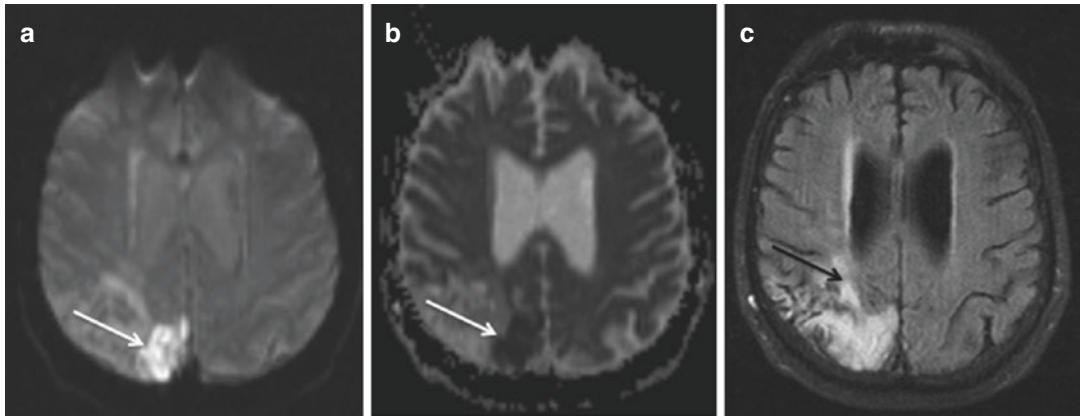


Fig. 3.3 Magnetic resonance imaging (MRI) of acute ischemic stroke in right posterior cerebral artery. (**a**) MRI diffusion weighted imaging (DWI) demonstrating a restriction of diffusion in the right occipital lobe (hypersignal area) (*white arrow*), corresponding with **(b)** abnormally low value on apparent diffusion coefficient (ADC) (hyposignal area) (*white arrow*) representing acute ischemic stroke. (**c**) Hyperintensity on T2 fluid-attenuated inversion recovery (FLAIR) in the same area as changes on DWI and ADC maps correlates with acute ischemic stroke in the right posterior cerebral artery territory (non-correlating hyperintense area on T2 FLAIR represents old infarction, *black arrow*)

various types of cognitive abnormalities have been observed in PCA strokes; in a study with pure cortical PCA strokes, memory impairment and aphasia affected up to 20% of patients [22].

Ischemic strokes in the territory of the *posterior choroidal artery (PChA)* arising from the PCA are rare and account for less than 10% of thalamic infarcts [30]. The two major clinical features are visual field defects and hemisensory loss, and, to a lesser extent, neuropsychological dysfunction (aphasia, memory disturbances) [31]. Additionally, spontaneous nystagmus or impaired fast-phase optokinetic response to the opposite side may be present due to involvement of the smooth pursuit pathways in the lateral geniculate body [32].

Characteristic visual field defects of the lateral branch of the PChA occlusion have been described as homonymous horizontal sectoranopia or wedge-shaped homonymous hemianopia. These unusual visual field defects are due to ischemia of the lateral geniculate body, which receives dual blood supply from the lateral PChA of PCA and anterior choroid artery of the internal carotid artery (Figs. 3.4 and 3.5).

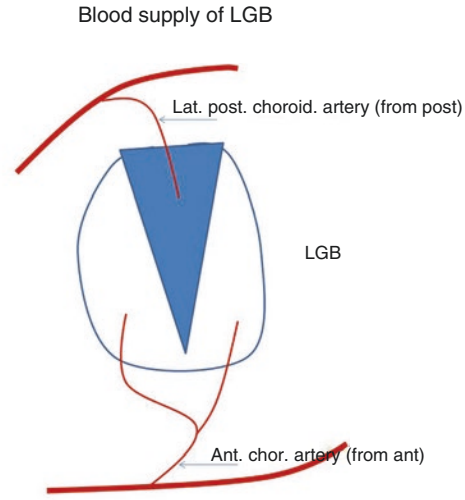
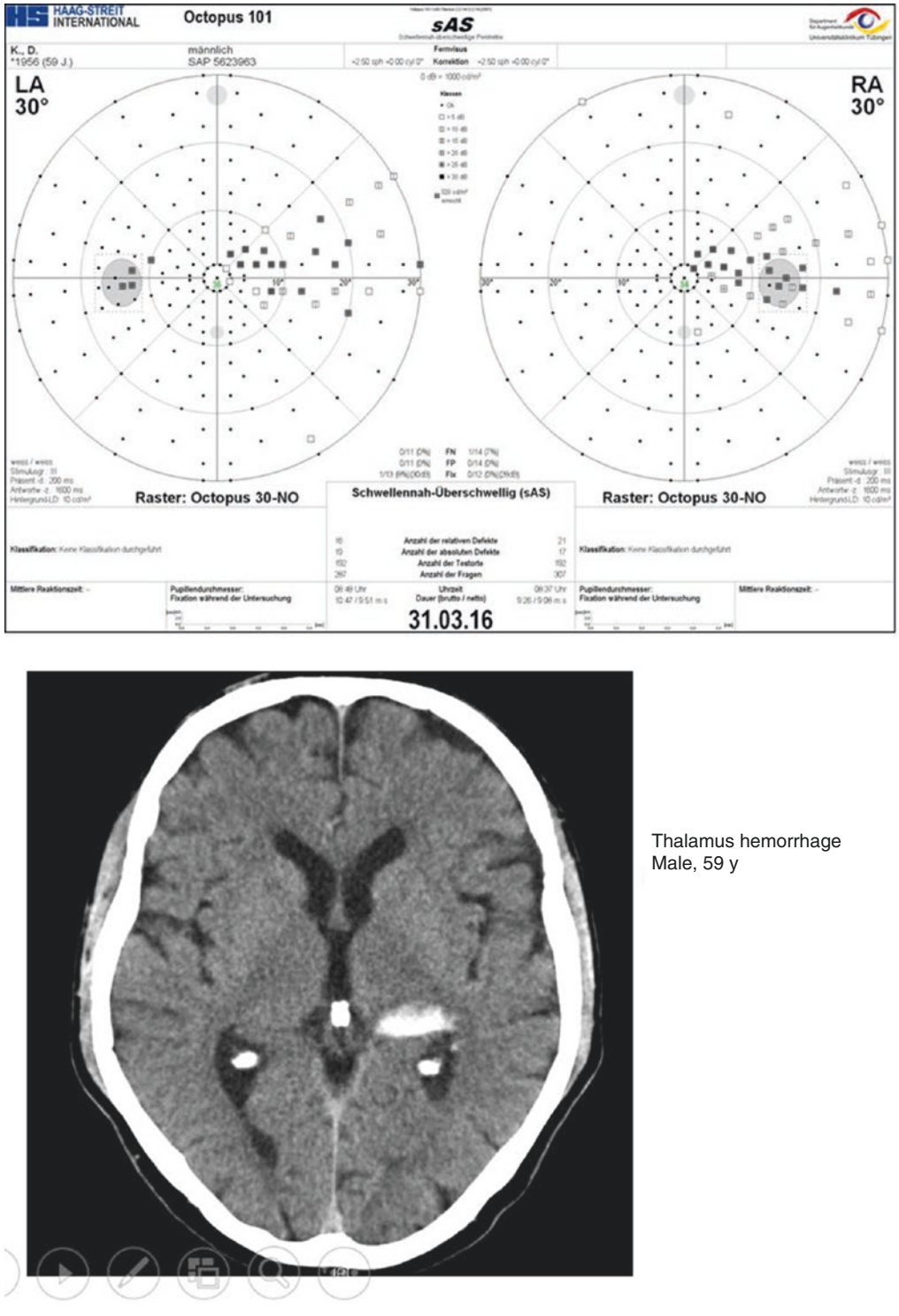


Fig. 3.4 Schematic drawing of the blood supply to the lateral geniculate body. Lateral posterior choroidal artery arises from the posterior cerebral artery, whereas the anterior choroidal artery is a branch of the internal carotid artery or the middle cerebral artery. This dual blood supply explains the specific wedge-shaped homonymous visual field defects that develop due to ischemia of the lateral geniculate body (Courtesy of Prof. Helmut Wilhelm, Center for Ophthalmology, University Hospital, Tübingen, Germany)



Thalamus hemorrhage
Male, 59 y

Fig. 3.5 Left thalamus hemorrhage in a 59-year-old male patient causing a right wedge-shaped homonymous visual field defect (sectoranopia) (Courtesy of Prof. Helmut Wilhelm, Center for Ophthalmology, University Hospital, Tübingen, Germany)

3.7 Stroke in the Territory of the Middle Cerebral Artery

The middle cerebral artery (MCA) is one of the three major paired arteries that supply blood to the brain. The MCA arises from the internal carotid and continues into the lateral sulcus where it then branches and projects to many parts of the lateral cerebral cortex. It also supplies blood to the anterior temporal lobes and the insular cortices. In the visual pathway it provides blood supply to the optic tract, in part to the lateral geniculate body and probably also to the Meyer loop of the optic radiation.

Clinical manifestations of stroke in the territory of the MCA depend on the clot localization and related extent of the ischemic lesion; however, the clinical picture is usually dominated by symptoms other than ophthalmological. Proximal occlusions of the MCA (also including intracranial internal carotid artery occlusions) are associated with more severe neurological deficits and worse functional outcome if the vessel is not recanalized. In general, infarction in the whole MCA territory has very poor prognosis, and only a limited number of patients reach functional independence in comparison with patients with M2/M3 territory infarctions or lacunar strokes [33, 34].

Proximal occlusions of the MCA are typically manifested as complete MCA syndrome: visual field deficits (contralateral homonymous hemianopia); contralateral motor deficit (palsy); central facial and/or tongue palsy; hemisensory deficits (hemihypesthesia or hemianesthesia); head and eye deviation to the side of occlusion; speech difficulties or dysarthria (motor speech disorder or slurred speech); and/or aphasia (impairment of language production and comprehension if the speech-dominant hemisphere is affected). Ischemia in speech nondominant hemisphere typically leads to the neglect syndrome.

Distal occlusions of the middle cerebral artery (M2/M3) usually manifest with less severe neurological deficits (mild brachiofacial paresis, aphasia, and/or cognitive disturbances). The particular symptoms listed above may occur, depending on the affected distal MCA territory. Occlusions of the inferior division of M2 MCA segment may also lead to visual fields defects (superior homonymous quadrantanopia or homonymous hemianopia on contralateral side) [35].

Specific homonymous visual field defects arise in stroke of the *anterior choroidal artery (AChA)*, which branches from the internal carotid artery or the middle cerebral artery and provides partly blood supply to the lateral geniculate nucleus. Typical is a contralateral homonymous wedge-shaped defect in the upper and lower quadrant of the visual field with sparing of the horizontal sector, which is supplied by the lateral posterior choroidal artery (branch of the posterior cerebral artery) as described above. Clinically dominant symptoms in AChA strokes are motor and/or hemisensory deficits due to the involvement of motor pyramidal tract and sensory thalamic nuclei [36].

Conclusion

Stroke is a devastating disease worldwide and a leading cause of homonymous visual field defects if the PCA is affected. Evaluation of visual field defects is a part of standardized neurology examination in acute stroke (a component of NIHSS). Homonymous hemianopia, due to an acute occlusion of PCA, represents indication to intravenous thrombolysis within a 4.5-h time window from symptom onset. The benefits of endovascular treatment in PCA territory remain uncertain. If a visual field defect corresponding to homonymous hemianopia is diagnosed by an ophthalmologist, even outside the time window for acute stroke treatment, the patient still needs to be examined by a neurologist. It is mandatory to do brain and vascular imaging. If an ischemic stroke in PCA territory is present, subsequent search for etiology must follow (e.g., 24-h Holter ECG monitoring, echocardiography, blood tests) and appropriate secondary prevention must be initiated.

Acute stroke care globally still has an insufficient logistic management; times from onset to calling the ambulance, from onset to hospital arrival, and from onset to treatment initiation are too long. Time is the most important factor in brain tissue fate (the “time is

brain" concept). Pre-hospital and in-hospital management, increased public awareness by campaigns, proper and periodic education of ambulance teams, and the desire for improving the in-hospital management should lead to more patients being treated early and successfully, with higher rates of functional recovery and independence after stroke.

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4 Neuro-Ophthalmological Examination in Homonymous Visual Field Defects

Eleni Papageorgiou and Evangeli Tsironi-Malizou

Abstract

Homonymous hemianopia is the hallmark of postchiasmal brain damage and a sign of serious underlying neurological disease. Patients are often unaware of their visual deficit and may present with vague symptoms. However, there are various neuro-ophthalmological signs, which will alert the clinician to the possibility of a homonymous visual field defect. First, precise history taking and questions about quality of life are of outmost importance in order to proceed to the appropriate diagnostic investigations. Although perimetry is the mainstay for diagnosis in patients with suspected homonymous visual field defects, there are numerous additional tests, which provide useful information regarding the etiology, extent, localization, and functional significance of the underlying brain lesion. Even in the era of modern neuroimaging, the clinician should assess visual acuity, color vision, ocular motility, reading ability, pupil responses, neuropsychological status, and also perform funduscopy and optical coherence tomography, in order to make an individualized assessment and choose the most appropriate therapeutic and rehabilitation interventions.

Keywords

Homonymous hemianopia • Stroke • Postchiasmal • Color desaturation • Hemifield slide • Hemianopic dyslexia • Confrontation perimetry • Bow-tie atrophy • Congenital hemianopia

4.1 Introduction

Homonymous visual field defects are a common manifestation after injury to the postchiasmatic visual pathway, as they affect approximately 30% of stroke patients [1]. If additional neurological symptoms, such as hemiplegia or hemianesthesia,

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are present, further investigation by means of modern neuroimaging usually determines the cause of vision loss. However, homonymous hemianopia may be also encountered as an isolated finding in a patient who visits the ophthalmologist due to visual disturbances, which do not always clearly point towards the underlying cerebral lesion. Hence, a thorough clinical examination will help the clinician to promptly identify a homonymous visual field defect and proceed to the necessary diagnostic investigations.

4.2 Taking a History

Taking a precise history is an essential part of the neuro-ophthalmological examination and will help the clinician differentiate the cause of vision loss. Some patients notice the visual field loss immediately, but others are not aware of an incipient hemianopia and often complain about monocular visual loss or bilateral "blurry" vision [2]. Hence the clinician should try to determine if the vision loss was monocular or binocular. It is not uncommon for a patient to misinterpret a right homonymous hemianopia as loss of vision in the right eye. Additionally, isolated hemianopia does not always lead the patient to see a doctor because they are unaware of the seriousness of their condition [3]. Especially if the visual field defect is peripheral and does not affect the macular area, it may remain undetected for a long time. Some patients with hemianopia seek medical advice weeks or even months after lesion onset, often because they or their family notice a compromise in their everyday visual functioning, and not because they are aware of the visual field loss. The clinician should try to determine the exact time of onset, severity, and duration of symptoms. An acute loss of vision (over minutes or hours) points towards traumatic or vascular causes, while a subacute or chronic presentation (over days or weeks) suggests an inflammatory, demyelinating, compressive, or degenerative etiology. Sometimes the patient may recall a recent episode of dizziness, numbness, or diplopia, suggesting an underlying transient ischemic attack (TIA) or stroke. Patients may also complain of disturbances of equilibrium, in particular a feeling that the projection of the body's center of gravity shifts towards the hemianopia, a condition sometimes termed "homonymous hemianopic visual ataxia." It was suggested that hemianopia increases lateral oscillations in patients in the standing position and the postural disturbance is due to tonic visual input from the intact hemifield [4].

Useful information can be gained if the clinician escorts the patient to the office. The patient's behavior in the waiting room, the patient's gait and navigational ability, response to handshaking, and movements of the face and eyes may provide useful clues about his visual field or level of vision. Patients with homonymous hemianopia may ignore or bump onto objects on their blind side, such as door-frames or people, and may find it difficult to navigate in unfamiliar and crowded places. An anomalous compensatory head posture, such as a head turn to the blind hemifield, should also be noted [3, 5].

Specific questions about quality of life and the activities that may be compromised in persons with hemianopia can provide information about the degree of visual field loss and associated neurological comorbidities. Patients with homonymous scotomas often complain about mobility problems, experience driving difficulties, and frequently lose their place or become frustrated during reading. There is a misconception that patients perceive a homonymous hemianopia as a dark curtain or an opaque black area. The loss from hemianopia reflects a void in the vision, and it seems that the brain fills it in perceptually to blend with whatever the patient is viewing [6].

Further questioning should be targeted to potential causes of a homonymous visual field defect (tumor, trauma, arteriovenous malformation, neurosurgery, demyelination, infection, perinatal injury, dementia, migraine). The majority of homonymous hemianopias results from stroke, due to embolus, thrombosis, hemorrhage, or dissection; hence, one should obtain the patient's cardiovascular status, such as blood pressure,

lipid profile, presence of diabetes mellitus, heart disease, body mass index, smoking history, and relevant medication [2].

4.3 Visual Acuity

Testing of the patient's best-corrected visual acuity is important. Carefully observe the patient during acuity testing, because patients with homonymous hemianopia may adopt a head turn to the affected field side in order to bring more visual information into their intact visual field. Additionally, they may consistently omit the left or right half of the eye chart [7]. Visual acuity in postchiasmal lesions is usually normal or near normal, unless there is superimposed ocular disease. Chiasmal processes lead almost always to visual acuity reduction of one eye and heteronymous visual field defects. For example, patients with the anterior junction syndrome due to chiasmal lesions may present with severe central vision loss and scotoma in one eye and a superior temporal scotoma in the contralateral eye. In cortical blindness due to bilateral infarctions of the posterior cerebral arteries, there is severe visual impairment with visual acuity of light perception only or worse.

4.4 Color Vision Testing

It is often useful to test for symmetry of color brightness in the two hemifields in order to explore the possibility of a homonymous visual field defect in respect to the vertical midline. Color desaturation refers to a qualitative change in color intensity and hue and is usually done with the red top of a cyclopentolate bottle [3]. Some authors have advocated the use of red pins, as a red bottle top may be too large for small scotomas. On the wards, in an emergency room, or when formal visual field testing is not available, this test may help detect bitemporal red desaturation from pituitary tumors or a relative homonymous hemianopia. Each eye is tested individually. With the patient fixing his or her eye on the examiner's nose, the red object is moved from one hemifield to the other. Alternatively, two bottles

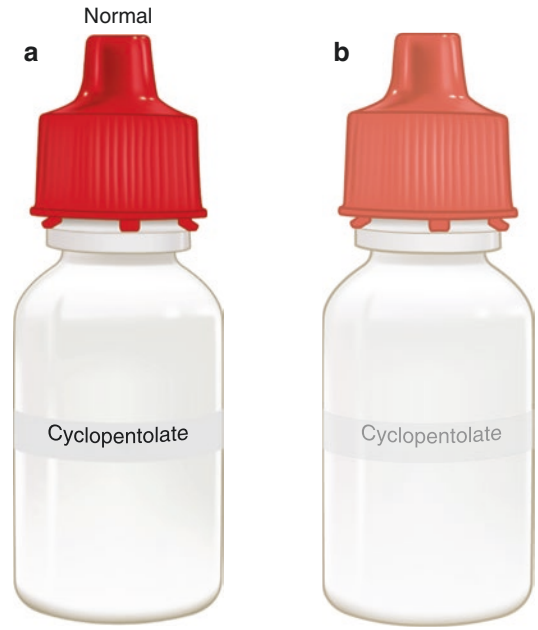


Fig. 4.1 (**a**) Cyclopentolate bottle viewed in an intact hemifield. (**b**) Red desaturation. The red colors of the same object appear duller or washed out, when viewed within the region of a homonymous visual field defect

are held simultaneously on either side of the vertical midline and the patient is asked whether the two objects look the same or whether one appears brighter or duller than the other [8]. A patient with "red desaturation" may report that the red color appears "washed out," duller, or darker when moved into the region of a visual field defect. If the point of transition is at the vertical midline, it is likely that the area of color desaturation represents a hemianopic field defect (Fig. 4.1).

4.5 Amsler Grid

The Amsler grid is a useful screening tool that can be used in persons with possible homonymous scotomas within the central 10°. Such small central or paracentral scotomas may be missed during standard 30° threshold automated perimetry, as, for example, in Humphrey perimetry the grid points are spaced 6° apart. The Amsler test is performed monocularly (with reading spectacles if needed), and the patient is asked to fixate on the central dot and then check if any areas of the

grid have missing or blurred lines. Corresponding areas of blurry vision in either eye may suggest a small central or paracentral scotoma due to occipital stroke [3].

4.6 Reading Ability

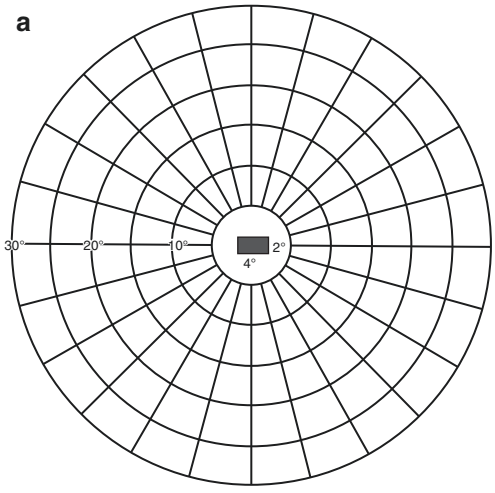
Testing for reading ability with the near correction in place may provide useful information about the central visual field. If funduscopy excludes macular disease in a patient with reading complaints, then a homonymous visual field defect is possible. Reading ability is commonly affected in homonymous scotomas, and patients have reading difficulties that reflect the laterality of the visual field defect and depend on the degree of macular sparing. Standardized assessment of reading speed is ideally performed by validated tests, such as the IReST (International Reading Speed Texts), which are provided in 17 languages and allow comparability of results before and after interventions.

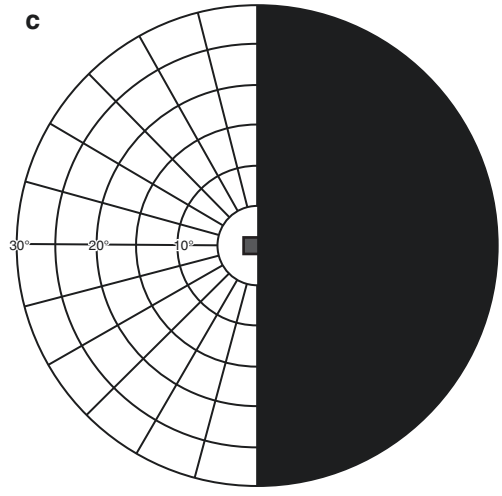
Fluent reading demands at least 2° of visual angle to the left and right and 1° above and below the central fixation point. Reading disorders of patients with homonymous visual field defects (HVFDs) result from the loss of parafoveal field regions that form a "perceptual window" for reading [3]. In western societies this reading window extends 3–4 characters to the left of fixation and 7–11 characters to the right; due to the asymmetry of this perceptual window, right-sided HVFDs cut a larger part of the reading window and therefore impair reading more than left-sided HVFDs. Left HVFDs cause difficulties with eye movements required to find the beginning of a new line, resulting in omissions of the first word or syllables of the line, because the left margin disappears into the scotoma as they scan rightward [7]. Right HVFDs cause more severe reading difficulties, with loss of the anticipatory parafoveal scanning process, and significant reduction of reading speed, resulting in a characteristic reading disorder termed "hemianopic dyslexia," which in some patients is nearly equivalent to spelling [7]. Reduced amplitude of reading saccades to the right and prolonged fixation lead to prolonged reading times. Reading speed improves with increasing degree of macular sparing (Fig. 4.2).

Bitemporal hemianopia, usually due to chiasmal processes such as pituitary adenomas, is another type of visual field defect associated with reading difficulties that are actually caused by unstable binocular alignment. In bitemporal hemianopia, the peripheral visual field loss is mild, because the function of each blind temporal hemifield is taken over by the nasal hemifield of the contralateral eye. The patients often complain about transient horizontal diplopia, disappearance or vertical splitting of the image during reading, in the absence of extraocular muscle palsies [9]. The symptoms arise due to the loss of binocular fusion, as there is absence of overlapping seeing retinal regions throughout the binocular visual field, and each hemifield is seen by one eye only [10].

This lack of retinal correspondence between the remaining nasal fields of both eyes decompensates any preexisting phoria into a tropia, with a resulting visual field defect often referred to as the "hemifield slide" phenomenon [9]. Depending on the phoria, the two nasal hemifields slide relative to each other horizontally or vertically, producing horizontal diplopia (with

Fig. 4.2 (**a**) Fluent reading requires a central intact visual field of at least 4° horizontally and 2° vertically. (**b**) Outside this central area visual acuity is degraded. (**c**) Right homonymous hemianopia with macular splitting leads to severe impairment of reading ability, called "hemianopic dyslexia." (**d**) In case of macular sparing, reading ability will be intact even in complete right homonymous hemianopia. (**e**) However, a small right homonymous paracentral scotoma can have deleterious effects on reading ability if it involves the central "reading window." (**f**) A left homonymous hemianopia with macular splitting will cause difficulties in finding the beginning of lines and words. (**g**) If there is macular sparing, reading ability will be intact. (**h**) A small left homonymous paracentral scotoma will result in reading difficulties, as the central visual field area will be affected





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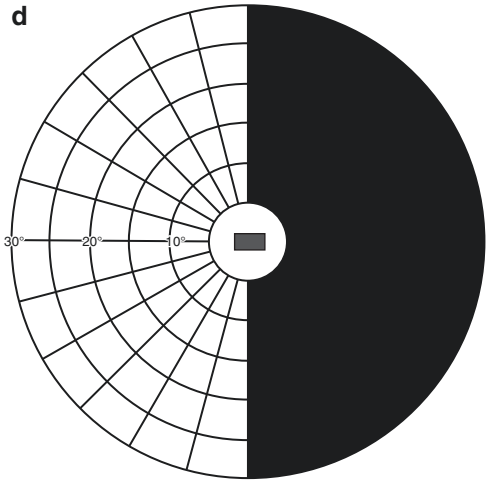
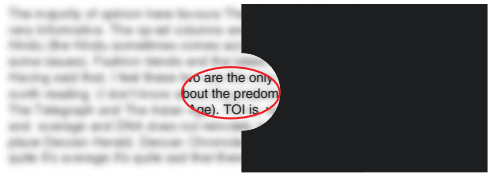
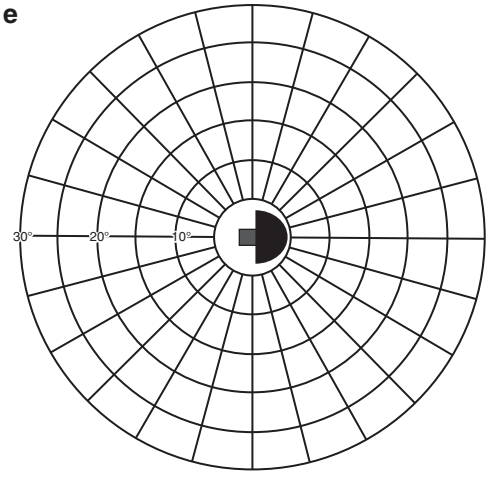
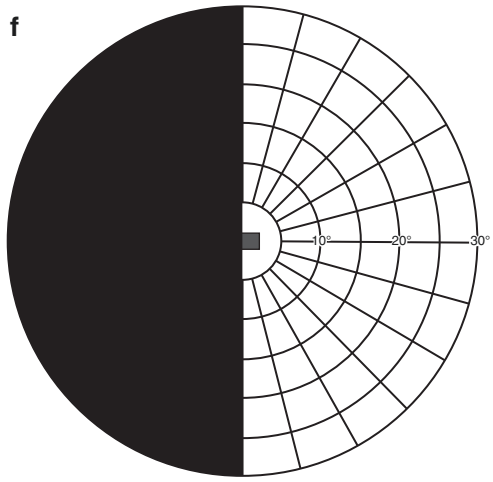
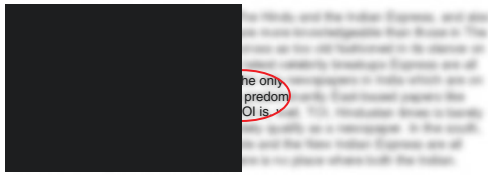
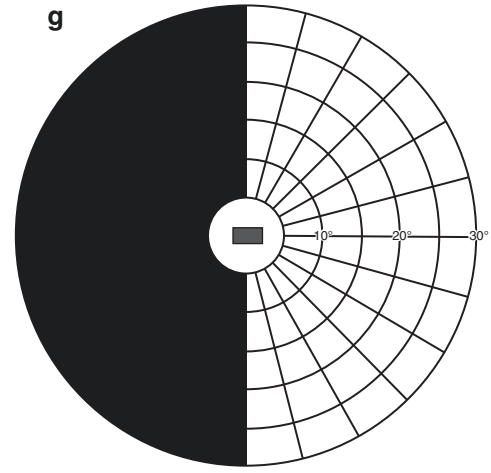


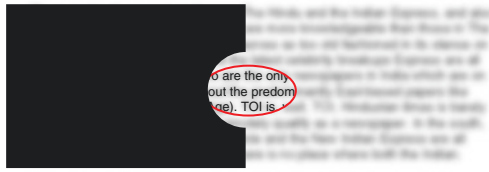


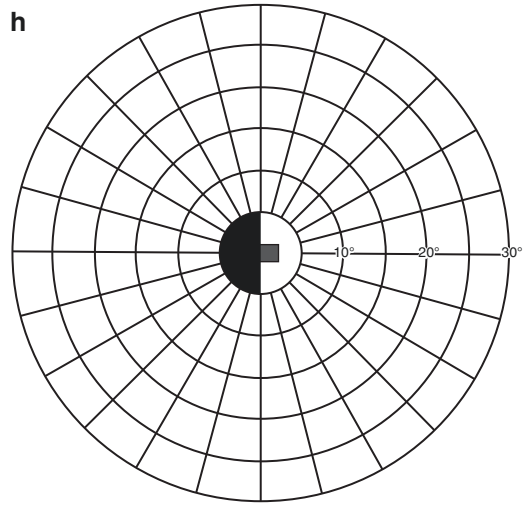












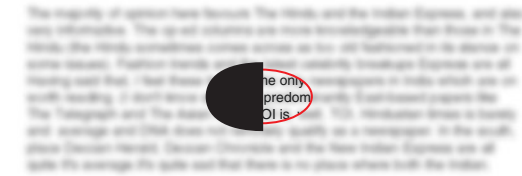


Fig. 4.2 (continued)

preexisting exophoria), sometimes combined with vertical splitting of the image (with preexisting hyperphoria). This type of diplopia can be quite bothersome and patients may patch one eye in order to avoid it, in spite of the resulting severe visual field loss [10]. On the other hand, patients with preexisting esophoria that decompensates in esotropia may notice shrinkage of an object of regard or report disappearance of some details in the object. This can be evident when reading long numbers or tables, but in general patients with decompensated esophoria and bitemporal hemianopia are less symptomatic. Bitemporal hemianopia may also cause a visual perception disorder termed "postfixational blindness," which is associated with impaired depth perception [10]. When viewing objects that are relatively close, there will be a blind area beyond the fixation point. Images posterior to the fixation point will fall into the blind temporal hemifield and will disappear. Patients will complain about problems with judging distance and precision tasks that require near central focusing, such as threading a needle (Fig. 4.3).

4.7 Pupils

Testing for a relative afferent pupillary defect (RAPD) by means of the swinging flashlight test should be used in any case of unexplained vision loss or possible afferent visual pathway damage. RAPD will be typically present in cases of pregeniculate lesions of the afferent visual pathway and also congenital postgeniculate lesions causing homonymous hemianopia [11]. For example, a lesion of the optic tract may cause a contralateral incongruous homonymous field defect, contralateral RAPD, and contralateral band optic atrophy. In patients with lesions of the brachium of the superior colliculus or the pretectal nucleus, a contralateral RAPD without field loss, known as "tectal RAPD," may be noted. However, even patients with postgeniculate lesions may occasionally demonstrate a subtle RAPD due to involvement of suprageniculate neurons in the vicinity of the lateral geniculate nucleus [12].

4.8 Ocular Motility

Ocular alignment, motility, and presence of diplopia should be carefully tested, because extraocular eye muscle palsies may accompany a homonymous scotoma and provide additional evidence of intracranial disease.

Smooth pursuit, optokinetic nystagmus (OKN), and saccades should also be assessed. Smooth pursuit eye movements are tracking eye movements used to stabilize the image of a moving object of interest on the fovea. Retinal image slip provides the stimulus for pursuit. In the smooth pursuit system, signals carrying information about target motion are extracted by motion processing areas in the visual cortex; the final motor pathway extends from the parieto-occipito-temporal junction, via the dorsolateral pontine nuclei of the brain stem, to the ipsilateral gaze center in the paramedian pontine reticular formation [13]. Smooth pursuit is tested by having the patient slowly follow a moving target with the head held still, and deficits can range from absence of tracking eye movements to saccadic (cogwheel) pursuit. Smooth pursuit may be irregular in brainstem-cerebellar disease, and injury to the pursuit pathways also affects the slow phase of the OKN [14].

Testing for symmetrical OKN may further provide information on the location of the underlying brain lesion. OKN is tested in both directions by a hand-held optokinetic drum or a striped band of cloth passed in front of the eyes. Optokinetic asymmetry in a patient with a homonymous scotoma suggests a parietal lobe lesion, and the OKN response is poorer when the OKN stimulus is moved toward the affected hemisphere than in the opposite direction. The explanation is that the smooth pursuit is controlled by the ipsilateral parieto-occipito-temporal junction [3]. If a patient with homonymous hemianopia has normal and symmetrical smooth pursuit and OKN, the hemianopia is likely caused by occipital lobe damage, which is usually infarction (Cogan's rule) [13].

Saccades should also be tested in the setting of homonymous hemianopia, by asking the patient

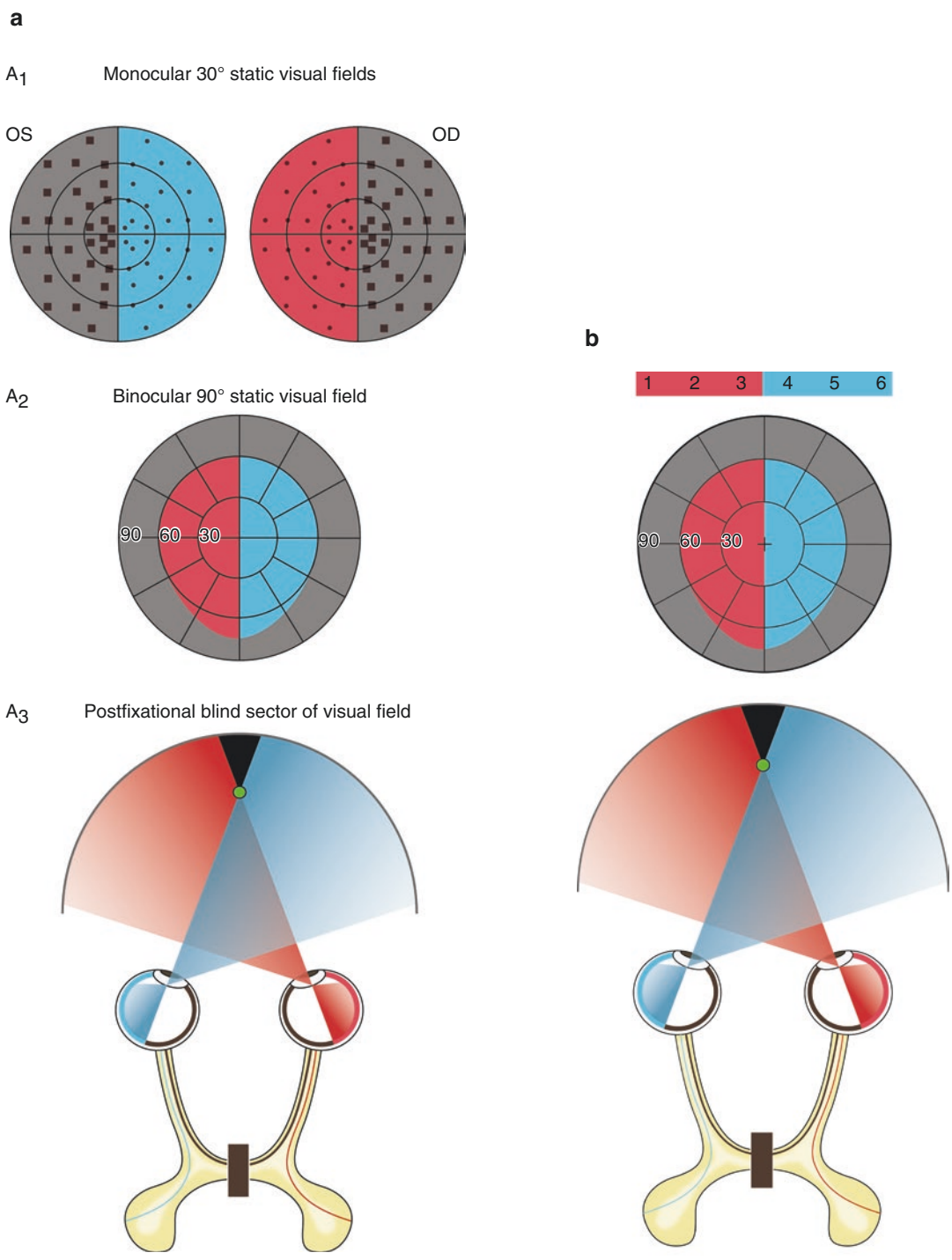


Fig. 4.3 (**a**) Postfixational blindness and the hemifield slide phenomenon in bitemporal hemianopia. A_1: monocular 30° static visual fields show bitemporal hemianopia. A_2: the corresponding binocular 90° visual field shows mild peripheral visual field loss. A_3: at near fixation there is a blind area beyond the fixation point. (**b**) In orthotropia there is only mild restriction of the peripheral visual field (the temporal crescents). (**c**) In left esotropia there is a vertical scotoma between the two nasal hemifields, resulting in disappearance of central parts of an image. (**d**) In left exotropia the purple area is diplopic due to overlapping of the two nasal hemifields. (**e**) In left hypertropia there is vertical splitting of the image

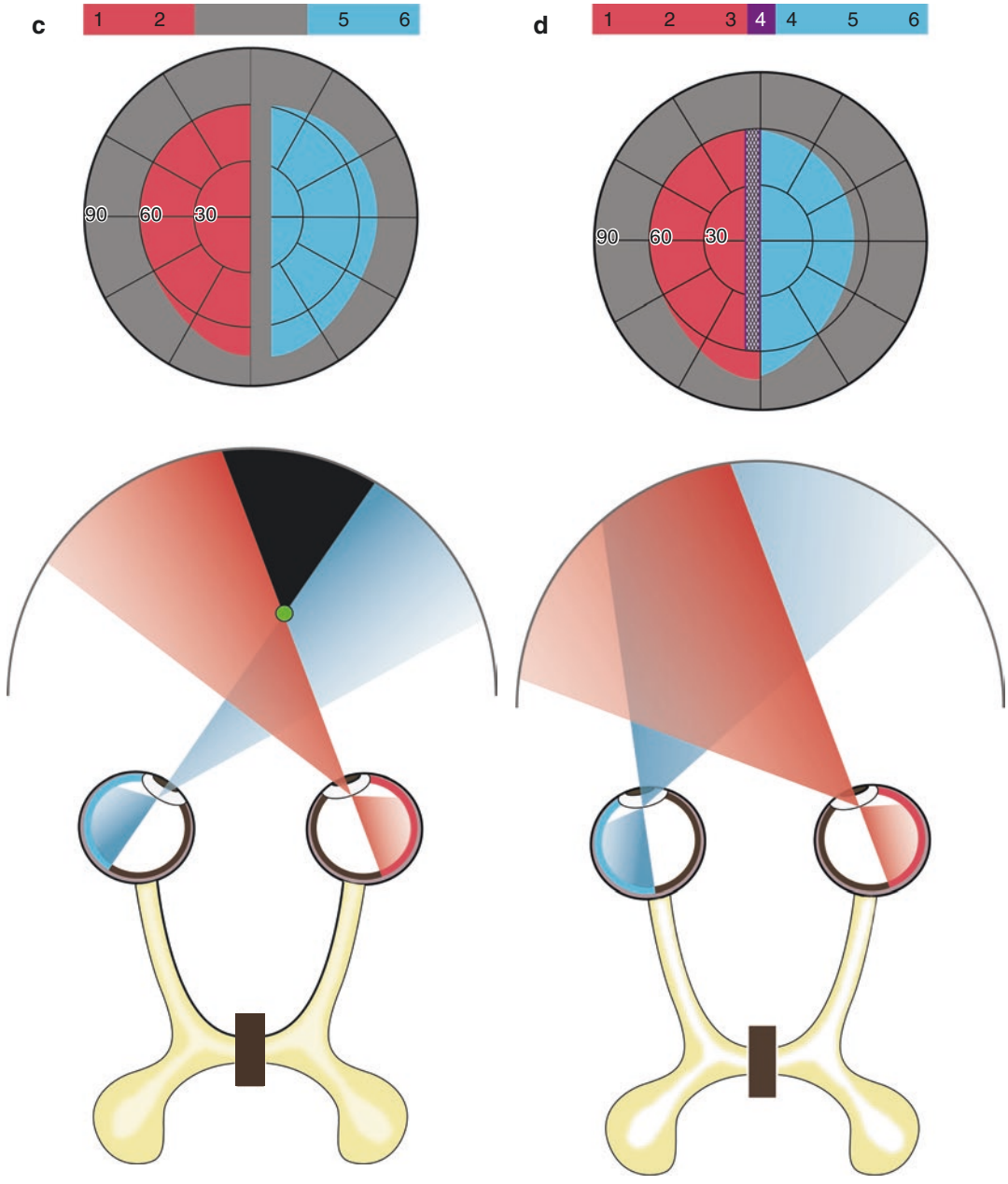


Fig. 4.3 (continued)

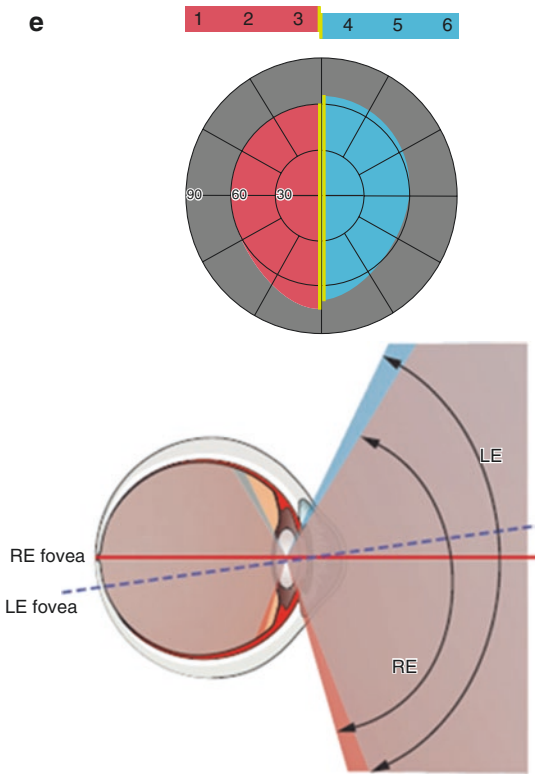


Fig. 4.3 (continued)

to look alternately at two targets held apart horizontally or vertically, usually the examiner's finger and nose. A variety of ocular motor strategies have been described in persons with homonymous hemianopia. For targets in the blind hemifield, patients may show a staircase strategy consisting of a series of safe but slow stepwise saccadic search movements to bring the target into the seeing visual field (stairstep strategy). In more chronic cases some patients adopt a more efficient strategy employing one large saccade calculated to overshoot the target, and they then make a corrective glissade to foveate it (overshoot strategy) [14].

4.9 Assessment of Visual Field

Testing of the visual field of both eyes in every patient with unexplained visual loss is the mainstay of accurate diagnosis in cases of suspected homonymous visual field loss. In cases where hemianopia is the sole manifestation, such as in patients with posterior cerebral artery stroke, the diagnosis can be missed by the clinician who neglects visual field testing. Visual fields, especially when associated with other symptoms, provide valuable information regarding the location of brain lesions. For example, patients with stroke involving the middle cerebral territory often display accompanying signs, such as hemiplegia, hemianesthesia, or dysphasia.

Central 30° threshold automated perimetry, such as Octopus and Humphrey perimetry, is routinely used for assessing visual field defects. Testing of the central 30° usually detects most types of homonymous visual field defects with the exception of the temporal crescent, because the representation of the central field is highly magnified in the brain. In fact, the central 30° of visual field are represented by about 80% of the posterior striate cortex [15].

Goldmann kinetic perimetry is probably more useful in detecting neurological visual field loss, but the device is not widely available, and its use requires more trained personnel. Recent advances in computer technology have facilitated computer-assisted Goldmann kinetic perimetry, such as the Octopus semiautomated kinetic perimetry, which has clear advantages in terms of sophisticated software, ergonomics, and easy operation. On the other hand, small defects within the central 10° of vision are better detected with automated than with Goldmann perimetry [3, 6] (Fig. 4.4).

If automated perimetry is not available, the visual fields should be tested by confrontation perimetry. This method is also used at bedside examinations, intensive care units, and when examining small children, uncooperative, or cognitively impaired patients [16]. Confrontation perimetry should be performed monocularly with the patient fixating on the examiner's nose. Many types of confrontation perimetry have been described in an attempt to assess the severity of the visual field defect. Hand motion, finger motion, and finger counting are the most

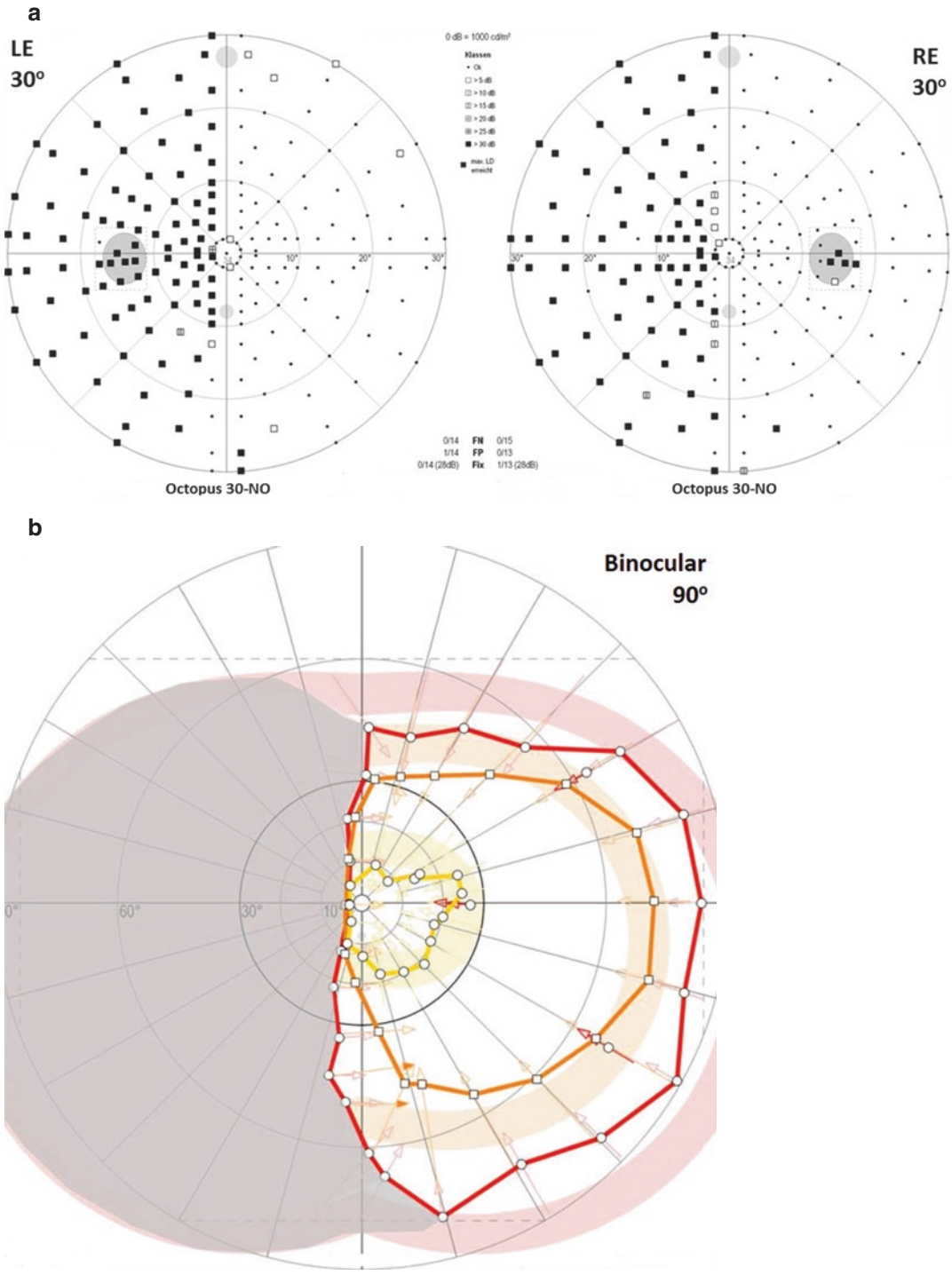


Fig. 4.4 (**a**) Perimetric results in a 32-year-old male patient after surgery for a parieto-occipital arteriovenous malformation. Monocular static automated perimetry within the central 30° visual field in the Octopus 101, demonstrating congruous complete left homonymous hemianopia with macular splitting. (**b**) Binocular 90° visual field using the Octopus 101 instrument's semiautomated kinetic perimetry (SKP). Graphical representation of the area of the visual field loss in the binocular visual field (gray transparent region obtained with stimulus III4e, angular velocity 3°/s). The patient has a left complete homonymous hemianopia

widely used confrontation tests [17]. Initially, the examiner holds his hands within both hemifields on either side of the vertical midline, and starts waving in only one hemifield at a time. The patient reports if he sees something moving. This test can be followed by the "finger wiggle testing," where the examiner holds his hands within both hemifields, but wiggles only the index finger rather than the entire hand. As a final step in the examination, the finger counting confrontation is performed [16]. The examiner holds his closed fists simultaneously in both hemifields to either side of the vertical meridian, and then raises one, two, or five fingers briefly, because other combinations are difficult to distinguish. The patient is asked to count the number of fingers [18]. Finally, simultaneous comparison of red desaturation between hemifields is possible by presenting two small red objects on either side of the vertical meridian, and can further assist in the detection of homonymous scotomas (see Sect. 4.4) [3]. Detailed testing of each of the four quadrants is possible in all of the above variations of confrontation perimetry (Fig. 4.5).

For infants and young children the examiner attracts his attention centrally, while an assistant introduces a toy or a light into various quadrants of the peripheral visual field. For example, the examiner can place a sticker on

Fig. 4.5 (**a**) Confrontation perimetry is performed monocularly with the patient fixating on the examiner's nose. The examiner closes her eye opposite to the eye the patient has closed and uses her monocular visual field for comparison to the patient's visual field. (**b**) The examiner holds his hands within both hemifields on either side of the vertical midline, and starts waving in only one hemifield at a time. The patient reports if he sees something moving. (**c**) During "finger wiggle testing" the examiner holds his hands within both hemifields, but wiggles only the index finger. (**d**) During finger counting confrontation the examiner holds his closed fists simultaneously in both hemifields to either side of the vertical meridian, and then raises one, two, or five fingers briefly, because other combinations are difficult to distinguish. The patient is asked to count the number of fingers

his nose and ask the child to observe it, while a brightly colored object is moved into the child's peripheral field. A shift in fixation, head or hand movement toward the target, or change in facial expression of the infant can indicate that the stimulus was perceived in the periphery. This test is referred to as "evoked saccadic technique" and is based on the principle that stimuli presented in the peripheral field generate reflex eye movements that bring the object of interest onto the central area (fovea) of the retina, movements that develop at a very young age (Fig. 4.6).

Older children can be shown how to mimic finger patterns, which is a simple alternative to the finger-counting confrontation. With the child fixating on the examiner's face, the examiner raises one, two, or five fingers briefly and asks the child to mimic the finger pattern. In children, an eye patch can be used for monocular viewing (Fig. 4.7).

Confrontation visual field is a quick and easy to perform test, which can be performed in any setting, but has a limited ability to detect more subtle defects; it is not quantitative and cannot be used for follow-up evaluations. For the clinical setting, Schiefer et al. [3] have described a practical modification of confrontation perimetry, a testing that is especially useful in cases of homonymous visual field loss. The patient fixes on the center of the examiner's face at a distance of about 30 inches, and he or she reports whether or not the entire face is simultaneously visible. Depending on the missing portions of the face, the examiner can estimate the extent of a homonymous defect (Fig. 4.8).

Fig. 4.6 (**a**) Confrontation perimetry in infants. The examiner attracts the infant's attention centrally, while an assistant silently introduces an interesting toy into the peripheral visual field. (**b–d**) A rapid eye, head, or hand movement toward the target indicates that the stimulus was perceived in the periphery

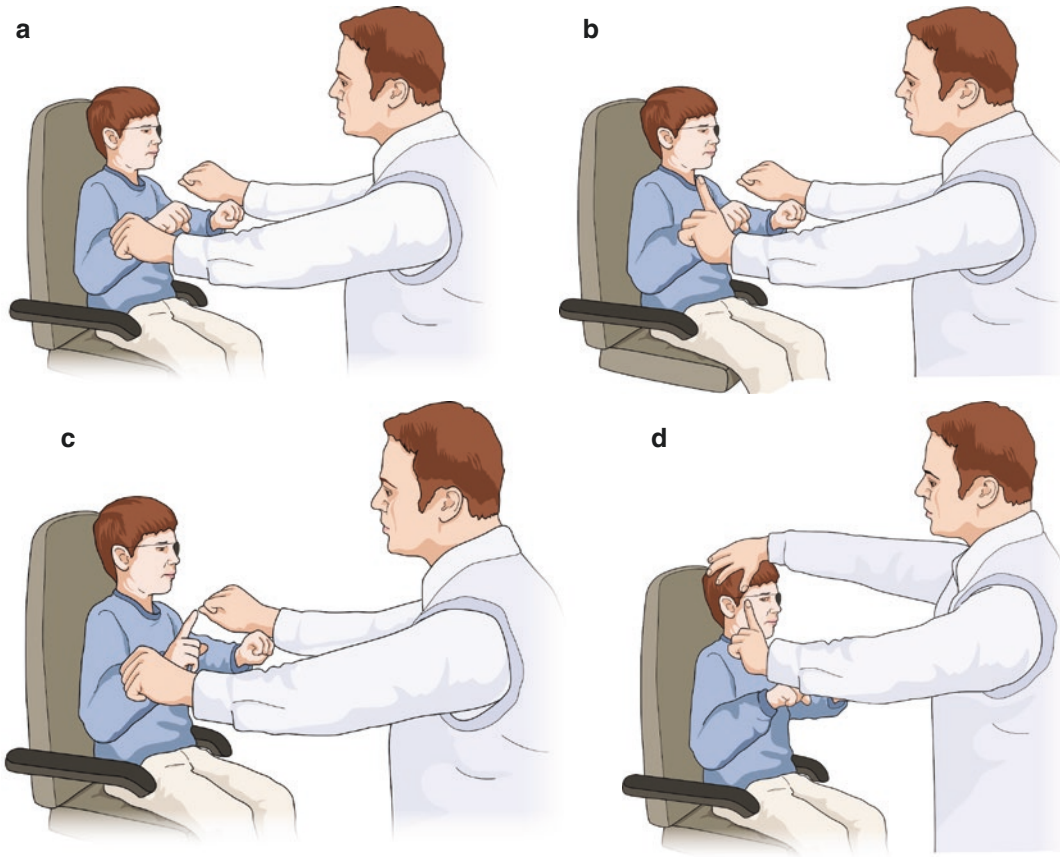


Fig. 4.7 (**a**) Confrontation perimetry in children. The child is asked to show the same number of fingers as the examiner. (**b**) The examiner tries to maintain the child's fixation centrally, while he quickly displays a number of finger in the peripheral hemifield. (**c**) The child mimics the examiner. (**d**) In order to avoid eye movements, the child's face can be turned away from the hemifield being tested

4.10 Funduscopy

Dilated funduscopy with particular attention to the optic disc is an essential part of the evaluation for homonymous scotomas. If optic disc pallor accompanies visual field loss respecting the vertical meridian, there is usually concern for intracranial pathology affecting the optic chiasm or the optic tract. The optic tract syndrome is characterized by a contralateral, incongruous homonymous hemianopia, contralateral RAPD, and contralateral optic atrophy known as "band atrophy" or "bow-tie atrophy" due to retrograde axonal degeneration [19]. The optic disc ipsilateral to the lesion shows temporal optic atrophy, while the optic disc contralateral to the lesion demonstrates a horizontal band-shaped pattern of optic atrophy. Sometimes the defect is more subtle and is seen only in a careful evaluation of the nerve fiber layer. The RAPD will be found in the eye contralateral to the optic tract lesion (with the temporal visual field loss). This is due to the increased number of decussating ganglion cell fibers compared with nondecussating fibers, or it may occur because the melanopsin-containing retinal ganglion cells found in the nasal retina have an increased sensitivity compared with those found in the temporal retina (Fig. 4.9).

Postgeniculate damage in the optic pathway is not typically associated with optic nerve head

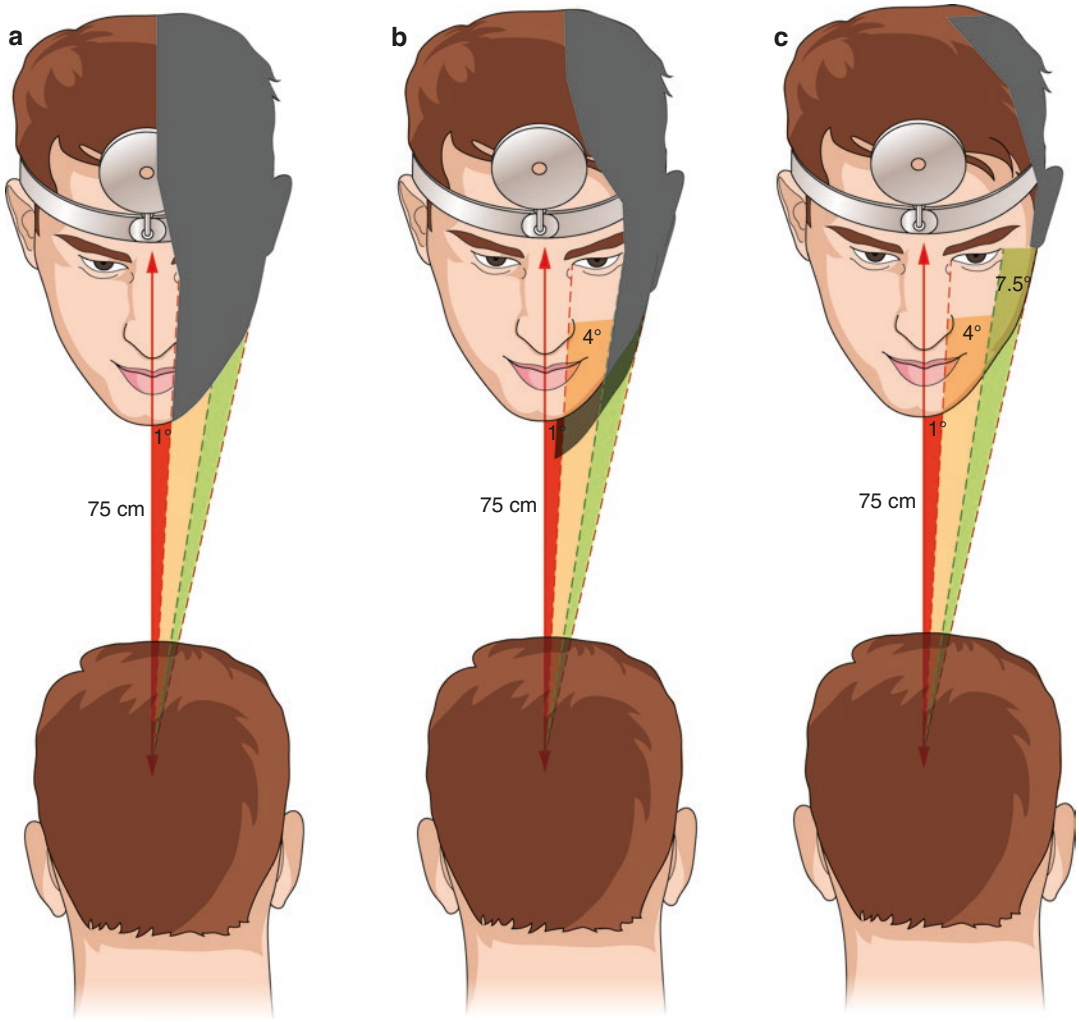
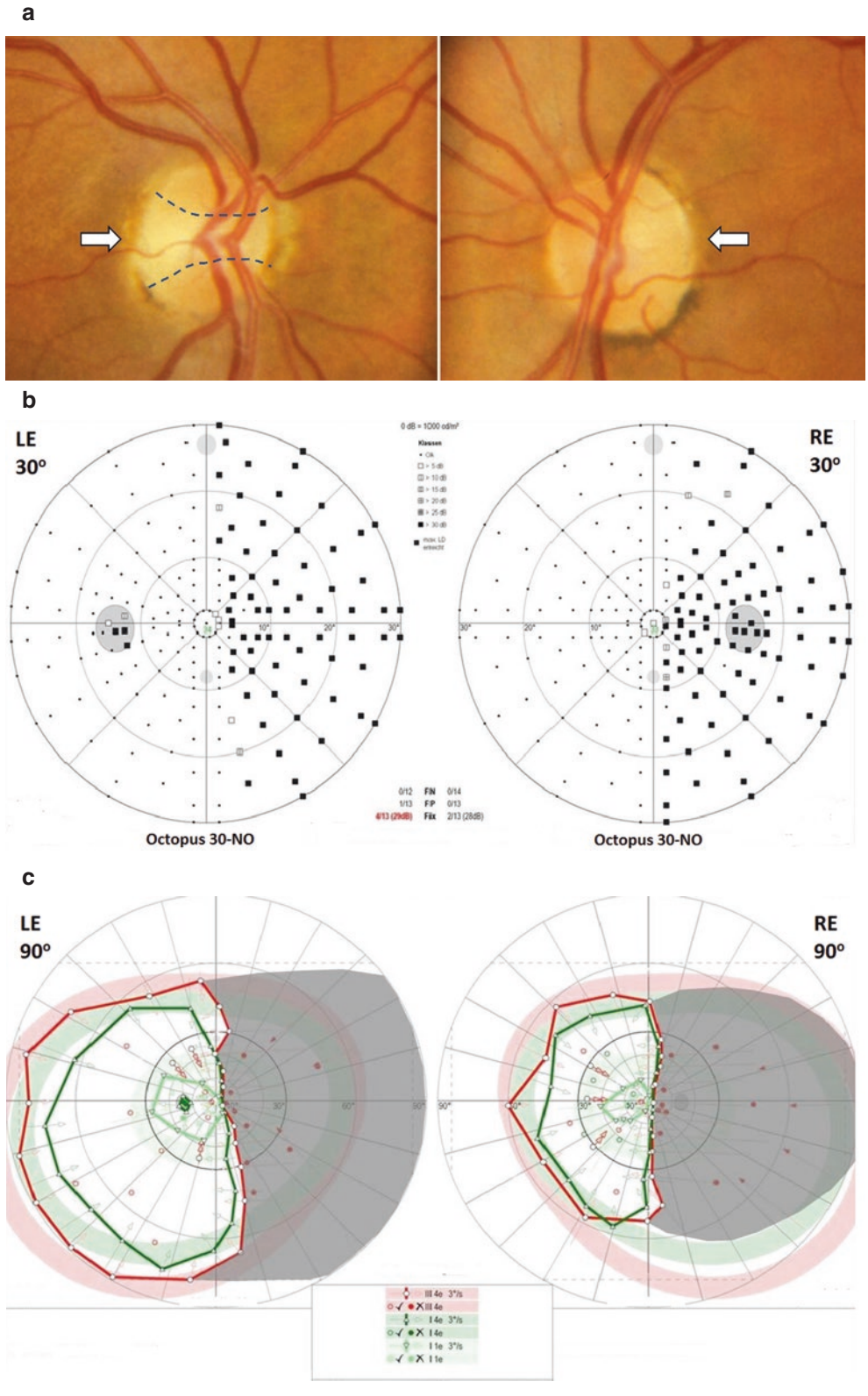


Fig. 4.8 (**a**) Estimation of macular sparing in a patient with a right homonymous hemianopia by means of a modified confrontation visual field test. The patient is asked to look at the examiner's nose from a distance of about 75 cm. If the examiner's right eye is not visible, then macular sparing is less that 1°. (**b**) If the examiner's right eye is just visible, then macular sparing is approximately 4°. (**c**) If the examiner's face is visible except for his right ear, then macular sparing is approximately 7.5°

findings on funduscopy. However, recent optical coherence tomography (OCT) findings have demonstrated retinal ganglion cell (RGC) layer and peripapillary retinal nerve fiber layer (RNFL) thinning corresponding to the hemianopic visual field loss in patients with acquired occipital lesions (see Sect. 4.11) [20, 21]. This finding provides evidence for transsynaptic retrograde degeneration, similar to that observed in congenital or early acquired occipital lesions that are accompanied by clinically detectable optic disc pallor and band atrophy. Finally, retinal vascular changes, such as arteriolar narrowing, arteriovenous nicking, changes in the arteriolar wall (arteriosclerosis), or diabetic retinopathy signs, should be carefully documented, as they may suggest a vascular etiology of the homonymous visual field defect.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4.11 Optical Coherence Tomography

Spectral-domain optical coherence tomography (SD-OCT) is a noninvasive tool that provides high resolution and accurate segmentation of the retinal layers. This technology enables the detection of subtle retinal changes that are not clinically visible and can describe the exact pattern of retinal nerve fiber layer (RNFL) loss in optic atrophy associated with homonymous hemianopia. The RNFL is made up primarily of the axons of RGCs that travel through the optic nerve, the optic chiasm, and the optic tract. The majority of these axons (around 90%) synapse in the lateral geniculate nucleus, and the remainder project to the pretectal region of the midbrain. The RGC axons in the nasal hemiretina subserve the temporal visual hemifield and cross at the optic chiasm, while the RGC axons in the temporal hemiretina subserve the nasal visual hemifield and do not cross at the optic chiasm.

A "bow-tie" atrophy of the optic disc in the contralateral eye in cases of optic tract lesions and also in congenital postchiasmal lesions is well established from clinical observation [19]. Parallel to the "bow-tie" atrophy observed clinically, OCT provides an objective proof of a "bow-tie" pattern of RNFL loss nasally and temporally to the eye contralateral to the brain lesion, and thinning in the superior and inferior temporal arcades in the eye ipsilateral to the brain lesion. Even where the band atrophy is clinically visible in the contralateral eye, OCT is especially useful in evaluating the thinning of the arcuate RNFL bundles at the ipsilateral disc that may not be detectable clinically.

In contrast to the well-established finding of optic atrophy in acquired optic tract lesion, it was previously thought that there are no clinical signs of optic nerve damage after acquired retrogeniculate damage. However, recent studies have provided evidence of retrograde transsynaptic degeneration in the human visual pathway, by demonstrating optic disc pallor, loss of retinal cells, and a relative afferent pupillary defect in retrogeniculate pathology [20, 21]. The pattern and the magnitude of peripapillary RNFL loss in acquired retrogeniculate lesions is similar to that observed in optic tract and congenital postchiasmal lesions [20]. Thinning of the peripapillary RNFL progresses within the first few months after brain damage and is more rapid in the first 2 years, with continued loss of thickness at a lower rate thereafter [20]. Those changes in the RNFL most likely represent RGC loss in both congenital and acquired cases, and thinning of the retinal ganglion cell complex (GCC) after cortical visual impairment has been indeed confirmed by OCT [21, 22, 23]. GCC thinning in the affected hemiretina suggests that retrograde neuronal degeneration can occur in the adult visual pathway and maintains the topographic distribution of the RGC layer as projected to the visual cortex [22, 24].

Fig. 4.9 (**a**) Bow-tie pattern of optic atrophy in a 44-year-old female patient with left optic tract lesion due to motor vehicle induced traumatic brain injury. The right optic disc (contralateral to the lesion) demonstrates a horizontal band-shaped pattern of optic atrophy (*dashed lines*), while the left optic disc (ipsilateral to the lesion) shows temporal optic atrophy (*white arrow*). There is also a right RAPD (Image courtesy of Prof. Ulrich Schiefer, Hochschule Aalen, Aalen, Germany). (**b**) Monocular static automated perimetry within the central 30° visual field in the Octopus 101, demonstrating incongruous right homonymous hemianopia with macular splitting due to a left optic tract lesion. (**c**) Monocular 90° visual field using the Octopus 101 instrument's semiautomated kinetic perimetry (SKP). Graphical representation of the right homonymous hemianopia in the above patient (gray transparent region obtained with stimulus III4e, angular velocity 3°/s)

OCT is important as an adjunct to visual field testing to confirm a visual field defect in a patient who is unable to undergo a reliable visual field test, or as a follow-up tool to monitor the progression and map the time course of transsynaptic degeneration. As thinning of the retinal nerve fiber layer follows both congenital and acquired lesions of the retrogeniculate visual pathway in humans, the differentiation between a congenital (or very long-standing) and acquired occipital lobe lesion should no longer be based on the presence of RNFL defects.

4.12 Neuropsychological Testing

Neuropsychological testing should be part of any clinical evaluation for homonymous visual field loss, because disorders of higher visual function such as visual neglect, object agnosia, simultanagnosia, color agnosia, prosopagnosia, and cerebral akinetopsia often accompany a homonymous hemianopia (see Chap. 10).

4.13 Congenital Hemianopia

The patient with isolated congenital or early-onset hemianopia is usually unaware of the visual field defect due to increased compensatory ability [24]. The field defect is often detected in adolescence or early adulthood as an incidental finding during a routine eye examination [25]. Frequently, the patient has engaged in sports and has been a driver for many years, although congenital hemianopias are usually complete and are not characterized by macular sparing. A congenital isolated hemianopia is usually caused by structural occipital lobe lesions, such as vascular malformations (i.e., Sturge-Weber syndrome, occipital arteriovenous malformations), cerebral hemiatrophy, occipital lobe dysplasia, porencephaly, colpocephaly, polymicrogyria, pachygyria, gangliogliomas, and periventricular leukomalacia due to prenatal injury to the periventricular white matter [26, 27]. In some cases, a congenital hemianopia may be discovered in early childhood if it is associated with other neurological disorders, primarily hemiplegia, temporal lobe or grand mal seizures, and developmental delays.

The majority of patients with congenital hemianopia show little or no evidence of visual impairment in everyday activities due to the development of adaptive strategies. A common finding in congenital hemianopia is a compensatory face turn to the side of the visual field defect [25]. Several theories have been proposed to explain this adaptive form of torticollis: This maneuver may serve to centralize the remaining intact visual field with respect to the body, or to position the head, so that a wider area towards the blind hemifield can be scanned by means of saccades. Additionally, many children with congenital hemianopia manifest a constant, nonalternating exotropia. The exotropic eye is ipsilateral to the visual field defect and is believed to enable the patient to expand his binocular visual field by achieving harmonious anomalous retinal correspondence [27]. Due to the frequent presence of exodeviations in neurologic disease, it is not clear if this finding is a compensatory adaptation. However, a child with a constant exotropia and a face turn towards the deviating eye should be evaluated for exclusion of a congenital hemianopia [28].

Additional typical changes of the optic discs and nerve fiber layer should alert the clinician towards the possibility of a congenital or long-standing lesion. The optic disc contralateral to the brain lesion shows band-shaped pallor, while the optic disc ipsilateral to the brain lesion shows temporal pallor [25]. This form of optic atrophy is termed “homonymous hemioptic atrophy” and is similar to the “bow-tie” atrophy encountered in optic tract lesions. Corresponding patterns of RNFL thinning are found in OCT, with the RNFL thickness at nasal and temporal sectors of the contralateral and those at superior and inferior sectors of the ipsilateral eye being significantly thinner than those of the fellow eye. As mentioned earlier, recent studies with OCT have demonstrated similar RNFL loss also in long-standing acquired lesions of the posterior visual pathway [29]. These data are most likely to represent transsynaptic retrograde degeneration

of retinal ganglion cells in both congenital and acquired hemianopias. Patients with congenital hemianopia also show a subtle RAPD in the eye with the band-shaped atrophy, namely, contralateral to the brain lesion. This relative afferent papillary defect is also attributed to transsynaptic degeneration of the pupillomotor fibers that synapse in the pretectal area of the midbrain [27].

Acquired homonymous hemianopia that occurs later in childhood is most commonly due to trauma and tumors [24]. In the pediatric group most lesions involve the optic radiations, followed by the occipital lobes, whereas in adults the lesions usually damage the occipital lobes, followed by the optic radiations. In approximately one third to one half of pediatric patients some spontaneous improvement can be expected within the first few months after lesion onset [26]. However, the recognition of homonymous hemianopia frequently is delayed in this population.

4.14 Functional Visual Loss

Nonorganic hemianopic visual field defects are occasionally encountered and may be psychogenic or caused by malingering. The predominant pattern is the "missing half" hemianopia, which is an ipsilateral hemianopia on the "affected" eye, normal visual field in the fellow eye, and a complete hemianopia toward the affected side on binocular visual field. The second most common pattern is ipsilateral blindness combined with hemianopia in the binocular visual field. This type of defect can be diagnosed by first performing visual field testing monocularly and then binocularly. The discrepancy between the monocular and binocular fields provides an immediate diagnosis of the functional nature of this alleged visual loss [30] (Fig. 4.10). Additionally, an organic monocular temporal hemianopia has never been described without an RAPD [31].

Other types of nonorganic visual field defects include bitemporal hemianopia, binasal hemianopia, and a nonspecific concentric visual field constriction, which is the most common type of nonorganic visual field defect in general. In case of an alleged hemianopic field defect, the most important examination is binocular perimetry. Goldmann perimetry is a valuable tool that may confuse a simulator due to its relatively complex procedure. Automated static perimetry is generally not helpful in the evaluation of suspected functional vision loss due to inconsistent responses and poor testing parameters [32]. For example, crossed or spiraling isopters in Goldmann may look like generalized constriction in automated perimetry. Correlation of the Amsler grid findings with the perimetric results will also help to differentiate organic from nonorganic vision loss. Hence, repeated perimetric testing with different methods and instruments may show discrepancies and diagnose a functional vision loss [33].

The presence of the physiologic blind spot in the temporal hemifield is also useful. In true homonymous hemianopia, the physiologic blind spot will be detectable in the eye with the temporal seeing hemifield during monocular perimetry [34]. In bitemporal hemianopia only the nasal hemifields are preserved; hence the physiologic blind spots will not be detectable during monocular or binocular perimetry. In binasal hemianopia, which is very rare, only the temporal hemifields are preserved; hence both blind spots will be detectable in binocular perimetry [3]. The blink response to a threatening gesture should be also absent in patients with true homonymous or heteronymous hemianopia, when the gesture is presented into the area of the visual field defect [7].

Additionally, in patients claiming homonymous visual field loss, testing of reading ability will produce reading disabilities, particularly when there is no macular sparing. Bitemporal and binasal hemianopias may present with similar reading disturbances in monocular viewing. When tested binocularly, patients with bitemporal hemianopia may manifest the hemifield slide phenomenon with impaired reading ability, which has been described in Sect. 4.6. In this case there are no corresponding parts of the remaining seeing nasal visual fields and each point in space is seen monocularly [34]. This

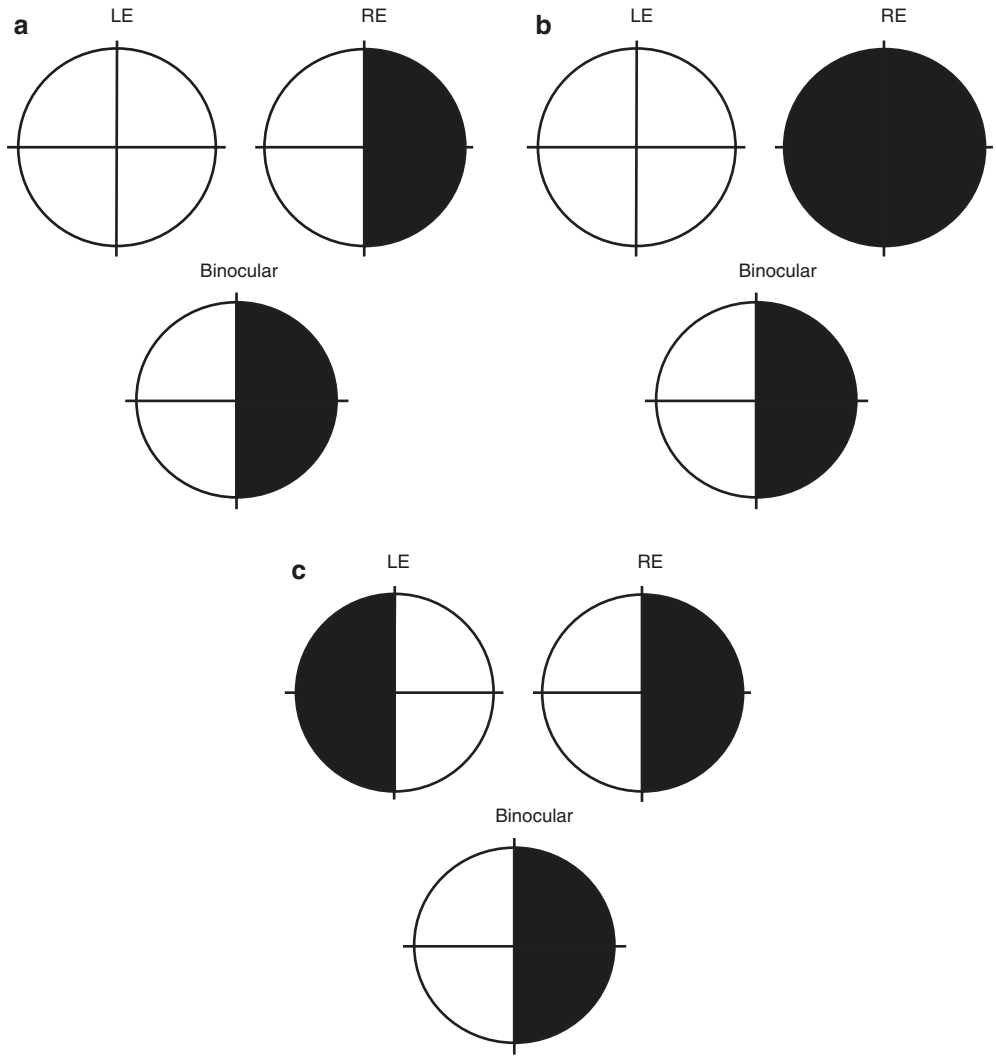

Fig. 4.10 (**a**) The most common pattern of hysterical hemianopia is the "missing half" hemianopia. This is an ipsilateral hemianopia on the "affected" right eye, normal visual field in the fellow eye, and a complete homonymous hemianopia toward the affected right side on binocular visual field. (**b**) Another type of functional visual field loss is right eye blindness combined with right homonymous hemianopia in the binocular visual field. (**c**) Less often patients report bitemporal hemianopia combined with right homonymous hemianopia in the binocular visual field

lack of motor control of binocular alignment leads to decompensation of underlying heterophorias and to horizontal separation (in preexisting esophoria), overlap (in preexisting exophoria), and/or vertical displacement (in preexisting hyperphoria) of the remaining nasal hemifields. Postfixational blindness can be also used to unmask a bitemporal hemianopia. When the patient with true bitemporal hemianopia fixates a close target, a small object 30 cm behind the fixation point becomes invisible because it falls within a triangular postfixational scotoma [10]. Finally, placement of a 20 prism diopters base-out prism in front of one eye in true binasal or bitemporal hemianopias will not induce any corrective movements, due to the lack of fusional vergence eye movements. However, in functional disease the prism will produce corrective eye movements in order to eliminate the diplopia [34].

Conclusion

Homonymous visual field defects due to postchiasmal damage are commonly encountered in clinical practice and may have deleterious effects on patients' quality of life and well-being. The combination of several different tests, such as careful history taking, testing of visual acuity, color vision, pupils, ocular motility, reading ability, perimetry, funduscopy, and OCT are the best guide towards correct diagnosis and the most appropriate interventions.

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Types of Homonymous Visual Field Defects

5

Eleni Papageorgiou and Evangeli Tsironi-Malizou

Abstract

Retrochiasmal brain damage can lead to various types of homonymous visual field defects (HVFDs), with the occipital lobe being the most common lesion location, followed by the optic radiation, the optic tract, and lateral geniculate nucleus (LGN). The etiology depends on the age of the patient. Older patients tend to have vascular lesions, whereas younger patients may have tumors, traumatic injuries, and arteriovenous malformations. HVFDs can be classified according to their size, shape, macular sparing, and congruency, giving rise to a variety of perimetric findings. Complete homonymous hemianopias are non-localizing and may be caused by lesions in any part of the retrochiasmal visual pathway, including the optic tract, LGN, optic radiation, and occipital lobe. However, a highly congruous complete homonymous hemianopia is usually due to an occipital lobe lesion. Homonymous quadrantanopias usually result from lesions of the occipital lobe and the optic radiation. Less frequent types of HVFDs are paracentral circumscribed homonymous scotomas due to small lesions at the tip of the occipital lobe, homonymous sectoranopias in lesions of the LGN, and peripheral HVFDs due to lesions in the intermediate striate cortex. A unique HVFD is the "temporal crescent," after damage to the most anterior portion of the occipital lobe. Bilateral homonymous visual field defects due to bilateral postchiasmatic lesions may present as checkerboard visual fields or bilateral altitudinal defects. Such deficits may pose a diagnostic dilemma, as they have to be differentiated from anterior ischemic optic neuropathy, ischemic retinal lesions, choroiditis, choroidal colobomas, glaucoma, optic nerve hypoplasia, tilted discs, or drusen.

Keywords

Homonymous hemianopia • Homonymous quadrantanopia • Horizontal sectoranopia • Quadruple sectoranopia • Peripheral hemianopia • Paracentral

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scotomas • Temporal crescent • Bilateral hemianopia • Checkerboard visual fields • Monocular hemianopia • Bitemporal hemianopia • Binasal hemianopia • Anterior junction syndrome • Cortical blindness

5.1 Introduction

Field defects respecting the vertical midline usually indicate chiasmal or retrochiasmal pathology. Unilateral damage to the retrochiasmal visual pathway, i.e., the optic tract, lateral geniculate nucleus (LGN), optic radiation, or striate cortex, results in homonymous visual field defects (HVFDs), which affect corresponding areas of the contralateral visual field in both eyes (Fig. 5.1). Stroke is the most common etiology for HVFDs, followed by traumatic brain injury, brain tumors, and other structural brain lesions. There is a variety of HVFDs, and certain types of HVFDs have been traditionally associated with damage to specific brain areas. Although lesions anywhere along the retrochiasmal pathway can produce virtually any type of HVFD, characteristics of the HVFD (type, shape, size, laterality, macular sparing, and congruity), along with other neurologic signs, may give some initial clues about localization of the underlying lesion and guide neuroimaging.

5.2 Homonymous Visual Field Defects

The location and cause of HVFDs depend on the age of the patient and the presence of other comorbidities. Among 850 patients with 902 homonymous hemianopias (HHs), who had undergone computed tomography (CT) or magnetic resonance imaging (MRI), the most common lesion location was the occipital lobe (45%), followed by damage to the optic radiations (32%), the optic tract (10%), LGN (1.3%), and multiple visual pathway segments (11%) [1]. Vascular lesions such as infarction (84%) and hemorrhage (16%) were the most frequent cause of HVFDs (69.6%), followed by trauma (13.6%), tumor (11.3%), neurosurgical procedures (2.4%), demyelination (1.4%), other miscellaneous causes (1.4%), and unknown etiology (0.2%) [1]. In children, the most frequent cause of HVFDs is traumatic brain injury (34%) followed by tumor (27%). Pediatric visual field defects often escape detection or their diagnosis is delayed, because children rarely complain about their visual field loss [2]. If formal visual field testing is not possible due to reduced cooperation, then the clinician should attempt to assess the visual field by confrontation perimetry, which is often more appropriate for younger children.

Almost half of all HVFDs are isolated and approximately 90% of patients with isolated homonymous hemianopia have ischemic infarcts of the posterior cerebral artery affecting the striate cortex [3]. In general, older patients tend to have vascular underlying lesions (infarction, hemorrhage), whereas younger patients may have congenital lesions, such as arteriovenous malformations, or nonvascular acquired lesions, such as tumors, abscesses, demyelinating disease, or traumatic injuries [4]. A careful history regarding the onset of visual field loss, sudden or progressive, will also help in differentiating the cause. A rapid onset is typical of vascular (ischemia, hemorrhage), traumatic, and inflammatory lesions, while compressive lesions (tumors) have a more progressive course, leading to gradual loss of the visual field from the periphery to the center [5]. If decompression of the visual pathway takes place, then improvement of the visual field is first noted at the center (macular region) and continues towards the periphery [4].

Characteristics of HVFDs (type, shape, size, macular sparing, and congruency), along with associated neurologic signs and symptoms, have been traditionally used for localizing the damage

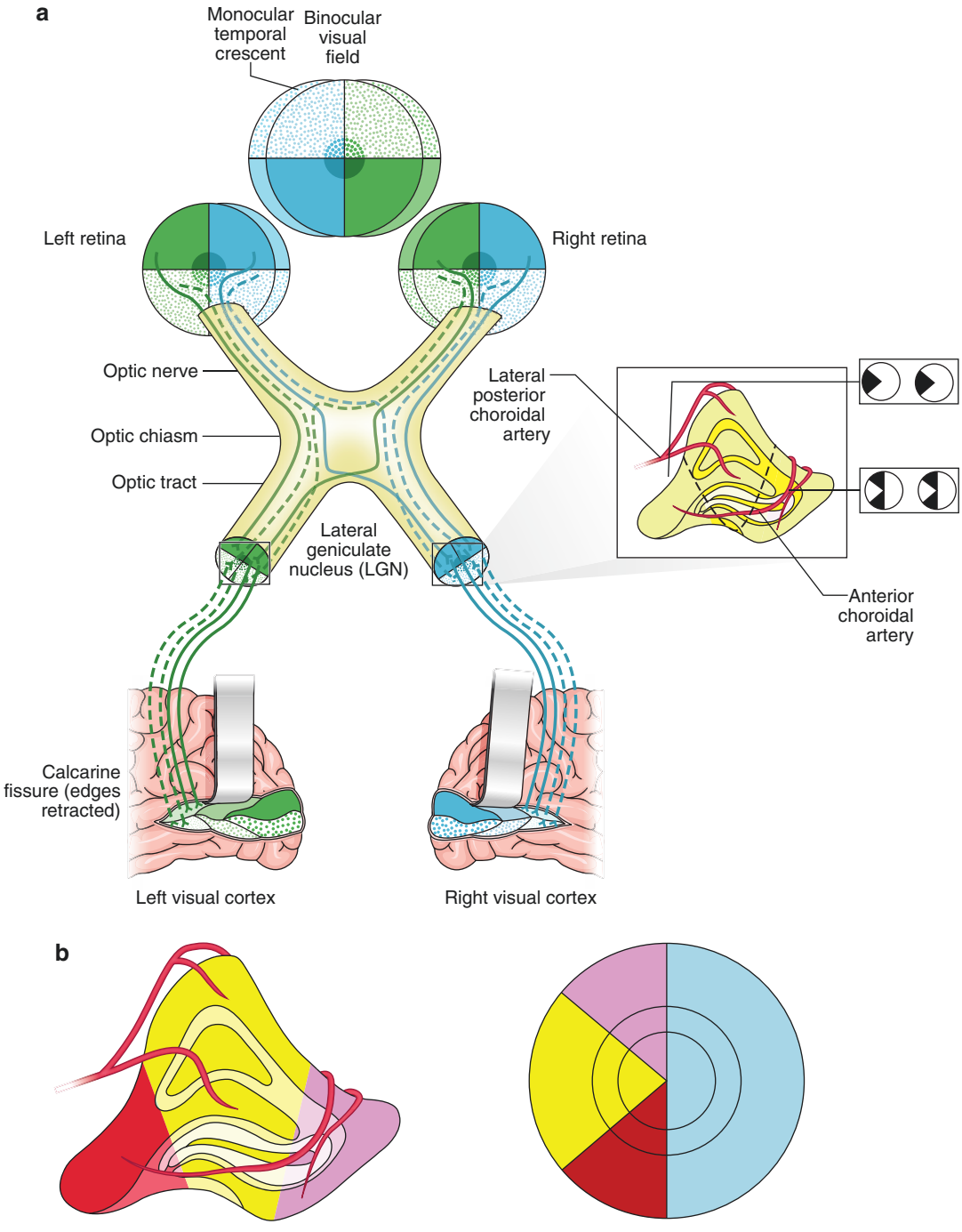


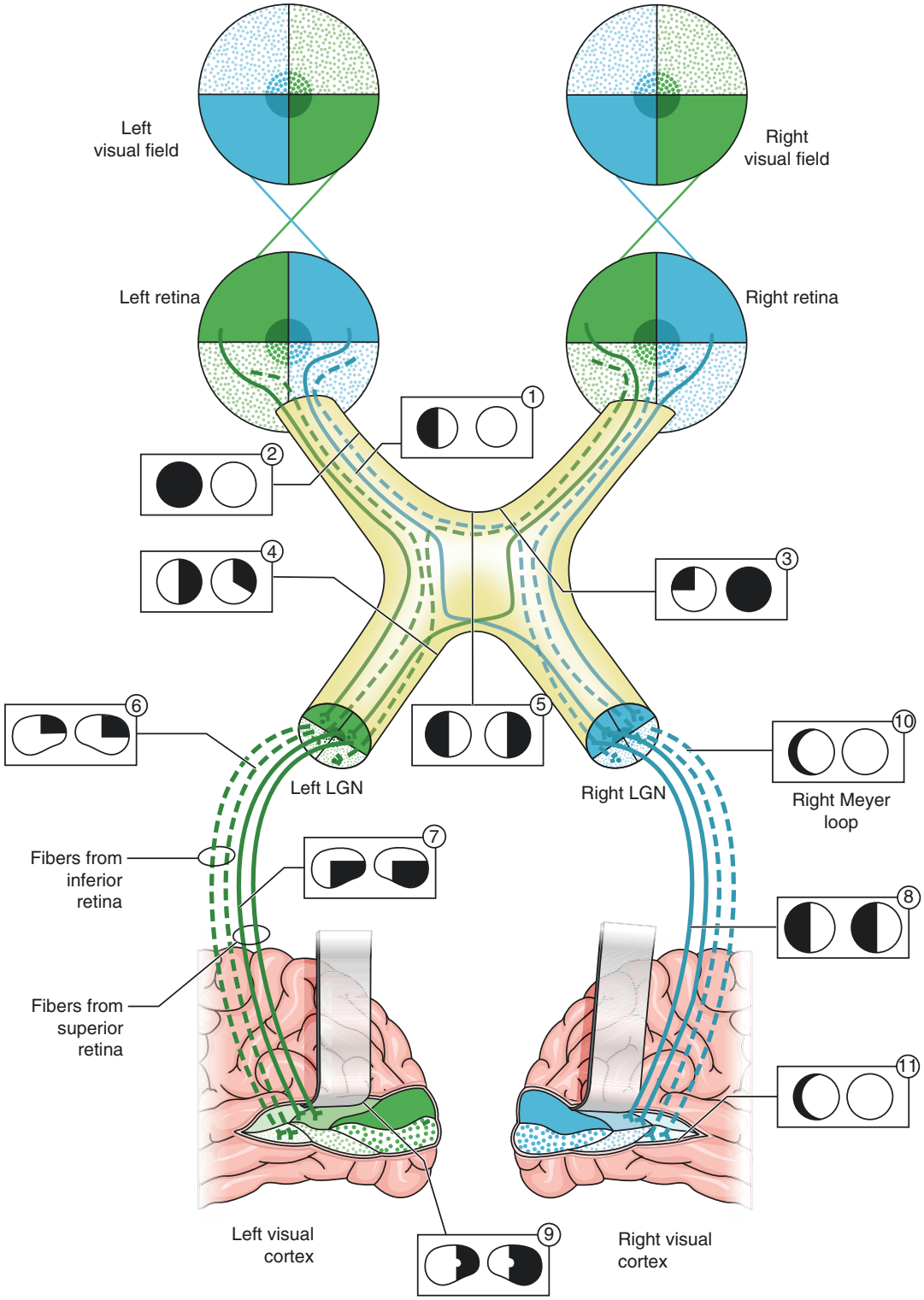
Fig. 5.1 (**a**) Projection of the visual fields onto the retina, lateral geniculate nucleus (LGN), and visual cortex. The four quadrants of the visual fields send signals to the primary visual cortices via the LGN. The superior visual fields are represented below the calcarine fissure and the inferior visual fields are represented above the calcarine fissure. The right lateral geniculate nucleus is supplied by the lateral posterior choroidal artery (hilum and midzone of the LGN), and the anterior choroidal artery (lateral and medial aspects of the LGN). Depending on the lesion site, partial infarctions of the right LGN produce a left horizontal sectoranopia or a left quadruple sectoranopia. (**b**) Anatomy of blood supply and representation of left visual field in the right LGN seen in coronal section from behind

in the retrochiasmal visual pathway, as there are typical HVFDs associated with damage of certain brain areas (Fig. 5.2) However, this is not always possible, as studies have shown that every type of HH, except for unilateral loss of temporal crescent and homonymous sectoranopia, can be found in all lesion locations along the retrochiasmal visual pathway. Additionally, a complete homonymous hemianopia has no localizing value, as it can occur with a lesion anywhere posterior to the optic chiasm [3]. In those cases the clinician should carefully seek for additional localizing neurological signs and symptoms prior to neuroimaging. The laterality of HVFD also provides information for neurological manifestations that may not have been obvious to the patient. Right-sided HVFDs are associated with reading or speech disorders, and left-sided HVFDs lead to visual hemineglect and difficulties with spatial orientation and face and color recognition.

In complete homonymous hemianopia the entire hemifield of both eyes is affected, while in incomplete homonymous hemianopia there is sparing of a portion of the visual field in at least one eye (Fig. 5.3). Incomplete HVFDs can be further classified as either congruous or incongruous. Congruous HVFDs have identical shape, depth, and size in both eyes, while in incongruous HVFDs the visual field is affected to a different extent in each eye. Due to the retinotopic organization of fibers within the visual pathways, the more posterior the location of a lesion to the visual pathway, the more congruous the visual field defect is likely to be [5]. Immediately posterior to the LGN, crossed and uncrossed fibers corresponding to the same area of contralateral hemifield are spatially separated. As these fibers course posteriorly through the optic radiation, they organize and they lie closer together as the optic radiations approach the occipital lobe. Hence lesions involving the occipital lobe characteristically produce congruous HVFDs, whereas the most incongruous hemianopias occur with optic tract and LGN lesions. However, this "rule of congruency" should be used with caution, as at least 50% of lesions in locations other than the occipital lobe also produce congruous homonymous visual field loss, especially if these lesions are stroke-related. Interestingly, it has been shown that 50% of optic tract lesions and 59% of optic radiation lesions produce congruous HVFDs, with the optic radiation being the most common location for conditions resulting in incongruous visual field defects [6].

Fig. 5.2 Sites of damage to the afferent visual pathway and corresponding visual field defects. Visual field loss in the monocular temporal crescent is associated with damage in the contralateral anterior occipital lobe, contralateral anterior portion of the temporal lobe (Meyer loop), or the ipsilateral nasal retina.

(1) Left monocular temporal hemianopia due to a left preschiasmal lesion affecting the fibers from the nasal hemiretina.
(2) Left optic neuropathy.
(3) Anterior junction syndrome due to damage of the anterolateral margin of the chiasm to the right side. The lesion involves the anterior Wilbrand knee, which carries fibers from the contralateral inferior nasal retina.
(4) Right incomplete homonymous hemianopia with poor congruence due to a left optic tract lesion.
(5) Bitemporal hemianopia from central chiasmal damage.
(6) Right superior homonymous quadrantanopia from damage to the left temporal lobe (inferior portions of the optic radiation).
(7) Right inferior homonymous quadrantanopia from damage to the left parietal lobe (superior portions of the optic radiation).
(8) Left complete homonymous hemianopia due to widespread damage of the right optic radiation in the vicinity of the occipital lobe.
(9) Right homonymous hemianopia with macular sparing from damage to the left occipital lobe.
(10) Left (monocular) crescentic scotoma due to a lesion of the right Meyer loop in the anterior temporal lobe.
(11) Left (monocular) crescentic scotma due to a lesion of the right anterior (rostral) visual cortex


Left visual field
Right visual field
Left retina
Right retina
1
2
3
4
5
6
7
8
9
10
11
Left LGN
Right LGN
Right Meyer loop
Fibers from inferior retina
Fibers from superior retina
Left visual cortex
Right visual cortex

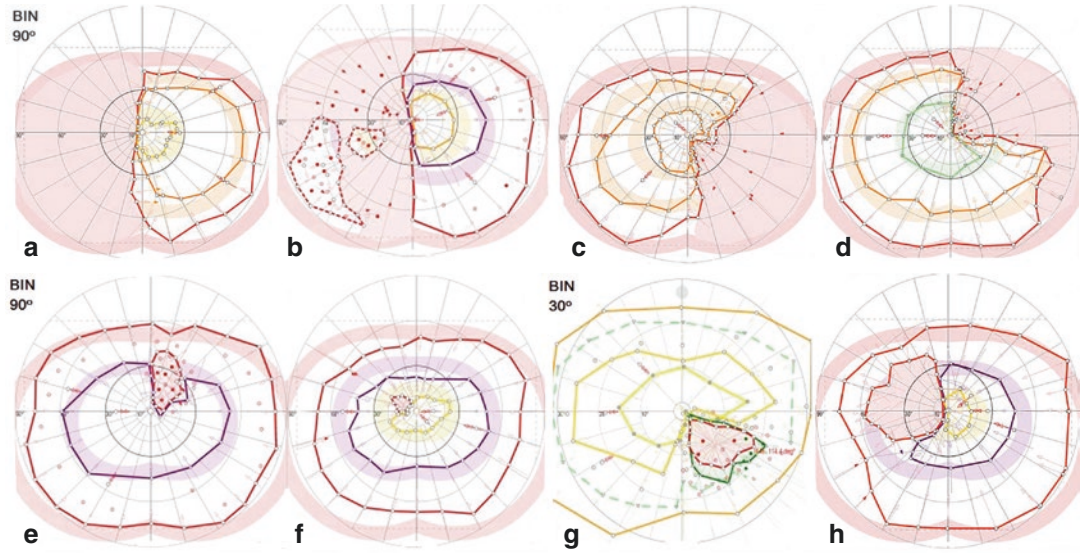


Fig. 5.3 Various types of homonymous visual field defects in the binocular 90° visual field (Octopus, semiautomated kinetic perimetry). (**a**) Left complete homonymous hemianopia (HH) without macular sparing due to brain surgery for a right parieto-occipital arteriovenous malformation (AVM). (**b**) Left incomplete HH due to ischemic infarction in the parieto-occipital region. There is sparing of the peripheral temporal crescent. (**c**) Right incomplete HH with macular sparing due to ischemic infarction of the left posterior cerebral artery (PCA). (**d**) Right homonymous superior quadrantanopia due to ischemic infarction of the left PCA. (**e**) Right incomplete homonymous superior quadrantanopia due to left occipital infarction. (**f**) Left homonymous superior paracentral scotoma due to infarction of the right occipital pole. (**g**) Right homonymous inferior paracentral scotoma due to infarction of the left occipital pole (binocular 30° kinetic perimetry). (**h**) Left incomplete HH without macular sparing due to traumatic injury of the right occipital lobe

5.2.1 Homonymous Sectoranopia

Homonymous sectoranopia is a wedge or sector-shaped homonymous visual field defect. Homonymous sectoranopias are mainly encountered in lesions of the LGN due to its distinct neuronal structure and dual vascular supply (see Fig. 5.1a). The LGN is organized retinotopically into 6 neuronal layers that are numbered 1 through 6 ventrally to dorsally and receive segregated input from both eyes. Visual information from the contralateral eye (crossed retinal projections) synapses in layers 1, 2, and 6, whereas from the ipsilateral eye (uncrossed retinal projections) in layers 2, 3, and 5. The macula is represented in the dorsal portion of the LGN, including the hilum, whereas the lateral horn represents the contralateral superior visual quadrant, and the medial portion represents the contralateral inferior visual quadrant. The lateral posterior choroidal artery supplies the hilum and midzone of the LGN, and the anterior choroidal artery supplies the lateral and medial aspects of the LGN (see Fig. 5.1b). Homonymous sectoranopias can be very congruous due to the sharp division between the vascular territories of the LGN [7].

The most likely cause of a sectoranopia is ischemic infarction, given the unique vascular anatomy of the LGN. Tumors (astrocytomas), arteriovenous malformations, and trauma are other causes of a sectoranopia [4]. Bilateral LGN damage has been reported in rare cases of central pontine myelinolysis, a syndrome associated with excessively rapid correction of hyponatremia, syphilitic arteritis, and methanol ingestion [8].

Homonymous horizontal sectoranopia, which lies along the horizontal midline, is a rare visual field defect that is usually produced by lesions of the geniculate hilum, an area supplied by the lateral posterior choroidal artery (see Fig. 5.1b). Small vascular lesions usually cause congruous defects, while compressive or infiltrative lesions tend to produce incongruous defects. Homonymous horizontal sectoranopia has been also described in damage to the anterior optic radiation, the entire

horizontal thickness of the intermediate portion of the optic radiation, and the occipital lobe in the region of the calcarine fissure. However, lesions of the occipital lobe produce more congruous sectoranopias, and there are no accompanying neurological symptoms and usually no optic atrophy [4]. Opposite to horizontal sectoranopia, ischemia of the medial and lateral portions of the lateral geniculate body that is served by the anterior choroidal artery will result in a quadruple sectoranopia (see Fig. 5.1a) [8]. There is loss of upper and lower quadrants with sparing of the horizontal sector along the horizontal meridian [9]. The unusual presentation of an "hourglass" shape to either the visual field defect or the region of spared vision has been attributed to presumed bilateral LGN damage.

Similar to lesions of the optic tract, lesions of the LGN are associated with corresponding sectorial optic atrophy of the optic disc due to retrograde axonal degeneration over time. There is "bow-tie" atrophy contralateral to the brain lesion and atrophy in the superior and inferior temporal poles of the optic disc ipsilateral to the brain lesion. The optic atrophy may be subtle in partial lesions of the LGN and may be seen only in a careful evaluation of the optic disc or demonstrated by means of spectral domain optical coherence tomography.

Homonymous sectoranopias are found infrequently in routine clinical practice, because isolated lesions of the LGN are rare, due to its small size, sheltered location, and rich anastomotic vasculature. The most common pattern of visual field loss in partial unilateral LGN damage is an incongruous hemianopia, similar to that seen with optic tract lesions. Additionally, in the majority of cases the underlying cerebral damage is diffuse and involves the neighboring optic tract and optic radiations as well, resulting in less characteristic visual field defects. A complete recovery of homonymous sectoranopias in cases of LGN damage is possible. In some cases the visual field defect may shrink to a small triangular paracentral scotoma, or there may be deterioration towards a complete homonymous hemianopia due to progression of the underlying disease [4].

5.2.2 Homonymous Quadrantanopia

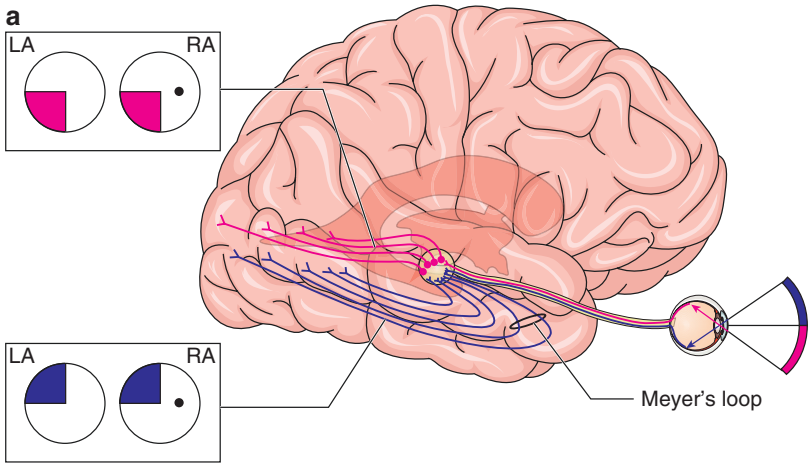
Homonymous quadrantanopias respect both the vertical and the horizontal meridian and they affect only one quadrant of the visual field, superior or inferior (Fig. 5.4a).

Depending on their extent and congruency, they are classified as complete or incomplete and congruous or incongruous. Congruous homonymous quadrantanopias point towards lesions of the occipital lobe. Damage to the superior or inferior fascicles of the posterior optic radiation or their terminations in cortical gray matter is usually the cause. On the other hand, incongruous quadrantanopias are due to lesions in more anterior portions of the visual pathway, such as the temporal or parietal optic radiation and the optic tract.

Superior Homonymous Quadrantanopia
Superior homonymous quadrantanopias may result from a lesion of the inferior fibers of the optic tract, the temporal loop of the optic radiation (Meyer loop), or the visual cortex below the calcarine fissure.

In the majority of cases, superior homonymous quadrantanopia is due to lesions of the inferior occipital lobe and the cause is an ischemic event of the posterior cerebral artery. In these cases the field defect is congruous. Immediately after the ischemic event some patients present with a complete homonymous hemianopia, which may gradually regress to a superior homonymous quadrantanopia. However, even after recovery, subtle functional deficits may still be evident in the inferior visual field, i.e., color vision disturbances [4].

The temporal loop of the optic radiation (the Meyer loop) contains fibers originating in the ipsilateral inferior temporal retina and the contralateral inferior nasal retina. Those fibers sweep anteriorly and laterally around the temporal horn of the lateral ventricle before transversing posteriorly to reach the occipital lobe. The Meyer loop hence carries information from the superior portion of the contralateral visual field. In lesions of the Meyer loop there is usually macular sparing, as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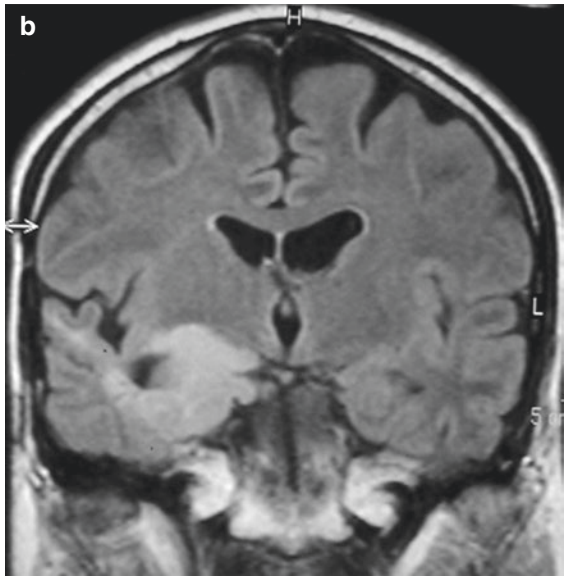
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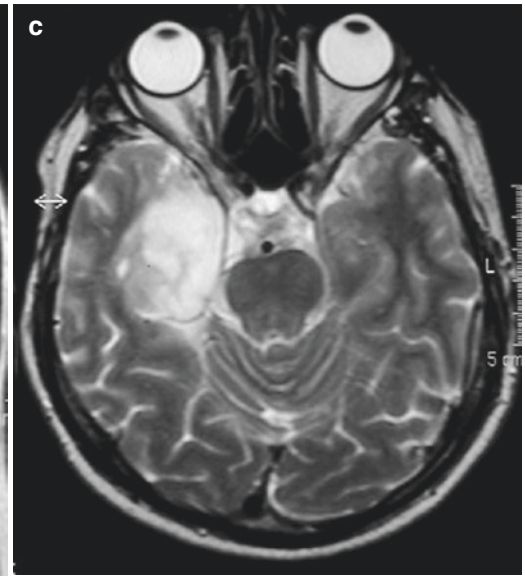
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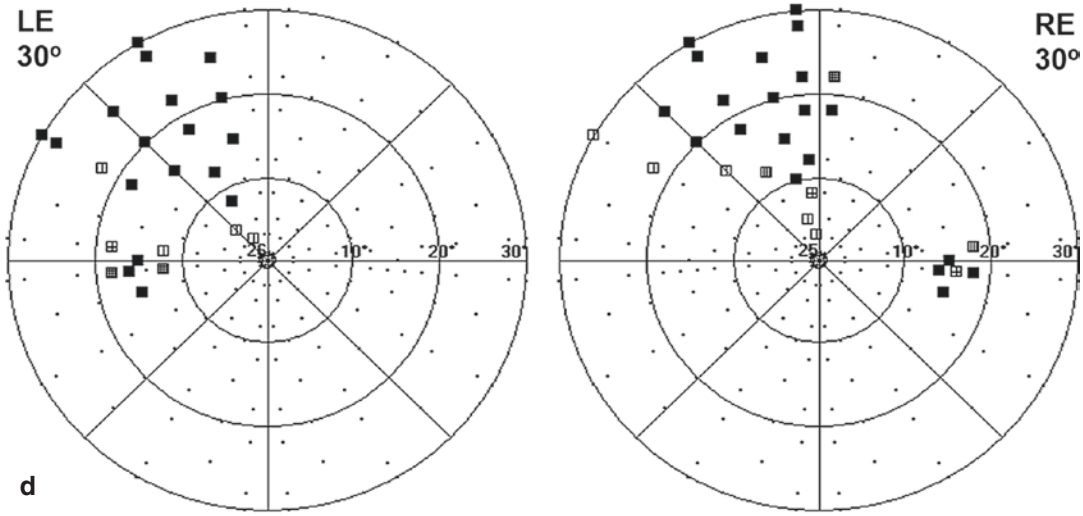
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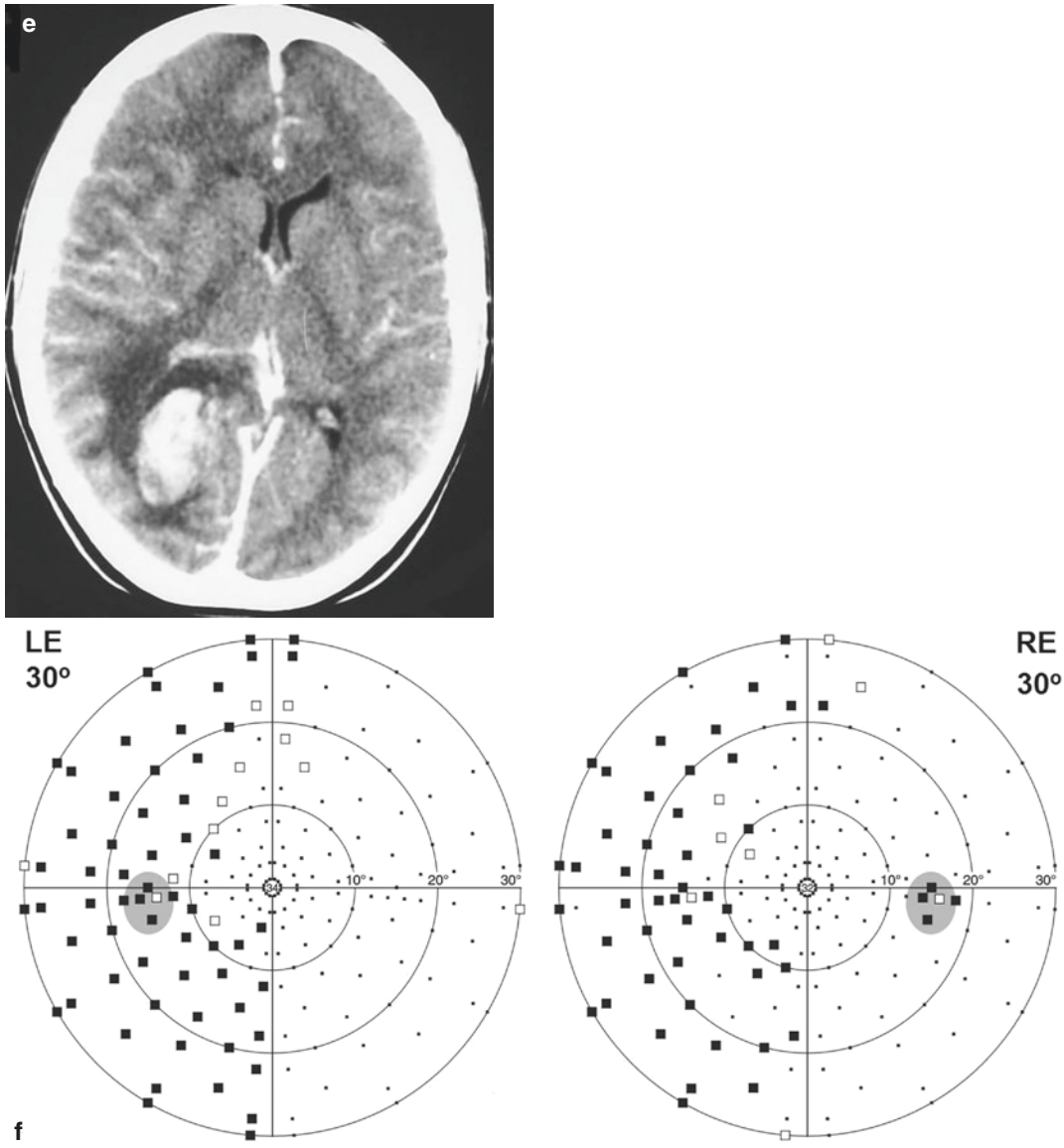

Fig. 5.4 (continued)

Fig. 5.4 (**a**) Lateral view of the right visual pathway. Information from the superior visual field (*blue)* is represented in the inferior retina and travels ventrally through the temporal lobe. Damage to this site leads to superior quadrantanopia. Information from the inferior visual field (*red*) is represented in the superior retina and travels dorsally through the parietal lobe. Lesion to this site produces an inferior quadrantanopia. (**b**) Preoperative postcontrast coronal T1 magnetic resonance image (MRI) of a 50-year-old male with an astrocytoma involving the right temporal lobe. (**c**) Preoperative T2 axial MRI of the same patient. (**d**) 30° Tuebingen automated perimetry (TAP) shows a left superior homonymous quadrantanopia presenting as "pie in the sky." The defect in the contralateral (left) eye is slightly smaller and also appears to spare points near the vertical midline. (**e**) Axial CT of a 23-year-old female with hemorrhage of an arteriovenous malformation (AVM) involving the right occipital lobe. (**f**) One week after AVM rupture there is a complete left homonymous hemianopia with macular sparing (30° TAP). (**g**) Six months after AVM rupture there is partial recovery of the homonymous defect to a left inferior quadrantanopia (Images 5.4b–g courtesy of Prof. Ulrich Schiefer, Hochschule Aalen, Germany)

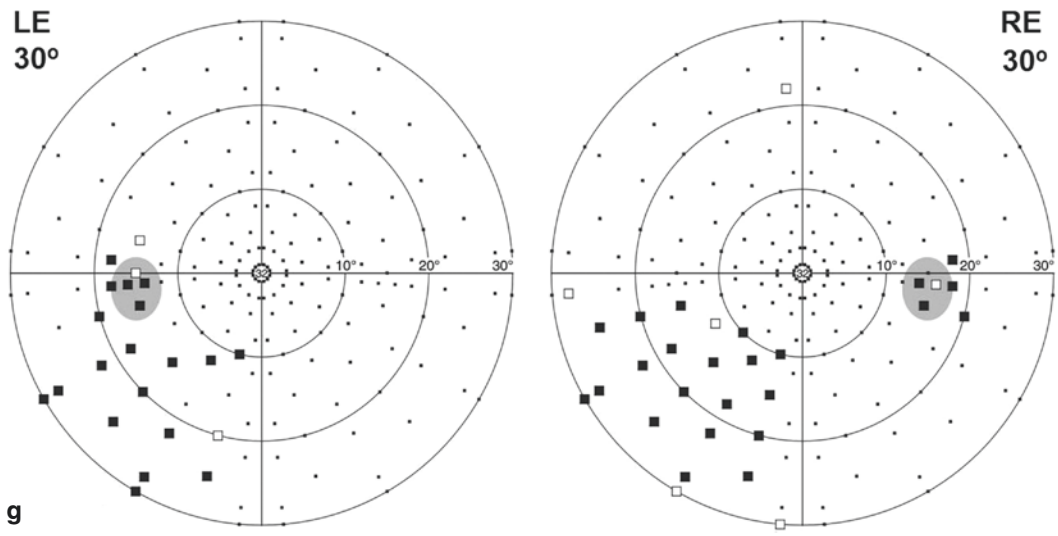

Fig. 5.4 (continued)

the fibers subserving the macula are not located anteriorly [5]. Damage of the Meyer loop within the anterior temporal lobe is associated with a contralateral homonymous superior wedge-shaped visual field defect ("pie in the sky") (Fig. 5.4b–d).

In temporal lobe lesions the superior quadrantic defect is usually incongruous, incomplete, denser above than below, and the inferior margin of the defect may cross beyond the horizontal meridian. The incongruity is not as severe as in optic tract lesions. Additionally, the defect is usually but not always larger and denser and also appears closer to the vertical midline in the ipsilateral than in the contralateral eye [10]. Those findings were based on studies of patients with temporal lobe resection and support the hypothesis that certain fibers from the ipsilateral eye travel more anteriorly and laterally in the Meyer loop. However, there are also reports from patients with temporal lobectomy, who showed more congruous visual fields with no consistent laterality regarding the severity, a finding that reflects the individual anatomic disposition of the nerve fibers within the temporal lobe [11].

Temporal lobe lesions are usually tumors or in some cases infections (abscesses). Congenital malformations, hemorrhage, infarction, demyelinating disease, and trauma (lobectomy) are encountered more rarely. In temporal lobe lesions, the patient may suffer from additional neurologic symptoms, such as complex partial seizures, headache, disturbances of memory, auditory agnosia, disturbance of hearing and sound discrimination, and auditory or formed visual hallucinations, which should prompt for a careful evaluation of the visual field.

A large area in the tip of the temporal lobe has no fibers of the Meyer loop. Studies on temporal lobectomy have shown that up to 4 cm of the anterior temporal lobe can be resected in most patients without producing a field defect [3]. Hence tumors in this area have to be relatively large, in order to produce a homonymous quadrantanopia. The tumor initially may cause only subtle incomplete defects in the superior visual field, but as it grows, the fibers of the Meyer loop are gradually affected, and the field defect progresses from the vertical down to the horizontal meridian in a stepwise fashion. With 5–7 cm resections most patients will have a superior homonymous quadrantanopia, whereas with temporal lobectomies extending beyond 8 cm, almost all patients end up with a complete homonymous hemianopia [3]. Due to the anatomical heterogeneity of Meyer loop, diffusion tensor tractography of the optic radiations is currently being used in order to assess an individual patient's risk of postoperative visual field defect [12, 13].

Inferior Homonymous Quadrantanopia Inferior homonymous quadrantanopia is encountered less frequently and is caused by damage to the optic radiation in the superior parietal lobe or the visual cortex superior to the calcarine fissure (Fig. 5.4e–g).

Compressive lesions that affect only the superior part of the optic tract are extremely rare (meningiomas, cerebral tuberculomas, meningeal carcinomatosis). More common causes of an inferior homonymous quadrantanopia are ischemic infarcts of the occipital lobe, or tumors (astrocytomas, oligodendrogliomas) and hemorrhages of the parietal lobe. Traumatic injuries are also associated mainly with inferior homonymous quadrantanopias. The reason is that traumas of the inferior occipital lobe, which would normally result in superior homonymous quadrantanopias, are often fatal due to their high complication rate and location in the vicinity of the cerebral sinuses [4].

Inferior homonymous quadrantanopias are usually more congruous than those produced by lesions of the temporal lobe. The congruity of the field defects increases as the causative lesion approaches the posterior optic radiation and visual cortex, because the retinotopic organization improves and the fascicles of visual axons become more compact. Hence lesions of the superior visual cortex or the termination of the optic radiation cause congruous inferior quadrantanopias respecting both the vertical and horizontal meridians. In anteriorly located lesions, HVFDs tend to be more incongruous: the defect may have sloping borders and cross the horizontal meridian. The reason is that within the parietal lobe the fibers of the optic radiation are not yet clearly separated into those serving the inferior visual quadrant and those serving the superior visual quadrant.

However, in contrast to the progressive nature of superior homonymous quadrantanopias in temporal lobe tumors, the visual field in the inferior quadrant is lost as a unit in cases of compressive parietal lesions, because the fibers of the optic radiation are affected as a group within the parietal lobe. Large lesions of the parietal lobe may even result in complete homonymous hemianopias with macular splitting.

If the lesion is located in the parieto-occipito-temporal junction, then an abnormal optokinetic response is present. The optokinetic nystagmus (OKN) response is poorer when the OKN stimulus is moved toward the affected hemisphere than when it is moved in the opposite direction [5]. Lesions of the parietal lobe are often accompanied by additional neurological symptoms. Patients may complain of numbness and tingling, suffer from visual neglect (usually left-sided neglect with lesions of the right parietal lobe), visual agnosia, and are often unaware of their visual field loss (anosognosia). Lesions of the dominant hemisphere can cause aphasia, apraxia, agnosia, acalculia, and agraphia.

5.2.3 Homonymous Paracentral Scotomas

A unilateral lesion at the tip of the occipital lobe causes a small, circumscribed, paracentral homonymous hemianopic visual field defect. Such defects are relatively rare. Even if their extent is limited to some degree only, they lead to severe impairment of reading ability, which is often the reason for the patient seeking medical advice [14]. Visual loss is sudden and is not associated with other focal neurological deficits. Paracentral homonymous hemianopic scotomas are circumscribed, respect both the horizontal and the vertical meridian, and are located adjacent to the area of central fixation, usually within the central 10° (Fig. 5.5) [15]. They may be perceived as "floaters," obstructing the central field of vision and leading to inability to read. Patients with right-sided defects present with hemianopic dyslexia, i.e., abnormally slow reading due to inability to see entire words and to find the following word. Patients with left-sided defects have difficulties in finding the next line. This condition has been described as "macular hemianopic reading disorder" by Wilbrand and Saenger [16].

Distance activities, such as driving or watching television, are less affected by the scotoma because the peripheral visual field is intact. Visual acuity is intact and the optic discs are normal, because the lesion is located at the tip of the occipital lobe. Interestingly, the majority of patients complain about glare, which is similar to the image which persists after looking into the sun. Photophobia has been attributed to the cortical origin of these scotomas, as patients with occipital strokes complain about similar symptoms [17, 18].

In general, homonymous paracentral scotomas result from lesions located at the occipital pole; hence defects that are located immediately adjacent to the central fixation point are usually congruous. However, there are some reports of incongruous homonymous paracentral scotomas, which leads some authors to believe that if the scotomas are

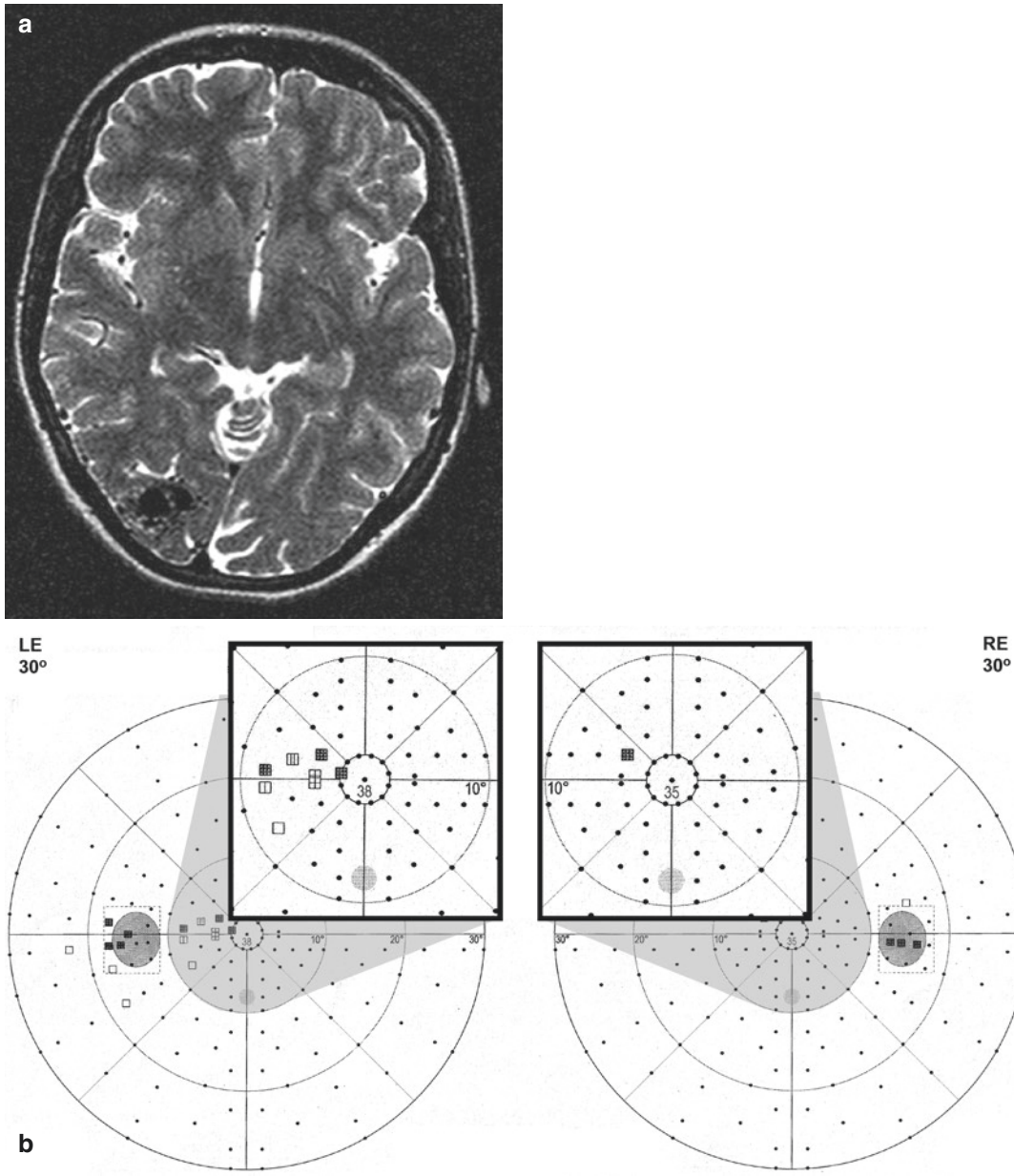

Fig. 5.5 (**a**) Axial T2 magnetic resonance image (MRI) of a 23-year-old female demonstrating resection of an arteriovenous malformation at the right occipital lobe. (**b**) Automated 30° static perimetry of the above patient 1 year after the operation. A small, left homonymous superior paracentral scotoma is shown in the central 10° (foreground). (**c**) Axial T1 MRI of a 78-year-old male showing a lesion of the left occipital pole due to an ischemic infarction of the posterior cerebral artery. (**d**) Automated 30° static perimetry of the above patient 6 months post-stroke. A small, right homonymous superior paracentral scotoma is shown in the central 10° (foreground) (From Ganssauge et al. [18], with permission)

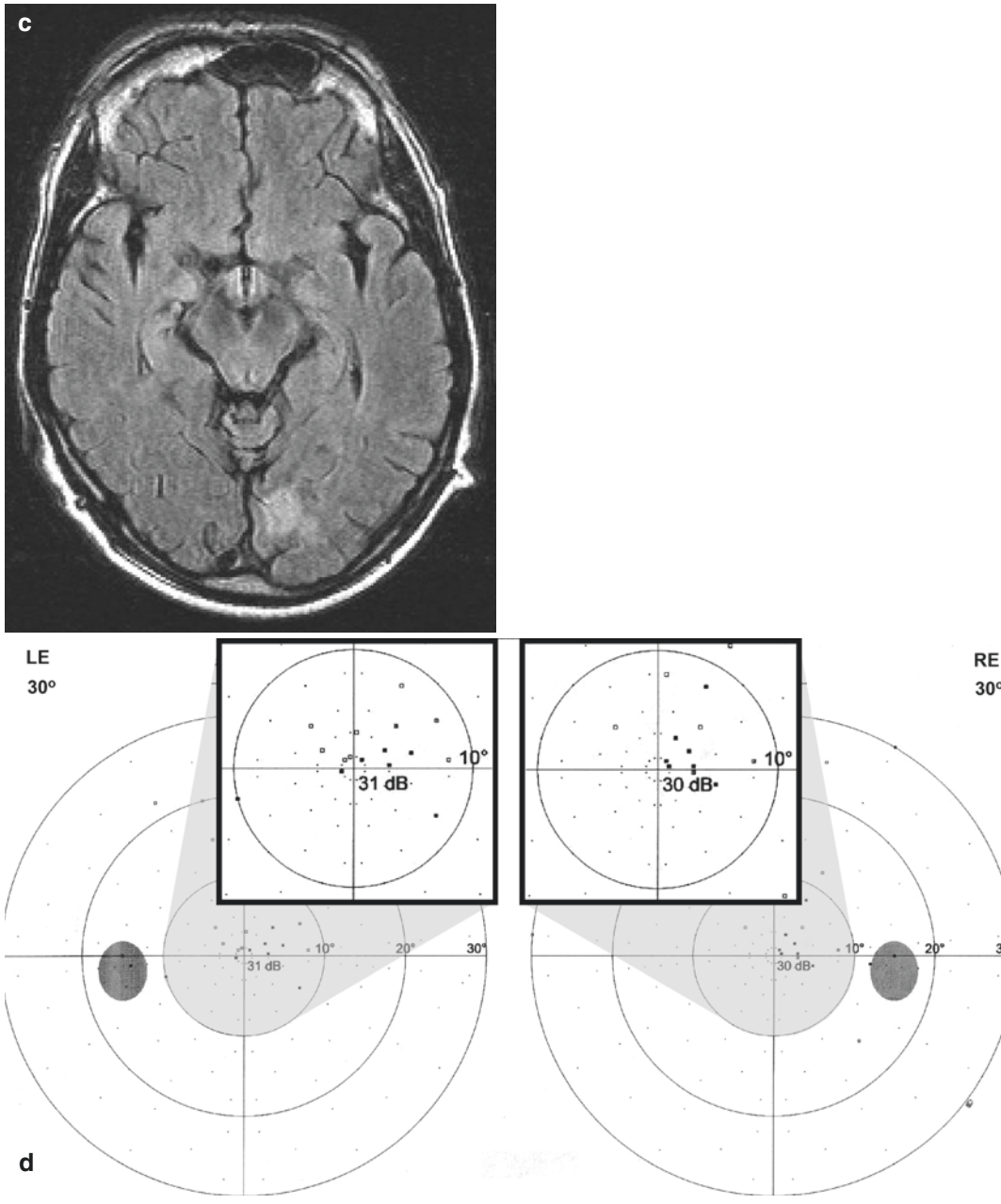

Fig. 5.5 (continued)

located further from the central fixation point, they are not necessarily congruous. This fact may actually provide evidence that retinal correspondence declines as the distance from the fovea increases.

Cerebrovascular accidents, in particular ischemic strokes, are the most common cause of paracentral homonymous scotomas, followed by traumatic brain injury. Tumors and demyelinating lesions are rare causes of homonymous paracentral scotomas [14]. A careful history, the age of the patient, the onset (sudden or gradual), and the presence of accompanying symptoms may help to differentiate the etiology and to request the appropriate neuroimaging and laboratory testing.

Due to their very limited extent and central location, paracentral homonymous hemianopic scotomas often go undetected during confrontation perimetry, and may also be misinterpreted as a nonspecific parafoveal depression or unstable fixation on standard automated perimetry [14]. Amsler grid testing is quick and effective in detecting such subtle paracentral scotomas, given that visual acuity is better than 20/40. If a small homonymous paracentral scotoma is suspected, automated perimetry should specifically assess the central visual field with a spatially denser perimetric grid.

5.2.4 Homonymous Hemianopia

Complete homonymous hemianopias may be caused by lesions in any part of the retrochiasmal visual pathway, including the optic tract, LGN, optic radiation, and occipital lobe. Hence a complete homonymous hemianopia is nonlocalizing, and the examiner should seek for other signs of neurological dysfunction prior to obtaining neuroimaging studies. Most lesions of the optic radiations and occipital lobe are associated with vascular disease, while most optic tract lesions are due to compressive masses. Additionally, HVFDs due to optic tract lesions tend to be incongruous, whereas lesions of the optic radiations cause only mild incongruity and occipital lobe lesions are highly congruous.

Lesions of the Optic Tract Etiologies of optic tract lesions are similar to those of chiasmal lesions, and combined damage to the optic tracts, chiasm, and optic nerve is not uncommon. The most frequent causes are tumors (pituitary adenomas, meningiomas, gliomas, and craniopharyngiomas) and aneurysms of the internal carotid artery, followed by cavernous angiomata, arteriovenous malformations, demyelinating disease, abscess, trauma, and neurosurgery (anterior temporal lobectomy, placement of intraventricular shunt) [1]. Congenital absence of the optic tract with contralateral homonymous hemianopia is a rare entity and has been attributed to either a primary failure of development or secondary atrophy due to focal injury during the perinatal period [19].

Lesions of the optic tract cause a triad of characteristic clinical findings that often permit localization of the lesion: homonymous hemianopia, a relative afferent pupillary defect (RAPD) and "bow-tie" optic atrophy, all contralateral to the brain lesion. In unilateral optic tract lesions visual acuity is usually spared unless there is bilateral tract damage or extension of the lesion to the optic chiasm or optic nerves. Optic tract lesion HVFDs are usually partial and produce markedly incongruous HVFDs due to the poor topographic alignment of corresponding retinal fibers from the two eyes [5]. However, there are exceptions to this rule, because approximately 50% of optic tract lesions produce congruous HVFDs [6]. Complete transaction of the optic tract is less frequent than partial lesions, and produces a congruous complete hemianopia.

Retrograde degeneration of the axons in the optic tract causes a distinct pattern of optic atrophy over time, which is evident in both eyes. The optic disc contralateral to the brain lesion demonstrates "bow-tie" atrophy in the nasal and temporal sectors, while the optic disc ipsilateral to the brain lesion has temporal disc pallor [20]. This pattern of optic atrophy can be explained by the underlying organization of the retinal ganglion cell layers: The affected optic tract contains crossed fibers from the contralateral nasal retina (nasal disc) and nasal half of the macula (temporal disc in the papillomacular bundle), and uncrossed fibers from the ipsilateral superior and inferior sectors that correspond to the temporal retina (temporal disc).

Lesions of the Optic Radiation The type of homonymous visual field loss in lesions of the optic radiation reflects the site of damage. The optic radiation can be affected in various locations during its course and produce characteristic

HVFDs. Large lesions of the parietal lobe produce complete homonymous hemianopias with macular splitting, because the entire optic radiation travels into the deep white matter of the parietal lobe. Mildly incongruous, incomplete homonymous hemianopias, denser below than above, may also occur in those cases. However, the HVFDs are more congruous than those observed in optic tract lesions. A complete homonymous hemianopia can also be caused by large lesions of the optic radiation close to its termination in the striate cortex. On the other hand, partial lesions of the dorsal fibers in the parietal lobe produce a contralateral inferior homonymous quadrantanopia, and lesions of the ventral fibers in the anterior temporal lobe cause a contralateral superior homonymous quadrantanopia, as described above (see Fig. 5.4). However, with damage extending beyond 8 cm from the anterior temporal tip, almost all patients will have a complete homonymous hemianopia, because both upper and lower optic radiations are affected.

Until recently it was thought that lesions of the retrogenicate pathway do not lead to optic atrophy (with the exception of some congenital lesions) or pupillary defects. However, recent optical coherence tomography advances have demonstrated that subtle retinal nerve fiber layer loss also occurs in retrogeniculate lesions, even if it is not visible clinically [21–23]. Unlike lesions of the optic tract, the most common causes of optic radiation damage are infarcts in the posterior cerebral or middle cerebral artery territories, followed by tumors, arteriovenous malformations, and infections.

Lesions of the Occipital Lobe In the striate cortex there is strict retinotopic organization of the fibers subserving the various portions of the visual field. The macula is represented at the posterior pole of the occipital lobe, and the far peripheral visual field at the anterior portion of the visual cortex, on the medial occipital surface [24, 25]. The most anterior bank of striate cortex (8–10%) represents the monocular temporal crescent (temporal 30° of the contralateral eye). This area receives input only from the contralateral eye, since the nasal hemifield of the ipsilateral eye does not extend beyond 60°.

Occipital lesions affecting both the upper and lower banks of the striate cortex cause highly congruous homonymous hemianopias. The most common causes of unilateral occipital lobe damage are vascular and traumatic, followed by arteriovenous malformations, infections, tumors, and demyelinating disease. The patient usually exhibits sudden visual loss and sometimes headache. If there is involvement of the entire striate cortex, then a macular splitting homonymous hemianopia is present. However, macular splitting homonymous hemianopias arise from lesions anywhere in the visual pathway; hence they do not have localizing value.

The macular area has a disproportionally large representation in the visual cortex retinotopic map, which is called cortical magnification (Fig. 5.6). Approximately 50–60% of the visual cortex represents the central 10°, and about 80% of the visual cortex represents the central 30° [24]. This cortical magnification offers an extremely high central acuity (spatial resolution of 60–100 cycles/degree), which declines towards the visual field periphery. A macular sparing hemianopia is one that spares an area of at least 3° of radius from fixation [5]. Macular sparing, which is considered characteristic for occipital lobe lesions, is most likely due to the large macular representation and the collateral blood supply from the middle cerebral artery, which protects the macular region from ischemia [4]. Strokes tend to produce macular sparing much more commonly than other causes, such as tumors or trauma. In contrast, more anterior lesions, for example in the optic radiation, produce macular splitting, because there is no collateral circulation. In general, a patient with a macular sparing homonymous hemianopia most likely has a lesion in the occipital lobe, and the cause is almost always a posterior cerebral artery infarction due to cardiac emboli or vertebrobasilar occlusive disease [4].

An occipital lesion can be restricted to either the upper or lower bank of the striate cortex, producing a highly congruous homonymous inferior or superior quadrantanopia, respectively. Isolated damage to the occipital lobe usually does not produce other neurologic manifestations, and the patient is fully or partially aware of the hemianopia, unless the lesion is more extensive or involves more anterior structures in the parietal lobe. In such cases there is anosognosia for the visual field loss, especially if the lesion is located in the right cerebral hemisphere.

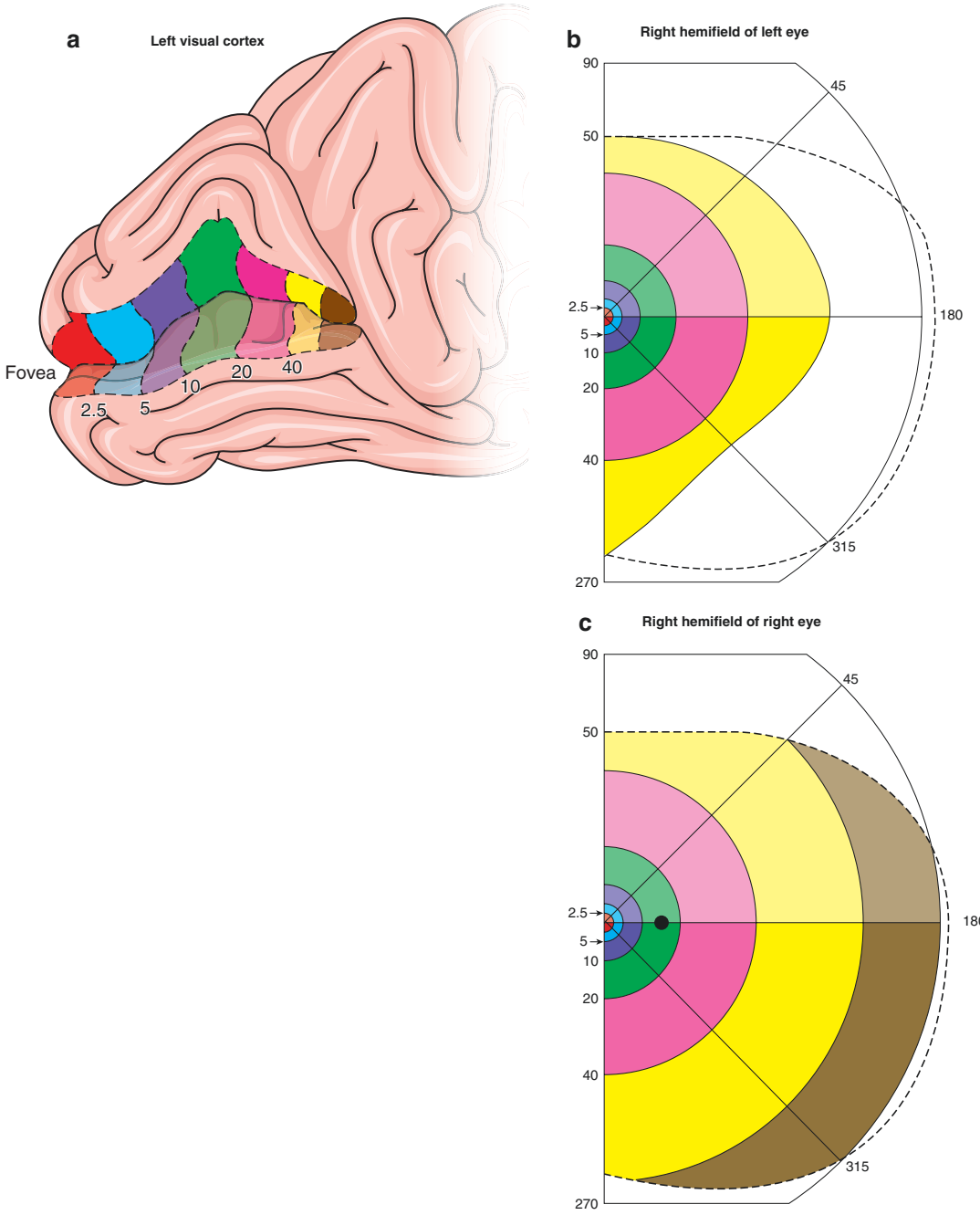

Fig. 5.6 Representation of the right visual field in the left visual cortex. (**a**) Retinotopic organization of the left visual cortex. There is disproportionate representation of the central visual field, termed "cortical magnification." (**b**) Corresponding right (nasal) hemifield of left eye. (**c**) Right (temporal) hemifield of right eye. The monocular temporal crescent is the most peripheral part of the visual field (*gray*)

5.2.5 Peripheral Homonymous Visual Field Defects

HVFDs typically involve the central 10° of vision. Peripheral homonymous scotomas, which extend beyond 30° from fixation, but spare the temporal crescent, are extremely rare (Fig. 5.7). Peripheral HVFDs commonly result from lesions in the intermediate area of the striate cortex, between the anterior and posterior confines, and spare the most anterior portion of the striate cortex and the occipital pole [26].

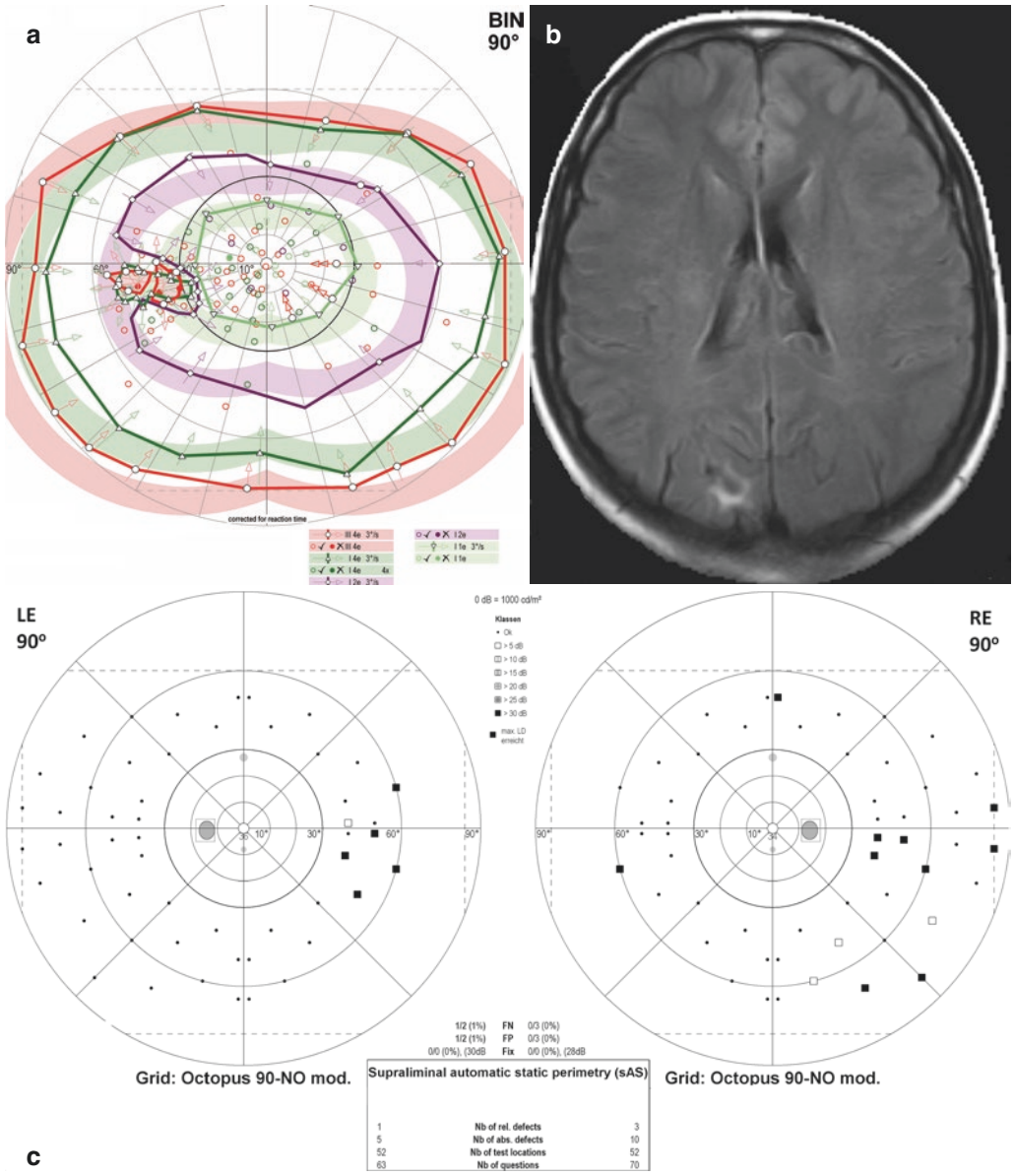

Fig. 5.7 (**a**) A 39-year-old female with left inferior homonymous peripheral scotoma, extending between 30° and 50° along the horizontal meridian (90° binocular semiautomated kinetic perimetry). (**b**) Axial fluid-attenuated inversion recovery (FLAIR) magnetic resonance image (MRI) of the above patient shows ischemic infarction of the right occipital cortex that spares the occipital pole and the most anterior part of the visual cortex. (**c**) A 54-year-old male with right homonymous peripheral scotomas extending between 30° and 60° are present in both eyes (90° static perimetry). (**d**) Axial FLAIR MRI of the above patient shows ischemia of the left occipital cortex with sparing of the occipital pole and anterior occipital lobe (From Papageorgiou et al. [27], with permission)

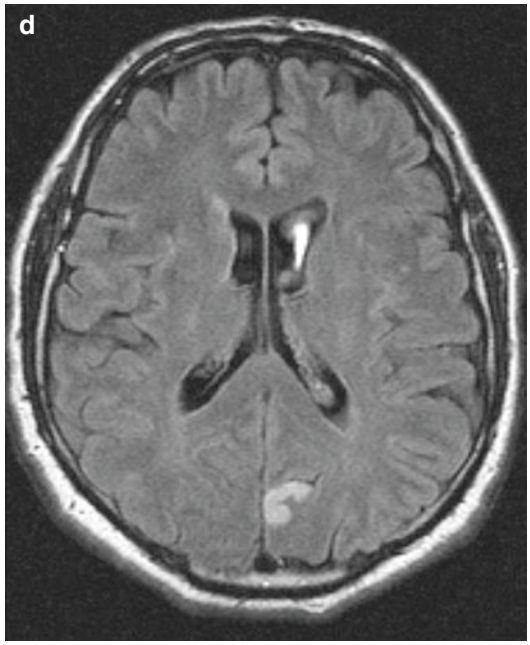

Fig. 5.7 (continued)

Such HVFDs may escape diagnosis for various reasons. First, the patient usually does not have severe symptoms, due to the low spatial resolution of the peripheral visual field. Second, routine visual field assessment involves automated static perimetry within the central 30°. Third, the development of collateral circulation may also explain the paucity of pure peripheral HVFDs. Peripheral HVFDs may present as subtle single-defect points on the outer border of the 30° visual field in both eyes and may sometimes be misinterpreted as perimetric artifacts [27]. However, if there is suspicion of a homonymous pattern the clinician should obtain kinetic or static perimetry of the 90° field (see Fig.5.7).

5.2.6 Temporal Crescent

In each eye, the portion of the temporal field between 60° and 90° from fixation has no correlate in the nasal field of the fellow eye. This so-called temporal crescent is represented at the most anterior portion of the contralateral occipital lobe. This area constitutes less than 10% of the striate cortex, is supplied by the parieto-occipital artery, and is susceptible either to selective damage or to selective sparing by disease processes [28]. Lesions in the posterior visual cortex tend to spare the temporal crescent, while those in the anterior visual cortex tend to involve it [29]. If the occipital lesion spares this anterior 8–10% of the striate cortex, there will be a contralateral homonymous hemianopia with a spared monocular temporal crescent (Fig. 5.8). The ipsilateral eye will show a nasal hemianopia, whereas the contralateral eye will show a temporal hemianopia with a spared crescent-shaped island of vision in the far periphery.

Conversely, a retrosplenial lesion along the parieto-occipital sulcus will produce a contralateral monocular temporal crescentic scotoma. This is also called a half-moon syndrome [30]. The differential diagnosis of a monocular temporal crescent scotoma includes a lesion in the ipsilateral retina (i.e., nasal retinoschisis), the contralateral Meyer loop, or the contralateral rostral visual cortex. The temporal crescent is not detected on 30° static automated perimetry and should be evaluated with Goldmann 90° kinetic perimetry [31].

The most rostral part of the Meyer loop, near the apex of the inferior horn of the lateral ventricle, contains fibers originating in the contralateral peripheral nasal hemiretina, which subserve the part of the visual field that is always monocular (the temporal crescent). Therefore, damage of this area can cause a contralateral temporal crescent scotoma as well. More extensive lesions involving the Meyer loop will produce a contralateral superior quadrantanopia, as described above.

5.2.7 Bilateral Homonymous Visual Field Defects

Bilateral homonymous visual field defects occur as a result of bilateral postchiasmatic lesions, which may be located at different sites along the right and left visual pathway (Fig. 5.9). Such lesions are not rare and constitute approximately 8% of HVFDs [5].

Bilateral HVFDs are usually the result of vascular occipital lobe lesions. The most common cause

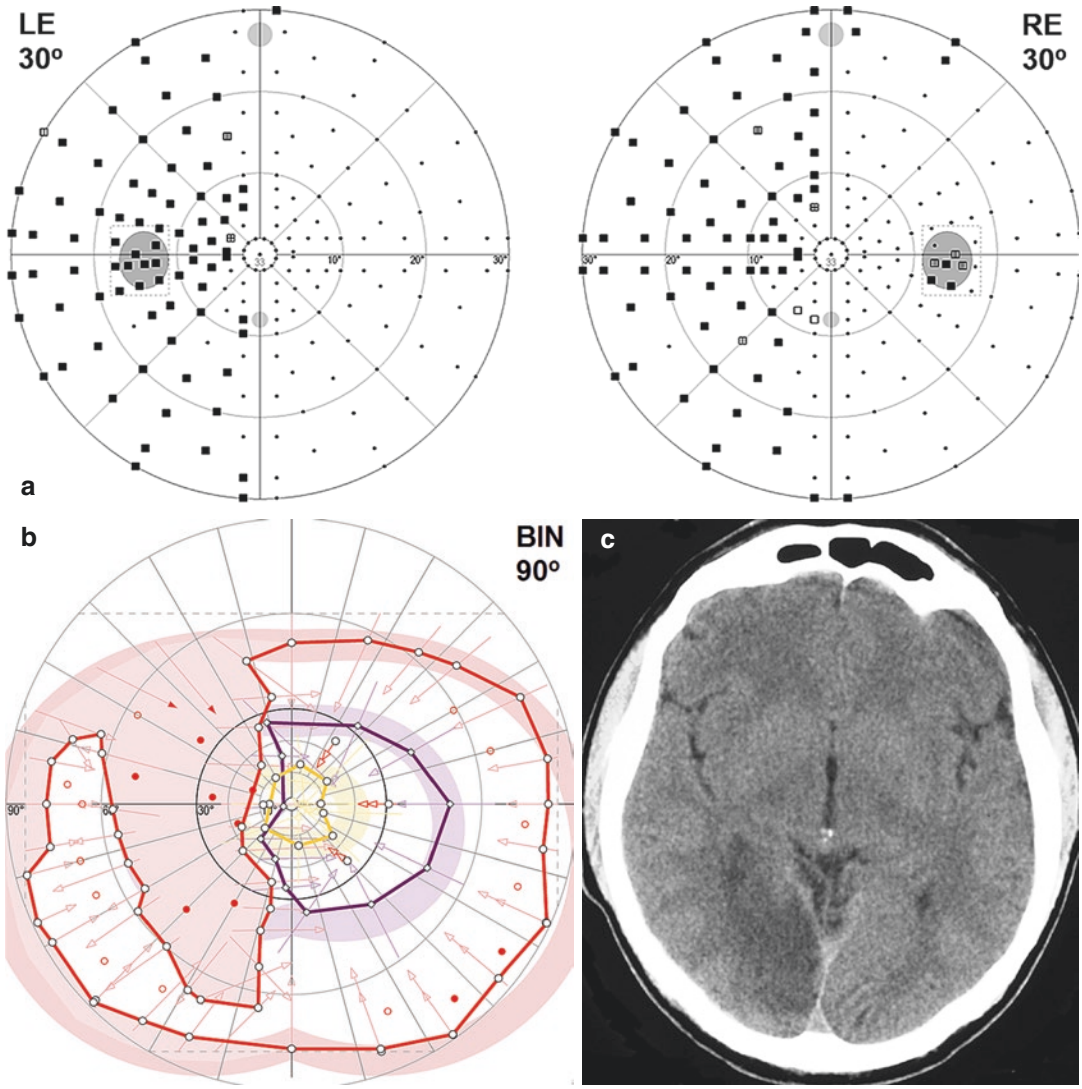

Fig. 5.8 (**a**) Octopus monocular 30° static automated perimetry of a 53-year-old male shows a left homonymous hemianopia with macular sparing. (**b**) Octopus binocular 90° semiautomated kinetic perimetry (SKP) reveals sparing of the temporal crescent beyond the peripheral 60°. (**c**) Axial CT demonstrates ischemic infarction of the right occipital lobe with sparing of its most anterior portion

is posterior cerebral artery infarction that can affect both striate cortices, either simultaneously or sequentially, due to the common origin of the right and left posterior cerebral arteries from the basilar artery. It has been estimated that 16% of patients with a unilateral occipital infarction develop bilateral infarction over 6 months [32]. Other causes of bilateral HVFDs are occipital tumors, trauma, inflammation, or infection affecting both striate cortices concurrently.

If both occipital lobes are simultaneously affected, there is complete vision loss, i.e., cerebral blindness, which is usually transient, lasting from minutes to days, and may recover to a variable degree of bilateral incomplete HVFDs with macular sparing.

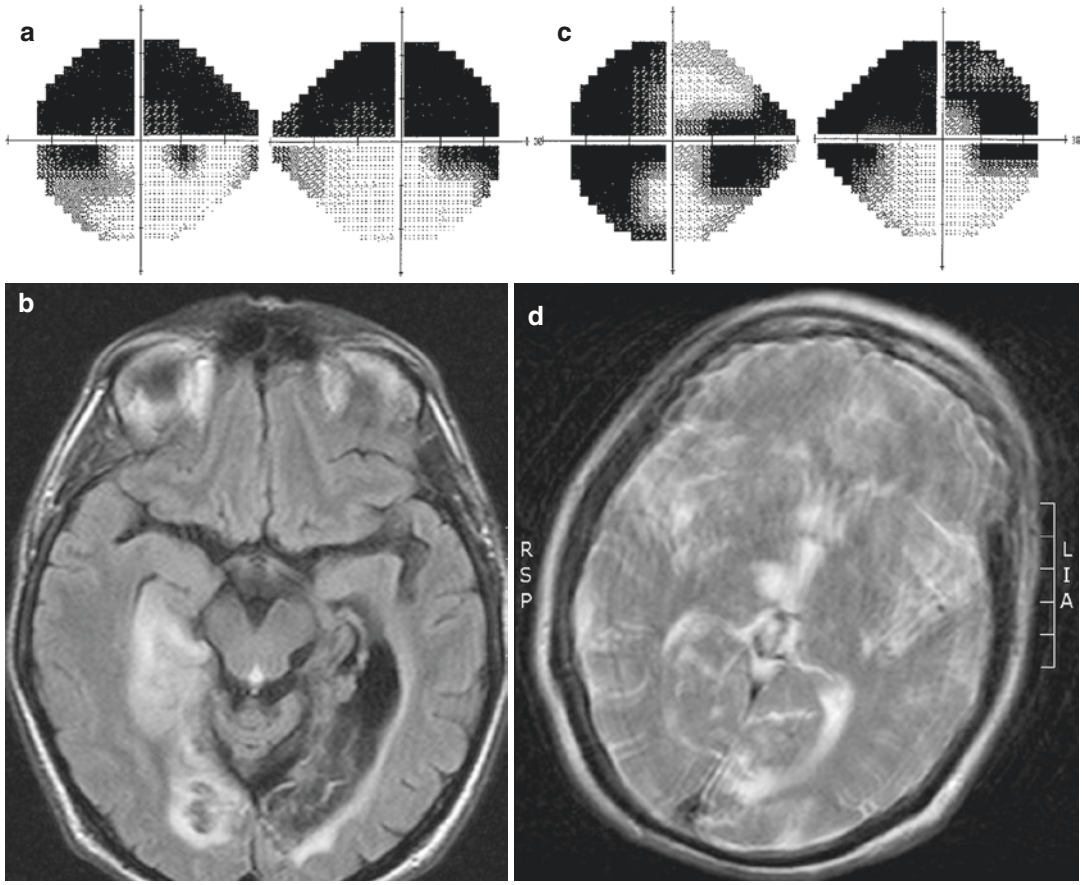

Fig. 5.9 (**a**) Humphrey 24–2 static automated perimetry of a 57-year-old male demonstrating bilateral superior homonymous quadrantanopia, which resembles superior altitudinal visual field defects. (**b**) Axial fluid-attenuated inversion recovery magnetic resonance image (MRI) showing bilateral lesions of the inferior occipital lobe. There is a subacute right posterior cerebral artery (PCA) territory infarct involving the right posterior temporal lobe and occipital cortex and an old left PCA territory infarct. (**c**) Humphrey 24–2 static automated perimetry of an 83-year-old female showing bilateral homonymous visual field defects, i.e., a left incomplete homonymous hemianopia and a right homonymous horizontal sectoranopia with macular sparing. (**d**) Axial T2 MRI demonstrates an acute infarct in the right thalamus and an old left PCA infarct

Much more commonly, bilateral HVFDs are associated with consecutive vascular infarctions of the posterior cerebral circulation. Except for the visual symptoms, occipital lobe lesions are generally not associated with other neurological problems; hence patients do not always present in the acute setting. In such cases it may be difficult to determine the exact time of onset of bilateral ischemic lesions and to decide if they were due to single or consecutive events [4]. Patients with unilateral brain lesions of the visual pathway are not always aware of the accompanying HVFD until they suffer a second event in the contralateral hemisphere weeks to years later, causing a more pronounced visual impairment.

Bilateral occipital lobe lesions either from a single or from consecutive events may lead to complete bilateral homonymous hemianopia with no macular sparing, which is called cortical or cerebral blindness. More often, however, there is some degree of macular sparing

giving rise to "keyhole" visual fields [10]. The degree of macular sparing may be different on each side, and reading ability depends on the residual central visual field. Affected individuals are severely handicapped in their everyday life, as they suffer from "tunnel vision" [5]. Occasionally bilateral paracentral HVFDs with macular sparing and intact periphery present as "ring" scotomas. In rare instances, bilateral HVFDs affect only the central area with preservation of the peripheral visual field, and manifest as bilateral central scotomas that may resemble ocular disease [4]. The presence of a vertical step on careful perimetric testing differentiates these defects from a true central scotoma due to retinal or optic nerve disease. Patients with bilateral central HVFDs do not have mobility problems, because the visual field periphery is preserved. However, they have difficulties with reading, face recognition, and other activities that require intact central vision.

Crossed homonymous quadrantanopias ("checkerboard" visual fields) present in lesions of the superior occipital lobe (above the calcarine fissure) on one side, and the inferior occipital lobe (below the calcarine fissure) on the opposite side [33]. Such defects are usually the result of sequential rather than simultaneous infarctions. In some instances, checkerboard visual fields occur after recovery from a single vascular event associated initially with cerebral blindness.

Other patterns of visual field loss in bilateral occipital disease include bilateral altitudinal defects, i.e., bilateral superior or inferior homonymous quadrantanopias, which occur when bilateral brain lesions are located below or above the calcarine fissure respectively (see Fig. 5.9a). Ischemic events of the posterior cerebral artery tend to produce mainly bilateral superior altitudinal hemianopias. On the other hand, bilateral inferior altitudinal defects usually result from tumors and traumas, such as bullet wounds. As mentioned above, the superior occipital lobe is more vulnerable to traumatic injuries. Traumatic lesions of the inferior occipital lobe are often fatal due to their location in the vicinity of the cerebral sinuses and the resulting hemorrhage [4]. Finally, the most common tumors of the occipital lobe leading to bilateral superior or inferior altitudinal HVFDs are meningiomas.

Bilateral HVFDs, especially in the form of incomplete hemianopias with macular sparing, central scotomas, ring scotomas, or altitudinal defects, must be distinguished from bilateral optic nerve or retinal disease. For example, bilateral superior or inferior altitudinal defects may occur due to bilateral retinal or optic nerve damage, such as anterior ischemic optic neuropathy, ischemic retinal lesions, choroiditis, choroidal colobomas, glaucoma, optic nerve hypoplasia, tilted discs, drusen, and intracranial masses affecting the chiasm or both optic nerves. Apart from the pathological fundus findings, careful observation of the perimetric results in the above cases reveals that the pattern of visual field loss is usually asymmetric and not homonymous, i.e., does not respect the vertical meridian. True bilateral HVFDs respect the vertical meridian; there are normal pupillary, oculomotor, and funduscopic findings, and visual acuity is usually normal or decreased symmetrically [10].

Cerebral Blindness Cerebral blindness is a general term that refers to bilateral severe vision loss from damage posterior to the lateral geniculate nuclei. Cerebral blindness can be persistent or transient. The most common cause of persistent cerebral blindness is infarction due to embolic or thrombotic events. Transient cerebral blindness can last hours to days and often recovers fully.

There are many causes of cerebral blindness, such as vertebrobasilar arteritis, subclavian steal, hypoxia, hemorrhage, generalized hypotension from antihypertensive medications such as nifedipine, and rupture of occipital mycotic aneurysms with endocarditis. Cerebral blindness can also complicate cardiac surgery, due to hemodynamic compromise or emboli. Causes of transient cerebral blindness include seizures (ictal or postictal), migraine, posterior reversible encephalopathy syndrome, demyelinating disease, metabolic insults (hepatic encephalopathy, hypoglycemia, alcoholic ketoacidosis, adrenoleukodystrophy, and acute intermittent porphyria),

eclampsia, hydrocephalus, cerebral venous thrombosis, and toxins, especially chemotherapeutic agents (cyclosporine and tacrolimus). Other etiologies include tumors, meningitis, radiation encephalopathy, Alzheimer disease, cerebral angiography, and infection (Creutzfeldt-Jakob disease, encephalitis, and abscess) [34].

Cortical Blindness Cortical blindness is a subset of cerebral blindness resulting from bilateral damage to the visual cortex. Visual acuity in cortical blindness is perception of light or worse, while pupillary responses and funduscopic findings are normal.

The most common cause of cortical blindness is infarction to both occipital lobes in the area supplied by the posterior cerebral arteries due to embolic or thrombotic events. With onset of the ischemic event there is usually complete blindness, but in most cases there is some recovery of the central visual field within the next few days or weeks [35]. Interestingly, some patients with unilateral occipital infarctions report total blindness during the first minutes of the ischemic event. Occasionally, an initial centripetal constriction of the visual field with subsequent improvement in a ring-like centrifugal direction is noted [4].

Transient cortical blindness can also complicate a severe head trauma due to traumatic vasospasm and cerebral edema. Those cases are usually associated with further neurological deficits, such as confusion, vertigo, headache, vomiting, and loss of consciousness. Approximately 1% of patients with severe closed head trauma experience posttraumatic cortical blindness, which occurs at the time of the injury or shortly after that [34]. Prognosis is favorable in children and adolescents and vision usually recovers fully within the next day. The course is more variable in adults, who occasionally suffer from residual visual field defects. Persistent cortical blindness due to head trauma is rare, because such patients usually have associated fatal injuries to the sinuses, the brainstem, and the cerebellum.

Cortical blindness has recently been recognized in patients with posterior cortical atrophy, which is an unusual visual variant of Alzheimer disease [36]. In those cases, cortical visual loss is usually severe and ranges from homonymous hemianopia to bilateral concentric constriction of the visual field. Visual disability is the predominant symptom and occurs prior to the onset of memory loss, dementia, and other psychiatric symptoms. A combination of history, clinical presentation, and neuroimaging points towards the correct diagnosis. MRI of affected individuals can be normal or demonstrate occipital, parietal, and temporal atrophy. Positron emission tomography scans are more characteristic and usually display hypometabolism in the brain areas corresponding to visual deficits [36].

Approximately 10% of patients with cortical blindness suffer from Anton syndrome, which is also known as visual anosognosia. Affected patients deny their blindness and behave as if they can see despite objective evidence of visual loss. However, Anton syndrome is not pathognomonic for lesions of the visual cortex, as it can also occur in some unusual cases of bilateral optic neuropathy with bilateral frontal lobe disease [37].

Cortical blindness must be differentiated from nonorganic visual loss in patients who claim complete blindness. Pupillary responses are normal in both cortical blindness and functional visual loss. However, patients with cortical blindness do not blink to threat or show OKN. The value of visual evoked potential (VEP) testing in this setting is limited due to the possibility of false positive results.

5.2.8 Monocular Hemianopia

Monocular hemianopia is typically a functional disorder or, less often, is associated with uncommon manifestations of organic disease.

Organic monocular temporal hemianopia is a rare disorder that may result from optic nerve damage immediately anterior to the optic chiasm or retinal disease, such as occlusion of central retinal arterioles, retinoschisis, retinal detachment, paraneoplastic retinopathy, inflammation, or

trauma ("pseudo-hemianopic" defect). In most cases it is caused by suprasellar or juxtasellar lesions such as pituitary adenomas, tuberculum sella meningiomas, craniopharyngiomas, and astrocytomas [38]. Monocular temporal hemianopia has been also attributed to dysversion of the optic disc, optic nerve hypoplasia, optic neuritis, and septo-optic dysplasia [39]. The lesion involves the ipsilateral optic nerve close enough to the chiasm in order to selectively damage the ipsilateral nasal crossing fibers, but spare the contralateral nasal crossing fibers from the fellow optic nerve. Unilateral nasal hemianopia is extremely rare, and, when organic, it has been attributed to subcapsular or traumatic cataract, and lesions compressing the temporal side of the optic nerve, such as meningioma, aneurysms, dolichoectatic carotid artery, optochiasmatic arachnoiditis, and pituitary tumors [40–44].

The persistence of hemianopia on binocular testing and the absence of a RAPD easily distinguish functional hemianopia from genuine hemifield loss [45]. Organic temporal monocular hemianopia has never been described with normal pupillary responses. Further signs, such as optic disc pallor, color vision abnormalities, and abnormalities on VEP testing, can help identify organic causes for the visual field loss. In those cases, one must perform neuroimaging with particular attention to the sella turcica and parasellar regions in order to exclude compressive lesions.

5.3 Heteronymous Visual Field Defects

Heteronymous visual field defects respect the vertical meridian, but affect opposite sides of the visual field in each eye, i.e., bitemporal or binasal hemianopia (Fig. 5.10).

5.3.1 Bitemporal Hemianopia

Bitemporal hemianopias are much more frequent than binasal hemianopias and indicate chiasmal pathology. Pituitary adenomas are the most common cause of bitemporal hemianopia (see Fig. 5.10d). Occasionally, other parasellar or suprasellar lesions, such as meningioma, craniopharyngioma, glioma, aneurysm, and trauma, can lead to bitemporal hemianopia. Rare causes of bitemporal hemianopia are inflammatory conditions such as atypical optic neuritis, Wegener granulomatosis, syphilis, sarcoidosis and brain abscess, and vascular disorders such as pituitary apoplexy, vascular malformations, cavernous sinus disease, and radiation neuropathy [5]. Internal hydrocephalus is an unusual cause of bitemporal hemianopia. Blockage of cerebrospinal outflow dilates the third ventricle, which compresses the chiasm [46].

Pituitary tumors and masses located inferior to the chiasm grow up out of the sella turcica and press on the underside of the chiasm. Due to the anterior inferior position of decussating inferior nasal fibers, such lesions initially produce superior temporal visual field defects, which then evolve to complete bitemporal hemianopia. In contrast, lesions located above the chiasm, such as craniopharyngiomas, tend to cause inferior temporal visual field defects initially, which then progress to complete bitemporal hemianopia [5].

Variable patterns of visual field loss in chiasmal processes are due to individual anatomical variations in the positional relationship between the chiasm and the diaphragma sellae [47]. In 9% of the population the optic chiasm is prefixed and lies anterior to the pituitary gland. In those cases suprasellar masses produce incongruous homonymous hemianopia or quadrantanopia by damaging the optic tract(s). In 11% of the population the chiasm is postfixed (posterior to the pituitary gland) and its compression causes monocular or highly asymmetric visual field loss field such as a junctional scotoma. In the majority of cases (80%) the chiasm lies directly over the pituitary fossa; therefore, upward extension of pituitary masses produces bitemporal hemianopia with the superior field more involved than the inferior. Bilateral loss of the temporal hemifields causes postfixational blindness and the hemifield slide phenomenon, which are described in Chap. 4.

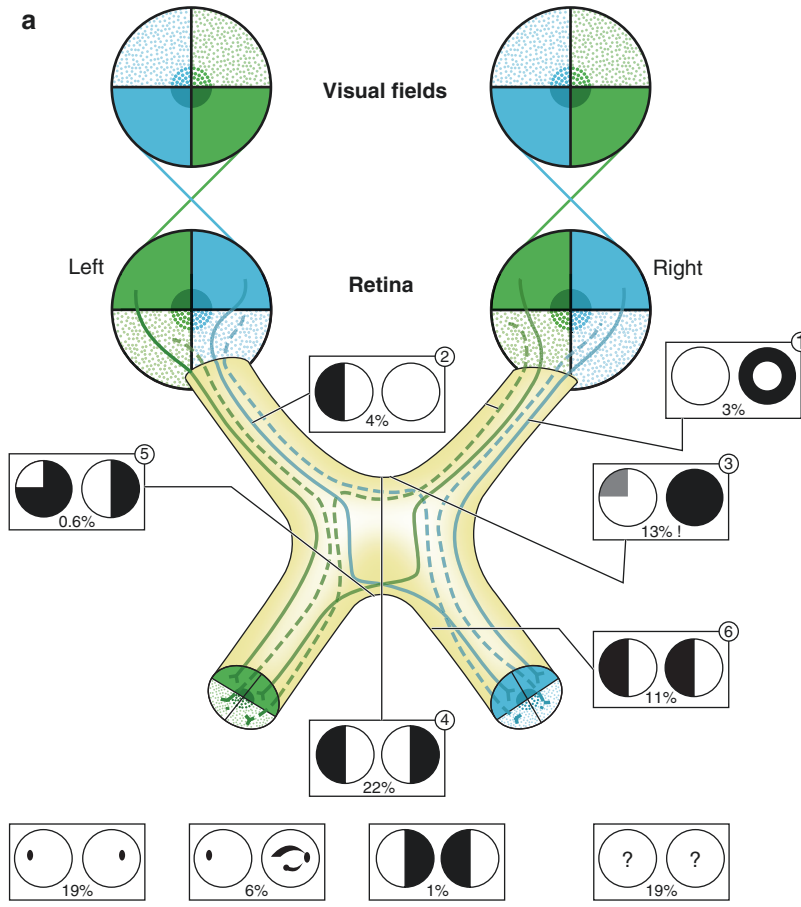

Fig. 5.10 (**a**) Projection of the visual fields onto the retina and course of the retinal ganglion cell axons in the region of the chiasm. Sites of damage and corresponding visual field defects with their frequency of occurrence are shown (modified from Schiefer et al. [5] and Schiefer et al. [47]). (1) Compressive optic neuropathies. (2) Partial prechiasmal lesion affecting the fibers, which carry signals from the nasal hemiretina and correspond to the temporal hemifield. (3) Anterior junction syndrome due to damage of the ipsilateral optic nerve and the anterior Wilbrand knee. Fibers from the contralateral inferior nasal retina that extend anteriorly into the affected ipsilateral optic nerve form the so-called anterior Wilbrand knee, and correspond to the superior temporal quadrant of the visual field. (4) Bitemporal hemianopia from central chiasmal damage. (5) Posterior junction syndrome due to damage to the posterior knee of Wilbrand, which carries signals from the ipsilateral superior nasal retina that correspond to the inferior temporal quadrant of the visual field. This ipsilateral inferior temporal scotoma is combined with a contralateral homonymous hemianopia. (6) Optic tract lesion. (**b**) Coronal section of the sellar and parasellar regions surrounding the pituitary gland. (**c**) Sagittal section of the chiasmal region. (**d**) Bitemporal hemianopia from central chiasmal compression, i.e., pituitary adenoma. (**e**) Anterior junction syndrome from compression at the level of the junction between the left optic nerve and chiasm

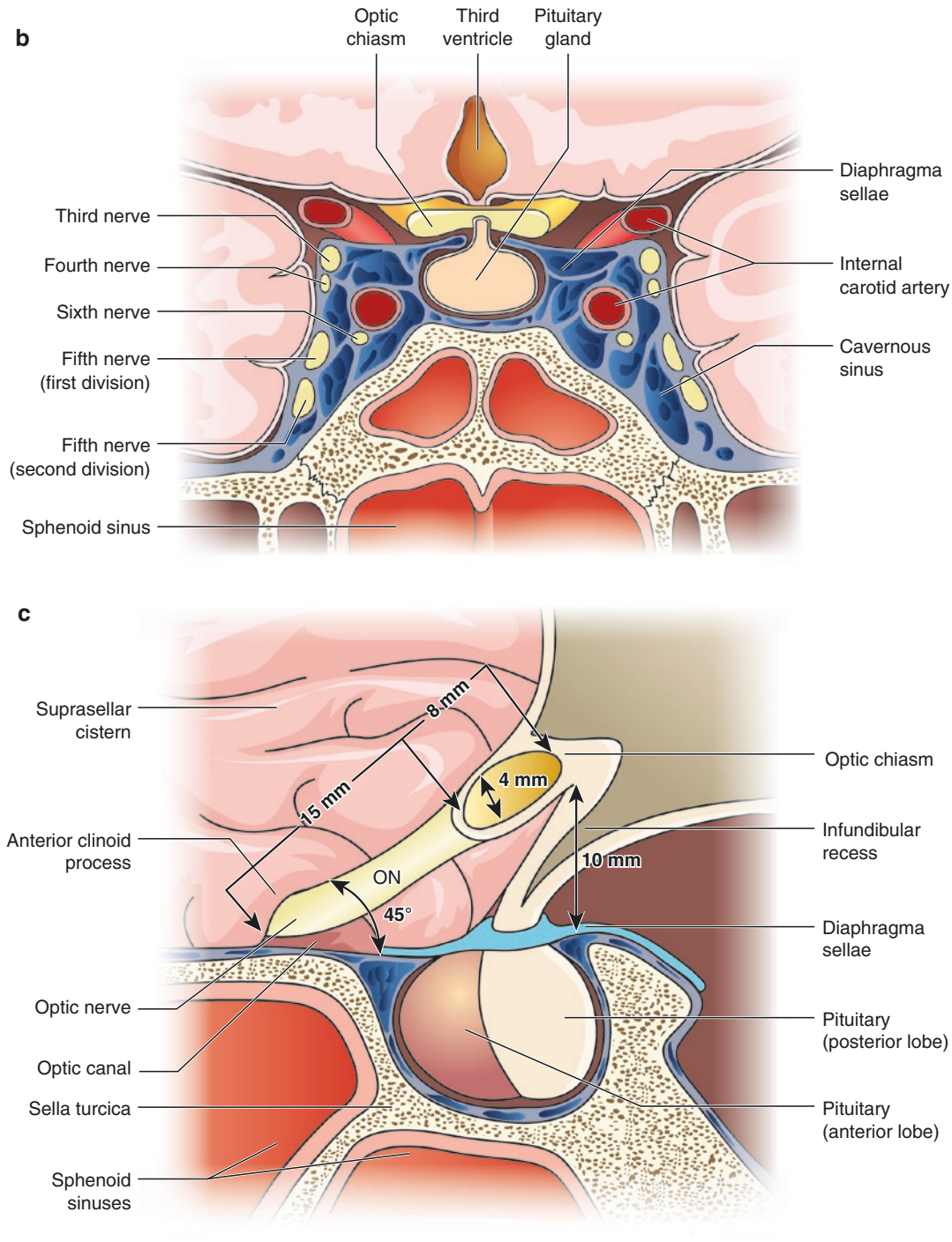

Fig. 5.10 (continued)

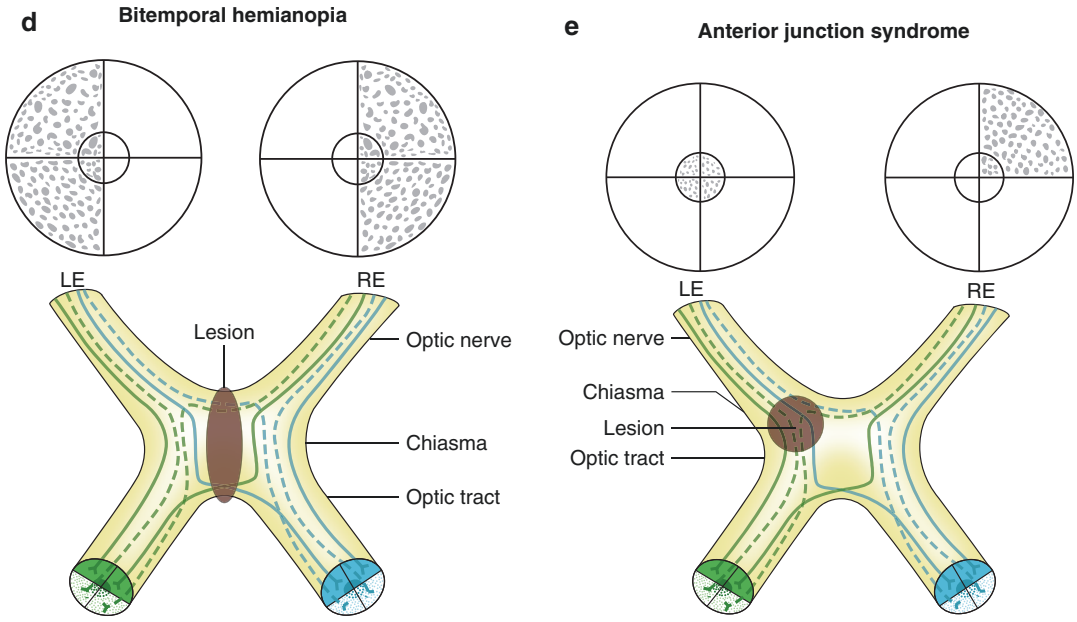

Fig. 5.10 (continued)

5.3.2 Anterior Junction Syndrome

The anterior junction syndrome refers to severe visual loss manifesting as advanced central scotoma in one eye, and a temporal defect (initially of the upper quadrant) in the healthier fellow eye (Fig. 5.11). This pattern of hemianopic visual field loss will be evident when perimetry is performed for both eyes, and careful analysis will reveal that the temporal deficit in the healthier eye respects the vertical meridian [47]. It is usually caused by lesions located at the anterolateral margin of the chiasm, such as meningiomas or supraclinoid aneurysms. The lesion involves the ipsilateral optic nerve producing an ipsilateral extensive field defect or total blindness, but also damages the crossed ventral fibers that originate from the inferonasal retina of the contralateral eye, resulting in a contralateral defect in the superior temporal field. The fibers from the contralateral eye (anterior Wilbrand knee), resulting in a contralateral defect in the superior temporal field.

5.3.3 Binasal Hemianopia

Binasal visual field defects usually represent nerve fiber bundle defects in cases of bilateral glaucomatous neuropathy. Genuine binasal hemianopia is a rare entity and may result from bilateral compression of the lateral aspect of the chiasm, i.e., due to bilateral intracavernous carotid aneurysms or calcified carotid arteries. Ocular causes, such as bilateral retinoschisis and papilledema, have been rarely described [5].

Chiasmal processes are often accompanied by early red desaturation within the temporal

hemifields, reduction in visual acuity, and optic atrophy of one or both eyes. The extent of optic atrophy does not correlate well with visual acuity loss. However, the prognosis for recovery of visual field and chiasmal function after surgical decompression is guarded in cases with disc pallor. Papilledema is an uncommon presentation in chiasmal disease unless a large mass compresses the third ventricle from below and obstructs the foramina of Monro.

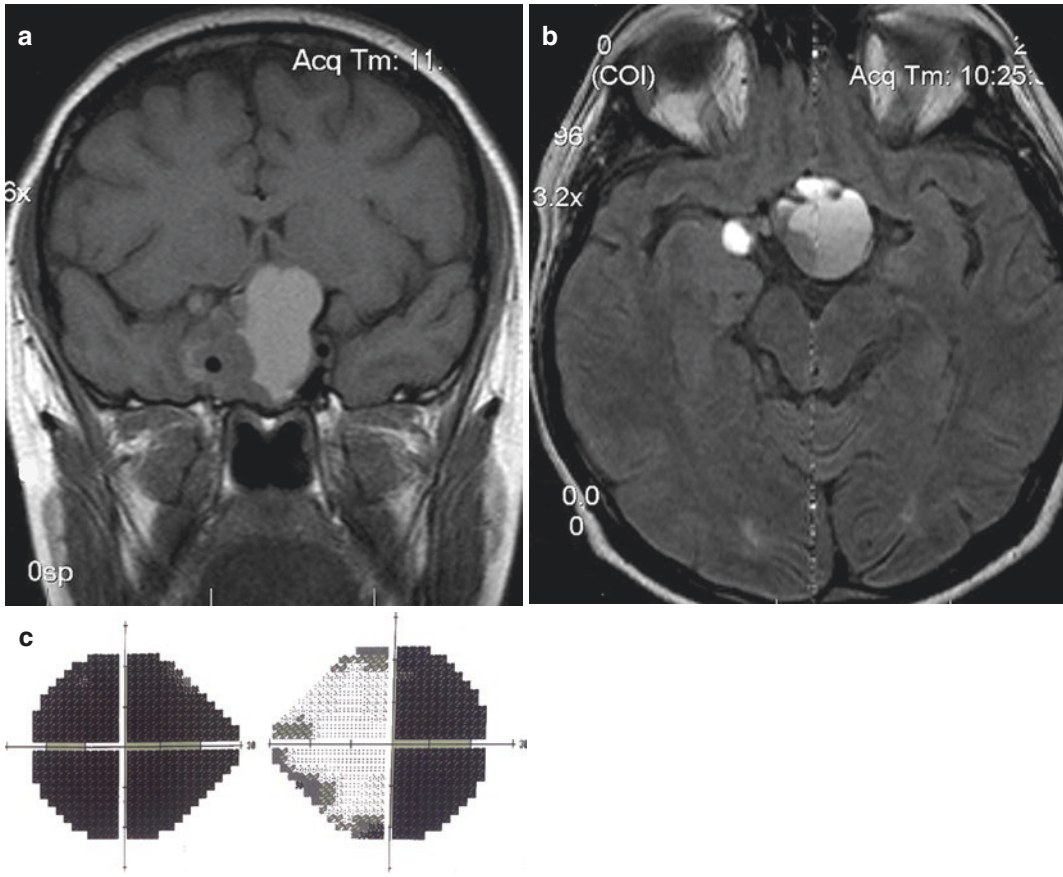

Fig. 5.11 (**a**) Coronal T1 magnetic resonance image MRI of a 30-year-old male demonstrates a pituitary adenoma, with elevation and compression of the optic chiasm mainly to the left side. (**b**) Axial fluid-attenuated inversion recover MRI of the above patient (sagittal view unavailable). (**c**) The patient has an anterior junction syndrome with advanced central scotoma of the left eye and temporal hemianopia of the right eye due to compression at the junction between the left optic nerve and the anterior chiasm. (**d**) Coronal T2 MRI after transnasal transsphenoidal resection of the prolactinoma. (**e**) Postoperative sagittal T2 MRI. (**f**) Perimetry 1 week after the operation shows partial recovery of the scotoma of the right eye to a superior temporal quadrantic scotoma

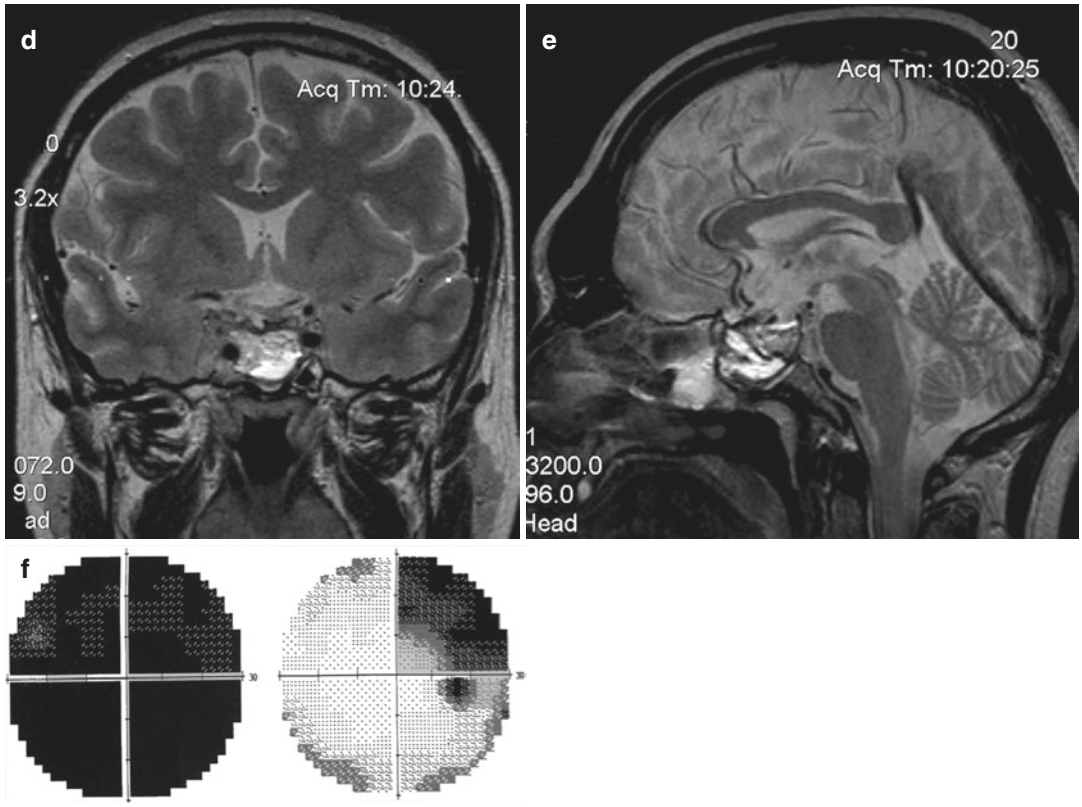

Fig. 5.11 (continued)

Conclusion

HVFDs occur with lesions in the retrochiasmal visual pathway: the optic tract, the LGN, the optic radiations, and the occipital cortex. Although it has been shown that almost every type of HVFDs can be found in all lesion locations along the retrochiasmal visual pathway, accurate classification of a HVFD is still important in seeking for accompanying neurological signs, guiding neuroimaging, identifying topographic-anatomic correlations, defining the vision-related quality of life, and choosing the appropriate rehabilitation interventions.

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Novel Imaging Techniques and Neuroradiologic Imaging

6

Njoud Aldusary, Birgit Hartog-Keisker, and Spyros Kollias

Abstract

The opportunity to apply various neuroimaging techniques to study the visual system has had a strong impact on the clinical assessment and management of visual pathologies. Advancements in the technology and the methodology of neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI), allow obtaining noninvasive structural, functional, and physiological information on the visual pathway. FMRI and DTI allow the noninvasive investigation of cognitive processes (fMRI), provide models of brain connectivity, and reveal abnormalities in white matter fiber structure (DTI). Combining these techniques with standard ophthalmology tests provides the clinicians with a powerful tool for the assessment and management of patients with visual field defects such as hemianopia.

Keywords

Magnet resonance imaging • Functional magnetic resonance imaging • Diffusion tensor imaging • MRI • FMRI • DTI • Visual field defect • Homonymous • Hemianopia

6.1 Introduction

Over the last two decades, the advances in technology and methodology of neuroimaging techniques had a strong impact on the clinical assessment of the visual system and its pathologies. The increased application of various imaging methods allowed a significant advancement in our understanding of the organization and the functional properties of the visual pathway in the human brain. Common conventional neuroimaging techniques, which

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structurally characterize the central and peripheral nervous system, include computed tomography (CT) and magnetic resonance imaging (MRI). More recent MRI methods as functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) allow the noninvasive investigation of cognitive processes (fMRI), provide models of brain connectivity, and reveal abnormalities in white matter fiber structure (DTI) [1].

The combination of improved and recently developed imaging methods with standard ophthalmological tests allows better characterization of symptoms for more accurate establishment of the clinical diagnosis in several visual pathway pathologies, including homonymous hemianopia [2]. The main cause of homonymous visual defects are retrochiasmal lesions because the retinal axons undergo a spatial realignment through the optic chiasm. When they enter the optic tract the adjacent fibers represent a spatial hemifield rather than a monocular field [3]. The most common etiologies of such lesions include ischemia, tumors, aneurysm, inflammation, and multiple sclerosis, involving the retrochiasmal visual pathway [4]. Additionally, recent studies by Kaeser et al. report that neurodegenerative disorders (e.g., Alzheimer) might also affect the retrochiasmal visual pathways, including the optic tract, lateral geniculate nuclei, optic radiations, and the visual cortex. The visualization of pathology affecting parts of these visual pathways provides important diagnostic and prognostic information for further successful treatment of homonymous visual field defects [2].

This chapter aims to provide comprehensive information about common neuroimaging techniques, which have been applied to characterize the visual pathway in vivo, and new advances in magnetic resonance imaging techniques, such as fMRI and diffusion-weighted/tensor imaging, to demonstrate their potential ability for characterizing structural and functional abnormalities causing homonymous visual field defects.

6.2 Structural Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging is a noninvasive structural and physiological imaging technology based on the principle of nuclear magnetic resonance coupled with radiofrequency waves to label and probe tissue without exposure to ionizing radiation. Over the past years MRI has become the most important diagnostic imaging modality in the clinical assessment of various pathologies, including neuro-ophthalmological ones. It allows optimal visualization of brain parenchymal abnormalities such as vascular lesions, demyelinating lesions, infections, congenital abnormalities, tumors, and traumatic brain injuries [5].

The MRI principle depends on a large superconducting solenoid coil, which creates a strong magnetic field inducing magnetization in protons of the exposed tissue. An excitation coil sends radiofrequency waves with specific frequency into the tissue. The energy from the radio waves will be absorbed by protons and later reemitted as MR signal when the radio waves are switched off. The remitted energy will be encoded by a set of gradient coils that provide information about the spatial variation in the signal, which allows the creation of a topographic image of the exposed (brain) structure [6].

Magnetic resonance imaging is now considered a conventional imaging method, used routinely in the clinical work-up of patients with ophthalmological symptoms. It allows detailed investigation of the integrity of the visual pathway, including the exact exploration of the chiasm and retrochiasmal visual pathway abnormalities [7]. The most common clinical protocol includes invariably, T1-weighted sagittal images and T2- and T1-weighted coronal sections without and with intravenous injection of a paramagnetic contrast agent, as suggested by De Champfleura et al. These sequences are complemented by high-resolution images in three planes (coronal, axial, and sagittal) to identify and demonstrate suspected optic chiasm lesions, and

whole brain T2 and T1 weighted IMAGES, without and with contrast administration, depending on the symptoms of the patient and the exact clinical indication. Diffusion-weighted imaging is indispensable for the exclusion of vascular (ischemic) lesions at the level of optic tracts or optic radiations. If necessary, perfusion imaging, spectroscopic imaging, and angiographic imaging will be required to further characterize the type of pathology (i.e., vascular, infectious, tumoral, etc.) for establishing a more precise and accurate diagnosis [8].

In patients suffering from homonymous visual defects due to tumoral or vascular lesions, the focus of the MRI investigation should be on the chiasm and retrochiasmal visual pathways. In the case of hemorrhagic stroke along the retrochiasmal visual pathway in the setting of a head trauma, a noncontrast rapid and low cost CT, available in any emergency room, is suitable. However, this protocol is sufficient neither to detect nonhemorrhagic ischemia nor to identify other lesions like tumors, demyelinating plaques, and infections. In case of such incidents, MRI is far more sensitive and accurate to detect the pathology at an early stage [9].

A careful and targeted MRI assessment should be considered in patients with symptoms of homonymous visual field defects because other neurological conditions (e.g., dementias, metabolic disorders, etc.) may mimic stroke and cause visual field defects. Vachalová et al. described a patient with the Heidenhain variant of Creutzfeldt–Jakob disease who was diagnosed with symptoms mimicking acute ischemic stroke presenting with acute inferior homonymous quadrantanopia. Four days after symptom onset, MRI revealed a medial occipital cortex ribbon-like high signal intensity and restricted diffusion typical for this neurodegenerative disease [10].

Exact knowledge of the various MRI sequences and their different contrasts between tissues is pivotal to achieve correct clinical diagnoses. Horton reported on a successful diagnosis of infarction in the lower right calcarine sulcus using fluid-attenuated inversion recovery (FLAIR) sequence in a patient with 10-day history of a shadow in her left visual field while CT and routine T2-weighted MRI failed to demonstrate the lesion. The available MRI sequences constantly improve; a successful diagnosis relies on the neuroradiological expertise to choose the most sensitive ones that will better demonstrate the pathology, depending on the clinical symptoms of the patient [9]. In summary, considering the above-mentioned aspects, MRI is the method of choice in the evaluation of patients with homonymous hemianopia.

6.3 MRI–DTI Tractography

Since the communication network of the brain consist of white matter fiber pathways, any alteration of these pathways will affect the signal transmission between brain regions and thus influence functional performance. Diffusion tensor imaging (DTI) is a MR method allowing non-invasive mapping of large white matter tracts in the human brain in vivo and investigation of white matter axonal integrity in a quantitative manner. It is based on the directional diffusion properties of microscopic water molecules in tissues. The mammalian white matter is a highly anisotropic structure. Barriers to free water diffusion include, among others, the myelin sheath and the cell membrane, which facilitate diffusion of the water molecules along the long axis of the fiber than perpendicular to its axis. The three-dimensional direction and speed of maximal diffusivity along axonal fibers in the white matter can be estimated for each voxel of the imaged volume.

Quantitative parameters of DTI include first, the fractional anisotropy (FA) index measuring the degree of anisotropic diffusion, ranging between 1 for maximum anisotropy, along one direction and 0 for isotropic diffusion, equal in all directions. The second quantitative parameter is the apparent diffusion coefficient (ADC) index, measuring the degree of diffusivity along each direction. Both measurements are used as

an expression of structural integrity of the tissue structure [11]. For example, reduced diffusivity of water molecules is observed when the integrity of the myelin sheaths in the white matter is affected, such as in demyelinating diseases, infiltration by a tumor, degenerative processes etc [12].

Diffusion information can be represented in the two-dimensional space as color-coded directionality images (FA maps), or three-dimensional reconstructions of specific white matter fiber tracts using diffusion tensor tractography (DTT) algorithms (Fig. 6.1) [11]. To start the tracking process and create 3D reconstructions of the visual pathway from the DTI data, an appropriate placement of regions of interest (ROIs) is required to selectively isolate specific white matter fiber systems that make part of the pathway. These ROIs are selected based on anatomical landmarks from high-resolution MR images of the same subject. For example, the ROI for starting the tracking of the optic tract should be placed over the chiasm with the end point in the lateral geniculate nucleus (LGN). The optic radiation reconstructions are performed by placing ROIs in the LGN and in the subcortical white matter of the occipital visual areas. For the reconstruction of individual fiber bundles that compose the optic radiations, ROIs should be placed along the paraventricular white matter in a more ventral location to reconstruct Meyer's loop, in a more central location for the central bundle, and more dorsal for the dorsal bundle [13]. It has to be noted that individual selection and positioning of the seed ROI's may result in a certain variability in the reconstruction of the fibers [12].

DT imaging has become an important tool for visualization of the macroscopic fiber tract architecture of the visual pathway in 3D [14]. Compared to conventional imaging methods, which do not demonstrate the anatomy of the posterior visual pathway effectively and cannot reveal microstructural changes in early stages of pathology, DTI provides the possibility to study the integrity of the entire visual pathway in greater detail. The ability of DTI to visualize white matter tracts, which connect different parts of the neural network in the brain, found an early application in presurgical planning and intraoperative guidance to avoid or minimize damage

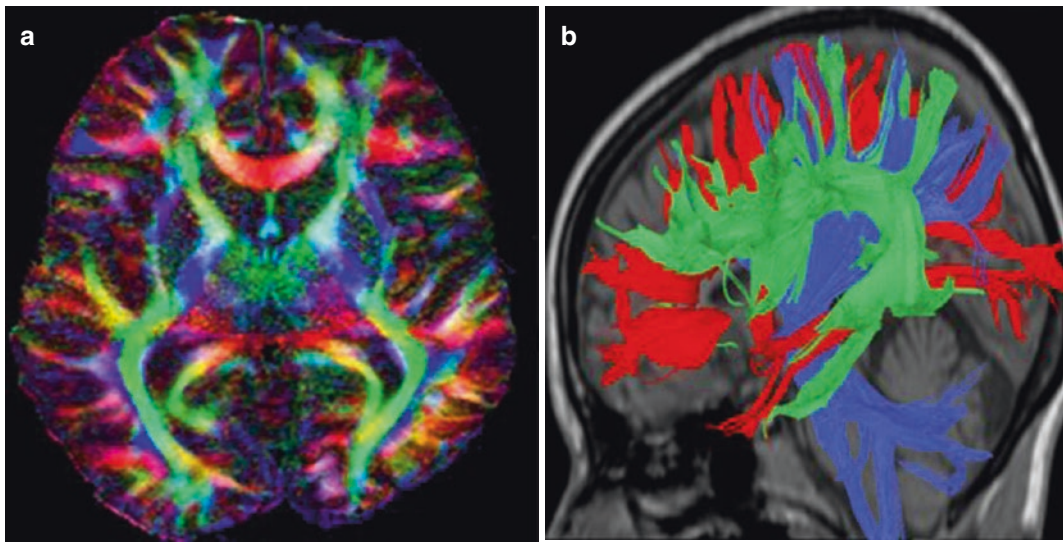

Fig. 6.1 **(a)** 2D diffusion tensor imaging (DTI) color-coded according to the orientation in the 3D space of the primary eigenvector within each voxel of the image (*red* for *left-right, green* for *anterior-posterior,* and *blue* for *superior-inferior*). **(b)** 3D reconstruction of fiber systems using the Fiber Assignment by Continuous Tracking (FACT) algorithm. Based on the localization and the specific main orientation, we can virtually reconstruct individual fiber systems of the white matter in great detail (From Kollias et al. [11], with permission)

during surgical intervention, i.e., removal of a tumor in the vicinity of the visual pathway [15].

DTI is also used in the clinical investigation of other neurological conditions and developmental disorders, which arise from disturbed white matter connections. Recent advances in the post-processing and analysis algorithms of DTI data promise increased specificity and improvements in the localization accuracy of the method and in relating lesion location to clinical/ophthalmological symptoms. In the case of multiple sclerosis, DTI imaging provides improved pathological specificity compared to conventional MRI; however, the pathological substrates underpinning alterations in brain tissue diffusivity are not yet fully delineated [16]. To better reveal the potential association between altered DTI diffusivity and the underlying tissue damage in multiple sclerosis, Klistorner et al. segmented a single tract of the optic radiation into separate groups based on their relationship to lesions. The calculation of diffusivity in predefined regions along the white matter tracts allowed a comparison of diffusion values with the corresponding segments of the nonlesional fibers in the same tract. According to their findings, the authors suggest that within the orbital radiation, parallel and perpendicular diffusivities are affected by tissue restructuring related to distinct pathological processes, providing evidence that DTI is a sensitive marker to investigate the tissue damage in lesioned and normal appearing white matter [16]. Furthermore, McNulty et al. assessed the impact of fiber tractography on the visualization of pathologies in the medial longitudinal fasciculus of multiple sclerosis patients suffering from internuclear ophthalmoplegia (INO). They found that DTI tractography allows improved visualization of fiber pathologies related to INO, which in turn supports monitoring of disease progression with refined association between lesion type and location and clinical symptomatology [17].

The usefulness of DTI for the assessment of patients harboring pathologies affecting the visual pathways was shown in several studies. Yeo et al. demonstrated the impact of DTI in the detection of a lesion in the optic radiation causing visual field defects in a patient with traumatic brain injury. The patient had right homonymous hemianopia following the brain trauma, which persisted for 6 months following the trauma and was diagnosed with Humphrey visual field testing. DTI demonstrated discontinuation in the mid-portion of the left optic radiation with decreased values of fractional anisotropy and increased values of the diffusion coefficient in the same region and the more distal parts of the radiations, as compared to healthy subjects [18]. Furthermore, Romero et al. in a case study of optic tract injury in neuromyelitis optica demonstrated the complementary role of a growing number of imaging modalities, including DTI and optical coherence tomography (OCT), in the investigation of patients with visual field defects [19].

DTI has found a prominent clinical application in presurgical planning including identification of the spatial/topographical relationship between an intracranial mass lesion and the visual pathway in order to avoid potential visual field defects following tumor resection [14]. Since most of the anterior temporal portion of the optic radiation passes through the temporal lobe, damage to the Meyer's loop during surgery is one of the most common causes of homonymous field defects following temporal lobe surgery. However, in contrast to the common structural MR sequences, which cannot identify the optic radiation, DTI tractography allows the in vivo demonstration of this structure and thus enables the surgeons to optimally plan tumor resections to preserve function with maximal possible tumor resection [20]. According to Powell et al., who found a superior homonymous quadrantanopia as prevalent complication after anterior temporal lobe resection, the preoperative application of DTI tractography is highly recommended for a better outcome [21]. In addition to the common application of DTI methods for presurgical planning, the intraoperative application of DTI allows immediate evaluation of the surgical intervention by combining mapping of the efferent visual system with microsurgical neuronavigation using intraoperative MRI technique [20]. This technique was applied recently in clinical practice during resection of lesions involving, or adjacent to, the optic radiation in order to maintain

patients' visual fields [20]. The DTI images were incorporated into the neuronavigation intraoperatively to provide the surgeon with exact information on the site of the lesion and the adjacent optic radiation [15].

Despite the promising applications of DTI fiber tracking in studying neurological disease of the brain, clinical investigations are limited to the assessment of major fiber tracts due to shortcomings inherited to the method. First, the voxel size of the data, which can be achieved in a clinically acceptable acquisition time, is much larger than the diameter of a single axon, which lies in the range of a few microns, so only major fiber bundles can be resolved. Other limitations, particularly relevant to the reconstruction of the visual pathway, are related to the increased susceptibility artifacts in the area of the chiasm, which result in signal loss in the DTI acquisitions, as well as the extensive fiber crossing within this area and the pronounced bending of the optic radiations, which are difficult to resolve with existing algorithms used routinely in the clinical work [22]. Recently, various data acquisition schemes (i.e., q-ball imaging and diffusion spectral imaging) and tracking algorithms have been proposed to overcome the existing limitations. However, they require extensive examination times that are often prohibiting for routing clinical use in daily patient care. The choice of an accurate tracking algorithm is pivotal for the reliable reconstruction of visual fiber tracks in the human brain (Fig. 6.2) [22]. Despite the above-mentioned challenges related to DTI, this new method can be requested by clinicians on an everyday basis in most clinical centers operating MRI scanners. The existence of several commercially available postprocessing softwares and neuroradiological expertise make it relatively easy to provide

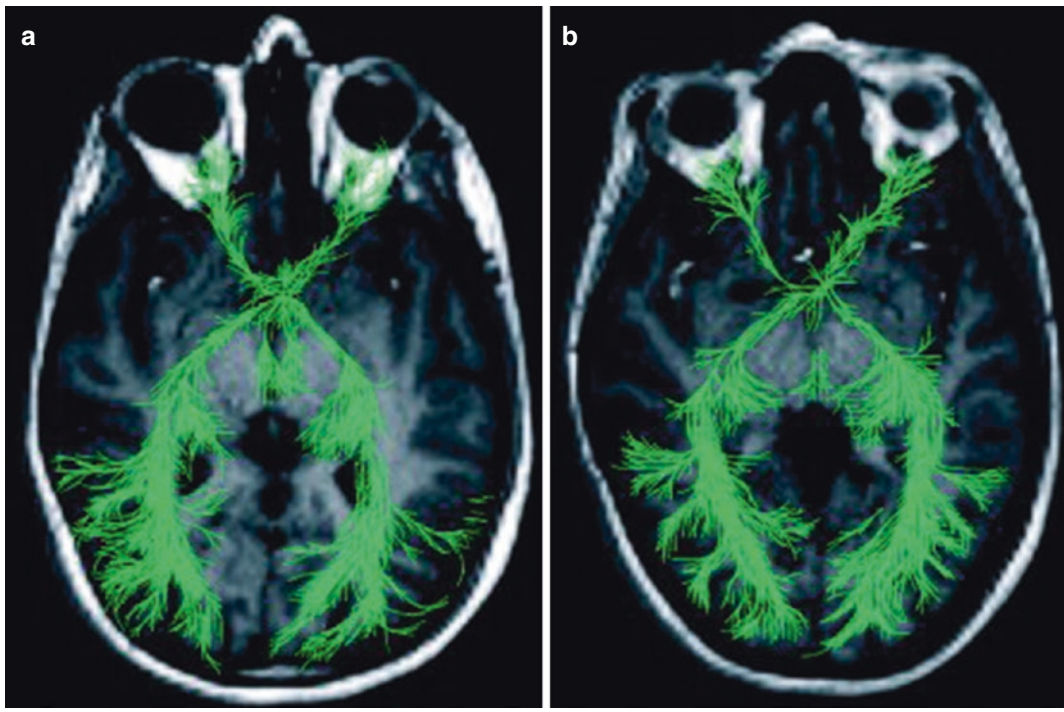

Fig. 6.2 Diffusion tensor imaging (DTI) fiber tracking**.** Fibers reconstructed from the center of the optic chiasm are shown. Trajectories calculated with the aFM (advanced fast marching algorithm) are depicted in *green*. In both hemispheres of the brain, the optic nerve, the optic tract, the connections to the lateral geniculate nucleus, and furthermore the optic radiation onto the area striata in the occipital lobe can be seen. The fibers emerging from the chiasm in the posterior direction most probably represent connections following the oculomotor nerve to its nuclei in the brain stem (From Staempfli et al. [22], with permission)

quantitative measures on the visual pathway for better correlation of clinical symptoms with underlying structural anomalies.

6.4 Functional Magnetic Resonance Imaging

Functional magnetic resonance imaging (fMRI), as a further noninvasive imaging method next to structural and DT imaging, allows the assessment of brain activity associated with sensory, motor, and cognitive behavior [1, 6, 23–26]. The application of fMRI in studies of the visual system provided researchers with the ability to sketch out the organization and functional properties of the human visual system, which in turn allowed improved understanding of altered function of neuro-ophthalmologic disorders [1, 27, 28].

The introduction of MR technology in the investigation of neuronal activity was facilitated by the finding that the MR signal could be made sensitive to changes in blood flow and blood oxygenation providing important physiological information related to brain function [1]. Previous imaging methods used for mapping brain activity, as positron emission tomography (PET), required the injection of radioactively labeled metabolites, which limited their applicability, whereas fMRI measures the naturally occurring blood oxygenation level dependent (BOLD) contrast (for details see below), which makes this method safe and thus well-tolerated by normal controls and patients [1, 6, 25, 26, 28]. Further advantages, which ushered fMRI to become the method of choice are: (a) fMRI provides both anatomic and functional information in a subject at the same session, allowing accurate determination of the anatomic site of the active regions; (b) due to its noninvasive nature, repetitive scans in a single subject are possible; (c) it is financially affordable for most medical centers operating clinical MRI scanners; and (d) it has better spatial and temporal resolution than other methods applying the same hemodynamic phenomena to localize neuronal activity [1, 25].

The principle of fMRI has its origin in the famous prediction of Roy and Sherrington who assumed that blood flow might depend on function [29]. Accordingly, task related neural activation causes a greater regional increase in blood flow than the moderate increase in the oxygen consumption by the neurons, implying that the blood flow is imperfectly coupled to the increased metabolic demands of neurons both in terms of spatial specificity and quantity [6]. Consequently, the relative concentration of oxyhemoglobin in the small venules draining the area of activated neurons increases. Oxyhemoglobin has diamagnetic properties, and thus the increased blood oxygenation can be detected by the oxyhemoglobin-sensitive fMRI as increased signal, serving as marker of brain function. This effect became known as the blood oxygen-level dependent (BOLD) signal [30, 31] for published reviews [1, 6]. A decade after Ogawa et al. demonstrated that MR technology could detect in vivo changes of blood oxygenation, the question, whether BOLD changes are related to axonal potentials, dendritic postsynaptic potentials, both or neither, could be elucidated [31]. According to simultaneous measurements of fMRI BOLD signal and electrophysiological activity in primates and also humans, rather postsynaptic potentials than action potentials seem to be the origin of the BOLD signal [6, 32].

The peculiarity of the neurovascular coupling lends fMRI experiments a dynamic character since signal changes after neuronal activity occur after 1–2 s and evolve over a period of 10–12 s. Thus, the progressive evolution of the signal provides information about the dynamics of the underlying physiological changes [1]. General fMRI designs aim at answering questions either related to *estimation* (e.g., "How did the BOLD response change over time in a particular brain region?") or to the *detection* of neuronal activity (e.g., "Which brain regions showed task-related neuronal activity?") [6]. To meet these questions whole brain images or particular brain regions (e.g., occipital lobe) are acquired at relatively high temporal (around 2–3 s) and reasonable spatial (3 mm) resolution using axial or coronal gradient echo-imaging sequences (e.g., echo-planar-imaging so-called EPI sequences) [1, 24–26]. To ensure accurate localization of

cortical brain activity, T1-weighted images with a spatial resolution of 1 mm are additionally acquired [1, 25, 26]. The collected fMRI data is usually subjected to several preprocessing steps, which measure and remove unwanted variability, caused, e.g., by head motion [6]. To allow comparison between subjects, the data is normalized prior to a statistical analysis that tests specific predictions about the relationship between the applied task and the evoked BOLD response. Thereby, a variant of the general linear model is used to evaluate the contribution of different explanatory variables to the observed activation pattern [6]. In the case of the relatively novel method of resting state analysis, the changes in correlation between (visual) areas are investigated while subjects are at rest, e.g., with the so-called independent component analysis ICA, which includes the comparison of temporal patterns of activity between independent components to elicit correlations that suggest connectivity [23, 27].

Cortical responses within the visual system are induced by simple stimuli like turning lights on and off, or flashing a large checkerboard or moving dots. However, such stimuli do not allow a distinction between cortical representations of peripheral versus central vision, which is relevant for tasks like reading [28]. A sophisticated paradigm, which allows the mapping of visual field eccentricity and angular position, is described by DeYoe and Raut. It consists of a slowly expanding checkered annulus and a slowly rotating checkered wedge, which are sequentially displayed. Due to the composition of the high-contrast checkerboard consisting of counter-phasing black and white checks, which flicker at 8 Hz, strong neural activation and also large increases in the BOLD fMRI signal in the responsive brain region can be achieved. Furthermore, the presentation mode of the stimuli is such that locations in the visual field, which differ in eccentricity or angular position, are stimulated at different times. The resulting maps both delineate visual cortex and identify multiple functionally distinct visual areas as well as subzones supporting vision at the center of gaze, relevant for reading and other daily activities [33]. To promote constant attention of the healthy individuals or patients during scanning, a button press task, including the fixation of a marker, which randomly disappears can be added. The application of both annulus and wedge as stimuli yield detailed retinotopic maps, so-called functional field maps (FFMap) with circles representing visually responsive voxels. The FFMap of healthy individuals contains circles distributed throughout the visual field while focal damage in patients will reveal missing or less numerous circles within the retinotopic zone of the affected visual field [28]. Thus, the FFMap visualizes the relationship between the focal pathology as cortical pattern and the resulting effect on the field of vision of the patient [33].

Functional magnetic resonance imaging vision mapping is predominantly applied in presurgical planning in patients with pathology of the visual pathways where resection is necessary [27, 28, 33, 34]. In order to avoid damage to visual cortex, which is critical for daily vision, fMRI maps provide additional information for resection planning which aims at gaining maximized therapeutic success with minimal resulting postoperative deficits [28, 33]. In addition, fMRI visual field mapping can also reveal abnormal functional brain organization, which is not easily discovered by conventional clinical tests. For example, DeYoe et al. report on an albinistic patient where FFmaps revealed that the opposite halves of the visual field projected onto the same left cortex [33]. Furthermore, Dem Hagen et al. (2008) compared fMRI and visually evoked potentials (VEP) to assess misrouting in albinism. They found that hemifield stimulation recorded with fMRI is highly sensitive and more effective than VEP to detect misrouting by using interocular comparison [35].

A further application of FFMaps is reported by Reitsma et al. in a study that investigated 25 patients with adult onset (stroke, tumor, or

trauma) and two patients with congenital pathology of the visual cortex. They identified atypical retinotopic organization in only three patients revealing an expanded ipsilateral field representation, which was on average 3.2 greater compared to healthy individuals. They concluded that under certain pathologic conditions, visual cortex might undergo large-scale retinotopic changes [36]. It can be speculated whether the change in cortical organization is true reorganization or unmasking of so-called normal subthreshold organizational features [33].

In another study, Hoffmann et al. assessed two achiasmatic patients, with complete visual fields and apparent integrity of the visual system, using fMRI-based retinotopic mapping to obtain visual hemifield representations on the cortical surface for each visual hemifield and each eye. They demonstrated that the gross topography of the geniculostriate and occipital callosal connections remains largely unaltered. Voxels of the primary visual cortex were better modeled with a bilateral receptive field rather than standard contralateral representations. They concluded that visual function is preserved by reorganization of intracortical connections instead of large-scale reorganizations of the visual cortex. Thus, developmental mechanisms of local wiring within cortical maps compensate for the improper gross wiring to preserve function [37], see also Millington et al. [27]. It is suggested that an interleaved representation of ipsi- and contralateral hemifields may allow visualization of the difference in response to the two hemifields; however, such an approach requires sufficiently high resolution in the range of 0.5 mm^3 [27]. An example of laminar high field fMRI (7 Tesla scanner) is shown in the study of Kok et al., which investigates the cortical response to illusory figures in the human primary visual cortex at different cortical depths. Applying a spatial regression analysis, in an attempt to explicitly unmix signals from the different layers, they were able to extract signals with less dependence on the actual voxel volume than previous interpolation approaches [38]. Although, the vast majority of research on visual processing and related disorders is performed using 3 T scanners, future studies will certainly benefit from increased signal-to-noise ratio, since more and more 7 T scanners can be afforded. In combination with sophisticated analyses, noninvasive recordings of neural activity will further promote our understanding of the visual system and its disorders.

The application of fMRI in patients with hemianopia deepens not only our knowledge about blindsight, plasticity, and recovery after brain injury, but it also provides important information about the visual system [27]. With the aid of Gabor stimuli presented with a spatial frequency of 1 cycle/°, Ajina et al. recorded contrast sensitivity in the human motion processing complex (MT+) in the damaged (primary visual cortex, V1) hemisphere of eight patients and aged-matched controls. They found that hMT+ no longer revealed early saturation but increased linear response in patients, which was comparable to the response of V1 in healthy controls. They concluded that V1 is essential for the marked contrast sensitivity and early saturation, which can be observed in normal hMT+ responses [39].

The validity of the BOLD response can be compromised when focal brain pathology disrupts the coupling cascade, without affecting the underlying neural activity [33]. The described effect, so-called neurovascular uncoupling (NVU), can cause incorrect activation maps, which can have devastating outcomes when applied in the context of presurgical planning. Therefore, testing for NVU, e.g., with the combined application of FFmaps and perimetric tests is highly recommended when applying fMRI for presurgical mapping [33]. Nevertheless, despite its limitations, fMRI, which is offered in most clinical centers applying MRI, provides (often in combination with other behavioral or imaging methods, such as DTI) valuable information on the functional consequences of pathologies affecting the visual system, which helps to improve diagnosis and treatment (Fig. 6.3) [1].

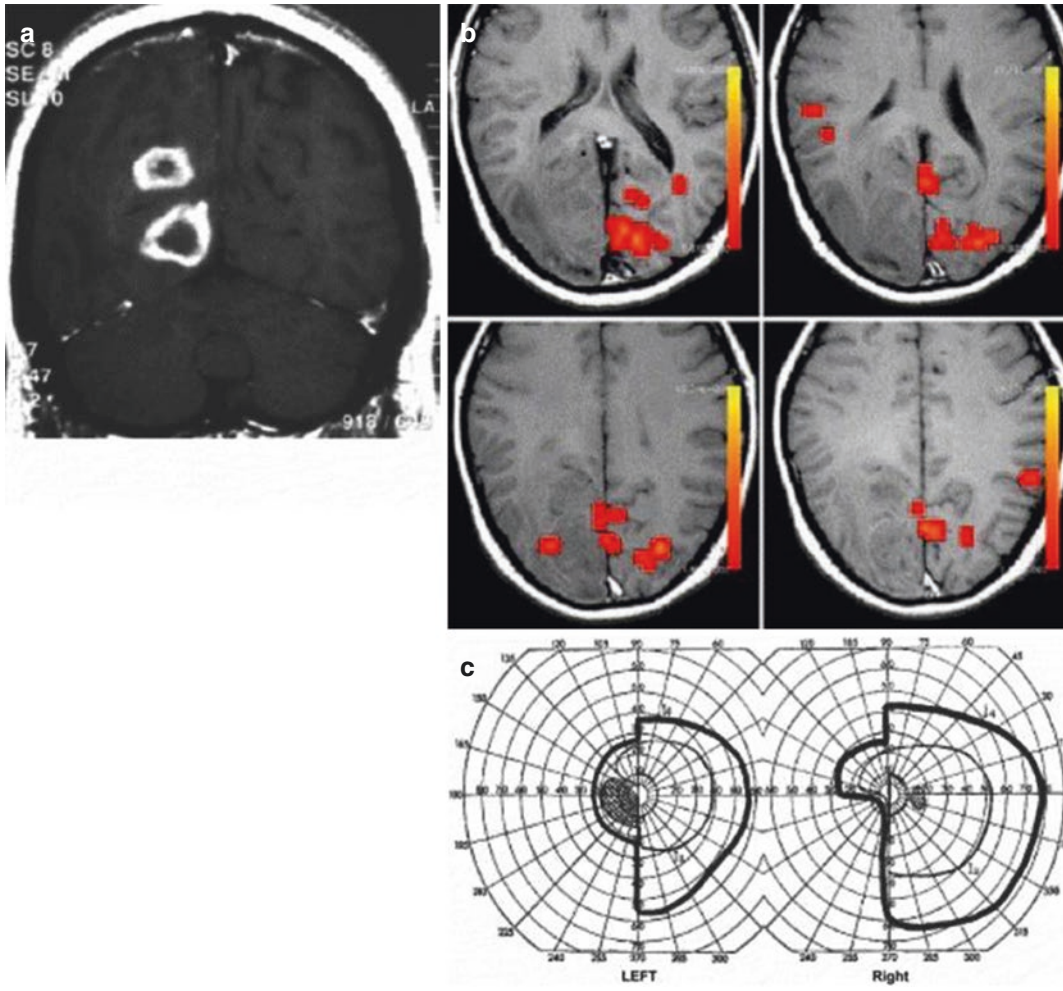

Fig. 6.3 Findings obtained in a 52-year-old-man with glioblastomas: (**a**) Coronal, T1-weighed magnetic resonance image with contrast showing the extension of the tumor above and below the parieto-occipital sulcus and the involvement of the right medial occipital lobe. (**b**) Functional maps acquired during binocular visual stimulation, overlaid on the corresponding anatomical images, clearly illustrates diminished activation of the right calcarine cortex which is indistinguishable from the infiltrating tumor. (**c**) Goldmann perimetry showing an almost complete left homonymous hemianopia with sparing of some of the upper central field on the left side (From Kollias et al. [1], with permission)

Conclusion

Recent advancements in technology and methodology of neuroimaging techniques had a significant impact on the assessment of the visual pathway and its pathologies: The progress of neuroimaging methods further strengthens our understanding of functional properties related to the visual pathway, which, in combination with standard ophthalmological tests, allows to define and confirm the clinical diagnosis of symptoms related to pathologies such as homonymous hemianopia. While DTI is commonly applied to visualize the degree of integrity of visual pathway fiber bundles, functional magnetic resonance imaging is a useful tool for evaluating visual function in the course of the disease or recovery. Both methods are also applied in presurgical planning and intraoperative mapping. The combination of fMRI and DTI is very

productive to assess cerebral visual field disorders in the acute phase and in the course of the disease [40]. Furthermore, the catenation of recent neuroimaging methods with clinical findings improves the prediction of clinical outcomes and helps to monitor disease recovery [41].

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Pupillary Disorders in Homonymous Visual Field Defects

7

Karolína Skorkovská, Barbara Wilhelm, and Helmut Wilhelm

Abstract

Classically, the pupil light reflex pathway is considered to be a simple reflex arc consisting of the retinal ganglion cells, intercalated neurons in the midbrain, the oculomotor nerve, and short ciliary nerves. However, there are some specialties in the structure of the afferent pupillary pathway that should be taken into account when interpreting pupillary disorders and that can help in the topodiagnosis of the lesion. Moreover, studies in patients with lesions of the retrogeniculate pathway showed that the pupillary pathway is more complex than previously assumed and the retrogeniculate visual pathway and the visual cortex are also involved in the pupillary light reaction. Clear anatomic evidence is still lacking but pupillographic measurements in patients with various disorders of the visual pathway support the existence of two pupillomotor channels that drive the pupil light reaction – the subcortical (more primitive, luminance channel associated with the intrinsically photosensitive retinal ganglion cells) and the supragenicular (responds to shifts in structured stimuli, is driven by the rods and cones, and receives input from the visual cortex and extrastriate areas). The chapter summarizes possible pupillary findings in patients with homonymous hemianopia.

Keywords

Pupil • Pupil light reflex • Relative afferent pupillary defect • Pupil perimetry • Chromatic pupillography • Swinging flashlight test • Hemihypokinesia • Hemiakinesia • Intrinsically photosensitive retinal ganglion cells • Melanopsin

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7.1 Introduction

The neural pathway of the pupillary light reflex as first described by Wernicke [1, 2] in 1880s consists of four neurons (Fig. 7.1). Afferent fibers of the retinal ganglion cells travel in the optic nerve and undergo hemidecussation at the chiasm before entering the optic tract. In the posterior third of the optic tract, the pupillomotor fibers separate from the sensory fibers, branch medial via the brachium of the superior colliculus to the lateral geniculate nucleus, and synapse in the ipsilateral pretectal nucleus in the dorsal midbrain. Intercalated neurons from each pretectal nucleus then project to both Edinger-Westphal nuclei and parasympathetic fibers from the Edinger-Westphal nuclei innervate the iris pupillary sphincter muscle. According to this model, the suprageniculate visual pathway should have no influence on the pupillary light reflex. However, studies in patients with lesions of the retrogeniculate pathway showed that the pupillary pathway is more complex than previously assumed and the retrogeniculate visual pathway and the visual cortex are also involved in the pupillary light reaction.

Homonymous hemianopia means vision loss on the same side of the visual field in both eyes and is indicative of a lesion involving the visual pathway posterior to the chiasm. Patients with a visual field defect should always have their pupils examined and this applies even more so in the case of homonymous visual field defects. This chapter should summarize possible pupillary findings in patients with homonymous hemianopia.

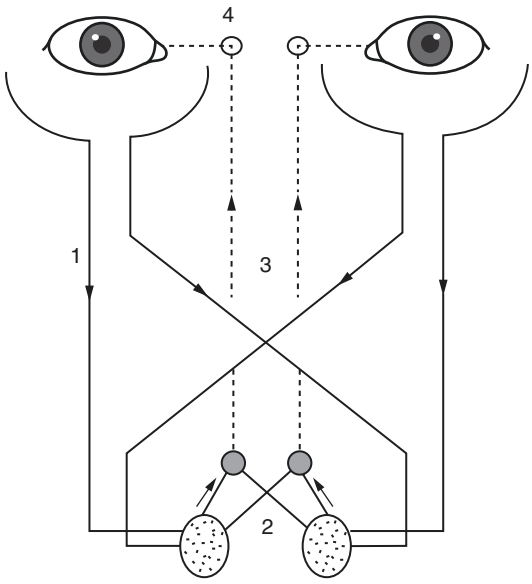


Fig. 7.1 The human pupillary pathway as first described by Wernicke consists of four neurons (excluding photoreceptors and bipolar cells in the retina): retinal ganglion cells (*1*), intercalated neurons in the midbrain (*2*), oculomotor nerve (*3*), and short ciliary nerves (*4*). The simplicity of this model can be no longer accepted (From Wilhelm [2], with permission)

7.2 Examination of Pupils

Examination of the pupils offers objective evaluation of visual function as well as of the vegetative pathways to the eye. Essential information is gathered within a short time. This makes pupillary inspection a valuable part of routine ophthalmological, neurological, and general medical examinations. Due to the proximity of pupillary pathways to various anatomic structures, pupillary dysfunction can be caused by a variety of disorders, some of which may be life threatening. Due to differences in the course of pupillomotor and sensory fibers, pupillary tests can help in the localization of a visual pathway lesion. The ophthalmologist plays a key role in detecting pupillary disorders and in directing further investigations. Therefore, one should have a good knowledge of the diagnostic significance of pupillary function and dysfunction.

There are several ways of how to examine the pupil light reaction. Some methods are based on the asymmetry in the afferent visual pathway, another on the examination of the visual field by means of measuring the pupil light reaction to focal light stimuli or on stimulation methods that are similar to multifocal electroretinography. Recently developed chromatic pupillography can identify pupil light response mediated by the rods, cones, or the intrinsically photosensitive retinal ganglion cells containing melanopsin.

7.2.1 Relative Afferent Pupillary Defect and Swinging Flashlight Test

The most frequently evaluated pupillary parameter in clinical practice is the relative afferent pupillary defect (RAPD). It is typically related to lesions within the anterior visual pathway and is almost always present in unilateral or asymmetric bilateral diseases of the optic nerve, chiasm, or the optic tract. It can be diagnosed by means of the swinging flashlight test and is characterized by diminished pupillary constriction on direct illumination with a normal consensual response to illumination of the contralateral eye.

Swinging flashlight test can be performed as follows: In a darkened room ask the patient to fixate an object in a few meters' distance. Shine with the ophthalmoscope in an angle of 45° from below and from the distance of 20–40 cm into the eyes. Move the light quickly from one eye to the other and observe the direct pupil light reaction of both pupils. Both pupils should be illuminated for the same time (ca. 2 s) and the switch between both eyes should be repeated at least five times. If a relative afferent pupillary defect is present on one side, then at the illumination of this eye both pupils will either enlarge without any previous contraction or this contraction will be smaller and shorter. RAPD can be quantified by means of neutral density filters and expressed in log units: A filter is placed between light source and the "good eye". If there is still a RAPD defect visible, a filter with higher density is chosen until the difference in pupillary constriction between both eyes disappears or even the RAPD switches side. The density of the filter necessary to compensate the side difference is a measure for the RAPD.

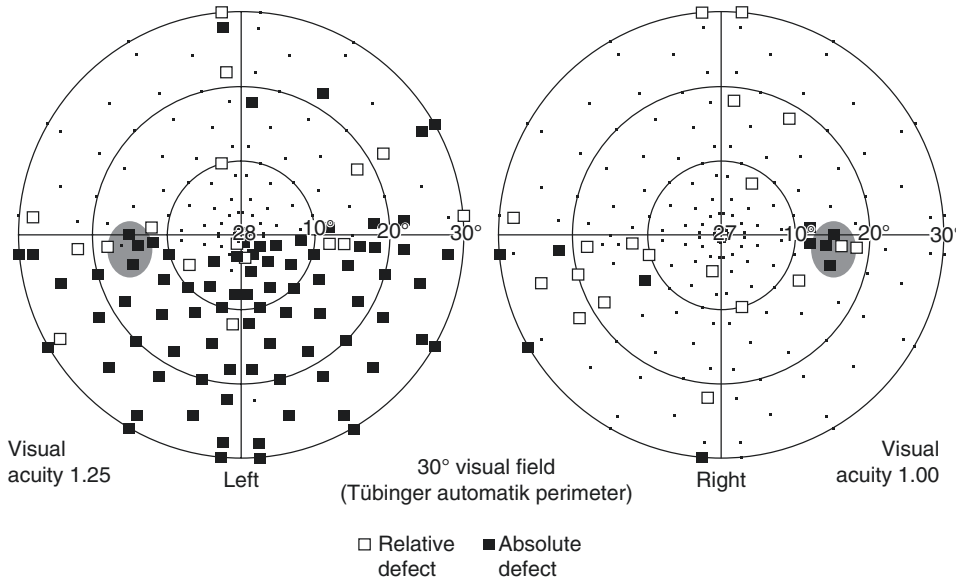
7.2.2 Pupil Perimetry

Pupil perimetry or campimetry is an objective visual field test that measures pupil light reaction (PLR) to focal light stimuli projected onto the retina. Light stimuli are presented at various locations in the visual field, similar as in standard perimetry. However, as the threshold for the pupil light response is higher than the differential light threshold in conventional perimetry, stimuli in pupil perimetry have to be brighter or larger. Brighter stimuli increase straylight, and larger stimuli reduce spatial resolution of pupil perimetry. This is the major problem of all systems applied in pupil perimetry. To overcome this, M-sequence techniques known from multifocal electroretinography have been applied but not yet tested against conventional pupil perimetry.

Visual field defects in pupil perimetry can be recognized by a reduced or absent pupil light reaction within these areas. Studies dealing with clinical applications of pupil perimetry have shown that most diseases affecting the retina and the visual pathway caused pupil field scotomata which match the defects found in standard perimetry (Figs. 7.2, 7.3, and 7.4) [3–5].

Pupil perimetry can be performed either by means of a special pupillographic device or by a modified standard perimeter. However, most of these devices serve for research purposes and only a few machines are available commercially. In our laboratory, the pupillographic device consists of a computer, a 19-inch CRT screen for the stimulus presentation, and a third monitor for continuous monitoring of fixation by observation (Fig. 7.5). Stimuli are displayed on the computer screen at a distance of 20 cm from the subject's eye. A small red spot is presented for fixation. Blinds around the device prevent stray light from the room disturbing the measurement. The pupil reaction is recorded by means of an infrared-sensitive video camera. The pupil edges can be determined by the contrast of the dark fundus and a very light iris infrared reflex. During the test the examiner can observe the quality of fixation, the stimulus sequence, as well as the continuous pupillographic curve. For the stimuli, white light is usually used and different stimulus intensities can be tested with a constant background luminance of 2.7 cd/m^2. The stimulus is usually presented for 200 ms every 2000 ms.

In contrast to standard visual perimetry, pupil perimetry represents a method for objective visual field examination. It can be very useful particularly in patients suspected of stimulation [6] or in patients who do not manage standard perimetry well enough.



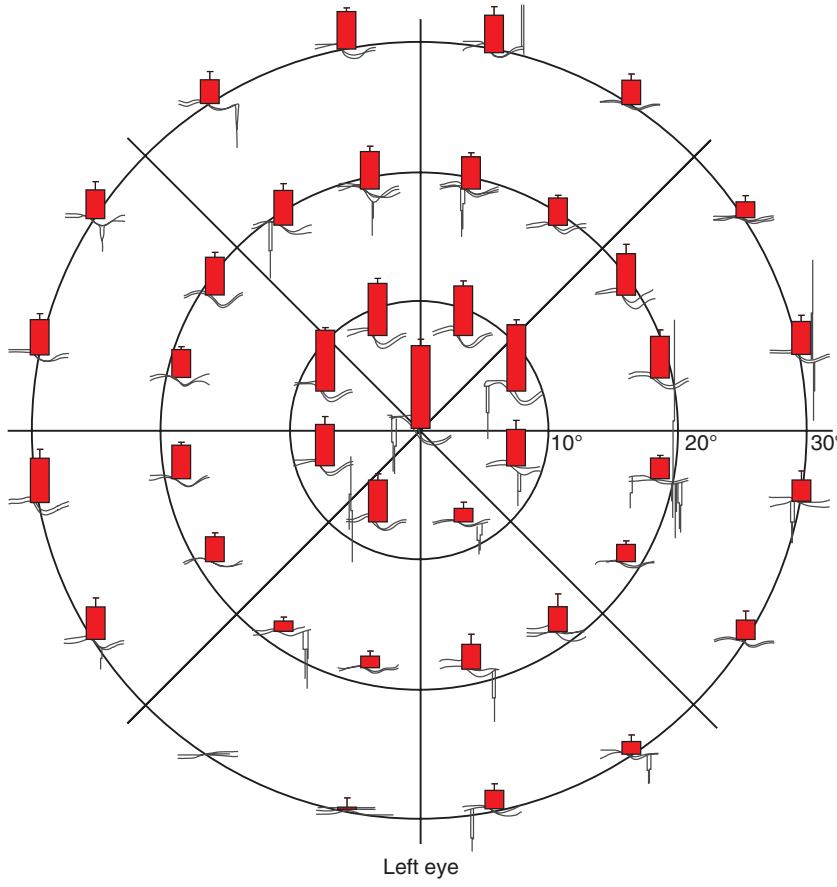
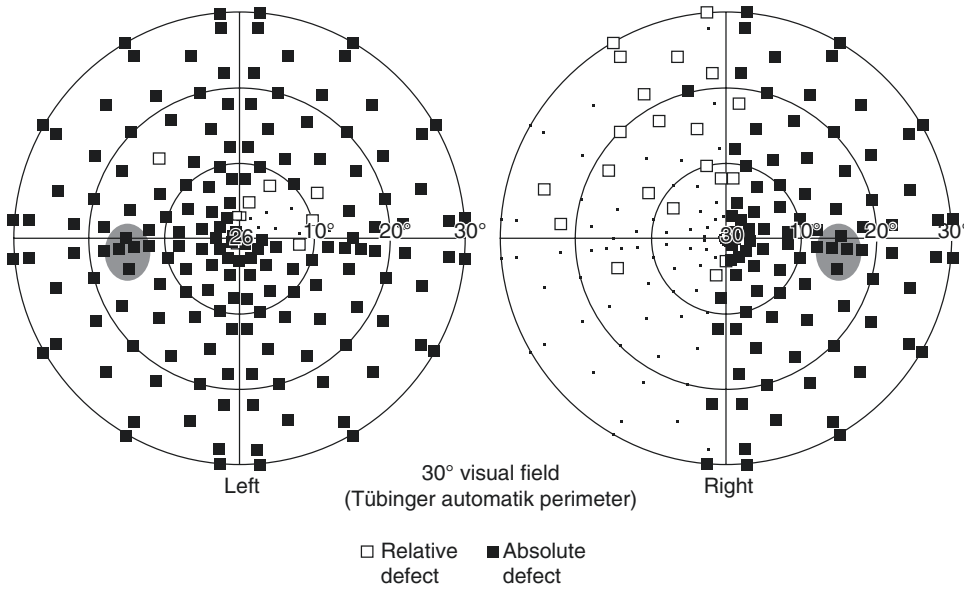


Fig. 7.2 (*Top*) Visual field in a patient with sphenoid wing meningioma causing a lower altitudinal defect in the left eye. (*Bottom*) Pupil field of the left eye as detected by means of pupil perimetry. The column represents the mean value of pupil light response amplitude in millimeters at each tested location in the visual field. Corresponding pupil field defect in the lower hemifield can be recognized by a reduced pupil light reaction in this area



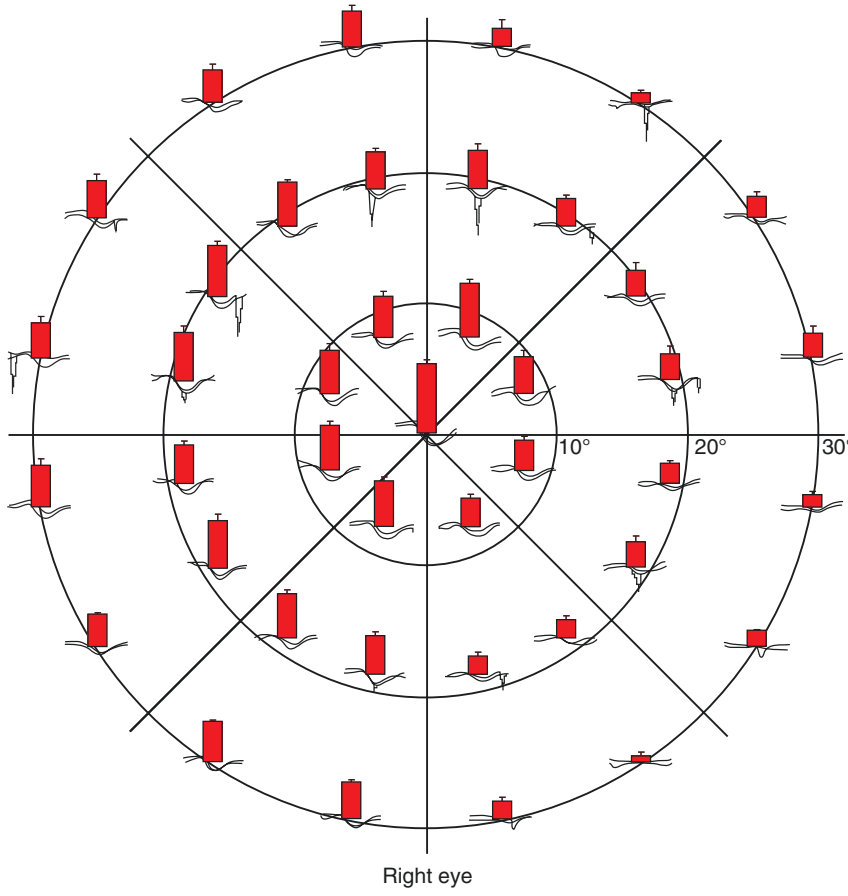


Fig. 7.3 (*Top*) Visual field in a patient with pituitary adenoma affecting the entire visual field of the left eye and the temporal hemifield of the right eye. (*Bottom*) Pupil field of the right eye showing a corresponding pupil field defect in the temporal hemifield

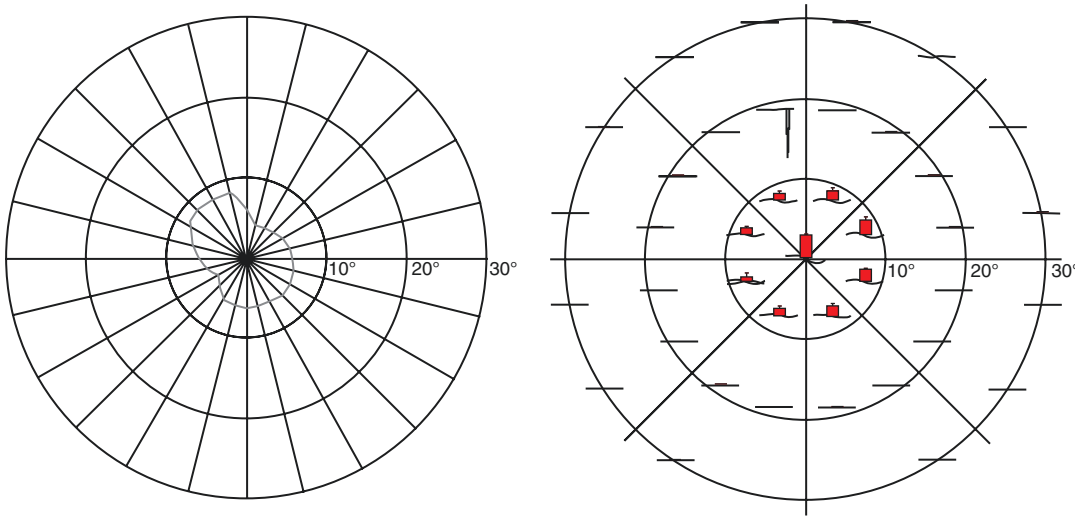


Fig. 7.4 (*Left*) Schematic drawing of advanced concentric visual field loss in a patient with retinitis pigmentosa as detected by kinetic perimetry (Goldmann stimulus V4). (*Right*) Corresponding pupil field with pupil light reaction present only within the preserved visual field (From Skorkovská et al. [4], with permission)

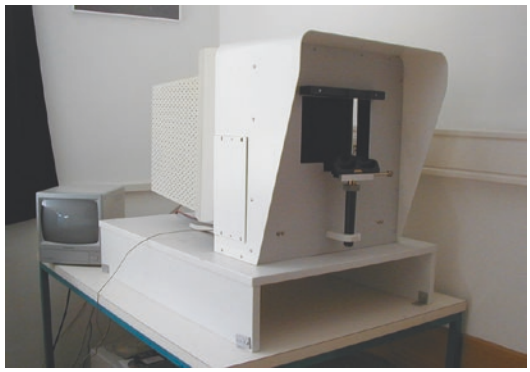


Fig. 7.5 Pupil perimetry (campimetry) in our pupil laboratory. The pupillographic device consists of a computer, a screen for the stimulus presentation, and a third monitor for a continuous monitoring of fixation. The examination is carried out in darkness, separately for each eye

7.2.3 Chromatic Pupillography

Recently it was found that not only the rods and cones, but also other retinal elements – retinal ganglion cells containing melanopsin (ipRGCs) – are intrinsically photosensitive and capable of phototransduction [7–10]. Unlike rods and cones they do not or only marginally contribute to image formation. They serve more as a detector of the surrounding light intensity and are involved in the management of circadian rhythm. In addition to that, axons of the ipRGCs are connected with the pretectal area and can drive pupil light reaction, particularly at high intensities of light (100 cd/m^2). This explains why people who lost sight because of a photoreceptor disease still may have normal pupil light reaction and circadian rhythm [11, 12].

Rods and cones are located in the outer retina, ipRGCs in the inner retinal layer. Each type of photoreceptors has its different wavelength sensitivity. The peak sensitivity of the ipRGCs is in the blue spectrum around 480 nm. By registering the pupil light reaction to light stimuli of different color and intensity, it is possible to separately test the function of different population of retinal photoreceptors, and like this evaluate and monitor the function of outer retina (rods and cones) and inner retina (ipRGC). This method is called chromatic pupillography and appears as a highly sensitive method for objective examination of neuroretinal function that might become a useful complement to electrophysiological tests, at this moment more for research purposes or clinical trials (Figs. 7.6 and 7.7) [13].

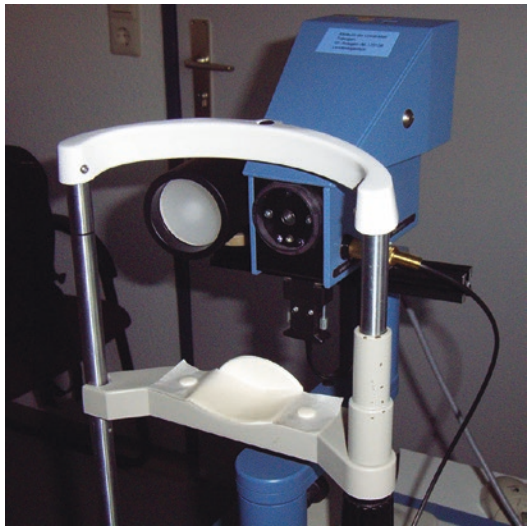


Fig. 7.6 Chromatic pupillography equipment in our laboratory. The stimulus is provided by a mini-Ganzfeld color LED stimulator to one eye and the consensual pupil light reflex of the nonstimulated fellow eye is measured by the compact integrated pupillograph (AMTech GmbH, Dossenheim, Germany)

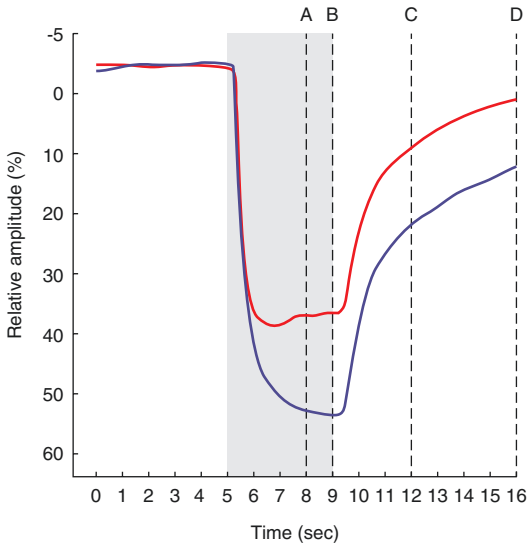


Fig. 7.7 The relative pupil light response amplitude to *red* and *blue light* stimulus in healthy subjects. With *blue light*, the relative amplitude is significantly greater and the time to maximal pupil constriction significantly longer compared to *red light* for all tested time points (*indicated by the vertical lines A–D*). *Blue light* evokes the "sustained" pupil contraction (driven by ipRGCs), while the *red light* rather the "transient" contraction (driven by rods and cones) (From Skorkovská et al. [13], with permission)

7.3 RAPD in Optic Tract Lesions

Optic tract lesions are characterized by homonymous visual field defects, asymmetric bilateral optic disc atrophy (more pronounced contralateral to the lesion), and contralateral RAPD (Fig. 7.8). The closer the lesion is located to the chiasm the more incongruent are the visual field defects. Visual acuity is usually not affected. The suggested causes for this contralateral RAPD in an optic tract lesion are a greater nasal photoreceptor density, a ratio of crossed to uncrossed fibers in the chiasm of 53:47, and a temporal visual field 61–71% larger than the nasal field [14]. A tract lesion disrupts fibers from the contralateral nasal retina and the ipsilateral temporal retina, thus disproportionally diminishing input from the contralateral eye and producing a corresponding RAPD. However, the magnitude of RAPD in patients with an optic tract lesion can range from 0.3 logE to 1.0 logE and this can, probably, be completely explained neither by the rather small asymmetry of crossed to uncrossed fibers nor the difference between temporal and nasal hemifield [15].

Patients with an optic tract lesion represent a unique model for studies of the hemifield organization of the afferent pupillomotor system. A complete tract lesion enables the comparison of the pupil light reaction from temporal and nasal retina without the disturbing influence of stray light because only the intact retinal half can participate in the pupil light reaction. Because of stray light such an estimation of the nerve fiber distribution in the pupillary pathway is not precisely possible in a healthy eye with both retinal halves functioning. By means of pupillography it could be shown that in case of separate light stimulation of either of the retinal halves in optic tract lesions, the pupil light reaction was always greater in the preserved temporal visual field ipsilateral to the site of the tract lesion, compared to the functional contralateral nasal visual field. So, RAPD in optic tract lesions probably reflects the difference in light sensitivity of the intact temporal and nasal visual field [16].

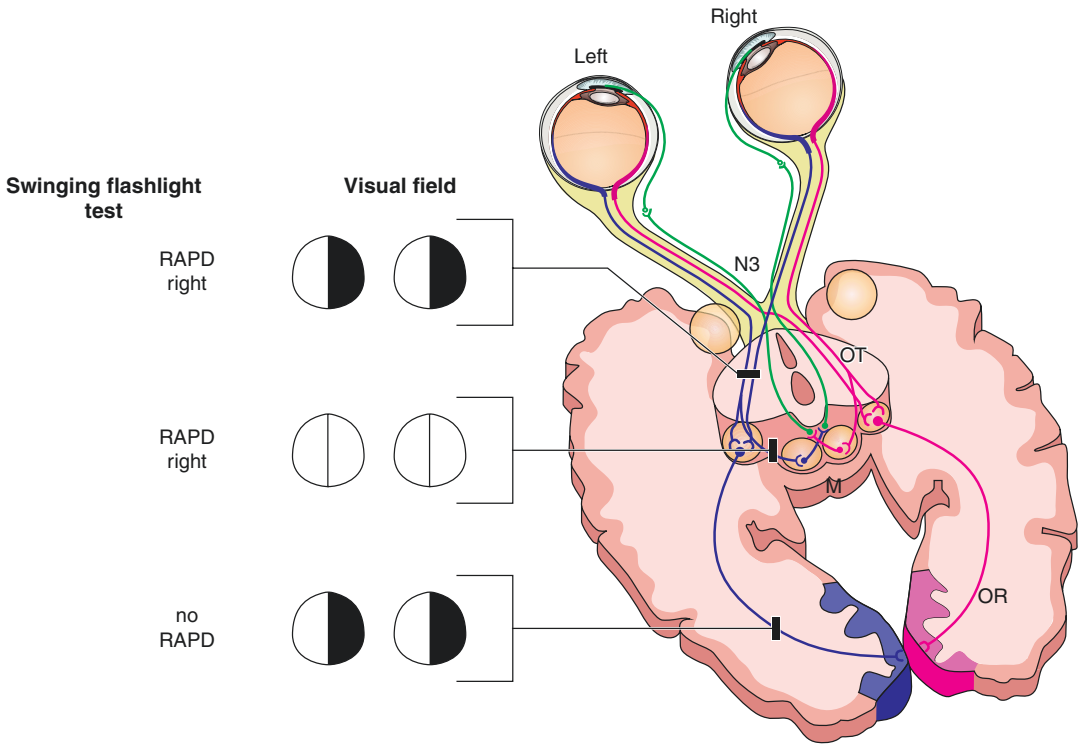


Fig. 7.8 Schematic representation of different findings according to the course of the pupil light reflex pathway (*OT* optic tract, *M* midbrain, *N3* oculomotor nerve, *OR* optic radiation). Lesions of the optic tract result in homonymous hemianopia with contralateral relative afferent pupillary defect (RAPD). Lesions of the brachium of the superior colliculus cause contralateral RAPD but no visual field defect. In suprageniculate lesions with sufficient distance from lateral geniculate body homonymous hemianopia without RAPD develops

7.4 RAPD Without Visual Field Loss

Prior to the termination of retinal ganglion cell axons in LGN, the pupillomotor fibers branch off and travel via the brachium of the superior colliculus to the ipsilateral pretectal nucleus, where they synapse with the next neuron of the pupillomotor pathway. This small region between the optic tract and pretectal area is called pretectal afferent pupillary pathway and is located inside the dorsal midbrain in the brachium of the superior colliculus. A pathology in this area will cause a contralateral RAPD without any visual impairment – that means no decrease in visual acuity, no visual field loss and no optic atrophy (Fig. 7.8). If the lesion was located more proximally (e.g., in optic tract), a visual field defect would be present and on the other hand, if the lesion was more distally (e.g., in Edinger-Westphal nucleus), an anisocoria would be observed.

There are several reports [17–19] in the literature dating back to 1920s that describe patients with a unilateral RAPD without any visual impairment. Most of the patients had a pathology in the dorsal midbrain and all authors considered the cause lesion of the pretectal afferent pupillary pathway in dorsal midbrain. Recently, it was shown by means of pupil perimetry that the pupil field in these patients looked exactly like the visual field in an optic tract lesion [20]. So, the RAPD without visual loss is simply a variant of the RAPD in an optic tract lesion, in which the site of the lesion is moved towards dorsal midbrain and leaves the visual function intact.

7.5 RAPD in Supragenicular Lesions with Homonymous Visual Field Defect

Detection of a RAPD in acute homonymous hemianopias has been commonly used in differentiating infrageniculate from supragenicular lesions, since neither optic atrophy nor a RAPD should occur in acquired affections of the optic radiation or the visual cortex. However, there are exceptions.

For instance, RAPD has been described in patients with congenital occipital hemianopia [21]. The suggested mechanism was transsynaptic optic tract atrophy after intrauterine or perinatal damage to the supragenicular visual pathway, which presumably affected also the afferent pupillary fibers to the pretectal area of the midbrain. This explanation sounds plausible and in accordance with what was written above.

Further, there are numerous studies, reporting disturbances of the PLR in patients with acquired HVFDs due to lesions not involving the optic tract, that are no more compatible with the traditional model of the pupillary pathway: either the presence of pupillary "hemiakinesia" or "hemihypokinesia" in the blind part of the visual field [3–5, 22–27] or RAPD contralateral to the brain lesion, as a response to full-field light stimulation [28, 29]. Results of these studies provide evidence that the pupil light reaction is not a pure subcortical pathway.

Further progress in understanding the underlying anatomic pupillary pathway could be achieved thanks to advances in neuroimaging. Modern methods of analysis enable us to define any lesion very precisely. Like this, clinically relevant RAPD, as a response to full-field light stimulation, could be limited to supragenicular lesions that were found closer than 10 mm to the LGN or involving it, but sparing the optic tract. In lesions located more than 18 mm from the LGN, RAPD did not occur [29]. It was concluded that RAPD was probably not caused by a lesion of the visual pathway itself, but by a lesion of the intercalated neurons between the visual pathway and the pupillomotor centers in the pretectal area of the midbrain, comparable to the lesions that cause RAPD without visual field loss. Further, using a new strategy of lesion analysis by combining subtraction techniques with the stereotaxic probabilistic cytoarchitectonic map it was found that a region in the early course of the optic radiation in the temporal white matter, close to the LGN, seems to be associated with the presence of RAPD. This finding is consistent with the hypothesis that the connection between visual pathway and pretectal area in the dorsal midbrain is probably closely related to the LGN and its involvement in supragenicular homonymous hemianopias can lead to RAPD. So, there seems to be more input from supragenicular neurons and the occipital cortex but the exact anatomy of this connection is still unclear. It may be that the critical area in the early course of the optic radiation near LGN is the site of integration of cortical signals in relation to the PLR into the pupillomotor pathway. Another explanation could be that some afferent pupillomotor fibers of infrageniculate origin bypass the LGN and then travel through this critical area to the mesencephalon.

In summary, the classical view of the pupillary pathway in postchiasmal lesions of the visual pathway is basically true. Infra- and supragenicular lesions can still be distinguished by the presence of RAPD. However, it must be kept in mind that RAPD can develop also in lesions in the surroundings of the pretectal area. And the situation is even more complicated in case of pupillary hemihypokinesia that is to be discussed.

7.6 Pupillary Hemihypokinesia

According to the classic idea of the pupillary pathway, infrageniculate lesions should present with a hypokinesia, supragenicular lesions should not. However, many studies [3–5, 22–27] in patients with retrogeniculate damage and homonymous visual field defects have provided evidence for impairment of pupil responses to small localized stimuli registered by pupillography. Early clinical reports dating back to 1940s were later reproduced by other groups using modern pupillometric techniques in patients well documented by magnetic resonance imaging or computed tomography, and currently there is no doubt that the retrogeniculate visual pathway or

even visual cortex is involved in the pupillary light reaction. In patients with retrogeniculate damage the so-called pupillary hemihypokinesia can be observed which differs from RAPD.

Pupillary hemihypokinesia (or akinesia) means a reduced or absent pupil light reaction to perimetric stimuli in the blind part of the visual field and was observed in all kinds of postchiasmal lesions (Fig. 7.9). The first pupillometric measurements in patients with suprageniculate lesions have been performed already by Harms in 1949 [22] and have challenged the Wernicke's description of the pupil light reflex. Harms found reduced pupil light reaction in war veterans with occipital lobe injuries. At that time, his results were called into question and the findings ascribed to the transsynaptic degeneration or to an overlooked pregeniculate damage. Harm's

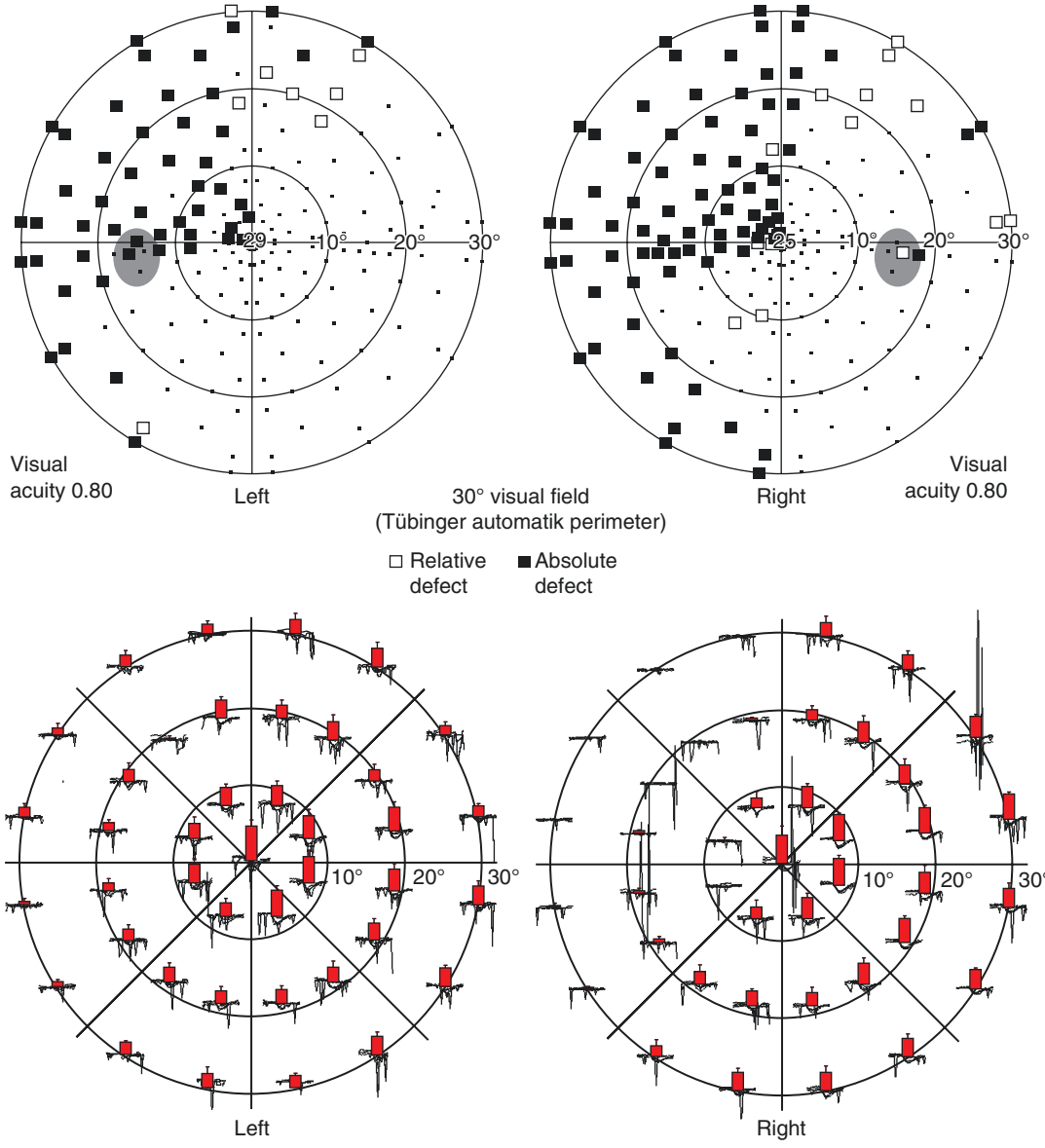


Fig. 7.9 (*Top*) Visual field in a patient with superior left homonymous quadrantanopia due to an ischemia. (*Bottom*) Pupil field of the same patient showing a reduced or absent pupil light reaction in the affected portion of the visual field (From Skorkovská et al. [4], with permission)

findings were eventually many times reproduced, later also with the help of modern pupillographic equipment and sophisticated imaging methods. Still, even today we can only speculate about the underlying cause of this phenomenon.

The findings, for example, can be explained by the view, that in pre- and retrogeniculate lesions different components of the light response may be involved to a different extent. The steady-state component of the pupillary light response regulates the resting pupil diameter depending on the ambient light level; it is characterized by a large spatial summation and a wide dynamic range. This component is represented basically by the subcortical pupillary pathway. The transient component of the pupil light response is responsible for the constriction of the pupil in response to brisk light stimuli. In the presence of this component, the steady-state signal is largely discarded. The transient component reflects merely novel changes in luminance contrast; it is characterized by a "limited spatial summation, band-pass temporal response characteristics, and high contrast gain" [30, 31]. It is obvious that the stimulus characteristics of pupil perimetry predominantly address this transient component. There is strong evidence that – after cortical processing of specific stimulus characteristics – projections from the extrastriate visual cortex contribute considerably to the transient pupil response component.

Indeed, pupillographic measurements with specific stimuli (isoluminant pattern stimuli, chromatic stimuli or moving stimuli) in patients with a retrogeniculate lesion indicate the possible existence of two separate pupillomotor channels: the PLR in the blind hemifield was reduced but not absent. However, all the other specific, "higher" pupil responses to stimulus attributes, like stimulus color, structure, or motion, were completely lost. On the other hand, studies in patients with Parinaud syndrome [32] demonstrated that there was a small, residual PLR and preserved reactions to pattern and color stimuli as well as preserved pupillary sleepiness-related oscillations. Again, the existence of a cortical input to the pupillary pathway was suggested, since the retinal afferent input to the pretectal nuclei had been apparently damaged.

Hence, it is considered that two or more distinct channels could serve the PLR: a more primitive "luminance channel," which connects the retina directly with the pretectal area and responds to diffuse light, and "pattern channel," which is mediated supragenículately and responds to shifts in structured stimuli, like isoluminant grating, motion, and isoluminant color stimuli. The PLR is primarily mediated by the luminance channel and to a smaller extent by the "weaker," supragenículate pattern channel (Fig. 7.10). It seems that the

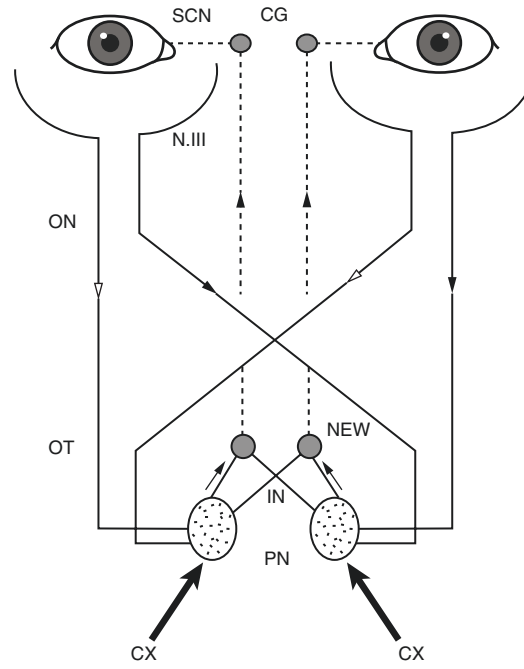


Fig. 7.10 Schematic drawing of the current view of the pupillary light reflex pathway. Afferent pupillomotor fibers travel in the optic nerve and undergo hemidecussation at the chiasm before entering the optic tract. In the posterior third of the optic tract, the pupillomotor fibers branch medial via the brachium of the superior colliculus to the lateral geniculate nucleus (LGN) and synapse in the ipsilateral pretectal nucleus (PN) in the dorsal midbrain. Intercalated neurons from each pretectal nucleus then project to both Edinger-Westphal nuclei. Parasympathetic fibers from the Edinger-Westphal nuclei (NEW) travel with the oculomotor nerve to the ciliary ganglion (CG) and via the short ciliary nerves (SCN) innervate the iris pupillary sphincter muscle. However, there seems to be more input from supragenículate neurons and the visual cortex (CX), although the exact anatomy of this connection is still unclear. It may be that stimuli with different attributes are processed at a different level – subcortically or by supragenículate neurons and the visual cortex. The proposed site of integration of cortical signals to the pupillary response should be located in the early course of the optic radiation near the LGN (From Papageorgiou et al. [29], with permission)

intrinsically photosensitive retinal ganglion cells operate merely on the subcortical level, while the cortical pathway may rely more on ganglion cells that carry predominantly cone inputs. Additionally, it needs to be considered that a pupillary constriction could also be evoked by temporarily canceling the inhibition of the Edinger-Westphal nucleus by the central sympathetic inhibiting system. This might provide a second pathway for pupillary constriction.

Conclusion

Pupillary findings in patients with pregeniculate lesions of the visual pathway are consistent with the subcortical course of the pupil light reflex arc. However, the evidence of pupillary hemihypokinesia in patients with homonymous visual field defects due to retrogeniculate lesions of the visual pathway supports the hypothesis that the afferent pupillary system is not purely a subcortical reflex arc but consists of two pathways: one of these via intrinsically photosensitive retinal ganglion cells (ipRGCs) directly reaching the dorsal midbrain, the other running through the normal RGCs via the visual cortex; although the exact anatomy of this pathway is still unclear. The subcortical pathway accounts for changes in pupil diameter to stimuli of high intensity, whereas the cortical part responds particularly to higher stimulus attributes like color, structure, or motion. Future research will certainly provide further understanding of the problem.

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Eye Movements and Visual Search in Homonymous Visual Field Defects

8

Jason J.S. Barton

Abstract

Eye movements in hemianopia can serve as an index of perceptual changes, residual visual function, or adaptive changes to altered vision. Central fixations are shifted towards the blind hemifield and saccades into the seeing hemifield are prolonged and less reliable. Targets in the blind hemifield are initially found with an inefficient series of small saccades, but some patients develop a compensatory search hypermetria. Blindsight studies have reported on the accuracy and reliability of saccades or pursuit responses to targets in the blind hemifield, with variable results. How hemianopic subjects scan visual information has been studied with search displays, line bisection and reading. The efficiency of scanning by hemianopic subjects is an important determinant of success in daily life activities such as driving.

Keywords

Hemifield • Dyslexia • Blindsight • Line Bisection • Visual Search • Driving • Saccade

8.1 Introduction

Why study eye movements in hemianopia? After all, homonymous visual field loss is a purely sensory deficit, the most classic and longest known visual effect of cerebral lesions. Eye movements have nothing to do with the origins of homonymous hemianopia. Hemianopia is the loss of processing of visual information coming from one half of the retina of each eye and eye movements are not responsible for this; thus, any changes in eye movements after hemianopia are merely an epiphenomenon. Nevertheless, as an

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epiphenomenon, eye movements may still reveal aspects about hemianopia that are informative for the researcher or critical for the patient.

For one, what we see determines where we look. In this sense, the change in visual experience caused by hemianopia will necessarily alter the eye movements made in response to visual input. Studying those eye movements may allow inferences about the processing of vision after hemianopia. Furthermore, there is the interesting finding that what we do not see in hemianopia may still influence where we look. 'Blindsight' rests on experimental data that show that visual stimuli in the blind hemifield of which the patient is unaware can still influence their responses to the world. Eye movements have had a prominent role in such research, and indeed these were the response measured by the first study that claimed to demonstrate blindsight in humans over 40 years ago [1].

The reverse is also true, however: where we look also determines what we see. This is particularly true in the case of hemianopia. Visual stimuli located within a blind hemifield are not seen, but can be perceived if the eyes are moved so that the stimuli now fall within the seeing hemifield. Eye movements thus play a critical role in the visual experience of the hemianopic patient. Some changes in eye movements represent important strategic adaptations of behavior that can reduce the impact of hemianopia in daily life. Studying whether these ocular motor changes are present, how they evolve and if they can be enhanced through rehabilitation are important and practical components of hemianopia research.

8.2 Fixation

Fixation is the simple task of maintaining the image of an object at the fovea, the central region of the retina with the highest spatial resolution, and most often also the point at which attention is focused. A common finding in hemianopic patients is a slight shift of central fixation into contralateral space [2–4]. This is likely a strategic adaptation that has a number of possible explanations. The most straightforward one is that since half of the foveal region is lost in complete hemianopia, placing fixation slightly towards the side of the hemianopia allows more of the fixated object to be seen, optimizing the perception of stimuli in the central field. If so, it should follow that hemianopic patients with sparing of macular vision would be less likely to show such a fixation shift. Whether this is true is not known.

Alternatively, such a fixation shift may reflect a perceptual shift of the hemianopic subject's estimate of the center of a visual scene. It has long been known that hemianopic patients show a small contralateral deviation in line bisection judgments [5, 6]. This may in turn have several explanations. First, the representation of visual space may be altered in hemianopia. From the retina to striate and extrastriate cortex, central regions of vision are more represented than more peripheral regions in the visual system [7, 8]. In someone with only one hemifield, this central magnification means that the part of the remaining visual field nearest to the blind field is more strongly represented, an effect which may be accentuated in hemianopia [9]. This can generate a small contralateral bias in line bisection judgments made by healthy subjects forced to view lines with only one hemifield [10]. Thus, as they scan the environment, the contralateral regions of space are emphasized, and the result may be a contralateral deviation of their estimate of where center is located. Second, there is an imbalance in spatial attention in hemianopia. Unlike the case of hemineglect, in which there is a pathologic failure to direct attention to contralateral space, patients with hemianopia direct more attention contralaterally, into the blind field, which is evident in fixation patterns they make during visual search [11]. This is a strategic adaptation to their deficit, and the increased emphasis of attention on contralateral space may lead to a deviation of the subjective estimate of center. Consistent with this adaptive hypothesis is the observation that the contralateral line bisection error is not seen in the acute stage of hemianopia [12]. Whether any of these perceptual explanations account for contralateral deviations of perceptual center as seen during line

bisection remains a subject of debate, with conflicting findings from studies in which hemianopia is simulated by virtual gaze-contingent displays in healthy subjects [13, 14].

8.3 Saccades to Targets in the Seeing Ipsilateral Hemifield

Although it is not intuitive, the intact ipsilateral hemifield of hemianopic patients may not be entirely normal, even when damage is strictly confined to one cerebral hemisphere. This is evident subjectively to some patients who complain of fatigue or blurring of their remaining vision and objectively to researchers who find in the seeing ipsilateral hemifield deficits in spatial and temporal contrast sensitivity [15], reduced sensitivity and increased response times to suddenly appearing visual targets, and reduction in the 'useful field of view' [16].

In eye movements, one might have postulated that responses to ipsilateral targets would be faster in the absence of competition from the blind hemifield. However, the latencies of both manual responses and saccades to moving or stationary targets in the seeing ipsilateral hemifield are actually prolonged, in the range of 20–100 ms, an effect that has been reported by numerous studies [16–21]. Furthermore, with paradigms that included catch trials on which no target appears, some hemianopic patients even failed on occasion to make saccades to targets in the seeing ipsilateral hemifield, an omission that does not occur in healthy subjects [21]. Older studies have also found that horizontal saccades to ipsilateral targets may be less accurate in a small minority of hemianopic patients, though this improved with repetition if target location did not change [3]. The reasons for these aberrations of visual processing in the ipsilateral hemifield are not entirely clear. Some postulate that this is evidence of excitatory influences from ipsilateral striate cortex that facilitate saccadic triggering in both right and left superior colliculi [20]. Others propose that a unilateral lesion reduces the information processing capacity and efficiency of the entire visual system, possibly reflecting damage to connection fibers both within and between hemispheres [16].

8.4 Saccades to Targets in the Blind Contralateral Hemifield

When hemianopic patients know that targets will appear in random locations in their blind field, they make a series of small searching saccades until the target is found [18, 22]. This can be used as a bedside test for functional hemianopia [23], as functional patients caught unawares will make an accurate saccade to something they claim not to see. These small searching saccades for a target on the blind side can also distinguish hemianopia from hemineglect in the initial weeks after onset [24]. Interestingly, this difficulty with locating targets in the blind hemifield is not confined to visual stimuli. Hemianopic patients also make a similar series of small searching saccades towards auditory stimuli, implying that hemianopia disrupts a common motor program used for any type of contralateral target, possibly at the level of the superior colliculus [20].

The latency of hemianopic patients to initiate a searching saccade to a target in a blind hemifield is often prolonged by 100 ms or more [21], even when the disappearance of the fixation light – along with the absence of a target in the seeing hemifield – is a reliable cue that something must have appeared in the blind hemifield [25]. Hence, triggering of a saccade reflects not just disengagement from fixation but is facilitated by a visible target.

This staircase pattern of small searching saccades persists when target location is unpredictable from trial to trial [18]. When auditory or visual targets are predictable in location, hemianopic patients learn their spatial coordinates and after only a few trials begin instead to make a single saccade that often overshoots the target [18, 20, 26, 27]. Thus, their visuospatial working memory is able to build up and maintain a position estimate of target location over several trials

and to use that in lieu of direct visual input to generate coordinates for saccadic programming.

With time some patients develop a more efficient strategy to find targets in their blind hemifield. They make one very large contralateral saccade that will place most of the previously unseen portions of the world into their seeing ipsilateral hemifield, allowing them to perceive the target quickly and then make an ipsilateral saccade to it [18]. Some healthy subjects experiencing a computer-simulation of hemianopia learn this strategy rapidly over minutes [13]. However, children may not develop this adaptive strategy naturally [28] and the same may be true of some adult patients: hence, some rehabilitative approaches specifically try to foster this 'search hypermetria' as a strategic compensation [29].

8.5 Blindsight Saccades

Early hypotheses about blindsight centered on the role of the superior colliculus and thus studies naturally focused on the ability to locate targets with saccades. Indeed, in monkeys with striate ablations, saccadic localization of contralateral targets is lost after a muscimol injection of the superior colliculus [30]. The first study [1] found a weak correlation between saccadic size and target position in four patients with incomplete hemianopia. Patient DB had a weak correlation of saccades with targets, but only for targets between 5° and 25° [31, 32], a result mainly driven by saccades to the target at 5°, which was a portion of the visual field that later recovered [33]. Interestingly, a later study of DB did not find evidence of saccadic localization when the targets varied in both horizontal and vertical position [34]. Nevertheless, another study [35] found some saccadic localization in two hemianopic patients, for targets with eccentricity of less than 30°.

Other studies found that only patients with conscious residual vision – who perceived the flashes as 'dark shadows' – reliably located targets in their blind hemifield with saccades [36, 37]. Another did not find any saccadic localization in three hemianopic patients [18]. A larger study found a weak correlation of saccadic amplitude with target position in only two of ten patients [25].

It has been suggested that blindsight saccadic localization might improve with training, as in monkeys [38]. In humans, the accuracy of saccadic search (as opposed to initial saccades) was weak or nonexistent in six subjects but improved with training [39, 40]. However, this probably represents learning of an adaptive strategy rather than development of blindsight.

Hemidecorticate patients show what is possible without striate and extrastriate cortex. Braddick et al. [41] found that two hemianopic infants were more likely to look to their blind hemifield when a target was presented there than when there was no target at all, suggesting some rudimentary subcortical target detection in the hemianopic region.

A slightly different question to that of localization is whether stimuli in the blind hemifield can reliably trigger saccades. One study used blocks that included both trials on which a target appeared in either the seeing or blind hemifield as well as catch trials on which no target appeared [21]. Four hemianopic patients initiated more saccades when blind field stimuli appeared than they did on the catch trials, even though they replied that they had not seen a stimulus. The amplitude of the saccades to the targets in the blind hemifield did not correlate with target location, however, indicating no blindsight ability to locate the target.

8.6 Blindsight Modulation of Saccades

An alternate blindsight strategy is to see how saccades to seen stimuli are affected by additional stimuli in the blind hemifield. Saccades show small curved deviations away from distractors placed along their trajectory [42, 43]. In two of five hemianopic patients, vertical saccades deviated away from distractors even though they were in their blind hemifield [44]. In the global effect, if the distractor is close to the target, the saccade lands at a position between the distractor and the

target [45]. This is attributed to spatial averaging of the neural activity generated by the distractor and target in some neural map, most likely in the superior colliculus [46, 47]. Curiously, two hemianopic patients displayed a paradoxical global effect, with saccadic endpoints that deviated away from rather than towards distractors in their blind hemifield [48].

Another study took a different modulatory approach. The antisaccade task requires subjects to make a saccade to a position in the direction opposite to the location of the target [49, 50]. The amplitudes of these antisaccades are more variable and inaccurate than those of saccades made to the location of visible targets [50]. One blindsight study showed subjects target in their seeing ipsilateral hemifield, which required them to make an antisaccade towards their blind contralateral hemifield. Antisaccades were more accurate and faster when the stimulus in the seeing hemifield was accompanied by a probe that was simultaneously flashed at the goal location in the blind hemifield [51].

Other studies using a modulatory approach have produced negative findings. In the ocular motor distractor effect, distractors far away from the target or saccadic trajectory tend to increase the latency of saccades rather than modifying the saccadic trajectory or endpoint. Blind distractors did not have any influence in hemianopic subjects in one study [52]. Another study examined the integration of visual and auditory information in hemianopic patients. While the presence of concurrent visual stimuli improves the accuracy of saccades to auditory targets by healthy subjects, seven hemianopic patients did not show any benefit from visual stimuli in their blind contralateral hemifield [53].

8.7 Blindsight Optokinetic and Pursuit Responses

Responses to moving stimuli have been a frequent choice in blindsight studies. This has been driven primarily by observations in monkeys that support the existence of a retino-tecto-pulvinar relay that bypasses striate cortex to project directly to extrastriate regions such as area V5, which is involved in motion perception. Striate lesions do not abolish motion responses in area V5 [54–56] or area V3A [57] unless accompanied by lesions of the superior colliculus [54, 58], though another study using optical imaging found that deactivation of striate cortex with muscimol abolished activity in area V5 [59]. In normal human subjects, physiologic studies using evoked potentials [60] or transcranial magnetic stimulation [61] have suggested that visual motion signals may arrive in area V5 before and independent of signals in striate cortex, though again this is not replicated by all studies [62].

In hemianopia, such evidence has spurred investigation of blindsight by studying eye movements to moving stimuli. For saccades, one study found that their accuracy was better to oscillating rather than stationary spots in one patient [63]. This contrasts with mixed results in manual pointing accuracy in two other studies: this was more accurate to moving than stationary gratings in only two of six patients [35], and no different for moving versus stationary squares in four hemispherectomized patients [64]. However, the more classic ocular motor responses to motion are the optokinetic response and smooth pursuit. Four children with cortical blindness were shown to have optokinetic nystagmus [65], though this is tempered by the fact that two may have had some residual vision. In the two children with congenital cortical blindness, the optokinetic responses elicited by monocular stimulation showed a temporo-nasal asymmetry, which is characteristic of the components of the optokinetic system located in the brainstem, namely the nucleus of the optic tract [66]. An adult with cortical blindness recovered some optokinetic responses after 5 months [67], but two other cortically blind patients did not [68, 69], nor were these elicited by motion stimuli in the blind hemifield of hemianopic patients [70]. The speed of the ocular pursuit of small moving targets weakly correlated with target speed in only one of ten hemianopic patients studied [25], and this did not depend on the integrity of the lateral occipitotemporal cortex, the location of the human homologue of area V5 [71].

One study also looked at whether moving stimuli in the blind hemifield can influence the pursuit of a moving target in the seeing hemifield [72]. This built on observations that, first, humans can generate smooth pursuit eye of an imaginary target whose location is indicated by moving flanking stimuli situated in parafoveal vision and, second, that pursuit is better when there are two such stimuli, one on either side, than if there is just one [73]. The natural question in blindsight is whether this is true even if the second parafoveal stimulus is located in the blind hemifield. In subject JS, the addition of the blind stimulus did not increase pursuit gain [72].

8.8 Scanning Patterns in Hemianopia

Beyond the metrics of saccades and pursuit eye movements, the distribution of ocular fixations made by hemianopic patients can reveal how these subjects sample their visual environment. Early studies concluded that chronic hemianopia does not affect the scanning of drawings [26, 74], but these used fairly coarse parameters. Subsequent work has since revealed several interesting findings. First, these have confirmed the expected, that the visual search of hemianopic patients is less efficient in general. Their overall search times, total number of fixations made and scanpath lengths (the sum of the amplitude of all saccades made during search) are all increased, and their fixation durations are longer and fixations more repetitive [75, 76]. Such findings are already evident in patients studied in the first few days following the onset of hemianopia after a stroke [77] and may be more severe in those with right hemianopia [75, 77]. Comparisons with the experimental effects of virtual hemianopia created in healthy subjects suggest that most of these effects are directly attributable to the hemianopia [78]; however, others suggest that some of the increased search duration and certain effects such as repetitive fixations may be due to damage to other brain circuitry [79]. Also, some of these changes may represent adaptations that allow hemianopic patients to attain a performance accuracy on complex tasks that is similar to that of controls [76]. With time, the efficiency of search can improve, in part through making larger and earlier saccades into the hemianopic side [77, 80].

In addition to these general effects, the pattern of search is also altered in hemianopic patients. For one, numerous studies have shown that hemianopic patients spend more time scanning the contralateral side of visual displays. This has been observed in numerous visual paradigms, such as dot-counting [75, 76, 78, 81, 82], uninstructed viewing of natural and degraded images [83], the search for randomly located targets [76] and virtual driving displays [84]. A more fine-grained analysis found that this contralateral emphasis of hemianopic search forms a gradient of fixations that increases towards contralateral space (Fig. 8.1), the opposite of what is seen in hemineglect [11]. This may reflect an adaptive gradient of attention that increases the visual exploration by hemianopic patients on their blind side, which some considered a marker of efficient strategic compensation for hemifield loss [85]. Studies with simulated hemianopia in healthy subjects show that this adaptive gradient develops very quickly, within about five trials after onset of hemianopia (Fig. 8.2), and then is slowly refined over many trials to become more efficient [86].

Altered scanning patterns can also be shown with other paradigms besides visual search. Line bisection is a classic task used to diagnose hemineglect. It can differentiate hemianopia from hemineglect: while patients with hemineglect tend to place bisection points too far towards the side of their lesion, as if they were unaware of the contralateral extent of the line, hemianopic patients tend to make a small error in the opposite direction [2]. During line bisection, healthy subjects concentrate fixations around the center of the line and rarely look at the peripheral ends of the line [2, 27, 82]. This may reflect the fact that the center of the line is most relevant during a bisection task, and hence attention is deployed to this region. In contrast, hemianopic patients have two peaks of fixations (Figs. 8.3 and 8.4), one at the end of the line on their blind side and a central

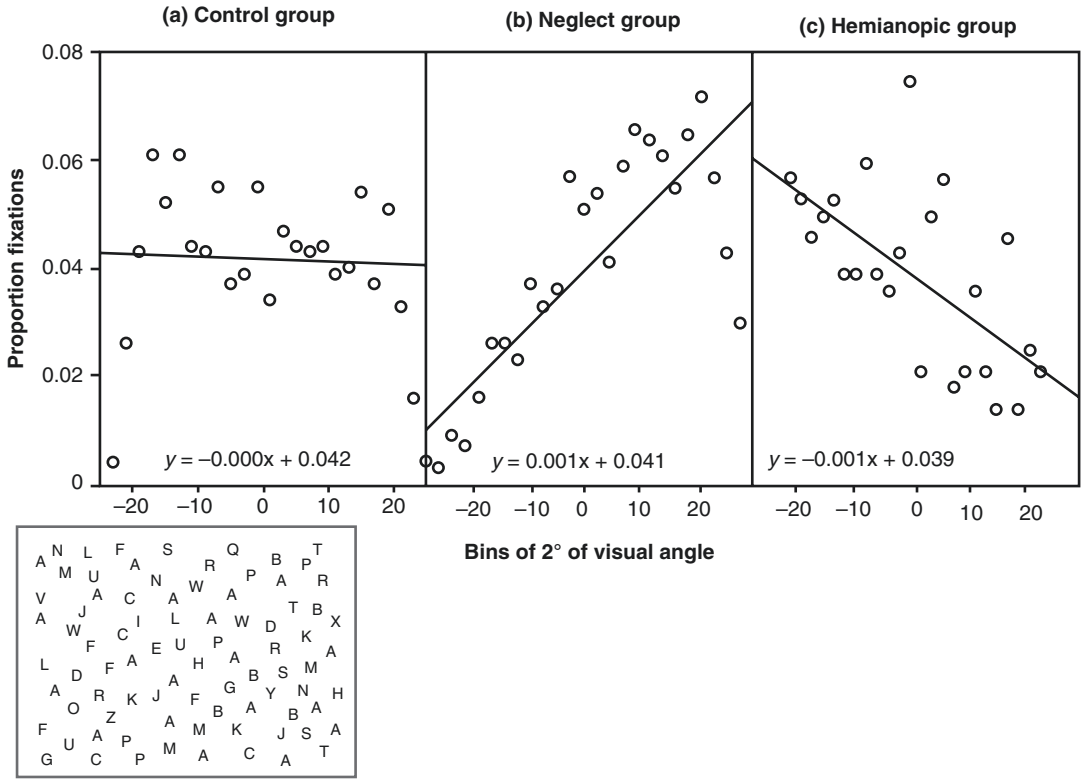

Fig. 8.1 Horizontal distribution of scanning during visual search. Subjects count the number of 'A's in the display shown at the lower left. The proportion of fixations allocated to each 2° bin of horizontal space is shown in the graphs, with 0 representing the bin at center, and positive values indicating bins to the right. Left graph shows data for healthy control subjects, middle graph for patients with left hemineglect, and right graph for patients with left hemianopia. While control subjects distribute their fixations evenly across the display, patients with hemineglect show a gradient that emphasizes the right side of space and relatively ignores the left. Patients with left hemianopia, however, show the reverse gradient, emphasizing the left side of space (Adapted from Behrmann et al. [11] with permission)

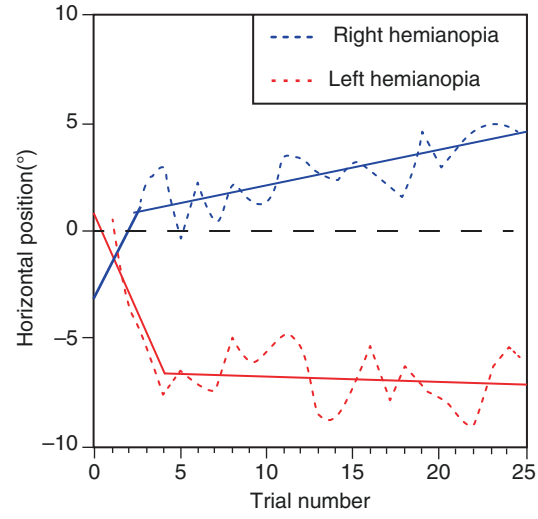

Fig. 8.2 Scanning during visual search in virtual hemianopia. Healthy subjects are made virtually hemianopic by using a gaze-contingent display with the eye-tracker. They search for letters with displays similar to those shown in Fig. 8.1. The *y*-axis plots the mean horizontal position of the fixations made during search on a trial, shown as *dotted lines*. This is plotted as a function of the trial number. As subjects begin the experiment, the mean position of their search is near the center of the display, but over the first five trials there is a rapid shift of search towards the blind side. Over the following 20 trials, there is a more gradual shift as subjects become more efficient at search. The *solid lines* show the best linear fits to the data of the first five and the last 20 trials (Adapted from Simpson et al. [86], with permission)

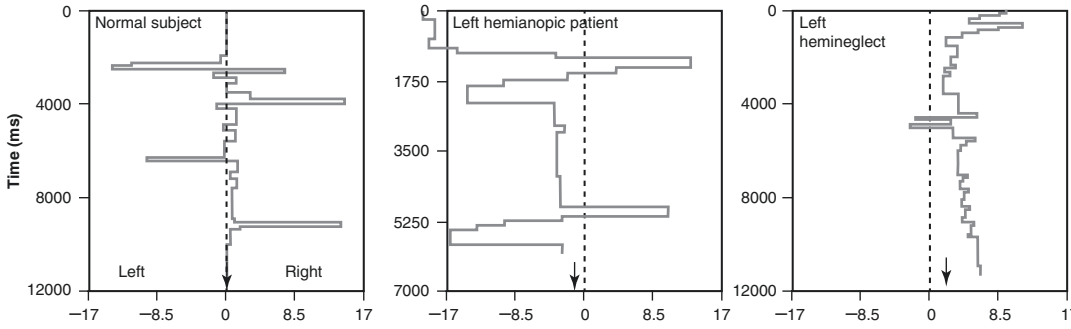

Fig. 8.3 Examples of scanning during line bisection. In each graph, the *x*-axis plots the horizontal position of fixations against the time point in the trial on the *y*-axis. The trial begins at the top (time point 0 ms). *Left graph* shows the scanning of a healthy subject, *middle graph* that of a subject with left hemianopia, and the *right graph* that of a subject with left hemineglect. The *dotted vertical line* shows the center of the line being bisected, while the *solid gray line* tracks the eye movements of the subject. The *black arrow at the bottom* shows the bisection judgment made by the subject. The healthy subject places most fixations near the line center, with occasional forays to the right or left periphery. The left hemianopic subject scans the left end of the line and a region near line center but offset towards the left side. The left hemineglect subject spends almost all their fixation on the right side of the line (Adapted from Barton et al. [2], with permission)

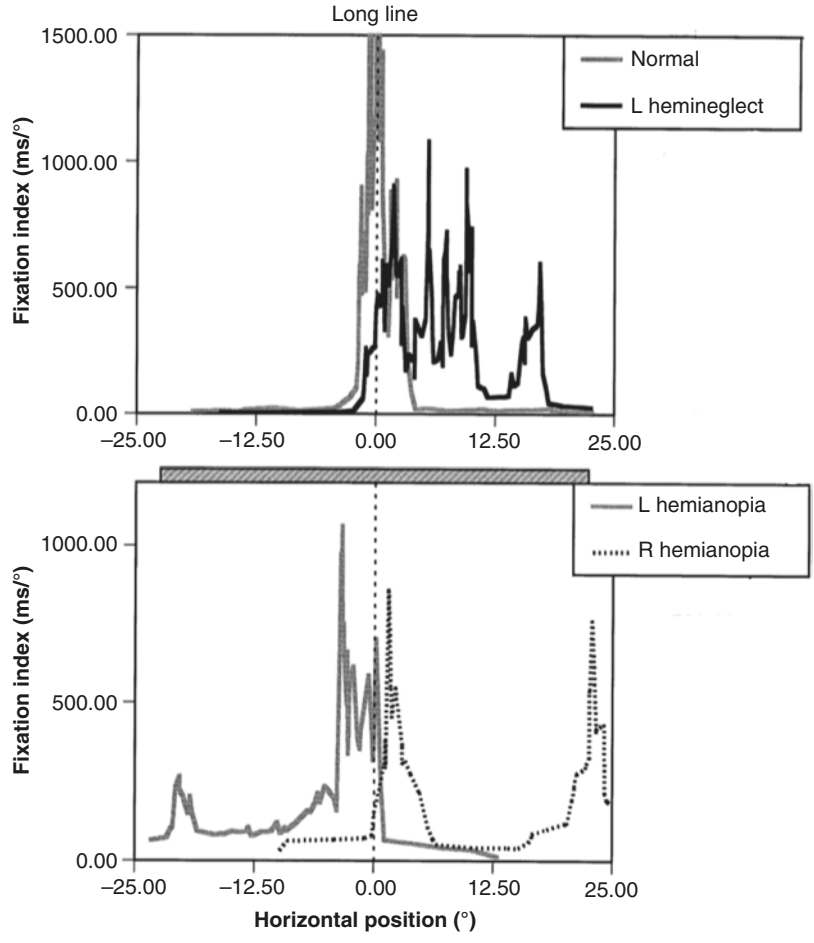

Fig. 8.4 Horizontal distribution of fixations during a line bisection task. The line being bisected is shown above the *bottom graph* as a *gray shaded bar*. The fixation index reflects the density of fixations in a particular region of space; 0 is the midline of both the line and space. In the *top graph*, controls scan mainly the line center, while patients with left hemineglect scan the right side of space. In the *bottom graph*, hemianopic patients show two peaks of fixations, one at the end of the line on their blind side and one near line center, shifted slightly towards their blind side (Adapted from Barton et al. [2], with permission)

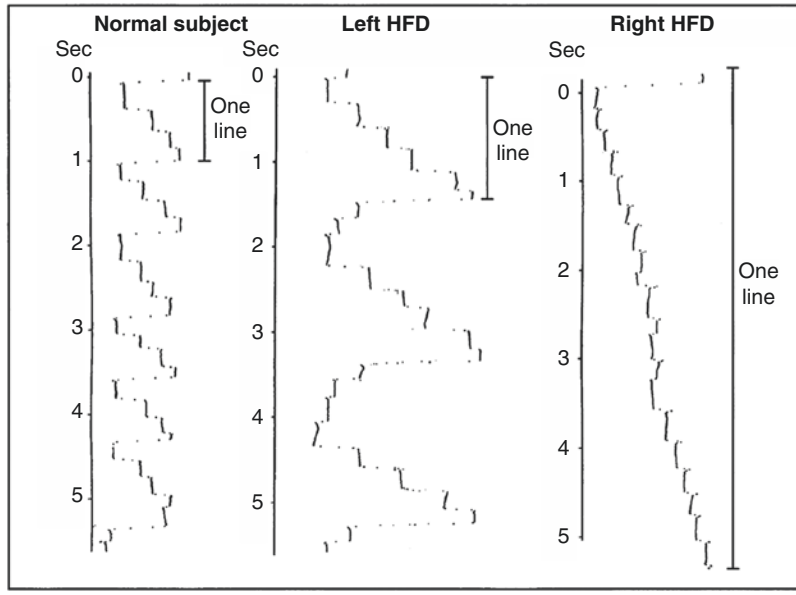

Fig. 8.5 Examples of scanning during reading of a paragraph. On the *Y*-axis is time, while the *X*-axis shows the horizontal position of the eye: *vertical segments* are fixations while *dotted horizontal transitions* are saccades. *Left trace* is from a healthy subject, *middle trace* is from a patient with left homonymous visual field defect [HVFD], and *right trace* is from a patient with right HVFD. The healthy subject makes about four fixations for each line, before returning with a single saccade to the start of the next line. The subject with left HVFD is slightly slowed, but their main difficulty is finding the start of the next line, having to hunt for it with several small saccades. The patient with right HVFD takes a long time to read a single line, using a series of very small rightward saccades to move along the line (From Trauzettel-Klosinski and Brendler [88], with permission)

peak [2, 82, 87]. Furthermore, the central peak is offset slightly contralaterally, which parallels the observation of a contralateral line bisection bias in hemianopia [5, 6].

Hemifield defects that involve the central 5° impair reading, leading to hemianopic dyslexia [88]. Reading is a classic example of the interplay of perception and eye movements, as it is accomplished by a series of fixations that each sample a portion of the line on a page followed by saccades that shift fixation further down the line. The direction of reading in a particular language and the side of the hemianopia interact to determine the effect of the field loss in a given subject. With languages written left to right, reading speed is more prolonged for patients with right hemianopia than for those with left hemianopia [88, 89]. Left hemianopia does not affect the rightward reading of a line much, but when the subject reaches the end and must move left to find the start of the next line, they experience difficulty because that start is now in their blind region. Healthy subjects simply make one large saccade to the beginning of the next line, with at most one small secondary corrective saccade. Patients with left hemianopia make a series of leftward saccades instead (Fig. 8.5), hunting for the beginning of the line, and sometimes ending on the wrong line [88, 90]. Right hemianopia is more problematic for two reasons. First, the span of information processed during a reading fixation is asymmetric and emphasizes the right field: it extends 15 letters or about 5° to the right but only four letters or about 1.3° to the left [91, 92]. Second, the inability to see what is coming up next on the line impairs the ability to plan the optimum location for the next fixation [93]. The end result is that subjects with right hemianopia read with a series of many, very small saccades (see Fig. 8.5), and their rightward progress along the line is often interrupted by small leftward ‘regressive’ saccades, as if they need to check

what they are reading [88–90]. Despite these difficulties, hemianopic dyslexia can improve with practice [88, 94]. Also, some report that hemianopic subjects who can improve the accuracy of saccades when targets are predictably located have better adapted reading behavior [27].

In addition to these alterations in shifting fixation along the line by saccades, one might question whether the efficiency of information acquisition during a fixation is reduced by hemianopia. If so, this might be reflected in longer fixation durations. This was indeed found in one study [90], but another reported that this was seen only if the remaining vision also showed reduced contrast sensitivity [89].

Although most of the data on ocular motor scanning in hemianopia are obtained in experimental settings, there is emerging evidence that scanning matters in real life. In addition to reading, driving is an important activity that is impacted by hemianopia. An on-road driving study using a video-camera to capture head and eye movements found that hemianopic drivers rated as safe, with better stability of their position in driving lanes and fewer episodes of sudden braking, make 50% more small head movements towards the blind hemifield than hemianopic drivers considered to be unsafe [95]. This was followed by observations with virtual driving simulators. Hemianopic subjects who show better ability to avoid collisions scan the display more, with larger saccades and more gaze shifts, and explore moving objects on their blind side more [84, 85]. Similarly, the detection of moving obstacles on a driving simulation is better in hemianopic subjects who explore a wider horizontal range of space with their gaze and show a greater shift of fixations towards the hemianopic side [96]. Hence, scanning with gaze shifts represents an important adaptation that can mitigate the effects of hemianopia on detection of critical objects during driving. There are promising results that training of search and reading can make the eye movements during these processes more efficient [80, 94, 97], and it may be that driving performance may show similar rehabilitative potential through training of scanning.

8.9 Summary

Eye movements can reveal many pathologic and adaptive effects in hemianopia. Fixation is displaced slightly towards the blind field, which may reflect either a distortion of perceptual space or a visual or attentional adaptive change. Saccades to targets in the remaining ipsilateral hemifield are less reliably triggered, being delayed or sometimes omitted. To targets in the blind hemifield, subjects usually make a series of small searching saccades, and this is also true if the target is a sound rather than a visual stimulus. They can use prediction to improve accuracy if the target has a consistent location, and with time they can learn a compensatory strategy to make a large saccade that will place the potential target locations in a seeing part of their field. Whether their eye movements reveal unconscious processing of unseen targets (blindsight) remains uncertain. Targets in the blind field may trigger saccades, but the accuracy of these is debatable; distractors in the blind field may modify the trajectory of saccades to visible targets but not to auditory ones. Scanning studies show that hemianopic patients are less efficient in searching displays and rapidly develop an adaptive gradient of fixations that emphasizes the contralateral space. Right hemianopia involving the central field can have a pronounced effect on reading, which is accomplished with a series of small saccades and many regressions. Driving studies show that the horizontal span of space explored with fixations is an important determinant of the performance of hemianopic subjects. Training of ocular motor behavior may enhance the strategic adaptation of these subjects to their perceptual deficit.

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Driving with Homonymous Visual Field Defects

9

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Abstract

Driving vehicles are part of an ultimate technology in modern societies allowing the user to travel and navigate short distances within urban regions as well as long routes within large-scale environments. Thereby, the ability to drive enables us to enlarge our own, biologically defined and restricted range of mobility in a nearly unlimited manner. Driving, that is, controlling a vehicle in a visually cluttered environment, involves the simultaneous use of central and peripheral vision and the execution of primary and secondary tasks (both visual and non-visual). As a vehicle moves through the environment, the visual input is rapidly changing and the driver is therefore often uncertain as to when and where a critical visual event will occur. Consequently, appropriate gaze behavior is a necessary cognitive tool for a safe drive in order to maximize information acquisition together with adequate interpretations and predictions of environmental situations based on memories.

In this chapter, the overall demands of driving are summarized and discussed in relationship with sensory, motor, and cognitive functions. Furthermore, several options to assess driving fitness in real (on-road) and virtual (simulator) environments together with the present regulations concerning the permission to drive are discussed respecting healthy drivers as well as visually impaired hemianopic patients. Finally, conclusions are provided by illustrating the complexity of the task of driving that leads to an overall high variability of behavioral strategies, which is in cause manifested in large individual differences.

Keywords

Hemianopia • Driving • Eye movements • Head movements • Compensatory patterns • Visual search • Brain lesions

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9.1 Driving Demands

The process of driving can be defined as a human-machine-environment interaction. Controlling and steering an automobile demands the driver with a variety of tasks and processes to handle in a proper way. Obviously, driving is a highly interactive as well as reactive task, demanding the interplay between perception and action behaviors capable to analyze and feedback the outer spatial environment with the appropriate driving operations (see Fig. 9.1). On the environmental side, driving complexity is defined by road design (e.g., motorways, rural roads, city roads), road layout (e.g., street curvature, inclination, junctions), traffic flow (high density vs. low density), and the overall potential-of-collision (i.e., the probability to intercept with obstacles). Concerning the capability of the driver, three main processes are crucial and linked to driver safety and driving performance and will be discussed in the following: sensory (perception), motor (action), and cognitive functions.

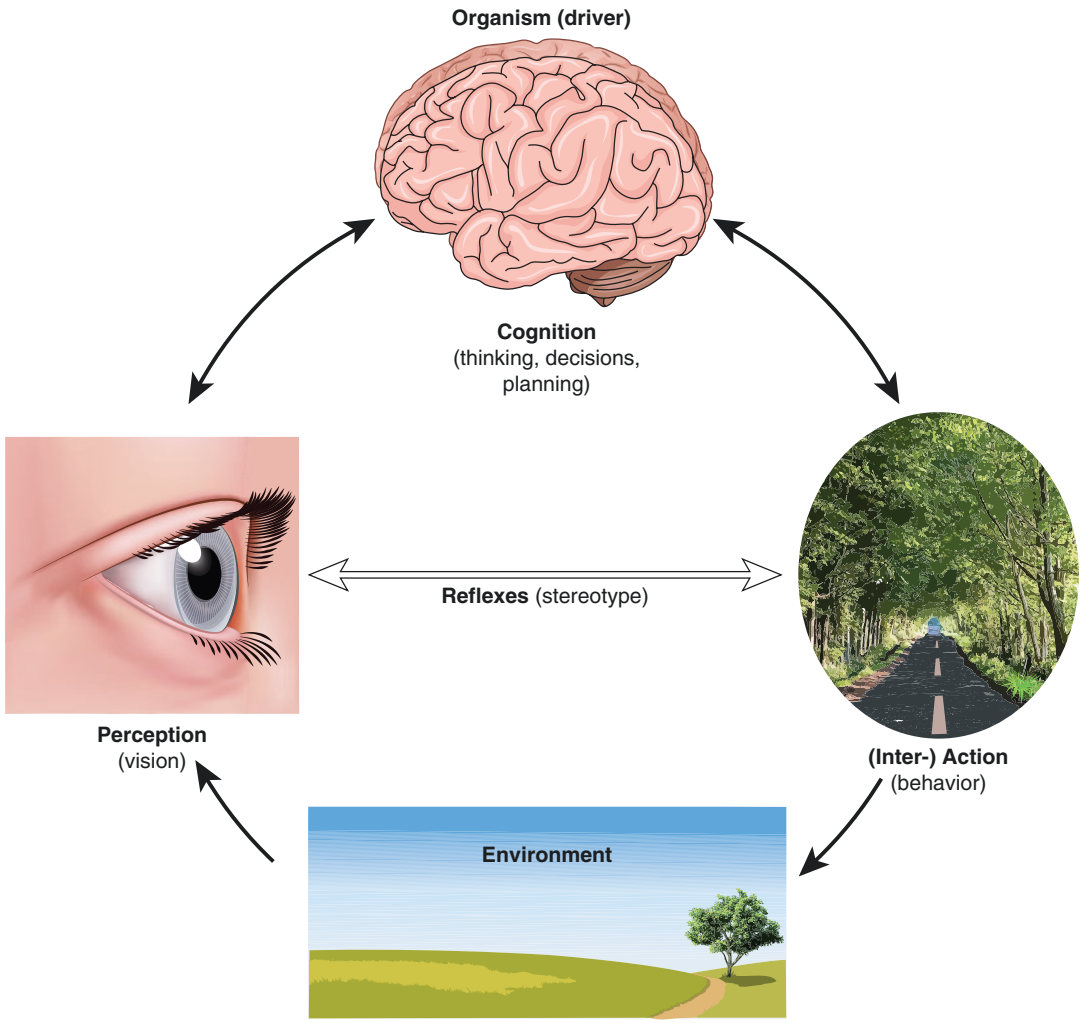

Fig. 9.1 The action-perception cycle related to the task of driving. Successful driving depends on effective measurement (i.e., *perception*), evaluation, and integration of information from the external environment to form internal representations (i.e., *cognition*) which drive task related and efficient behavior (i.e., *inter-action*). Stereotyped stimulus response connections (i.e., *reflexes*) can bypass cognition but restrict behavior to an inflexible action

Sensory processes Sensory processes are primarily restricted to vision as the predominant distal sense, since environmental information belonging to other senses are largely suppressed by the vehicle body or are negligibly required in driving. The main important visual functions for driving are visual acuity, visual field size, contrast sensitivity, and visual processing speed [1]. The assessment and relevance of these functions in hemianopes is explained below. Furthermore, all visual functions serving object and scene recognition have to be considered when discussing requirements for a safe drive.

Motor processes Motor processes are restricted on the one hand to steering behavior involving hands and feet of the driver and on the other hand to spatial exploration behavior for the purpose of information acquisition by combined head and eye movements, that is, gaze shifting behavior [2]. While the control of steering of a vehicle is not known as restricted in hemianopic patients, their completion of adequate gaze movement behavior is often considerably impaired. Here, restrictions of the hemianopes' visual field play a causal role [3–6], but also deficits in working memory functions were shown as an influential factor concerning gaze control [7–9]. Interestingly, the constraints regarding the usable size of the visual field in hemianopic patients are often (functionally) compensated by additional (excursive) gaze movements in cooperation with spatio-temporal integration processes in visual working memory (see Sect. 9.2.1).

Cognitive processes Cognitive processes interconnect sensory with motor functions (see Fig. 9.1), thus enabling a top-down driven, complex, and adaptive behavior. Regarding driving, cognition involves attention, memory (i.e., working memory and long-term memory), spatial and task planning, as well as decision making. Obviously, overt attention is needed for guiding gaze movements towards the most informative spatial locations. Such attentional shifts can be driven simply by the conspicuousness (saliency) of external features or objects (stimulus-based) or by intentions or expectations of internal mental states (knowledge-based [10–12]). Attention is also closely related and functionally linked with working memory in that both processes may bidirectionally impact one another [13] since they share reliance on a common cognitive resource. Working memory is part of a larger cognitive network providing planning and decision making. Planning is involved when complex multitasks have to be handled ensuring the appropriate allocation of re-sources as well as the correct sequence of execution (e.g., navigational purpose: planning a route to drive; perceptual purpose: planning a sequence of gaze shifts). Decision-making is essential when several perceptual or behavioral options occur, but just a single one can be processed at a given moment in time [14, 15].

9.2 Assessment of Driving Fitness

Driving fitness is assessed based on visual functions, such as the examination of the visual field, visual acuity, contrast sensitivity, and color vision. Details on these examination methods and their association with different types of hemianopia have been provided in the Chaps. 3 and 4. Based on these assessments, patients with homonymous hemianopia (HH) are usually considered unsafe drivers, leading thus to driving prohibition in many countries [16–18]. Few countries, namely, the Netherlands, Belgium, the United Kingdom, Canada, and parts of the United States, offer an individual on-road driving assessment for this patient group. In case the driving test is absolved successfully, the patients are allowed to keep the driving license despite the visual impairment.

Different methods are known form the literature to assess the driving fitness of patients with hemianopia, namely, police charts, self-reported accidents, driving simulation, and on-road studies. The majority of simulator and on-road studies with hemianopic patients have reported difficulties with lane keeping, unstable steering, and inadequate hazard detection [3, 19–22]. A general consensus from these studies is that there

is a wide variation regarding the driving fitness of patients with hemianopia.

In the following, we provide an overview on individualized assessment of driving fitness in driving simulators as well as on-road studies.

9.2.1 Individual Assessment of Driving Fitness in Simulated Environments

Driving simulators and other computerized assessments using virtual reality provide a safe, controlled environment in which many potentially hazardous events can be presented to the participants to investigate their driving abilities in an experimental way.

Simulator studies conducted so far reported various results regarding the driving fitness of patients with hemianopia. More specifically, there is a high variability in the pass rates reported by these studies, which is associated with different designs of the simulator environment (fixed-base, moving-base, advanced virtual reality expose, screen-based tasks), the stimuli design, patient inclusion criteria (etiology), other study parameters, and the number of patients.

Most of these simulator studies [23–27] that have investigated the driving ability of subjects with binocular visual field loss (including hemianopic patients) have either reported the percentage of patients who were fit-to-drive without recording their eye and head movements or have assessed various driving behavior parameters (e.g., hazard detection performance, lane keeping ability, steering steadiness) without linking them to a driving test outcome measure. Furthermore, hemianopic patients have been usually considered as one group and compared to healthy-sighted subjects.

In an early simulator study by Lövsund et al. [23], the authors looked at the driver's detection performance for stimuli of different sizes appearing in 24 different positions on a screen. Six participants with HH were included in the study, from which one showed good detection abilities. However, the experimental setting, that is, the detection task, is a rather unrealistic one. Furthermore, the setting was quite simple, although using a high number of events. In 1993, Szlyk et al. [21] assessed the driving fitness of six patients with hemianopic visual field defects (three out of these patients with neglect). The authors reported that the driving performance of the patients was either worse than, or similar to, that of the older control [21]. Despite the small patient group, different etiology might explain the high variability of the results with regard to the driving fitness. In a later study by Schulte et al. [28], the driving performance (i.e., driving speed, reaction time, and driving error rate) of nine patients with homonymous binocular defects was compared with that of a control group of ten subjects. The authors reported that they found no differences regarding the tested parameters between the patients and the healthy-sighted subjects [28]. This confirms the hypothesis that individuals with hemianopic visual field defects may show safe driving behavior.

A relatively large patient group was included in a study by Lundqvist et al. [29], who investigated neuropsychological aspects of driving after a stroke both in a driving simulator and on road. The authors included 30 patients and 30 control subjects in the study. For both tests, it was reported that patients performed significantly worse than control subjects and that they had significantly greater difficulties in allocating processing resources to a secondary information processing task during driving in both settings [29].

In a later simulator study by Bowers et al. [3], the authors investigated the impact of HH for 12 patients on the detection of pedestrians appearing in several hazardous situations. As reported by the authors, most of the HH drivers were rated as not fit-to-drive with regard to the blind-side detection rates. However, some HH subjects showed detection rates similar to the control group. Furthermore, the authors reported that most of the HH drivers took a lane position that increases the safety margin on their blind side [30]. Despite the limitations in the study design, for example, restricted field-of-view in the simulated environment, virtual pedestrian figures appeared abruptly and remained stationary without representing a collision risk, no involvement

of eye- or head-tracking, results from this study underscore the importance of individualized assessments. In a later work from the same author group, the detection performance of HH subjects was examined in a more realistic approaching pedestrian paradigm for both stationary and approaching pedestrian figures that appeared at small (4°) and large (14°) eccentricities [25]. The results from this study confirm previous findings from [3], namely, that most of the HH subjects had deficits with regard to blind-side detection or delayed response that could potentially result in a collision in real-world driving [25].

In recent publications examining a large cohort of patients with homonymous visual field defects (i.e., 20 with hemianopia and 10 with quadrantanopsia) together with (healthy-sighted) control subjects, a group of authors investigated factors causally affecting the performance in a dynamic collision avoidance task [6, 9, 11, 31]. In this task, using virtual reality, gaze tracking, and a natural field-of-view stimulation, subjects had to actively approach an intersection (driving distance to the intersection was about 200 m) where a varying number of cars crossed with a constant speed of 50 km/h. The traffic densities included two difficulty levels that would generate collisions in 50% or 75% of the trials should subjects not adjust their own approaching speed properly. Here, subjects could adjust their own speed between 18 and 61.2 km/h by means of a joystick in order to avoid a collision with any vehicle of the cross traffic. In summary, the authors found in patients and controls, traffic density as primary factor for an increased collision rate as well as a positive correlation between collision rate and age [6]. Furthermore, patients with a higher extend of visual field loss showed an enhanced potential-of-collision. Interestingly, by splitting up the collective of patients concerning their performance (i.e., the number of collisions), the authors identified the group of 'adequate' patients (in contrast to the 'inadequate' patients) as performing within the range of healthy subjects, since they adapted successfully to their visual deficit by achieving compensatory gaze patterns [9]. Such distinct gaze patterns were characterized by increased exploratory gaze movements, that is, more fixations on vehicles and fewer fixations on the intersection, an overall increased gaze eccentricity, and, particularly, more fixations towards moving objects of interest on the blind side. This compensatory behavior became especially evident during the more demanding task, that is, the high traffic density condition. Thus, the compensatory pattern of the 'adequate' patients brought more visual elements into their seeing hemifield and, hence, enabled them to analyze almost all vehicles regarding the potential-of-collision.

Besides appropriate gaze strategies, 'adequate' patients were also found to differ with respect to the affected brain areas identified by lesion mapping. Such mapping revealed that right-hemispheric damage in 'adequate' patients was more frequent in the parieto-occipital region and posterior cingulate gyrus, while left-hemispheric damage in 'inadequate' patients was more likely to involve the inferior occipital cortex and the fusiform (occipito-temporal) gyrus [31]. These and other brain lesion results [7, 32] indicate that 'inadequate' patients might lack (at least partly) in their cognitive competence related to working memory functioning (i.e., object recognition, control of attention, memory storage or retrieval, and memory guided saccades). To conclude, the strategy of increasing gaze exploration allows sufficient uptake of visual information by 'adequate' patients. Subsequent integration of information in an intact working memory enables successful compensation. On the other hand, reduced working memory availability and lack of gaze movements in the 'inadequate' patients are associated with ineffective visual adaptation (see Fig. 9.2).

In a recent study, Kübler et al. [5, 33] investigated exploratory gaze patterns and driving performance measures that are associated with successful driving performance in a simulated driving test. The authors included in their study three patients with complete HH, two patients with incomplete HH, and three patients with incomplete homonymous quadrantanopsia. Driving performance and visual search behavior were compared to that of (healthy-sighted) control subjects who were gender and age-matched to the patients. The study was conducted in a

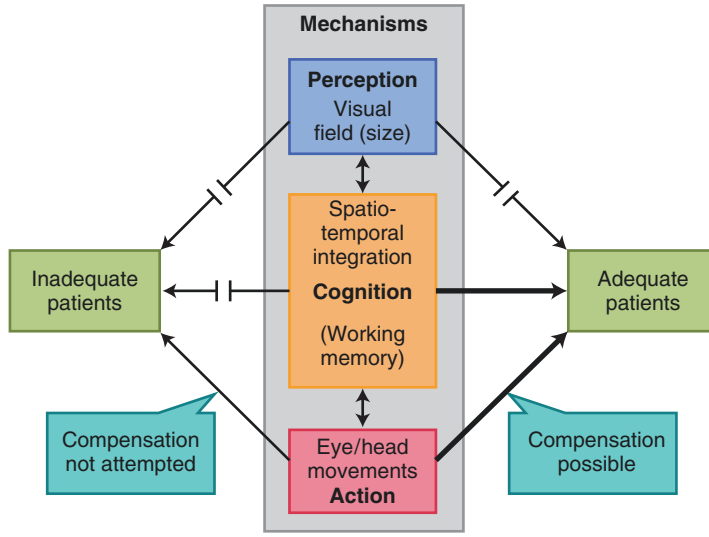

Fig. 9.2 Mechanisms and functions enabling dynamic collision detection compared between 'adequately' and 'inadequately' performing patients with homonymous visual field defects. Three mechanisms are crucial: (1) The size of the (intact/usable) visual field determines stimulus acquisition (*perception*). (2) Eye and head movements enable the relocation of the intact visual field (*action*). (3) The spatio-temporal integration in working memory allows to establish adequate task representations (*cognition*). By definition, all patients with homonymous visual field defects lack in visual field size. The group of 'inadequately' rated ones have difficulties in building spatio-temporal representations and, hence, fail in utilizing compensatory eye and head movements. Whereas 'adequate' patients show widely unimpaired working memory functions enabling them to compensate the visual field defect by gaze compensation

most advanced moving-base driving simulator at the Mercedes-Benz Technology Center in Sindelfingen, Germany. This driving simulator includes a 360° virtual environment, contains a whole car body, and simulates acceleration effects, which enable a very realistic driving experience. In fact, the Kübler et al.'s study [5] is to date the first study that combines a most realistic driving experience (since the subjects experience full inertial characteristics of an actual motor vehicle) with the advantage of having identical, controlled experimental settings. Each subject absolved a driving route of 37.5 km length facing nine hazardous situations during the course. The authors compared the study parameters across control subjects, patients who passed, and patients who failed the test. By means of eye- and head-tracking technology, the explicit visual exploratory behavior could be assessed throughout the drive.

Kübler et al. [5] reported that when all patients were analyzed as a group, they showed more inadequate driving responses in hazardous situations compared to control subjects. However, the individual assessment of the driving behavior showed that 50% of the patients were rated as fit-to-drive. The authors further reported that hemianopic drivers who were rated as fit-to-drive did not differ from the control subjects in their driving behavior regarding speed management and lane keeping capability. Furthermore, no association between the side of the visual impairment and the side of the hazardous event that caused a failure of the driving test was found.

Kübler et al. [5] found increased head movements and longer saccades in patients who were judged as fit-to-drive. Indeed, compensation by increased saccadic amplitudes in hemianopic drivers has been reported by various authors [9, 32]. In the Bowers et al. study [24], the authors also quantified head scanning and found that HH drivers had impaired detection of blind side stationary pedestrians at simulated intersections, either due to not scanning or an insufficient scan

magnitude. The same authors found that successful detection of a pedestrian moving on a collision course in the blind field was associated with a saccadic eye movement towards the target [3]. Similarly, in another simulator study, more frequent compensatory saccades to the affected side, but no head movements were found for one patient who had no collisions [34]. Other studies investigating visual search behavior of patients with homonymous visual field defects in everyday tasks have confirmed the use of compensatory eye and head movements [35].

9.2.2 Individual Assessment of Driving Fitness in On-Road Studies

The most realistic assessment of individual driving fitness can be obtained by means of on-road studies. As summarized in [36], several settings have been employed in a variety of research studies to measure driving performance on open roads (i.e., public roads with natural traffic environment) or closed-road circuits. Here, we focus on individual assessment of driving fitness in patients with homonymous visual field defects. Due to the high effort associated with on-road studies with patients with homonymous visual field defects, the number of studies conducted so far is quite low compared to simulated driving tests. In the following, we will summarize the main outcomes from such studies.

Several on-road studies with patients with homonymous visual field defects have found poor steering control, incorrect lane position, difficulties in gap judgment, and inadequate detection of potential hazards to be the primary reasons for failing the on-road driving tests [4, 20, 21, 26, 37, 38, 39]. With regard to the different patient etiology and experimental setting, the pass rates reported by these studies show a high variation. However, a consensus is achieved, as all studies consistently report of a subgroup of patients that show driving performance similar to that of control subjects despite the visual impairment. De Haan et al. [37] reported a positive correlation between visual field size and viewing behavior and operational handling during driving. However, they found no indication for a cut-off point below which all participants were unfit to drive. The majority of the on-road studies including hemianopic and quadrantanopic patients have in contrast reported that the extent of hemianopic visual field loss is of minor importance with regard to driving performance [4, 20, 38, 40]. Therefore, the extent of visual field per se cannot predict fitness to drive. On-road studies that have analyzed the gaze behavior of patients with homonymous visual field defects have reported that some patients are able to compensate for the visual impairment by means of gaze scanning. Indeed, Wood et al. [20] and Kasneci et al. [4] reported that patients who passed the on-road driving test showed a higher percentage of gaze towards their visual field defect than patients who failed. Furthermore, patients who were rated as fit-to-drive demonstrated increased exploration in terms of head and shoulder movements and received superior ratings regarding scanning activity. By means of sophisticated eye tracking, the authors [4] showed that effective visual scanning into the area of visual field defect is associated with superior driving performance.

Additionally, in the study of Kasneci et al. [4], patients rated as fit-to-drive focused longer on the central area of the visual field than patients who failed the test. This interesting result is in agreement with a recent study, suggesting a significant bias of fixations and viewing time towards the center of the screen for both healthy subjects and hemianopic patients during a visual search task in a static display [41]. The authors suggested that this central bias could be related to functional specialization of the human visual field. Saccadic eye movements are performed in order to overcome acuity limitations of the visual field and shift its center to new objects of interest [41]. Several explanations have been suggested for the tendency to fixate the center of the scene when freely viewing images. First, the central bias may result from motor biases that favor small amplitude saccades over large amplitude saccades. Second, the bias may arise from the distribution of image features. In addition, the center of the screen may be an optimal location for early

information processing of the scene. Alternatively, the center of the screen may be a convenient location from which to start oculomotor exploration of the scene. Finally, the central bias may reflect a tendency to re-center the eye in its orbit [42].

9.3 Conclusion and Future Work

In conclusion, the discussed body of work indicates that some patients with hemianopic visual field loss, who do not meet the legal requirements for driving, are nevertheless judged as fit-to-drive in simulated or on-road tests. This confirms the frequently stated hypotheses that visual field related parameters per se are inadequate for assessment of driving fitness and more individualized approaches are required. Similarly, the prediction of driving safety in patients with hemianopic visual field defects by evaluating the causative brain lesion on clinical neuroimaging has not been successful [43]. While imaging studies do suggest that certain brain regions are linked with specific parameters of driving performance, this may not necessarily result in an unsafe driver [43]. Therefore, individualized approaches are required to assess the driving fitness of an HH patient.

Although individualized on-road driving assessment can be a good means to keep the driving license, such tests are quite costly, and therefore, not always practical. More research needs to be conducted to design simple tests that can predict the driving performance of individuals. For example, a new test procedure allowing the assessment of the so-called exploratory field-of-view (EFOV) (i.e, the field-of-view of a person when eye movements are allowed) was introduced in [44]. In contrast to perimetric procedures, during EFOV testing, the subject is encouraged to move the eyes towards the presented stimulus in order to fixate it. Thus, EFOV testing can capture the visual exploration capability of a subject and reveal the real impact of a visual field defect on daily tasks. Although a promising approach, detection performance in EFOV and driving performance have not been linked yet. In a recent work by Smith et al. [45], the authors introduced two computerized tests including a pedestrian detection task in simulated driving and evaluated 12 patients with homonymous visual field defects and 12 control subjects. Based on their visual search performance, two subgroups of patients were identified: patients who were able to 'adequately' compensate for their visual deficit and others who were not. It is noticeable that the 'adequately' compensated group showed better performance than the 'inadequately' compensated patient group, although reaction times were slightly slower than controls [45]. Thus, such a search task [45] can be used to predict the compensation capability of hemianopic persons to a certain extent.

Another promising approach of evaluating the ability of HH patients to functionally compensate for their visual field defect should include working memory tests. Here, the ability to represent and generate spatial coordinates to plan effective saccadic behavior by using memory functions (i.e., memory guided saccades) would need to be analyzed. Indeed, some studies point out that memory-guided saccades may serve as essential compensation strategy in patients with HH [8, 9].

Finally, and in light of the above finding, we think that standardized tests in driving simulators, including the detection of potential hazards while recording gaze patterns, should be continued and expanded, since they provide ecologically valid measures to individually assess the driving as well as the compensation capabilities of hemianopic drivers [46, 47].

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10 Neurological and Neuropsychological Investigation in Patients with Homonymous Visual Field Defects

Martin Pail, Sabina Goldemundová, Karolína Skorkovská, and Milan Brázdil

Abstract

Visual information is transferred via the optic pathway and processed by an interaction of the striate cortex with visual associative areas. These areas evaluate different properties of the signal and contribute to an overall perception of the visual environment. Lesions of associative cortices in humans cause the so-called central visual disorders that may accompany homonymous visual field defects. An understanding of the functions of these areas is important, as many of these patients will first contact an ophthalmologist, usually with vague complaints that may be difficult to specifically define. This chapter gives an overview of central visual disorders that can be found in patients with homonymous visual field defects and of the principles of neurological and neuropsychological examination in these patients.

Keywords

Central visual disorder • Visual cortex • Associative area • Agraphia • Alexia • Agnosia • Achromatopsia • Neglect • Allesthesia • Akinetopsia • Anomia • Blindsight • Visual attention • Visual hallucination • Visual aura migraine • Neuropsychology

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10.1 Introduction

To evaluate the function of an eye it is common for ophthalmologists to examine the visual acuity, visual field, orthoptics, color vision, and to perform a slit lamp examination. However, the eye may function well and yet the patient is still unable to master some visual tasks or to cope with his surroundings. The patient may find it difficult to perceive a complex image, to recognize a familiar person, or to name a seen object or follow its movement. These complaints have nothing to do with the eye itself but are sign of damage to the central nervous system and should be investigated by a neurologist and neuropsychologist.

The striate cortex is not just an afferent structure receiving information from the lateral geniculate nucleus. In fact, the striate cortex is the beginning of a complex system of visual analysis that leads to global awareness of the visual environment. Disorders that may occur from damage to the visual cortex and its occipitofugal connections with associative visual areas are called central visual disorders or disorders of the higher cortical function.

The site of damage predisposes patients with homonymous visual field defects not only to a visual field defect but also to symptoms like aphasia, agraphia, alexia, agnosia, visual neglect, visual hallucionations, etc., due to the simultaneous impairment of visual associative areas and their projections. Neurological and neuropsychological examinations based on the knowledge of the processing of visual information may be crucial for a proper evaluation of patients with homonymous visual field defects.

10.2 Cortical Visual Areas

So far, five cortical areas (V1–V5) that may have clinical importance in humans have been identified. From V1 (striate cortex or Brodmann area 17), the visual input is projected to higher visual association areas that are responsible for the perception of objects, letters, faces, colors, and orientation. Visual association areas are classified into ventral and dorsal pathways (Fig. 10.1) [1]. The ventral pathway projects from the striate cortex to the angular gyrus (language processing),

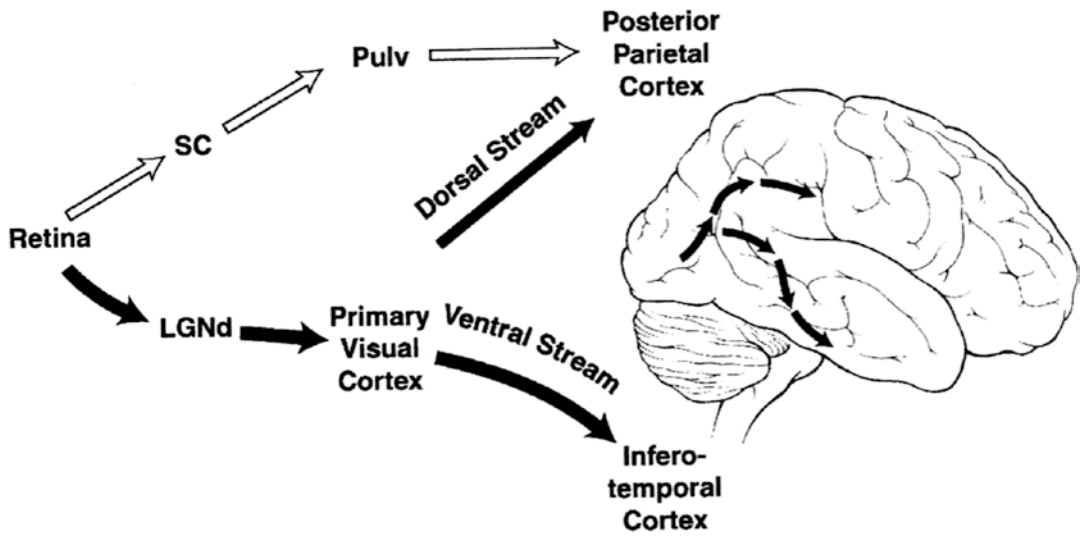

Fig. 10.1 Parallel visual processing pathways in the human. Diagram of the major routes passing from the retina into the dorsal and ventral streams (*LGNd* lateral geniculate nucleus, pars dorsalis, *Pulv* pulvinar, *SC* superior colliculus) (Artist: David Fisher. From Goodale et al. [1], with permission)

the inferior temporal lobe (object identification), and limbic structures. The ventral pathway is often called the "what" pathway because it serves object recognition. The dorsal pathway projects to the posterior parietal cortex and superior temporal cortex (visuospatial analysis) and then continues forward to the premotor frontal cortex [2] This dorsal or "where" pathway serves the localization of objects in visual space and their movement. Naming the what and where pathway of visual processing is an oversimplification of how these cortical areas function as there is a lot of interaction among the individual regions as well. However, it serves as a good clinical model of cortical visual processing. Damage to the ventral stream results, for example, in visual object agnosia, pure alexia, anomia, prosopagnosia, and achromatopsia. Bálint syndrome, visual inattention, and hemispatial neglect are examples of dorsal stream disorders [2].

10.3 Principles of Neurological Examination

The diagnostic balance sheet in neurology proceeds from the detection of symptoms to a syndromological, topical, and nosological diagnosis, or ideally to the disclosure of the etiology of the disorder. Syndromological diagnosis means a summary of the various manifestations of the disease (subjective symptoms and objective signs revealed during a neurological and neuropsychological examination) grouped in a combination characteristic for a particular syndrome. Topical diagnosis defines the level of impairment within the peripheral or central nervous system. Nosological diagnosis describes the disease by means of the detected neurological syndrome, clinical course of the disease, response to treatment, etc. Usually, the cause of the disease cannot be determined with certainty only from the patient's history and clinical examination. To verify a clinical suspicion, it is often necessary to perform other tests such as computed tomography (CT), magnetic resonance imaging (MRI), examination of cerebrospinal fluid, electroencephalography (EEG), electromyography (EMG), evoked potentials (EP) studies, etc. Moreover, in certain cases specific auxiliary diagnostic methods (clinical neurophysiology, biochemistry or molecular genetics) may be helpful.

The basic task is to detect whether a given patient has suffered damage to the peripheral or central nervous system and to determine the location of the damage as precisely as possible. Associated focal neurological signs and symptoms, as well as visual field characteristics, may help to determine the site of the causative brain lesion. Also, the "general" examination of the patient is as important as the neurological part and may help to reveal the diagnosis. Only with all necessary data can a differential diagnosis, diagnostic evaluation, and treatment plan be generated. However, quite frequently the situation may be impeded by the fact that the clinical picture in a given patient is expressed incompletely, or combines symptoms of impairment at both the peripheral and central levels.

Taking the patient's history is the most important part of a neurological examination and should be performed prior to all other procedures unless it proves impossible (i.e., the patient is unconscious). The time profile of visual problems (temporary or permanent) and mono- and binocular nature of the disorder are essential for the localization and etiology of the disability. Acute and subacute disorders usually have a vascular and inflammatory origin, while chronic and progressive disorders are usually caused by compression, infiltration, or a degenerative process. Understanding the neurological condition of the patient at the time of questioning is important to get an idea as to which neurological systems could be affected. Then it is necessary to focus on the neurological examination and to investigate in detail the functions whose disability is suspected.

10.3.1 Specific Tests of Visual Function

Visual field test Visual field testing is used to detect signs of pre- and postchiasmatic damage to the visual pathways. Visual field defects may be

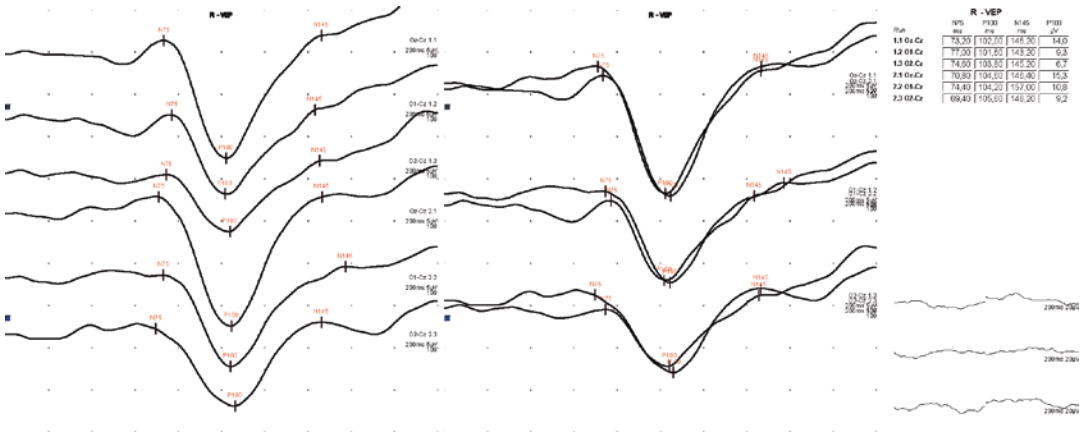

Fig. 10.2 Visual evoked potentials wave patterns (R-VEP – pattern reversal VEP) of a healthy volunteer (bipolar montage Oz-Cz, O1-Cz, O2-Cz, length of the recording is 200 ms, average responses number in one recording is 200, 2 runs)

plotted in a number of ways: confrontation visual field, tangent screen, automated static, or Goldmann kinetic perimetry [3, 4]. Simple, bedside confrontational testing of the visual field is even nowadays the most important component of a basic neurological examination. Confrontational visual field examination should be performed by an experienced neuro-ophthalmologist or neurologist using hand movement, finger counting, and color comparison (red saturation across the vertical meridian). Each eye should be tested separately as the patient looks at the examiner's eye, and stimuli should be presented in each quadrant. This method will, however, detect only absolute visual field defects. Subtle visual field defects such as small central scotomas are likely to be missed. Double simultaneous stimulation may reveal visual neglect, which may or may not be accompanied by a homonymous visual field defect.

Visual evoked potentials The terms visual evoked potentials (VEP) or visual evoked response (VER) refer to electrical potentials, initiated by brief visual stimuli (either a flashing stimulus or a checkerboard stimulus with units that reverse from black to white, typically at 2 Hz frequency), which are recorded at the scalp overlying the visual cortex. The light-evoked signal, small in amplitude and hidden within the normal electroencephalographic (EEG) signal, is amplified by repetitive stimulation and time-locked, signal-averaging techniques, separating it from the background EEG readings. The VEP comprises a series of negative and positive waves, of which the most reliable and useful is the P100 wave elicited usually with a latency of close to 100 ms after the stimulus presentation (Fig. 10.2). VEPs are used to measure the functional integrity of the visual pathways from retina to the visual cortex of the brain. Any abnormality that affects the visual pathways or visual cortex can affect the VEP (increase the latency or decrease the amplitude of the individual peaks). Flash stimulus VEP is more useful in patients with substantial visual loss.

10.4 Neuropsychological Investigation in Central Visual Disorders

Neuropsychological examination should be carried out by a neuropsychologist who is usually part of a neurological department. Numerous,

well-recognized tests used in everyday clinical practice can help reveal central visual disorders.

The horizontal line bisection task is a common clinical test introduced in 1894 by the German physician Axenfeld, who published a case report about line bisection as a "simple method to diagnose hemianopia" [5]. The examiner draws a line on a paper in front of the patient asking him to make a mark right in the middle of the line. The score is the length by which the patient's estimated center deviates from the actual center. It should be pointed out that even normal subjects tend to make the mark a little to the left (1 or 2 mm). It also depends on the length of the line – the longer it is, the more deviation from the center there may be [6].

The symbolic functions should be examined by asking the patient to read a text aloud and to write something spontaneously or by dictation. The patient should describe a complex picture like the cookie theft picture from the Boston diagnostic aphasia examination (Fig. 10.3) [7], draw a picture (a human figure, a flower, a tree, a house, do the Clock Test, or copy a figure, e.g., in terms of the Rey Complex Figure Test). Observing the patient in such situations can provide a lot of information. We should also ask about the patient's left-right orientation.

Fig. 10.3 The "cookie theft picture" from the Boston Diagnostic Aphasia Examination. The information in the picture is scattered into four visual field quadrants. A patient is asked to describe the events in the picture. A person with simultanagnosia is able to describe only disconnected fragments of the scene such as the cookie jar or the faucet and is not able to describe the events related to the scene (From Goodglass et al. [7], with permission)

Homonymous hemianopia may occur together with visual inattention (visual neglect), but these conditions are not necessarily linked. Observing the patient in daily life can help us to distinguish the two entities: a woman with neglect would comb just half of her hair, in case of hemianopia she would turn her head (and eyes) during combing so that she can see better. There may also be other symptoms of hemispatial inattention apart from visual deficit; for example, patients may not react to sound stimuli coming from the ignored side, etc. Patients with neglect are not able to compensate their deficit (in contrast to those with hemianopia). Again, there are tests used to diagnose different symptoms associated with unilateral visual neglect like the star cancelation, key cancelation, line crossing, and apples cancelation (Fig. 10.4) [8]. Another test used for the evaluation of neglect is the Bells Test. First, the patient becomes familiar with the target figure (the bell) and all the distractors. Then, on the task sheet the patient is asked to circle all the bells in the picture. The scoring sheet (Fig. 10.5) [9] is divided into seven parts (one central, three to the left, three to the right). The score consists of the number of circled bells and the time necessary for completion of the test [9]. The use of distractors instead of line crossing enables detection of mild and moderate neglect more readily because the patient has to develop a consistent search strategy [10].

Sometimes in a patient with visual problems a possible psychogenic cause or simulation may be suspected. One of the most common psychogenic disturbances in ophthalmology is decreased visual acuity [11]. Psychogenic visual field defects may present as homonymous hemianopia, though this is rather rare. After excluding an organic cause, we should calm the patient with

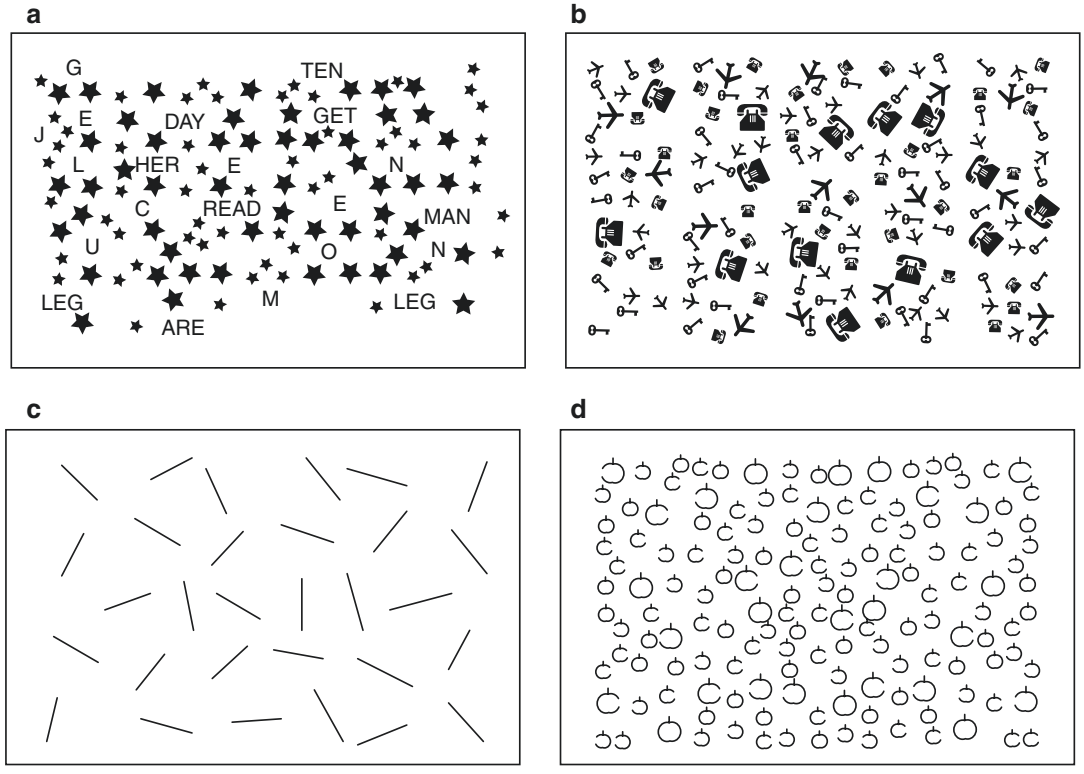

Fig. 10.4 Examples of tests frequently used to diagnose heterogeneous symptoms associated with unilateral visual neglect, which can provide measure of deficits associated with impaired control of attention either (**a**–**c**) across space, i.e., egocentric frame of reference and/or (**d**) within objects, i.e., allocentric frame of reference. Common cancelation tests: (**a**) star cancelation, (**b**) key cancelation, and (**c**) line crossing, all administered by asking patients to cross targets (*small stars*, *keys*, or *lines* respectively) evenly distributed on the centrally placed sheet of paper – deficits are measured by target omissions on either left or right side of space. Gap detection tests: (**d**) apples cancelation, administered by asking patients to cross only full targets (*full circles* or *full apples*, respectively) evenly distributed on the centrally placed sheet of paper – deficits are measured by counting missing targets on either left or right side of space as well as false-positive responses, i.e., crossing objects with either left or right openings (From Chechlacz et al. [8], with permission)

reassurance that the situation will eventually improve. Most patients report they are able to manage daily life activities despite their visual problems; therefore there is no need to intervene. If the patient's situation is complicated, we should recommend a more thorough psychological examination and follow-up psychotherapy. In case of simulation, mostly it is not necessary to confront the patient, but the situation should be clarified.

Last but not least, homonymous hemianopia may be associated with the impairment of daily activities, particularly with difficult orientation to surroundings. Patients may fear falling, slipping, or running into objects. Consequently, they may prefer to stay isolated at home, not risking the danger outside. This can cause serious mental problems like panic attacks, phobias, and depression that should not be underestimated.

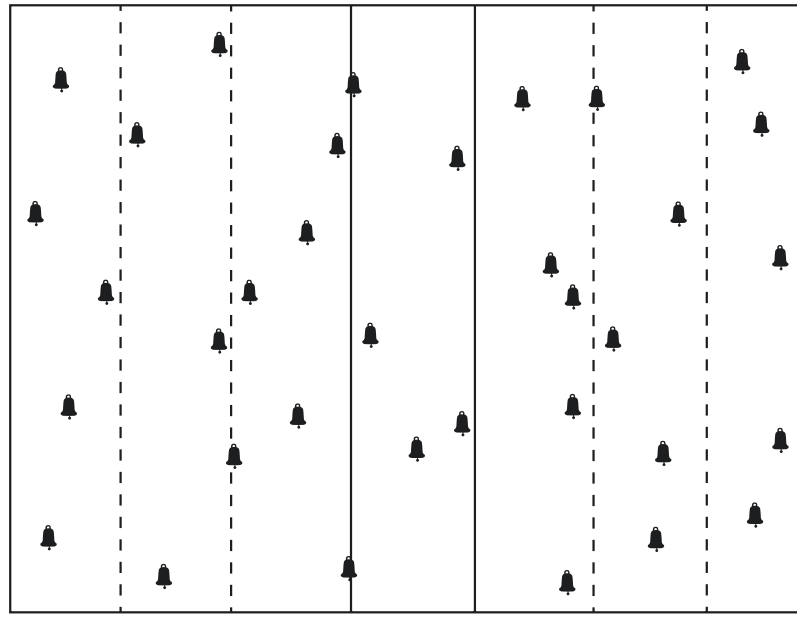

Fig. 10.5 The bells test (From Gauthier et al. [9])

10.5 Neuropsychological Symptoms and Syndromes Associated with Homonymous Visual Field Defects

Homonymous visual field defects may be accompanied by different neuropsychological symptoms and syndromes that depend on the location of the lesion. Lesions of the associative areas often go unnoticed and, unlike the HVFDs, may be only temporary. Still, they can significantly affect patient's life.

10.5.1 Lesions of the Optic Tract

An isolated complete optic tract lesion causes a characteristic clinical triad of neuro-ophthalmological findings: (1) homonymous hemianopia, (2) relative afferent pupillary defect (RAPD), and (3) atrophy of the optic disc [12]. All these findings are found contralateral to injured optic tract, and a temporal optic disc pallor is seen ipsilateral to the lesion. Either a complete or an incomplete homonymous hemianopia can be seen in patients with optic tract lesion, and about half of the optic tract lesions manifest by congruous homonymous hemianopia [13]. Involvement of the hypothalamus, pituitary infundibulum, or pituitary gland (structures adjacent to the optic tract) may lead to autonomic or endocrine dysfunction. If cerebral peduncles are affected, contralateral hemiparesis may be present. Disturbances of memory and seizures may occur with impairment of the temporal lobe [3].

10.5.2 Lesions of the Lateral Geniculate Nucleus

Isolated lesions of the lateral geniculate nucleus (LGN) are uncommon, but if they occur, then the most common pattern is an incongruous homonymous hemianopia, often with a specific wedge-shaped pattern due to the dual blood supply of the

LGN by the anterior choroidal artery and the lateral posterior choroidal artery. The impairment of nearby structures may result in superimposed neurological deficit like contralateral hemiparesis, hemianesthesia, central pain, etc. [3].

10.5.3 Lesions of the Optic Radiation

Lesions of the optic radiation in the temporal lobe lead to contralateral upper homonymous quadrantanopia, while lesions located in the parietal lobe result in contralateral lower homonymous quadrantanopia. In case of a complete lesion of the optic radiation a contralateral homonymous hemianopia is present. A varying degree of hemiparesis or hemianesthesia may also be found due to damage to the internal capsule [2, 3].

Hemianopia caused by lesions of the optic radiation may be accompanied by other hemispheric symptoms that may be revealed with detailed neurological testing. Temporal lobe lesions lead to defects of personality, temporal epilepsy, memory disturbances, Wernicke aphasia, or Klüver-Bucy syndrome (hypersexuality, hyperorality, visual and auditory agnosia and apathy). Dominant parietal lobe lesions manifest with conductive aphasia, Wernicke aphasia, alexia with or without agraphia, Gerstmann syndrome (finger agnosia, agraphia, acalculia, failure of left-right orientation), or tactile agnosia. Nondominant parietal lesions manifest by a left-hand syndrome, neglect, or constructional apraxia and apraxia of dressing in association with left-sided hemianopia. Patients with parietal lobe lesions involving the optic radiation are often unaware of their visual field defects. This condition is called anosognosia and is most often seen with nondominant parietal lobe lesions. Moreover, dysfunctions of higher sensory integration may be discovered, including astereognosis, agraphesthesia, and impaired two-point discrimination. Deep parietal lesions may lead to homonymous hemianopia and abnormalities in smooth pursuit eye movements to the ipsilateral side. Visual disturbances in lesions of the parieto-occipital border or the occipital lobe itself – Bálint syndrome or cortical blindness – can occur in dementia caused by Creutzfeldt-Jakob disease, progressive multifocal leukoencephalopathy, or Alzheimer disease [2, 3, 12, 14].

10.5.4 Lesions of the Occipital Lobe (Area V1-V5)

Unilateral lesions of the occipital lobe typically lead to congruent contralateral homonymous hemianopia with a typical central (macular) sparing. Incomplete homonymous hemianopia is more common than complete hemianopia, and homonymous quadrantanopia is the most common type of incomplete homonymous hemianopia [14]. Explanation of the preserved central vision is twofold: (1) the macular visual cortex is a “watershed zone” receiving dual blood supply from the middle and posterior cerebral arteries, and (2) double-sided representation of the macula in the cortex [3]. Bilateral cortical lesions above or below the calcarine fissure lead to altitudinal hemianopia respecting the horizontal dissecting line.

Contralateral homonymous hemianopic central scotoma is indicative of a unilateral lesion of the visual cortex with preserved visual acuity; nevertheless, vision is reduced in bilateral affections of the pole. Generally, both-sided retrochiasmal lesions are associated with a varying degree of decreased visual acuity; however, the decrease is symmetrical. In case of an asymmetric decrease of visual acuity, the presence of prechiasmatic lesions can be suspected. Patients with a hemianopia due to occipital ischemia usually have normal optokinetic nystagmus, whereas in occipital tumors with edema extending to the parietal lobe, optokinetic nystagmus is missing.

Cortical blindness is the result of a bilateral lesion of the visual cortex. Patients do not react with blinking upon a rapid approach of an object or person, and optokinetic nystagmus cannot be elicited. Some patients may experience photopsias or other visual hallucinations in the blind hemifield [12]. *Charles Bonnet syndrome* is the name for visual hallucinations that frequently occur in patients who lose vision in both eyes, regardless of the location of the causative lesion.

The hallucinations may be simple (e.g., brief flashes of light, phosphenes, various shapes etc.), or complex (specific objects, people, countryside, animals, etc.). Patients are generally aware that the images are not real, but they can cause significant anxiety, and thus patients should be educated regarding the benign nature of this syndrome [12].

Some patients may confabulate visual perception to mask their visual loss or deny their blindness. This is called *Anton syndrome* or *visual anosognosia*. The patient cannot see and bumps into objects while walking, but he adamantly behaves as if he could see. It is an uncommon form of anosognosia that may follow extensive damage to the striate cortex [15]. Although Anton syndrome usually accompanies geniculostrate lesions, it may occur from any etiology, including blindness from prechiasmal disorders such as optic neuropathies and retinal detachment [2]. There are several theories regarding the etiology of Anton syndrome. Denial of blindness may be due to damage to higher cognitive areas or due to lesions of the geniculostriate pathway that disrupt input to and also interfere with output from the visual cortex to areas involved in the conscious awareness of visual perception [16]. Further, patients with Anton syndrome often have altered emotional reactivity similar to patients with frontal lobe lesions [17].

Other symptoms of impaired visual cortex function include the *covert vision sign* [18], *unaware vision (blindsight),* or impaired perception of static objects with preserved perception of moving stimuli in the blind hemifield (*Riddoch phenomenon*) [19, 20]. Blindsight refers to a condition sometimes observed in humans who experience severe damage to one or both occipital lobes. Under experimental conditions the direction of moving objects in the blind hemifield is correctly given by the patients, colors recognized, or a target object and its displacement is detected. The significance of this phenomenon is topically low [2]. Some authors attribute these perceptions to preserved islands of striate cortex [21] or multifocal damages [18]. Blindsight may also be explained by the transmission of visual signals through the primitive extrastriate subcortical visual pathway (see Fig. 10.1) involving particularly the superior colliculus and pulvinar [19, 20] or, alternatively, by a pathway from the LGN to the associative visual areas that bypasses the striate cortex [22, 23]. Considerable controversy still surrounds the existence of blindsight in humans and further studies are needed to explain this phenomenon.

Cerebral achromatopsia is a rare acquired defect of color perception, usually as a result of damage to the ventromedial visual cortex. It may be complete (which is rare) or affect only one hemifield [24]. These patients cannot match up the colors of the surrounding world but see the environment completely devoid of color, only black and white, in shades of gray, or washed out [23]. If discrimination of the main colors is preserved, but the ability to discriminate subtle colors is reduced, then it is referred to as cerebral (hemi)dyschromatopsia [25]. Most often, the pathology in patients with achromatopsia is localized in the posterior fusiform and lingual gyri [23]. Cerebral achromatopsia may be associated with a superior homonymous visual field defect from damage to the inferior striate cortex. In such cases, the residual inferior field on that side is achromatopic [2]. Achromatopsia may be accompanied by other symptoms like prosopagnosia, topographagnosia, visual object agnosia, pure alexia, and defects of visual memory [2], resulting from a lesion of the ventral occipitofugal pathway. If the lesion extends to the temporal lobe, global amnesia may be present as well [2]. Due to intact chromatic pathways from the retina to the striate cortex, patients with acquired cerebral achromatopsia show, in comparison with congenital achromatopsia, preserved trichromacy and intact cortical responses to chromatic visual evoked potentials [26]. Because of preserved function of the wavelength-selective cells in the striate cortex, achromatic patients may perform well in tests with pseudoisochromatic plates [27].

Akinetopsia (also mentioned under the dorsal pathway disorders) is a rare disorder usually associated with damage to the ventrolateral occipital gyri or attributed to a bilateral lesion of the parieto-occipito-temporal transition of area V5. Patients with akinetopsia are unable to detect

motion. They perceive moving objects as stationary objects that suddenly appear, disappear, and jump from one place to another and so change their position [28]. Also in this case, possible hemiakinetopsia may be associated with incomplete homonymous field defects and so be obscured.

Visual aura migraine is localized in one hemifield (corresponding to the impairment of the primary visual cortex of one occipital lobe) and is characterized by a scotoma and irritative symptoms like scintillations, zig-zag lines, and phosphenes. These types of visual disturbances tend to start in the center of the visual field and move outward, or spread. Quite typical is a gradually expanding, scintillating scotoma with flickering light on the edge. Visual aura migraine usually occurs within an hour before the onset of headache and lasts less than 60 min. Unlike classical migraine, retinal migraine occurs as a transient visual loss in the visual field of the affected eye.

Other symptoms of central visual disorders include *polyopia* (multiple vision, perception of one object as few), *palinopsia* (persistence of visual perceptions), and *optical allesthesia* (abnormal orientation of objects in space). Hemianopia caused by occipital lobes ischemia due to vertebrobasilar thrombosis may be associated with brainstem (especially oculomotor nerve lesions) and cerebellar symptoms.

10.5.5 Lesions of the Associative Visual Areas

In the case of lesions of the associative visual areas, symptoms occur that cannot be explained by failure of the primary visual cortex only. For example, when a lesion affects the splenium of the corpus callosum or the adjacent periventricular white matter of the dominant hemisphere, then pure alexia as part of the dysconnection syndrome may occur (the inability to recall vocabulary for visual information processed in the intact right occipital lobe). A bilateral lesion of the medial temporo-occipital area (impaired lower longitudinal fascicle) results in visual agnosia as well as in prosopagnosia. Left-sided neglect syndrome is the sign of damage to the right parietal lobe. Additionally, bilateral lesions of the parieto-occipital area (important brain regions for foveal fixation and visual attention) cause the so-called Bálint syndrome. It is usually accompanied by lower altitudinal hemianopia due to the currently affected area above the calcarine fissure.

Lesions of the Dorsal Occipito-Parietal Pathway The dorsal or "where" pathway begins in area V1 and projects through V2 and V3 to area V5 (area MT). The information is conveyed along the dorsal longitudinal fascicles to the posterior parietal cortex, frontal motor areas, and frontal eye fields (FEF) [1]. The posterior parietal cortex combines characteristics of both motor and sensory areas and serves as a junction between multimodal sensory input and motor output [1]. This pathway is associated with spatial localization, visuomotor search, guidance (guidance of eye, head and arm movements), and visuospatial synthesis [29]. Lesions of the occipito-parietal pathway cause visual hallucinations and disturbances of visual attention and of the processing of objects in space [30].

Bálint syndrome is defined as a combination of acquired oculomotor apraxia, simultanagnosia, and optic ataxia. These individual symptoms do not necessarily occur together, but may be detected in isolation or in association with other disorders of visuospatial perception [31, 32]. Bálint syndrome is caused by a bilateral lesion of the parieto-occipital regions, which are important for attention and visual foveal fixation [32]. Symptoms are usually accompanied by lower altitudinal hemianopia due to the simultaneously affected area above the calcarine fissure. Acquired oculomotor apraxia or spasm of fixation is characterized by the loss of voluntary eye movements with persistence of fixation on a target [2]. In contrast to congenital oculomotor apraxia, saccades are easily made to peripheral targets in the absence of a fixation target. Other oculomotor symptoms include defective smooth pursuit eye movements and impaired optokinetic nystagmus in both directions, while volitional saccades are relatively preserved, but are hypermetric and inaccurate.

Patients with simultanagnosia can perceive whole shapes, but they cannot recognize whole scenes because they are unable to shift visual attention. Patients with this condition require multiple fixation, and they complain of tunnel vision or of the sudden appearance or disappearance of objects. They have problems when reading or interpreting images while performing an action [31, 33, 34]. They thus behave as if they were blind even though they have intact visual fields. Simultanagnosia can be diagnosed, for example, by the "cookie theft picture" (see Fig. 10.3). This scene requires higher-order synthesis of multiple objects scattered throughout four quadrants of the picture to achieve a global understanding of the image. Optic ataxia means the inability to grasp an object during visual inspection or, in other words, to perform accurate limb movements under visual control. Thus, patients reach for targets within an intact field as if they were blind.

Unilateral (or hemispatial) *neglect* is a neuropsychological disorder of attention, perception, and orientation in one half of the space, usually left, without breaking the primary motor and sensory functions [2, 35–37]. Hemispatial neglect may affect multiple sensory modalities, but visual inattention is often the most prominent feature. Left-sided neglect syndrome is a sign of the right nondominant hemispheric lesion that may occur without left-sided hemianopia. However, extensive parietal lobe lesions usually lead to both neglect syndrome and hemianopia. In these cases, it is rather difficult to prove neglect. Besides right parietal lesions, neglect syndrome may also be due to the damage of the left parietal lobe, the right prefrontal areas, the cingulate gyrus, striatum, thalamus, and posterior arm of the internal capsule [38]. Hemianopic patients have difficulties on the side of the visual field defect due to impaired exploration, while neglect patients seem to lose awareness of space on the affected side. The least serious form of disability, reflecting a focal lesion of the right parietal lobe, shows in diagnostic tests often only during double simultaneous stimulation. That means that a patient with left-sided neglect is able to perceive individual stimuli in the right and left side of the visual field, but only the right stimulus is perceived if both stimuli are presented at the same time (i.e., extinction sensation). Severe forms of neglect are usually caused by ischemia in the territory of the right middle cerebral artery and damage to two-thirds of the parietal lobe. It disturbs all perception of left-sided stimuli, including body sensations (hemiasomatognosia); head and eyes are twisted to the right, and while looking left, the eyeballs do not cross the medial line. Unlike hemianopic patients, patients with neglect syndrome are usually capable of capturing elementary visual stimuli from the left half of the visual field (light stimuli during a perimetric examination), and visual evoked potentials show normal results. Left-sided neglect manifests with mistakes when drawing a picture (Fig. 10.6) – e.g. in the clock test the patients tends to place all digits or most of them into the right half of the dial [39]. When the patient is asked to split a horizontal line in half, the patient places a hyphen to the right of the center. Similarly, in the cancellation test the patient crosses out certain characters only in the right half of the paper. Neglect syndrome often remains undiagnosed, and affected patients are not recognized. Past studies, however, show that the marginalization of half of the space and other difficulties associated with the reported diagnosis often limit the patient more seriously than, for instance, disorders of speech and right-sided hemiparesis [36].

Hemiasomatognosia is part of the neglect syndrome in which the patient does not recognize the left (rarely, the right) half of his body or its parts. The patient, e.g., shaves only the right half of his face, his left extremity seems foreign (belonging to another person lying in the bed), etc. He also generally neglects the left half of the space and may suffer from a simultaneous visual hemifield disturbance. The syndrome is a manifestation of a right parietal lobe lesion and usually is accompanied by a left-sided hemiparesis.

Visual allesthesia is a disorder of visuospatial perception in which the retinotopic visual field is rotated, flipped, or even inverted. The lesion is usually localized in the right occipito-parietal

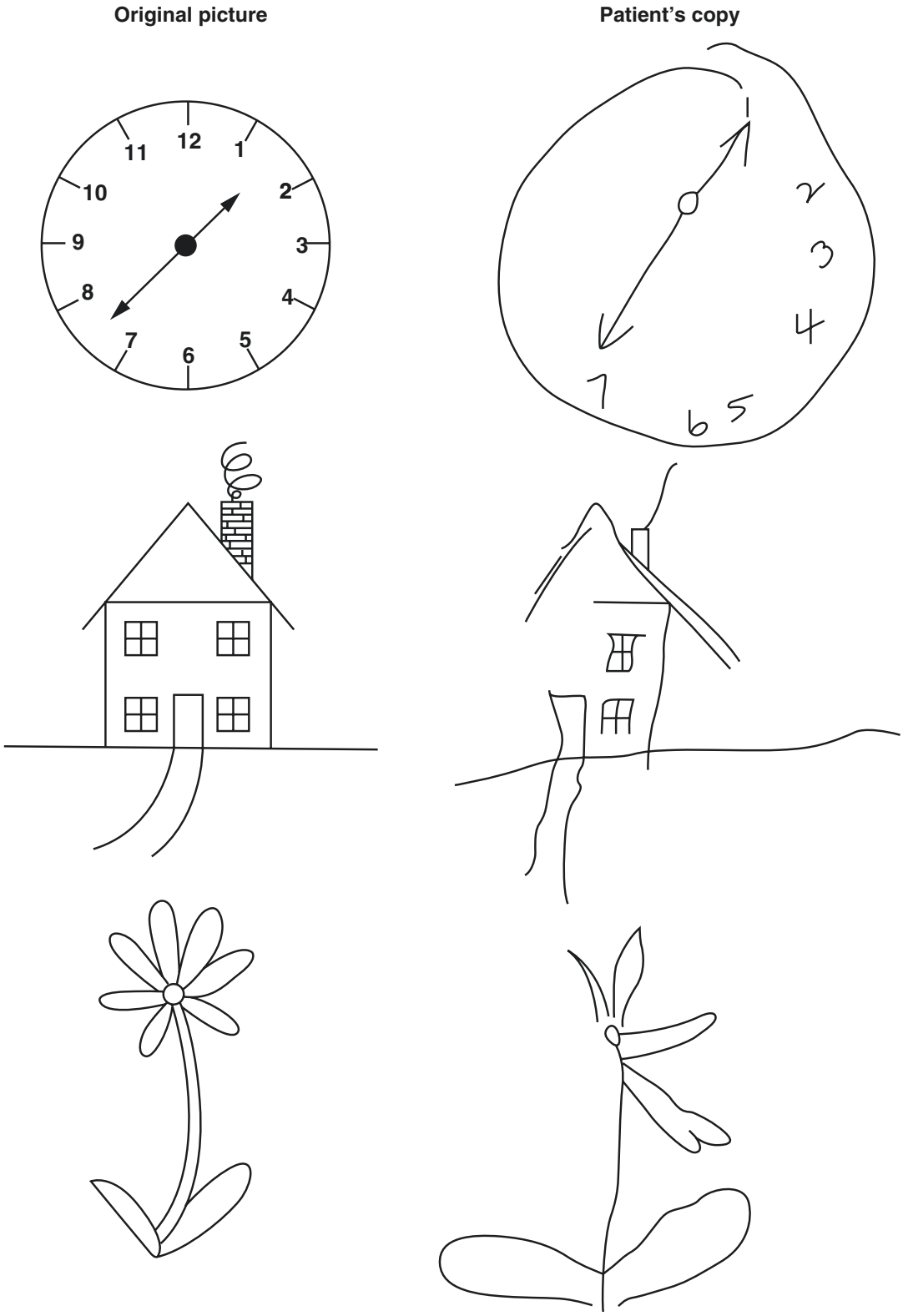

Fig. 10.6 Neglect syndrome: the drawings are missing their left halves, which is due to damage to the right parietal lobe (From Brown [39])

area. An explanation for this phenomenon is not clear; there may be an error in the integration of visual information with signals from the vestibular system [2].

Lesions of the Ventral Occipito-Temporal Pathway The ventral occipitofugal or "what" pathway is conducted mainly via the inferior longitudinal fascicles. It originates in V1 and projects through V2 and V4 to specific inferior temporal cortical areas, the angular gyrus, and limbic structures. Lesions of the occipitotemporal pathway cause primarily visuoassociative deficits and hallucinations [30]. Lesions of this pathway are often divided into three types of disconnection syndromes: (1) visual-visual disconnection (agnosia), (2) visual-verbal disconnection (alexia, anomia), and (3) visual-limbic disconnection (deficits in visual memory and emotion) [2]. However, the separation between these cerebral processes involved in visual perception, object identification, and naming is not distinct and patients seldom display completely isolated manifestations of these syndromes [2]. Also, all lesions are often associated with upper homonymous unilateral or bilateral visual field defects from extension of the damage to the inferior striate cortex.

Visual agnosia is a disorder of object recognition that cannot be explained by a sensory or speech disorder or global cognitive dysfunction. A patient with visual agnosia cannot recognize seen objects, and can provide neither the name nor the associative features of an object, like describing its function. However, patients can recognize these objects if they can touch them or hear them, for example, the characteristic sound of a bunch of keys. Visual agnosia is a sign of bilateral affection of the medial occipitotemporal areas involving both lower longitudinal fascicles connecting the primary visual cortex with visual associative areas within the temporal lobe.

The general mechanism of agnosia is a disorder of association (*associative agnosia*) or integration (*apperceptive agnosia*) of sensory stimuli ensued from loss, breach, or unavailability of the relevant subject image (memory trace) in the association cortex [40]. Patients with apperceptive agnosia have impaired object recognition due to perceptual difficulties in which elementary visual function remains intact [2]. Patients are unable to integrate visual information to form an internal image of an object and have difficulty matching, copying, and recognizing even simple shapes. These patients often have visual field defects, but their perceptual deficit cannot be explained by the field loss. Apperceptive agnosia usually develops in association with diffuse lesions to the posterior parts of brain. In contrast to apperceptive agnosia, patients with associative agnosia are unable to identify objects or categories of objects visually; however, they have intact perception and can draw and match objects [40].

Patients with *dorsal simultanagnosia* can perceive whole shapes, but their perception of these shapes is restricted to a single visual area because of their inability to shift visual attention. Patients fail to integrate information into a global image; they describe only fragments of a scene. Peripheral visual field defects may simulate simultanagnosia and must be excluded [2]. This symptom results from bilateral lesions to the dorsal occipitofugal pathway and was initially considered as part of Bálint syndrome (see above). *Ventral simultanagnosia* may be another consequence of a lesion to the ventral occipitofugal pathway, particularly to the left inferior temporal region of the brain. In this case patients are able to shift attention to multiple objects, in contrast to dorsal simultanagnosia; however, they cannot integrate single components into a whole object [36]. For example, they are unable to recognize a complex object like a car, even though they can identify the components of the car, such as the tires.

Prosopagnosia ("face blindness") is a special form of agnosia, manifesting by the inability to identify familiar faces or to memorize new ones [41]. However, the affected person is able to identify the appropriate person by other distinguishing marks, such as by voice. Prosopagnosia is usually due to bilateral damage to the inferior portions of the occipitotemporal cortex, notably the lingual and fusiform gyri. As with all lesions in the ventral stream, prosopagnosia is often associated with superior homonymous unilateral or bilateral visual field defects from extension of

damage to the inferior striate cortex. Often a left homonymous hemianopia is present [2].

Visual-spatial agnosia manifests by impaired orientation in space, loss of topographical memory, and constructional apraxia. The patient is unable to trace images, especially if they show spatial relationships, and usually suffers from other disorders, such as finger agnosia, apraxia of dressing, etc. The underlying lesion is usually in the posterior part of the right (nondominant) parietal lobe.

Object anomia should be distinguished from object agnosia and is characterized by a generalized defect in visual naming. The patient is able to describe objects and their function but is unable to recall the names of objects, as long as he sees them only. Only the touch or a characteristic noise leads to the recall of the object name [33]. Object matching and recognition are intact.

Color anomia is the inability to name colors. There is no achromatopsia (isochromatic tests are recognized successfully) and no agnostic deficit. Color anomia may occur in conjunction with an aphasic disorder and pure alexia. The semantic recall of colors remains intact, and so the patient can identify colors by the colors of known objects (the color, for example, of an orange, banana, or tomato).

Patients with *pure alexia* (alexia without agraphia) suffer from the loss of reading ability (even words they have just written) with preserved language, retained speech and writing skills [42]. Some patients are completely unable to identify words, letters, or symbols. Other patients are able to read letters and identify words by tracing and letter-by-letter reading strategy [33]. Affected patients usually have a right homonymous hemianopia, or the defect is limited to the upper quadrant. Many cases of pure alexia are overlooked or wrongly attributed to the hemianopic defects frequently seen in these patients. However, the alexia is not caused by the visual field defect only, but rather by disruption of visual inputs to higher order linguistic centers. Pure alexia, similarly to color anomia or object anomia, results from the disconnection of visual inputs to the dominant angular gyrus from damage to the left striate cortex and the splenium of the corpus callosum usually due to ischemia of the left posterior cerebral artery. More extensive lesions of the left angular gyrus may also cause—apart from alexia with agraphia—the so-called *Gerstmann syndrome*: finger agnosia, acalculia, and failure of left-right orientation [2, 33]. Lesions of the splenium (callosal disconnection) may cause a left hemialexia associated with other signs such as tactile anomia and agraphia with the left hand [3, 33]. Additionally, depending on the extension of the lesion, other properties conveyed by the ventral occipitofugal pathway may be affected, resulting in agnosia and memory deficits that may be easily confused with anomia [2]. If disturbances of spontaneous speech; speech understanding; and impaired repetition of speech, writing, and spelling are noted, it is necessary to consider aphasic alexia, where reading is secondarily involved [2, 33].

10.5.6 Functional Visual Disturbances

Functional visual disorders are relatively common, representing up to 5% of all visual difficulties for which patients visit an ophthalmologist or a neurologist. They can be either unconscious (dissociative disorder) or deliberate (simulation). The most commonly reported problems include bilateral or unilateral blindness, visual field defects, and monocular diplopia. The most common pretended visual field loss is concentric visual field loss and hemifield defects. Several tests may help distinguish functional from organic visual loss:

- Absence of a linear improvement or deterioration in vision by changing the test distance; e.g. in organic concentric visual field loss the visual field will enlarge if the test distance is doubled. In feigned concentric visual field loss, the borders of the visual field will be given by the patient as previously so that the so-called tunnel vision can be observed.
- Normal color and spatial vision (stereopsis).
- Normal defensive response (blink reflex) to quickly approaching hands.
- Normal optokinetic nystagmus.
- Normal VEP and mfVEP (however, abnormal VEP does not confirm an organic cause, since

abnormalities can be achieved on purpose by eccentric fixation or convergence and accommodation).
- Normal electroretinography and electroencephalography.
- Absence of RAPD in unilateral vision loss.

Conclusion

Homonymous hemianopia is an indicative of a retrochiasmal disease, and is one of the most common features of central nervous system damage. However, this visual disability may be accompanied by changes in the perception of the visual environment that cannot be explained by the visual field defect only. They are caused by concurrent damage to associative visual areas of the brain and may dispose the patient to severe handicap. Neurological and neuropsychological examination is crucial in the investigation of patients with homonymous hemianopia. Associated focal neurological signs and symptoms, as well as visual field characteristics such as their location and congruity, may help to more precisely determine the site of the causative brain lesion. Understanding neurological syndromes will enable ophthalmologists and neurologists to identify patients with central visual disorders and perform appropriate testing. Only at that point can a differential diagnosis, diagnostic evaluation, and treatment plan be generated.

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Adaptation and Rehabilitation in Patients with Homonymous Visual Field Defects

11

Susanne Trauzettel-Klosinski

Abstract

Hemianopia leads to severe impairment of spatial orientation and mobility. In cases without macular sparing an additional reading disorder occurs. Persistent visual deficits require rehabilitation. The goal is to compensate for the deficits to regain independence and to maintain the patient's quality of life. Spontaneous adaptive mechanisms, such as shifting the field defect towards the hemianopic side by eye movements or eccentric fixation, are beneficial, but often insufficient. They can be enhanced by training, e.g., saccadic training to utilize the full field of gaze in order to improve mobility and by special training methods to improve reading performance. At present only compensatory interventions are evidence-based.

Keywords

Hemianopia • Orientation disorder • Reading disorder • Rehabilitation • Compensatory methods • Training • Quality of life

11.1 Introduction

In recent years, many new treatment options were achieved in neuro-ophthalmology. However, visual deficits often persist and cannot be treated by pharmacological or surgical interventions. Those will require rehabilitative interventions with the goal to compensate for the deficits to regain independence and to maintain the patient's quality of life.

The aspects of daily living determining quality of life that are most impacted by homonymous visual field defects are reading, orientation, and mobility, as well as social demands related to communication [1–3].

The literature research regarding rehabilitative interventions in homonymous hemianopia (HH) focused on using Cochrane Reviews (http://www.cochrane.org/) and randomized controlled trials (RCTs) in PUBMED for the period 1990 to January 2016. The main interventions were: substitutive, restitutive, and compensatory.

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11.2 General Aspects of Rehabilitation

11.2.1 Aspects of Disability

The International Classification of Functioning Disability and Health (ICF) can be well applied to the visual system (Fig. 11.1) [4, 5]. Three different fields should be considered:

1. Vision impairment: morphology and visual function are assessed on the basis of the organ.
2. Limitations of activity, based on functional vision, are related to the person. Two main areas need to be considered: Near distance tasks, especially reading, are impaired by visual field defects involving the visual field centre. Distance tasks, such as mobility and communication, are impaired by peripheral visual field defects.
3. Restricted participation in society caused by the resulting problems in the patient's social environment.

11.2.2 The Significance of Spontaneous Adaptive Mechanisms

Spontaneous adaptive mechanisms are of special interest for understanding the underlying pathology and for developing rehabilitation programs:

- Are they functionally beneficial?
- Which kinds of patients develop them, which do not?
- Can they be enhanced by training?

11.2.3 The Significance of Interventional Studies

For any interventional studies, three main aspects should be considered:

1. Specificity: Spontaneous recovery needs to be excluded. It has been shown in patients with HH that spontaneous recovery is observed in 38% of them, and it occurs with decreasing

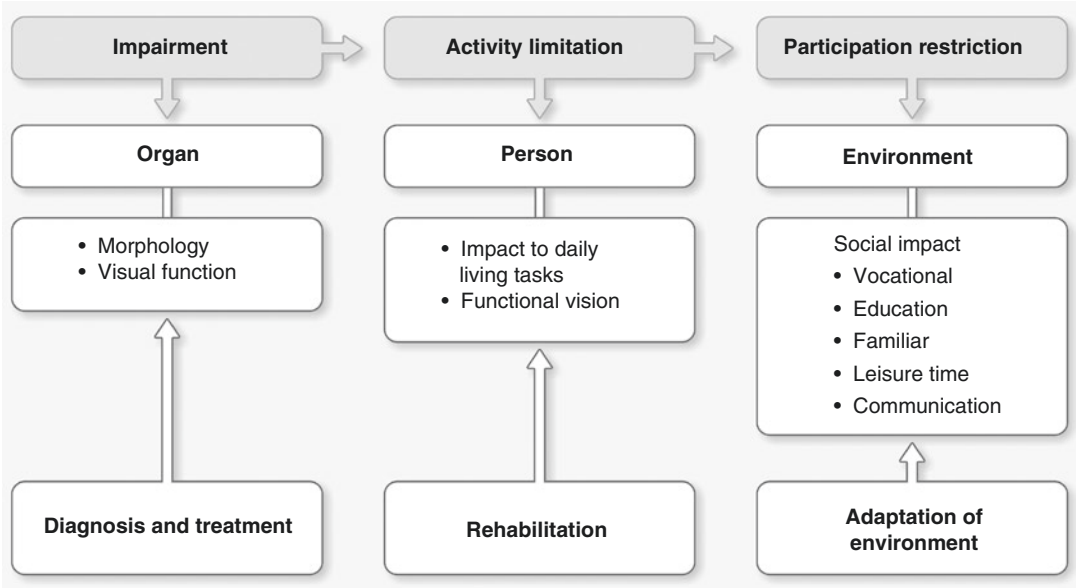

Fig. 11.1 World Health Organization (WHO) classification applied to the visual system (International Classification of Functioning, Disability and Health; WHO 2004) (Modified from Trauzettel-Klosinski [5], with permission)

probability during the first 6 months after onset [6]. Additionally, a placebo effect should be excluded by using a control group.
2. Quality of testing methods:
   (a) Reliability (e.g., repeatability, precision)
   (b) Objectivity
   (c) Validity (does the test show causal relations)
3. Aim of the intervention:
   (a) Clinical relevance of the effect
   (b) Persistence of the effect after training

11.3 The Hemianopic Reading Disorder

Reading is a key function in developed societies. It means independence, participation, mental agility, and quality of life.

11.3.1 Normal Reading

The visual preconditions for reading are [5, 7]:

(a) *Sufficient resolution* of the retinal area used for reading (for reading common newspaper print at a distance of 25 cm a visual acuity of at least 0.4 or 20/50 is required)
(b) *Sufficient size* of the retinal area during one fixation, which requires a minimum of 2° right and left of fixation [8, 9]

In skilled readers, the total "perceptual span" or "reading visual field" during one fixation can be extended in the reading direction. For fluent reading, a total perceptual span of 5° (or 15 letters) right and 1.3–2° (or 4–6 letters) left of fixation is necessary, which was shown in scrolling window experiments in normal subjects [10], and in patients with HH [11]. The perceptual span offers a preview benefit by providing information about word length, word shape, etc., which is useful to guide the next saccade to the appropriate landing position [12]. The perceptual span is a dynamic parameter that is also influenced by linguistic (grammatical, contextual) mechanisms. Recordings of reading eye movements in healthy subjects show a typical staircase pattern, a sequence of saccades and holding positions. The significance of the central visual field is indicated by the high cortical magnification: the central 10°, which account for approximately 2% of the total visual field, cover more than 50% of the primary visual cortex [13].

11.3.2 The Clinical Picture

Reading performance in HH depends strongly on the configuration of the field defect and its distance to the visual field centre, i.e., the size of the reading visual field (Fig. 11.2) [14]. In macular splitting, half of the reading visual field is obscured (see Fig. 11.2a). In macular sparing, the reading visual field is preserved and reading can be normal dependent on the amount of sparing (see Fig. 11.2b). On the other hand, a small paracentral homonymous scotoma causes severe reading problems because it covers half of the reading visual field (see Fig. 11.2c). Such small paracentral scotomas can easily be overlooked in automated perimetry if the grid of test points is not dense enough. Therefore, an especially dense grid in automated perimetry should be chosen, or manual perimetry should be performed, which allows the examiner to search for small scotomas in a goal-directed manner.

The degree of the hemianopic reading disorder is also influenced by the side of the field defect. If the hemianopic field defect is in the reading direction, reading is extremely impaired. Figure 11.3 shows the eye movement recordings during reading of one line of text: In Fig. 11.3a for a healthy subject; in Fig. 11.3b for a patient with left HH. The patient gets through the line quite well, but needs additional steps during the return sweep, indicating the difficulties in finding the beginning of the next line. Figure 11.3c displays the recording of a patient with right HH who needs many more forward saccades per line and makes several backward saccades to get through the line.

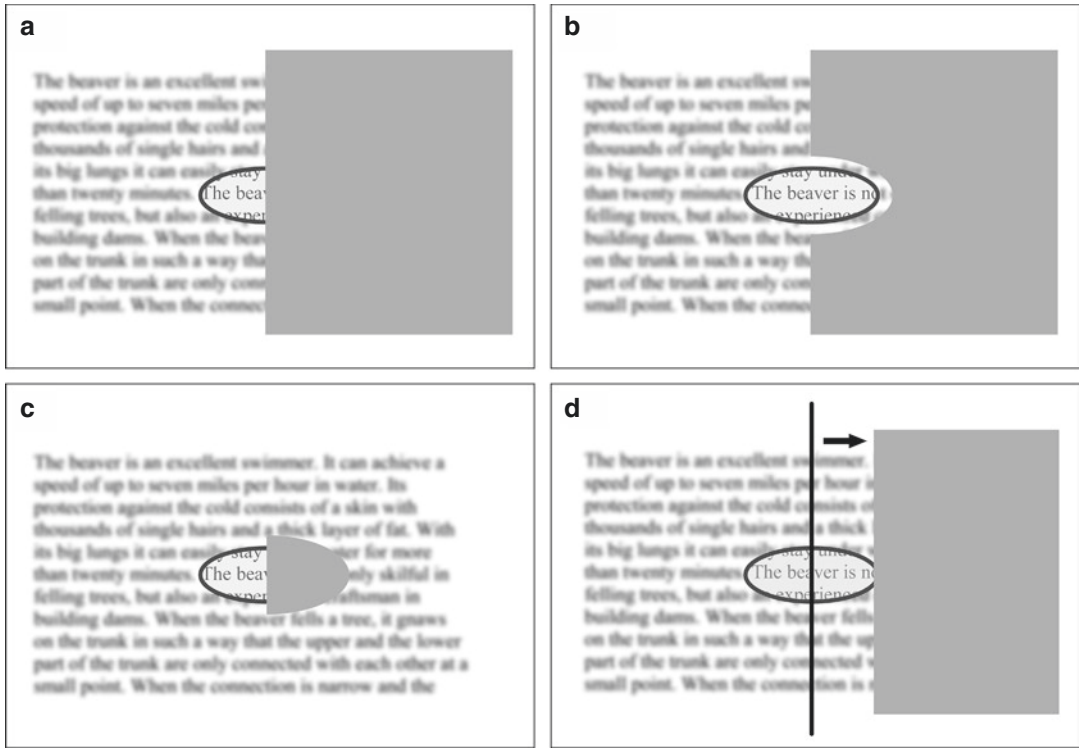

Fig. 11.2 The impact of a homonymous field defect on reading performance: Right homonymous hemianopia related to the text: (**a**) In macular splitting, half of the reading visual field is functionless and reading ability is severely impaired. (**b**) In macular sparing, reading ability is preserved, even though there is a large field defect causing spatial orientation problems. (**c**) A small paracentral homonymous scotoma causes severe reading problems. (**d**) Eccentric fixation shifts the field defect towards the blind side, which creates a small perceptual area along the midline (Modified from Trauzettel-Klosinski [14], with permission)

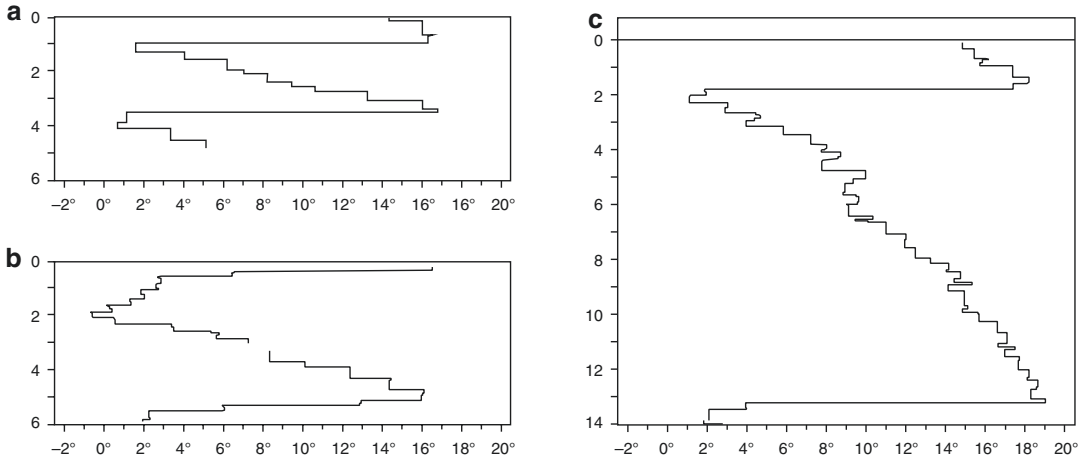

Fig. 11.3 Eye movements while reading one line of text. (**a**) The normally-sighted subject makes eight saccades and needs approximately 1.5 s to get through the line. An accurate return sweep follows to the beginning of the next line. (**b**) A patient with left homonymous hemianopia (HH) has no major problems getting through the line, but has difficulties finding the beginning of the next line, indicated by several additional steps during the return sweep. (**c**) A patient with right HH shows an increased number of saccades and several regressions per line, has a markedly prolonged reading time, but has no problems with the return sweep (Modified from Trauzettel-Klosinski [5], with permission)

11.3.3 Spontaneous Adaptive Mechanisms

Eccentric Fixation About 18% of patients with macular splitting are able to use slightly eccentric fixation despite normal foveal function [15, 16]. This occurs in both eyes as homonymous (!) eccentric fixation: The patients shift the visual field defect border towards the hemianopic side, thus creating a small strip of 1–2° of seeing visual field along the vertical midline, which expands the perceptual span for reading. Hence, these patients sacrifice a bit of visual acuity and gain a bit of reading visual field (see Fig. 11.2d). In conventional perimetry, this shift can be misinterpreted as a recovery of the visual field.

This compensatory process indicates cortical plasticity: the eccentric fixation locus is not only used as the new centre of the visual field, but also as the new centre of the reading eye movement coordinates, which means a shift of the sensory and motor references. It should be noted that these patients have intact foveal vision but can learn to use eccentric fixation if it is required by the task, such as reading. However, in a high-resolution task, as in visual acuity testing, they use their foveola [15].

Eye Movements: Fixational and Scanning During continuous fixation of a fixation cross, patients with HH show an asymmetric distribution of their fixational eye movements: they make more saccades towards the blind side, thus shifting the visual field border towards the hemianopic side. This mechanism is present during continuous fixation of a cross, but can be enhanced by performing scanning eye movements for improving orientation (see below). Figure 11.4 shows the asymmetric distribution of the fixational eye movements in right HH [16].

Dysmetric Saccades Hypometric saccades are often observed in HH [16]. During the return sweep they are an ineffective, time-consuming strategy (see Fig. 11.3b). On the other hand, hypermetric predictive saccades can be a beneficial adaptive mechanism that makes finding the beginning of the next line easier.

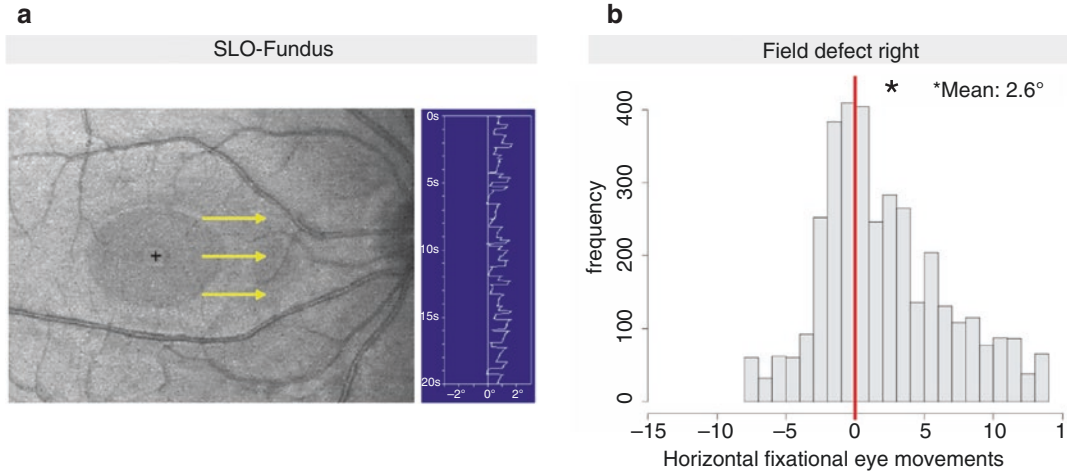

Fig. 11.4 (**a**) (*left*) SLO-image of the fundus with a fixation cross. The image shows the absolute position of the fovea related to the stimulus, which allows direct fixation control without calibration. (*right*) Asymmetric fixational eye movements towards the hemianopic side (individual example). (**b**) Distribution of fixational eye movements during continuous fixation of a single cross (20 s) in 25 patients with right homonymous hemianopia and with sparing of <4°. A positive mean value corresponds to a shift of the distribution to the right: here centered at +2.6° (mean). The distributions are significantly different from a normal distribution centered at 0° ($P < 0.0001$) (Modified from Reinhard et al. [16], with permission)

11.3.4 Rehabilitation

From a clinical perspective, it is helpful to improve the orientation on the page by visual and tactile tools, especially to find the beginning of the new line in left HH, for example, with the index finger, a ruler, or other tools with a guiding line. Another help in left HH may be training predictive saccades to improve finding the beginning of the next line. Turning the text so that the lines run vertically or diagonally could be beneficial. However, these methods have been examined only in normally-sighted subjects [17, 18] and have not yet been validated in scientific studies on patients with HH.

Special reading training has been applied in patients with HH by *scrolling the text*. Earlier studies without sufficient level of evidence reported a beneficial effect [19–21], but there is only one RCT showing scrolled text training to be effective in right HH with an average improvement of reading speed of 20 words per minute [22].

Another approach is the presentation of *single words*, which also yielded an improvement of reading speed [23]. Further, it was shown also that *nonword search tasks* can improve reading performance. The effects of an oculomotor task during presentation of single words or nonword material did not show a difference [24]. In a recent RCT, the reading training consisted of a nonword search task among words in a horizontal line [25].

11.4 The Hemianopic Orientation Disorder

11.4.1 The Clinical Picture

HH causes severe impairment of mobility and spatial orientation. However, most patients are unaware of their visual field defect. This is why HH is often not diagnosed in the early stage after a stroke [5], because other symptoms, e.g., hemiplegia, can be too dominant. Instead, the patients notice that they have "accidents" such as bumping into objects and people. Furthermore, they feel insecure while walking, especially in a complex environment with many people or objects surrounding them, and they can have problems with finding their way. Additionally, communication can be impaired, because the patients do not see familiar people approaching them in their blind hemifield. These impairments lead to reduced participation in social life and to a diminished quality of life [1–3].

11.4.2 Spontaneous Adaptive Mechanisms

Scanning Eye Movements Patients spontaneously perform saccadic eye movements towards the blind side to utilize their field of gaze. Figure 11.5a shows the perceived environment while looking straight ahead. In this condition, the information from the hemianopic side is missing. During scanning eye movements, the full field of

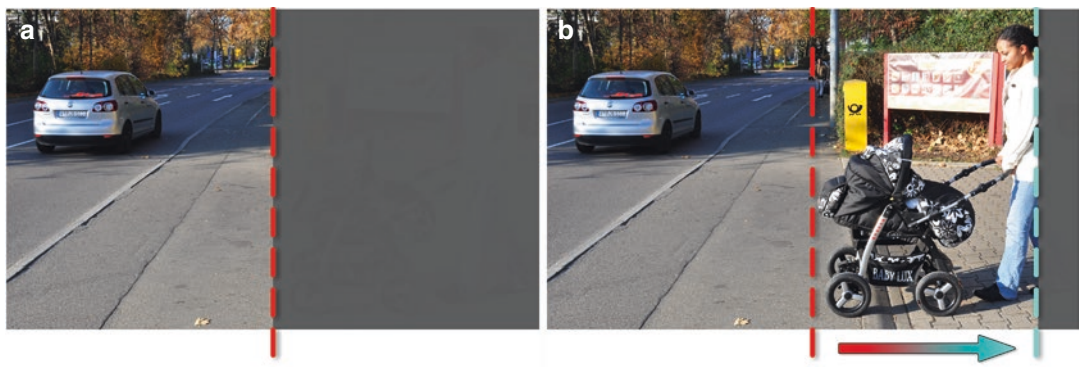

Fig. 11.5 When looking straight ahead (**a**), information from the blind side is missing. The obstacle, here, the baby carriage, becomes visible by making scanning eye movements (**b**)

gaze can be utilized to gather information from the blind side and to avoid collisions, here with the baby stroller (Fig. 11.5b). This mechanism normally is not sufficient for complete compensation, but can be enhanced by saccade training.

Saccadic Tasks Dysmetric saccades often occur while performing tasks that require saccades, so that the accuracy of "landing places" as well as fixation stability after landing is decreased [16]. Using mainly hypometric saccades is an ineffective, time-consuming strategy. Some patients learn to switch from hypometric saccades at onset to predictive saccades after training to find a unique target. Such short-term adaptation was reported by Meienberg et al. [26]. On the other hand, Reinhard et al. did not find a correlation between the number of dysmetric saccades and the duration of the disease, which indicates that long-term adaptation with more effective strategies did not, or only insufficiently, occur [16]. As a consequence, for rehabilitation simple saccade training in addition to using search tasks can be considered.

Head Turn Turning the head in yaw is a common habit in patients with HH. However, Fig. 11.6

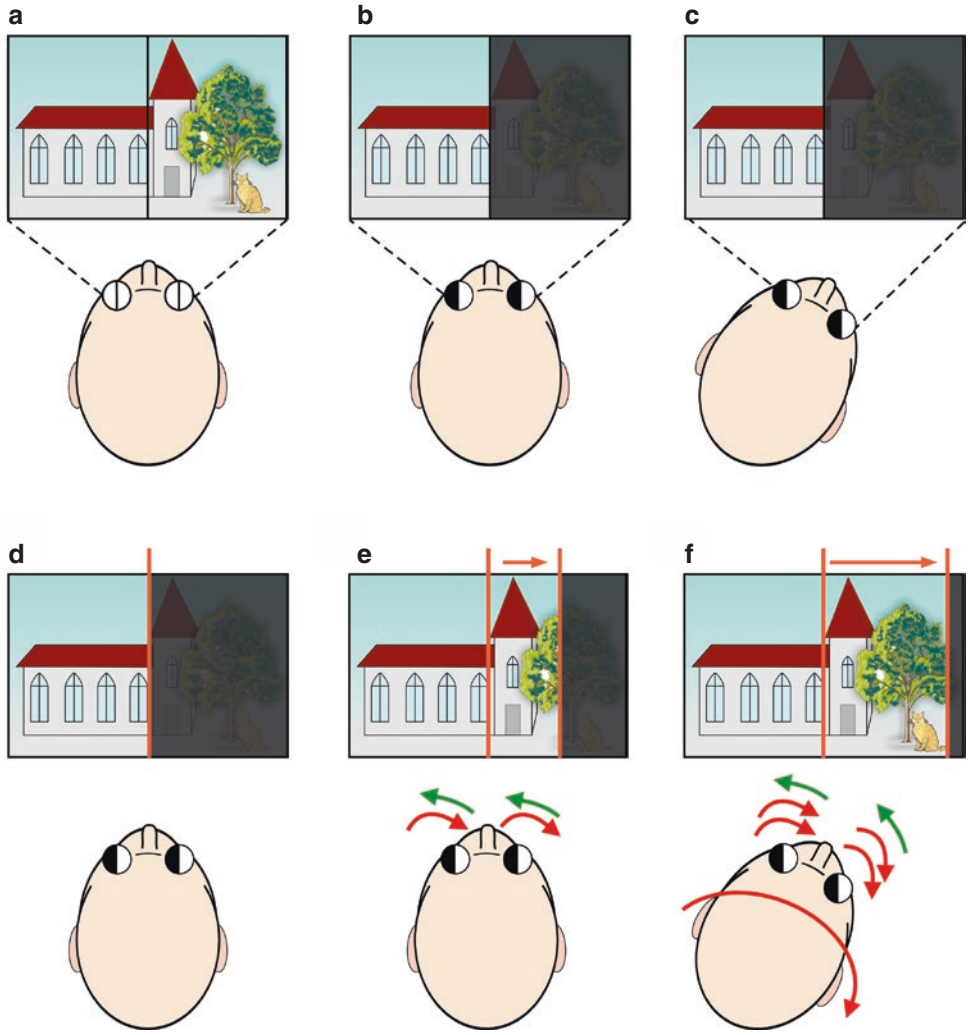

Fig. 11.6 Visual field seen in normal conditions (**a**) and in patients with right homonymous hemianopia. *Upper row* Head turn: (**b**) looking straight, no information from the blind side; (**c**) head turn alone does not change the visual field. *Lower row* Eye movements and head turn: (**d**) without eye movements no information from the blind side, (**e**) scanning eye movements utilize the field of gaze and enlarge the "functional visual field", (**f**) scanning eye movements plus head turn enhance this effect (Modified from Paysse and Coats [27], with permission)

shows that head turn alone does not change the visual field. On the contrary, the disadvantage of continuous head turn is torticollis without any functional improvement. If head turn is combined with scanning eye movements, the "functional" visual field is extended by using the full field of gaze [27].

Exotropia Exotropia with anomalous retinal correspondence leads to extension of the binocular visual field (Fig.11.7) [28–30]. In such cases, it should be considered that strabismus surgery would be contraindicated [31].

Shift of Attention Normally, conscious visual attention is connected with the centre of the visual field. In scanning a visible scene with eye movements, a sequence of events involving reflex-like, transient attention is necessary [32]: (1) Disengage attention, (2) move attention to the new stimulus, (3) reengage attention there, (4) disengage fixation, (5) move the eye to the new stimulus, and (6) reengage fixation there. This means that all scanning saccades are preceded by movements of attention [33].

The special features of attention in HH for saccades are the following: The stimulus on the blind side is not visible. Sustained attention is controlled by volition and can initiate saccades into blind areas of the visual field [32], i.e., into the blind side in HH. Therefore, a consciously controlled saccade can be performed in order to bring the stimulus onto the seeing hemifield. After that, transient attentional mechanism can take over again.

11.4.3 Rehabilitation

The Compensatory Approach Compensating training aims to enlarge the "functional visual field" by utilizing the field of gaze with scanning eye movements into the blind hemifield and by consciously shifting attention to the blind side. In earlier studies, this kind of training, either in search tasks or as saccade training, has been shown to be beneficial at improving the utilization of the blind hemifield [19, 21, 34, 35]. As these earlier studies could not prove the specificity of the intervention without a control group, Roth et al. performed the first RCT using explorative saccade training (EST) based on a search task, which clearly showed the beneficial effect compared with a control group: EST selectively decreased reaction times for a digit search task (multiple search targets) and for a natural search task (objects on a table) [3]. This improved natural scene exploration and quality

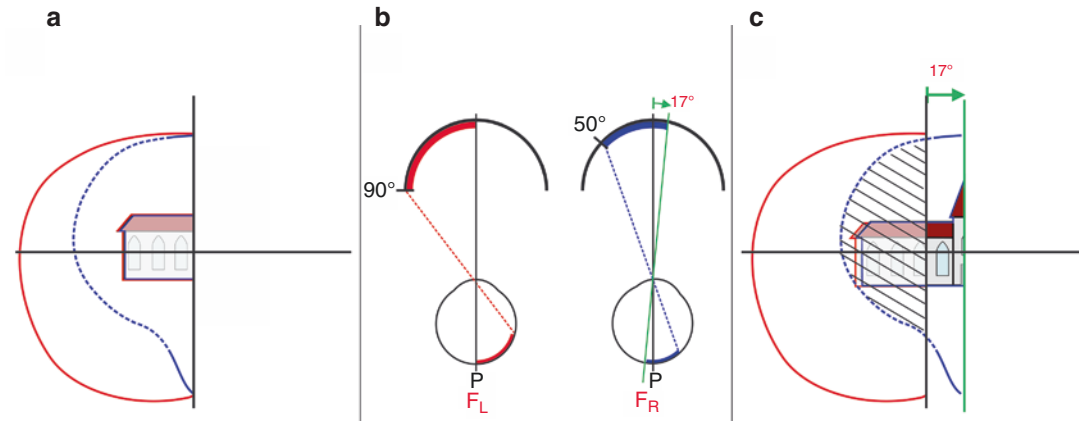

Fig. 11.7 Exotropia of the eye on the hemianopic side (right homonymous hemianopia, HH) with anomalous retinal correspondence leads to extension of the binocular visual field. (**a**) Binocular visual field in right HH with normal binocular vision. (**b**) Exotropia of the right eye (RE) with anomalous correspondence related to the fundus (*bottom*; *FL* fovea left eye, *FR* fovea RE) and to the monocular visual fields (*top*). (**c**) Exotropia of RE of 17° extends the binocular visual field towards the hemianopic side (The marked section represents the area of double vision in the case of normal correspondence) (Modified from van Waveren et al. [30], with permission)

of life scores in the social domain. The newly learnt saccadic strategy could be applied to everyday life. The training effect remained stable after the end of the training. Even patients with long-standing HH for many years improved, which indicates that the spontaneous adaptation had not been sufficient. In a recent as yet unpublished study with age-matched normally-sighted subjects, we found that the average improvement of the reaction times of the HH patients even reaches normal levels [unpublished data].

The control group that received visual field stimulation training (a flickering letter at 22° eccentricity) showed neither a change in exploration behavior nor in the extent of the visual field. The EST software (www.visiocoach.de) was designed to be easy to handle and can be used independently by the patient at home, even without previous personal computer experience. Other software is also available with different saccadic or search strategies [19, 34, 35]. Meanwhile, more RCTs have been conducted, showing audio-visual stimulation to be more effective than visual training alone [36], and oculomotor and attentional training to have the same benefit [37]. A recent study compared a combined reading and exploration training with a control training (attentional tasks) and found enlargement of the field of gaze, and improvement of activities of daily living and reading speed [25]. In another RCT, a horizontal saccadic training improved mobility [38].

Other approaches do not yet allow final conclusions: Studies with a very small sample and without patient control group reported that a ramp-step paradigm improved visual search [39], which was then applied in a larger patient group as a Web-based training [40]. Regarding multisensory stimulation, a review of 21 studies cited beneficial effects in 20 of them; however, the quality of these studies was judged as insufficient for a valid conclusion that this is an effective intervention [41].

Antisaccade training by stimulation of consciously controlled attention in combination with a saccadic adaptation procedure yielded positive effects on different tasks [42].

During the rehabilitative consultation, it is generally important to explain the special nature of the visual impairment to patients and their relatives in detail. The goal is to make them aware of their impairment and to make them understand that driving a car is illegal in Europe. There are some states in the United States, where, dependent on local legal regulations, a restricted driving license can be given limited to a familiar environment. In the future, it might be an option that HH patients may regain a restricted driving license after compensative saccadic training, when their reaction times during scanning tasks normalize and they pass a special driving test.

Substitutive Interventions: Optical Devices Binocular sector prisms have been shown to be ineffective in HH, but helpful in neglect [43]. Most patients find monocular prisms and mirrors too unpleasant because of the resulting confusion and diplopia in the centre (see Fig. 11.6). A newer approach applied monocular sector prisms placed across the whole width of the lens, but only in the *peripheral* part of the glasses. This was reported to be beneficial by expanding the visual field without central diplopia, based on the finding that after 1 year 47% of these patients were still wearing the prisms [44]. However, these studies were performed without control group. A recent randomized crossover trial found higher acceptance and greater improvement of mobility in the group with real prisms, based on subjective reports [45]. In order to come to a conclusive judgment about the benefits, future studies should employ this method using objective outcome variables.

Restitutive Training The aim of restitutive training is to reactivate incompletely damaged neurons in the blind hemifield and to enlarge the visual fields by visual stimulation. Earlier studies performed visual stimulation *along the vertical border* of the field defect, and reported visual field enlargement [46, 47]. However, these effects could not be confirmed in studies using conventional perimetry [48, 49], nor by fundus perimetry with simultaneous fixation control [50]. Fixational eye movements shift the field defect towards the blind side [16, 51, 52] and can be

misinterpreted as an enlargement of the visual field [50, 53–55].

Studies that applied stimulation of the visual field in a *more peripheral* area, thus reducing the risk of eye movements towards the stimulus, did not yield enlargement of the visual fields [3, 56], but rather increased contrast sensitivity in two patients [56], which might be an effect of an extrastriate activation (see below).

In summary, at present, there are no evidence-based studies in the literature that could show the effect of restitutive training on improvement of visual fields [57]. However, regeneration of neurons in V1 has to be distinguished from the blindsight phenomenon, which is based on extrastriate activation (see below).

Plasticity of the Adult Visual Cortex *Perceptual learning in the normal visual cortex* has been shown in many studies (see the review by Sasaki et al. [58]). It is characterized by an improvement in different functions such as motion direction, orientation, Vernier acuity, and texture discrimination. The underlying mechanisms have been described as an increase in response strength, tuning of individual neurons, changes in contextual modulation (rather than large-scale spatial reorganization [59]), or long-term potentiation of synaptic responses [60].

In cases of *bilateral retinal lesions*, reorganization in the occipital cortex (V1) has been found to be very limited, and the interpretation of earlier data regarding cortical remapping has been seriously questioned [61, 62].

In cases of *damage to the visual cortex*, perceptual relearning for specific motion direction stimuli has been reported [63–65]. This finding is based on visual *training of extrastriate cortex* [63].

The "blindsight" phenomenon is mediated by mostly unconscious perception of visual stimuli via the superior colliculus to extrastriate regions bypassing V1 [65]. These "phylogenetically old" pathways can be reactivated by intensive training, which can lead to mainly unconscious perception in some patients [64]. Whether this kind of residual vision can be improved by the blindsight training to a level of everyday-life relevance is still an open question.

On the other hand, *compensatory plasticity after V1-damage* is indicated by changes in gaze strategy: "a compensatory, higher-level, integrative plasticity, which supports interaction between the person and the environment" [63]. This view is supported by a functional magnetic resonance imaging study that yielded bilateral activation of *extrastriate cortex* after eye movement training [66].

11.5 Associated Symptoms

Patients with brain damage often show rather unspecific ophthalmological symptoms, which can be very impairing and that interfere with rehabilitation efforts. These symptoms can be related to crowding, glare, reduced contrast sensitivity, oculomotor disorders, and asthenopia due to accommodation deficits and diplopia. Diplopia (14.6% in one study [5]) and hypo-accommodation can particularly be very disturbing and require early treatment with prisms and appropriate near addition lenses, respectively. Furthermore, HH is frequently associated with other neurological deficits such as hemiplegia and cognitive and attentional deficits. Hemineglect can be present in combination with HH. The line dissection test, for example, can help to assess the additional effect of neglect [67, 68], but not in acute cases [69]. In isolated HH the line is slightly shifted to the blind side, but in hemineglect, to the seeing side. The rehabilitation of these patients requires an interdisciplinary approach.

11.6 Diagnostics

The following test battery is important for specific rehabilitative measures:

- Assessment of visual acuity for far and near distance, refraction, accommodation, and adaptation of optimal corrections are essential. Appropriate glasses are a precondition for an effective visual rehabilitation.
- Neuro-ophthalmological/orthoptic examination assesses binocular vision, eye position, motility, saccades, pursuit, optokinetic nystagmus.

- Visual field examination is crucial. If standard perimetry (see Chap. 4) cannot be performed, confrontational perimetry or tangent screen campimetry (focusing on the central part of the field) are semiquantitative methods to be applied. When looking for small paracentral defects, a specially dense grid of test points or a thorough manual strategy should be used.
- Contrast sensitivity can be important for reading and for orientation. These activities can be improved by augmented illumination and/or by marking the patient's environment with special high contrast landmarks.
- Reading speed is an important measure. A suitable tool are the International Reading Speed Texts (IReST), which are standardized paragraphs to be read aloud. A set of ten equivalent texts is linguistically adapted for contents, length, difficulty, and linguistic complexity in order to be used for repeated measurements. They were developed in 17 languages and are therefore comparable, not only within one language, but also between different languages (www.amd-read.net.) [70, 71].
- Recording eye movements during reading is a valuable method for detailed analysis of reading performance that allows quantitative assessment of reading parameters, such as number and amplitude of forward and backward saccades, fixation durations, and return sweep.

11.7 Summary and Conclusions

The main effects of HH are impairment of reading and spatial orientation. Reading performance depends on the side of the field defect (unfavorable if in the reading direction), the size of a macular sparing, and spontaneous adaptation.

Spontaneous adaptive mechanisms are mostly beneficial, but often insufficient. However, they can be supported by compensatory training. They aim to enlarge the "functional visual field" by utilizing the field of gaze.

For rehabilitation, at present only compensatory methods are evidence-based *For reading*: scrolled text for right HH [22], search task in a line [24, 25], and single word reading [23].

For orientation: Visual search tasks [3], audiovisual search tasks [36], saccadic tasks [25, 38], and attentional training [37].

Remark: The author has no personal financial interest in any products mentioned.

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