Dean McKay
Eric A. Storch
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Handbook of Child and Adolescent Anxiety Disorders

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ISBN 978-1-4419-7782-3 e-ISBN 978-1-4419-7784-7
DOI 10.1007/978-1-4419-7784-7
Springer New York Dordrecht Heidelberg London

Library of Congress Control Number: 2011922751

To Dawn & Rebecca, for a fun, rich and full life.

—Dean McKay

To my children Noah and Maya for being the perfect playmates. And, to my bride Jill.

—Eric A. Storch

About the Editors

Dean McKay, Ph.D., ABPP, is Professor, Department of Psychology, Fordham University. He currently serves on the editorial boards of *Behaviour Research and Therapy*, *Behavior Modification*, and *Journal of Anxiety Disorders* and is an Associate Editor of *Journal of Cognitive Psychotherapy* (term beginning 2008). He has published more than 130 journal articles and book chapters and has more than 150 conference presentations. Dr. McKay has been a member of the Obsessive Compulsive Cognitions Working Group since 1995. He is Board Certified in Behavioral and Clinical Psychology of the American Board of Professional Psychology (ABPP), is a Fellow of the American Board of Behavioral Psychology and the Academy of Clinical Psychology, as well as a Clinical Fellow of the Behavior Research and Therapy Society. He is also a Fellow of the American Psychological Association (Divisions 5 (Measurement, Evaluation, and Statistics), 12 (Clinical), 29 (Psychotherapy), and 42 (Community of Psychologists in Independent Practice)) and the American Psychological Society. Dr. McKay has edited or coedited eight books dealing with treatment of complex cases in children and adults, obsessive-compulsive disorder, disgust in psychopathology, and research methodology. His research has focused primarily on Obsessive-Compulsive Disorder (OCD), Body Dysmorphic Disorder, and Hypochondriasis and their link to OCD as well as the role of disgust in psychopathology. His research has also focused on mechanisms of information processing bias for anxiety states. Dr. McKay is also the director and founder of Institute for Cognitive Behavior Therapy and Research, a private treatment and research center in Westchester County, New York.

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Part I

Foundations in Child and Adolescent Anxiety

Classification of Child and Adolescent Anxiety Disorders

1

Dean McKay and Eric A. Storch

Classification in psychopathology has moved through several important stages, based on the trajectory of the Diagnostic and Statistical Manual from its first edition to the most current, and the upcoming fifth edition. The initial two editions were marked by a unifying theoretical basis, whereby specific diagnoses were conceptualized in psychodynamic terms. This tradition is similar to the formulation of taxonomies in other branches of science. For example, in biology the reliance on a hierarchical arrangement from kingdom down to species is based on a specific theoretical framework, whereby all newly discovered organisms may be readily classified. While not totally without controversy, such as the recent movement toward cladistics (whereby organisms are classified by ancestry rather than present biological structure; Scott-Ram, 2008), these represent mere refinements rather than sea-change level alterations in classification. Another example is in chemistry, where elements are classified by a theory-driven framework regarding the organization of atoms, with specifications within the periodic table of elements (such as noble gases, metals, etc.) that also readily guides researchers in how to classify newly discovered entities. Again, controversies exist (e.g., cloud theory versus heliocentric theory of atomic structure; Cox, 1996), but these do not substantially alter the manner of utilizing the classification system.

Unlike other branches of science, however, psychiatry, psychology, and their associated professions are not unified by a single theory of mind, and most conditions likely have multiple determinants. Further, most users of the original DSMs noted the limited reliability of the taxonomy it laid out, and with the third edition came a radical change in how psychiatric classification was conceptualized: purely descriptive and atheoretical. This allowed users to arrive at diagnoses with much greater precision, and the aim was to establish a set of conditions that had ecological and syndromal validity. This has served the field well, and has lead to important advances in assessment, treatment, and etiological understanding. However, unlike classification systems in other branches of science, should a new condition arise, there is no inherent mechanism for classifying it. Instead, any new diagnosis must wait until the revisions are planned for the next edition of the DSM, whereupon the proposed diagnosis is determined by committee.

This process of committee-driven descriptive diagnoses has lead to a growth of diagnoses, but rarely have any been eliminated. In the anxiety disorders, two disorders stand out as illustrative of this point. On the one hand, panic disorder without history of agoraphobia has been in the DSM since the arrival of the third edition. However, this particular diagnosis has long been recognized as either so rare as to not exist, or when actually diagnosed to likely have had a

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_1, © Springer Science+Business Media, LLC 2011

panic-related origin even if panic is completely and successfully avoided by the sufferer (McNally, 1994). On the other hand, of the very few diagnoses that have been eliminated is overanxious disorder of childhood. Interestingly, this diagnosis was only eliminated in that the criteria for a different disorder (Generalized Anxiety Disorder) were extended to encompass diagnosis in children. While these are two examples, they typify the approach to the DSM as contemporarily construed. Committees determine putative diagnoses for larger categories, based on the existing literature on etiology, incidence, and prevalence. At the same time, existing diagnoses are very rarely eliminated, even if infrequently encountered or its basis is seriously questioned by the broader community of researchers for that disorders member class.

This may be changing, as it applies to the anxiety disorders. Many of the proposed changes for the fifth edition of the DSM include the potential role of fear circuitry modeling for conceptualizing candidate disorders (i.e., Britton & Rauch, 2009). Problematic in this regard is that the fear circuitry approach to conceptualizing anxiety is not yet fully understood, and the ability to predict the full range of anxiety problems is incomplete. For example, in the case of obsessive-compulsive disorder (OCD), the fear circuitry conceptualization has been vigorously promoted by some researchers (discussed in Poulton, Pine, & Harrington, 2009), but has also been subject to questions about its validity. In the case of OCD, the heterogeneity of the disorder has made it difficult to reduce it to a single biological mechanism, or group of mechanisms such as that implied by the fear circuitry approach (Abramowitz, Taylor, & McKay, 2009). Further, the fear circuitry is hypothesized to increase the probability of learning-feared associations (Debiec & LeDoux, 2009; LeDoux & Schiller, 2009). However, in the case of OCD, many of the symptoms have limited or no clear learning mechanism associated with its manifestation. This leaves us with the curious problem of a biologically based theoretical framework from which many disorders will be classified but that also fails to adequately explain a serious and debilitating condition that is considered a putative member. And, although other etiological features are considered in this framework, there is the distinct possibility of an inaccurate bias toward a neurobiological explanation for disorders against a more holistic understanding that incorporates multiple determinants.

Current Standing of Childhood Anxiety Diagnosis

At the present, most of the anxiety disorders in the DSM are age-downward extensions of adult diagnoses. The exceptions to this are: separation anxiety, school refusal, and selective mutism. While there are exceptions, all anxiety disorders, when present in children, have unique manifestations that call for special clinical skill in assessment and intervention. One important distinction between childhood and adult manifestations of anxiety is that it is not required or even expected that children have clear insight into the nature of their fears. The only adult disorder where insight is not required is OCD, and in this case the modifier "with poor insight" is available in the DSM, and this manifestation has come under specific scrutiny as a poor prognostic indicator for treatment response (i.e., McKay, Taylor, & Abramowitz, 2010).

A second major distinction involves the behavioral manifestation of different anxiety disorders. In children, it is not unusual for the presentation to have clear developmental consequences. For example, children with school refusal, when untreated, face significant developmental limitations resulting from reduced socialization and limited opportunities for establishing normative age-related behaviors. This is likewise true in social anxiety, and the dimensionally less severe problem of chronic shyness, whereby the inhibition associated with the disorder leads to developmental lags (Beidel & Turner, 2006). Given the importance of socialization to cognitive and emotional growth (Konner, 2010), when treating children with anxiety disorders, it is often also necessary to attend to socialization problems resulting from the avoidance behaviors involved.

A third major distinction involves the role of caregivers in the etiology and maintenance of anxiety.

While this is in part associated with socialization (i.e., Okagaki & Luster, 2005), it is unique in that each is mutually dependent. This unique association can lead to anxiety problems in children if one or both caregivers are themselves anxious, or if they engage in behaviors designed to accommodate anxious avoidance (see Chap. 15). This is distinct from mere genetic transmission, since there are specific behaviors parents may exhibit that propagate anxiety exclusive of heritability by virtue of reducing the child's anxiety. Indeed, genetic data have been inconclusive with respect to transmission of anxiety disorders, while behavioral theory has offered an empirically robust method of describing disorder onset and maintenance (see Chap. 5). Instead, it could be better stated that anxiety begets anxiety, but that there are no specific risks conferred on individual anxiety disorders.

Future Directions in Classifying Childhood Anxiety Disorders

The adequacy of a purely descriptive model of psychopathology, with specific reference to anxiety disorders in childhood, is limited. Formerly, theoretically driven models seem inadequate given the difficulties in operationalization and reliability (such as that noted in the early editions of the DSM). Modern medical conceptualizations (such as the fear circuitry) do not yet have adequate empirical support to use in developing a classification scheme. Further, purely biological models are often viewed as overly reductionistic, ignoring other important sources of influence such as behavioral and cognitive theory (Taylor, Asmundson, Abramowitz, & McKay, 2009).

This leaves the field in a difficult predicament. It appears that, in consolidating a research agenda that would advance our approach to classification, it will be necessary to identify the variables associated with the greatest amount of variance in the developmental trajectory of anxiety per se, and all its manifestations. This would no doubt narrow the class of disorders, but would also allow for a comprehensive theory for which classification would readily flow without simply adhering to a diagnosis by committee approach to classification. It would also require that researchers remain open to a wide range of disparate theoretical influences (i.e., biological, psychological, developmental) to converge into a single meaningful theoretical framework.

Since the state of the field is not integrated into a meaningful theoretical framework, there are numerous perspectives on conceptualization, diagnosis, and treatment. It is our hope that the field will continue to advance, whereby the multiple perspectives in the field may be meaningfully integrated to allow practitioners to seamlessly provide high-quality services. In the meantime, this text is intended to provide a critical analysis of the state of the field in child and adolescent anxiety disorders across multiple perspectives.

Structure of the Present Text

We have arranged the book into five major sections. The first is a foundational section related to diagnostic issues and the directions anticipated in the coming years with respect to anxiety classification in children. The second section examines the full scope of alternative ways of classifying, the adequacy of these approaches, and limitations. The third section covers a wide range of additional complicating features associated with childhood anxiety, such as attention problems, low cognitive functioning, personality, family functioning, and emotional regulation. The fourth section is devoted to specific childhood anxiety disorders and their treatment, as well as integrative approaches to therapy (such as cognitive-behavioral therapy and psychopharmacology). Finally, the fifth section covers novel and emergent areas within the anxiety disorders in children.

It is our hope that this book will serve the multiple goals of providing clinicians with a deeper understanding of the full breadth of childhood anxiety disorders, their assessment, treatment, and a critical understanding of classification. We also hope that this book will advance multiple research agendas such as those in specific anxiety disorders, as well as in areas that are debilitating but have as yet received limited research scrutiny.

Finally, and perhaps most importantly, we hope that this book will vastly improve the lives of children affected by anxiety disorders.

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Issues in Differential Diagnosis: Phobias and Phobic Conditions

2

Marjorie Crozier, Seth J. Gillihan, and Mark B. Powers

The purpose of this chapter is to summarize the current status of research with respect to the clinical features, course, and prognosis of specific phobia, social phobia, panic disorder, and separation anxiety disorder (SAD) in children. In this context we will consider the salient factors involved in the differential diagnosis of these four disorders. Finally we will provide some directions for improvement in the assessment of these disorders in children.

Specific Phobia

Description of the Disorder

Specific phobias are the most prevalent anxiety disorder according to nearly all epidemiological studies of the general population (e.g., Kessler et al., 2005). Defined in Diagnostic and Statistical Manual-IV-TR (DSM-IV-TR; American Psychiatric Association, 2000) as intense fears of specific objects or situations, specific phobias (formerly simple phobia in DSM-III-R) can develop in response to nearly anything (Marks, 1987) (Table 2.1). Commonly occurring fears include animals, heights, enclosed spaces, or darkness. Because children naturally experience developmentally appropriate fears, it is important to distinguish phobias from those fears that are typical for the developmental stage of the child. A phobia diagnosis should be considered when the fear is excessive and causes marked interference in the child's life. In children the fear must be present for at least 6 months. According to DSM-IV-TR, specific phobia should be diagnosed when all of the following criteria are met: These symptoms should not be better explained by other mental disorders, such as obsessive-compulsive disorder, posttraumatic stress disorder, social phobia, or panic disorder.

The criteria listed above are those for diagnosing specific phobias in children and have been slightly modified from the criteria for diagnosis in an adult. The ICD-10 has similar diagnostic criteria but identifies fewer subtypes. The DSM-IV-TR categorizes specific phobias into five subtypes: Animal type (e.g., spiders, dogs, snakes), natural environment type (e.g., storms, heights, or water), blood-injection-injury type, situational type (e.g., bridges, elevators, flying), and another category for fears that do not fit into one of these specific categories (e.g., choking, vomiting, loud sounds, costumed characters).

Avoidance behaviors in children often take the form of tantrums, crying, and hiding. When the feared stimuli are present, the severity of the fear response and avoidance behaviors indicate the extent of the child's distress. Often the child is brought in for treatment not because of the fear itself but rather due to severity of the disruption to the family's daily routine as a result of the avoidance and distress-related behaviors.

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_2, © Springer Science+Business Media, LLC 2011

Table 2.1 DSM-IV-TR diagnostic criteria for specific phobia

Marked and persistent fear that is excessive or unreasonable, cued by the presence or anticipation of a specific object or situation (criterion A)
Exposure to the phobic stimulus almost invariably provokes an immediate anxiety reaction, which might reach the severity threshold of a situationally bound panic attack. In children the anxiety reaction may be expressed in crying, tantrums, freezing, or clinging (criterion B)
The person recognizes that the anxiety is excessive or unreasonable, although this recognition is not always present in children (criterion C)
The situations or objects are avoided or endured with intense anxiety or distress (criterion D)
The avoidance, anticipatory anxiety, or distress in the feared situations(s) interferes significantly with the person's normal routine, academic functioning, or social activities or relationships, or there is marked distress about having the phobia (criterion E)

Note. Adapted from American Psychiatric Association (2000, pp. 410–411)

Epidemiology

Prevalence. In international community samples, prevalence rates for specific phobias in children and adolescents are 2.6–9.1% with the average near 5% (Ollendick, King, & Muris, 2002). Some of the higher prevalence rates have been found in the United States but it is likely that these differences are a result of variations in assessment methods. Along with generalized anxiety disorder and SAD, specific phobias are one of the more commonly diagnosed anxiety disorders in children (Costello & Angold, 1995). Additionally, Costello and Angold found that specific phobias in a community sample occur more frequently without comorbid diagnoses than any other anxiety disorder in children. Community samples have also shown that adults with a specific phobia are significantly more likely to have had a specific phobia as an adolescent but no other previous anxiety diagnoses (Gregory et al., 2007).

Comorbidity. Clinical samples have shown different rates of co-occurring anxiety and internalizing disorders in children. A sample of children referred to an outpatient anxiety center showed a prevalence rate of 15% with specific phobia as the primary diagnosis; 64% of children with a primary specific phobia met diagnostic criteria for a secondary diagnosis (Last, Strauss, & Francis, 1987). A similar study found that 72% of children between the ages of 6 and 16 that were referred to a phobia treatment clinic had at least one comorbid diagnosis (Silverman et al., 1999); some of the more common comorbid conditions included an additional specific phobia (19%), separation anxiety (16%), and ADHD (6%) (Silverman et al., 1999). Additionally, there has been some evidence that phobias, specifically fears of the dark, in children and adolescents increase the likelihood of a co-occurring major depressive disorder (Pine, Cohen, & Brook, 2001).

Cultural differences. The rates for specific phobias have been reported to be higher in African Americans and Mexican Americans born in the US when compared to Caucasians (Karno et al., 1989; Robins & Regier, 1991). There have also been higher rates of specific phobias reported in Brazil than in the US (Da Motta, de Lima, de Oliveira Soares, Paixao, & Busnello, 2000). Lower risk for specific phobias has been reported among Asians and Hispanics (Stinson et al., 2007) compared to Western countries. A number of factors, including differences in operational definitions and ages sampled, may have contributed to differences in sampling, so it is difficult to determine whether these results reflect true cultural differences or methodological differences.

Age and gender differences. Studies indicate that the prevalence of specific phobias tends to be higher in children and adolescent than in adults (Emmelkamp & Wittchen, 2009). Most adults that meet diagnostic criteria for a specific phobia report an early age of onset but little longitudinal research has been done to confirm these reports. However, there is research suggesting that the typical age of onset for specific phobia is between

10 and 13 years of age (Strauss & Last, 1993). For animal, environmental, or blood-injection-injury type phobias the age of onset is typically 12 years or younger (Becker et al., 2007; Kessler et al., 2005; Wittchen, Lieb, Schuster, & Oldehinkel, 1999). Stinson et al. (2007) replicated this result in the largest epidemiological study ($n=43{,}093$) to date for specific phobias, finding that the highest prevalence rates were in children and adolescents.

Research on gender effects in children with specific phobias has generally shown few significant differences under the age of 10 years (Strauss & Last, 1993). However, Anderson, Williams, McGee, and Silva (1987) reported that boys were six times more likely than girls to meet DSM-III criteria for a simple phobia. Contrary to this finding, a more recent German study found that more girls than boys were diagnosed with specific phobia in a community adolescent sample (Essau, Conradt, & Petermann, 2000). Strauss and Last (1993) have suggested that this gender difference may be either based on methodological differences or a reflection of the different rates of referral for treatment in boys vs. girls.

Despite the varied results of gender prevalence across studies, there have been some consistent findings related to the prevalence of specific subtypes of phobias. Environmental phobias tend to have an earlier age of onset in boys, though they are not necessarily more prevalent in males vs. females (Wittchen et al., 1999). The blood-injury-injection subtype has been shown to be significantly more prevalent in females (Marks, 1988). Animal phobias are also more common in girls with a 3:1 ratio clearly present by age 10 years (Wittchen, Nelson, & Lachner, 1998). Though not specific to children and adolescents, phobias involving lightning, enclosed spaces, and darkness have all been found to be more prevalent in females (Goisman et al., 1998). In her book on gender differences in anxiety disorders, Craske (2003) described adolescence as a period during which women develop fears and phobias more rapidly than men do. While several environmental factors may contribute to this difference, it is clear that gender differences in prevalence rates of specific phobia become apparent in adolescence (Craske, 2003).

Specific phobias and subtypes. Some of the more commonly occurring phobias in children include fear of heights, darkness, injections, dogs, loud noises, small animals, and insects (Essau et al., 2000; King, 1993; Silverman & Rabian, 1993; Strauss & Last, 1993). However, there have been few studies specifically examining the prevalence of subtypes, and most studies have focused on adult populations. Most recently, the National Epidemiological Study on Alcohol and Related Conditions examined prevalence rates among adults. The most commonly reported phobias involved animals and heights and comprised more than half of the diagnosed cases of specific phobia. Claustrophobia and fear of flying were found to be significant in about one third of the individuals diagnosed with a specific phobia, while blood-injury-injection phobias were among the least common (Stinton et al., 2007).

Structure of Fear

A recent study (Cox et al., 2003) using both exploratory and confirmatory factor analyses examined the factor structure of all the specific phobias and found the following factors:

- *Agoraphobia*: Public places; crowds; being away from home; travel by car, train, or bus
- *Speaking*: Public speaking; speaking to a group; talking to others
- *Heights/water*: Flying; heights; crossing a bridge; water
- *Being observed*: Public eating; public toilet use; writing in front of others
- *Threat*: Blood/needles; storms/thunder; snakes/animals; being alone; enclosed spaces

Higher-order analyses showed two second-order factors: social fears and specific fears.

Another factor analytic study of specific phobia subtypes used data from a large sample of young adults from 11 countries. Results of this study

showed some evidence for blood-injection-injury subtypes and also an animal subtype of phobia (Arrindell et al., 2003). Environmental (e.g., storms, heights) and situational (e.g., flying, elevators) phobias were grouped together on one factor in this sample. Additional studies have found similar results suggesting that there may be few differences between environmental and situational phobias (Fredrikson, Annas, Fischer, & Wik, 1996). While these studies have been primarily with adults there has been some research specifically examining children. Muris, Schmidt, and Merckelbach (1999) found similar results in a sample of children, indicating that environmental and situation types of phobias tend to cluster together in factor analyses. These consistent results across samples indicate that phobia subtyping may need to be refined.

Genetic Patterns

There has been some evidence in family studies that there is a moderate degree of concordance for specific phobia diagnosis among family members. Another consistent finding has been the relationship between the fears of a mother and her child (Emmelkamp & Scholing, 1997). For example, mothers who fear insects may also have children who exhibit fear in the presence of insects. While there are a variety of factors such as temperament and modeling that may contribute to the familial relationship among anxiety disorders, genetic factors may also be responsible for some of the co-occurrence of this diagnosis.

Bolton et al. (2006) studied over 4,500 6-year-old twins to determine genetic and environmental influences on the development of early-onset anxiety disorders. For specific phobias the heritability was around 60% with the remaining 40% of variance attributed to differences in environment. As this study was conducted on young children and differs in results from other studies done on older children or adults, it is likely that early-onset phobias may be more genetically determined than are those developing later in childhood or adulthood (Bolton et al., 2006). These findings provide support for a non-associative model of phobias which suggests an evolutionary basis to fears rather than a conditioned fear model (Menzies & Clarke, 1995). Another study examining heritability of specific phobias used a sample of 319 sets of twins between the ages of 8 and 18 (Stevenson, Batten, & Cherner, 1992). The results of this study suggested that differences in genes accounted for 29% of the variance in specific phobia diagnosis, with shared and non-shared environmental factors each accounting for a remaining third of the variance.

While there has been a range of results found for the heritability of specific phobias, the heritability of anxiety more generally has been demonstrated consistently in the literature. Fyer et al. (1995) found moderate aggregation for specific phobias in families where one family member had an anxiety disorder. Hettema, Neale, and Kendler (2001) found similar results in a meta-analysis of the heritability of anxiety disorders in both family and twin studies. Hettema, Prescott, Myers, Neale, and Kendler (2005) examined anxiety disorders in a community sample of twins and determined that for all the anxiety disorders there appears to be two genetic factors that contribute to the development of symptomology. One of these factors is specifically associated with situational and animal phobias but no other forms of anxiety. Because these two subtypes of phobias are loaded together but separated from other forms of anxiety, it suggests that there may be a unique genetic factor related to the development of these two specific types of phobia making them distinct from the etiology of other forms of anxiety. Additional evidence has shown that individuals with the blood-injection-injury subtype of specific phobia have more relatives with similar problems indicating that this subtype may be a separate category (Marks, 1987; Öst, 1992). The presence of unique physiological attributes in blood-injection-injury phobia, including the risk for fainting which is rare in other phobia subtypes (Connolly et al., 1976), also supports differentiating this subtype from other specific phobia subtypes.

Contrary to the above results, the VATSPSUD study (Kendler & Prescott, 2006) found the lowest

rates of *specific* heritability for blood-injection-injury phobias (7%). That is, those with a relative with this specific type of phobia are not as likely to inherit that particular phobia. Kendler and Prescott also found similarly low rates for the specific heritability of situational phobias (15%). However, this study did find common genetic factors contributing to all phobias, with the largest contribution for animal (21%) and blood-injection-injury (22%).

Disgust Sensitivity

Disgust sensitivity refers to the propensity for experiencing disgust in a wide variety of settings. This sensitivity has been proposed to contribute to the development of a variety of disorders, particularly blood-injection-injury phobias, animal phobias, and OCD (Olatunji & Deacon, 2008). Individuals with phobias related to spiders frequently report feelings of disgust rather than fear (Davey, 1992). In fact, disgust responses to images of spiders have been shown to be present even when fear is not present (Olatunji, 2006). While little research has examined disgust responses to in vivo spider exposure, the results have shown that people with spider phobias report more disgust than do non-phobic individuals (e.g., Olatunji & Deacon, 2008). There is also some evidence that disgust predicts avoidance of spiders better than does anxiety (Olatunji & Deacon, 2008; Woody, McLean, & Klassen, 2005). There are a few studies suggesting that disgust sensitivity may be related more to concerns about cleanliness and potential for disease rather than concern related to physical harm in the presence of spiders and other small animals and insects (Davey, 1992; Olatunji & Deacon, 2008).

Despite the general conception that disgust sensitivity is a genetically based vulnerability there is little evidence of a genetic component. Correlations in twin studies have shown very small genetic contribution ($r=0.29$ for monozygotic twins and $r=0.24$ for dizygotic twins; Rozin, Haidt, & McCauley, 2000). While a significant relationship exists between parent and child levels of disgust ($r=0.52$; Rozin et al., 2000), there are environmental factors that could be contributing to this relationship other than genetics. Additionally, some researchers have suggested that gender differences in specific phobias may be related to gender differences in disgust sensitivity (Davey, 1994). While early studies in this area have been inconclusive, a recent study (Connolly, Olatunji, & Lohr, 2008) found that disgust sensitivity mediated the association between gender and specific phobias.

Social Phobia

Description

Social phobia is characterized by intense fear or discomfort in social situations. This fear can be limited to one specific situation (e.g., eating in front of others) or it can be generalized to all social settings. Individuals with this type of anxiety fear embarrassment in these situations which often includes fear of being ridiculed, laughed at, or disliked by peers. Individuals often have an overestimated perception of how anxious they appear physically. In children symptoms must persist for at least 6 months and must result in significant interference in the child's social functioning. In addition to these criteria DSM-IV-TR (pp. 416–417) requires that there be:

- A marked and persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others. The individual fears that he or she will act in a way (or show anxiety symptoms) that will be humiliating or embarrassing.
- Exposure to the feared social situation almost invariably provokes anxiety, which may take the form of a situationally bound or situationally predisposed panic attack.
- The feared social or performance situations are avoided or else are endured with intense anxiety or distress.

These symptoms vary slightly from those necessary for an adult diagnosis, according to DSM-IV-TR. Adults additionally are required to see

their symptoms as excessive. In children, these symptoms must be present in social situations involving similarly aged peers and not only around adults. In addition, the child must demonstrate the capacity to engage in age-appropriate social interactions with individuals with whom the child is familiar. The distress and avoidance seen in social settings is often demonstrated in tantrums, crying, clinging to caretakers, and hiding.

Social phobia in children and adolescents is associated with a number of long-term negative outcomes. Children and adolescents with social phobia are at a high risk for developing substance use earlier than their peers and tend to have a shorter interval between first use of substances and problems associated with substance use (Marmorstein, White, Loeber, & Stouthamer-Loeber, 2010). There is some evidence that those who receive treatment for an anxiety disorder in childhood are less likely to have problems with substance use in later adolescence (Kendall, Safford, Flannery-Schroeder, & Webb, 2004). Children with social anxiety are also at a much higher risk for major depression (Last, Perrin, Hersen, & Kazdin, 1992) and educational problems particularly in later adolescence (Kessler, Foster, Saunders, & Stang, 1995).

Epidemiology

The lifetime prevalence of social phobia in an adolescent population has been reported as 1.6% (Essau, Conradt, & Petermann, 1999b). Prevalence rates of social phobia in children in the general population range from 1 to 6% (Verhulst, van der Ende, Ferdinand, & Kasius, 1997). One possible reason for this large range in prevalence rates is the way certain forms of social anxiety are coded by researchers. For example, both school phobia and fear of public speaking could be classified under either social anxiety or specific phobia. Different studies have chosen to categorize these types of fears differently which may contribute to the inconsistent prevalence rates across studies. In a more recent study conducted with 8–13-year-olds in Norway, 2.3% of all children were reported to have significant symptoms of social anxiety (Van Roy, Kristensen, Groholt, & Clench-Aas, 2009). The rates of social phobia among a clinical population have been reported around 15% (Last et al., 1987). As with all anxiety disorders there is a high level of comorbidity in social phobia with one sample reporting that 63% of children with social anxiety had a comorbid anxiety disorder (Last et al., 1987).

Additionally, there is some evidence of sociodemographic differences in the prevalence of social phobia. Inconsistent findings have been reported for gender differences in social phobia. One study of a clinical sample found that boys were more likely to have social anxiety than were girls (Compton, Nelson, & March, 2000), while other studies have found that up to 70% of clinical samples of social phobia are females (Beidel & Turner, 1988). There has been little cross-cultural research or research related to racial background in social phobia. There is some evidence, however, that European American children are more likely to report more symptoms of social anxiety than are African American children in a community sample (Compton et al., 2000) but these findings have not yet been replicated.

Panic Disorder with and Without Agoraphobia

Description

The hallmark symptom of panic disorder is the presence of recurrent and spontaneous panic attacks that cause the individual great anticipatory anxiety. Panic attacks themselves are brief periods of numerous physiological symptoms accompanied by intense fear. For a majority of individuals experiencing panic disorder there is also agoraphobic avoidance – that is, avoidance of situations from which escape might be difficult in the event of a panic attack. Panic disorder was once thought to be a disorder found only in adults and very rarely in adolescents. This notion was based on the idea that there is a strong cognitive component

to panic disorder that children were incapable of experiencing (Nelles & Barlow, 1988). However, there is now a large body of evidence showing that panic disorder does occur in children (e.g., Kearney, Albano, Eisen, Allan, & Barlow, 1997). Despite the evidence showing that it does occur in children (Wittchen et al., 2008), the typical age of onset for panic disorder is late adolescence into adulthood (Kessler et al., 2005). For many individuals with panic disorder the first panic attack occurred during a time of psychosocial stress (Craske, 1999).

Symptoms of Panic

According to DSM-IV (pp. 395) a panic attack is a "discrete period of intense fear or discomfort, in which four (or more) of the following symptoms developed abruptly and reached a peak within 10 minutes (See Table 2.2).

In order for panic attacks to be considered part of panic disorder they must be recurring with persistent concern about having another attack, worry about the implications of the attacks, or a significant behavior change related to having these attacks. In children, making a diagnosis of panic disorder can be challenging as some of the fears may present differently. For example, young children may report a fear of becoming ill without any clear physical symptoms reported.

Table 2.2 DSM-IV-TR symptoms of panic attacks

Palpitations, pounding heart, or accelerated heart rate
Sweating
Trembling or shaking
Sensations of shortness of breath or smothering
Feeling of choking
Chest pain or discomfort
Nausea or abdominal distress
Feeling dizzy, unsteady, lightheaded, or faint
Derealization (feelings of unreality) or depersonalization (feeling detached from oneself)
Fear of losing control or going crazy
Fear of dying
Chills or hot flushes

Note. Adapted from American Psychiatric Association (2000, p. 395)

In older children reports of anxiety about becoming sick are common, as are fears of uncontrollable vomiting. Only in adolescence do individuals tend to start reporting fears related to specific physiological symptoms.

In a study examining the frequency of panic symptoms in children aged 8–17 years, results showed that heart palpitations, nausea, shakiness, dizziness, sweating, headaches, and depersonalization/derealization were the most frequently experienced symptoms (Kearney et al., 1997). The study found no age differences in the frequency of reported panic symptoms. Essau, Conradt, and Petermann (1999a) studied adolescents in an epidemiological study in Germany and found similar results. This sample found that palpitations, shakiness, nausea, chills, and abdominal distress were the most commonly reported symptoms of panic attacks. A third study examining symptom frequency found that depersonalization/derealization is less common in younger children but reported no other significant trends in symptom presentation (Moreau & Follett, 1993).

Agoraphobia

According to the DSM-IV-TR, agoraphobia can occur with or without the presence of panic disorder and is defined by extreme anxiety in situations where escape is difficult or in which help may not be readily available in the event of an emergency. Usually this anxiety leads to avoidance of situations that provoke the anxiety. These situations often include large crowded places, public transportation, going out alone, crossing bridges, and standing in line. Generally in agoraphobia these "situations are either avoided (e.g., travel is restricted) or else endured with marked distress or with anxiety about having a panic attack or panic-like symptoms, or require the presence of a companion" (p. 396). Phobic avoidance may be motivated by unrealistic fears of the *consequences* of having panic symptoms in particular situations where the person feels trapped or far from help.

Agoraphobia is common in children and adolescents with panic disorder and in some cases is also diagnosed in adolescents without the presence of panic attacks (Wittchen, Reed, & Kessler, 1998). In a study of US adolescents, Roberts, Ramsay, and Yun Xing (2007) found a 1-year prevalence rate of 4.5% which was significantly higher than the rates found in adults. In fact, this study found that agoraphobia was the most frequently occurring anxiety disorder in their sample although the prevalence dropped to 1.6% when impairment was required for a diagnosis. Wittchen et al. (2008) used a large community sample of German adolescents to examine the prevalence of agoraphobia in the community. Adolescents with panic disorder or panic attacks were only moderately more likely to develop subsequent agoraphobia, while the majority of adolescents meeting criteria for agoraphobia had never experienced a panic attack.

Table 2.3 DSM-IV-TR diagnostic criteria for separation anxiety disorder

Recurrent excessive distress when separation from home or major attachment figures occurs or is anticipated
Persistent and excessive worry about losing, or about possible harm befalling, major attachment figures
Persistent and excessive worry that an untoward event will lead to separation from a major attachment figure (e.g., getting lost or kidnapped)
Persistent reluctance or refusal to go to school or elsewhere because of fear of separation
Persistently and excessively fearful or reluctant to be alone or without major attachment figure at home or without significant adults in other settings
Persistent reluctance or refusal to go to sleep without being near a major attachment figure or to sleep away from home
Repeated nightmares involving the theme of separation
Repeated complaints of physical symptoms (such as headaches, stomachaches, nausea, or vomiting) when separation from major attachment figures occurs or is anticipated

Note. Adapted from American Psychiatric Association (2000, p. 113)

Separation Anxiety Disorder

Description

SAD is a somewhat unique diagnosis in that it is the only anxiety disorder limited to children and adolescents. Previous versions of the DSM had other childhood anxiety disorders; however, SAD is the only one to have survived the revisions made for DSM-IV. SAD is defined in DSM-IV-TR (p. 113) as: "developmentally inappropriate and excessive anxiety concerning separation from home or from those to whom the individual is attached, as evidenced by three or more of the criteria listed in Table 2.3.

To be considered clinically significant these symptoms must be present for at least 4 weeks and be developmentally inappropriate for the age of the child. Many of these symptoms would be considered developmentally appropriate in children aged 7 months to 6 years (Bernstein & Borchardt, 1991), and thus it is important to consider both age and developmental level when making a diagnostic determination. The underlying fear found in SAD is an exaggerated fear of losing or becoming separated from parents or other primary caregivers. In addition to these fears, many children experience nightmares related to becoming separated from caregivers (Bell-Dolan & Brazeal, 1993).

Symptom differences have been found between ages but not between genders (Francis, Last, & Strauss, 1987). Young children (ages 5–8 years) are most likely to report fears of harm to self or caregivers, nightmares, and school refusal. Children between the ages of 9 and 12 years present with more excessive distress at the time of separation, while adolescents are more likely to experience somatic symptoms and school refusal. Additionally, older children and adolescents are most likely to experience a smaller number of symptoms than younger children.

Epidemiology

While SAD can be present in children of all ages, it is most common in preadolescent age ranges. Typically, the onset is acute and follows a

significant change in the child's life (e.g., start of school, moving, death of a parent or close relative) or developmental changes (Last, 1989). Several studies have shown that SAD follows an intermittent course over time. Children often experience remissions and relapses around times of school holidays, vacations, and life stressors (Hale, Raaijmakers, Muris, van Hoof, & Meeus, 2008). When followed over a period of 4 years, 96% of children initially diagnosed with SAD no longer met diagnostic criteria, the highest recovery rate of any anxiety disorder studied (Last, Perrin, Hersen, & Kazdin, 1996).

Prevalence rates in community samples for SAD ranged from 2.0 to 12.9% (Anderson et al., 1987; Kashani & Orvaschel, 1988). The range in rates may be attributable to the age at which symptoms were assessed. The lower rates of prevalence were in studies examining adolescents, while the higher rates were found in community samples of younger children. Rates among clinical populations are higher, with 33% of a sample of anxious children meeting diagnostic criteria for SAD (Last, Francis, Hersen, Kazdin, & Strauss, 1987). Results of this study also indicated that 41% of the children with a primary diagnosis of SAD had a comorbid anxiety diagnosis of some sort.

A number of sociodemographic variables have been associated with SAD. Most samples examining SAD have been primarily with children of European descent, although this finding may reflect biased sampling rather than true cultural differences (Strauss & Last, 1993). As with most other anxiety disorders, rates of SAD are higher in females than males (Compton et al., 2000); however, a few published reports found no gender differences (Bird, Gould, Yager, Staghezza, & Canino, 1989; Last et al., 1992). Additionally, lower SES and parental education levels have been associated with higher rates of SAD in children (Bird et al., 1989; Last et al., 1987).

Role of Avoidance

In addition to the many fears that children with SAD experience, avoidance plays a large role in the symptom presentation of this disorder. There is a large range of avoidance behaviors common to children with SAD. Types of avoidance may also vary by the age of the child. Milder forms of avoidance can be hesitation to leave the house, requesting that the caregiver be accessible via phone during outings, and frequent questions about schedules. More moderate forms of avoidance in younger children can include clingy behaviors with parents or caregivers. They may also follow the parents or other caregivers around the house to avoid being alone in a room. Older children may be more likely to have difficulty leaving the house without caregivers or refuse to participate in social activities with peers if the caregiver is not present. More serious forms of avoidance can include faking illnesses, school refusal, or refusal to sleep alone at night.

Avoidance behaviors may slowly increase over time. Albano, Chorpita, and Barlow (2003) describe a pattern of increasing avoidance that starts with occasional nightmares and subsequent requests to sleep with parents. From this relatively mild behavior change, the child can become increasingly avoidant until he or she is sleeping with one or both parents every night. Similarly, Livingston, Taylor, and Crawford (1988) describe a pattern of increasingly serious physical complaints on the part of the child. This behavior often progresses from very vague complaints of not feeling well to frequent complaints of stomach or headaches. Frequently it is these avoidance behaviors that will prompt the parent to bring the child in for treatment.

Differential Diagnosis

Developmentally Appropriate Fear vs. Anxiety Disorders

An important diagnostic issue to consider in children is whether the anxiety is developmentally appropriate or is part of a disorder. Anxiety and its various associated physiological symptoms are considered to be basic human emotions (Barlow, 2002). In young children common developmental fears include: fear of the dark, fear of new

situations including the first day of school, fear of separation from parents or other caretakers, and fear of large animals. In adolescents common developmental fears include: anxiety related to job interviews, college applications, and dating.

An important distinction between developmentally appropriate fears and phobias is both the duration and severity of the anxiety. In order for the anxiety to become clinically significant it must persist for a period of at least 6 months and include significant avoidance and interference in daily functioning (Albano, Causey, & Carter, 2001). While this distinction often is based on clinical judgment, there has been research showing that a specific phobia diagnosis can be reliably achieved through the use of structured clinical interviews and standardized self-report measures (Schniering, Hudson, & Rapee, 2000). One common assessment used for the diagnosis of anxiety disorders in children is the Multidimensional Anxiety Scale for Children (MASC; March, Parker, Sullivan, Stallings, & Conners, 1997). This self-report scale is used to differentiate clinical from nonclinical samples as well as distinguish different forms of anxiety. It has been found to be sensitive to the differences in these groups (Dierker et al., 2001). The Anxiety Disorders Interview Schedule for Children (ADIS-C; Silverman & Albano, 1996) is another useful structured interview for diagnosis of anxiety disorders in children.

Distinguishing Between Different Anxiety Disorders

Given the substantial overlap in symptoms across the disorders presented in this chapter, it may be difficult at times to identify which diagnosis a given child's symptom presentation warrants. The task can be all the more challenging in light of children's difficulty at times in reporting clearly what they are experiencing. Even if they are willing to discuss their experiences, at times they have limitations in their vocabulary or their concept formation to fully describe their fears. Accurate diagnosis is important for case conceptualization such that the most appropriate treatment can be administered. For example, a cognitive-behavioral clinician would expose an individual with panic disorder to interoceptive cues (e.g., pounding heart) but would follow a different treatment plan for an individual with SAD. The following section covers common distinctions that must be made in the differential diagnosis of specific phobia, social phobia, panic disorder, and SAD. In most cases the correct diagnosis can be derived by understanding what is at the core of the patient's fears.

Specific phobia vs. social phobia. Of the disorders under consideration, the two that share the most symptom criteria may be the most straightforward to distinguish, based simply on the content of the fears. Specific and social phobia overlap in nearly all of their diagnostic criteria except that social phobia involves a fear of social situations (e.g., talking to a group, answering questions in class), whereas specific phobia involves a fear of other stimuli. In cases where the distinction may be somewhat difficult – for example, fear of clowns – the differential diagnosis is based on whether the fear is primarily social (e.g., being publicly embarrassed by the clown) or involves fear of the stimulus itself (e.g., being attacked by the clown).

Specific phobia vs. panic disorder. Children with specific phobias often will experience many physiological symptoms of panic, and may even develop a panic attack, when confronted with the feared stimuli. The presence of panic attacks is not sufficient to warrant the diagnosis of panic disorder, given that only a small minority of individuals who experience panic attacks go on to develop panic disorder; results from the National Comorbidity Survey Replication revealed a 22.7% lifetime prevalence estimate for panic attacks vs. a 3.7% rate for panic disorder (Kessler et al., 2006). Specific phobia is indicated when the child's fear, including panic attacks, is provoked by the phobic stimulus itself – for example, a dog. The content of the fear in this case would have to do with the possibility of injury as a result of contact with the dog. At the core of panic disorder, on the other hand, is a fear of the panic attacks themselves (the so-called "fear of fear"; e.g., Chambless, Caputo, Bright, & Gallagher, 1984).

Differential diagnosis can be more difficult when the feared stimulus or situation is one that commonly is associated with panic disorder – for example, a fear of elevators. In these cases it is imperative that the diagnosing clinician ascertain whether the patient is afraid of panicking in these situations or simply is afraid of the situations themselves (e.g., fears that the elevator will fall). Finding that the individual fears several situations that provoke panic attacks (e.g., car trips, elevators, crowds) makes a diagnosis of panic disorder more likely than diagnosis of a specific phobia to multiple situations.

Specific phobia vs. SAD. Specific phobia and SAD both may include significant levels of avoidance. The primary distinction between these disorders is based on whether the avoidance is driven by fear of the avoided stimulus, as in specific phobia, or by fear of separation from attachment figures, which defines SAD. Although children with specific phobia may cling to their caregivers when confronted with the phobic stimulus, the clinging behavior represents the child's looking to the caregiver for safety and protection. In contrast, the core fear in SAD is separation from the caregiver in and of itself. For this reason the fear of separation is likely to be more pervasive than in specific phobia in which fear of separation is provoked by the presence of a relatively limited range of stimuli (e.g., dogs).

Social phobia vs. panic disorder. A child who presents with panic attacks and a fear of social situations could be suffering from either panic disorder or social phobia. Both conditions also lead to avoidance of social situations, such as school refusal. It is relatively common in panic disorder for a person to fear embarrassing him/herself in some way by panicking in public. Indeed, the Panic Appraisal Inventory (Telch, *The panic appraisal inventory*. University of Texas, Unpublished manuscript, 1987), which is commonly used to measure panic-related concerns, comprises a subscale of panic consequences that include social concerns. For example, a child may fear that he will panic in school, faint, and have to be carried out of the classroom while the whole class watches. In this case the child is unlikely to fear social situations per se, but rather the possibility of having a panic attack in a social setting. Children with social phobia similarly may fear embarrassing themselves in public due to their anxiety response – for example, that they will shake, trip over their words, or blush. In this case the child will fear the social situation itself, not his possible public panic response.

Social phobia vs. SAD. As with panic disorder, SAD also can resemble social phobia in some respects. For example, school refusal may be driven by social anxiety or by the distress associated with separating from one's caregiver. Careful questioning of the child and, if necessary, the parents may reveal what the underlying fear is. For example, if the child has no trouble socializing with peers when the parents are present but refuses to go to school, sleepovers, and other events where the parents are not present, a diagnosis of SAD is likely. On the other hand, if the child still is terribly afraid of social settings even in the presence of the parents, the accurate diagnosis likely is social phobia.

Panic disorder vs. SAD. The final differential diagnosis, between panic disorder and SAD, can be one of the more difficult distinctions to make. In fact, there is strong evidence that SAD is a risk factor for panic disorder (for a review see Silove, Manicavasagar, Curtis, & Blaszczynski, 1996). Both disorders may include clinging to "safe" persons, often the parents. Once again, making the right diagnosis depends on identifying the child's specific fear. In panic disorder, the strong desire to be close to a safe person is driven by fears related to panic – for example, the agoraphobic's concern that she will have a panic attack when help is not available. In this case the safe person provides a sense of comfort in the face of a potential panic attack, similar to the function of having a bottle of benzodiazepines always nearby. With SAD, the fear is related to separation from the caregiver in its own right. Unwanted separation from the caregiver may trigger a bout of anxiety that leads to a panic attack, but the root of the anxiety is the separation and not the panic symptoms.

Diagnostic Reliability

In light of the often difficult differential diagnosis of the disorders described in this chapter, it is imperative that these diagnoses can be made reliably. Our current diagnostic system was adopted in an attempt to increase the reliability of diagnosis across clinicians. Attempts to determine diagnostic reliability often rely on test–retest or interrater reliability approaches. Studies on criteria for panic disorder and specific phobia have shown that the test–retest reliability is between good and excellent (Williams et al., 1992) on the established ranges for reliability (Di Nardo, Moras, Barlow, Rapee, & Brown, 1993). Interrater reliability for these disorders is also in the excellent range (Brown, Di Nardo, Lehman, & Campbell, 2001). The reliability of diagnosis specifically in children has also been found to be good when using structured diagnostic interviews (Schniering et al., 2000). This high level of reliability has improved the ease of communication between mental health professionals about a given patient's clinical status.

While there are positive aspects of the current diagnostic system, there also are significant limitations of the way that disorders are defined. First, many diagnoses contain words like "persistent," "clinically significant," and "excessive" without defining the threshold for such criteria. This vagueness can lead to disagreement across clinicians. With respect to children specifically, the current DSM does not address developmental norms that can be expected across ages. It also does not address how specific disorders may present themselves differently in different age groups. Therefore, the clinician often must make a judgment call as to whether a particular behavior falls outside the realm of developmentally appropriate behavior in a child, creating a lack of reliability in diagnosis. By improving this definition, a clearer threshold would be established that would ideally incorporate developmental norms for diagnosis in children. A clearer definition of this threshold would dramatically improve diagnostic reliability as much of the lack of diagnostic agreement in this area is caused by differing definitions of what is "developmentally appropriate" (Albano et al., 2003).

Second, diagnosis could be improved by increasing the reliability of subtypes of specific phobias. There is significant co-occurrence of multiple subtypes in individuals diagnosed with specific phobias and a lack of empirical support for the current subtypes. Blood-injection-injury phobias seem to have both different physiological responses and psychometric properties and likely represent a clear subtype. However, the other subtypes do not seem to have the same psychometric differentiation. As with social phobia, it may make sense to refer to specific phobias in terms of simple type (one specific phobia), and generalized type (more than one specific phobia) (Piqueras, Olivares, & López-Pina, 2008).

Third, symptoms of panic disorder should more clearly be differentiated by age range. There is evidence that children of different ages report different types and numbers of symptoms. This developmental variability needs to be reflected in the diagnostic criteria for children. There may also be a need for the addition of several symptoms currently missing from the diagnostic criteria for children.

Finally, there have been criticisms of the validity of the current diagnostic categories. There is high comorbidity of the current diagnostic criteria which often results in multiple diagnoses, although it is unclear whether the current disorders represent distinct entities. One proposed option is for a quantitative hierarchical model for diagnosis (Watson, 2005). Under this model, diagnoses are categorized by empirically supported phenotypic and genotypic similarities. This system would decrease the overlap of diagnosis and aim to increase the validity of the diagnostic system while maintaining reliability.

Summary

Anxiety disorders, including specific phobia, social phobia, panic disorder, and SAD, are common in children. Correct diagnostic assignment requires an understanding of the core fears in each of these

disorders and the various ways that children may manifest these fears. In specific phobia and social phobia, anxiety is provoked by confronting the feared stimulus. Panic disorder is defined by fear of having panic attacks and of what their implications might be, whereas SAD is driven by fear of being separated from one's parents or other attachment figures. While the current diagnostic system represents an improvement over previous versions of the DSM, changes in several areas of the system could lead to more reliable diagnosis and clearer differentiation between anxiety disorders.

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3 Issues in Differential Diagnosis: Considering Generalized Anxiety Disorder, Obsessive-Compulsive Disorder, and Posttraumatic Stress Disorder

Jeremy Cohen, Matthew Mychailyszyn, Cara Settipani, Sarah Crawley, and Philip C. Kendall

An accurate diagnosis provides a foundation for case conceptualization and facilitates effective treatment practices. Accurate diagnoses are also critical to the organization of participants in empirical research. Although not without its own problems, the *Diagnostic and Statistical Manual of Mental Disorders – Text Revision* (DSM-IV-TR), currently in its fourth iteration (American Psychiatric Association, 2000), is the most frequently used taxonomic system for organizing psychological disorders. Within this framework, disorders are presented as categories (discrete entities) characterized by specific criteria. However, one of the shortcomings associated with a categorical approach is the existence of considerable overlap in symptomatology among disorders. Moreover, comorbidity is common and, among youth with anxiety disorders, it is the norm (Kendall, Brady, & Verduin, 2001). For example, Curry, March, and Hervey (2004) found that 30–65% of children who met criteria for an anxiety disorder also met criteria for an additional disorder. Differential diagnosis among disorders (i.e., the anxiety disorders) poses challenges to both researchers and clinicians.

The diagnostic assessment of children and adolescents carries with it additional considerations not present when working with adults. First, *DSM-IV-TR* identifies some developmental differences in diagnostic criteria. Consider criteria for diagnosing OCD, for example: children are not required to recognize that obsessions or compulsions are unreasonable to obtain an OCD diagnosis. Thus, features that may serve to differentiate disorders among adults may not apply to youth. In addition, both children and parents typically provide information about the presenting problem. However, the agreement between parent and child reports of anxiety disorders is usually quite limited (Choudhury, Pimentel, & Kendall, 2003). Clinicians can resolve this discrepancy by assigning a diagnosis if the child meets criteria by either the child's report or the parents' report. Nevertheless, the reasons underlying parent–child discrepancies may be important to diagnosis, case conceptualization, and treatment and should not be overlooked (De Los Reyes & Kazdin, 2005). For example, differences may be contingent upon the observability of the symptoms being reported (Comer & Kendall, 2004). Given the limited number of studies specific to issues of differential diagnosis among youth, the present discussion draws upon findings from the adult literature when necessary. However, it is clear that further research is needed before conclusions can be drawn regarding differential diagnosis among youth.

This chapter addresses issues of differential diagnosis pertaining to generalized anxiety disorder (GAD), obsessive-compulsive disorder (OCD), and posttraumatic stress disorder (PTSD), with an

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_3,

emphasis on the potential diagnostic confusions among these three disorders. As is often the case among psychological disorders, GAD, OCD, and PTSD share similar symptom features. Perhaps most prominent, all three disorders are characterized by the presence of intrusive, repetitive cognition that causes distress. Among adults and children, it can be difficult to delineate the boundaries between these diagnoses. For example, a child may report that she frequently experiences thoughts of her mother in a car crash. This presentation could suggest worry regarding the safety of family members, obsessional thinking, or flashbacks of an earlier trauma, corresponding to GAD, OCD, and PTSD, respectively. Further examination is necessary to accurately assess the nature of the presenting problem.

This chapter will first provide a description of the essential diagnostic features of GAD, OCD, and PTSD in youth along with a brief overview of epidemiological findings. The chapter then examines areas of diagnostic overlap and confusion. These domains are organized into five categories of symptoms: (1) fear/anxiety, (2) recurrent thoughts, (3) intrusive images, (4) physical symptoms, and (5) avoidance. These symptom domains are present in nearly every anxiety disorder. However, these domains can help distinguish anxiety disorders from other disorders and may facilitate differential diagnosis. Given the high rate of comorbidity, symptom overlap, and heterogeneity within diagnostic categories, a nuanced examination of youths' symptomatology within each domain will help our understanding. Last, this chapter will discuss current research findings in terms of their diagnostic implications.

Essential Features of GAD, OCD, and PTSD

Generalized Anxiety Disorder

The hallmark of GAD is the presence of excessive, uncontrollable, and persistent worry about a number of events or activities, more days than not for at least 6 months (American Psychiatric Association, 2000). Worry has been defined as "a chain of thoughts and images, negatively affect-laden and relatively uncontrollable" (Borkovec, Robinson, Pruzinsky, & DePree, 1983, p. 10). For youth, these worries frequently concern health, school, and personal harm (Silverman, La Greca, & Wasserstein, 1995) and must be associated with at least one physiological symptom (i.e., feeling keyed up or on edge; being easily fatigued; difficulty concentrating or mind going blank; irritability; muscle tension; or sleep disturbance). In addition, the worry or physical symptoms must cause distress or impairment in important areas of functioning, which for youth often include school/academics, peer relationships (i.e., Verduin & Kendall, 2008), and family/home life.

Critical to differential diagnosis, the focus of the anxiety and worry present in GAD cannot be better accounted for by features of another Axis I disorder. For example, if the excessive and interfering worry is only about peer evaluation, Social Anxiety Disorder may be more apt than GAD. In addition, the symptoms of GAD cannot occur solely during the course of a Mood Disorder, a Psychotic Disorder, or a Pervasive Developmental Disorder and the disturbance must not be attributable to the effects of a substance or a general medical condition.

GAD is associated with an earlier age of onset than most other anxiety disorders, occurring between childhood and mid-adolescence (Brown, Barlow, & Liebowitz, 1994; Kendall, Hedtke, & Aschenbrand, 2006; Rapee, 1991). However, the age of onset for GAD may be difficult to determine as most individuals report an insidious development of chronic worry as opposed to a sudden onset (Rapee, 2001). A modest increase in GAD in middle adolescence has been observed (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003), and the likelihood of receiving a diagnosis of GAD has been found to increase with age (Carter, Wittchen, Pfister, & Kessler, 2001). The gender ratio for GAD is approximately 2:1 in favor of females in adult samples (Wittchen, Zhao, Kessler, & Eaves, 1994); the opposite ratio may hold among children (Anderson, Williams, McGee, & Silva, 1987; McGee et al., 1990).

Obsessive-Compulsive Disorder

OCD is characterized by the presence of obsessions or compulsions. Most individuals with OCD experience both obsessions and compulsions, and the presence of pure obsessions is uncommon (Foa et al., 1995). Obsessions are defined as recurrent and persistent thoughts, impulses, or images that are intrusive, inappropriate, and experienced as distressing (American Psychiatric Association, 2000). The most common obsessions among clinic-referred youth involve themes of contamination, harm or death, and symmetry (Hanna, 1995). Children with OCD often try to ignore, hold back, or neutralize obsessive thoughts and related feelings with some other thought or by performing compulsions. Compulsions are repetitive, intentional behaviors performed to reduce anxiety or distress and are often performed stereotypically or according to rigid rules. Unlike adults, children do not have to recognize that the obsessions or compulsions are excessive or unreasonable. Given the presence of intrusive thoughts and images in the general population, symptoms must be distressing, time-consuming (lasting for more than 1 h per day), or interfering with academic functioning, social activities, or relationships to warrant a diagnosis of OCD.

Regarding differential diagnosis, *DSM-IV* specifies that obsessions are not simply excessive worries about real-life problems. Moreover, the obsessions and compulsions cannot fall within the circumscribed content domains of other disorders. For example, obsessions related to one's own appearance may better fall under the diagnosis of Body Dysmorphic Disorder. Likewise, hair pulling may be better accounted for by a diagnosis of Trichotillomania in the absence of other compulsive behavior. As with other disorders, the disturbance cannot be due to the direct physiological effects of a substance or a general medical condition.

Similar to GAD, OCD likely develops between childhood and mid-adolescence, with the average age of onset falling between 7.5 and 12.5 years (Geller et al., 1998). Several epidemiologic studies conducted in adolescent populations in the United States and elsewhere report prevalence rates ranging from approximately 2 to 4% of the pediatric population (Geller, 2006). Among clinic-referred youth, the lifetime prevalence rate is approximately 15% (Last, Perrin, Hersen, & Kazdin, 1992). About twice as many females as males have OCD in adult samples (Rasmussen & Tsuang, 1986). The gender ratio is not as clear in children: Some data suggest that OCD is more common in boys (Geller et al., 1998; Zohar et al., 1997), whereas other data indicate no difference in sex distribution (Chabane et al., 2005).

Posttraumatic Stress Disorder

PTSD is characterized by a constellation of symptoms that develop in response to a trauma in which the individual experienced or witnessed an event involving actual or threatened death, serious injury or threat to the physical integrity of self or others (American Psychiatric Association, 2000). Furthermore, the individual's response must have been characterized by intense fear, helplessness, or horror, which in youth may be expressed by disorganized or agitated behavior. It is very important to note that not all youth who experience trauma develop PTSD, and there is evidence to suggest that age, gender, and environmental factors may all play a role in differential outcomes (e.g., Bokszczanin, 2007, 2008; McNally, 1993). To meet criteria for PTSD, the traumatic event has to be persistently re-experienced (i.e., recurrent and intrusive distressing recollections of the event, which in young children may be expressed by repetitive play involving themes of the trauma). In addition, there must be three symptoms of persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness not present before the trauma (i.e., avoidance of activities, places, or people associated with the trauma; restricted range of affect). Furthermore, there must be at least two persistent symptoms of increased arousal (i.e., hypervigilance). The disturbance must last for longer than 1 month and cause meaningful distress or impairment in important areas of functioning.

A history of adverse or traumatic events can be present in individuals with diagnoses other than PTSD. In fact, the stress associated with traumatic events may serve as a catalyst for the manifestation of an underlying vulnerability, as described in the diathesis-stress model. Thus, the presence of a traumatic event is necessary but not sufficient for a diagnosis of PTSD. Additional considerations of differential diagnosis for PTSD in adults, specifically combat veterans, have been presented by Schillaci et al. (2009). The authors emphasized the centrality of the connection between PTSD symptomatology and trauma-related themes and stimuli. Moreover, differential diagnosis was informed by the timing of symptom onset. As noted in *DSM-IV*, symptoms of avoidance, numbing, and hyperarousal associated with PTSD cannot be present before the trauma. Based on this framework, symptoms of PTSD were distinguished from psychotic hallucination, agoraphobia, specific phobia, and depression. Of course, the presence of PTSD does not exclude the presence of other disorders, as evidenced by the high comorbidity rates of individuals diagnosed with PTSD (Brady, 1997).

Surveys of adolescents in community samples have found a 3–6% prevalence rate for PTSD (Cuffe et al., 1998; Reinherz, Giaconia, Lefkowitz, Pakiz, & Frost, 1993). A large-scale survey of PTSD in children aged 2–5 revealed a much lower prevalence rate of 0.1% (Lavigne et al., 1996). Some researchers contend that the diagnosis of PTSD in younger children may not be optimally represented by the current DSM diagnostic criteria. These critics suggest that a modified algorithm for assessing PTSD that involves reducing the number of necessary avoidance symptoms and removing the requirement of emotional response at the time of the trauma may be optimal for identifying PTSD in the 2–5 year old group (Meiser-Stedman, Smith, Glucksman, Yule, & Dalgleish, 2008). Interestingly, the modified algorithm did not offer an advantage over *DSM-IV* criteria when both parent and child reports were available for children 7–10 years of age.

Domains of Symptom Overlap

Fear/Anxiety

All anxiety disorders are characterized by the presence of fear or apprehension in some form. The presence of fear/anxiety can help differentiate anxiety disorders from other psychopathology, such as mood disorders. This domain can include fear of specific stimuli, situations, or feelings. Fear of specific stimuli is characteristic of OCD and among the possible symptoms of the disorder. It may also be present in GAD and PTSD, but it is not explicitly included as a symptom of the disorders. Likewise, fear of a specific situation (e.g., riding the bus) may be present in GAD, OCD, and PTSD, requiring a more specific understanding of the fear. For example, a child with GAD may fear that the bus will get lost or will cause him to be late, whereas a child with OCD may fear that every time the bus hits a bump it is running over a person; a child with PTSD may have previously been in a bus accident.

Fear of fear (e.g., Goldstein & Chambless, 1978), frequently referred to as anxiety sensitivity, is often thought of as the signature feature of panic disorder, but it may also be present in GAD (Cox, Fuentes, Borger, & Taylor, 2001) and PTSD (Taylor, Koch, & McNally, 1992). Individuals with heightened anxiety sensitivity evidence a fear of physiological symptoms of anxiety due to the belief that those sensations are deleterious to their physical, psychological, and/or social well-being (Reiss & McNally, 1985). In GAD, anxiety sensitivity has been associated with worry regarding uncertainty (Floyd, Garfield, & LaSota, 2005). Regarding PTSD, anxiety sensitivity has been thought to be a vulnerability and maintenance factor (Elwood, Hahn, Olatunji, & Williams, 2009) and has been implicated as such in children and adolescents (e.g., Kiliç, Kiliç, & Yilmaz, 2008). Research is needed to better inform diagnosticians about how anxiety sensitivity and its features (i.e., physical, psychological, and social concerns) differentially relate to anxiety disorders in youth.

Intolerance of uncertainty (IU) has been defined as "the tendency to react negatively on an emotional, cognitive, and behavioral level to uncertain situations and events" (Dugas, Buhr, & Ladouceur, 2004, p. 143). Research has demonstrated a strong relationship between OCD and IU (Sica et al., 2004; Steketee, Frost, & Cohen, 1998), although this may only hold for individuals with pathological self-doubt and checking behavior (Tolin, Abramowitz, Brigidi, & Foa, 2003). IU has also been associated with the severity of GAD in adults (Dugas et al., 2007) and the pathological worry characteristic of GAD (e.g., Ladouceur, Gosselin, & Dugas, 2000). Although IU does not appear to differentiate between OCD and GAD, it may be useful in distinguishing the two disorders from other diagnoses. Investigators have only begun to examine IU in youth. A measure of IU has been found to differentiate youth with anxiety disorders from non-referred community youth (Comer et al., 2009). Further research is needed to examine the utility of IU in youth for differentiating among the anxiety disorders.

Recurrent Thoughts

The fact that there is a similar presentation of recurrent, intrusive thoughts among GAD, OCD, and PTSD (and other psychopathology) is perhaps one of the most challenging aspects of differential diagnosis. Research and theoretical discussions have emphasized the similarities of intrusive cognition for youth with GAD and OCD (Comer, Kendall, Franklin, Hudson, & Pimentel, 2004) and youth with OCD and PTSD (Huppert et al., 2005). The lion's share of the discussion has focused on adults, but nevertheless has some applicability with youth.

Turner, Beidel, and Stanley (1992) suggested that there were five primary similarities between adult worries and obsessions: (1) both are present in clinical and nonclinical populations, (2) the form and content of both phenomena are similar in clinical and nonclinical populations, (3) both are experienced as more frequent and uncontrollable in clinical populations than nonclinical populations, (4) both are associated with negative mood and attentional biases, and (5) both have a vulnerability factor that distinguishes clinical and nonclinical populations. Given the overlap, some have suggested that obsession and worry may coexist on a single continuum (Langlois, Freeston, & Ladouceur, 2000b). Huppert et al. (2005) demonstrated that items on rating scales, such as "unpleasant thoughts come into my mind against my will and I cannot get rid of them," and "I find it difficult to control my own thoughts" are characteristic of both OCD and PTSD. It is not surprising, and it is understandable, that clinicians and researchers find it difficult to capture the exact nature of an adult's or child's cognitive intrusions. This effort may be further complicated by the social context of threat that emerge during times of terrorism (Comer & Kendall, 2007)

Obsessions and worry are also often frequently conflated with rumination. Rumination, with reference to its role in depression, has been defined as "repetitively focusing on the fact that one is depressed; on one's symptoms of depression; and on the causes, meanings and consequences of depressive symptoms" (Nolen-Hoeksema, 1991). Other definitions of rumination have emphasized the negative inferences made regarding past stressful events (Alloy et al., 2000). Worry may be differentiated from rumination in temporal orientation, such that worry is more future-oriented, whereas rumination is past-oriented (Papageorgiou & Wells, 1999). These distinctions between worry and rumination have been replicated in adolescent samples (e.g., Hong, 2007; Muris, Roelofs, Meesters, & Boomsma, 2004). Confusing matters, however, worry is often present in the context of depression (Starcevic, 1995) and rumination in the context of anxiety (Nolen-Hoeksema, 2000). Additionally confusing, features of rumination may play etiological and maintenance roles in anxiety. For example, the compulsion to ruminate and repeatedly ask questions such as "why" and "what if" have been associated with the onset and maintenance of PTSD (Michael, Halligan, Clark, & Ehlers, 2007).

Although there is a meaningful overlap among the various forms of recurrent thoughts, some

cognitive features may help to differentiate between them. One distinction is the content of recurrent thought. As described by *DSM-IV*, worries characteristic of GAD consist of "everyday matters," such as health, relationships, school, and finances. In contrast, obsessions tend to be more irrational and bizarre (Turner et al., 1992; Wells & Morrison, 1994). The content of obsessions tend to fall into more circumscribed areas, including dirt/contamination, sex, aggression, self-doubt, and order. Children's worries seem to be more logical, whereas obsessions have an illogical (disconnected) quality (Comer et al., 2004). The content of recurrent thoughts present in PTSD is typically associated with re-experiencing the trauma. However, such cognition is not limited to the recollection of the trauma per se and may also include themes of danger, negative self-schema, and evaluation of the meaning of the trauma (De Silva & Marks, 1999).

Distinctions have also been made regarding the evaluation of the thought content. In particular, content of obsessions tend to be experienced as contradictory to one's own beliefs and values, whereas worries tend to be experienced as consistent (Langlois, Freeston, & Ladouceur, 2000a; Langlois et al., 2000b; Turner et al., 1992). Given the contradictory nature of some obsessions, they may be accompanied by feelings of responsibility for having the thoughts (Langlois et al., 2000a; Salkovskis, 1985). However, this distinction may vary by the content area of the obsessions (Wells & Papageorgiou, 1998).

The presence or absence of identifiable triggers may help to distinguish between different forms of recurrent thought; although as with other phenomena should not be considered in isolation. Studies have demonstrated that adults with intrusive worries are more aware of specific external or internal precipitants of the recurrent thoughts as compared to adults with intrusive obsessions (Langlois et al., 2000a; Turner et al., 1992). A key feature of PTSD is the psychological and physiological distress in response to triggers associated with the trauma, which are often avoided. However, individuals with PTSD are frequently unaware of the triggers that give rise to intrusive memories (Ehlers, Hackmann, & Michael, 2004). These triggers may only be loosely associated with the trauma and may not be directly meaningful to the individual.

Thought-action fusion is a meta-cognitive construct that may help differentiate between OCD and other disorders. This construct consists of (1) believing that the presence of a thought increases the probability of an event actually occurring and (2) that the presence of a thought that is inconsistent with one's beliefs is equivalent to actually carrying out the thought (Shafran, Thordarson, & Rachman, 1996). Higher thought-action fusion was found in adults with obsessive thinking than in adults with pathological worry (Coles, Mennin, & Heimberg, 2001). It has also been suggested that thought-action fusion may play an etiological and maintaining role in additional disorders, such as GAD, depression, and certain psychotic disorders (Starcevic & Berle, 2006), although research is needed, particularly with youth, regarding this assertion. Attention should be paid to the interaction between thought content and meta-cognitive processes. The presence and quality of recurrent thoughts should be considered within the full constellation of symptoms.

Intrusive Images

The symptom presentation of both OCD and PTSD may include intrusive images. Intrusive images associated with PTSD are related to the initial trauma and are frequently fragmented sensory memories (Ehlers et al., 2004). Although images in OCD are typically characterized as bizarre or irrational in nature, it is important to note that individuals with OCD can also experience intrusive images associated with a prior adverse event (De Silva & Marks, 2001; Lipinski & Pope, 1994; Speckens, Hackmann, Ehlers, & Cuthbert, 2007). Regarding the distinction between OCD and GAD, studies have found that obsessions more frequently occur in the form of intrusive images than do worries (e.g., Turner et al., 1992). Pathological worry typically takes the form of verbal cognition rather than visual images and has been described as a "chain of

thoughts" (Borkovec et al., 1983). In contrast, intrusive images are characterized as brief mental flashes that are shorter in duration (Langlois et al., 2000a).

Physical Symptoms

Somatic symptoms are commonly experienced by children with anxiety disorders and have been associated with anxiety severity and impairment (Ginsburg, Riddle, & Davies, 2006; Storch, Merlo, et al., 2008). Indeed, for children to meet criteria for a diagnosis of GAD they must exhibit at least one physical symptom associated with worry. Similarly, to meet criteria for a diagnosis of PTSD individuals must exhibit at least two symptoms of increased arousal. Children with anxiety frequently report headaches, stomachaches, muscle tension, sweating, and jittery feelings (e.g., Eisen & Engler, 1995; Last, 1991). In a study of somatic complaints across anxiety disorders in children, based on primary diagnosis, 56% of those with GAD, 44% of those with OCD, and 25% of those with PTSD reported somatic symptoms (Last, 1991).

The substantial overlap among the physical symptoms associated with the various anxiety disorders in youth makes it difficult to determine a diagnosis based on this factor alone. Hofflich, Hughes, and Kendall (2006) found that children with GAD, social phobia, and separation anxiety disorder did not differ in the frequency with which they reported somatic symptoms or with regards to the presence of any specific somatic symptom. Interestingly, children with a principal diagnosis of GAD reported a wider variety of physical symptoms than those listed in *DSM-IV-TR*, including feeling shaky and jittery, having chest pain, feeling strange, weird or unreal, heart racing or skipping beats, and feeling sick to their stomach. Given the lack of significant group differences across anxiety disorders in this study, these somatic complaints may not be specific to GAD. The number of somatic complaints reported by children with GAD has been shown to increase with age, suggesting that children may be better able to identify their physiological symptoms associated with anxiety as they mature (Choudhury et al., 2003).

Although evidence of somatic complaints is not required for a diagnosis of OCD, physical symptoms are common among youth with the disorder. The most frequently experienced physical symptoms include tension and restlessness (Storch, Merlo, et al., 2008). Storch, Murphy, et al. (2008) found that sleep-related difficulties were associated with anxiety severity in children with OCD and may be relatively common among these youth. Children with OCD and hoarding symptoms have been found to exhibit higher levels of somatic complaints relative to non-hoarders with OCD, suggesting that physical symptoms may vary within OCD (Storch et al., 2007). The role of physical symptoms in OCD is particularly nuanced as somatic concerns also characterize the nature of some children's obsessions and/or compulsions (Ivarsson & Valderhaug, 2006). Thus, it may be difficult to differentiate between a child's actual experience of somatic complaints and preoccupation with such concerns. Gathering detailed information regarding children's true physical symptoms, beliefs about bodily sensations, and mental/behavioral responses may aid clinicians in distinguishing OCD from other anxiety disorders.

Somatic symptoms appear to be a common reaction to trauma in children (Bailey et al., 2005; Escobar, Canino, Rubio-Stipec, & Bravo, 1992; Gobble, Swenny, & Fishbein, 2004) and warrant specific attention as they are associated with negative social, emotional, and academic outcomes (Campo, Jansen-McWilliams, Comer, & Kelleher, 1999). A study of PTSD symptoms among children in the New Orleans area following Hurricane Katrina found headaches, nausea, and upset stomach to be the most commonly reported somatic symptoms (Hensley & Varela, 2008). Consistent with the earlier discussion of anxiety sensitivity in PTSD, children in the study with high anxiety sensitivity and high trait anxiety may have had a higher risk of developing PTSD and somatic symptoms following exposure to the traumatic event. Knowing whether children possess these characteristics may help identify youth who are most likely to develop trauma reactions, which can in turn aid with diagnosis and intervention.

Garnering information about the situations that typically surround the onset of physical symptoms is likely to be more useful in determining a diagnosis than solely assessing the presence of a particular somatic complaint. If physical symptoms are the primary presenting problem, it is necessary to carefully analyze the context in which these symptoms occur. When a child reports a physical symptom it can merit parental attention – more attention than would be assigned if the child only felt emotionally unsettled. Indeed, the functional impact of a child's reporting physical complaints (stay home from school, receive care) may unwittingly buttress such reports.

Avoidance

Avoidance is central to the disorders under discussion, but avoidance is not unique to GAD, OCD, and PTSD. Avoidance, a hallmark of anxiety, is characteristic of the anxiety disorders generally, and may be present in other forms of psychopathology. Individuals with an anxiety disorder tend to avoid an event, outcome, or thought which is greatly feared. Avoidance is the mechanism by which individuals minimize or obviate the potential for a negative outcome. It is important to determine the details of the avoidance: (1) what is actually being avoided (e.g., an object, a situation, a thought)? (2) what is the function of the avoidance? (3) when does the avoidance take place? and (4) what, if any, circumstances facilitate coping? Answers to these questions inform an accurate diagnosis and effective treatment.

Research suggests that in GAD, worry *itself* may be the vehicle of avoidance. The process of worry has been defined as an attempt at problem-solving to prevent the occurrence of negative outcomes (Borkovec et al., 1983). Evidence has shown that worry serves an avoidant function by suppressing the body's somatic anxiety response and thus diminishing the corresponding experiential discomfort (Borkovec & Hu, 1990; Borkovec, Lyonfields, Wiser, & Deihl, 1993). Finally, worry has been found to act as a method of distraction used by anxious individuals to avoid thinking about even more emotionally distressing issues than those at the center of the worry (Borkovec & Roemer, 1995). Overall, the evidence supports the "avoidance theory of worry" (Borkovec, Alcaine, & Behar, 2004), suggesting that a primary function of worry in GAD is to enable individuals to avoid negative outcomes, negative bodily feelings, as well as other even more distressing thoughts. Of interest, this notion has applicability to the parents of anxious youth (Tiwari et al., 2008).

Individuals with OCD engage in a wide range of compulsions that are meant to deactivate and avoid threatening outcomes. According to Salkovskis (1985, 1989), this behavior stems from a person's faulty belief that they have control over whether such outcomes will occur (recall thought-action fusion). The implied responsibility that comes with this way of thinking translates into a pattern of behavioral neutralizing responses which reflect attempts to escape or avoid the feared outcome (Salkovskis, 1996). These avoidance-focused efforts include compulsions that are consistent with the associated fear (i.e., repetitive hand washing to avoid catching germs) as well as those that lack a rational connection (i.e., touching objects in a symmetrical fashion to prevent harm from befalling a loved one). Additionally, internal avoidance may be present in the form of mental rituals such as repetitively thinking about a word or phrase until the interfering discomfort has been alleviated. There has been limited discussion in the literature regarding the differences in frequency, quality, and function of covert compulsive behaviors versus pathological worry, and it is not yet possible to draw any firm conclusions (see Comer et al., 2004). Cognitive processes present in adults with OCD that have been linked to compulsions, such as appraisals of responsibility, have been found to exist in children with OCD as well. However, many of these processes were not found to distinguish between youth with OCD and youth with other anxiety disorders (Barrett & Healy, 2003). Such findings provide further evidence of the considerable diagnostic overlap between disorders.

Youth with PTSD are likely to engage in avoidance with the express purpose of distancing themselves from stimuli associated with the trauma.

During a traumatic event, an association is formed with corresponding contextual cues which then come to signal the presence of danger. This association leads youth to try and stay away from places, people, and activities that trigger painful memories. In addition to being directed at external triggers, avoidance in PTSD can also be directed at internal experiences. Youth with PTSD will often make a concerted effort to avoid thoughts and feelings that might remind them of the immense distress they previously experienced. Within the adult literature, clinical cases of PTSD have been described in which individuals manifest cognitive compulsions such as coming up with "'good thoughts' to cancel out the images of a dying friend" (De Silva & Marks, 2001, p. 173). These compulsive urges can strictly occur within the context of PTSD and are not necessarily indicative of a comorbid diagnosis of OCD. However, the presence of such symptoms warrants comprehensive assessment to rule out the presence of OCD.

Implications

The essential features of GAD, OCD, and PTSD, as currently defined by *DSM-IV*, have been considered, as has the substantial degree of commonality between the disorders that makes differential diagnosis difficult. Consideration of this issue begs the question of whether the disorders under examination truly reflect distinct entities, each with their own unique etiology and underpinnings, or whether anxiety is better conceptualized as a unified construct with varying manifestations. Speaking to this question, symptoms of anxiety are typically not specific to one particular disorder. Treatment strategies that emerge from a cognitive-behavioral framework (Kendall, 2006), though applied with some variations for the specific disorders, are similar and consistent and have been found to be effective for several of the anxiety disorders in youth (see Ollendick & King, 1998). Additionally, there is evidence that the genes for anxiety disorders may be shared, as opposed to distinct (Hudson & Rapee, 2004) and that similar changes in the brain occur in several anxiety disorders (see Sinha, Mohlman, & Gorman, 2004). As advances in the fields of genetics and neuropsychology continue to provide findings, a reconceptualization of anxiety may be warranted. This conceptualization has important implications for how anxiety disorders are understood, studied, and treated.

Overall, anxiety may be better viewed as a dimensional, rather than a categorical construct. For example, it may be difficult to distinguish between developmentally appropriate anxiety and pathological anxiety (Costello & Angold, 1995; Pine, 1997). Although one or two symptoms may distinguish between persons with or without a diagnosis according to *DSM-IV* classification, in actuality these individuals may look quite similar to their nondiagnosed counterparts. Since the inception of *DSM*, the number of childhood diagnoses has expanded quite rapidly and additional diagnoses are continually being suggested (Silk, Nath, Siegel, & Kendall, 2000). However, before the field incorporates new diagnostic categorizations, bigger and overarching issues surrounding classification – categorical or dimensional approaches (Drabick, 2009; Maser et al., 2009), should be addressed (see also Jensen, Hoagwood, & Zitner, 2006). A refinement of our classification scheme, reflecting the empirical research, will likely facilitate better understanding and care for youth with anxiety and its disorders.

As the current classification system stands, diagnostic categorization can serve both to facilitate and hinder accurate assessment and effective treatment. That is, categorical distinctions help organize constellations of symptoms and participants into cohesive groups, and these distinctions can provide a framework for identifying commonalities among individuals with similar problems. On the other hand, given the symptom overlap among diagnostic categories and the heterogeneity within diagnostic categories, disorder-level distinctions may obscure fundamental characteristics of the psychopathology present at the symptom-level. The present discussion of such issues as they relate to GAD, OCD, and PTSD emphasizes the importance of exploring the form, function, quality, and associated features of symptoms within their context.

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Part II

Diagnostic Components in Child/ Adolescent Anxiety Disorders

Cognitive Behavioral Models of Phobias and Pervasive Anxiety

4

Brian Pilecki and Dean McKay

Over the last several decades, the expansion of cognitive behavioral models of anxiety disorders has led to improvements in therapeutic interventions and treatment outcomes. Behavioral models are dependent on learning processes and conditioning potentials (such as the nonassociative account; Menzies & Clarke, 1995). Further, contemporary learning theories suggest that anxiety serves as a conditioned response, as well as an unconditioned response, leading to future conditioning for anxiolytic stimuli (Bouton, Mineka, & Barlow, 2001).

There are two major perspectives that inform a purely cognitive perspective on anxiety disorders. On the one hand, cognitive therapy-based models have emerged that posit two central dimensions of anxiety which include an overestimation of danger, threat, and fear, as well as an underestimation of one's abilities to cope with such threats (Beck, Emery, & Greenberg, 1985). On the other hand, an extensive literature describes cognitive biases based on automatic processing of environmental stimuli (Williams, Watts, MacLeod, & Mathews, 1997). The former perspective is predicated on the ability of individuals to articulate cognitive errors that occur in response to specific events, while the latter is not reliant on client report, but instead on reaction time and biases evident for subtle cues related to anxiety (Matthews & MacIntosh, 1998). Recent literature supports the findings related to reaction time differences for subtle cues, and has shown that cognitive biases have clear neurological correlates (McKay, Thoma, & Pilecki, 2009). These findings have collectively shown the robust nature of specific cognitive biases in understanding the etiology and maintenance of anxiety in general. At the same time, cognitive errors that are articulated by anxious individuals have been effective at determining methods of intervention (see, for example, McKay & Storch, 2009)

The aforementioned research describes complementary perspectives on anxiety disorders that have, for the most part, been integrated into a comprehensive framework constituting cognitive-behavioral theory for anxiety. This line of work has been highly influential in the development of treatment for anxiety for all ages. Indeed, the majority of empirically supported treatments for anxiety disorders are cognitive-behavioral in origin (Chambless & Ollendick, 2001).

Common to models of specific anxiety disorders is threat appraisal in conjunction with learning as per the above description. Specific components are introduced intended to isolate the ways a specific disorder differs from others, and the arrangement and constellation of components that result in anxiety are also deemed unique. The aim of this chapter is to critically consider the degree those components of anxiety disorders models are unique to the disorders they purport to describe (see Table 4.1).

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_4, © Springer Science+Business Media, LLC 2011

Table 4.1 Common features of anxiety disorders: two experimental perspectives

Cognitive errors	Information-processing biases
Overestimation of danger/threat	Encoding process selectively biased towards threat
Overestimation of fear	Interpreting ambiguous information as threatening
Underestimation of coping abilities	Memory biases favoring recall of threatening info.
Overactive threat/ danger schemas	

Cognitive Models of Anxiety: General Considerations

Several models have attempted to describe the cognitive processes occurring in childhood anxiety disorders. One early model emphasized the role of schemas and cognitive deficit and distortion. From this point of view, schemas related to danger and threat are believed to be overactive in children with anxiety (Kendall & Ronan, 1990). Additionally, such children also lack or are unable to use adaptive coping skills and suffer from cognitive processes that are biased or erroneous. Conversely, another model emphasized a stage-process approach, whereby childhood anxiety could be understood in the context of information flowing through the information-processing system (Crick & Dodge, 1994). Six stages were identified as part of normal cognitive processing. During *encoding*, information can be attended to for further processing, or ignored. If attended to, information then undergoes *interpretation*, whereby meaning is attached by the individual. Next, the *goal clarification* or *construction* stage involves the activation or construction of a new goal to meet situational demands. *Response access* or *construction* involves the cognitive process of decision-making, whereby one or more responses are recalled from memory or created for the situation. Finally, the individual undergoes *response selection*, whereby responses are evaluated in terms of a variety of factors, and the individual finally produces the selected response through *enactment*. According to Dodge's information-processing system model, anxiety disorders are the result of dysfunctions occurring during one or more of these stages.

A third model works to integrate Kendall's theory of childhood anxiety (Kendall & Ronan, 1990) with Dodge's model of information-processing to highlight distortions and deficits that occur throughout the stages of processing (Daleiden & Vasey, 1997). Specifically, the encoding process of children with anxiety disorders may be influenced by a narrowing focus and selective attention to threatening information. There is evidence for such an attention bias in both normal (Field, 2006) and anxious children (Watts & Weems, 2006; Murrary, Creswell, & Cooper, 2009). Such children may also interpret ambiguous information as threatening, make negative attributions about new information, expect negative outcomes, and have low self-efficacy in coping with threatening situations. Such biases in the encoding and interpretation stage may also lead to an increased reliance on avoiding and escaping threatening situations, as opposed to engaging in problem-focused coping. While these models have been helpful in understanding general processes that occur in childhood anxiety disorders, there is still much to be done in order to better understand cognitive dysfunctions that are specific to each of the anxiety disorders. Similar to this model, Weems and Watts (2005) posit that childhood anxiety may be related to three cognitive processes: selective attention, memory biases, and negative cognitive errors. In other words, children with anxiety tend to pay more attention to threatening stimuli, remember threatening information, and have more biased interpretations of events and situations as fearful or threatening. Evidence for this latter model has shown that selective attention, memory bias, and cognitive errors are correlated with childhood anxiety problems, but is unable to show specific relationships between these three cognitive processes and specific anxiety symptoms or disorders (Watts & Weems, 2006).

In summary, contemporary cognitive models encompass elements from the original notion of cognitive errors that were articulated by Beck et al. (1985), and emphasize the way information is processed (i.e., directed attention, encoded, and

recalled) in the etiology of childhood anxiety disorders. Behavioral models associated with learning are involved insofar as learning leads to selective encoding of material. Nevertheless, treatment for childhood anxiety, regardless of specific disorder, emphasizes both cognitive approaches as well as behavioral interventions.

Content-Specificity Hypothesis

The idea that various disorders have specific and unique cognitive processes is not new and goes back to early cognitive models positing that anxiety and depression are caused by specific types of cognitive dysfunctions unique to each disorder and has been termed the *cognitive content-specific hypothesis* (Beck, 1976; Beck et al., 1985). For example, the content of cognitions that gives rise to social anxiety disorder would be distinctive from the content of cognitions that gives rise to panic disorder. Therefore, treatment for mental disorders would involve identifying and modifying the specific cognitive distortions or biases that are presumed to give rise to each disorder. In adults, some evidence for the content-specific hypothesis has provided support for the specificity of cognitions in identifying and treating various anxiety disorders (Clark, 1999; Clark and Fairburn, 1997; Foa, Franklin, Perry, & Herbert, 1996; Stopa & Clark, 2000). However, a larger meta-analysis failed to find support for the content-specificity hypothesis (Beck & Perkins, 2001). Less research has examined the content-specificity hypothesis with anxiety disorders in children and suggests a need for further investigation into the ability of cognitive models of anxiety to inform treatment and predict outcome. However, as will be seen below, the research that has examined the content-specificity hypothesis with anxiety disorders in children is mixed and suggests only partial support for the specificity of cognitions amongst disorders. One major difficulty in linking specific cognitions with specific anxiety disorders is the high degree of comorbidity found amongst anxiety disorders (Last, Perrin, Hersen, & Kazdin, 1992; Last, Strauss, & Francis, 1987; Micco & Ehrenreich, 2010; O'Neil, Podell, Benjamin, & Kendall, 2010; see also Chaps. 2, 3, and 13 this volume). Because of this overlap amongst diagnostic categories, it is difficult to demonstrate specificity amongst cognitive content without also experiencing similar degrees of overlap.

One early study investigating the content of cognitions compared the measurements of cognitions in a group of depressed, anxious, and mixed depressed-anxious fourth, fifth, sixth, and seventh graders, and found few differences between groups (Laurent & Stark, 1993). While no differences in anxious cognitions were found between depressed, anxious, and mixed depressed-anxious groups, the depressed group did endorse more depressive cognitions than the other two groups. While this study did not find support for specificity of cognitions amongst anxiety disorders, it did lend backing to the theory that positive and negative affects are two dimensional variables important in understanding anxiety and depression.

One small study compared the interpretations of ambiguous events of four anxious children with obsessive-compulsive disorder (OCD), separation anxiety disorder (SAD), social phobia, and panic disorder to interpretations provided by a group of eight nonanxious controls and found evidence that anxious children have a tendency to interpret ambiguous material as threatening (Chorpita, Albano, & Barlow, 1996). Furthermore, when asked about how they would react to the ambiguous situations, anxious children tended to express plans involving avoidance and assign a higher probability that threatening events will occur. A similar study investigated the cognitions of various groups of children by providing them with an ambiguous situation involving either physical or social threat, and then asking them to interpret the event and say what they would do about it. When comparing the cognitions of anxious children with SAD, overanxious anxiety disorder, simple phobia, and social phobia to a nonclinical control group, evidence for a threat interpretation bias was found within the anxious group (Barrett, Rapee, Dadds, & Ryan, 1996). However, when dren, the anxious group actually showed less threat interpretation bias. Therefore, this particular cognitive bias was useful in distinguishing anxious from nonanxious children, but lacked

specificity in distinguishing between children with oppositional defiant disorder and anxiety disorders. It is unknown to what extent this shortcoming can be attributed to methodological factors in the way these studies were conducted. That is, because each study grouped all anxiety disorders under one category, it is not possible to know if children with different disorders provided distinctive types of responses when interpreting ambiguous information. Furthermore, for the latter study, the ambiguous situation involved only physical or social threat, and may not have included enough of a variety of situations necessary to capture the divergence of cognitions amongst anxiety disorders.

Yet still another study investigating the interpretations of ambiguous situations compared a group of children with anxiety disorders including SAD, generalized anxiety disorder (GAD), panic disorder, OCD, social phobia, and simple phobia to both a nonclinical control group and a group of children with externalizing disorders including oppositional disorder, attentional deficit and hyperactivity disorder, and conduct disorder (Bogels & Zigterman, 2000). Here, it was found that anxious children had more negative cognitions than the externalizing group and nonclinical group; the former difference was significant, while the latter difference only approached significance. Contrary to the findings by Barrett et al. (1996), it was found that the group of anxious children also interpreted the situation as more threatening than the other two groups. Other research has also confirmed this threat bias in children with anxiety disorders (Hadwin, Frost, French, & Richards, 1997; Muris et al., 2000). While these findings offer support for differences in cognitions between anxiety and externalizing disorders, they still lack specificity in association with each of the anxiety disorders and instead point to support for a general threat bias among children with any anxiety disorder.

The first study to directly investigate the content-specificity hypothesis in children failed to find support for distinctive cognitions based upon anxiety disorder. Reactions were recorded from a group of children without anxiety disorders who were exposed to stories characterized by social anxiety, separation anxiety, or generalized anxiety (Muris et al., 2000). While high levels of anxiety were associated with greater threat perception, high ratings of threat, high levels of negative feelings and cognitions, and an early detection of threat, no differences in cognitions were found between the anxiety-specific content of the stories. However, one potential reason for this failure may be due to the sample's high degree of comorbidity between social anxiety, separation anxiety, or generalized anxiety as measured by the Screen for Child Anxiety Related Emotional Disorders (SCARED), an anxiety assessment. Additionally, it was noted that though each of the three stories were separated by theme, separate sentences within stories may have included themes from other stories. Therefore, it is difficult to parse out the unique effects of each anxiety disorder on the types of responses provided by the participants in this study.

Another study also attempted to identify specific cognitive interpretations in children with social anxiety, separation anxiety, and generalized anxiety by exposing children to ambiguous situations and analyzing their interpretations and action plans (Bogels, Snieder, & Kindt, 2003). Again, only limited support was found for the content-specificity hypothesis. Children with separation anxiety did report more overestimations of the danger of being abandoned and more underestimations of their independent functioning compared to children with GAD or social anxiety. However, socially anxious children reported more overestimation of criticism and rejection, and underestimation of their social competence compared to children with SAD, but not compared to children with GAD. Additionally, cognitive interpretations associated with generalized anxiety did not differ amongst the three groups. This latter finding may be due, again, to the high degree of comorbidity between anxiety disorders. Similarly, children with SAD and social phobia showed a negative interpretation bias relevant to their fear, though these groups could not be distinguished from each other. Also, children with GAD did not show any distinguishable differences in their negative interpretation bias.

As mentioned above, one study has shown that selective attention, memory bias, and cognitive errors are associated with anxiety symptoms in children (Watts & Weems, 2006). Of interest to the content-specificity hypothesis is the degree to which cognitive errors alone can account for differences in the expression of anxiety symptoms. In the aforementioned study, cognitive errors were measured by The Children's Negative Cognitive Error Questionnaire (CNCEQ), an assessment targeting four major forms of cognitive errors (catastrophizing, overgeneralization, personalizing, and selective abstraction). However, measures that were used to assess anxiety, The Revised Child Anxiety and Depression scales (RCADS) and its parent version (RCADS-P; Chorpita, Yim, Moffitt, Umemoto, & Francis, 2000), assessed for a range of anxious and depressive symptoms to produce an overall score and were not able to provide information about specific diagnosis. While scores on these anxiety measures were significantly and positively correlated with the CNCEW total and subscale scores, it was not possible to investigate whether particular anxiety disorders were associated with unique types of cognitive errors as assessed by the CNCEQ. An earlier study also investigated the relationship between specific cognitive errors as measured by the CNCEQ, and measures of anxiety as measured by the Childhood Anxiety Sensitivity Index (CASI; Silverman, Fleisig, Rabian, & Peterson, 1991), The Revised Children's Manifest Anxiety Scale (RCMAS; Reynolds & Richmond, 1978), and The State Trait Anxiety Inventory for Children-Trait Version (STAIC-T; Spielberger, 1973) (Weems, Berman, Silverman, & Saavedra, 2001). A measure of depression, The Children's Depression Inventory (CDI), was also included. Again, results found support for a positive relationship between cognitive errors and child anxiety. Additionally, partial correlations controlling for depression indicated that catastrophizing and overgeneralizing were related to all measures of anxiety, and that personalization was related to most measures of anxiety. While these findings lend credence to the notion that different types of cognitive errors contribute to anxiety, it remains unknown whether or not each of the measured categories of cognitive errors are specific to the various anxiety disorders present in children.

Specific Disorders: Posttraumatic Stress, Obsessive-Compulsive, and Generalized Anxiety Disorders

Posttraumatic Stress Disorder (PTSD) has been found in both adults and children, although until recently most research on cognitive models of PTSD has been focused on adults. More recently, cognitive models of adult PTSD have been applied to working with children with this disorder (Vickers, 2009). An adult model proposed by Ehlers and Clark (2000) was applied to understanding the presentation and treatment of two children with PTSD. This model views PTSD as a paradoxical disorder characterized by intense fear of a future threat propagated by a severely terrifying event that happened in the past. Because this event has been processed in a way that the threat of danger remains current, individuals with PTSD are observed to engage in a variety of avoidance behaviors that are ineffective at reducing threat. This model of PTSD views cognitions and the personal meaning of the terrifying event as a core process, rather than simply emphasizing conditioning as earlier models of PTSD have done. The two cases presented by Vickers (2009), along with several other studies applying the Ehlers and Clark model, have offered some promising, though limited, support for using an adult model of cognitive processes in explaining a childhood anxiety disorder (Stallard, 2003; Ehlers, Mayou, & Bryant, 2003).

OCD is another disorder that is present in both adults and children. While there has been evidence to support the specificity of cognitions associated with OCD in adults (e.g., Salkovskis et al., 2000; Frost & Skeketee, 1997), less research has been conducted to determine whether or not similar cognitions occur in childhood OCD. One study that did focus on children investigated whether cognitions found in adult OCD were also found in childhood OCD, including inflated

responsibility, overimportance of thoughts, and perfectionism (Libby, Reynolds, Derisley, & Clark, 2004). Results showed that children with OCD displayed higher levels of inflated responsibility as compared to a group of children with other anxiety disorders and a nonclinical control group. Results also showed a higher level of thought-action fusion, the belief that one's thoughts can have direct effects on the environment, in children with OCD as compared to children with other anxiety disorders and a nonclinical control group. And while perfectionism was not found to be uniquely associated with childhood OCD, a subscale of the perfectionism measure, concern over mistakes, was significantly related to children with OCD as compared to children in the other two groups.

Finally, GAD is a disorder present across age ranges. Most models of GAD emphasize the role of worry control and catastrophizing in the etiology and maintenance of the disorder (Borkovec, Alcaine, & Behar, 2004). Some research supports the role of catastrophizing in worry process (Davey & Levy, 1998) and its interfering role in information-processing (McKay, 2005). However, this does not suggest specificity of catastrophizing or worry to GAD. Indeed, it may not necessarily be the case that these cognitive processes are specific. Recent treatment trials targeting worry, and associated cognitive processes, have shown positive outcome in children with GAD as well as those with separation anxiety and social anxiety (Kendall, Hudson, Gosch, Flannery-Schroeder, & Suveg, 2008; Suveg, Sood, Comer, & Kendall, 2009).

Selective Mutism

Current conceptualizations of selective mutism (SM) suggest two major types: anxious and/or oppositional. For the present purposes we will restrict our focus to the anxious type, which has been considered similar to social anxiety (Beidel & Turner, 2007; Freeman, Garcia, Miller, Dow, & Leanard, 2004). One factor that has been considered a significant contributor to SM in relation to children is behavioral inhibition (Beidel & Turner, 2007), a temperament that is present from a very early age. However, the research has generally suggested that behavioral inhibition is a risk factor for a wide range of anxiety disorders and is not specific to SM (summarized in Lonigan & Phillips, 2001). There have not been any investigations evaluating cognitive factors contributing to SM.

Separation Anxiety Disorder

As noted above regarding GAD, treatment of several common factors associated with anxiety generally appears to confer a benefit on children suffering from separation anxiety (i.e., Kendall et al., 2008). With respect to SAD specifically, several factors have been implicated in the etiology and maintenance of the disorder. Among these are anxious attachment style, parental anxiety, and comorbid psychiatric conditions (summarized in van Dyke & Albano, 2009). However, these do not represent a comprehensive model of the disorder's unique characteristics. Nevertheless, treatment relying on general cognitive behavioral principles such as coping skills, anxiety management, and exposure has collectively lead to significant improvement (Kendall et al., 2008; Suveg et al., 2009; Walkup et al., 2008).

Specificity of Treatment for Unique Cognitive Features of Anxiety Disorders

From the available literature, it appears that treatment for childhood anxiety disorders using cognitive-behavior therapy is highly efficacious. Indeed, meta-analytic reviews have shown large effect sizes associated with treatment (Abramowitz, Whiteside, & Deacon, 2005; Silverman, Pina, & Viswesveran, 2008). This is encouraging since anxiety disorders are associated with significant disability and can impair academic and social functioning in lasting ways.

Table 4.2 Content-specificity in anxiety disorders

Disorder	Unique components	References
Separation anxiety	Overestimation of the danger of being abandoned	Bogels et al. (2003)
Disorder	Underestimation of independence	
	Anxious attachment style	van Dyke and Albano (2009)
	Parental anxiety	
	Comorbid psychiatric conditions	
Social anxiety	Overestimation of criticism and rejection	Bogels et al. (2003)
Disorder	Underestimation of social competence	
Selective mutism	Behavioral inhibition	Beidel and Turner (2007)
Posttraumatic	Intense fear of a future threat due to manner of	Ehlers and Clark (2000)
Stress disorder	Processing of prior threatening event	
Obsessive-compulsive	Inflated responsibility	Libby et al. (2004)
Disorder	Overimportance of thoughts	
	Perfectionism	

Table 4.3 Mixed or limited support for specificity of hypothesized cognitive content

Generalized anxiety disorder
Anxiety disorders in general
Anxiety disorders vs. depressive disorders
Anxiety disorders vs. oppositional defiant disorder/ conduct disorder
Phobia
Panic disorder

Note: this list is derived from research examining content specificity either among disorders or between disorders in children

While the news is encouraging, it has become increasingly important that specific mechanisms associated with the development of disorders be clearly articulated in order to advance our understanding of how to prevent specific psychological problems, as well as to improve the efficiency of current interventions. What this review has shown is that whereas treatment as currently conceived is effective, there are few unique cognitive or behavioral factors tied to individual anxiety disorders (see Tables 4.2 and 4.3). Cognitive variables such as coping or proneness to catastrophizing are instead more likely to be components evident across anxiety disorders, and the alleviation of these features produces a general therapeutic benefit. Insofar as there are specific behavioral manifestations, it appears that directly targeting these using behavioral interventions alone is also efficacious.

This leads to an important distinction that has been drawn in recent years regarding the role of behavioral interventions in cognitive therapy (i.e., behavioral experiments) vs. exposure per se. Some have argued that the behavioral experiments allow therapists to access cognitions that are either unique to the individual or to the disorder in question (i.e., Bennett-Levy et al., 2004). Alternatively, it has been argued that behavioral experiments provide a mechanism, through exposure, to provide corrective feedback that alters cognitive processes indirectly (McMillan & Lee, 2010). This would suggest that a typology of environmental cues could be developed that would serve a similar diagnostic value to the current Diagnostic and Statistical Manual. The prospect of a behavioral typology that would lead directly to specific interventions has been entertained in the past (Kanfer & Saslow, 1969). These have not lead to systematic diagnostic schemes, but point to the possibility that models should be developed with specificity in mind.

Conclusion

In conclusion, the evidence supporting a content-specificity hypothesis for anxiety disorders is mixed and in need of further review. While there is strong evidence that cognitive errors are associated with anxiety and depression in general, the degree to which particular disorders map onto specific cognitive errors is still unknown. Such a mapping

is important in bolstering a cognitive model of anxiety disorders in children, as well as adults, because it clearly identifies the mechanism involved in the development of an anxiety disorder in an individual. Without such knowledge, current cognitive models remain muddled and vague, limiting themselves to only pointing at general patterns rather than the more detailed cognitive processing involved in etiology and maintenance of anxiety that one would desire in treatment.

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Genetics of Childhood and Adolescent Anxiety

5

Paul D. Arnold and Stephanie Taillefer

There is considerable evidence that genetic determinants play a major role in the etiology of anxiety. However, the genetic etiology of anxiety disorder is complex (Elston, 2000), involving the interaction of multiple genes of small or modest effect and gene–environment interactions. For such complex traits, genetic risk factors are probabilistic rather than deterministic in nature (Page, George, Go, Page, & Allison, 2003). In addition to genetic complexity, the marked phenotypic heterogeneity of anxiety poses a challenge to genetic investigators, since it is highly unlikely that our current diagnostic categories "carve nature at its joints" with regard to the underlying genetic architecture. Despite these challenges, significant advances in our understanding of the genetic basis of anxiety have been made in recent years. This chapter attempts to provide a critical review of current knowledge regarding the genetic determinants of anxiety.

In the first section of this chapter, genetic epidemiological approaches including family, high risk, and twin studies are briefly reviewed. Genetic epidemiological studies have clearly established the importance of genetic determinants in anxiety disorders and provide an essential backdrop to the second and largest section on molecular genetic approaches. In this section, current gene-finding approaches (linkage and association) are briefly outlined followed by a comprehensive review of molecular genetic findings for categorical DSM-IV anxiety disorders and continuous anxiety-related traits. The final section describes novel approaches in psychiatric genetics, including the study of putative endophenotypes and gene–environment interaction. The chapter concludes with a brief discussion of anticipated future trends in anxiety genetics.

Although the majority of psychiatric genetic studies continue to define groups based on categorical diagnoses, it is generally acknowledged that genetic determinants are unlikely to closely map on to conventional diagnostic categories (Smoller, Gardner-Schuster, & Misiaszek, 2008), and many investigators have therefore chosen to focus their efforts on quantitative anxiety-related traits that cross diagnostic boundaries. In this chapter, genetics of anxiety disorders and quantitative traits are discussed. The focus throughout the chapter is on the studies of anxiety disorders or traits in children or adolescents whenever possible. However, relevant adult studies are also summarized from topic areas where little is known regarding children, or if the findings are clearly of high general relevance to anxiety in all age groups. Given the burgeoning literature on genetics of anxiety in recent years, this review is by necessity selective, highlighting recent and exciting trends in the literature.

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_5, © Springer Science+Business Media, LLC 2011

Genetic Epidemiology: Family, High Risk, and Twin Studies

Family studies: Family studies constitute the first step in establishing that genetic determinants are important. There is significant familial aggregation for all anxiety disorders, as demonstrated in a meta-analysis of family studies in which odds ratios ranged from 4.0 to 6.0 for first-degree relatives (Hettema, Neale, & Kendler, 2001). Early onset may be associated with increased genetic risk; for example, OCD has been shown to be more common in relatives of child compared with adult onset probands in large, controlled studies (Nestadt et al., 2000; Pauls, Alsobrook, Goodman, Rasmussen, & Leckman, 1995). In one large study, no cases of OCD were detected in relatives of probands with onset greater than 18 years (Nestadt et al.). Controlled family studies of pediatric OCD (do Rosario-Campos et al., 2005; Hanna, Himle, Curtis, & Gillespie, 2005) identified a remarkably consistent recurrence risk of 23% for OCD in first-degree relatives, with odds ratios ranging from 11 to 32 due to differing rates of OCD in controls.

High-risk studies: A complementary design to the family study is a prospective study of "high-risk" individuals, typically the offspring of individuals with a disorder. Prospective studies have indicated that children of anxious parents are at increased risk of developing anxiety disorders (Black & Gaffney, 2008; Black, Gaffney, Schlosser, & Gabel, 2003; Merikangas, Lieb, Wittchen, & Avenevoli, 2003). In a high-risk study of children of OCD probands (Black et al.), 23% of the high-risk offspring met the criteria for OCD at 2 year follow-up, a proportion significantly higher than that for control offspring and remarkably congruent with the 23% of first-degree relatives meeting criteria for OCD in the family studies of pediatric probands noted above (do Rosario-Campos et al., 2005; Hanna et al., 2005). High-risk offspring were more likely to meet criteria for an anxiety disorder generally (particularly overanxious disorder or separation anxiety disorder) and scored higher on dimensional measures of anxiety/depression and somatic complaints.

Twin studies: Twin studies in which the concordance of monozygotic twins and dizygotic twins are compared have suggested that between 20 and 40% of risk for anxiety disorders is due to additive genetic factors, depending on the disorder studied (Hettema et al., 2001) with similar estimates for trait anxiety (Kendler, Aggen, Jacobson, & Neale, 2003). These heritability estimates strongly support a genetic contribution but leave substantial unexplained variance, suggesting an important role for environmental factors. Studies of large population samples of preschool twins, which may illuminate pathways of early developmental risk for anxiety disorders, suggest that shyness/inhibition may be the most highly heritable form of childhood anxiety, followed by obsessive–compulsive traits (Eley, Bolton, et al., 2003). In contrast to other anxiety disorders, twin data on OCD diagnosis is very limited in both adults and children, with the best evidence for the heritability of OCD symptoms coming from large twin studies measuring obsessive–compulsive symptoms as quantitative traits distributed continuously throughout the population (van Grootheest, Cath, Beekman, & Boomsma, 2005). Such twin studies have demonstrated substantial heritability in child and adolescent populations, ranging from approximately 55 to 65% (Eley, Bolton, et al.; van Grootheest, Bartels, et al. 2008). Caution should be exercised in placing excessive weight on the magnitude of heritability estimates which tell us little about the actual "genetic architecture" of disorders and how many genes are involved. For example, heritability of 80% could represent the additive effects of four loci each contributing 20% to risk or 100 loci each contributing 0.8% (Smoller, Block, & Young, 2009). Twin (and family) studies also suggest substantial overlap between anxiety disorders with regard to shared genetic risk, and some of this risk may also be shared with depression (Mosing et al., 2009).

In summary, family, twin, and high-risk studies support a substantial genetic contribution to anxiety disorders and traits. These studies provide an essential foundation for the molecular genetic studies discussed in the next sections.

Gene Discovery in Anxiety Disorders: Linkage and Association

Strategies for discovering risk genes are based on the complementary methods of linkage and association. Linkage studies involve genotyping evenly spaced DNA markers in order to determine chromosomal segments shared by affected individuals within families, thereby indicating the approximate chromosomal location of the susceptibility gene(s). Sampling strategies include large pedigrees with multiple affected individuals or affected relative pairs (usually siblings). The strength of linkage is summarized in various ways, the most widely used method being the "Logarithm of the Odds" (LOD) score, with the odds reflecting the likelihood of linkage being present divided by the likelihood of no linkage. Sometimes the linkage approach will be used on a selected region of the genome identified in a previous whole genome scan. Although linkage studies have the advantage of not requiring *a priori* hypotheses regarding which genes are involved, compared with candidate gene studies they have limited power to detect genes of small or modest effect (i.e., a relative risk of less than two) (Risch & Merikangas, 1996).

Association analysis is another strategy for gene discovery. The classic design for an association study is based on comparison of allele frequencies in cases and controls. The case–control strategy requires correction for population differences between groups in order to avoid spurious results in which genetic effects are identified that are unrelated to the disease (population stratification). Alternatively, this problem can be reduced by using family-based association methods (Ewens & Spielman, 2001), exemplified by the transmission disequilibrium test (TDT) (Spielman, McGinnis, & Ewens, 1993), in which one tests for transmission of candidate gene variants from parent to affected offspring.

Almost all the genetic association studies in anxiety disorders involve candidate genes selected for hypothesized involvement in disease pathogenesis. Candidates are typically identified based on location (when a specific chromosomal region has shown linkage), or function. In addition to selection of candidate genes, it is equally important in association studies to choose appropriate polymorphisms (gene variants) within a given gene. Apparently contradictory results for a given gene by different investigators may often be explained by testing different polymorphisms, which may give rise to discrepant results depending on their true proximity (linkage disequilibrium) to the actual genetic site causing the illness within a given gene. Furthermore, studies of the same variant may lead to discrepant (even opposite) results due to different patterns of background linkage disequilibrium in different populations (Lin, Vance, Pericak-Vance, & Martin, 2007).

As in other complex disorders, candidate gene studies of anxiety disorders are limited by the likely small effect and low *a priori* probability of any given single gene, increasing the risk of spurious findings (Wacholder, Chanock, Garcia-Closas, El Ghormli, & Rothman, 2004). While the candidate gene approach has come under increasing criticism (Sullivan, 2007), the availability of comprehensive and cost-effective microarrays (Couzin & Kaiser, 2007) has increasingly led researchers investigating complex traits to conduct genome-wide association studies (GWAS). Using the GWAS approach, association tests are conducted on all common variants across the genome (current standard is over 500,000 markers). GWAS studies have initially focused on common (>5% minor allele frequency) single nucleotide polymorphisms (SNPs). However, with advancing technology investigators have been increasingly interested in assaying rare and common copy number variants (CNVs), structural rearrangements of the genome including deletions, duplications, and insertions which are greater than 1 kb in size.

GWAS studies performed in common complex disorders have revealed that most common variants have small effect sizes. Odds ratios of 1.1–1.5 are typical, with odds ratios greater than 2.0 being an exception (Altshuler, Daly, & Lander, 2008). As a result of these small effect sizes, and to overcome the multiple testing burden of examining so many variants, GWAS requires large sample sizes

(thousands of subjects), typically involving multiple collaborative sites . Using such genome-wide methods, investigators have achieved some success in other neuropsychiatric disorders including schizophrenia, bipolar disorder (The International Schizophrenia Consortium et al., 2009), major depressive disorder (Lewis et al., 2010), autism (Weiss, 2009), and ADHD (Franke, Neale, & Faraone, 2009). There is also an international effort, known as the Psychiatric Genomics Consortium, to combine data from multiple studies in order to increase power to detect genetic effects, although currently this does not include anxiety disorders (Psychiatric GWAS Consortium Steering Committee, 2009). To date, there have been five published GWAS studies examining common SNPs in anxiety phenotypes, including two for panic disorder (PD) (Erhardt et al., 2010; Otowa et al., 2009) and three for the anxiety-related trait, neuroticism (Shifman et al., 2007; Terracciano et al., 2010; van den Oord et al., 2008), as reviewed below. Results from an international collaborative GWAS of OCD are expected within the year (Dr. David Pauls, personal communication), and this approach is likely to be attempted in other anxiety disorders in the near future. No studies have been reported to date systematically assessing copy number variation in anxiety disorders.

The GWAS approach holds great, as yet largely untapped, possibilities for gene discovery in anxiety disorders. However, as noted above, GWAS platforms are designed to detect common variants and more recently have been used to identify rare large CNVs. According to the common-disease common variant hypothesis (Iyengar & Elston, 2007), complex genetic diseases are largely attributable to common variants of low effect that would be amenable to such an approach, although requiring large sample sizes. However, it is likely that common complex genetic disorders have a highly heterogeneous etiology, with common polygenic forms caused by common low-effect polymorphisms and subtypes of the disorder causes by rare variants specific to a given family (common disease rare variant hypothesis). In fact, it has recently been suggested that many of the GWAS findings in complex disorders may be "synthetic associations" resulting from rare variants of large effect that lie nearby the association signals (Dickson, Wang, Krantz, Hakonarson, & Goldstein, 2010). Ultimately, the only way to conclusively resolve the debate over common versus rare variants will be to sequence the entire genome in large samples of individuals characterized for a disorder or trait. Although this approach is currently prohibitively expensive, the costs of sequencing are decreasing rapidly. It is predicted that the cost of sequencing an entire human genome will cross a threshold of $1,000 within 5 years, which will make this approach feasible for many research groups (Cirulli & Goldstein, 2010).

Summary of linkage and association findings in anxiety disorders and traits: In the following paragraphs, major linkage and association findings from anxiety disorders and anxiety traits are described. The emphasis is on linkage and association findings in children or adolescents, or at least in samples in which age of onset of symptoms is known to be early. Emphasis is placed on studies in which there has been some consistency of replication by two or more independent groups.

Obsessive–Compulsive Disorder

Linkage studies: There have been three independent published genome-wide linkage (GWL) scans of OCD (Hanna et al., 2002, 2007; Shugart et al., 2006). Stronger findings (LOD = 3.7 on chromosome 14) emerged from a fourth study, based not on OCD diagnosis but on the OCD symptom of hoarding (Samuels et al., 2007). All four studies (from two different research groups) were based on samples of children or individuals with onset of symptoms before age 18, and although each study has produced suggestive linkage peaks there is no overlap between the regions identified. A fifth GWL study is currently underway based on families ascertained due to childhood onset OCD from an isolated region of Costa Rica. Preliminary results indicate some suggestive peaks, and no substantial overlap with previously reported GWL studies (Dr. Carol Mathews, personal communication). Although

based on 77 sibling pairs affected with Tourette's Syndrome (TS), another genome scan focused on the phenotype of hoarding and identified linkage to 4q (in close proximity to a region previously linked to TS), 15q, and 17q (Zhang et al., 2002).

GWL studies of OCD have suggested candidate genes lying within linkage peaks. In the first published genome scan, a region of suggestive linkage was found in chromosome 9p24 based on seven multigenerational large pedigrees with multiple affected individuals (LOD = 2.25). The 9p24 finding was subsequently replicated through linkage analysis on 38 small nuclear pedigrees using the same set of 13 markers (Willour et al., 2004). As described below, multiple candidate gene studies of *SLC1A1* have found positive associations with SNPs within this gene. In their second GWL study of 26 extended pedigrees, Hanna et al. (2007) identified a region of suggestive linkage on 10p15 (LOD = 2.43). Family-based association analyses performed on 35 SNPs within the 10p15 region detected significant association ($p < 0.05$) with three adjacent SNPs in the 3′ region of the gene Adenosine Deaminase Acting on RNA 3 (*ADAR3*), a finding which has yet to be replicated. In the largest GWL study of 219 families ascertained for OCD (Shugart et al., 2006), the strongest linkage signal was identified at 3q27-28 (LODALL = 2.67, $p = 0.0003$), a region which contains the gene encoding the serotonin 3C receptor. Although a reasonable candidate for OCD, there are no reported association findings for this gene.

Summary of linkage studies: To our knowledge, there have been three published and one unpublished GWL study for OCD, and two for the hoarding phenotype (one based on subjects with TS). They have produced three distinct suggestive linkage peaks (9p24, 3q27-28, and 10p15) for OCD and one significant linkage peak for hoarding (on chromosome 14) which do not overlap between studies. The distinction between hoarding and non-hoarding families with regard to genetic loci is consistent with other clinical and neurobiological evidence suggesting hoarding as a distinct subtype of OCD, possibly a separate disorder. Additional, fine mapping and association studies are required to narrow the broad genomic regions identified using GWL approaches. To date, the 9p24 locus is the one linkage finding that has subsequently led to multiple findings of associations with a biologically plausible candidate gene, the glutamate transporter gene *SLC1A1* (as described in the next section).

Candidate gene association studies in OCD – serotonin transporter (*SLC6A4*): Most candidate gene studies have been based on adult OCD probands, although there have been a growing number of studies based on child and adolescent subjects. The majority of candidate gene studies in OCD to date have been based on serotonergic hypotheses. In particular, the gene encoding the serotonin transporter (*SLC6A4*) is the most studied gene in OCD with 25 published reports as of this writing, and two meta-analyses (Bloch, Landeros-Weisenberger, Sen et al. 2008; Lin, 2007). No genome-wide studies have found linkage or association in or near the region of Chromosome 17 containing the serotonin transporter gene *SLC6A4*, nonetheless *SLC6A4* has been regarded as a prime candidate gene for all anxiety disorders and traits. The majority of candidate gene studies in OCD and other anxiety phenotypes have focused on a functional variant in the promoter region known as the serotonin transporter (5HTT)-linked polymorphic region (5HTTLPR), composed of either 14 (short or "*S*" allele) or 16 (long or "*L*" allele) repeated elements. This variant has been demonstrated to induce changes in 5HTT activity, with the *S* allele producing decreased 5HTT activity compared with the *L* allele (Murphy et al., 2008).

Early studies (Bengel et al., 1999; McDougle, Epperson, Price, & Gelernter, 1998) suggested an association with the *L* allele, but subsequent studies produced mixed findings and two recent meta-analyses reached different conclusions. The first meta-analysis (Lin, 2007) included results from 13 case–control studies (1,242 OCD cases, 2,203 controls), and excluded family-based association studies. In their pooled data analyses, Lin and colleagues found a small but significant association between OCD and the *S/S* homozygous genotype (OR = 1.21), an inverse association with the *L/S* genotype ($R = 0.79$, $p = 0.03$) but no single allele effects. However, these reports should be interpreted with caution since sensitivity tests revealed

that removal of a single study (Hu et al., 2006) resulted in nonsignificant findings. In the more recent and comprehensive meta-analysis (Bloch, Landeros-Weisenberger, Sen, et al., 2008), the same 13 case–control samples were augmented with three more recent studies and six family-based association studies, for a total of 1,797 OCD cases, 3,786 controls, and 486 proband–parent trios. In their overall analysis, Bloch and colleagues found no significant association between *SLC6A4* and OCD. However, when they performed stratified meta-analyses they found significant associations with the *L* allele specific to family-based association studies, studies based on child probands (Dickel et al., 2007; Walitza et al., 2004), or studies based on Caucasian cases/probands (excluding two studies from Asian populations). The findings in Caucasian and family-based association samples may be due to the reduction of population stratification effects noted above (N.B. the child studies were also family-based).

Interpretation of association with the 5HTTLPR has been complicated by discovery of a SNP (rs25531) within the *L* allele which alters transcriptional activity. The discovery of this variant effectively makes the 5HTTLPR a "tri-allelic" system and forces a re-examination of previously published association studies involving this polymorphism. The high activity *L (A)* allele (frequency 50% in US Caucasians) is associated with increased transcription, whereas the *L (G)* allele (frequency 15%) and *S* alleles are both associated with decreased transcription. A collaborative study between David Goldman's group at NIH/NIAA and our group in Toronto discovered a positive association between the *L(A)* allele and OCD in a case–control as well as an independent family-based sample (Hu et al., 2006). This finding was not replicated in a subsequent large case–control study which examined the triallelic 5HTTLPR–rs25531 combination (Wendland, Kruse, Cromer, & Murphy, 2007). Intriguingly, however, when the same group examined additional SNPs which also influence expression of SLC6A4, they identified a strong association ($p = 0.01$, OR = 1.63) with a "gain-of-function" haplotype containing the high-expressing alleles at three loci (5HTTLPR-rs25531, rs25532, and rs16965628) (Wendland, Moya, et al., 2008). More recently, 17 variants spanning *SLC6A4* were genotyped in 1,241 individuals from 278 pedigrees collected by the OCD Collaborative Genetics Study (Voyiaziakis et al., 2011). These investigators did not find an association with the *L(A)* allele considered alone, but were not able to test the gain-of-function haplotype identified by Wendland, Moya, et al. (2008) since they did not genotype the rs25532 and rs16965628 SNPs. They also noted that their sample differed from most case–control and trio studies since their ascertainment was based on multiple affected individuals per family, which might have led to different results.

Four groups (Baca-Garcia et al., 2007; Ohara et al., 1999; Saiz et al., 2008; Voyiaziakis et al., 2011) reported a positive association with a variable nuclear tandem repeat (VNTR) variant in the second intron of *SLC6A4*, whereas another group that examined this variant found no association (Wendland et al., 2007). There is some inconsistency in the alleles of this VNTR that have been associated with OCD, with three of four studies reporting an association with the 12 repeat allele, whereas the largest study (Voyiaziakis et al.) implicated the 9/10-repeat genotype. Future studies of *SLC6A4* should consider this variant, however, great care needs to be taken to quality control as it is difficult to genotype reliably (Wray et al., 2009).

In addition to the common variants just described, a rare A/G transversion in transmembrane domain 8 produces an isoleucine–valine substitution (I425V). The rare G (valine) variant was identified in two OCD probands and their families and co-segregates with a rather severe, atypical phenotype including multiple comorbid disorders (Ozaki et al., 2003). Expression studies indicate that this is a "gain of function" mutation, which produces an approximately twofold increase in uptake activity (Kilic, Murphy, & Rudnick, 2003). This gain of function effect is consistent with the haplotype findings of Wendland et al. (2008). An independent group reported the I425 V variant in three OCD patients and one control subject. As reviewed by Wendland, Deguzman, et al., 2008, cumulative

data from 530 European Caucasian OCD patients and 1,300 control subjects (from four Caucasian populations) (Delorme et al., 2005; Ozaki et al., 2003; Wendland, Deguzman, et al., 2008; Wendland, Martin, et al., 2006) suggest that the 425V variant is significantly more frequent in OCD patients compared with controls (1.5 vs. 0.23%, $p = 0.004$, OR = 6.54). However, it should be noted that the frequency of this variant in unselected OCD cases is undetermined, as the cases with the 425V variant have come from only five unrelated families. More recently, Voyiaziakis et al. (2011) screened their large sample for the I425V variant and identified three carriers, two of whom had either OCD or obsessive-compulsive personality disorder (OCPD). However, all three carriers were parents of affected OCD sib-pairs and none of them passed on the variant to their OCD-affected offspring. In summary, the I425V variants may cause a rare, familial subtype of OCD but does not always co-segregate with OCD and is not likely to contribute much to OCD risk on a population level.

Summary of findings regarding the serotonin transporter gene: Overall, the findings for *SLC6A4* support a role for increased *SLC6A4* expression in OCD. Furthermore, they suggest that investigators need to shift their focus from studying any single variant such as 5HTTLPR and test for multiple functional variants that are now being discovered in this intensively studied gene (Kraft, Slager, McGrath, & Hamilton, 2005; Murphy et al., 2008; Prasad et al., 2005). Interestingly, a study of rigid-compulsive behaviors in autism found that it was the aggregate effect of common and rare functional variants that explained the association with *SLC6A4* rather than single variants alone (Sutcliffe et al., 2005).

Other candidate genes affecting serotonin neurotransmission: A second serotonergic candidate susceptibility gene for OCD is the gene encoding the serotonin 1B receptor (*HTR1B*, also known as 5HT1B or 5HT1Dbeta), a presynaptic autoreceptor that regulates serotonin release. Most studies have concentrated on the common G861C polymorphism, which occurs within the coding region but does not cause changes in the amino acid sequence (Lappalainen et al., 1995). The first report of an association between *HTR1B* and OCD came from the Toronto group who found increased transmission of the more common G allele of the G861C polymorphism in two family-based association studies using overlapping samples (Mundo, Richter, Sam, Macciardi, & Kennedy, 2000; Mundo et al., 2002). Subsequently, three groups reported positive findings in male probands – a Mexican family-based study (Camarena, Aguilar, Loyzaga, & Nicolini, 2004), an Afrikaner case–control study (Lochner et al., 2004), and a Korean case–control study which only included males (Kim, Namkoong, Kang, & Kim, 2009). However, four negative studies, two based on adult probands (Denys, Van Nieuwerburgh, Deforce, & Westenberg, 2006; Di Bella, Cavallini, & Bellodi, 2002) and two on child probands (Dickel et al., 2007; Walitza et al., 2004), have been published. Possible reasons for this inconsistency include genetic heterogeneity, or low power due to small sample sizes. Most importantly, genotyping of polymorphisms other than G861C is needed to clarify the inconsistent findings with this gene.

A number of candidate gene studies in OCD have focused on the gene encoding the serotonin 2A receptor (*HTR2A*), utilizing the closely linked markers rs6311 (−1438G/A) and rs6313 (T102C). The rs6311 variant may affect gene expression due to its location in the promoter region, though its actual functional effects have not been established; the rs6313 variant is located in the coding region but does not change amino acid sequence and has no known functional effect. Positive associations between OCD and either rs6311 or rs6313 have been reported in case–control studies of adult (Enoch et al., 1998; Hemmings et al., 2003) and child (Walitza et al., 2002) populations. Enoch, Greenberg, Murphy, and Goldman (2001) reported a sex-specific finding of association between rs6311 and OCD in females in a population consisting largely of subjects with early onset OCD. Five other case–control samples found no association with either the rs6311 or rs6313 variants (Frisch et al., 2000; Hemmings et al., 2003; Meira-Lima et al., 2004; Nicolini et al., 1996; Saiz et al., 2008; Tot, Erdal, Yazici, Yazici, & Metin, 2003), although one of these studies identified an association with

symptom severity (Tot et al., 2003). While their study did not implicate the rs6313 polymorphism, a Brazilian group found an association with the C516T variant, an example of the importance of examining more than one polymorphism in a gene (Meira-Lima et al., 2004). In the only family-based association study of *HTR2A* in OCD, Dickel et al. (2007) did not find an association between rs6311 and OCD in their total sample based on child probands but identified a positive association in probands with comorbid tic disorders.

Candidate genes affecting dopamine neurotransmission: Dopamine genes have also been investigated in candidate gene studies, based on a number of lines of evidence including: the putative role of dopamine in tic disorders (hypothesized to be genetically linked to OCD), the well-established efficacy of dopamine antagonists as augmenting agents for OCD patients refractory to SRI treatment (McDougle, Epperson, Pelton, Wasylink, & Price, 2000), and the fact that stereotypic behaviors resembling compulsions or complex tics have been induced in humans or animals with various dopaminergic agents such as amphetamine and l-Dopa (Berridge, Aldridge, Houchard, & Zhuang, 2005; Joel & Doljansky, 2003). A functional 48 bp VNTR polymorphism located in the third exon of the dopamine D4 receptor (*DRD4*) gene has attracted a lot of interest (Tarazi, Zhang, & Baldessarini, 2004). A number of groups have reported associations between OCD and this VNTR, but have been somewhat inconsistent with regard to the major alleles identified, including decreased transmission of the 2-repeat allele (Millet et al., 2003), reduced frequency of the 2/4 genotype(Billett et al., 1998), and decreased transmission of the 4-repeat allele (Camarena, Loyzaga, Aguilar, Weissbecker, & Nicolini, 2007; Walitza, Renner, Wewetzer, & Warnke, 2008) although the latter study failed to replicate their case–control findings in an independent family-based sample. Negative results have been reported in other case–control studies from different populations (Frisch et al., 2000; Hemmings et al., 2003). An earlier case–control study demonstrated an increase in frequency of the 7-repeat allele in patients with OCD with tics compared to those without (Cruz et al., 1997), consistent with two family-based association studies of Tourette Syndrome patients, suggesting an association between TS and the 7-repeat allele (Diaz-Anzaldua et al., 2004; Grice et al., 1996). Overall, methodological limitations in most of the studies described preclude making any conclusions regarding the association between the *DRD4*-VNTR and OCD, however, the preliminary positive findings and functional importance of this variant should provide impetus for further study.

Catechol-*O*-methyltransferase (*COMT*), an enzyme involved in the metabolism of noradrenaline and dopamine, contains a common functional variant (rs4680, or Val158Met) with wild-type A (valine, high activity) and methionine (G, low activity) alleles. *COMT* has been reported to have a sex-specific association with OCD, and has been the subject of two meta-analyses. The first meta-analysis of did not support any general or sex-specific associations with the *COMT*-Val158Met polymorphism (Azzam & Mathews, 2003). A more recent meta-analysis including a much larger number of subjects from all extant case–control samples found an association (OR = 1.23) of the Met allele which was present in men (OR = 1.88) but not women. This latter study did not consider evidence from family-based association studies, and a more recent family-based study based on child probands failed to find any association (Walitza, Scherag, et al., 2008). Overall, there is some evidence for a sex-specific effect of *COMT* in OCD. However, further research is warranted on *COMT* in both case–control and family-based studies to confirm this association, including testing additional important variants and haplotypes that have been shown to influence gene expression (Nackley et al., 2006).

Candidate genes affecting glutamate neurotransmission: In recent years, investigators have increasingly been testing genes in the glutamate system, based on mounting evidence for a role of altered glutamate neurotransmission in the pathogenesis of OCD (D. R. Rosenberg & Keshavan, 1998). Indirect support for the glutamate hypothesis comes from animal models in which altered glutamate neurotransmission is found in

mice characterized by perseveration and compulsive motor behaviors (Nordstrom & Burton, 2002) or excessive grooming (Welch et al., 2007). More direct support for the role of glutamate in OCD is provided by investigations using proton magnetic resonance spectroscopy (1-H MRS), suggesting a pharmacologically reversible glutamatergically mediated thalomocortical-striatal dysfunction in OCD (Rosenberg et al., 2000, 2004). The glutamate transporter gene *SLC1A1* (Solute-linked carrier, family 1, member 1) has attracted particular interest given that it is located within the 9p24 region, one of the strongest linkage peaks in OCD, and therefore represents an excellent positional as well as functional candidate for OCD. Initially reported by our group in Toronto (Arnold, Sicard, Burroughs, Richter, & Kennedy, 2006) and a group of investigators at the University of Michigan (Dickel et al., 2006), an association between *SLC1A1* and OCD has now been reported by a total of five independent groups (Shugart et al., 2009; Stewart et al., 2007; Wendland et al., 2009), although the precise variants associated with OCD vary between studies.

Four out of the five groups (the lone case–control study (Wendland et al., 2009) being the exception) have reported stronger findings in males. Using publicly available genotype and gene expression data, Wendland et al. found that two SNPs within *SLC1A1* were expression quantitative loci (eQTL) influencing messenger RNA levels. Wang et al. have gone on to screen *SLC1A1* for mutations using capillary electrophoresis and have identified four novel polymorphisms, one of which is a rare (only identified in one pedigree) variant that alters the coding sequence of the protein. Taken together, the association studies combined with the earlier GWL peak in 9p24 strongly suggest a role for *SLC1A1* in OCD, particularly in males. However, further research, including targeted re-sequencing of *SLC1A1*, is needed to confirm the actual functional variant(s) contributing to the OCD phenotype. Other glutamate system genes that are interesting candidates but have not been as well studied in OCD include: the glutamate receptor, ionotropic, NMDA subunit 2B gene (*GRIN2B*) (Arnold et al., 2004), and kainate glutamate receptors (*GRIK2* and *GRIK3*) (Delorme et al., 2004).

A few investigators have recently reported on *DLGAP3*, which became an attractive candidate for OCD when it was reported that the *DLGAP3* knockout mouse exhibits marked compulsive grooming behaviors that are reversible with SSRI treatment (Welch et al., 2007). *DLGAP3*, also known as *SAPAP3*, encodes a postsynaptic scaffolding protein, highly expressed in striatum, which has been shown to affect glutamate functioning (Welch et al.). Association studies of common variants in OCD have either been weakly positive (Arnold et al., unpublished results) or negative, although one group reported a positive association with grooming disorders (e.g., trichotillomania), which are highly comorbid with OCD (Bienvenu et al., 2009). Sequencing of *DLGAP3* revealed a number of novel variants, and that the total number of mutations was increased in OCD cases compared with controls (Zuchner et al., 2009).

Brain-derived neurotrophic factor (BDNF): *BDNF* influences neuronal development with other known functions including modulation of serotonergic transmission (Mossner et al., 2000) and enhancing phosphorylation of the postsynaptic NMDA receptor subunit 1 (Suen et al., 1997). *BDNF* contains a functional variant known as rs6265 (Val66Met) which has been widely studied. In an initial large study of 164 families ascertained for OCD, a distinct *BDNF* haplotype (including the Met allele of rs6265) was under-transmitted, particularly to probands with early-onset disorder, suggesting a protective function for the Met allele (Hall, Dhilla, Charalambous, Gogos, & Karayiorgou, 2003). A more recent case–control study in a Spanish population also identified a protective haplotype containing the Met allele of rs6265 (Alonso et al., 2008). Other studies based on genotyping of one or two SNPs did not find an association in samples based on adult (Wendland et al., 2007; Zai et al., 2005) or child (Dickel et al., 2007; Mossner et al., 2005) probands. One study found a weak, gender-specific association in the opposite direction (Met allele increasing rather than decreasing risk for OCD, Hemmings et al., 2008). Taken together, these findings suggest that specific haplotypes in the region of rs6265 may be associated with OCD, but further work is needed to replicate this finding.

Studies of OCD symptom dimensions or subtypes: In OCD genetic studies there is great interest in studying empirically-derived symptom dimensions (groups of symptoms that tend to cluster together in patients) as phenotypes rather than OCD diagnosis which is presumed to be more etiologically heterogeneous and therefore less tractable for genetic studies. A recent meta-analysis of 21 studies including 5,124 participants (Bloch, Landeros-Weisenberger, Rosario, Pittenger, & Leckman, 2008) has confirmed four basic symptom dimensions ("forbidden thoughts," symmetry, cleaning, and hoarding), derived from factor analyses that are largely consistent across populations of all ages, temporally stable, have distinct neurobiological profiles, and are associated with differential treatment response (Leckman, Bloch, & King, 2009). There is evidence from family and segregation analyses that OCD symptom dimensions have distinct genetic correlates in clinical (Katerberg et al. 2010b) and nonclinical (Taberner et al., 2009; van Grootheest, Boomsma, Hettema, & Kendler, 2008) samples. Preliminary results from candidate gene studies suggest that OCD symptom dimensions may be associated with specific genes (for recent examples see Katerberg et al., 2009, 2010a).

Summary of genetic findings in OCD: The most replicated candidate gene in OCD is *SLC1A1*, although as is typical of studies of complex disorders the variant identified differs between studies. Most studies of this gene have suggested an association that is strongest in males. Despite conflicting findings including two meta-analyses that differ in their conclusions regarding the 5HTTLPR, *SLC6A4* remains of high interest. There is evidence that multiple variants of this gene, both within and outside of the promoter region, may be associated with OCD. There is evidence from one meta-analysis of a sex-specific association between *COMT* and OCD in males, however, this gene has been less extensively investigated compared with *SLC6A4*, and studies have been restricted to a single functional polymorphism. Positive findings have also been reported in more than one study for *HTR1B*, *HTR2A*, *DRD4*, and *BDNF*. *DLGAP3* remains of high interest given the *a priori* evidence from an animal knockout model of compulsive behavior, however, results to date have not provided strong evidence for involvement of this gene. Results from a GWAS, currently in progress, are eagerly anticipated and expected to provide new clues regarding the genetic basis of OCD. Further refinement of the OCD phenotype, including studies of specific OC symptom dimensions, may also facilitate discovery of risk genes.

Panic Disorder

Genome-wide studies: Genetic studies of PD have been conducted almost exclusively in adults, possibly due to the later age of onset for the condition. A total of 10 GWL scans have been reported for PD with the most promising peaks found within 13q, 14q, 4q, 22q, and 9q (reviewed in Maron, Hettema, & Shlik, 2010; Smoller, Gardner-Schuster, & Covino, 2008). The first published GWAS of any anxiety disorder was published for PD, based on genotyping approximately 500,000 SNPs in a sample of 200 cases and 200 controls from a Japanese population (Otowa et al., 2009). Although no SNPs met standard criteria for genome-wide significance, seven SNPs fell below a threshold of $p < 1 \times 10^{-6}$. None of the SNPs overlapped with genetic markers previously associated in candidate gene studies. The same group attempted to replicate 32 of their top SNPs in an independent sample of 558 Japanese patients and controls, resulting in no significant findings (Otowa et al., 2010). Both stages of this study were likely under-powered and further replication is needed using genome-wide assays in larger populations.

A second group of investigators recently reported on a second, much larger GWAS of PD (Erhardt et al., 2010). In combined analysis of a total of 909 PD cases and 915 controls from three independent samples, a two-SNP haplotype of the gene *TMEM132D* had a *p* value that fell just short of genome-wide significance ($p < 1.2 \times 10^{-7}$). The risk genotype for one of these two SNPs was furthermore found to be associated with expression in postmortem frontal cortex. In a final validation step the investigators also demonstrated association of *TMEM132D*

expression with anxiety in a mouse model, and association with a *TMEM132D* SNP in a cross-breeding study with high and low-anxiety mice (Erhardt et al.). In summary, this elegant series of experiments provided convergent evidence that *TMEM132D* may be an important risk gene in PD and other forms of anxiety. A large international consortium has reportedly already been formed in order to generate larger GWAS data sets (Maron et al., 2010) and it is hoped that this collaborative effort will lead to further identification of risk genes for this disorder.

Candidate gene association studies: According to one recent review, over 76 discrete candidate genes have been studied in PD (Hamilton, 2009). As in OCD, functional variants within *SLC6A4* and *COMT* have been the focus of intense interest and subjected to meta-analysis. The 5-HTTLPR does not appear to be associated with PD, as confirmed by meta-analysis of 10 studies (Blaya, Salum, Lima, Leistner-Segal, & Manfro, 2007) and more recent studies accounting for the triallelic nature of the 5HTTLPR (Strug et al., 2010). However, Strug et al. identified a three-SNP haplotype outside the promoter region that was associated with PD (OR = 1.7) in a case–control study that included rigorous control for population stratification. A follow-up study of this haplotype block identified a functional SNP (rs3813034) which may influence protein translation in a variety of ways mediated by its effects on polyadenylation signaling. This SNP was also found to be significantly associated with PD ($p < 0.007$) (Gyawali et al., 2010). It is interesting that a comprehensive survey of *SLC6A4* reveals a more complex and interesting story in PD compared with analysis of the 5HTTLPR alone, similar to recent findings in OCD.

COMT is a strong functional candidate for PD, and also a positional candidate since it lies close to the linkage peak in 22q noted above. The first meta-analysis of *COMT* found no consistent association with PD (Zintzaras & Sakelaridis, 2007). A subsequent, larger meta-analysis found no association in the total sample, but found that the Val (high activity) allele of rs4680 was associated with PD in Caucasians, particularly in females (Domschke, Deckert, O'donovan, & Glatt, 2007). The same group then went on to demonstrate, using functional MRI, increased activation in the right amygdala on exposure to fearful faces in PD patients with at least one Val allele (Domschke, Ohrmann, et al., 2008) (for more on fearful faces paradigm see below in Section "Endophenotypes").

Summary of genetic findings for panic disorder: GWL scans for PD have produced a number of significant peaks but with no overlap between studies. Candidate gene association studies have implicated a small number of candidate genes, with *COMT* being the most strongly supported according to multiple reports, an association which is likely sex-specific according to meta-analysis. Two GWA studies have produced interesting preliminary findings and more such studies, including combined analysis of data from different studies, are likely to yield other more strongly significant findings in future.

Other DSM-IV Anxiety Disorders

One group of investigators reported GWL scans for social phobia and simple (specific) phobia, based on small samples ascertained through PD probands. The strongest finding for social phobia was suggestive linkage to chromosome 16, a region containing the norepinephrine transporter protein *SLC6A2* (Gelernter, Page, Stein, & Woods, 2004). The strongest finding for the genome scan of simple phobia was significant linkage on chromosome 14q (Gelernter et al., 2003). Interestingly, an anxiety-related trait (open-field activity) in mice has been mapped to the equivalent chromosomal region (Flint et al., 1995). There are no consistently replicated candidate gene findings associated with anxiety disorders other than OCD and PD, although many findings from anxiety traits may be highly relevant for these conditions (see next section).

Candidate genes derived from rodent models: Rodent models of anxiety are well-developed and can suggest candidate genes for human studies. For example, a group of Finnish investigators tested 13

known human homologues of genes (208 SNPs in total) whose expression levels correlate with anxiety across strains of laboratory mice. Using this approach they identified three genes associated with different anxiety disorders including prosaposin (*PSAP*) in PD, *ALAD* (delta-aminolevulinate dehydratase) in social phobia, and *DYNLL2* (dynein light chain 2) in generalized anxiety disorder (Donner et al., 2008). These interesting findings require replication.

Trait Anxiety

In contrast to anxiety disorders analyzed as categorical variables, linkage and association studies of anxiety-related traits typically involve comparison of genotype groups based on a continuous trait score, either by comparing individuals in the extreme high end of the distribution with extreme-low individuals (extreme trait approach) or performing a quantitative trait analysis on the entire distribution. To date, most investigators wishing to examine anxiety-related traits have focused on Neuroticism (N). Neuroticism (Canli, 2008) is a broad trait reflecting a propensity towards negative affect which can lead to either anxiety or depression, with expression varying between individuals and at different time points within the same individual.

Linkage studies: Several GWL scans have been published for neuroticism based on large samples. Only one published report (Gillespie et al., 2008) has focused on neuroticism in adolescents. This study included 1,280 Australian adolescent twins (12–16 years of age) and their siblings assessed using the Junior Eysenck Personality Questionnaire. The highest linkage peaks in this study were on chromosomes 16 and 19, although these results fell short of the accepted threshold for significant linkage. The overlap between GWL studies has been greater than that seen in OCD or PD, and for some of the linkage peaks there is convergent evidence from quantitative trait loci for anxiety behaviors in mice. Convergence of human findings with genes implicated in mouse models may be a particularly powerful approach for trait anxiety, for which excellent models exist. As an example of this convergence between human and animal studies, GWL studies have identified suggestive or significant linkage peaks on Chromosome 14q for neuroticism (Wray, Middeldorp, et al., 2008) and other broad anxiety traits (Kaabi et al., 2006; Middeldorp et al., 2008) in humans; and the homologous genomic region has been linked with anxiety behaviors in mice. The other most promising and replicated findings for linkage scans include peaks on 10p (Fullerton et al., 2003; Wray, Middeldorp, et al.), 12q (Fullerton et al.; Kuo et al., 2007) (strongest results in females in both cases), and 18q (Kuo et al.; Wray, Middeldorp, et al.).

Genome-wide association studies: There have been three published GWAS studies of trait anxiety. The first study of neuroticism (Shifman et al., 2008) employed DNA pooling and a multi-stage design. DNA pooling is a cost-effective technique in which equal amounts of DNA are pooled from each participant and then pools are compared with regard to allele frequencies. In the first stage of this study 2,000 individuals were selected based on the extremes of age and sex-corrected *N* scores from a general population cohort of over 88,000 adults from Southwest England. High and low *N*-scoring individuals were then compared for allele frequencies of approximately 450,000 SNPs. Although no SNP met genome-wide significant thresholds, they selected 19 top SNPs for genotyping in an independent sample of 1,534 individuals with extreme *N* scores (drawn from their original population). Only one SNP, lying within the gene phosphodiesterase 4D (*PDE4D*), was replicated in this second sample. However, the same SNP was not replicated in a third sample of 2,199 individuals (Shifman et al.). In a second GWAS of neuroticism (van den Oord et al., 2008), 1,227 US individuals were genotyped for a similar number of SNPs (420,000). Again, no results reached genome-wide significance but the top 63 SNPs were genotyped in a replication sample of 1,880 German individuals. Using this combined approach, the most promising finding was for the gene *MAMDC1*, which is expressed in the neocortex and pons and is thought

to be involved in neuronal migration. The most recent GWAS of neuroticism involved 3,972 individuals within a genetically isolated population in Sardinia (Terracciano et al., 2010). This group examined five major personality dimensions including neuroticism. The strongest finding for neuroticism (although falling short of genome-wide significance) was a SNP in Intron 1 of the gene synaptosomal-associated protein of 25 kDa (*SNAP25*) which is a good functional candidate gene and has been previously associated with ADHD and other psychiatric disorders.

Candidate gene association studies: As in other anxiety disorders, both *SLC6A4* and *COMT* have been repeatedly studied for possible association with anxiety traits. A widely cited association between the short (*S*, low-activity) allele of the 5HTTLPR variant and neuroticism was first reported by Lesch et al. (1996). Two meta-analyses (total of over 5,000 subjects) found a highly significant association between the *S* allele of 5HTTLPR and neuroticism but not harm avoidance or other anxiety traits, indicating that the choice of inventory can produce discrepant results (Schinka, Busch, & Robichaux-Keene, 2004; Sen, Burmeister, & Ghosh, 2004). A study using a child/adolescent version of a harm avoidance scale was similarly unable to demonstrate an association with 5-HTLPR (Becker, El-Faddagh, Schmidt, & Laucht, 2007). Although the association between 5HTTLPR and neuroticism is statistically significant and robust, the effect size is small (e.g., $d=0.23$ (Schinka et al.)). This small effect size in turn suggests that there are likely to be multiple other unexplained genetic and nongenetic factors involved in the development of neuroticism, a common scenario with complex genetic traits that has been labelled the "missing heritability" problem (Manolio et al., 2009).

In a methodologically rigorous study, Hettema and colleagues selected a total of 1,128 twins scoring at the extremes of scores on a latent genetic risk factor (Hettema et al., 2006) shared by neuroticism, major depression, and anxiety disorders (GAD, PD, agoraphobia, and social phobia). They then genotyped *COMT* markers using a two-stage design, in which initial genotyping of one third of the samples (Stage 1) was followed by genotyping of the most promising markers in the remainder of the sample in Stage 2. Combined analysis of Stage 1 and Stage 2 revealed a strong, female-specific association between a haplotype containing the Valallele of rs4680 and another SNP (rs165599, $p=2\times10^{-5}$). Using a similar design on a large sample, an Australian group of investigators found no association between *COMT* variants and neuroticism (Wray, James, et al., 2008), and earlier smaller studies identified weak associations between *COMT* and neuroticism (Eley, Tahir, et al., 2003; Stein, Fallin, Schork, & Gelernter, 2005) or other anxiety-related traits (Enoch, Xu, Ferro, Harris, & Goldman, 2003). A meta-analysis might help clarify these discrepant findings regarding *COMT* variation and trait anxiety.

Childhood anxiety traits: Behavioral inhibition (BI) is a temperamental style first identifiable in infancy characterized by fear and withdrawal in response to unfamiliar settings, people, or objects. BI is measured in a standardized laboratory paradigm based on ratings by independent observers and is therefore a more objective measurement of behavior than self-report. Longitudinal studies have demonstrated that preschool children with BI are at elevated risk of developing anxiety disorders in later life, particularly social phobia (Hirshfeld-Becker et al., 2008; Schwartz, Snidman, & Kagan, 1999); and therefore BI represents an excellent intermediate phenotype for social phobia and childhood anxiety in general. Shyness, a personality trait measure by self- or parent-report rather than in the laboratory, overlaps with BI and has also been the subject of genetic studies.

The gene *RGS2* (regulator of G-protein signaling 2) was suggested as a candidate for human anxiety since it lies within a quantitative trait locus for anxiety in mice (Yalcin et al., 2004). Using a family-based design, Smoller et al., 2008 identified associations between nine *RGS2* SNPs and BI in children. Furthermore, a haplotype block spanning these SNPs was also significantly associated with BI ($p=3\times10^{-5}$). Four of these nine SNPs also showed association (either individually or when considered as a haplotype) with

the social anxiety-related trait of introversion in an independent sample of adults. One SNP (rs4606), associated with both BI and introversion and previously found to alter gene expression, accounted for 15% of variance in amygdala activation and 10–15% of variance in insular cortex activation on functional MRI during a facial emotional processing task. SNP rs1081152 was also associated with left insular cortex and amygdala activation. Taken together, these findings suggest that genetic variation leads to decreased expression of *RGS2*, which in turn leads to increased reactivity of limbic structures responsible for modulating anxiety.

Like *RGS2*, other candidate genes for BI have been suggested by studies of anxiety in laboratory rodents. Testing four such candidate genes in a small sample of children characterized according to BI, Smoller and colleagues identified a nominal association between BI and variation in the gene encoding the 65 kDa isoform of glutamic acid decarboxylase (*GAD2*), an enzyme which synthesizes GABA from glutamate (Smoller et al., 2001). This finding is in contrast to another study in which the phenotype was a latent trait underlying anxiety disorders, neuroticism, and depression (described above). In the latter study there was no association between *GAD2* and trait anxiety, although an association was identified with variants in the related gene *GAD1* which was replicated in a second stage (Hettema et al., 2006). Other candidate genes have also been examined for association with behavioral inhibition or shyness with mixed results, including *SLC6A4* (Arbelle et al., 2003) and corticotrophin-releasing hormone (*CRH*) (Smoller et al., 2003, 2005).

Endophenotypes

One novel approach to studying genetics of anxiety disorders and traits has been the study of endophenotypes. Theoretical predictions have suggested that endophenotypes will be more etiologically homogeneous and more closely linked to the action of genes than clinical diagnostic categories (Gottesman & Gould, 2003), however, this assumption has yet to be proven and has been criticized by some authors (Flint & Munafo, 2007). A strict definition of endophenotype requires that such phenotypes meet a number of criteria including heritability, state-independence, co-segregation within families, and greater frequency in unaffected family members compared with the general population (Gottesman & Gould). It has been suggested that the classic endophenotype definition is too stringent for certain traits (Meyer-Lindenberg & Weinberger, 2006). For example, there is a high cost to conducting imaging studies on a sufficient number of family members to demonstrate heritability and therefore most imaging phenotypes have not been thoroughly investigated for heritability and co-segregation within families. Even without established heritability, imaging phenotypes have been successfully used to explore mechanisms of illness (Meyer-Lindenberg & Weinberger) through in vivo study of individuals characterized according to genotype.

Endophenotypes for anxiety have been suggested from a number of sources including cognitive tasks, physiological measures, and neuroimaging (Domschke & Dannlowski, 2009). For example, facial emotional processing tasks reveal attentional biases towards threatening stimuli, and fMRI performed during such tasks has consistently implicated the amygdala (Arnold, Hanna, & Rosenberg, 2010). Beginning with Hariri et al. (2002), a number of studies have demonstrated an association between the *S* allele of the 5HTTLPR in *SLC6A4* and amygdala activation during viewing of emotional faces. The relationship between the 5HTTLPR and amygdala activation has now been confirmed in a meta-analysis of healthy, depressed, and anxious adults that suggested that this variant may account for up to 10% of variance in this fMRI phenotype (Munafo, Brown, & Hariri, 2008), an effect size much larger than that typically seen for gene effects on behavioral traits. This finding has also been replicated in healthy adolescents, although interestingly the direction of association in depressed and anxious adolescents is opposite to

that seen in healthy adolescents or adults (*S* allele associated with under-activation as opposed to increased activation of the amygdala (Lau et al., 2009)), suggesting possible differences depending on developmental stage and presence of psychopathology. These large effect sizes support the theoretical proposition that brain processes visualized using magnetic resonance imaging are closer to the expression of genes compared with behavior, are likely influenced by fewer genes of larger effects, and are therefore better candidates for gene mapping (Hariri, Drabant, & Weinberger, 2006). As noted above, variants of *RGS2* have also been associated with amygdala activation (Smoller et al., 2008).

All the aforementioned studies of amygdala activation have been based on a candidate gene approach. Recently, however, the first published GWAS of an imaging phenotype in child psychiatry (Liu et al., 2010) identified a nominally significant association between right amygdala activation and a single SNP within the gene *DOK5* in a small sample of adolescents with bipolar disorder compared with controls, although this finding fell short of genome-wide significance. Future GWAS studies of amygdala activation in children with anxiety disorders are sure to follow.

Other endophenotypes that have been examined in non-OCD anxiety disorders include: extinction learning (Lonsdorf et al., 2009; Soliman et al., 2010), acoustic startle reflex (Brocke et al., 2006), evoked response potentials during error processing (Althaus et al., 2009), and blushing propensity (Domschke, Stevens, et al., 2008).

Endophenotypes in OCD: A group at Cambridge University were the first to report that adult patients and unaffected relatives showed delayed response inhibition on the Stop-Signal task (SST) compared to controls (Chamberlain et al., 2007). Impaired SST performance was associated with reduced gray matter in orbitofrontal and right inferior frontal regions and increased gray matter in cingulate, parietal, and striatal regions (Menzies et al., 2007). The same investigators found reduced activation of cortical regions, such as lateral orbitofrontal cortex, during reversal learning in patients and unaffected relatives (Chamberlain et al., 2008). However, there have been no published molecular genetic studies based on these promising endophenotypes.

In OCD, we have reported an association between glutamate system genes and brain volume in the following regions of interest previously implicated in OCD: thalamus, orbitofrontal cortex, and anterior cingulate cortex (Arnold, Macmaster, Hanna, et al., 2009). Based on MRS in medication-naive children and adolescents with OCD, we identified an association between decreased glutamate concentration in the anterior cingulate cortex and a promoter region variant of the gene glutamate receptor ionotropic *N*-methyl-D-asparate subunit B (GRIN2B) (Arnold, Macmaster, Richter, et al., 2009). In all cases, the putative risk variant of the gene (based on candidate gene studies of OCD) was associated in the expected direction with the imaging phenotype based on previous OCD versus control comparisons.

Gene by Environment Interactions

Twin studies suggest that environmental factors play an important role in the etiology of anxiety disorders. Similar to the literature on imaging genetics, most studies of gene–environment interaction for anxiety have focused on *SLC6A4* with more limited evidence from other genes (e.g., *BDNF* (Gatt et al., 2009)). In a landmark study, Caspi et al. (2003) showed that the *S* allele of 5-HTTLPR only conferred risk to depression in the presence of negative life events. Although this finding has been replicated many times, it has recently been called into question with a meta-analysis by Risch et al. (2009) which did not support the association. However, this meta-analysis has been criticized on methodological grounds (Rutter, 2010). Interestingly, as pointed out by Uher and McGuffin (2010), many non- or partial replications of this effect come from adolescent studies, with studies of adults more consistently supporting the gene by environment interaction. There have been studies in which a gene by environment interaction was found with the

high-expressing *L* (or *L (A)*) allele rather than the *S* allele (Laucht et al., 2009). For example, in one study (Veletza et al., 2009), individuals carrying the *S* allele that were exposed to serious past adversities scored higher on a variety of psychopathology measures, including anxiety and phobic anxiety; whereas individuals not exposed to serious past adversities, individuals homozygous for the *L* allele had increased levels of depression, anxiety, and phobic anxiety. This finding was interpreted as reflecting vulnerability to more "endogenous" psychopathological tendencies among *L/L* individuals compared to the more environmentally dependent phenotype displayed by *S* carriers. Finally, in a study of behavioral inhibition, children homozygous for the *S* allele of the 5HTTLPR that had experienced low social support were at increased risk for exhibiting BI in middle childhood (Fox et al., 2005).

One of the main differences between studies of gene–environment interactions has been the way that life events or stressors were measured. Using an innovative approach, Gunthert et al. (2007) examined the relationship between the triallelic 5HTTLPR polymorphism and anxiety measures based on multiple daily recordings from each individual. They found that mood reactivity was significantly moderated by genotype, even after controlling for neuroticism. Specifically, individuals possessing the *S* or *L (G)* alleles reported increased anxiety on days with more stressors compared to *L (A)* homozygotes.

In summary, there is evidence for significant gene–environment interaction involving *SLC6A4* and anxiety, but the relationship is complex and may depend on developmental stage and the way in which life events are measured. Given the clinical relevance of early life events in development of child anxiety, validating these findings of gene by environment interaction involving the 5-HTTLPR remains of high interest, and further work is needed to determine if gene by environment effects apply to other genes.

Gene–environment interactions and PTSD: PTSD is an anxiety disorder for which major life trauma is not just a risk factor but a core clinical criterion, and therefore it is not surprising that researchers in this area have focused on gene by environment interactions. A number of studies have focused on *SLC6A4*, but the findings have been somewhat contradictory. For example, two recent studies found an interaction between the low-expressing *S* allele of the 5HTTLPR and environmental events associated with development of PTSD (Kilpatrick et al., 2007; Kolassa et al., 2010), whereas another study found the high-expressing *L(A)* allele to be associated with development of PTSD (Xie et al., 2009). The gene *FKBP5* is thought to impact glucocorticoid receptor (GR) sensitivity, making it a good candidate for PTSD in which abnormalities of the HPA axis have been repeatedly demonstrated. Four *FKBP5* SNPs (rs9296158, rs3800373, rs1360780, and rs9470080) significantly interacted with child abuse severity to predict the level of adult PTSD symptoms (Binder et al., 2008). As no main effect was found when looking at the SNPs alone and no significant interaction between SNPs and non-child abuse, the authors suggest that the gene–environment interaction observed may be specific to childhood trauma.

Pharmacogenetics

The study of the influence of genetic variation on drug response is known as pharmacogenetics. Limited evidence suggests that response to selective serotonin reuptake inhibitors (SSRIs) in adults is associated with 5HTTLPR variation (Perna, Favaron, Di Bella, Bussi, & Bellodi, 2005; Stein, Seedat, & Gelernter, 2006). Kwon et al. (2009) identified an association between *SLC1A1* and atypical antipsychotic-induced obsessive–compulsive symptoms. As more genome-wide association data become available for anxiety disorder samples, genome-wide studies of drug response will become possible. Although little is known about genetics of drug response in anxiety disorders (and all studies to date have been in adults), more findings are likely to accumulate in the coming years, holding out the prospect of identifying genetic predictors that will enable better tailoring of medications to individual patients.

Conclusions and Future Directions

The rapid pace of technological advance is expected to revolutionize molecular genetic studies in the near future. Currently, the emphasis is on GWAS. Research efforts will increasingly shift to targeted re-sequencing and eventually whole genome sequencing approaches as the cost of these technologies become affordable to more investigators. As investigators identify actual causal variants, an array of techniques including in vitro studies, gene expression, and mouse models will be employed to elucidate the functional effects of these alterations in DNA sequence. Current SNP-based strategies will be complemented by studies which incorporate copy number variation and epigenetic approaches (Petronis, 2010) which will reveal different biological mechanisms underlying anxiety disorders.

Endophenotypes will be increasingly emphasized in future studies of anxiety. Brain imaging abnormalities represent particularly promising phenotypes for genetic studies. Future studies will also benefit from increasingly sophisticated approaches to modeling gene–gene and gene–environment interaction. Although it may take many years to fully elucidate how genes lead to pathological anxiety, it is thought that the genetics of drug response may be somewhat less complex and will therefore result in practical applications in the relatively near future (Mrazek, 2010). The genetic variants involved in drug response are not necessarily the same as those involved in pathogenesis of pathological anxiety, and therefore more studies specifically targeting the pharmacogenetics of anxiety are needed.

In summary, future knowledge regarding the genetic determinants of anxiety will likely be derived from advancing technological applications, examination of neuroimaging profiles and other endophenotypes, and increasingly sophisticated modeling of gene–gene and gene–environment interactions. Pharmacogenetics is a field of untapped potential in anxiety at this point in time. There are now numerous convergent and exciting findings emerging, which, given the rapid acceleration in our knowledge of the human genome, will likely result in a more definitive understanding of the genetic roots of these complex conditions in the near future.

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Neuropsychological Considerations in Child and Adolescent Anxiety

6

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Anxiety is characterized by feelings of apprehension, persistent worry, and frequent somatic complaints (American Psychiatric Association, 2000). Symptoms present along a continuum from mild fear when a child is separated from his or her parents, to incapacitating flashbacks of previous traumatic events. With a wide range of symptoms and presentations, it is not surprising that the relationship between behavioral manifestations of anxiety and neuropsychological functioning is very complex.

Emotional and affective variables can strongly influence neuropsychological assessment results, interpretation, and diagnosis. For example, some children show neurologically based emotional dysregulation following head injury or tumor resection that can be misinterpreted as personality-based emotional lability. Similarly, emotional adjustment reactions to newly acquired disability or longstanding chronic illness can manifest as symptoms of more severe psychopathology; premorbid emotional difficulties can either enhance or mask neuropsychological symptom presentation; and, performance/evaluation anxiety can significantly depress neuropsychological test scores leading to incorrect diagnoses (Strauss, Sherman, & Spreen 2006). It is, therefore, important that evaluators assessing the cognitive or academic functioning of a child or adolescent understand the potential influence of emotional and affective variables on assessment results and appropriately consider these variables in diagnostic case formulation.

This chapter provides a broad overview of the interactions between neuropsychology and symptoms of child and adolescent anxiety, including the contribution of anxiety to neuropsychological test performance, major brain areas involved, and links between neurologic insult and anxious behavior. We discuss the neuropsychological presentations of the most common anxiety disorders and end with a review of how technological advances in structural and functional neuroimaging have bolstered our understanding of brain–behavior relationships associated with anxiety.

The Role of Anxiety on Neuropsychological Test Performance

Test anxiety is a multifaceted construct consisting of an individual's physiological, cognitive, and behavioral responses that stimulate negative feelings about an evaluation (Nicaise, 1995). Such anxiety during test performance is common across many cultures during evaluations in both academic and clinical settings. Early studies of test-related anxiety conducted by Sarason and Mandler (1952) showed higher scores on

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_6,

measures of intelligence in individuals with low test anxiety relative to their high-anxiety counterparts. A large number of subsequent studies consistently indicate poorer performance in high test-anxious individuals across a variety of outcome measures, including on classroom-based tests, standardized achievement tests, and measures of self-motivation and self-evaluation (e.g., Chappell et al., 2005; Everson, Millsap, & Rodriguez, 1991).

Not surprisingly, individuals with heightened levels of test anxiety perform poorly on tests commonly used in both child/adolescent and adult neuropsychology, such as finger tapping (Chavez, Trautt, Brandon, & Steyaert, 1983), digit span (Firetto, 1971), block design (Buckelew & Hannay, 1986), verbal fluency (Buckelew & Hannay, 1986), the Stroop test (Batchelor, Harvey, & Bryant, 1995), the Wechsler Memory Scales (Cannon, 1999), and scales of intelligence (Oostdam & Meijer, 2003). A possible contributing factor to reduced performance on these tests is heightened anxiety due to timing of performance, as many of these tests (e.g., finger tapping, block design) are timed. We should also note additional research that suggests test anxiety does not reliably affect performance on some neuropsychological tests such as the Trail Making Test Parts A and B and Digit Symbol (Chavez et al., 1983).

Due to its potential for suppressing effects on neuropsychological test performance, test anxiety may contribute to false-positive diagnoses or invalid inferences made from neuropsychological test results (Tramontana, Hooper, Watts-English, Ellison, & Bethea, 2009). For example, neurologically healthy children with an "anxious-depression" presentation show deficits in the executive skills of sequencing, task-switching, and problem solving (Emerson, Mollet, & Harrison, 2005). Similarly, children with high levels of test-related anxiety show more frequent negative self-evaluations and off-task thoughts that lead to poorer cognitive test performance than children with low levels of test anxiety (Bodas & Ollendick, 2005). Such patterns of performance may mimic possible cognitive deficits in a child or adolescent with attention deficit hyperactivity disorder (AD/HD), traumatic brain injury (TBI), or other neurological illness; incorrect classification of abilities may lead to the inappropriate provision of expensive services instead of more appropriate treatment of the anxiety-related symptoms.

Interactions Between Neurological Insult and Anxiety

A growing number of studies report an interaction between neurological insult or disease, anxiety, and neuropsychological functioning. Recent work in adults with brain injury suggests anxiety and general "negative affect" have compounding negative effects on cognitive performance (Larson, Kaufman, Kellison, Schmalfuss, & Perlstein, 2009). That is, disproportionate decrements in cognitive functioning are present in survivors of TBI with increased levels of anxiety and negative affect, relative to their matched TBI counterparts whose anxiety and negative affect are well regulated. Similarly, Ponsford, Draper, and Schonberger (2008) report that individuals with poor outcomes 10 years after a TBI showed considerably higher scores on a measure of anxiety than those with good outcomes. While causation cannot be inferred from the correlational data presented in these studies, the authors suggest that the increased levels of anxiety are associated with attempts to cope amidst considerable cognitive disability. However, it is likely that the relationship between anxiety and cognitive functioning after TBI is reciprocal, rather than unidirectional.

In children and adolescents, increased levels of anxiety are common sequelae of neurological insult or dysfunction (e.g., Bloom et al., 2001). Childhood survivors of TBI show increases relative to preinjury estimates in many symptoms of anxiety, including hyper-vigilance, separation anxiety, specific phobias, and obsessive–compulsive symptoms (Vasa et al., 2002). Similarly, children and adolescents with epilepsy show psychiatric comorbidity rates as high as 40–50%, with anxiety disorders accounting for the highest rates of diagnosis (Caplan et al., 2005).

Child and Adolescent Anxiety Disorders from a Neuropsychological Perspective

Neuropsychologists have historically focused on differentiating organic, or "brain-based", cognitive disturbances from those that are more functional, or "psychosocial", in origin. Research over the last 20 years, however, disputes this dichotomy – particularly in relation to psychiatric disorders. Estimates of neuropsychological impairments in children and adolescents with psychiatric disorders range from less than 5 to 60% (Hertzig, 1982; Tramontana et al., 2009; Tramontana, Sherrets, & Golden, 1980), with increased duration since diagnosis associated with more severe neuropsychological impairments (see Teeter et al., 2009 for review). A considerable number of studies show psychopathology-related structural and functional abnormalities on neuroimaging and neurochemical studies (see Tramontana et al., 2009). Given the potential for neuropsychological changes associated with psychiatric disorders, as well as the distinct contributions of different neural systems to anxiety disorder presentation, research is beginning to focus on distinct neuropsychological profiles that differentiate psychiatric disorders. This research, however, is in its infancy and stems primarily from the experimental psychology literature.

Despite recent advances in the specificity of neuropsychological profiles associated with different disorders, the brain regions implicated in anxiety disorders may in fact be relatively disorder nonspecific, due to the observation that many of the same regions show abnormalities across the various anxiety disorders (Mathew, Coplan, & Gorman, 2001). Indeed, a confluence of research implicates structures in the medial temporal lobes, including the amygdala and hippocampus, as well as the anterior cingulate cortex, the insular cortex, and the orbitofrontal and prefrontal cortices in dysfunction associated with several anxiety disorders (Damsa, Kosel, & Moussally, 2008). The specific brain areas contributing to anxiety-related dysfunction are primarily being researched using structural and functional neuroimaging techniques, but can also be examined using neuropsychological tests with known structure–function relationships (e.g., the hippocampus and tests of list learning or paragraph recall). In the following section, we present emerging findings about the unique neurocognitive profiles of different child and adolescent anxiety disorders and the areas of the brain hypothesized to be involved in specific anxiety disorder presentation. In some instances, because research in children and adolescents in the area is sparse, we refer to findings from the adult literature to make general inferences.

Obsessive–Compulsive Disorder (OCD)

A growing body of evidence suggests that OCD is associated with dysfunction of the frontal lobes and basal ganglia, particularly the areas of the striatum (Cottraux & Gerard, 1998; Greisberg & McKay, 2003; Tramontana et al., 2009). *Due to these primarily fronto-striatal abnormalities*, the majority of OCD-related neuropsychology research has focused on executive functions. For example, Shin et al. (2008) reported that, relative to healthy controls, children with OCD made significantly more errors and completed fewer categories on the Wisconsin Card Sorting Test (WCST; Heaton, 1981), a measure of problem solving, and showed higher levels of impairment on perceptual-organization tasks that require organization, planning, and rapid completion (e.g., Block Design and Object Assembly subtests of the Wechsler Intelligence Scale for Children-Third Edition; WISC-III; Wechsler, 2003). In addition, children with OCD showed some organizational difficulties when copying the Rey-Osterreith Complex Figure (ROCF; Rey, 1941), although the differences between children with OCD and controls did not reach statistical significance. These findings of poor planning, problem solving, and organization, coupled with intact performance on tests of memory, attention and concentration, and verbal abilities, are consistent with the hypothesis of fronto-striatal dysfunction in children with OCD (Shin et al., 2008).

Earlier studies of children and adolescents with OCD report mixed findings. Behar et al. (1984) used computerized tomography (CT) scan results in conjunction with neuropsychological test findings to show adolescents with OCD have visuospatial organization difficulties similar to individuals with frontal lobe lesions, including poor visuospatial rotation ability and poor ability to learn rules in order to appropriately navigate mazes. Beers et al. (1999) administered an extensive neuropsychological test battery, including measures of executive functions, planning, response inhibition, verbal fluency, manual dexterity, and memory, to children with OCD and healthy controls and found no statistically reliable differences between groups on any measures. Thus, while there is some research pointing to difficulties in the fronto-striatal functions of planning, organizing, and problem solving in children with OCD, continued research in this area is necessary to elucidate a more precise neurocognitive profile.

Research on adults with OCD, however, shows a consistent pattern of deficits in fronto-striatal executive functions, particularly in utilization of organization strategies, as well as some evidence for memory impairments (Greisberg & McKay, 2003). The pattern of deficits in executive skills is demonstrated in multiple studies using a variety of executive tasks, including tests of planning, problem solving, and set shifting (Gambini, Abbruzzese, & Scarone, 1993; Mataix-Cols, Jungque, & Sanchez-Turet, 1999; Veale, Sahakian, Owen, & Marks, 1996). Each of these studies reports OCD-related impairments in the ability to shift set, organize and plan, and quickly solve problems.

Memory functions in adult OCD, however, are more variable. The preponderance of research suggests that individuals with OCD experience memory impairments; however, these impairments are primarily due to insufficient organization strategies to effectively encode and retrieve the presented information (Greisberg & McKay, 2003). For example, Savage et al. (2000) gave individuals with OCD and healthy control participants measures of both verbal and nonverbal memory, including the ROCF and the California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987). Results indicated that adults with OCD were impaired on both the verbal and nonverbal memory measures. Importantly, the reported memory impairments were mediated by organizational strategy. That is, those individuals who used poor organizational strategies during encoding of the memory information were most likely to show subsequent memory impairments. Of note, the individuals with OCD recalled a significantly higher proportion of words during the semantically cued recall portion of the CVLT, indicating that when an external structure is provided memory performance improves. Thus, while more information is clearly needed in this area, the OCD-related memory impairments are likely related to executive difficulties, rather than direct impairments to learning and memory systems.

Of particular import in the discussion of neuropsychological functioning in individuals with OCD, particularly with regard to executive functioning vs. learning/memory impairments, is the heterogeneity in OCD-symptom presentation. It is quite possible that memory or executive difficulties could differ depending on the primary presenting symptoms (e.g., hoarding subtype vs. contamination). Future research examining the neuropsychological profiles of specific subtypes of OCD is a logical next step.

Posttraumatic Stress Disorder (PTSD)

PTSD is consistently being linked to deficits in the medial temporal lobes, particularly the amygdala and hippocampus, the prefrontal cortex, and some white matter structures, including the corpus callosum, in children (Jackowski, de Araujo, de Lacerda, de Jusus Mari, & Kaufman, 2009). Thus, similar to the cognitive profile of individuals with OCD, children with PTSD often show difficulties in executive functioning, learning/memory, and attention. For example, Beers and De Bellis (2002) studied neuropsychological functioning in maltreated children diagnosed with PTSD. Children with PTSD showed decreased performance relative to controls on the interference portion of the Stroop Color-Word

Test (Stroop, 1935), the WCST, and measures of verbal fluency (Benton & Hamsher, 1976). Children with PTSD also performed more poorly than demographically matched children on measures of attention, including Digit Vigilance (Lewis & Rennick, 1979) and the color/word portion of the Stroop test (Beers & De Bellis, 2002). These findings are consistent with neuroimaging studies reporting prefrontal cortex abnormalities in children with PTSD. Of note, the children with PTSD did not significantly differ from controls on the broad constructs of language, visual–spatial abilities, and psychomotor skills. However, some differences between groups were noted on specific tests of memory such as the California Verbal Learning Test for Children (CVLT-C; Delis, Kramer, Kaplan, & Ober, 1994), where children with PTSD performed worse than controls on both the short and long delay portions.

Consistent with these findings, two additional studies in children and adolescents report PTSD-related impairments in learning and memory. Moradi et al. (1999) showed decreased overall and prospective memory performance relative to psychiatrically healthy controls on the Rivermead Behavioral Memory Test (Wilson, Cockburn, & Baddeley, 1985). More specifically, children with PTSD had significantly lower scores on the immediate story memory, delayed story memory, and total memory profiles. Yasik, Saigh, Oberfield, & Halamandaris (2007) compared learning and memory scores on the Wide Range Assessment of Memory and Learning (WRAML; Adams & Sheslow, 1990) in children exposed to trauma and diagnosed with PTSD, children exposed to trauma and not diagnosed with PTSD, and nontraumatized control children. Children diagnosed with PTSD showed considerably worse performance than the nontraumatized control children on the Learning, General Memory, and Verbal Memory indices of the WRAML. In contrast, children exposed to trauma with and without PTSD only differed on measures of verbal memory – suggesting such verbal memory impairments are specific to PTSD, rather than the result of general exposure to traumatic events.

Decreased scores on measures of intelligence are also present in children with PTSD, and it has been proposed that intelligence impairments may, in part, be the consequence of chronic child abuse experiences (De Bellis et al., 1999). Taken together with the difficulties in memory and executive functions, the observed cognitive declines associated with PTSD are an important cause for concern because failure to develop cognitive skills may result in pervasive difficulties as these children progress through life.

Social Phobia (Social Anxiety Disorder)

Recent theories suggest that social anxiety disorder might be reconceptualized as a chronic neurodevelopmental illness, rather than an episodic de novo adult disorder (Mathew et al., 2001). As such, early identification and intervention of social anxiety disorder are important, with better understanding of the affected brain regions being quite beneficial toward that end. Regions of the medial temporal lobe, basal ganglia, and orbitofrontal cortex are implicated in the neural instantiation of social anxiety (Damsa et al., 2008). Given this, it is not surprising that children with social anxiety demonstrate deficits and delays in a number of cognitive domains. For example, a recent study by Kirstensen and Torgersen (2008) investigated the contribution of neurodevelopmental deficits and delays in language and motor function to social anxiety symptoms in children. Verbal ability, as measured by the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999), was significantly lower in children with social anxiety disorder as compared to children with no disorder; there were no between-group differences in performance ability. The children with social anxiety disorder also showed poorer performance in motor skills. Maternal report of developmental language or motor delay generally corroborated the results of the standardized testing, indicating that the socially anxious children were more often reported by their mothers to be delayed compared to children with no disorder. Nonetheless, it is unclear whether these difficulties contribute to

the presence of social anxiety, whether they are partly the result of the disorder, or whether the cognitive deficits and the social anxiety have a common underlying cause.

Children with social anxiety may also present with memory complaints. Vasa et al. (2007) reported that children with a diagnosis of social phobia displayed deficits in visual, but not verbal, memory after controlling for intelligence, symptoms of separation anxiety disorder, and symptoms of generalized anxiety disorder (GAD). As discussed previously, this may be related to medial temporal lobe dysfunction in social anxiety, such that dysfunction in this region may be associated in a parallel fashion with both memory deficits and anxiety disorders. Psychosocial stressors may also disproportionately affect the cognitive performance of individuals with social phobia. For example, a study of adults with social phobia showed greater levels of impairment relative to healthy controls during the stressful experience of being videotaped on measures of executive function and problem solving, spatial memory, and the executive skills of working memory and set shifting; however, verbal attention and working memory performance were preserved (Graver & White, 2007). Although this effect has not been examined in children to date, it is expected that they would demonstrate a similar pattern of performance.

Generalized Anxiety Disorder (GAD)

The superior temporal gyrus, frontal lobes, and temporal lobe structures, most notably the amygdala, are strong contributors to neuropsychological dysfunction associated with pediatric GAD (De Bellis et al., 2000; Krain et al., 2008; Krain et al., 2006). The majority of published findings implicating a specific cognitive profile for children with GAD are based on experimental research paradigms, rather than describing the profiles using neuropsychological test batteries that are commonly used in clinical settings. For example, Dalgleish et al. (2003) used an experimental paradigm known as the dot-probe test, in which emotionally salient words (either threat-related words or depression-related words) were paired with neutral words. These were presented to the participants on a computer screen one pair at a time. The participants were informed that some word pairs would be followed by a small dot, and they were instructed to respond as quickly as possible to this dot with a button press. Children with GAD demonstrated an attentional bias toward threat-related material relative to depression-related material. The study also revealed no significant differences between anxious and nonanxious children for level of vocabulary or reading skills.

While there are few reports of neuropsychological performance in children with GAD, the adult literature helps to understand possible cognitive difficulties these children might face in adulthood. For example, one study found that 19% of adults diagnosed with GAD are cognitively impaired in at least one neuropsychological domain, as compared with 3.6% in the general population (Gualtieri & Morgan, 2008). The most prominent domain of cognitive impairment in individuals with GAD is complex attention, as measured by the Stroop test, Shifting Attention Test (SAT; Gualtieri & Morgan, 2008), and Continuous Performance Test (CPT; Gualtieri & Morgan, 2008). Mantella et al. (2007) found that elderly individuals with GAD performed worse than their normal counterparts on short-term and delayed memory. They also showed greater difficulties on set-shifting tasks (i.e., Trail Making Test Part B). However, another recent study found no difference in memory performance between children with and without GAD, though this null result may have been due to low statistical power (Vasa et al., 2007). There is clearly need for expanded research regarding the cognitive functioning of children and adolescents with GAD, before making inferences about GAD-related cognitive changes.

Other Anxiety Disorders

The existing literature indicates that brain regions implicated in other anxiety disorders are similar to those already described. Examples include increased amygdala, anterior cingulate cortex,

and insular cortex activation in specific phobia (Goossens, Schruers, Peeters, Griez, & Sunaert, 2006) and increased amygdala and prefrontal cortex activation in panic disorders (Domschke et al., 2008). In addition, a gray matter deficit in the anterior cingulate cortex and gray matter increase in left insular cortex and left superior temporal gyrus are reported for panic disorders (Uchida et al., 2008). As noted above, research to date generally indicates brain regions implicated in anxiety disorders are relatively disorder nonspecific because many of the same regions show abnormalities across the various anxiety disorders (Mathew et al., 2001). Nevertheless, it is possible that there may be slight neurobiological differences that are disorder specific.

The neuropsychological profiles of individuals (children, adolescents, or adults) diagnosed with other anxiety disorders (including specific phobias, separation anxiety, and panic disorder) are not well characterized. This could be due to lack of observed cognitive impairment in these disorders, lower base rates in the general population, or the confound of common comorbid diagnoses, such as GAD, among the anxiety disorders. For example, a study by Pine et al. (1999) explicitly stated that they did not include individuals with specific phobias in their study of psychopathology and neuropsychological abilities due to low rates of impairment.

The Role of Neuroimaging in the Assessment and Treatment of Childhood Anxiety Disorders

Recent advances in technology allow for the increased use of neuroimaging techniques in the study of mental illness and the evaluation of treatment modalities. Detectable differences in brain structure and function may be used to help elucidate the underlying pathology that accompanies observable behaviors. Further, functional neuroimaging may eventually aid in the diagnosis of mental disorders and improve our ability to evaluate the effectiveness of psychotherapeutic and pharmacological treatments. There are now a variety of neuroimaging methods available for research in pediatric anxiety and each one provides unique information about brain integrity and functioning. We include here a brief description of child anxiety research from the standpoint of both structural and functional neuroimaging approaches.

Structural Magnetic Resonance Imaging

Structural magnetic resonance imaging (sMRI) studies indicate significant differences in the volumes of certain subcortical brain structures in children and adolescents with anxiety disorders, relative to their counterparts with no diagnosis. Hippocampus, amygdala, and temporal lobe volume reductions are among the most often observed in various anxiety disorders. The stress response is mediated by areas of the hippocampus, amygdala, and medial prefrontal cortex (Bremner, Elzinga, Schmahl, & Vermetten, 2008). In concert with these findings, sMRI studies have found structural differences in the hippocampus and amygdala in individuals diagnosed with anxiety compared to their nonanxiety-prone counterparts.

Hippocampus: Hipppocampal volume reductions are generally observed in chronic adult PTSD (Karl et al., 2006). Elevations in cortisol levels associated with the stress response detrimentally target the hippocampus, resulting in decreased dendritic branching and neuronal cell loss in the CA3 region of the hippocampus (Magarinos, Verdugo, & McEwen, 1997). Another potential explanation for the reduction in hippocampal volume arises from suppressed neuroregeneration of the dentate gyrus in response to stress (Gould, Tanapat, McEwen, Flugge, & Fuchs, 1998). Specific research on these mechanisms is ongoing.

In contrast to findings of reduced hippocampal volume in adults with PTSD, studies of children with PTSD do not show a reliable pattern of hippocampal volume reductions (Carrion et al., 2001; De Bellis et al., 1999), though total intracranial volumes are reported to be significantly reduced in children with PTSD (De Bellis et al., 1999). Interestingly, however, recent evidence indicates

hippocampal volumes actually decline with increased age and time since diagnosis, suggesting that there may be a developmental component to the PTSD response in the brain, with the full structural consequences of the trauma being manifested only after a prolonged period of time (Carrion, Weems, & Reiss, 2007). Indeed, the prolonged hyper-arousal of medial temporal structures during development can lead to the long-term development of maladaptive neural networks that put traumatized individuals at increased risk for neurocognitive dysfunction and mental health difficulties (Cook, Ciorciari, Varker, & Devilly, 2009; Felitti et al., 1998). Neurodevelopmental plasticity may also play a role in masking the structural effects of traumatic stress in childhood PTSD, since grey matter structures typically show an increase in volume until the third decade of life (De Bellis et al., 1999). Despite inconsistent imaging results for the hippocampus in children diagnosed with PTSD, there is no question that these children still show the associated deficits in memory and attention (Yasik et al., 2007); as normative studies of brain development in children become more advanced, it may be possible to trace age-related changes that are specifically associated with PTSD.

Amygdala: The amygdala receives a considerable amount of attention in the study of anxiety disorders due to its role in the recognition and processing of fearful stimuli. The amygdala coordinates the automatic threat response by integrating information from sensory features, context, and prior learning via both cortical and subcortical inputs (Damsa et al., 2008). The neurocircuitry of the fear response involves projections of sensory inputs from the anterior thalamus to the amygdala, which then initiates behavioral and autonomic nervous system responses by means of projections to motor regions and brain stem nuclei. Results of studies of amygdala volume in adult PTSD are mixed. One meta-analysis found no significant difference in amygdala volume between PTSD and control groups (Woon & Hedges, 2008), whereas another meta-analysis (Karl et al., 2006) reported some evidence of a smaller left amygdala in PTSD subjects compared with healthy controls.

There are few imaging studies to date that investigate the morphometric properties of the amygdala in childhood anxiety disorders. One pilot study of children with GAD reported right amygdala volume increases (De Bellis et al., 2000), whereas another study observed relative decreases in left amygdala volumes (Milham et al., 2005). Future research on the morphometric properties of the amygdala in childhood anxiety are needed to elucidate these potential changes.

Cortical thickness: Regional cortical thickness measurements also show distinctive patterns of relative cortical thickness for different anxiety disorders. For example, increased cortical thickness for individuals with animal phobia as compared to healthy control participants was reported in the paralimbic and sensory cortical regions (Rauch et al., 2004), whereas decreased volumes in these paralimbic regions were observed in other anxiety disorders such as PTSD (Rauch, 2003), OCD (Szeszko et al., 1999), and panic disorder (Vythilingam et al., 2000).

Diffusion Tensor Imaging (DTI)

DTI is a relatively new neuroimaging technique which capitalizes upon the diffusion properties of water in order to identify white matter tracts in the brain. Fractional anisotropy (FA) and the apparent diffusion coefficient (ADC) are some of the commonly used DTI measures of white matter integrity. FA reflects the relative directionality of water molecules along white matter tracts and is influenced by the thickness of the myelin sheath and the axons. Values of FA are on a scale from 0 to 1, with 0 corresponding to maximum isotropic diffusivity (e.g. free diffusion in all directions), and 1 corresponding to maximum anisotropic diffusivity (e.g. diffusion that is parallel to the white matter tract). Relatively few studies have utilized DTI in anxiety research to date, especially in children. However, white matter abnormalities in the anterior cingulate gyrus region are reported in adult OCD (Cannistraro et al., 2007; Szeszko et al., 2005). This observation is consistent with the current understanding that the

anterior cingulate plays a role in monitoring and resolving conflict during information processing (Braver, Barch, Gray, Molfese, & Snyder, 2001); however, the relevance of these findings to the development of pediatric anxiety disorders remains unclear. Reduced FA in the medial and posterior corpus callosum was reported in children with PTSD (Jackowski et al., 2008). This region is associated with circuits that mediate the processing of emotional stimuli and various memory functions, which are commonly disturbed in PTSD.

Functional Magnetic Resonance Imaging (fMRI)

Rapid advances in the technology and methodology of *f*MRI have added an exciting new set of tools for research regarding the development and course of psychiatric disorders. Functional MRI has important potential use in translational research, where scientists involved in basic research provide clinicians with new tools for use in patient assessment and treatment. Functional MRI may also become an important tool in personalized medicine, in which disease risk factors and response to treatment can be tracked for individual patients (Horner & Siegle, 2008). This section considers the technical considerations for using *f*MRI in pediatric populations, followed by a review of progress from basic research into the neural mechanisms that underlie child anxiety disorders as well as studies of treatment response; we conclude this section with a review of the potential and possible pitfalls for future *f*MRI research in this area.

Technical considerations: Functional MRI measures levels of oxygen during blood flow in the brain, which is interpreted as a reflection of neural activity in response to specific stimuli or tasks. Functional imaging studies are often based either on the contrast in brain activity between two or more conditions, such as viewing a series of emotional vs. nonemotional stimuli (block designs), or on the brain response to specific stimuli or tasks, such as response to a startling noise (event related designs). Functional MRI has excellent spatial resolution – down to the millimeter – allowing for the identification of precise regions that are associated with specific behavioral functions. *fMRI* is noninvasive and does not involve any ionizing radiation; it is, therefore, safe for use with individuals of any age, as well as for repeated/longitudinal studies. Because of strict movement tolerances, however, *f*MRI is generally not practical for studying young children below 10 or 11 years old. Additionally, discomfort caused by loud noise of the scanner, and/or the confined space of the scanner bore, may make it difficult for some children to participate in research studies.

Research on basic mechanisms: Pine and colleagues (reviewed in Pine, Guyer, & Leibenluft, 2008) have conducted a series of behavioral and neuroimaging studies of atypical attention modulation in children diagnosed with anxiety disorders. Specifically, anxious children take longer than nonanxious children to respond to the neutral "dot-probe" after viewing angry faces; there is no difference after viewing neutral faces, suggesting that the anxious children show a greater attentional bias to the threatening stimuli. Animal models for this task implicate the role of attentional modulation by the amygdala. Indeed, during an *f*MRI task that displayed threatening angry faces for 17 ms, anxious adolescents showed significantly increased amygdala activation over the comparison group; amygdala activation was significantly correlated with behavioral measures of task performance (reaction time) and the severity of anxiety symptoms (Monk et al., 2008). An earlier *f*MRI study (Monk et al., 2006) showed no between-group differences in amygdala activation when threat stimuli were displayed for 500 ms, whereas there was significantly less activity for the anxious group in the ventrolateral prefrontal cortex – an area that is actively involved in processing information from, and providing feedback to, the amygdala. In healthy adolescents doing the same dot-probe task, self-reported trait anxiety was significantly, positively correlated with right dorsolateral prefrontal cortex activity while viewing threatening faces, and with ventrolateral

prefrontal cortex while viewing all faces regardless of emotional expression. Summarizing all these findings, Pine et al. (2008) suggest a two-stage mechanism for anxiety in which the initial response to threat (in the amygdala) is too strong, while the subsequent modulation of the response (from frontal cortex) is not strong enough.

A slightly different study of attention to threat in anxious adolescents, by the same research group (McClure et al., 2007), found that hyperactivation of the amygdala and connected frontal regions was more prominent when the anxious group was focused on their own subjective experience of fear. Beesdo et al. (2009) report similar amygdala activation in response to subjective ratings of fear while viewing fearful faces in two pediatric patient groups: one diagnosed with anxiety and the other with major depression. Guyer et al. (2008) report increased amygdala activation in adolescents diagnosed with social anxiety, while viewing faces of peers that they had previously rated as likely to make negative social attributions about the participant. Altogether, attentional and attitudinal contexts are probably both important mediators of the fear response in anxiety disorders.

Krain et al. (2008) conducted an *f*MRI study of 16 anxious (GAD or social anxiety) adolescents and 13 matched controls using a decision-making task that varied the probability of a correct response. Although there were no overall between-group differences in activation levels of key brain regions, the authors indicate that those in the anxiety group who self-reported high levels of "intolerance for uncertainty" (as a marker for worry, Krain et al., 2008) showed significantly more activation of orbitofrontal and amygdala regions than those in the anxiety group who reported low intolerance for anxiety. An earlier study by the same research group (Krain et al., 2006) demonstrated developmental changes in adolescence for the relationship between behavioral ratings of worry and anxiety and activation in the anterior cingulate cortex, which may provide a marker of maturational changes in GAD-related brain mechanisms and possible links to the onset of symptoms of depression.

There have been few *f*MRI studies regarding other types of pediatric anxiety conditions. Yang, Wu, Hsu, and Ker (2004) studied a very small sample ($n=5$) of adolescent earthquake survivors who were diagnosed with PTSD vs. a comparison group of survivors without PTSD. While viewing earthquake-related imagery, the PTSD group showed a pattern of significantly more activation of bilateral visual cortex, bilateral cerebellum, and left parahippocampal gyrus; while the comparison group showed significantly more activation of anterior cingulate. This may reflect activation of imagery and spatial memory involved in flashbacks and other symptoms in the PTSD group. A study of pediatric OCD found some evidence for reduced orbitofrontal activation and, in general, additional support for models of frontostriatothalamic dysregulation in OCD, similar to findings from the adult literature (Woolley et al., 2008).

Research on treatment response: Research on basic neural mechanisms is clearly relevant for designing interventions that are targeted more directly toward the foundations of anxious behavior rather than the more overt symptom manifestations. Much of this research is yet to be done: for example, behavioral treatments that train stressed college student adults to successfully modify attention modulation have shown reduced stress; however, there is to date no published application of this idea to children with anxiety disorders.

*f*MRI studies of treatment outcome have thus far only been conducted with adults, but are very promising. For example, a prepost scan study of exposure therapy for spider phobics reported an increase in orbitofrontal activation that is likely related to inhibitory control (Schienle, Schafer, Hermann, Rohrmann, & Vaitl, 2007). In a study of healthy adult volunteers, individuals taking the anti-anxiety drug lorazepam showed dose-dependent decreases in amygdala and insula activation while participants were viewing emotional faces (Paulus, Feinstein, Castillo, Simmons, & Stein, 2005). This research shows promise, as *f*MRI could likewise be used to track activity of key brain regions such as the amygdala and prefrontal cortex as one measure of treatment response in children.

Future directions for fMRI: As noted throughout this chapter, one of the most difficult challenges for research regarding pediatric anxiety disorders is to establish the specificity of neuropsychological impairments across the various definitions of anxiety (e.g., GAD vs. social anxiety). Likewise, research to identify particular neuropsychological deficits in anxiety vis-à-vis other neuropsychiatric conditions of childhood (such as mood disorders, autism spectrum disorders, and AD/HD) has had only limited success. Nonetheless, many of the behavioral symptoms of anxiety are clearly different from those seen in other disorders, and *f*MRI has tremendous potential for discovering intermediate endophenotypes that demonstrate group-level and individual-level differences in the basic processes and timing involved in tasks such as working memory or response inhibition (Greene, Braet, Johnson, & Bellgrove, 2008; South, Wolf, & Herlihy, 2009).

Perhaps the most important application of *f*MRI, but certainly the most difficult to bring to fruition, would be in personalized medicine. That is, in the ability to diagnose and plan treatment for individual patients based on their unique patterns of brain activation (Paulus et al., 2005). To date, virtually all *f*MRI studies report findings from group comparisons: clinical utility for individual cases is yet to be demonstrated. The expense of doing *f*MRI scans precludes the development of large, normative database. The complexity of normative processes and especially the heterogeneity of symptom expression and underlying genetic and neural systems will likely require theoretical and statistical models that are being developed. Work to improve phenotypic definitions, including dimensional approaches that range beyond the narrow categorical definitions of the DSM-IV, is just as important as work on the technology or cost of the scans themselves (see Paulus et al., 2005; South et al., 2009).

Summary: Developmental Research for Developmental Conditions

This chapter reviewed a number of interactions between neuropsychology and anxiety in children and adolescents. There is substantial evidence to show that anxiety supplemental to, or as a result of, neurological or neuropsychological deficits affects performance on neuropsychological testing and should be carefully accounted for during diagnostic assessment and intervention planning. In general, behavioral testing of children with anxiety disorders indicates deficits in executive functions such as organization, flexibility, and working memory. Memory problems in anxious individuals may be secondary to these executive difficulties. Executive functions and memory are, therefore, good targets for behavioral intervention in pediatric anxiety. Neuroimaging is proving to be an important addition to behavioral research, highlighting the delicate interplay between arousal and moderation/inhibition in response to threatening stimuli. Nonetheless, the specification of underlying neural mechanisms and, subsequently, targeted treatment for these conditions is likely to follow dimensional constructs rather than broad categorical definitions. Discovering different patterns of interaction between the amygdala, prefrontal cortex, and the hippocampus may be the key to defining specific neural phenotypes across the various anxiety disorders and other child psychiatric conditions.

Despite some clear patterns of neuropsychological and neurophysiological deficits in anxiety disorders, there remains considerable inconsistency across research studies, especially in pediatric samples. Neurological, emotional, and cognitive development is extremely fluid in children. There is, therefore, a pronounced need for developmentally oriented studies of normative as well as psychiatric populations that can compare and contrast changes in brain structure and function, and disentangle the relative relationships between anxiety and various neuropsychological constructs including language and executive functions (see Lenroot et al., 2009). Although there are now many more technical tools available to understand the neuropsychology of anxiety in children, the goal remains constant: to intervene as early and specifically as possible to break the interactive cycle of biogenic and psychogenic factors associated with childhood anxiety that are so disruptive in the lives of these children and their families.

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7 Empirical Approaches to the Study of Latent Structure and Classification of Child and Adolescent Anxiety Psychopathology

Amit Bernstein and Michael J. Zvolensky

The need to identify and classify anxiety psychopathology among youth is of great public health and scientific importance (Albano, Chorpita, & Barlow, 2003). Anxiety psychopathology is highly prevalent among youth (e.g., Costello & Angold, 1995a, 1995b), associated with significant suffering and life impairment (e.g., Albano & Detweiler, 2001), and often related to long-term negative outcomes (e.g., chronic mental health problems; Achenbach, Howell, McConaughy, & Stanger, 1995). Consequently, a variety of research and clinical efforts are focused on understanding, measuring, preventing, and treating anxiety psychopathology among children and adolescents. One fundamental element of building this knowledge base involves taxonomic study of anxiety psychopathology among youth. Such taxonomic study broadly strives to validly "carve nature at its joints" by "drawing boundaries between adjacent syndromes, and between these syndromes and normality, where there are genuine discontinuities, either in symptomatology or in etiology" (Kendell, 2002, p. 7), and concurrently designing a system of classification grounded in this evolving knowledge of the constructs' latent structure(s). This area of scholarship is foundational to the progress and scientific veracity of our collective efforts to study anxiety psychopathology among youth. Indeed, the degree to which the work of clinical researchers focused on understanding various aspects about the nature of anxiety psychopathology among youth, such as its prevalence, course, or its etiology and maintenance, is scientifically sound and clinically useful relies in large part on the premise that the various phenotypes of anxiety psychopathology (disorders or syndromes) that we study and that guide our work are themselves empirically founded and valid in the first place (Kendell, 2002). Thus, in the context of anxiety psychopathology phenotypes of limited validity, our clinical capacity to understand, measure, prevent, and treat anxiety psychopathology among youth may be greatly impeded (Achenbach, 1995).

Due to the centrality of the study and classification of psychopathology to the ultimate success of science and practice related to psychopathology and psychopathology among youth specifically, there has been considerable effort placed into this activity. Perhaps not surprisingly, a long-standing spirited debate has also emerged regarding the best approach(es) for achieving these ends (Achenbach, 1995; Joffe, 2004; Lilienfeld, Waldman, & Israel, 1994; Meehl, 2001; Rutter, 1994; Widiger & Ford-Black, 1994; Zimmerman & Mattia, 1999). Interestingly, unlike many areas of anxiety

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_7,

psychopathology research and scholarship, in which research was first conducted among adults and subsequently among youth, advances in taxonomic study of psychopathology among youth preceded similar study among adults (Achenbach, 1966). Since the initiation of this area of research, scholars have argued for the importance of clarifying these nosological (psychiatric classification of psychopathology into categorical disorders) and taxonomic (classification of psychopathology that reflects empirically observed syndromes) (Achenbach, 2008) issues. Although the scope of the scientific study of classification of psychopathology and anxiety psychopathology specifically may perhaps at first seem overwhelming due to the volume and nuance of issues relevant to this domain, a number of focal questions have guided much of the thought on taxonomic research related to psychopathology across the lifespan: (1) Is a given form of anxiety psychopathology a categorically distinct, naturally occurring syndrome (taxon); or, is that form of anxiety psychopathology more accurately conceptualized as dimensional? (2) Where and how do we identify the boundary(ies) between a disorder and other forms of anxiety disorders/syndromes, normative levels of anxiety, and other forms of psychopathology among youth (e.g., mood disorders)? (3) Is the co-occurrence and multi-morbidity between anxiety disorders/syndromes a sign that these nosologically distinct disorders co-occur and may substantively (e.g., causally) relate to one another, or alternatively, an indication that our operational definitions of disorders/syndromes need revision to better account for syndromal phenomenology? (4) Should psychiatric disorders be organized as a function of their descriptive phenomenology or their causes? (5) What approach should be adopted to develop and refine the classification of psychopathology among youth (e.g., a top–down nosological approach or a bottom–up statistical approach)? (6) How should we evaluate and develop classification of psychopathology in light of the likelihood that psychopathology and its diagnostic or syndromal criteria may change over the course of development? As described in this chapter, some, but not all, of these questions, and others, have begun to be addressed in contemporary anxiety disorder research among youth.

The broad-based purpose of the present chapter is to provide a synopsis of past and contemporary empirical approaches to the study of latent structure and classification of anxiety psychopathology among youth. To achieve this aim, the chapter is organized around three sections related to the extant literature. In the first portion of the chapter, we briefly present the historical context for understanding and classifying anxiety psychopathology. In this same section, we present an emerging statistically based hierarchical model of psychopathology (it includes, but is not limited to, anxiety disorders) informed by scholars such as Achenbach, Krueger, and Watson, among others, relevant to classification of anxiety psychopathology among youth and adults (e.g., Achenbach, 2008). This model is discussed to illustrate an example of innovative empirical work in the area of latent structure and taxonomy. This type of work could be fruitfully incorporated into future taxonomic study of anxiety psychopathology among youth, efforts to empirically guide classification of anxiety psychopathology, as well as to potentially guide broad-based study, assessment, and intervention of anxiety. In the second section, we describe some key statistical methods to answer taxonomic questions about the latent structure of anxiety and other forms of psychopathology and that may therefore be important for advances in their classification and study. We conclude with a discussion of the clinical implications of empirical approaches to understanding and classifying anxiety disorders and promising next steps for further scientific pursuit. We also want to highlight that many of the ideas presented here are anxiety psychopathology across the lifespan. Indeed, the idea of approaching the understanding and classification of anxiety psychopathology empirically and from a developmentally informed perspective is arguably relevant to conceptualizing and studying anxiety psychopathology across among children, adolescents, and adults.

Classification of Anxiety Psychopathology: Historical Context

Dominant Model

The vast majority of anxiety psychopathology research has been driven by conceptual models that posit – even explicitly assume – that discrete mental conditions exist as natural categories (Lilienfeld et al., 1994). This corpus of work has been strongly influenced – socio-politically and scientifically – by the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV; American Psychiatric Association (APA), 1994). Within our current nosological system, the DSM-IV-TR (American Psychiatric Association, 2000), anxiety psychopathology among youth is not classified separately from adult anxiety psychopathology; with exception of separation anxiety disorder (SAD), which is classified under Other Disorders of Infancy, Childhood, or Adolescence. In the DSM-III (APA, 1980) and DSM-III-R (American Psychiatric Association, 1987), anxiety disorders of childhood were classified separately. In the DSM-IV-TR (APA, 2000), the issue of developmental factors related to diagnosis and classification of anxiety disorders is incorporated within the *Specific Culture*, *Age*, *and Gender Features* sub-section, within the description of each diagnostic category. This means of classifying and diagnostically distinguishing between anxiety psychopathology among adults and youth has been critically evaluated (e.g., Costello & Angold, 1995a, 1995b).

The basic premise to the DSM-based nosological approach is that in order to meet criteria for a particular disorder, a person must meet diagnostic criteria, at a clinically significant level, a specified number of symptoms and related life impairment within a specific period of time, thereby coinciding with pre-established diagnostic criteria. Using this classification approach, there is, by definition, a multitude of permutations of symptoms (or criteria) that could qualify an individual for a specific diagnosis. Thus, two individuals could meet criteria for the same disorder by virtue of endorsing a different constellation of symptoms. This approach is strictly categorical in nature; simply meaning, meeting criteria for a particular disorder is conceptualized on an a priori basis as falling into or out of a category. Due to the permutations allowed for entry into this (theoretically presumed) category, it is implicitly guided by what has been labeled an underlying *polythetic subtyping* scheme (Clark, Watson, & Reynolds, 1995); a term intended to simply communicate that there may be multiple permutations of symptoms to meet criteria for a given disorder.

The categorical polythetic approach has indeed been fruitful (Clark et al., 1995). Progress yielded by progressive advances in nosological classification is evident when examining the relative inroads made in the study of psychopathology among youth and adults (including anxiety and other types of disorders) prior to, and following, the influence of the DSM-III (e.g., Mash & Dozois, 2003). For instance, Nathan (1998) observed that the diagnostic labeling of specific conditions derived via the DSM system has yielded enhanced communication between clinicians and scholars that would not otherwise be possible. Additionally, in the case of anxiety psychopathology, efficacious prevention and treatment approaches have been developed for a large number of specific anxiety disorders (e.g., Albano et al., 2003). Moreover, integrated theoretical models explicating the etiology and maintenance of these conditions have been developed (Barlow, 2002). Thus, the identification and classification of anxiety disorders as discrete entities has served as an organizational framework, whereby systematic lines of empirical inquiry can be pursued and critically evaluated.

Examples of Gaps in Scientific Knowledge

Despite the noted progress within anxiety disorder research among youth, there are important gaps in our existing knowledge. For example, extant treatment for anxiety disorders, although often producing meaningful positive behavior change and reduced impairment, is not effective or has only limited effectiveness for a meaningful

proportion of youth and adults (Cartwright-Hatton, Roberts, & Chitsabesan, 2004). Although this issue may not entirely or solely be driven by problems in classification, numerous scholars have suggested that the complex nature of classification may be playing a key role in hindering success in matching treatments to particular disorders (Schulte, 1996).

As a second example, there are often large amounts of unexplained variance in tests of contemporary models of anxiety psychopathology (Albano et al., 2003). Conceivably, we would be better able to account for, and thereby understand, a given form or forms of anxiety psychopathology insofar as our classification of anxiety psychopathology best matched its latent structure(s). Specifically, the more valid the match between our classification of anxiety psychopathology and its putative latent structure(s), the better the opportunity for models (e.g., etiological models) of such problems (i.e., phenotypes) to be developed.

Third, real-world presentations of anxiety symptoms may be clinically and functionally important but may not map isomorphically onto contemporary nosological diagnostic criteria for any one disorder, or be comprehensively accounted for by any single diagnostic category (Achenbach, 2008; Eifert, 1992). This may be particularly the case for youth for whom developmentally grounded anxiety disorder diagnostic categories are not specified (cf. SAD; American Psychiatric Association, 2000). For example, a person may demonstrate clinically significant impairment across numerous domains of anxiety or disorders, but fail to reach a "diagnostic threshold" for any one of them for a variety of reasons (e.g., exclusion rules used in a diagnosis process; Brown & Barlow, 1992). In other instances, a condition may share features with a range of disorders, and again, not be most accurately accounted for by any one diagnostic category (Hollander & Rosen, 2000).

As a final example, scholars struggle to understand and accordingly revise classification as a function of the relative degree of overlap between anxiety disorders with one another and other forms of mental illness (Brown & Barlow, 2002; Robins, 1994).[1] The empirical literature is replete with findings and discussion of work documenting high rates of co-occurrence and multi-morbidity between anxiety and other psychiatric conditions (e.g., Brown, Campbell, Lehman, Grisham, & Mancill, 2001; Mineka, Watson, & Clark, 1998). Although such co-occurrences and multi-morbidity are not specific to the anxiety disorders (Giaconia, Reinherz, Paradis, Hauf, & Stashwick, 2001; Kessler et al., 1994; Van Praag, 1996; Widiger & Sankis, 2000), the best way to interpret such co-occurrence(s) and its implications for models of the etiology and maintenance of anxiety psychopathology have yet to be fully delineated and remain an important focus of debate and study (Rutter, 1994; Spitzer, 1994).

Together, a key point inferred from the foregoing discussion is that alternative ways to study and classify anxiety psychopatholgy should be explored and systematically evaluated in order to further enhance our understanding of anxiety psychopathology across the lifespan. As numerous scholars have argued, competing models of anxiety and other types of psychopathology can be compared to one another, or at a minimum, conducted with more explicit reference to one another (Achenbach, Bernstein, & Dumenci, 2005; Achenbach & Edelbrock, 1984; Jensen, 2003; Klein & Riso, 1993; Krueger, 1999). In this way, the type of model that can best capture the underlying nature of anxiety psychopathology can be identified and employed in the day-to-day activities of science and practice. This work would, in theory, improve efforts to understand and treat anxiety disorders because of the more accurate elucidation of the latent structure of these conditions. Thus, programmatic study of the taxonomy of anxiety psychopathology, especially across the lifespan, promises

[1] Historically, some scholars refer to the co-occurrence between one or more disorders as "comorbidity," whereas others have argued for the use of terms such as "multi-morbidity" or "covariation" or "co-occurrence." From the broadest perspective, all these terms are intended to reflect the fact that mental disorders are (generally) correlated with one another (e.g., Lilienfeld et al., 1994). In the present chapter, we use the term co-occurrence to reflect instances of two clinical conditions and multi-morbidity of instances when more than two conditions are present.

various theoretical and clinical implications and therefore merits increased scientific attention.

Contemporary Empirical Study and Classification of Anxiety Psychopathology

In large part, there has been a working assumption that anxiety disorders exist as a discrete class of conditions (APA, 2000), and as a consequence, taxonomically oriented research has predominately aimed to understand the nature of anxiety disorders and how they relate to other forms of mental illness. Due to this a priori nosological stance, most scientific work has been focused on addressing questions such as: what are the boundaries between anxiety disorders and other forms of anxiety disorders/syndromes and what are the distinctions between clinical and nonclinical presentations of anxiety? The main point being that the study of anxiety psychopathology and the dominant nosological model has largely assumed that anxiety disorders are a discrete class of presumably related disorders. It also has largely assumed that they are distinct as a class from other forms of psychopathology.

Some scholars have argued convincingly that the dominant, contemporary approach to classification in science and practice has a number of key limitations (Achenbach, 2008; Krueger & Piasecki, 2002). Numerous challenges have been raised, including: nosology is categorically based as opposed to dimensional; not derived from population-based studies that employ representative sampling methods; assigns diagnostic criteria to disorders in a way that may not be valid; and draws boundaries in a top–down fashion (Krueger & Piasecki, 2002; Watson, 2005). Dominant models and the approaches used to study them have been challenged because they do not fully account for the full spectrum of phenomenology of co-occurrence, including multi-morbidity between anxiety disorders and other forms of psychopathology (i.e., co-occurrence of more than two disorders; Achenbach, 1995; Krueger, 1999; Krueger, McGue, & Iacono, 2001; Krueger & Piasecki, 2002; Watson, 2005). Inspection of this body of work makes clear that the issue of how best to understand the "co-occurrence of disorders" has predominately influenced the type of research questions being addressed – a valid issue at the heart of psychiatric taxonomy. Indeed, prevalence rates of multi-morbidity make clear the importance of this issue for critically evaluating the classification of anxiety psychopathology and for understanding co-occurrence (Kessler et al., 1994). To effectively empirically evaluate and understand such multi-morbidity, multivariate models may be useful.

Relative to research grounded in contemporary psychiatric nosology, there has historically been less work using statistical strategies to develop and study a taxonomy of anxiety psychopathology (but see Krueger, 1999; Krueger, Caspi, Moffitt, & Silva, 1998; Middeldorp, Cath, Van Dyck, & Boomsma, 2005; Watson, 2005, for illustrative exceptions). Driven by the work of Achenbach, Krueger, Watson, and others, there is an emerging multivariate perspective of anxiety and other mental disorders (e.g., Achenbach, 1995; Krueger, 1999; Watson, 2005). This approach differs from the dominant "top–down" nosological system (i.e., DSM), in that it attempts to model psychopathology from the "bottom–up" (Achenbach et al., 2005). "Bottom–up" is intended to reflect an approach to organize classification and derive a taxonomy of psychopathology based on the empirical co-occurring pattern of disordered behaviors or syndromes as they are observed to occur without any predetermined hypothesis(es) regarding syndrome structure. In contrast to this approach, the current nosological approach is based on classification primarily rooted in expert review of wide range of extant research literature (APA, 2000).

Although various aspects of a statistically based approach to taxonomy of psychopathology have been evident to varying degrees in the literature for many years (e.g., Achenbach, 1966), it has not always had wide-ranging influence in all domains of anxiety disorder research and practice. In the area of anxiety psychopathology research among youth as well as adults, DSM-based diagnostic categories have largely reflected the dominant unit and operational definitions of study (Barlow, 2002). Indeed, most research in the area of anxiety psychopathology has been focused on the study of nosologically

based disorders defined by the DSM in contrast to statistically derived internalizing syndromes, or a statistically based taxonomy of anxiety psychopathology (e.g., Achenbach et al., 2005; Krueger, 1999). Yet, this type of multivariate approach to psychopathology, which includes, but is not limited to, anxiety disorders, may also represent a theoretically and clinically compelling and effective way to understand anxiety psychopathology relative to the traditional, nosological classification system.

Hierarchical models of psychopatholgy have been influenced and guided initially by the work of Achenbach and colleagues, and more recently, Watson, Krueger and their respective colleagues. Although an extensive discussion of this type of modeling of psychopathology is beyond the scope of the present chapter (see Achenbach, Dumenci, & Rescorla, 2003; Krueger, 1999, 2005; Krueger & Piasecki, 2002; Tellegen, Watson, & Clark, 1999; Watson, 2005), we overview one application of this approach to taxonomic study to illustrate the function of such approaches more broadly. It is also important to observe that there are significant distinctions between different empirically derived hierarchical models of psychopathology (Achenbach et al., 2003; Krueger, 2005; Watson, 2005). In this chapter, we portray the commonalities of this type of approach at a broad-based level rather than explicate the distinctions between specific hierarchical models.

Hierarchical models organize psychopathology symptoms along a number of statistically derived dimensions that relate to specific syndromes – the empirically observed pattern of co-occurrence of symptoms. These syndromes, in turn, are related to a higher-order co-occurring group of syndromes/disorders. That is, syndromes relate to a higher-order factor, and by extension, such hierarchically linked syndromes are related to one another as a function of their common, higher-order dimensional structure. This hierarchical approach does not begin with the assumption that there are necessarily a given number of distinct disorders, be they categorical entities or dimensions, but simply analyzes the actual co-occurring pattern of observable symptoms and identifies these co-occurring dimensions as syndromes. Furthermore, this approach statistically models patterns of co- and multi-morbidity observed in nosological study of psychopathology by identifying higher-order factors linking co-occurring but distinct syndromes and includes these higher-order syndromes within the taxonomic system. As a result, this approach has the tendency to carve far fewer joints – it is designed to "lump" rather than "split," and thereby, provides an alternative account of co-occurrence and multi-morbidity of nosologically based categorical entities. Consequently, hierarchical models of classification obviate the "problem" of co- and multi-morbidity in the current nosology between anxiety and other disorders that leads to questions about the validity of nosological classification that has historically increasingly "split" rather than "lumped" (Krueger, 1999, 2005; Krueger & Piasecki, 2002; Tellegen et al., 1999). On the other hand, it is noteworthy that lumping in favor of splitting too early in the development of a descriptive taxonomic system may result in failure to comprehensively study and clinically measure and treat more narrow syndromes that may be lumped together within this type of broad-based system (Lilienfeld et al., 1994).

Study of psychopathology adopting this statistically based hierarchical model indicates that there are two higher-order factors reflecting internalizing and externalizing symptoms and syndrome spectra (Achenbach et al., 2003; Achenbach & Edelbrock, 1984; Krueger, 2005; O'Connor, 2002; Watson, 2005). These higher-order factors are indicative of vulnerabilities, broadly conceived, to experience negative affect (internalizing symptoms) and/or disinhibition (externalizing symptoms) and consequently elevated levels of one or more syndromes that are lower-order factors/syndromes. Extant evidence suggests that the internalizing factor corresponds most closely to disorders involving anxiety and depressive features, whereas the externalizing factor reflects substance use disorders and antisocial personality disorder (O'Connor, 2002; Watson, 2005). Research indicates that the internalizing factor can be further divided into separate lower-order dimensions of distress and fear (Krueger & Markon, 2006). More specific symptom presentations can then be categorized from these distress and fear dimensions. For example, major depression and GAD symptoms tend to fall within the distress category and panic disorder and specific phobias

tend to fall within the fear dimension (Krueger, 2005). Among youth, anxious/depressed, withdrawn/depressed, and somatic complaints are lower-order factors/syndromes of the higher-order internalizing factor (Achenbach & Rescorla, 2001). On the externalizing side, various conditions involving disinhibition processes such as aggressive behavior and rule-breaking behavior lower-order factors/syndromes fall within this higher-order dimension (Achenbach & Edelbrock, 1984; Krueger, 2005). It is noteworthy that the cross-national study of psychopathology has indicated a strong degree of consistency in the observed hierarchical model among youth and adults (e.g., Hunt, Issakidis, & Andrews, 2002; Ivanova et al., 2007; Krueger, Chenstova-Dutton, Markon, Goldberg, & Ormel, 2003).

Statistical Technologies in the Study of the Latent Structure of Anxiety Psychopathology

From an applied perspective, the utility in statistical procedures rests squarely with the type(s) of information they can provide, and by extension, the type(s) of questions they can help answer. Thus, understanding the types of statistical procedures available and the information they can provide is key to forwarding programmatic taxonomic study of anxiety and related psychopathology, and thereby, advance classification of anxiety disorders. To this end, we now briefly highlight some of the statistical techniques available to answer pressing questions concerning the latent structure of anxiety psychopathology across the lifespan and what information they can provide in guiding classification. Please see Table 7.1 for a summary of the data analytic approaches reviewed below.

Factor Analysis

Of the various statistical tools available to study latent structure, anxiety researchers have largely utilized factor analytic methodology. Factor analysis is part of the multiple general linear hypothesis family of procedures (Brown, 2006). In exploratory factor analysis (EFA), the goal is to uncover the underlying structure of a relatively large set of variables (Brown, 2006). In EFA, any indicator may be associated with any factor. EFA is the most common form of factor analysis in anxiety disorder research. There is generally no or limited prior theory guiding this type of work and one uses factor loadings and various factor extraction strategies to intuit the factor structure of the data. In confirmatory factor analysis (CFA), the goal is to determine if the number of factors and the loadings of measured (indicator) variables on them conform to what is expected on the basis of pre-established theory (Brown, 2006).

There are many ways that factor analysis can be employed to facilitate understanding of latent structure and classification of anxiety psychopathology. In anxiety disorder research and practice, examples of the application of factor analysis have often included tasks such as reducing a large number of variables such as putative symptoms to a smaller number of syndromal factors. Such analysis can thereby be used to empirically define the composition of individual dimensional syndromes, delineate their boundaries with independent and related syndromes, and document the nature of their relations with one another (e.g., hierarchical) and putatively distinct forms of psychopathology. As another example, factor analytic strategies can be used to select a subset of variables, such as diagnostic criteria, from a larger set; to drop proposed diagnostic criteria or putative symptoms that may not discriminate between

Table 7.1 Data analytic approach as a function of observable variable and latent variable type

Data analytic approach	Observable variable	Latent variable
Factor analysis	Continuous	Continuous
Latent trait analysis	Categorical	Continuous
Taxometric (CCK) analysis	Categorical or continuous	Categorical
Latent class analysis	Categorical	Categorical
Latent profile analysis	Continuous	Categorical
Factor mixture model analysis	Categorical or continuous	Categorical and continuous

putatively distinct syndromes; or to evaluate the validity of a syndromal factor by evaluating that its constituent items or putative symptoms load as theoretically or nosologically predicted (e.g., Asmundson, Stapleton, & Taylor, 2004).

Factor analysis can therefore test questions about the uni- vs. multi-dimensionality of a construct(s) or set of variables or behaviors, and the higher-order structure of a construct or those variables or behaviors. Consequently, factor analytic approaches can help delineate syndromal patterns of symptoms, and thereby, empirically delineate boundaries and relations between dimensional syndromes. Furthermore, factor analytic strategies can further help identify the empirical relations, or pattern of co-occurrence of these syndromes, in relation to one another and in relation to higher-order factors or syndrome spectra consistent with a hierarchical model of classification. These approaches, however, cannot answer many other fundamental questions relevant to latent structure and taxonomy. For example, factor analysis cannot test whether a given form of anxiety psychopathology is taxonic (e.g., dichotomous categorical latent variable) or dimensional, and by definition, assumes the latter for all latent variables. Factor analytic strategies also cannot empirically delimit the boundaries between it and normative levels of and forms of anxiety, but simply reflects dimensions in factor space. As a final example, factor analytic research cannot determine why, theoretically, these specific symptoms and syndromes co-occur.

Taxometrics

Taxometrics is a family of statistical procedures that provides a set of tools to investigate the latent class structure of constructs by evaluating whether or not they are taxa, dichotomous, categorical latent class variables (Haslam, 2007; Meehl, 1973, 1999; Ruscio, Haslam, & Ruscio, 2006; Schmidt, Kotov, & Joiner, 2004). Here, we are highlighting Meehl and colleagues' Coherent Cut Kinetic (CCK) taxometric procedures and approach to studying latent structure specifically (Meehl & Golden, 1982; Waller & Meehl, 1998). Meehl's taxometric procedures are designed to test the existence of latent taxonic structure, and indicate nontaxonicity when the latent structure of a construct is either dimensional or composed of more than two discrete classes (e.g., 3 or more classes). In that sense, although potentially less powerful in terms of identifying more complex multi-class models, these CCK taxometric procedures nevertheless provide tests of a specific, taxonic, latent class structure (Waller & Meehl, 1998). The epistemological rigor of taxometrics, involving risky consistency tests of a specific, falsifiable conjecture about the latent taxonic structure of latent variables offered by taxometrics, make taxometrics a uniquely powerful approach (e.g., Meehl, 2004; Schmidt et al., 2004).

In addition to distinguishing between latent anxiety dimensions and taxa and delineating the boundaries between anxiety psychopathology and normative levels of and forms of anxiety (e.g., Haslam, 2003, 2007; Schmidt et al., 2004 for reviews), taxometric procedures can similarly be utilized to understand comorbidity (Brown, 2001; Meehl, 2001). Taxometrics can similarly be utilized to detect latent comorbidity between two co-occurring taxa such as two categorical anxiety disorders. Specifically, taxometrics can be used to empirically evaluate whether putative taxa (e.g., two anxiety disorders) are indeed distinct taxa that sometimes co-occur, or whether they are not distinct taxa and therefore not, technically speaking in terms of their latent structure, comorbid categorical disorders (cf. dimension(s), single comorbid taxon). Moreover, taxometrics cannot be used to evaluate latent class structures more complex than dichotomous categories. In recent years, taxometric procedures have been increasingly utilized to evaluate the latent structure of various forms of anxiety psychopathology and nosologically based diagnostic categories (e.g., Broman-Fulks et al., 2006; Kollman, Brown, Liverant, & Hoffman, 2006; Kotov, Schmidt, Lerew, Joiner, & Ialongo, 2005; Olatunji, Williams, Haslam, Abramowitz, & Tolin, 2008; Schmidt et al., 2007).

Latent Class, Latent Profile, Latent Trait, and Factor Mixture Analyses

Latent class analysis (LCA) shares some conceptual similarity to taxometric procedures, in that it

is aimed principally at the explication of mutually exclusive underlying classes or groups of cases. LCA is a statistical method for finding subtypes of related cases (latent classes) from multivariate categorical data. Unlike Meehl and colleagues' CCK taxometric procedures (Waller & Meehl, 1998), LCA is not constrained to distinguishing between dimensional and taxonic latent structure (dichotomous latent class structure) and instead can be used to detect multiple latent classes (Ruscio et al., 2006). LCA has a similar function to finite mixture estimation, a form of cluster analysis (Day, 1969; Lazarsfeld & Henry, 1968; Titterington, Smith, & Makov, 1985; Wolfe, 1970). Latent profile analysis (LPA) is an extension of LCA, but is used to model latent class structure using observable *continuous* variables. Latent trait analyses, in contrast to LCA and LPA, is a form of factor analysis for binary (dichotomous) or ordered-category data that may be used to test latent dimensional structure using observable categorical variables. More recently, there have been advances that build upon latent class and common factor analysis, that model categorical *and* continuous latent variable structure concurrently, named factor mixture models (e.g., Lubke & Muthén, 2005). Factor mixture modeling tests the latent categorical structure of a construct(s) and its within-class dimensional (factor) structure(s) concurrently. Thus, factor mixture modeling evaluates the concurrent categorical *and* continuous latent structure of latent variables and can do so using categorical and continuous observable indicators (Muthén, 2008).

Latent class and latent profile analyses can be used to model the presence, number, and composition of latent classes underlying a set of observable indicators, such as putative diagnostic criteria or symptoms. In comparison, latent trait analysis can be used to model the dimensional structure of a latent trait underlying a set of observable indicators, such as putative diagnostic criteria or symptoms. A key distinction between factor analytic in comparison to taxometric and latent class/profile analytic strategies is that the former is concerned with the structure of variables (i.e., their correlations), whereas the latter is concerned with the structure of cases (i.e., the latent taxonomic structure). Therefore, LCA-related procedures can be used to answer certain taxonomic questions. For example, LCA-related procedures can be used to evaluate the dimensional vs. taxonic structure of a putative syndrome. Unlike CCK taxometric procedures, LCA-related procedures can also be used to model putative (multi-class) categorical sub-types of a diagnostic category (e.g., Kessler, Stein, & Berglund, 1998) or multiple diagnostic categories from a set of observable indicators (i.e., symptoms) that putatively compose a theoretically related group of discrete disorders (e.g., anxiety disorders). LCA-related procedures can also be used to identify the boundary(ies) between a taxon/taxa (or latent class(es)) and other forms of anxiety disorders/syndromes, between it and normative levels of and forms of anxiety, and between it and other forms of psychopathology (e.g., mood disorders) (e.g., Kessler, Chiu, Demler, & Walters, 2005). Furthermore, LCA-related procedures may similarly be used to evaluate and explicate putative comorbidity and multi-morbidity (e.g., Kessler et al., 2005). There are currently unfortunately few such studies focused on anxiety psychopathology in the published literature, reflecting an understudied yet promising area for increased research attention. In light of the likelihood that anxiety psychopathology could theoretically demonstrate categorical and dimensional structure (Pickles & Angold, 2003), factor mixture modeling may be particularly promising in future taxonomic study of anxiety psychopathology across the lifespan. Indeed, factor mixture modeling and related advances in latent variable "hybrid" modeling (Muthén, 2008) may be a particularly promising future direction for advances in taxonomic research.

Contemporary Issues in the Empirical Study and Classification of Anxiety Psychopathology

In this final section, we highlight a few ideas that future research may pursue to continue to meaningfully move this body of work forward.

Sequencing Tests of Latent Structure Within a Programmatic Framework of Taxonomic Research

One of the most striking observations of extant latent structural work on the anxiety disorders across the lifespan is that it has proceeded in a manner that does not necessarily consider a macro-level sequencing of taxonomic questions and tests. At a meta-scientific level, extant work has not been consistently pursued programmatically or systematically across the field. For instance, some research has been conducted with a working premise rooted in an (often) empirically untested assumption that certain fundamental latent structural questions have been addressed. One broad-based implication of this sort of meta-scientific problem involves calling for an increasingly unified, comprehensive, and programmatic commitment by researchers to sequentially and systematically evaluate taxonomic questions relevant to the classification of anxiety psychopathology. As one example, it may be helpful to organize research around an organized sequence of taxonomic questions (e.g., (1) What symptom-level behaviors co-occur syndromally? (2) Is a putative syndrome dimensional, taxonic, and/or multi-class? (3) What are its boundaries and relations with other syndromes? (4) How do we conceptualize co- and multi-morbidity in the context of syndromal structure and relations, and how do we refine classification in light of patterns of co-occurrence?).

Connecting Latent Structural Research to Anxiety Research and Theory

Evaluation of latent structural research on anxiety and its disorders among youth might lead one to assume that this body of work is influenced largely by statistical tools more so than theoretical models of anxiety psychopathology. There has been a relative lack of attention paid to linking such latent structural work to more basic areas of science on anxiety and affective states more generally. This relative degree of neglect, although perhaps to be expected at an early developmental stage, is unfortunate. Indeed, there are large, fast-moving sources of empirical data on the neurobiology and emotional learning directly relevant to understanding anxiety. This problem of the latent structural and taxonomic research alludes to one of the long-standing questions at the heart of taxonomy – whether to develop a descriptive or etiologically based taxonomy of anxiety psychopathology? As noted by scholars in recent conceptual work related to psychiatric taxonomy (Zachar & Kendler, 2007), although a descriptive taxonomy is likely more scientifically feasible and clinically pragmatic, it should nevertheless be directly informed by the broader anxiety research literature. In this regard, the nosological approach used to construct the DSM (APA, 2000) that incorporates extant literature on psychopathology reviewed by experts, *in combination with* the application of advances in empirically based and statistical strategies used to answer empirical latent structural and taxonomic questions, may offer a promising comprehensive meta-scientific approach to advancing classification. This approach appears to be an explicit aim in the development of the DSM-V (e.g., Kupfer, First, & Regier, 2002; Widiger, Simonsen, Krueger, Livesley, & Verheul, 2005).

Multi-Modal Measurement of Multiple Response Systems and Latent Structural Research

Building from the immediately preceding discussion, another key issue of note in the extant latent structural work on anxiety disorders is that it has largely been completed from a uni-method approach. Specifically, self-report or interview-based instruments have been employed to index symptoms. Such study and measurement of anxiety, however, does not comprehensively reflect prevailing theoretical models of the nature of anxiety and fear states in the sense that it fails to include analyses across response (cognitive, physiological, and behavioral) systems (Craske, 1999; Lang, 1994). Thus, there is notable disconnect between theoretical knowledge and empirical support for a multi-systemic conceptualization of

anxiety and its disorders and how the vast majority of latent structural work in this domain has been developed and evaluated. There are numerous points of substantive concern related to this limitation of extant study, including but not limited to, the possibility that method biases influence observed results; a lack of understanding as to how one response system relates to another (e.g., self-report anxiety symptoms and psychophysiological responsivity to theoretically relevant stimuli); and the possibility that volitional types of responding may fail to capture and accurately reflect automatic aspects of responding at numerous levels (behavioral, cognitive, and physiological). To the extent multiple response systems are not included in latent structural research (e.g., as observable components of anxiety syndrome phenotypes), it will be difficult to convincingly connect taxonomic work to more basic research on anxiety and fear states.

A Multi-Taxonomic Approach to Classification of Anxiety Psychopathology

There also is a need to utilize a multi-taxonomic approach to classification of anxiety disorders (Achenbach et al., 2005). A multi-taxonomic approach to classification operates from the assumption that any single classification system will likely reify *hypotheses* about anxiety and its syndromes/disorders. Consequently, a multi-taxonomic approach to the classification of anxiety psychopathology among youth is based on the notion that more than one (competing or complementary) classification system may be used to organize the same set of symptoms. Specifically, the multi-taxonomic perspective proposes that we ought to develop, evaluate, and compare various models of latent structure and classification of the same set of symptoms and syndromes (e.g., a nosological system, a statistically based hierarchical system); and that doing so not only will protect against taxonomic reification but is theoretically likely to potentiate scientific progress by affording concurrent study of multiple (hypothesized) operational definitions of anxiety psychopathology (Achenbach et al., 2005). Indeed, and as we have noted in this chapter, two or more classification schemes may be more or less likely to "lump" or "split" the same set of symptoms and syndromes, conceptualize a syndrome dimensionally or categorically, draw boundaries between syndromes differently, or account for co- and multi-morbidity in various ways. In a related area of scholarship, scholars have debated the distinctions and merits related to causalism vs. descriptivism, essentialism vs. nominalism, objectivism vs. evaluatism, internalism vs. externalism, entities vs. agents, categories vs. continua, and other philosophical and scientific questions that challenge adherence to a single taxonomic system (Zachar & Kendler, 2007). Consequently, the threat of reification of diagnostic categories or syndromes of anxiety psychopathology is both an important epistemological and scientific point of interest. Thus, multi-taxonomic approaches that explicitly relate to diagnostic categories and syndromes as working hypotheses and taxonomy/nosology as a working hypothesized organizational system may merit greater empirical attention and may augment both advances in classification of anxiety psychopathology as well as, more broadly, the study of anxiety and its disorders across the lifespan.

Summary

The study and classification of anxiety psychopathology across the lifespan, and among youth specifically, is a central task in efforts to explicate the intricate nature of anxiety and its putative syndromes and disorders. There has been substantial progress in the empirical study of anxiety disorders among children, youth, and adults. Promising steps forward in latent structural research have been identified, including, but not limited to, hierarchical models of psychopathology. Future work in this area needs to continue to apply advances in statistical methods to test latent structural models of anxiety psychopathology. It is likely that such work will be facilitated when conducted within a meta-scientific programmatic framework for taxonomic research, integrates

knowledge from basic areas of science and theory on anxiety, and incorporates multi-taxonomic approaches to classification.

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Dimensional Diagnosis of Anxiety in Youth

8

Melanie W. Moretz and Dean McKay

Dimensional Diagnosis of Anxiety in Youth

The diagnosis of anxiety disorders in children and adolescents is associated with several problems including high comorbidity and low clinical utility of diagnostic categories. This chapter will begin by outlining the weaknesses of the current categorical diagnostic system and reviewing the history and evidence for taking a dimensional approach to the diagnosis of anxiety disorders in children and adolescents. The problem of the high comorbidity of anxiety and depression in youth will be discussed, followed by a review of several quantitative structural models which have been proposed to differentiate between the shared and specific components of anxiety and depression. Based on the research indicating that anxiety disorders are best classified as highly correlated symptom clusters comprising internalizing syndromes, approaches to assessment and diagnosis will be covered in the last section of this chapter. Tools that have been validated to measure anxiety and depression dimensionally in youth will be presented, as well as measurement of narrow traits that have been found to put children and adolescents at risk for the development of pathological anxiety. Finally, we will discuss the need to move toward a system of classification that corresponds more directly to effective interventions for anxiety disorders in youth.

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DSM-IV Diagnostic Categories of Anxiety Disorders

Currently the diagnostic categories for anxiety disorders are rationally derived. That is, they are grouped together according to phenotypically similar symptoms. However, the tradition in psychology is to evaluate dimensionally, as evidenced by the types of measures used to assess symptom severity. The current diagnostic system has attempted to include a dimensional quality by including the global assessment of functioning (GAF) scale, but this scale is not considered a psychometrically adequate measure since it is a single item that groups together multiple constructs (e.g., suicidality, basic daily functioning, interpersonal relatedness). Therefore, there is tension between the clinically relevant practice of rating symptom severity dimensionally and assigning a categorical diagnosis.

Notably, there were only three categories of anxiety disorders in the second edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-ll*; American Psychiatric Association, 1968). There are 12 categories in the current edition (*DSM-IV-TR*; American Psychiatric Association, 1994). Brown, Chorpita, and Barlow (1998) argued that the increasing

D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_8,

number of anxiety diagnoses indicates that the "classification systems have become overly precise to the point that they are now erroneously distinguishing symptoms and disorders that actually reflect inconsequential variations of broader, underlying syndromes" (p. 179). This reflects the "splitting" movement, whereby disorders are defined in increasingly narrow domains. Accordingly, with this level of specificity, existing diagnoses can in some instances lack syndromal validity and fail to offer distinctions that allow for effective treatment planning.

Dimensional Approaches – A Brief History

Dimensional models of psychopathology have been advocated for some time now, and the arguments advanced for this approach include several important points. First, categorically based diagnosis assumes that each disorder is a discrete entity (Carson, 1991). This is generally an inaccurate view, but it is the one understood by the architects of the symptom-based DSM (Frances et al., 1991). Second, since diagnoses in the current DSM are formulated based on consensus agreement in committees and task forces, rather than based on medical and/or psychological etiology from agreed upon theoretical concepts, the diagnoses are potentially arbitrary entities whose existence is based on a posteriori reasoning (for a discussion of different taxonomic methods and models, see Blashfield, Keely, & Burgess, 2009). Third, dimensional models permeate other medical sciences, where severity and complicating factors play a prominent role in classification. These factors are critical in any taxonomy because they contribute to prediction of course and treatment outcome (again, see Blashfield et al.). And finally, a guiding principle in the development of many categories in the current DSM was the degree that clinicians would be likely to accept the diagnosis, and thereby utilize it in evaluating clients (Carson, 1991). This last difficulty is perhaps most problematic since it undermines the very utility of a diagnostic system by formulating diagnosis on the basis of consensus rather than syndromal validity.

Since the earlier recommendations that a dimensional approach be adopted, a growing effort to develop statistical methodologies for identifying entities that are either continuous or taxonic has emerged. This approach, referred to as taxometric analysis, has allowed for the identification of conditions that may be taxonic (that is, composed of some discrete point whereby levels of a psychopathological indicator would suggest a unique and separate entity) or may be on a continuum of severity. Two notable examples from the anxiety disorder literature illustrate this. The first involves dissociation, which is commonly associated with trauma and acute anxiety and has been shown to be taxonic. That is, scores on a major measure of dissociation can be categorized where some individuals are considered nondissociators (or to a very limited degree) and those scoring above that point are considered dissociators (Waller, Putnam, & Carlson, 1996). On the other hand, anxiety sensitivity (AS) has been examined for taxonic status. AS refers to the degree that changes in internal bodily state are experienced as dangerous, and it is commonly present in most anxiety disorders (Taylor, 1999). Research has shown that this construct is nontaxonic, or dimensional (Broman-Fulks et al., 2010).

In the case of the major constructs used to understand anxious psychopathology, the majority are dimensional in nature. Among those that are dimensional in nature are worry (Olatunji, Broman-Fulks, Bergman, Green, & Zlomke, 2010), post-traumatic reactions (Ruscio, Ruscio, & Keane, 2002), and obsessive-compulsive symptoms and beliefs (Haslam, Williams, Kyrios, McKay, & Taylor, 2005). Likewise in children, there is a high degree of dimensionality evident in anxiety disorder relevant constructs. Notably, AS (Bernstein, Zvolensky, Stewart, & Comeau, 2007) and trauma (Goodman et al., 2003) both have been found to have a dimensional structure. There have been far fewer taxometric studies involving children, likely due to the large sample sizes necessary for stable estimates of effect (see Waller & Meehl, 1998, for a technical discussion of taxometric analysis).

What this suggests is that most psychological indicators involved in conceptualization and

assessment of anxiety disorders have a dimensional quality. This would rule out a categorical approach since such models eliminate a great deal of information regarding symptom severity and relevant treatment components.

The Problem of Comorbidity

From an epidemiological perspective, the current DSM system has resulted in a high probability of comorbid conditions. Brady and Kendall (1992) reported a 16% comorbidity rate in a community sample of children and adolescents that were not seeking treatment and comorbidity rates ranging from 28 to 62% in clinical samples of youth that were seeking treatment. As was discussed above concerning the problem of dimensional vs. discrete categories, the problem of comorbidity rate has been addressed in the literature. For example, Mineka, Watson and Clark (1998) described "excessive diagnostic splitting" as a potential cause of comorbidity with regard to highly similar disorders (e.g., overanxious disorder and generalized anxiety disorder [GAD] in children; Caron & Rutter, 1991). Researchers have also provided excellent suggestions for handling this issue in conceptualization and treatment planning. For example, Rachman (1991) offered four recommendations for handling comorbidity, including (a) behavioral analysis of presenting symptoms; (b) assessment of subjective experience of all comorbid conditions to identify overlapping features; (c) commonalities in psychophysiological responses; and (d) semantic overlap among diagnoses.

Around this same time, it was widely recognized that depression and anxiety tend to co-occur, or exist together at sub-threshold levels, but collectively lead to serious psychological disturbance (Barlow & Campbell, 2000). This emerged due to the frequent finding that, regardless of sample, depression and anxiety tend to correlate. In the case of self-report measures, the correlation between depression anxiety is typically greater than 0.6, even after removing items that could reasonably reflect the other construct and thereby inflate the correlation (Barlow, 1991). Similar results have been observed for other methods of assessing these constructs, indicating that this is not due to common method variance.

Among youth, there is significant amount of overlap between symptoms of anxiety and depression. In particular, Brady and Kendall (1992) found that the correlation between self-report measures of anxiety and depression ranged from $r = 0.50$ to 0.70 among children and adolescents. Although this high correlation may be due in part to similar item content on self-report measures of anxiety and depression, previous research has found that there is still substantial correlation when overlapping items are removed (Cole, Truglio, & Peeke, 1997; Stark & Laurent, 2001).

Generally, the net result has been to recognize that each is dimensional, rather than discrete entities, given the robustness of such a finding. Some in the psychiatry profession have called for a purely dimensional approach given that (a) depression and anxiety are commonly experienced in the general population and (b) severity is not tied to a reliable biological substrate (Goldberg, 2000). Indeed, consider that, even in the realm of behavioral genetics where the aim is to identify phenotypic signs of psychiatric disturbance, the field relies on dimensional models (Kendler, 2006). This is largely because there is recognition of the range of disturbance present in individuals suffering from psychiatric problems, and the dimensional approach permits greater reliability in findings given the increased variability and hence greater power in statistical tests (DiLalla, 2004).

Alternate Conceptualizations of Anxiety Disorders

Because of the high level of comorbidity, it has been suggested that a quantitative approach to diagnosis be used to uncover actual, rather than perceived, similarities among mood disorder diagnoses. Several models have been proposed in which correlated syndromes are grouped together in the same diagnostic class. These models aim to explain the shared and specific factors contributing to the etiology of anxiety and depression and serve to identify relevant treatment targets.

Negative Affect and Positive Affect

Negative affect (NA) is the tendency to experience negative moods (e.g., sadness, fear, guilt, and hostility) and has been described as a stable trait. It has been proposed that NA should be considered a main vulnerability factor for the development of anxiety and depression (Clark, Watson, & Mineka, 1994). Positive affect (PA), on the other hand, has been suggested as a vulnerability factor specifically related to depression. Watson, Clark, and Tellegen (1988) described PA as reflecting "the extent to which a person feels enthusiastic, active, and alert" (p. 1063), with low PA reflecting anhedonia. Tellegen (1985) theorized that these personality dimensions could be used to differentiate between anxiety and depression. Specifically, he hypothesized that NA is a nonspecific factor related to both anxiety and depression, and that the existing symptom overlap and resulting comorbidity are due to this shared trait. Furthermore, he suggested that PA is a specific factor that could be used to distinguish between anxiety and depression because they found that PA was related (negatively) to depression diagnoses in adults, but PA was not correlated with anxiety disorders (Watson, Clark, & Carey, 1988).

Among a nonclinical sample of elementary school–aged children, Crook, Beaver, and Bell (1998) did not find support for this model. Rather, they found that NA was significantly related to both self-reported depression symptoms ($r = 0.66$, $p < 0.001$) and self-reported anxiety symptoms ($r = 0.68$, $p < 0.001$). They also found that PA was negatively correlated with both depression symptoms ($r = -0.50$, $p < 0.001$) and anxiety symptoms ($r = -0.34$, $p < 0.001$). Although these initial results seemed to refute the specific relationship of PA to depression symptoms, Crook et al. also performed hierarchical regression to examine the partial correlations of PA and NA with measures of anxiety and depression, and they found that PA had a significant negative partial correlation with depression scores when anxiety and NA scores were controlled, whereas PA was unrelated to anxiety scores when depression and NA scores were controlled.

Tripartite Model

Clark and Watson (1991) expanded upon the original two-factor model of anxiety and depression by introducing another factor. They proposed the tripartite model as a means of differentiating anxiety and depression despite their high symptom overlap and diagnostic comorbidity, which posits that depression and anxiety both share the common component of NA. Depression, however, is specifically characterized by low PA, whereas anxiety is associated with high physiological hyperarousal (PH). While NA and PA have been described as stable temperaments or personality traits, PH has not. However, Clark et al. (1994) have related the concept of PH to AS, and AS has been described in the literature as a trait that is a risk factor for the development of anxiety disorders (McNally, 1990).

Barlow, Chorpita, and Turovsky (1996) have also described a very similar three-factor model for conceptualizing anxiety and depression which attributes the development of these disorders to problems with three basic emotions: anxiety (or anxious apprehension), fear, and depression. Their model indicates that (a) general distress (i.e., high NA) leads to *anxiety* (anxious apprehension), (b) autonomic arousal leads to *fear/panic*, and (c) anhedonia (i.e., low PA) and hopelessness lead to *depression*. As in the tripartite model, autonomic arousal is theorized to be specific to anxiety diagnoses while anhedonia/low PA is related only to depression. High NA/distress is hypothesized to be a common factor to both anxiety and depression.

Although the tripartite model was developed to explain the relationship between anxiety and depression in adults, it has been shown to be relevant to children and adolescents as well. For example, in a large sample of anxious and depressed youth, Lerner et al. (1999) found factors from measures of anxiety and depression that corresponded to the models described in Clark and Watson (1991). Furthermore, in a large unselected sample ($N = 1{,}289$) of children, similar findings were obtained using a different assessment of depression and anxiety, and were replicated in a smaller second sample ($N = 300$) (Chorpita, Daleiden, Moffitt, Yim, & Umemoto, 2000).

The relationship among NA, PA, and PH was further examined among inpatient children and adolescents, and support was again found for the tripartite model among youth (Joiner & Lonigan, 2000). Although many studies have supported the tripartite model, there is some evidence that the relationship among the three variables (i.e., NA, PA, and PH) may not be identical across all of the anxiety disorder diagnoses. In particular, there is evidence that predictions made using the tripartite model do not hold for youth diagnosed with Social Anxiety Disorder.

Brown et al. (1998) examined the structural relations among NA, PA, and PH in a large sample of individuals with one of five DSM-IV diagnoses: GAD, Depression, Panic Disorder, Obsessive-Compulsive Disorder (OCD), and Social Phobia. The use of structural equation modeling allowed the researchers to test the tripartite model with a dimensional approach to the DSM diagnostic categories as opposed to other approaches that would require the researchers to confirm a categorical diagnosis. Brown et al. found that all paths from NA to the DSM-IV disorder factors were statistically significant, which supports the notion that NA is a general dimension common to mood and anxiety disorders. The strength of the relationship varied across diagnosis, with the strongest relationships existing between NA and Depression and NA and GAD. The smallest association was found between NA and Social Phobia. When PA was added to the structural models, there was a significant negative path from PA to Depression. Notably, after creating a path from PA to Depression, the modification indices suggested that a path should also be added from PA to Social Phobia. A significant negative path was found between PA and Social Phobia, and the results indicated that the fit of this model was so good that it would not be improved by adding additional paths from PA to any other latent variable (i.e., other DSM-IV anxiety diagnoses). Furthermore, the strength of the path between PA and Depression (−0.29) was comparable to the strength of the path from PA to Social Phobia (−0.28). Finally, the addition of PH to the structural models did not improve the fit of the models. In terms of the different anxiety disorders, the strongest path from PH was found to Panic Disorder/Agoraphobia. The paths from OCD and Social Phobia to PH were not significant. Notably, the path from GAD to PH was significant and negative.

Turner and Barrett (2003) found that the tripartite model was consistent across three age groups (ages 8–9, 11–12, and 14–15) suggesting that the three major components of the model are not developmentally dependent. The balance of research has generally supported the tripartite model, but much of this has involved self-report measures or assessments that do not necessarily pose a strict test of the model (Anderson & Hope, 2008). However, the tripartite model has shown considerable promise in assessment of anxiety in youth, may be relatively robust across major anxiety diagnoses, and illustrates the potential clinical utility of a dimensional model of nosology.

Hierarchical Models

Although there has been empirical support for the tripartite model of depression and anxiety, this structural model asserts that all anxiety diagnoses are characterized by the shared component of high autonomic arousal, which differentiates anxiety from depression. Researchers have instead proposed that a hierarchical model of anxiety disorders may be more appropriate to account for the heterogeneity of anxiety diagnoses (Brown et al., 1998; Zinbarg & Barlow, 1996). In this model, each anxiety disorder has unique and shared components, with the shard component representing a higher-order factor of anxious apprehension (i.e., high NA). This model not only accounts for the high correlation among anxiety disorder diagnoses due to this shared component but also accounts for the high comorbidity among anxiety and depression because high NA is common to depression as well as anxiety.

Mineka et al. suggested a more comprehensive structural model that combines the tripartite model with the hierarchical model described above based on the fact that it is unlikely that each is equally and adequately explained by the dimension of

autonomic hyperarousal as proposed by those models. Therefore, Mineka et al. proposed the integrative hierarchical model, which suggests that syndromes have both common and unique components. As in previous models, high NA/distress is considered to be the shared component of both anxiety disorders and depression, but anxious arousal (AA) is not viewed as broadly characteristic of all anxiety disorders. Instead, each individual anxiety disorder is presumed to have some unique component that differentiates it from all others. AA is viewed as the specific component of panic disorder alone.

Support for this model has been found in children using structural equation modeling. In a sample of children, Spence (1997) examined four models to see which best explained the structure of self-reported anxiety symptom data (i.e., a single-factor model, a six-uncorrelated-factor model for each specific DSM-IV anxiety diagnosis, a six-correlated-factor model, and a higher-order model with six first-order factors loading onto a single second-order factor). The results indicated that the correlated six-factor model with these six factors loading onto a higher second-order "anxiety" factor provided the best fit to the data. Additionally, she found that the major proportion of variance in anxiety symptoms was explained by this higher-order anxiety factor, which suggests that while there are distinguishable anxiety diagnostic categories, the high comorbidity can be explained by a high correlation among the diagnoses in youth.

The integrative hierarchical model need not be confined to anxiety disorders and depression alone, but can be broadened to encompass other disorders that are characterized by high NA (Mineka et al., 1998). Krueger and Piasecki (2002) proposed the hierarchical spectrum model, which was an attempt to capture the correlation among DSM diagnoses by clustering symptoms to comprise syndromes with these syndromes comprising broader families of disorders or spectra. The broadest categories identified are the internalizing and externalizing disorders, with the internalizing disorders being comprised of depression and the anxiety disorders. Externalizing disorders include substance dependence, antisocial behavior, and disinhibited behavior diagnoses. This model has been promising in understanding anxiety disorders (Taylor, Abramowitz, McKay, & Asmundson, 2010), but has not yet been extensively examined in youth.

Krueger (1999) analyzed data from the National Comorbidity Study (NCS) to find that a three-factor structure best accounted for the relationship among psychiatric diagnoses. The three latent factors were Anxious-Misery (which included major depression, dysthymia, and GAD), Fear (which included panic disorder, agoraphobia, Social Phobia, and simple phobia), and Externalizing disorders (which included alcohol dependence, drug dependence, and antisocial personality disorder). The Anxious-Misery and Fear latent factors were highly correlated and thus were found to comprise a second-order factor of Internalizing disorders, which collectively form a group of conditions that tend to co-occur in varying levels. Interestingly, while the three-factor structure was found for the total NCS sample, in a treatment-seeking sample, the lower-order latent factors of Anxious-Misery and Fear could not be recovered. This suggests that among individuals experiencing functional impairment the individual diagnoses are even more highly correlated in a "superclass" of emotional disorders (Clark & Watson, 2006; Krueger & Markon, 2006; Watson, 2005).

The presence of such a superclass of disorders provides additional weight to the need for a dimensional approach to diagnosis since the underlying phenotype of anxiety confers a higher risk for a wide range of putative psychiatric conditions. Hereditability data have borne this out, whereby no single diagnosis increases the risk for anxiety disorder in offspring. Instead, the presence of any anxiety disorder increases the risk of any anxiety disorder in offspring (Hettema, Neale, & Kendler, 2001).

Measuring Anxiety Along a Dimension in Children

In general, the procedures used to assess and diagnose anxiety in children and adults are quite similar and typically include diagnostic interviews, self-report measures, and behavioral assessment.

However, it is important to consider developmental differences throughout the assessment process because due to speed of physical, emotional, and cognitive development in childhood, assessment strategies will differ according to age. For example, a multi-informant, multi-method approach is recommended to gather comprehensive information about symptoms and impairment. Thus, in addition to clinical interview, observation, and self-report, reports from parents and teachers are recommended when assessing emotional symptoms in a child, and the amount of collateral data needed from caretakers is typically inversely related to the age of the child. Furthermore, when assessing young people, it is also necessary to have knowledge of normative development, so that manifestations of "normal fears" are not considered abnormal behaviors (Beidel & Turner, 2005).

The Child Behavior Checklist (CBCL; Achenbach, 1991; Achenbach, Demenci, & Rescorla, 2003) and Teacher Report Form (TRF; Achenbach, 1991) are the most widely used parent and teacher reports. The CBCL is a standardized assessment that asks parents to report on behaviors, problems, and competencies in children aged 4–18 years. The TRF is completed by teachers and is identical in content to the CBCL. The clinical scales of the CBCL and TRF are comprised of a Total Problems score, Internalizing Problems, Externalizing Problems, and eight syndromes (i.e., Aggressive Behavior, Delinquent Behavior, Withdrawn, Somatic Complaints, Anxious/Depressed, Attention Problems, Social Problems, and Thought Problems). These syndrome scales were not developed to reflect DSM-IV diagnoses, but they were derived through multivariate statistical analyses to identify separate empirically validated syndromes in line with the hierarchical models described above. Specifically, with regard to anxiety, it was determined that anxiety and depression were so highly correlated that they represent a singular syndrome in youth.

Although the CBCL and TRF were originally developed with this empirically based approach to identifying symptoms along a continuum, Achenbach et al. (2003) created DSM scales by asking pediatric psychologists and psychiatrists from diverse cultural backgrounds to rate how consistent CBCL/TRF items were with a specific DSM category. Achenbach et al. selected items that were reliably rated as "very consistent with the DSM category" to create the DSM scales. A six-item Anxiety subscale was developed through this approach. Kendall et al. (2007) noted that these six items do not include any somatic symptoms, and this omission calls the validity of the Anxiety subscale into question given that somatic symptoms are a necessary criterion for many of the DSM-IV anxiety disorder diagnoses. Thus, Kendall et al. derived an alternative measure of anxiety based on the CBCL/TRF items.

Kendall et al. (2007) developed an initial list of 22 items by asking experienced clinicians with a specialty in childhood anxiety disorders to select CBCL/TRF items related to the diagnosis of an anxiety disorder. Of these items, 18 achieved item-total remainder estimates above 0.40 and were retained in their anxiety scale. These researchers found that their anxiety scale significantly discriminated anxious and nonanxious children aged 9–13 years, and their anxiety scale better predicted an anxiety disorder diagnosis than did the Anxious/Depressed and Internalizing Scales of the CBCL and TRF. In addition, they found that their anxiety scale was sensitive to treatment effects. Participants who received treatment demonstrated a significantly lower score after treatment, while those on the waitlist showed no significant change in score. Therefore, Kendall et al.'s (2007) anxiety subscale of the CBCL seems to be a good predictor of pathological anxiety in children and adolescents and can be used to identify gains made in treatment. However, there is some evidence that its utility may depend on the reporter. Kendall et al. found that when compared to the CBCL Anxiety Subscale developed by Achenbach et al. (2003), their anxiety scale better predicted anxiety disorder status according to mother report, while the Achenbach et al. Anxiety Subscale better predicted anxiety disorder status according to father report.

Another dimensional measure that may be useful for measuring factors related to anxiety is the Positive and Negative Affectivity Scale – Child

version (PANAS-C; Laurent et al., 1999). The PANAS-C is a 20-item self-report measure consisting of two scales: PA and NA. Respondents are asked to rate how often within the last week they have experienced 20 mood adjectives. The 10 positive-mood adjectives and 10 negative-mood adjectives are rated on a 5-point Likert-type scale. The scale choices are "very slightly or not at all," "a little," "moderately," "quite a bit," and "extremely." The findings suggest that the children's version of the PANAS has a similar structure as the adult counterpart. Since the development of this scale, several investigations have shown that it performs consistently across different cultural groups (Kiernan, Laurent, Joiner, Catanzaro, & MacLachlan, 2001), in unselected elementary and high school children (Jacques & Mash, 2004), and in children with diagnosed anxiety disorders (Hughes & Kendall, 2009). This last study identified difficulties in discriminant validity for the scale, however, with higher than anticipated relations with social anxiety and depressive symptoms. In some ways, this is not surprising, and reflective of the aforementioned long-standing difficulty in distinguishing anxiety from depression (see, for example, Rapee & Barlow, 1991).

A third measure that has been developed to measure mood symptoms along a dimension is the Mood and Anxiety Symptom Questionnaire (MASQ; Watson et al., 1995a, 1995b). The MASQ was created as a specific measure of the tripartite model described above. It is a 77-item self-report measure with three subscales: (1) General Distress: depressive symptoms (12 items), anxious symptoms (11 items), and mixed symptoms (15 items); (2) Anxiety-specific (AA, 17 items); and (3) Depression-specific (Anhedonic Depression [AD], 22 items). Buckby, Yung, Cosgrave, and Killackey (2007) found support for the clinical use of the MASQ to differentiate between anxious and depressed adolescents and young adults. Using ROC analyses, these authors found that the AD scale accurately predicted the presence of a mood disorder (72.8%) and the AA scale predicted anxiety disorders (61%). Thus, it seems that the AD scale may be superior to the AA scale in predicting the presence of the particular disorder it is intended to measure. Notably, the AA scale did better at identifying the absence of an anxiety disorder (83.5%). Furthermore, Buckby et al. (2007) found that AA and AD scores were highly and significantly correlated in all participants with a current Axis I disorder ($r = 0.59$). This high correlation calls into question the assumption that these are separate constructs, which is in line with the hierarchical models which indicate that these both fall on the broader spectrum of internalizing disorders.

Narrow Traits and Risk Factors in Youth

Given that heredity studies suggest that the presence of an anxiety disorder in a biological parent predicts development of *any* anxiety disorder in offspring (Hettema et al., 2001), it is assumed that a general tendency to develop anxiety disorders (i.e., anxiety proneness) is inherited rather than a specific anxiety disorder (Turner, Beidel, & Roberson-Nay, 2005). Thus, it is recommended that assessment also includes attention to these personality traits and temperaments that have been identified as risk factors for the development of anxiety disorders.

Behavioral Inhibition

Behavioral inhibition (BI) is a temperamental trait that is characterized by the tendency of children and adolescents to become uncomfortable in, and avoid, novel social situations. These youth are extremely shy and are reluctant to engage in adventurous activities or participate in unfamiliar social situations (Kagan, Reznick, & Snidman, 1988). BI has consistently been found to be related to the development of anxiety disorders, particularly Social Anxiety Disorder (Hirshfeld-Becker et al., 2008). Furthermore, BI seems to be most predictive of anxiety disorders when it is found among the children of parents with anxiety disorders (Biederman et al., 2001).

BI is typically measured using objective standardized laboratory observation protocols which involve exposing toddlers and preschoolers to unfamiliar people and situations. There are also

several parent, teacher, and self-report measures of BI. For example, the Behavioral Inhibition Questionnaire (BIQ; Bishop, Spence, & McDonald, 2003) may be used to assess BI in preschool-aged children (i.e., 3–5 years old). There are both parent and TRFs of the BIQ. In older children and adolescents (i.e., 11–18 years old), the Behavioral Inhibition Instrument (BII; Muris, Merckelbach, Wessel, & van de Ven, 1999) can be used.

Anxiety Sensitivity

AS refers to a person's beliefs that his or her anxious physical symptoms will lead to aversive physical, psychological, and social consequences (Reiss, 1991; Reiss, Peterson, Gursky, & McNally, 1986). In other words, AS can be understood as the likelihood for an individual to report that normal bodily changes associated with anxiety are likely to have extreme negative consequences. For example, an individual with high AS is likely to believe that heart palpitations are a sign of a heart attack, whereas an individual low on AS perceives heart palpitations to be nothing more than brief physical discomfort. Those with high AS have been described as having the "fear of anxiety" (Reiss, Peterson, & Gursky, 1988, p. 341).

AS has consistently been shown to be higher among youth with anxiety disorders as compared to those without anxiety (Hayward et al., 1997; Weems, Hayward, Killen, & Taylor, 2002). This indicates that AS likely serves as a risk factor in the development and maintenance of anxiety disorders in young people. AS is measured using the Childhood Anxiety Sensitivity Index (CASI; Silverman, Fleisig, Rabian, & Peterson, 1991).

Anxiety Control

Anxiety control (AC) is a cognitive construct that is defined as a person's perceived control over his or her emotional and bodily reactions due to anxiety (e.g., internal physiological reactions) as well as his or her perceived control over external events or threats that cause anxiety (Rapee, Craske, Brown, & Barlow, 1996). Low AC has been identified as a factor that can differentiate between youth who have been referred to a clinic for anxiety treatment and controls, and AC has been shown to predict anxiety disorder status among children and adolescents when controlling for anxiety symptoms (Weems, Silverman, Rapee, & Pina, 2003).

The Anxiety Control Questionnaire for Children (ACQ-C; Weems et al., 2003) may be used to measure AC. The ACQ-C measures beliefs along two dimensions: (1) Internal Reactions (e.g., "I can take charge and control my feelings") and (2) External Threats (e.g., "When something scares me, there is always something I can do"). In a recent study, Marin, Rey, Nichols-Lopez, and Silverman (2008) found that both dimensions of AC predict anxiety symptoms in youth, but they found a different pattern for boys and girls. Specifically, in boys, low perceived control over Internal Reactions predicted anxiety symptoms. However, in girls, low perceived control over External Threats predicted anxiety symptoms.

Diathesis–Stress Model

The presence of any one of these identified risk factors alone is likely not sufficient to lead to the development of an anxiety disorder. In other words, even if a child is anxiety prone, a disorder's onset will probably be triggered by the interaction of the biological predisposition with environmental/psychological factors (e.g., parenting factors) as described in the diathesis–stress model. In fact, there is evidence that some of these inherited vulnerability factors may be mitigated by environmental factors. For example, BI, which has been identified as a relatively stable temperamental trait, has been shown to be reduced among young children if parents are instructed in the risks associated with over-protective parenting and how to intentionally expose their child to novel social situations (Rapee, Kennedy, Ingram, Edwards, & Sweeney, 2005). There is ample empirical support for the usefulness of measuring these narrow traits as part of dimensional diagnosis of anxiety disorders in youth. Because many of these traits are currently measured via self-report, Turner et al. (2005) recommended that physiological reactivity can be used as a measure of anxiety proneness that is not dependent on subjective report.

Correspondence to Treatment Models Rather than Diagnostic Categories

A shift in diagnostic classification from a categorical to dimensional conceptualization can lead to a fuller understanding of the components that underlie anxiety and mood problems. The current DSM-IV criteria focus on the differential diagnosis of anxiety problems at the risk of neglecting aspects relevant to the amelioration of these anxiety problems. However, a dimensional model, which supports an understanding of mood disorders as highly related disorders residing together in a broader spectrum and consisting of common and unique components, can be used to hone in on relevant aspects of the disturbance in therapeutic interventions. Specifically, cognitive behavioral treatments have been shown to be effective treatments for anxiety disorders in children and adolescents (e.g., Kendall, 1994) and the adoption of a dimensional model may ensure that all relevant cognitive aspects are addressed in treatment even though they may not be narrow (i.e., unique) symptoms associated with a particular diagnosis. For example, treatment of Social Anxiety Disorder without attention to the identified correlate of low PA may not be as effective, but this relationship that has been shown empirically is not reflected in the diagnostic criteria. Similarly, Marin et al. (2008) found that different aspects of AC were useful for predicting anxiety disorders for boys and girls, which suggests that cognitive behavioral interventions may have separate targets for the different genders. As the literature covered in this chapter amply illustrates, there are many advantages that can be conferred on treatment of children with anxiety disorders by relying on dimensional perspectives. Further research into quantitatively derived models for the dimensional diagnosis of anxiety in youth promises to inform and improve our treatment of these disorders by highlighting the relevant personality traits, cognitive factors, and emotional and behavioral responses that will lead to increased functioning. This can also provide a rich understanding of what dimensions may potentially form distinct categories at the extreme boundaries based on empirically based evaluations. In contrast to the large and diverse number of diagnoses that currently exist, it appears that there are in fact numerous dimensions but few distinct binary categories. Refinement of dimensional models would permit better treatment decisions based on severity level and the rarer categorical psychiatric conditions.

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Part III

Ancillary Components of Child and Adolescent Anxiety

Differential Diagnosis and Comorbid ADHD in Childhood

9

Alasdair Vance

Anxiety disorders and Attention Deficit Hyperactivity Disorder (ADHD) are both common conditions in children and adolescents. Further, there is a known significant association between them, evident in epidemiological and clinical studies (Anderson, Williams, McGee, & Silva, 1987; Biederman, Newcorn, & Sprich, 1991; Jensen et al., 2001). This chapter explores how ADHD affects the diagnosis, clinical presentation, assessment and treatment of anxiety disorders. There is a particular emphasis on key differential diagnoses to consider in a comprehensive approach to assessment and composing more specific and targeted treatment plans for young people with anxiety disorders and comorbid ADHD.

ADHD and the Diagnosis of Anxiety Disorders

ADHD is characterised by developmentally inappropriate levels of inattention, and/or impulsiveness overactivity (American Psychiatric Association, 1994). There are three main subtypes of ADHD, ADHD-combined type (ADHD-CT), ADHD-hyperactive-impulsive type (ADHD-HI) and ADHD-inattentive type (ADHD-IA) (American Psychiatric Association, 1994). A patient must present with more than six symptoms of inattention and less than six symptoms of hyperactivity-impulsiveness to meet the threshold criteria for ADHD-IA, more than six symptoms of hyperactivity-impulsiveness and less than six symptoms of inattention to meet the threshold criteria for ADHD-HI and more than six symptoms of inattention and hyperactivity-impulsiveness to meet the threshold criteria for ADHD-CT. Further criteria stipulate that the symptoms must have been present and caused some clinically significant impairment before the child was 7 years of age, and the impairment must be present in two or more settings over the preceding 6 months. The diagnosis of ADHD is made only if the symptoms are not better accounted for by any other disorder such as a pervasive developmental disorder, psychotic disorders, mood disorders, personality change due to a medical condition or any substance-related disorder.

Similarly, a number of different anxiety disorders are recognised in the current Diagnostic and Statistical Manual for Mental Disorders (DSM) nosology (American Psychiatric Association, 1994). Importantly, like the three ADHD subtypes, they share a number of clinical, aetiological risk factors and treatment response features in common. However, there are also key differences: for example, generalised anxiety disorder (GAD), separation anxiety disorder (SAD), social phobia (SoPh) and specific phobia (SpPh) form a coherent group of anxiety disorders that are closely aligned (Fonesca & Perrin, 2001;

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_9, © Springer Science+Business Media, LLC 2011

Vance, 2005). In contrast, obsessive–compulsive disorder (OCD) has a distinctive clinical presentation, set of aetiological risk factors and psychological and/or medication treatment response (Fonesca & Perrin, 2001; Vance, 2005). This essential heterogeneity in both ADHD and anxiety disorders presents a significant hurdle for the clinician and the researcher to overcome; for instance, the sheer number of possible ADHD subtype and anxiety disorder combinations to be considered and the potential additive risk or ameliorating effect of given different combinations of ADHD and anxiety disorders (Fonesca & Perrin, 2001; Vance, 2005). For example, children with ADHD and GAD may have a better performance on some aspects of executive functioning while those with ADHD and OCD may have a worse performance. These performance differences may contribute to worsening comorbid oppositional defiant disorder (ODD) or conduct disorder (CD) symptoms. Nevertheless, while much research is yet to be done to elucidate these complexities, there have been significant gains in theoretical understanding, clinical knowledge and treatment approaches over the past decade (Tannock, 2009).

Epidemiological studies suggest point prevalence rates from 2 to 24% for anxiety disorders, defined in various ways, categorically and/or dimensionally, and from 1 to 17% for ADHD, again variably defined, categorically and/or dimensionally (Tannock, 2009). Categorical diagnostic rates are almost always lower than those that are questionnaire derived. GAD, SpPh, SAD and SoPh are the four most common anxiety disorders, while OCD and panic disorder are less common, particularly pre-puberty. In epidemiological samples, ADHD-IA is the most common subtype of ADHD followed by ADHD-CT, while ADHD-CT predominates in clinical samples (Biederman, Faraone, & Keenan, 1991; Taylor, Everitt, et al., 1986; Taylor, Schachar, Thorley, & Wieselberg, 1986). This is broadly consistent with increased rates of ODD associated with ADHD-CT compared to ADHD-IA (Cantwell & Baker, 1992), for ODD is a common reason for a child's or adolescent's referral to mental health services (Loeber, Burke, & Lahey, 2000). Of course, there are other factors that also affect this difference; these are beyond the scope of this chapter. Approximately thirty to forty percent of patients with ADHD will have comorbid anxiety disorder(s) (Biederman et al., 1996) while 15–30% of those with anxiety disorders are noted to have ADHD (Last, Hersen, Kazdin, Orvaschel, & Perrin, 1991). Twenty-five to thirty-three percent is a consistent average range from clinical and epidemiological samples (Biederman, Faraone, & Mick, 1991; Jensen et al., 2001), confirming the greater-than-chance association of anxiety disorders with ADHD. Interestingly, child, adolescent and recently adult samples confirm the enduring association between anxiety disorders and ADHD across key developmental stages (Schatz & Rostain, 2006). Also, this association is evident across different social groups, cultures and nations (Buyn, Yang, & Lee, 2006). Further, gender does not moderate the association between anxiety disorders and ADHD in children, adolescents or adults (Biederman, Faraone, & Mick, 1991).

Early studies noted the robust association between anxiety disorders and ADHD-IA compared to ADHD-CT (Hynd et al., 1991; Lahey et al., 1988; Stanford & Hynd, 1994). In contrast, recent studies, using clinical samples, failed to demonstrate any differences between these two ADHD subtypes: for example, Willcutt, Pennington, Chabildas, Friedman, and Alexander (1999) studied ADHD-CT, ADHD-IA and comorbid GAD and anxiety symptoms, from parent and child reports, using a school-derived sample of twins and found no differences between them. Wolraich, Hannah, Pinnock, Baumgaertel, and Brown (1996) investigated a school-based sample of children with ADHD-CT and ADHD-IA and found increased rates of anxiety disorders in the children with ADHD-CT compared to ADHD-IA. In particular, increased rates of SAD were reported with ADHD-CT (DSM-III equivalent) compared to ADHD-IA (Cantwell & Baker, 1992). Our group has reported point prevalence rates of 20–40% child self-reported anxiety disorders in medication naïve children with ADHD-CT (Vance, Luk, Costin, Tonge, & Pantelis, 1999). We have also noted the weak correlation between

parent- and child-reported anxiety disorders and the decrease in child-reported anxiety disorders over time while there is no change in parent-reported anxiety disorders (Vance et al., 2002). Further, we have reported that the child self-report of SAD was the only parent or child self-reported anxiety disorder to be significantly increased in the anxiety disorders and ADHD-CT compared to the anxiety disorders-alone group (Vance, 2005). This suggests an additive or multiplicative effect between SAD and ADHD-CT that requires further investigation using epidemiological data with larger numbers, particularly in the anxiety disorders-alone group: our calculation of the effect sizes of anxiety disorders alone: ADHD-CT alone (Cohen's $d=0.05$) compared to ADHD-CT and anxiety disorders: anxiety disorders alone (Cohen's $d=0.68$) compared to ADHD-CT and anxiety disorders: ADHD-CT alone (Cohen's $d=0.70$) suggested a multiplicative effect. These divergent parent and child report findings are consistent with studies that have shown only approximately 50% of children with self-reported anxiety have been noted to also be reported with anxiety by their parents (Pliszka, 1992), and that the parent and child report may have different origins: the parent report of their given child's anxiety disorder(s) may represent their child's "negative affectivity and associated behavioural problems" rather than "neurotic anxiety suffered by children with anxiety disorders alone [*sic*]" (March et al., 2000). Further, significant clinical correlates, such as levels of self-confidence and impairments in activities of daily living, may be associated with the child anxiety self-report alone (Tannock, 1994).

Indeed, it appears that ADHD-IA and ADHD-CT, the two most common subtypes of ADHD in epidemiological and clinical samples, do not differ in their greater-than-chance association with anxiety disorders, or in the specific types of anxiety disorders with which they are comorbid. Interestingly, parent- and child-reported anxiety disorders have similarities and differences from childhood into adolescence, although their underlying nature is congruent. Our group used hierarchical log-linear analyses to study the relationships between parent-reported anxiety disorders in their children and, separately, child self-reported anxiety disorders in ADHD-CT and anxiety disorders and anxiety disorders-alone groups (Vance, 2005). Anxiety disorders were only allowed in the models, as per convention, if two-way contingency tables provided expected frequencies in excess of five. Parent and child reports of anxiety disorders differed in the relationships between specific anxiety disorders that were allowed entry into the models. Parent-reported OCD in the anxiety disorders-alone and with ADHD-CT group was separate to the related four most common anxiety disorders (GAD, SAD, SoPh, SpPh), consistent with the known aetiological differences between these two broad types of anxiety (Sallee & March, 2001). Importantly, child-reported OCD was not allowed entry into the model, while the four most common anxiety disorders were, in the anxiety disorders-alone and with ADHD-CT groups. Therefore, the above parent-reported difference could not be investigated in the child self-reported data.

Anxiety disorders and ADHD can persist or actually worsen from childhood into adolescence (Barkley, Fischer, & Smallish, 1996). Further, additional comorbid conditions such as ODD/CD and/or depressive disorders may develop (Biederman, Monuteaux, & Mick, 2006). These conditions invariably confer additional functional impairment in one or more academic, social, home or occupational domains.

The exact nature of comorbid anxiety disorders with ADHD remains unclear. Current possibilities include (1) the ADHD (usually ADHD-IA) symptoms being secondary to the primary anxiety disorder (for example, OCD), (2) the anxiety disorders arising from a maladjustment of the patient to a primary ADHD (usually ADHD-CT), (3) both disorders arising from common biological and/or psychosocial antecedent risk factors and (4) the association between both disorders arising from their separate association with a third disorder such as ODD, CD or depressive disorders such as dysthymic disorder (DD) and/or major depressive disorder (MDD).

A number of lines of evidence are emerging to support option (4). At the phenomenological level, the association of anxiety disorders, ADHD and early onset depressive disorders with ODD

symptoms has been examined (Vance, Arduca, & Sanders, 2005). The greater-than-chance association of ODD with ADHD-CT, depressive disorders and anxiety disorders is a replicated finding (Angold, Costello, & Erkanli, 1999). Angold et al. (1999) reported median joint odds ratios from a meta-analysis of 10.7 (95% CI = 7.7–14.8) with ADHD (primarily ADHD-CT), 6.6 (95% CI = 4.4–11.0) with depressive disorders and 3.0 (95% CI = 2.1–4.3) for anxiety disorders. Recently, Maughan, Rowe, Messer, Goodman, and Meltzer (2004) noted previous epidemiological studies that had reported this association and confirmed it using data from their recent epidemiological study: 19.1 (95% CI = 12.5–29.3) for boys with ADHD (primarily ADHD-CT), 6.3 (95% CI = 2.1–18.7) for boys with depressive disorders and 5.4 (95% CI = 3.3–8.7) for boys with anxiety disorders. Within the ADHD-CT literature, the greater-than-chance association of ADHD-CT with ODD, depressive disorders and anxiety disorders has also been noted (Lahey, McBurnett, & Loeber, 2000; Vance, 2005; Vance, Arduca, & Sanders, 2005). We studied one hundred and eighty-nine children aged from 6 to 12 years with ADHD-CT (DSM-IV criteria), defined through a semi-structured clinical interview with the child's parent(s) and by the parent and/or teacher report of the subscale scores of the core symptom domains of ADHD-CT being greater than 1.5 standard deviations above the mean for a given child's age and gender. ADHD-CT symptoms (15% of the variance) and DD symptoms (8% of the variance) made independent significant contributions to the prediction of ODD symptoms. The three independent variables in combination contributed a further 21% of the variance. Altogether 44% of the variance in ODD symptoms was predicted by knowing scores on these three variables. Although the correlation between anxiety disorder symptoms and ODD symptoms was 0.27, anxiety disorders did not contribute significantly to the regression. Apparently, the relationship between anxiety disorder symptoms and ODD symptoms is mediated by the relationships between ADHD-CT symptoms, DD symptoms and ODD symptoms. This finding extends Angold et al.'s (1999) reported association of CD with anxiety disorders via each disorder's link with depressive disorders by specifically demonstrating the association between ODD and DD symptoms within a primary school age ADHD-CT sample.

A second line of evidence supporting option (4) involves underlying biological risk factors. We examined the association of neurodevelopmental deficits (NDD) with anxiety disorders, ADHD and DD in primary school age children. A cross-sectional study was undertaken of NDD in 99 6- to 12-year-old children with categorically and dimensionally defined anxiety disorders alone, ADHD-CT alone, DD alone and 20 age-matched healthy children. The ADHD-CT and DD groups had significantly increased total neurological subtle signs compared to the anxiety disorders group and the healthy control group. The anxiety disorders group also had significantly increased neurological subtle signs compared to the healthy control group (ADHD-CT: anxiety disorders Cohen's $d = 0.87$; ADHD-CT: controls Cohen's $d = 1.59$; DD: anxiety disorders Cohen's $d = 0.57$; DD: controls Cohen's $d = 1.69$; anxiety disorders: controls Cohen's $d = 0.74$). These significant group differences remained after controlling for full scale IQ, which had a significant independent association with total neurological subtle signs, gender, which did not have a significant independent association and, separately, age, which did. The findings replicated earlier work by Taylor, Everitt, et al. (1986), Taylor, Sandberg, Thorley, and Giles (1991) and Taylor, Schachar, et al. (1986) and are consistent with results reported by Piek, Pitcher, and Hay (1999). Shaffer, Schonfeld, and O'Connor (1985) findings were extended through demonstrating that (1) within the rubric of "affective diagnoses", DD rather than anxiety disorders may better explain the reported association between "emotional" disturbance and neurological "soft signs" and (2) "emotional *and* behavioural disturbance" are associated with neurological subtle signs, as the strength of the association with neurological subtle signs does not significantly differ between DD and ADHD-CT, compared to healthy children, although the magnitude of the difference for ADHD-CT is large and for DD is moderate

compared to primary school age children with anxiety disorders.

A third line of evidence supporting option (4) involves underlying cognitive risk factors. We extended our investigation of biological risk factors associated with each condition by examining the association of anxiety disorders and ADHD and separately DD and ADHD on a robust cognitive neuroscience construct, spatial working memory (SWM). Of particular interest is whether comorbid anxiety disorder differs from comorbid DD in its effects on SWM performance and the putative prefrontal cortical neural networks known to subserve this measure. The extant literature suggests that comorbid anxiety disorder should have an independent impairing effect on SWM (Tannock, Ickowicz, & Schachar, 1995), while to our knowledge there is no literature that supports a directional hypothesis for SWM function in DD, separate from MDD. A total of one hundred and twenty-five children (aged 7–12 years) were identified: ADHD-CT alone ($N=25$), ADHD-CT and anxiety disorder(s) ($N=25$), anxiety disorder(s) alone ($N=25$), ADHD-CT and DD ($N=25$) and DD alone ($N=25$). Anxiety disorders were defined as DSM-IV GAD, SAD, SoPh and SpPh (American Psychiatric Association, 1994), diagnosed through a semi-structured clinical interview with the child's parent(s) (Silverman & Albano, 1996) and by the parent and/or child report of the total anxiety scores being greater than 1.5 standard deviations above the mean for a given child's age and gender (Achenbach & Edelbrock, 1983; Reynolds & Richmond, 1985). The children were all stimulant, anxiolytic and antidepressant medication naïve. All groups were matched for age, gender, verbal/performance/full scale IQ, spelling, arithmetic and social adversity. Children with ADHD-CT had worse SWM, ability to generate strategy and spatial span than anxiety disorder, whether comorbid "anxiety" was present or not. Further, the children with ADHD-CT and anxiety disorder, whether comorbid or not performed the SWM task in the same way. As age increased, SWM ability improved in all groups, although ADHD-CT had a worse SWM performance, whether anxiety disorder was present or not. In contrast, children with ADHD-CT and DD were indistinguishable on their SWM performance and differed in their approach to completing the SWM task: the ADHD-CT group relied on spatial span and strategy while the DD group depended on strategy alone. As age increased, SWM ability improved in all groups, which were unable to be differentiated.

In summary, our studies suggest that comorbid anxiety disorders with ADHD may arise from common biological risk factors (NDD). Further, their association may also arise from their separate association with a third disorder such as DD. Of course, there may be myriad additional biological and psychosocial risk factors and further mediating third disorders yet to be characterised. Such factors and disorders may affect the children's response to medication and/or psychological treatments offered.

ADHD and the Clinical Presentation of Anxiety Disorders

Children with anxiety disorders and comorbid ADHD manifest features of both disorders in a variety of situations – mainly the home environment, the school classroom and peer social interactions. It remains unclear whether the features of anxiety disorders and/or ADHD are affected by the presence of the other. The Multimodal Treatment Study of Children with ADHD (MTA) (Jensen et al., 2001; Newcorn, Halperin, and Jensen, 2001) data implied that inattention rather than hyperactivity-impulsiveness characterised children with "anxiety" and ADHD and that this group had lower teacher rated impulsiveness than children with ADHD and ODD/CD. However, subsequent observation of these children did not discern significant differences in their inattention, motor overactivity and/or impulsiveness in the school environment (Abikoff, Jensen, & Arnold, 2002). Earlier studies were similarly inconclusive: Pliszka (1992) also reported that teacher-rated inattention and hyperactivity and core ADHD symptoms during standardised testing were decreased in comorbid anxiety disorders and ADHD. In contrast, Livingstone, Dykman, and Ackerman (1990) noted increased core

ADHD symptoms and aggression in these children compared to those with ADHD alone. At present, there are no compelling explanations for these inconclusive results. Core anxiety disorder symptoms and separately ADHD symptoms can be better in some individuals while worse in others with additional comorbid ODD and/or CD symptoms. ADHD and anxiety disorders may be similar to each other in presentation via observation. Also, it may be harder to identify anxiety disorders in the presence of core ADHD symptoms because of a clinician bias to focus preferentially on the latter. Certainly, different contexts affect the manifestations of both types of disorder. This is particularly pertinent for the anxiety disorders.

Generalized anxiety disorder, SpPh, SAD and SoPh are the most frequent anxiety disorders comorbid with ADHD. Children's worries about how well they are performing compared to their peers, how accurate they are, how quick they are, checking for errors, and repeated requests for reassurance are common, although the worries will vary depending on the child's situation and context. Specific fears of the dark, particular strangers or dogs may occasionally motivate avoidance behaviours that can be repetitively impulsive. Fears about moving from a low threat, easily managed environment, such as the home living room, to perceived higher threat environments where there are many more novel cues and competing stimuli to manage and prioritise, are a particularly important form of anxiety. As noted above, such separation anxiety is especially comorbid with ADHD-CT and may indeed worsen with age and the degree of defiance (Cantwell & Baker, 1992; Vance, 2005). Further, they may become a main driver for school refusal behaviour as can social anxiety, especially the fear of being critically appraised by peers and/or teachers and found wanting. This type of anxiety is especially crippling from late childhood into adolescence when peer group interactions become normative for young people, aside from their family of origin. Together, these forms of anxiety are associated with children being more tentative about engaging with new situations, novel tasks, taking appropriate risks to facilitate their learning, and trying new things repeatedly in order to consolidate their skills base.

Less commonly, checking and counting behaviour with or without excessive cleaning suggests comorbid OCD. Elaborate number systems that may also arise from a need for symmetry and rarely aggressive OCD themes characterise these children. Post-puberty, sexual OCD themes can emerge as in adults with the disorder. Usually, the ADHD symptoms are more easily identified while the OCD features remain more hidden. Children often try to hide them because of their embarrassment about their nonsensical, irrational nature. Further, children feel trapped by their obsessive and compulsive symptoms because of the intense unpleasant feelings associated with them that are trying to minimise. Indeed, these children often have severe and frequent tantrums associated with severe mood lability and marked defiance that can predispose them to developing early onset depressive disorders such as DD and/or MDD (Fonesca & Perrin, 2001). The exact mechanisms for these outbursts can be hard to uncover clinically without careful interview of multiple informants and occasionally direct observation over a number of days in an inpatient setting.

Similarly, panic attacks are relatively rare pre-puberty and tend to occur in older children and adolescents once their cognitive capacities are sufficiently well developed. The younger the child with panic attacks, the more likely the presence of a depressive disorder (Fonesca & Perrin, 2001).

Acute stress disorder and post-traumatic stress disorder are also relatively rare pre-puberty. However, there has been considerable debate in the health and welfare literature about the possibly different phenomenology and clinical presentation of these disorders in younger patients. Nevertheless, both anxiety disorders and ADHD are known to worsen in the context of traumatic life events, particularly when repeated and/or of chronic duration.

Perhaps one of the most challenging clinical decisions is separating anxiety symptoms from inattentive symptoms as the main driver for a given child's presentation. Further, there are children who manifest both equally. Usually on careful history taking, the child with a primary

anxiety disorder will self-report a number of key anxiety symptoms that complete the impairing pattern of symptoms of one or more of the anxiety disorders above. ADHD inattentive symptoms, with and without hyperactive-impulsive symptoms may be present but will be less frequent, less severe and clearly linked to worsening anxiety symptoms and better as they abate. In contrast, the converse is true for a child manifesting primary ADHD (parent and teacher report) with secondary, more fragmentary self-reported anxiety symptoms. However, when both are equally present, there is similar frequency, severity and timing of onset of both.

ADHD and the Assessment of Anxiety Disorders

When taking the history, there are a number of key factors to identify that increase the risk of anxiety disorders and ADHD, separately: these include for ADHD, a positive family history of first-degree relatives with ADHD (Biederman, Faraone, & Keenan, 1990), maternal smoking during their child's pregnancy (Linnet, Dalsgaard, & Obel, 2003), perinatal complications (for example, birth hypoxia) (Ben Amor, Grizenko, & Schwartz, 2005) and a vulnerable temperament with high levels of motor activity, inattention and distractibility (Sheese, Voelker, Rothbart, & Posner, 2007). Similarly, for anxiety disorders, a positive family history of first-degree relatives with anxiety disorders, shyness and behavioural inhibition in infancy, increased frequency of adverse life events across developmental life stages and social adversity (for example, multiple parental relationship breakdowns) (Leech, Larkby, & Day, 2006; Phillips, Hymnen, & Brennan, 2005). Such factors form non-specific risks for ADHD and anxiety disorders, amongst other internalising and externalising disorders.

In addition, there are three more specific factors that may be particularly important to identify in children with anxiety disorders and comorbid ADHD: First, it is known that children with ADHD and anxiety disorders have first-degree relatives with substantially increased rates of anxiety disorders although similar levels of ADHD compared to children with ADHD alone (Biederman, Faraone, & Keenan, 1991). Importantly, anxiety disorders and ADHD appear to be transmitted independently in families (Braaten, Biederman, & Monuteaux, 2003). This suggests that the familial risk of anxiety disorders is separate from that of ADHD. This adds more weight to models that predict that anxiety disorders and ADHD are not directly related but rather are associated through the presence of biological and/or psychosocial risk factor(s) and/or disorder(s) that they have in common. Second, maternal anxiety, over-protectiveness and the lack of positive parenting are associated with anxiety disorders comorbid with ADHD (Pfiffner & McBurnett, 2006). These interpersonal factors emphasize the environmental contribution to the onset and progression of anxiety disorders. Further, they suggest key targets for the effective treatment of anxiety disorders. Third, antenatal maternal stress, especially "anxiety", are associated with increased rates of core ADHD-CT symptoms, ODD symptoms, CD symptoms, aggression, anxiety and depressive disorder symptoms and more difficult temperament during infancy (Huizink, Mulder, & Medini, 2004; O'Connor, Heron, & Golding, 2003; Van den Bergh, Mulder, & Mennes, 2005). Indeed it has been estimated that the risk of anxiety disorders comorbid with ADHD doubles if maternal anxiety levels are in the top 15% (Van den Bergh, Mennes, & Oosterlaan, 2005).

The key risk gestational phase appears to be from 12 to 22 weeks during the pregnancy (Van den Bergh & Marcoen, 2004): a time of peak neuronal migration, proliferation and differentiation (Nowakowski & Hayes, 2002). This would necessarily contribute to aberrant prefrontal cortical, basal ganglia, medial temporal lobe and parietal lobe neural network formation. These anomalous neural networks are known to subserve working memory, response inhibition, mood and arousal regulation difficulties associated with both anxiety disorders (lesser extent) and ADHD (greater extent) (Vance et al., 2006; Vance, Silk, & Cunnington, 2007). Possible mechanisms by which antenatal maternal anxiety

may contribute to such neural network dysfunction include (1) vulnerability gene by environment interaction, (2) enhanced maternal hypothalamic-pituitary-adrenal (HPA) axis function (hypercortisolaemia) leading to alterations in the foetal HPA axis that influences the developing foetal brain and (3) alterations in foetal blood flow affecting circulation in the developing foetal brain (Sjostrom, Valentin, & Thelin, 2002; Talge, Neal, & Glover, 2007). Regardless of these possible mechanisms, this increased antenatal maternal anxiety along with paternal anxiety and parenting style are important targets for psychological and/or medication intervention.

Examination of the child with comorbid anxiety disorders and ADHD should involve assessment of cognition. There is emerging evidence that children with comorbid "anxiety" and ADHD are impaired in their performance of cognitive tasks that require progressively more short-term memory and working memory (Tannock et al., 1995). It remains unclear which specific anxiety disorders may be associated with this impairment and whether there are other types of "anxiety" that enhance performance. In contrast, tasks that are focussed on reaction time with minimal working memory demands are usually performed better by this comorbid group (Pliszka, 1992). This pattern of results may be due to a modicum of increased anxiety leading to an increased allocation of working memory processing resources and alternative strategies within working memory that are overwhelmed by tasks requiring large working memory reserves (Eysenck, Derakshan, & Santos, 2007). Levy (2004) recently articulated a succinct neurophysiological model to explain such findings: altered tonic/phasic dopaminergic firing in mesolimbic systems drives core ADHD symptoms while impaired prefrontal cortical and hippocampal gating of amygdala-linked fear "anxiety" activity at the level of the nucleus accumbens drives "anxiety". Both these theories help explain the academic underachievement and social difficulties these children experience that exacerbates their low self-esteem and "giving up" attitude. For both academic literacy and numeracy, tasks and the interpersonal cues involved in making and keeping friends require considerable working memory processing and strategising resources. These resources may be habitually, continually and progressively more overwhelmed as these children move from one developmental stage to the next. Further, these theoretical models suggest clear medication and/or psychological treatments that may aid children with comorbid anxiety disorders and ADHD.

ADHD and the Treatment of Anxiety Disorders

There are a variety of psychological and/or medication treatment options available for children with comorbid anxiety disorders and ADHD that have been shown to be effective. These include cognitive behavioural therapy (CBT) and medication options (Jensen & The MTA Group, 2002; Silverman & Berman, 2001). CBT includes response prevention, mood and arousal regulation, social skills training and desensitisation techniques, parent management training, and educational school-based interventions. To date, key issues remain such as whether ADHD affects the response of children with anxiety disorders to CBT with or without selective serotonin reuptake inhibitors (SSRIs), anxiety disorders affect the response of children with ADHD to stimulant medication, whether ADHD medication treatment also helps anxiety disorders, whether the psychological and/or medication treatment of anxiety disorders helps ADHD and whether an optimal treatment algorithm can be formulated for the treatment of anxiety disorders comorbid with ADHD. In this section, each of these key issues is addressed.

There is an emerging literature that notes the deleterious effect of ADHD on the response of children with OCD to CBT (Storch, Merlo, Larson, Bloss, et al., 2008). Further, this same effect of ADHD has been reported in children with OCD treated with SSRI medication (Geller et al., 2003). At present, it remains unclear how comorbid ADHD is exerting this treatment non-responsive effect. Possible mechanisms include the increased difficulty of children with ADHD have developing insight into their situation in life,

inhibiting their responses, planning, organizing and prioritising their thoughts and actions, regulating their feelings and mood and controlling their level of anxiety and/or aggression. In addition, children with ADHD tend to have a greater severity of OCD and associated anxiety disorder symptoms. Future systematic investigation of these potential pathways is needed.

A number of early studies suggested that children with ADHD and comorbid anxiety disorders had an attenuated response to stimulant medication and experienced more adverse effects, particularly autonomic adverse effects such as stomach ache, headache, nausea, dysphoria and irritability (Buitelaar, Van-der-Gaag, Swaab-Barneveld, & Kuiper, 1995; Pliszka, 1989; Taylor et al., 1987). However, recent controlled investigations have suggested that core ADHD symptoms improve regardless of the presence of anxiety disorders and that approximately 20% of patients have significantly improved "anxiety" symptoms (Abikoff, McGough, & Vitiello, 2005; Diamond, Tannock, & Schachar, 1999). The MTA (Jensen et al., 2001; The MTG Cooperative Group, 1999) study data revealed that the ADHD and "anxiety" group responded to the psychological intervention-alone arm, while the ADHD alone and ADHD and comorbid ODD/CD groups did not. They also required a lower dose of stimulant medication and optimally responded to both stimulant medication and psychological treatment together. Interestingly, the comorbid ADHD and "anxiety" and ODD/CD group required combined medication and psychological treatment while medication alone was sufficient for the ADHD alone and ADHD and ODD/CD groups. Adverse effects were not increased in this comorbid anxiety disorders and ADHD group.

The response of cognitive deficits associated with ADHD to stimulant medication when anxiety disorders are evident remains unclear. These cognitive deficits, such as impaired working memory, are important because they contribute to educational underachievement as well as social skills difficulties, particularly the separate processes of making and keeping friends (Gathercole & Alloway, 2006). Future systematic examination of this issue is needed, particularly parsing out specific anxiety disorders on their own vs. being associated with an additional comorbid disorder such as a depressive disorder [MDD, DD] that has an independent separate effect on these cognitive functions (Vance, 2005; Vance, 2007). In fact, it is crucial to not "miss" anxiety disorders associated with an early onset depressive disorder such as DD and/or MDD comorbid with ADHD: such a depressive disorder may affect the patient's response to the medication and/or psychological treatment provided (Vance, 2007). For example, there is evidence that the presence of DD can be associated with an attenuated response of core ADHD symptoms to stimulant medication through increased prefrontal cortical neural network dysfunction (Vance, 2007). Conversely, there is evidence that increased depressive disorder symptoms can increase the responsiveness via enhanced insight of children and adolescents with OCD to CBT, whether ADHD is comorbid or not (Storch, Merlo, Larson, Marien, et al., 2008).

Atomoxetine, a selective noradrenaline reuptake inhibitor, may be helpful for decreasing ADHD, anxiety and depressive symptoms, when these conditions occur together (Stock, Werry, & McClellan, 2001). However, more controlled trials focussed on again separating anxiety disorders from comorbid DD and/or MDD are needed (Vance, 2007). In contrast, there is ample evidence supporting the effectiveness of SSRIs for a range of anxiety and depressive disorders (Geller, Donnelly, & Lopez, 2007). Interestingly, to date, there is not compelling evidence that the SSRIs in association with stimulant medication improve comorbid anxiety symptoms while the core ADHD symptoms are improved by stimulant medication, regardless (Abikoff et al., 2005). Similarly, a recent trial of SSRIs and atomoxetine in this comorbid group revealed that core ADHD symptoms alone improved (Kratochvil, Newcorn, & Arnold, 2005). There are no controlled trials of other key third-line medications for ADHD such as clonidine, imipramine or risperidone. However, there are published case reports (Huffman & Stern, 2007) combined with clinical experience that allow some further pertinent observations: Clonidine, a central noradrenergic agonist that

decreases the functional level of activity of the noradrenaline system, has been shown to decrease the core symptoms of ADHD. There may be a subset of children with anxiety disorders comorbid with ADHD who also gain benefit for their anxiety symptoms because of this reduced noradrenaline drive. Imipramine is remarkably similar to atomoxetine in its pharmacodynamic and pharmacokinetic effects, apart from its potential cardiotoxic (conduction anomaly) adverse effects that atomoxetine does not share but clonidine does. Imipramine has known benefits for anxiety and depressive disorder symptoms along with core ADHD symptoms. However, because of potential cardiotoxic effects, imipramine and clonidine should only be used by specialist psychopharmacology units and practitioners after a thorough assessment that includes a cardiac history and examination and an electrocardiogram prior to using these medications (Vance, 2008). Risperidone, an atypical neuroleptic medication with particular dopamine (D2): serotonin (5HT2) receptor blockade effects, helps reduce anxiety and depressive symptoms and core ADHD symptoms, particularly in low dose for children with autistic spectrum disorders and/or intellectual disability. Again, because of its potential motor adverse effects, especially tardive dyskinesia, risperidone should only be used by specialist psychopharmacology units and practitioners (Vance, 2008).

Chapter Summary

There are a number of assessment and treatment points that emerge from this overview of comorbid ADHD and childhood anxiety disorders: Early recognition of the comorbid state is crucial for many parents, teachers and children, themselves, do not understand that they may have anxiety disorders in addition to ADHD and that both disorders need specific, targeted treatment. Multi-informant reports are imperative because parents and teachers are better at identifying externalising problems such as ADHD while children are best at revealing anxiety and depressive problems that are affecting their lives at home, in the school classroom and in the school playground. Detailed symptom patterns of different anxiety disorders are needed, especially as the clinical research fields begin to work out which anxiety disorders confer risk and which anxiety disorders may be helpful for comorbid ADHD symptom domains and associated cognitive deficits such as working memory. Also, possible third disorders, like DD and/or MDD, exerting an effect on the relationship of anxiety disorders with ADHD need to be carefully and systematically uncovered and treated if children's response to treatment is to be optimised. Structured clinical interviews and parent, teacher and child questionnaires can be very helpful and efficient ways of obtaining this information. Details of family history, particularly of anxiety disorders in first-degree relatives, maternal antenatal stress and family over-protectiveness and the lack of positive parenting practices are especially relevant for comorbid anxiety disorders and ADHD. Finally, overt signs of physiological anxiety need to be noted such as motor tension, restlessness, autonomic arousal (including dilated pupils, sweating, fine peripheral tremor), variations in speech volume, rate, emotional inflection and abnormal involuntary movements (including tics, mannerisms, stereotypies).

The first treatment issue is to ensure parent, child and teacher awareness of the comorbid state and to emphasize that both anxiety disorders and ADHD need specific and targeted treatment, monitoring of treatment outcomes and clear ongoing prioritisation of psychological and/or medication treatments depending on the child and family's response. A range of psychological treatments and/or medication treatments are available and the possible options should be discussed with each child and their parents, using a benefits/adverse effects/crisis plan/review plan treatment planning model. The effects of treatment will vary from the home environment to the school classroom and playground for both anxiety disorders and ADHD. Finally, the current literature suggests that specific, single psychological and medication intervention should be trialled first and evaluated in each patient before combining treatments. This is crucial to avoid

potential adverse effects being augmented when benefits remain modest. As the clinical research field matures, these potential psychological and medication treatment combinations will be continually refined to ensure their optimal synergism. So, maximal developmental and functional outcomes for these children will be facilitated and achieved.

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Comorbid and Secondary Depression

10

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A high rate of comorbidity between anxiety and depressive disorders has been demonstrated in children and adolescents as well as adults. Rates of depressive disorders in children and adolescents with anxiety disorders range as high as 70%, higher than one would expect by chance (Angold, Costello, & Erkanli, 1999; Kovacs & Devlin, 1998). This significant comorbidity has been reported in both community and clinical samples of youth (Angold, Costello, & Erkanli, 1999; Brady & Kendall, 1992; Kovacs & Devlin, 1998; Seligman & Ollendick, 1998). Comorbidity is associated with a more severe course of psychopathology than anxiety or depressive disorders alone (Brady & Kendall, 1992; Seligman & Ollendick, 1998), including more severe depressive symptoms (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Merikangas et al., 2003; Moffitt et al., 2007) and greater risk for suicidality (Foley, Goldston, Costello, & Angold, 2006). For example, Hammen, Brennan, Keenan-Miller, and Herr (2008) found that among youth with early onset depression, those with comorbid anxiety disorders were at particular risk for recurrent depression. Similarly, Wittchen and Fehm (2003) report that individuals with comorbid social anxiety disorder and depression were more likely to experience additional depressive episodes and less likely to experience a remission in depression than individuals without social anxiety disorder. In this chapter, we present an overview of issues pertinent to the understanding of comorbid anxiety and depression among children and adolescents. Specifically, we will discuss models of conceptualizing comorbidity and the risk factors, outcomes, and clinical implications of comorbid anxiety and depression.

Comorbidity Among Specific Anxiety Disorders

Researchers have recently begun to investigate differences in comorbidity among specific anxiety disorders; findings indicate that individual anxiety disorders are not comorbid with depression at the same rate. While generalized anxiety disorder (GAD) and social anxiety disorder are highly comorbid with depressive disorders (Beesdo et al., 2007; Verduin & Kendall, 2003; Wittchen & Fehm, 2003), results are less consistent for separation anxiety disorder, with some studies reporting separation anxiety disorder to be associated with the lowest rates of depressive disorders (i.e., 2 vs. 17.4% in GAD and 15% in social anxiety disorder; Verduin & Kendall, 2003). Researchers have begun to distinguish between anxiety disorders related to the emotion of fear (i.e., panic or phobia) and those related to the emotion of anxiety (i.e., overanxious or GAD; Krueger & Markon, 2006), including the

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_10,

associations between fear- and anxiety-related disorders and familial major depressive disorder (MDD). Warner, Wickramaratne, and Weissman (2008) found that fear-related disorders, but not anxiety-related disorders, mediated the association between parental MDD and offspring MDD, while nonfamilial MDD may be associated with either fear- or anxiety-related disorders. These results lend support to the distinction between fear- and anxiety-related disorders in some children and suggest that treating children of depressed parents with fear-related disorders may help prevent the subsequent onset of depression.

Depression Secondary to Anxiety Disorders

In addition to high rates of comorbidity between depression and anxiety, research has consistently shown the onset of anxiety disorders to generally precede the onset of depressive disorders in children and adolescents (Avenevoli, Stolar, Li, Dierker, & Ries Merikangas, 2001; Brady & Kendall, 1992; Kessler & Wang, 2008). In studies of youth with comorbid anxiety and depression, the anxiety disorder preceded the depressive disorder in two-thirds of cases (Brady & Kendall, 1992; Seligman & Ollendick, 1998). Risk of secondary depression is two to four times greater among adolescents with an anxiety disorder than among those without significant anxiety (Wittchen, Kessler, Pfister, & Lieb, 2000), and presence of anxiety has longitudinally predicted depression in children and adolescents (Costello et al., 2003; Mazza et al., 2009). Particular characteristics of anxiety disorders also increase the risk of secondary depression (Bittner et al., 2004; Wittchen, Beesdo, Bittner, & Goodwin, 2003; Wittchen et al., 2000). Specifically, secondary depression is associated with the number of anxiety disorders, severity of anxiety disorders at baseline, frequency of avoidance, and presence of panic attacks. However, recent research suggests that this temporal pattern may not be present for all anxiety disorders. Specifically, while individuals with overanxious disorder (Bittner et al., 2007; Pine, Cohen, Gurley, Brook, & Ma, 1998), social anxiety disorder, and GAD appear to be particularly at risk for the development of subsequent depression (Beesdo et al., 2007; Bittner et al., 2004; Kessler et al., 2008; Wittchen & Fehm, 2003; for exceptions, see Avenevoli et al., 2001; Bittner et al., 2007), onset of panic disorder has not preceded depression onset (Avenevoli et al., 2001).

While the phrase "secondary depression" is often used to refer to the temporal pattern of anxiety and depression onset in youth, this usage is inconsistent with the medical definition of a secondary condition (Angold, Costello, & Erkanli, 1999). In medicine, the adjective "secondary" is used to describe a condition caused by a primary condition. Although certain medical conditions – and psychological conditions – may be comorbid, one does not necessarily cause the other. Further research is necessary to better determine the nature of the temporal association. Therefore, this chapter focuses more broadly on research regarding the comorbidity of anxiety and depression and its effects on youth. We will use the term "secondary depression" to refer to studies in which the researchers specifically investigated the temporal association of the disorders.

Models of Comorbidity

Several models have been developed to explain the relationship between anxiety and depression (Olino, Klein, Lewinsohn, Rohde, & Seeley, 2008; Seligman & Ollendick, 1998; Wittchen et al., 2000). Two of these models argue whether anxiety and depression represent one underlying condition or two distinct conditions. Some researchers propose that anxiety and depression are simply expressions of the same underlying process. Krueger and Markon (2006) provide empirical support for the development of two broad dimensions, internalizing and externalizing. Both anxiety and depressive disorders comprise the internalizing dimension, and comorbidity represents this single construct. For example, twin studies have suggested that GAD and MDD may be different forms of the same disorder, as certain types of depression are indistinguishable

from GAD (Kendler, Gardner, Gatz, & Pederson, 2007; Kendler, Neale, Kessler, Heath, & Eaves, 1992). Other researchers, however, support the idea that depression and anxiety are distinct disorders. Although some common underlying characteristics may exist, depression and anxiety consist of factors that are unique to each disorder. This theory is best reflected in Clark and Watson's (1991) tripartite model of anxiety and depression. According to this model, anxiety and depression both share high levels of negative affect, but while low positive affect is unique to depression, high physiological arousal is unique to anxiety. In a recent longitudinal study of depression in adolescents, Olino et al. (2008) found strong support for a three-factor model, similar to the tripartite model, as opposed to a one-factor model such as an internalizing dimension. While depressive and anxious disorders loaded onto a common factor, each also loaded onto a unique factor. These findings suggest that although an underlying common factor is present, factors specific to depression and anxiety account for the difference in symptom presentation. Researchers suggest that high negative affect and physiological arousal may underlie comorbid depression and anxiety in youth (Anderson & Hope, 2008; Chorpita, Albano, & Barlow, 1998; Compas, Connor-Smith, & Jaser, 2004). However, further research is necessary to understand the tripartite model among children and adolescents. Research on the tripartite model has been limited by use of self-report measures rather than interview or objective measures, and research has primarily focused on adult samples (Anderson & Hope, 2008). In addition, research has only recently begun to examine clinical severity in the tripartite model (Chorpita et al., 1998). The tripartite model may not perform similarly across anxiety disorders. For example, negative affect may be related to GAD as well as depression, and physiological hyperarousal may be more strongly associated with panic disorder than other anxiety disorders (Anderson & Hope, 2008). This may help to explain the differential comorbidity between specific anxiety disorders and depression.

Findings of the strong temporal relationship between the disorders and increased risk for depression among youth with an anxiety disorder have led to a third model suggesting that presence of an anxiety disorder may actually be a risk factor for depression (Hammen et al., 2008; Seligman & Ollendick, 1998; Wittchen et al., 2000). Although this is the least empirically investigated of the models explaining anxiety and depression comorbidity, researchers hypothesize as to the nature of this relationship. Some suggest that the consequences of anxiety, such as deficits in social and academic functioning, are depressogenic factors that may lead to the later development of a depressive disorder (Brady & Kendall, 1992; Seligman & Ollendick, 1998). However, while interpersonal deficits may be related to both depression and social anxiety, each disorder may be related to different interpersonal factors. For example, Starr and Davila (2008) found that among adolescents, social anxiety was associated with peer interpersonal factors, while depression was associated with family interpersonal factors. Further research is necessary to determine the precise nature of this relationship, as it is unclear whether temporal sequencing suggests that early anxiety increases the risk for later depression, increases exposure to depressogenic factors, or is merely a developmental expression of underlying pathology.

A Developmental Approach to Comorbidity

A growing body of evidence supports a developmental approach toward understanding the temporal relationship between childhood anxiety and adolescent depression (e.g., Compas, Oppedisano, Sameroff, Lewis, & Miller, 2000; Kovacs & Devlin, 1998; Rice, van den Bree, & Thapar, 2004). This approach takes into account the developmental differences in the onset of anxiety and depression and examines how the relationship between these two disorders changes as a function of time. In general, this perspective posits that youth may have a greater capacity to manifest symptoms of anxiety during childhood and depression during adolescence, with a transitional phase where they may be at greater risk to display symptoms of both disorders (i.e., comorbid anxiety and

depression). Thus, children may exhibit more anxiety symptoms and adolescents may display more depressive symptoms simply because of age at assessment (Kovacs & Devlin, 1998).

Although not explicitly defined by a single theory or model, this approach has been indirectly supported by numerous studies suggesting that the relationship between anxiety and depression changes over time with development. Olino et al. (2008) propose that the temporal relationship between anxiety and depression may be due to the presence of a common factor early in development (e.g., an internalizing factor; Fergusson, Horwood, & Boden, 2006), with anxiety-specific and depression-specific factors differentiating later in development. They also suggest that an anxiety-specific factor may have a primary presentation early in development, with depression-specific and common factors developing as the individual matures. With regard to the tripartite model, positive affect may increase one's ability to cope with the negative affect that underlies both anxiety and depression (Tugade & Fredrickson, 2004). Children may be protected from depressive symptoms by positive affect until later in development, when physiological and neurological maturation degrades the ability to experience reward and positive affect (Forbes et al., 2009; Poletti, 2009). Kovacs and Devlin (1998) propose that childhood anxiety may be a manifestation of developmental "readiness" related to the psychophysiology of emotional dysregulation and associated psychopathology. They suggest that the younger the child, the more likely that the onset of such pathology will take the form of anxious symptoms.

This developmental approach has also been supported by family and genetic studies. Weissman et al. (2005) investigated three generations of family members at high and low risk for developing psychopathology and found that anxiety was a reliable early sign of depression in offspring. The authors suggested that this disparate age-dependent manifestation of the same underlying disorder might be evidence of anxiety serving as a genetic precursor to depression in high-risk children. Rice et al. (2004) examined the association between common and unique risk factors for early symptoms and found evidence suggesting that childhood anxiety may be temporally associated with adolescent and later depression because of shared genetic etiologies, and not because of a shared phenotypic risk factor for subsequent depression.

Research has also demonstrated that the impact of environmental risk factors on youth internalizing problems is critically dependent on the timing of exposure. Numerous studies have supported the notion that early childhood (as opposed to mid-childhood or late-childhood) is a period of particular developmental vulnerability, during which children may be more negatively affected by exposure to specific risks (Cicchetti & Toth, 1998; Essex, Klein, Cho, & Kraemer, 2003; Rice et al., 2004). Karevold, Røysamb, Ystrom, and Mathiesen et al. (2009) reported that children are more vulnerable to factors such as maternal distress, family adversity, and lack of social support before the age of 5 years than during middle childhood. In addition, specific factors may cause heightened vulnerability at even earlier ages.

One crucial advantage of approaching comorbidity from a developmental perspective is that it does not necessarily exclude alternative models or theories of comorbid anxiety and depression. By utilizing a developmental perspective, it may be possible to account for variance between competing models of comorbidity. For example, some evidence suggests that comorbidity models emphasizing a single mixed factor may fit best for young children, while two-factor models may be a better fit for older children (Cannon & Weems, 2006; Cole, Truglio, & Peeke, 1997). While a developmental approach may be an advantageous first step toward understanding the unique relationship between early anxiety and depression, much is still unknown regarding this unique symptomatology.

Risk Factors for Comorbid Depression

Various biological, psychological, and environmental factors have been implicated in the etiology of early-onset anxiety and depression. While research explicitly investigating comorbid anxiety and depression is limited, research investigating

anxiety or depression alone often contributes to an understanding of an underlying common etiology, making each body of literature relevant for the other and for understanding the co-occurrence of the disorders (Brady & Kendall, 1992; Chorpita, Plummer, & Moffitt, 2000; Lengua, West, & Sandler, 1998). Early findings regarding comorbidity consistently suggest that how and when these factors interact with each other may be more important with regard to vulnerability than whether they are present at all. In the following sections, we examine some of the specific factors involved in the etiology of anxiety and depression that are also implicated in the comorbidity of the disorders.

Biological Risk Factors

Genetics Research

Parental depression, comorbid anxiety and depression, and – to a lesser extent – anxiety have been strongly associated with an increased genetic risk for comorbid anxiety and depression in offspring (Beidel & Turner, 1997; Micco et al., 2009; Weissman, Wickramaratne, et al., 2006). Family and twin studies indicate at least a moderate influence of genes on risk for comorbid anxiety and depression in children, with some studies finding most of the covariation of anxiety and depressive symptoms in child twins due to a common genetic influence (Boomsma, van Beijsterveldt, & Hudziak, 2005; Merikangas, Risch, & Weissman, 1994; Thapar & McGuffin, 1997). It should be noted, however, that genetic effects for comorbidity may differentially affect children based on sex and age (Eley & Stevenson, 1999). For example, increased genetic liability is found among females and after puberty (Angold, Costello, & Worthman, 1998; Hyde, Mezulis, & Abramson, 2008; Silberg, Rutter, & Eaves, 2001; Simonds & Whiffen, 2003). Further, specific anxiety disorders comorbid with depression have different genetic risk profiles (Kendler et al., 1995). Genetic research also provides support for the temporal pattern of onset. Specifically, Eaves, Silberg, and Erkanli (2003) found that genes that increased risk for childhood anxiety directly influenced the later development of depression. Likewise, genes that increased risk for early anxiety were also associated with increased exposure to negative life events and sensitivity to adversity.

In twin studies, shared environment consists of the common family environment, which is influenced by factors such as socioeconomic status (SES), parental education, and rearing practices. Nonshared environment is the residual factor, encompassing child-specific influences that are not attributable to common factors within a household. Along with genetics, shared environment specifically influences the development of anxiety symptoms and disorders (Ehringer, Rhee, Young, Corley, & Hewitt, 2006; Thapar & McGuffin, 1995). Nonshared environment, in contrast, has a small to moderate effect on the development of comorbid anxiety and depression in children and adolescents (Cerdá, Sagdeo, Johnson, & Galea, 2010; Thapar & McGuffin, 1997). The exact influence of shared versus nonshared environments, however, cannot be determined, as shared environment may differ for siblings, contributing to the individual's nonshared environment (Plomin, Asbury, & Dunn, 2001; Topolski et al., 1999). Genetic influence on comorbid anxiety and depression may also be influenced by heritable neurological and cognitive risk factors. For example, temperament and early environment account for 38% of the variance in males' and 25% of the variance in that of females' comorbid symptoms of anxiety and depression in early adolescence (Karevold et al., 2009). Finally, neuroticism, which is strongly related to comorbid anxiety and depression in children, has a moderate genetic loading (Krueger, Caspi, Moffitt, Silva, & McGee, 1996; Wray, Birley, Sullivan, Visscher, & Martin, 2007).

Neurobiology Research

The amygdala and hippocampus are implicated in fear, memory, and other emotions. Reduced volume of the amygdala has been correlated with increased activation of this region (Goldsmith, Pollak, & Davidson, 2008; Siegle, Thompson, Carter, Steinhauser, & Thase, 2007). Depressed children have been found to have smaller amygdalae than healthy children, and children with anxiety disorders display a left lateral amygdala reduction similar to that found in adult MDD

(Milham et al., 2005; Rosso et al., 2005). Few studies have examined volumetric alterations among children and adolescents with comorbidity, but those that do suggest greater alterations in anxiety than in depression (MacMillan et al., 2003). Child and adolescent anxiety and depression are correlated with altered amygdala activation to fearful faces, although there may be distinct activation differences between the disorders even when comorbidity is present (Beesdo et al., 2009; Roberson-Nay et al., 2006; Sheline et al., 2001; Thomas et al., 2001). Some studies indicate decreased hippocampal volumes in child and adolescent depression, but the presence of comorbid anxiety contributes no influence (McKinnon, Yucel, Nazarov, & MacQueen, 2009).

Abnormal alpha wave activation patterns in the cortex may be useful in predicting depression with and without anxiety, but children with comorbidity display different activation patterns than do adults. Greater relative right to left frontal activation is associated with withdrawal emotions, such as sadness or fear, in children and depression in adolescents and adults (Davidson, Elkman, Saron, Senulis, & Friesen, 1990). In adult electroencephalographic (EEG) studies, comorbid anxiety and depression is associated with greater relative right to left frontal activation (Bruder et al., 1997; Heller & Nitschke, 1998; Mantovani et al., 2007; Pizzagalli et al., 2002). In contrast, a study of children and adolescents with comorbidity did not demonstrate this abnormal frontal asymmetry, and only those children with pure depression displayed similar posterior alpha asymmetries to those found in adults with comorbidity (Kentgen et al., 2000). It is important to note that definitive structural and functional differences in depression and anxiety are not found among adults; child studies are further complicated by developmental stage, as maturational differences complicate the study of the brain (Hare et al., 2008; Koolschijn, van Haren, Lensvelt-Mulders, Hulshoff Pol, & Kahn, 2009; Yurgelun-Todd, Killgore, & Cintron, 2003).

HPA Axis Research

The amygdala, hippocampus, and prefrontal cortex are also involved in hypothalamus-pituitary- adrenal (HPA) axis regulation, which is implicated in both depression and anxiety (Bao, Meynen, & Swaab, 2008; Kallen et al., 2008). Chronic activation of the HPA axis, which results in higher levels of cortisol, can disrupt functioning in regions of the brain responsible for regulating emotion and therefore interfere with the ability to cope effectively with stress. Studies do not suggest HPA axis dysfunction in anxiety disorders to the same extent as shown in depression. Among adults, comorbidity has been associated with greater elevation of the HPA response to stress than found among those with depression or anxiety alone (Cameron, 2006). While depression specifically disrupts the HPA response to stress, anxiety appears to be more relevant in noradrenergic disruption. Thus, HPA disruptions in anxiety disorders may be due to the influence of comorbid depression. While depression has been associated with HPA axis anomalies among children, only anxiety subscales, and not the anxiety disorder itself, have been associated with such anomalies (Kallen et al., 2008). Additional research on the role of the HPA axis is necessary regarding comorbidity in general and among children and adolescents specifically (Kallen et al., 2008; Lopez-Duran, Kovacs, & George, 2009).

Neurotransmitter Research

Several candidate genes related to neurotransmitters implicated in depression and anxiety have been investigated in recent years. Polymorphisms of the serotonin transporter gene promoter (5-HTTLPR) may increase risk for both anxiety and depression in adolescents, although particular alleles may confer different risks for comorbid anxiety and depression depending on the developmental period and sex (Laucht et al., 2009; Uher & McGuffin, 2008; Verhagen et al., 2009; also see Risch et al., 2009). The allelic variants of 5-HTTLPR may also be related to cognitive, psychological, and neurological risk factors for comorbid anxiety and depression, such as neuroticism, shyness, behavioral inhibition, and amygdala activation (Arbelle et al., 2003; Caspi et al., 2003; Fox, Henderson, Marshall, Nichols, & Ghera, 2005; Lau, Goldman, Buzas, Fromm, et al., 2009; Lesch et al., 1996;

Lotrich & Pollock, 2004; Sen, Burmeister, & Gosh, 2004; Sheikh et al., 2008). Other polymorphisms implicated in depression and anxiety, such as monoamine oxidase A (MAOA), dopamine receptor D_4 (DRD4), tryptophan hydrolase, and brain-derived neurotrophic factor, have been investigated among adults with mixed results (for a review, see Gasic et al., 2009; Lau, Goldman, Buzas, Hodgkinson, et al., 2010; Serretti et al., 2003). Polymorphisms related to risk factors or neural activations among children and adolescents have received more attention.

Prenatal Adversities

Prenatal adversities have been implicated as risk factors for the development of early-onset anxiety and depressive disorders. Animal studies have demonstrated the mediational effects of gestational stress on anxiety- and depression-like symptoms in offspring (Seckl & Meaney, 2004). Accumulating evidence from population-based studies implicates maternal anxiety during pregnancy in cortisol alterations among pre- and post-pubertal children (Glover, O'Connor, & O'Donnell, 2010; O'Connor et al., 2005). However, only one study has found the cortisol alterations to be correlated with depressive symptoms, and then only among females (Van den Bergh, Van Calster, Smits, Van Huffel, & Lagae, 2008).

Psychological Risk Factors

Temperament

Temperament refers to the personality characteristics of the child that are thought to be innate or present from birth, such as shyness or fussiness. Evidence suggests that certain types of temperament serve as vulnerability factors for the development of psychopathology (Clark, Watson, & Mineka, 1994; Krueger et al., 1996). For example, behavioral inhibition is associated with anxious and depressive disorders, and it may confer a specific risk for early-onset social anxiety disorder that could lead to depression in adolescence (Hirshfeld-Becker et al., 2008; Kagan & Snidman, 1999; Merikangas, Swendsen, Preisig, & Chazan, 1998). Among children, behavioral inhibition is associated with increased startle to threatening stimuli and enhanced reactivity of the amygdala (Perez-Edgar et al., 2007; Schmidt & Fox, 1998).

Neurotic traits, such as high emotional reactivity to stress and high negative affect, are strongly related to both anxiety and depression in children (Barlow & Campbell, 2000; Lonigan, Vasey, Phillips, & Hazen, 2004). Positive affect may serve as a buffer against risk factors for depression and is noted to be high in some anxiety disorders. The interaction of negative affect and physiological hyperarousal may underlie comorbid depression and anxiety in youth (Anderson & Hope, 2008; Chorpita et al., 1998; Compas et al., 2004). Anxiety sensitivity, defined as a sensitivity to anxiety-related physiological sensations (Reiss & McNally, 1985), is highly correlated genetically with both anxiety and depression and is moderately correlated with measures of cognitive biases (Bale, 2006; Zavos, Rijsdijk, Gregory, & Eley, 2010). These traits may moderate relationships between stress, depressive symptoms, and measures of cognitive bias (Charbonneau, Mezulis, & Hyde, 2009; Hyde et al., 2008).

Effortful Control

Recent literature in temperament has suggested that the regulatory factor of effortful control may be particularly relevant in understanding the etiology of child psychopathology (Muris & Ollendick, 2005; Rothbart & Bates, 1998). Preliminary data suggest that high levels of effortful control may serve as a protective factor for at-risk youth, assisting in the maintenance of emotional stability by mitigating the harmful effects of factors such as behavioral inhibition and neuroticism. For example, highly anxious individuals may not develop the ability to inhibit negative affect. Negative affect then interacts with social factors, potentiating negative affect and leading to depression (Lonigan et al., 2004; Muris, van der Pennen, Sigmond, & Mayer, 2008). Effortful control has also been found to influence attentional bias to threat-related stimuli, as only children with low effortful control and high negative affect demonstrate an attention bias to threat stimuli (Lonigan & Vasey, 2009).

Interpretations of Ambiguous Stimuli

Childhood anxiety is associated with a higher number of threat interpretations of ambiguous information (Bogels & Zigterman, 2000; Waters, Craske, Bergman, & Treanor, 2008). A similar bias has been found among samples of depressed youth, although interpretations have been found to be more associated with self-referential ambiguous information (Dearing & Gotlib, 2009; Grillon et al., 2005). As development progresses, the interpretation of life events as being threatening or stressful may interact with perceived unpredictability, contributing to avoidance behaviors, anxiety, and later depression (Barlow, 2000). Although comorbidity has not been specifically investigated, negative interpretations of ambiguous stimuli are strongly associated with negative psychosocial sequelae and may be a target of intervention or prevention programs for high-risk youth.

Cognitive Biases

Cognitive biases may be seen as more of a correlate of anxiety and depression than as a risk factor, as their etiological influence on the disorders has not been definitively established (Seligman & Ollendick, 1998). Research suggests that cognitive biases, such as the cognitive triad (i.e., negative view of the self, world, and future) and cognitive distortions, are similar among children with anxiety or depressive symptoms alone and comorbid anxiety and depression (Epkins, 1996). However, Fresco, Alloy, and Reilly-Harrington (2006) found that individuals with comorbid depression and anxiety were especially likely to endorse internal, stable, and global attributions for negative events, and those with comorbidity reported more depressogenic attributions than those with depression or anxiety alone. Differences in specific cognitions have also been proposed. Beck suggests that in depression, cognitions involve themes of loss, while anxious cognitions involve threat-related themes (Beck, Rush, Shaw, & Emery, 1979). Research regarding differences in cognition theme has been mixed. While some have found that threat-related cognitive biases are specific to anxious symptoms, others have found no clear differences (Alfano, Beidel, & Turner, 2002; Taghavi, Neshat-Doost, Moradi, Yule, & Dalgleish, 1999). Negative cognitive style has been shown to interact with negative life events to predict depressive but not anxious symptoms (Hankin, 2008). Further, depression has been associated with personalizing, but not externalizing, schemas, while anxiety has been associated with only catastrophizing schemas (Leung & Poon, 2001). Although the role of cognitive bias in the etiology of comorbid anxiety and depression is unclear, its role as a correlate for both depression and anxiety has strong implications for treatment, assessment, and future research in comorbidity.

Contextual Risk Factors

Parental Psychopathology

Parental psychopathology is among the most reliable and clinically salient risk factors for the development of internalizing problems and associated pathological behavioral outcomes in children. Various longitudinal studies have demonstrated these vulnerability effects, with studies utilizing clinical samples reporting the risk to be elevated three- to four-fold (e.g., Weissman, Pilowsky, et al., 2006), and those using community samples reporting a two- to three-fold increase (e.g., Beardslee, Keller, Lavori, & Staley, 1993). Weissman et al. (2005) found that multigenerational MDD (i.e., the presence of MDD in both a parent and a grandparent) compounds this effect by elevating offspring to more than a five-fold risk of developing psychopathology. These familial studies highlight the mediational role of parental psychopathology and, more importantly, the moderational role of grandparental depression on the association between parental depression and grandchild diagnosis. These studies further support the critical need for early identification and intervention for this particularly vulnerable population of at-risk offspring.

Subsequent research on familial diagnostic history has begun to focus on potential moderating effects of parental illness. For example, Kessler et al.'s (2008) recent comorbidity study found little variation in factors such as number of disordered parents, sex of disordered parent, or match between sex of disordered parent and child. Results regarding sex of disordered parent conflict

with previous work in this area, which has shown that maternal illness is more strongly associated with child outcome than paternal illness. This is suspected to be a function of mothers' emotional influence on children's social and emotional development (Connell & Goodman, 2002; Klein et al., 2004). Kessler et al. (2008) additionally examined the predictive ability of comorbidity rates in this population and found that parental history of major depressive episodes, GAD, substance disorder, and panic disorder were all predictive of both GAD and MDD in offspring. However, effects of parental disorders on GAD were highly confined to childhood-adolescent onsets, while the effects on major depression were consistently significant through adulthood.

Additional Contextual Risk Factors

Beyond parental psychopathology, researchers have identified additional contextual risks that they believe may increase children's vulnerability for developing early internalizing problems. Early exposure to family adversities, including maltreatment, loss, and other trauma, is often identified as a major contextual risk factor (Kendler & Karkowski-Shuman, 1997; Kessler, Zhao, Blazer, & Swartz, 1997). Kessler, Davis, and Kendler (1997) examined the association between loss events and the onset of early anxiety and mood disorders and found significant associations between loss and onset, but not prevalence, and both disorders. Other researchers have focused on demographic factors such as SES. Essex et al. (2006) found that children from high SES families displayed a different pathway to symptom severity than those from lower SES families and suggested that as a result, it may be possible to identify high-risk children from high SES families much earlier than those from low SES families.

Outcomes

Early-onset anxiety and depression are associated with an array of short-term and long-term negative outcomes. Studies focusing on the effects of pure early-onset anxiety (i.e., without subsequent or comorbid depression) are limited in number and have produced somewhat mixed results. In general, youth anxiety disorders – particularly social phobia and separation anxiety – are associated with high levels of short-term impairment including social dysfunction, school avoidance, and academic failure (Beidel & Turner, 1998; Turner, Beidel, & Costello, 1987). However, in general, these children go on to sustain relatively well-adjusted behavioral and psychosocial outcomes and experience a moderate risk for residual, clinically significant pathological outcomes (Last, Hansen, & Franco, 1997; Last, Perrin, Herson, & Kazdin, 1996; Pine, Cohen, & Brook, 2001; for an exception see Otto, Pollock, Rosenbaum, Sachs, & Asher, 1994).

In contrast, the adverse effects of early-onset depression are well documented and appear to be salient across both clinical and community populations, as well as consistent in both MDD and sub-clinical depressive symptomology (Angold, Costello, Farmer, Burns, & Erkanli, 1999; Lewinsohn, Solomon, Seeley, & Zeiss, 2000). Youth depression is associated with immediate clinical and social consequences including problematic peer and family relationships, social disengagement, loneliness, academic difficulties, high dropout rates, health problems, eating and disruptive behavioral disorders, and heightened risk for suicidal behaviors (Garber, Gallerani, Frankel, Gotlib, & Hammen, 2009; Lewinsohn, Rohde, Klein, & Seeley, 1999). Further, it has been suggested that the development of dysfunctional psychosocial processes during adolescence may contribute to recurrent pathological behaviors and a potential lifetime course of depression (Fombonne, Wostear, Cooper, Harrington, & Rutter, 2001; Lewinsohn et al., 1999; Weissman et al., 1999).

Whereas comorbidity inherently confounds and complicates evidence of etiology, comparing pure and comorbid outcomes facilitates a more comprehensive understanding of the compounded effect of youth depression comorbid with anxiety. This is particularly useful with regard to the development and implementation of innovative therapeutic interventions for youth suffering from this distinct symptomatology. Although research examining comorbid outcomes is preliminary, early findings suggest that children and adolescents suffering from comorbid anxiety and

depression tend to exhibit outcomes characteristic of – but more severe than – those who suffer from pure depression (Costello et al., 2003; Merikangas et al., 2003; Moffitt et al., 2007). For example, (Foley et al. 2006) examined proximal psychiatric risk factors for suicidality in youth and found that while no pure anxiety disorder increased risk for suicide, and pure depression increased risk greater than any single diagnosis, comorbid depression and GAD had the greatest suicide risk of any pure (including all anxiety disorders) or comorbid diagnosis. Further, only comorbid depression and GAD discriminated youth independent of severity of psychopathology (Foley et al., 2006). These results are particularly interesting because they suggest that comorbid GAD and depression may in fact index a different profile of risk factors compared with youth who exhibit pure patterns of anxious symptomology. Such an effect may be viewed as further evidence that in some children, comorbid childhood anxiety may be an age-dependent manifestation of adolescent depression.

Other literature suggests that comorbid symptomology may lead to deleterious long-term effects, including a life course of psychopathology. Numerous studies have demonstrated that the lifetime prevalence of unipolar MDD has increased in each age cohort of birth since World War II (e.g., Klerman & Weissman, 1989; Lewinsohn, Rohde, Seeley, & Fischer, 1993). A national comorbidity survey conducted by (Kessler et al. 1996) presents evidence that this secular change was caused by depression secondary to the onset of other conditions, primarily youth anxiety, and not by an increase in pure depression. Such findings raise essential questions regarding the fundamental disparity between the pure and comorbid forms of these disorders.

Clinical Implications of Comorbid Depression

Assessment

Neither anxiety nor depression are unitary phenotypes, thus complicating the assessment of these disorders. Depression and anxiety inventories are highly correlated, demonstrating a lack of discriminant validity in the measures and an overlap in symptomatology (Kendall, Kortlander, Chansky, & Brady, 1992). As researchers attempt to create new measures that better discriminate between depression and anxiety, difficulties in doing so indicate the lack of specificity between disorders (Cox, Taylor, & Enns, 1999). Researchers have suggested two reasons for the significant correlation between anxiety and depression measures. First, this may be due to symptoms shared by the two disorders, such as insomnia and diminished ability to concentrate. Second, the significant correlation may support the theory that anxiety and depression are aspects of a single underlying construct, such as negative affect or an internalizing dimension (Anderson & Hope, 2008; Brady & Kendall, 1992; Chorpita et al., 2000; Lengua et al., 1998). The assessment of positive affect may differentiate anxiety from depression, as both disorders are associated with negative affect but only anxiety is associated with high positive affect (Clark & Watson, 1991; Seligman & Ollendick, 1998). Given the high rates of comorbidity between the disorders and the implications for outcomes and treatment, clinicians should assess for comorbidity in children and adolescents.

Treatment

As discussed above, youth with comorbid anxiety and depression often experience more severe symptoms of both disorders and more deficits in functioning than youth with only one disorder. In addition, depression is more difficult to treat when anxiety is comorbid (Young, Mufson, & Davies, 2006). While research supports a number of empirically based treatments for anxiety and depression (see Chaps. 26, 27, 29, and 30), few studies have investigated treatment outcomes for youth with comorbid anxiety and depression (Kendall et al., 1992). Therefore, the treatment implications of comorbid anxiety and depression among children and adolescents must be considered.

Comorbid conditions may have implications for the successful treatment of the primary

diagnosis. While comorbid disorders generally do not impact outcomes for anxiety disorder treatments, comorbid anxiety disorders are associated with a poorer outcome for depression treatment among children and adolescents (Ollendick, Jarrett, Grills-Taquechel, Hovey, & Wolff, 2008). This suggests that the issue of comorbid anxiety may necessitate additional consideration when the primary problem is a depressive disorder. However, research suggests that depressed youth with comorbid anxiety disorders may benefit most from the use of evidence-based treatments, such as cognitive-behavioral or interpersonal therapies (Ollendick et al., 2008).

Treatments for primary anxiety or depressive disorders can not only improve the primary condition but also lead to improvements in the comorbid condition. In their treatment outcome study of cognitive-behavioral therapy for children with anxiety disorders, Kendall, Brady, and Verduin (2001) reported that comorbid internalizing and externalizing disorders did not impact children's response to treatment. Further, even though the treatment specifically addressed anxiety, the rate of comorbid diagnoses decreased significantly at post-treatment and follow-up. In an investigation of individual and family-based cognitive-behavioral therapy for children and adolescents with anxiety disorders, Suveg et al. (2009) reported significant decreases in depressive symptoms at post-treatment and 1-year follow-up. Although the interventions were anxiety focused, the therapeutic techniques used may have been effective in targeting both anxiety and depressive symptoms.

Similar effects on comorbidity are seen when depressive disorders are the focus of treatment. Improvement in anxiety symptoms was often reported among adolescents whose depression improved during treatment (Young et al., 2006). Depression-focused treatments for children and adolescents have resulted in improvements in both depressive and anxious symptoms (Stark, Reynolds, & Kaslow, 1987). For example, Reynolds and Coats (1986) reported that relaxation training for depressed adolescents also improved anxious symptoms, and these symptoms continued to improve at 5-week follow-up. However, improvement in anxiety symptoms during depression-focused treatment may depend on anxiety severity. Young et al. (2006) suggest that while adolescents with mild to moderate anxiety may continue to benefit from depression-focused treatments, those with more severe anxiety may benefit from focusing specifically on anxiety symptoms in treatment. While more disruptive anxiety may need to be addressed along with depression, initial treatment of depression may provide skills and techniques that can be useful in the subsequent focus on less severe or more circumscribed anxiety (Kendall et al., 1992).

Three explanations for improvements in depressive symptoms following treatment for anxiety have been proposed (Borkovec, Abel, & Newman, 1995; Brown & Barlow, 1992). First, therapeutic techniques used to treat anxiety may generalize to comorbid diagnoses. For example, an individual may apply cognitive restructuring techniques originally taught for anxious cognitions to depressive cognitions, thus generalizing the skill to a comorbid condition. Second, improvements in symptoms of anxiety that overlap with symptoms of depression may result in a reduction of comorbid diagnoses. Finally, treatments for anxiety may address an underlying mechanism that is shared by depression, such as negative affect in the tripartite model of anxiety and depression, thereby resulting in an improvement in both disorders.

While cognitive-behavioral therapy is supported for the treatment of childhood anxiety disorders (i.e., Walkup et al., 2008), treatment of comorbid anxiety and depression may require modifications based on the nature and severity of presenting symptoms, the client's developmental level, and his or her level of functioning. Kendall et al. (1992) present modifications to empirically based treatment strategies for use in the treatment of comorbid anxiety and depression in youth. Affective education, a common technique in both anxiety and depression treatments, focuses on teaching the individual to identify affective states and corresponding thoughts. Youth with comorbid anxiety and depression may benefit from learning to identify and distinguish thoughts and emotions associated with each disorder, as well as identifying positive emotions in addition to negative

emotions. Behavioral techniques such as exposure, behavioral activation, and relaxation training are also used to treat comorbid anxiety and depression. When behavioral interventions seem to contradict treatment of depression or anxiety, such as the possibility of exposure therapy increasing negative affect, clinicians should proceed with the exposure slowly, allowing the client to build mastery, and simultaneously focus on positive techniques such as pleasurable activity scheduling. It may also be helpful to address anxious and depressive symptoms separately. As both anxiety and depression are associated with cognitive distortions and unrealistic goal setting, cognitive therapy techniques and problem-solving skills are likely to be effective for both disorders. However, the temporal focus of cognitive therapy may differ based on cognition, as anxiety is associated with the anticipation of events and depression is often associated with a focus on past events. Social skills and parent training can also be effectively modified and used to address the unique needs of youth with comorbid anxiety and depression.

Given that models of comorbidity suggest that anxiety and depression comprise one broad dimension or are related by common factors, researchers have begun to develop transdiagnostic approaches that emphasize commonalities among diagnoses (Norton, Hayes, & Hope, 2004). Rather than focusing treatment on anxiety or depression specifically, Brown and Barlow (2009) suggest that treatment should address common factors that underlie both disorders, such as difficulties in emotion regulation. For example, a transdiagnostic treatment should incorporate cognitive-behavioral principles common to both anxiety and depression and address deficits in emotion regulation, which are found in both disorders, making the intervention effective for all anxiety and depressive disorders. This model has been utilized in the development of a transdiagnostic emotion-focused treatment for youth that simultaneously addresses anxiety and depression (Trosper, Buzzella, Bennett, & Ehrenreich, 2009).

While youth with comorbid depression and anxiety often experience more severe symptoms and tend to be more difficult to treat than youth with either disorder, research indicates that treatment of the primary disorder often has a positive effect on comorbid conditions. In addition, existing empirically supported treatment techniques can be modified to take into account the comorbid condition and used with youth with comorbid anxiety and depression.

Summary

Comorbid depression presents unique challenges to the understanding, assessment, and treatment of anxiety in children and adolescents. Children and adolescents with comorbid anxiety and depression have been shown to experience more severe symptoms of depression than those with depression alone, and comorbidity may be associated with a life course of psychopathology. While research has consistently demonstrated that the onset of anxiety precedes that of depression, the exact nature of this temporal relationship is uncertain. In fact, the National Institute of Mental Health assigned a workgroup to investigate childhood anxiety disorders as a precursor to depression (Costello et al., 2002), confirming the importance of further research in this area. Although risk factors specifically associated with comorbid anxiety and depression have been little investigated, the evidence regarding risk and developmental specificity underscores the importance for the early identification of at-risk youth, as well as the development and implementation of prevention and intervention efforts. Further, the effect of the interplay of different biological, psychological, and environmental risk factors over time on the developmental trajectories of anxiety, depression, and comorbidity must be considered. While treatment of a primary disorder is often effective in improving the symptoms of a comorbid disorder, therapeutic techniques may be tailored to address comorbid anxiety and depression, and interventions are being developed to address a common factor underlying both disorders. Given the high rates of comorbidity among children and adolescence and the associated negative outcomes, specific attention to this topic is warranted in research and clinical work.

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The Role of Disgust in Childhood Anxiety Disorders

11

Melanie W. Moretz, Jon Rogove, and Dean McKay

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During the past several years, there has been extensive research into the role of disgust in a wide range of psychopathology (Olatunji & McKay, 2007). Most of this research has focused on anxiety disorders where disgust may figure prominently in avoidance. The early work in this area focused on specific phobias and avoidance of contact with disease and contagion (Matchett & Davey, 1991). Since that time, the range and nature of disgust's involvement in psychopathology has become refined and includes a multifaceted conceptualization, drawing on the postulates of the emotion as described by Rozin and Fallon (1987). This chapter focuses on the conjoint roles of disgust and development in childhood anxiety.

The Role of Disgust in the Maintenance of Avoidance Behaviors

Disgust has been described as "the forgotten emotion of psychiatry," (Phillips, Senior, Fahy, & David, 1998), a description that, until recently, was far from unwarranted. Despite the central role of disgust in several influential theories and accounts of emotion (e.g., Darwin, 1872/1998; Ekman, 1992, 1999), the disease-avoidance and social functions ascribed to disgust (Keltner & Haidt, 2001; Matchett & Davey, 1991), and the growing appreciation for the role of disgust in adult psychopathology (Olantunji, Cisler, McKay, & Phillips, 2010; Olatunji & McKay, 2009), it was only after the publication of Matchett and Davey's (1991) disease-avoidance model that researchers began to recognize the pertinence of disgust to anxiety disorders and their treatment. The field has since witnessed a significant increase in the number of articles and book chapters published specifically addressing the role of disgust in the phenomenology and maintenance of anxiety disorders and other conditions characterized by avoidance behaviors. This is especially true of contamination-related obsessive-compulsive disorder (OCD; e.g., Moretz & McKay, 2008; Olatunji, Sawchuk, Lohr, & de Jong, 2004; Tolin, Woods, & Abramowitz, 2006), animal phobias (e.g., de Jong, Andrea, & Muris, 1997; Matchett & Davey, 1991), and blood-injection-injury (BII) phobia (e.g., Olatunji, Williams, Sawchuk, & Lohr, 2006; Sawchuk, Lohr, Westendorf, Meunier, & Tolin, 2002).

While it appears that there is considerable support for the role of disgust in anxiety disorders, the majority of this research has focused on adults. Nonetheless, the limited research that has investigated the role of disgust in childhood anxiety disorders is promising and seems to resemble

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_11,

the findings from the adult literature. The aim of this chapter is to summarize the major findings for the role of disgust in specific anxiety disorders, including the extant literature detailing this relationship in children. Where literature is limited or absent, we will provide predictions and directions for future research in the area. The following section provides an overview of disgust in general, and its impact on psychopathology. First, disgust will be defined and essential theoretical issues presented. Second, the assessment of disgust in children and its relationship with anxiety disorders will be discussed.

Disgust Defined

Disgust has been defined as an emotion characterized by "a feeling of revulsion or profound disapproval aroused by something unpleasant or offensive" (Lindberg 2002, p. 389). Rozin and Fallon (1987) provided a detailed theoretical account that describes how disgust may operate both behaviorally and cognitively. According to their definition, disgust is "revulsion at the prospect of (oral) incorporation of an offensive object. The offensive objects are contaminants; that is, if they even briefly contact an acceptable food, they tend to render that food unacceptable" (p. 23). Both of these definitions adequately capture the fundamental essence of disgust, namely the feeling of repugnance or intense aversion that is triggered by exposure to a distasteful or offensive object or situation. Disgust sensitivity is the trait-like predisposition of a person to become disgusted in response to a particular group of stimuli, known as disgust elicitors (Woody & Teachman, 2000).

Disgust is conceptualized as a universally-experienced emotion that was evolutionarily selected to help humans solve a specific recurring threat to survival via avoidance of contamination (Oaten, Stevenson, & Case, 2009). Over time, disgust has come to serve additional adaptive functions, such as defending against ideological contagions, regulating relations between social groups, safeguarding social order, and protecting the soul from moral transgressions (Keltner & Haidt, 2001; Rozin, Haidt, & McCauley, 2004, 2009).

A closer inspection of the disgust state reveals a topography that distinguishes disgust from other basic emotions, such as fear, anger, guilt, sadness, and joy (Ekman, 1999). The first defining component of disgust lies in its eliciting stimuli. Disgust is elicited by stimuli that have the potential to contaminate (Rozin & Fallon, 1987). Disgust elicitors are well known to many as a result of socialization and include stimuli such as spoiled, dirtied, or socially unacceptable food (e.g., moldy yogurt, monkey meat, food that is infested with cockroaches, ketchup on ice cream), body envelope violations (e.g., mutilated or missing body parts, exposed innards, sores, deep wounds), body products (e.g., feces, urine, mucus, vomit), death and dead bodies (e.g., rotting corpses, graveyards, ashes of a cremated person), animals (e.g., maggots, cockroaches, flies, rats), sexual behaviors that may be considered unacceptable within specific cultural groups (e.g., sex with animals, incest), poor hygiene (e.g., body odor, dirt under fingernails, greasy hair, sticky hands), and general violations of social and moral norms (e.g., cruelty, bad manners, vulgarity) (Haidt, McCauley, & Rozin, 1994). Although there are some cross-cultural differences with regard to the kinds of stimuli that people find disgusting, these seven domains of disgust elicitors appear to be consistent across cultures (Olatunji et al., 2009).

Disgust is also unique on the basis of its distinctive facial expression (Cisler, Olatunji, & Lohr, 2009; Ekman, 1999). Izard (1977) described the typical disgust facial expression as looking as if "one is gagging or spitting out" (p. 336). Specifically, when disgusted, people typically open their mouth, raise their upper lip, and wrinkle their nose. The tongue may also be protruding. The person may lower his or her eyebrows and squint his or her eyes as a result of drawing up the nose and upper lip (Izard, 1971). It has been shown that there is cross-cultural agreement in recognition of the disgust facial expression (Ekman & Friesen, 1986; Izard, 1971), which indicates that it is likely a universal human expression. This facial expression is found across cultures (Ekman, 1999), and in human infants when administered bitter tasting substances (Steiner, 1979).

In addition to its unique facial expression, disgust is characterized by unique autonomic nervous system activity (Cisler et al., 2009; Ekman, 1999; Vrana, 2009). Physiological studies have consistently indicated a heart rate deceleration for disgusting compared to fear-inducing and neutral stimuli (see Cisler et al., 2009; Vrana, 2009). This is likely reflective of activation of the parasympathetic nervous system (Page, 1994). In contrast, disgust imagery has been found to increase heart rate (Vrana, 1993, 1994). McKay and Tsao (2005) offered an explanation for this apparent inconsistency. According to these authors, imagery "may better address anticipatory reactions. In this case participants may label the anticipatory reaction as anxiety, leading to sympathetic activation, while live exposure more likely produces the diphasic reaction, with parasympathetic arousal then occurring as well" (p. 356). Similar to other negatively-valenced emotions, disgust has also been linked to an augmentation in the magnitude of startle reflex upon presentation of disgust pictures, an increase in corrugator supercilii EMG activity, and increased skin conductance (Vrana, 2009).

Disgust can also be set apart from other emotions on the basis of associated cognitive phenomena (Cisler et al., 2009; Ekman, 1999; Teachman, 2006; Williams et al., 2009; Woody & Teachman, 2000). Central to this, is the transferability of disgust via the laws of sympathetic magic. The two laws of sympathetic magic shape the circumstances under which people may perceive an unrealistic threat of contamination, when there is no actual danger of becoming contaminated. First, the cognitive processing of disgust-related information is often biased by the *law of contagion* (Rozin, Millman, & Nemeroff, 1986), which states that objects pass on some of their properties when they touch other things in such a way that the effect of contact is sustained even after the connection has been broken (i.e., "once in contact, always in contact," p. 703). For example, a patient may avoid touching an object that he fears to be contaminated prior to entering his own bedroom out of fear that his hand will contaminate his room, which he considers to be a contaminant-free "safe haven." The processing of disgust-related material also has a propensity to be biased by the *law of similarity* (Rozin, Hammer, Oster, Horowitz, & Marmora, 1986). According to this law, if a neutral stimulus resembles a disgusting stimulus, there is a greater likelihood that it too will be perceived as being disgusting (i.e., "the image equals the object," Rozin et al., 1986, p. 703). For example, people may refuse to consume chocolate that is shaped like dog feces.

The cognitive processing of disgust-relevant information seems to differ from that of other emotions (e.g., fear) on the basis of primary disgust appraisals. Applying Salkovskis' (1985) model of OCD-related appraisals to disgust, Teachman (2006) differentiated between primary and secondary appraisals. In contrast to secondary appraisals, which have to do with the consequences of becoming disgusted, Teachman posited that primary disgust appraisals reflect beliefs about the properties of a stimulus (e.g., "blood and guts are disgusting"), or the likelihood of feeling disgusted (e.g., "if I look at the screen, I will feel sick"). Thus, the content of primary disgust appraisals is thought to be related to disgust or contamination, while the content of primary fear appraisals is believed to be related danger (Woody & Teachman, 2000). Lastly, it appears that the cognitive landscape of disgust may be characterized by unique attention, perceptual, and memory biases. If this is the case, then these biases may have important implications for the treatment and maintenance of disgust-related disorders. For example, Charash and McKay (2009) have shown that individuals with elevated contamination fear showed a bias in interpretation for vague situations that could be associated with disgust, but not attention or biases for memory. Recent analyses have also shown that disgust biases are more consistent than fear biases, and that disgust facilitates recognition of otherwise phobic stimuli (Wiens, Peira, Golkar, & Ohman, 2008). Williams et al. (2009) provide a detailed discussion of cognitive biases associated with disgust.

Finally, the action tendency associated with disgust is behavioral avoidance (Ekman, 1999), a characteristic shared with fear and anxiety.

Similar to fear-based avoidance, the disgust reaction is characterized by the avoidance of objects or situations determined to be upsetting or disturbing (Woody & Teachman, 2000). For example, an adolescent who is easily disgusted by spoiled foods would theoretically be more likely to avoid consuming buttermilk or blue cheese than would a disgust-insensitive child. Similarly, a child who finds body envelope violations to be objectionable might avoid looking at television shows depicting surgery. However, fear- and disgust-related avoidance are conceptualized as serving different functions. In contrast to fear-related avoidance, which is believed to have served the function of distancing humans and other organisms from imminent threats to physical survival (Barlow, 2002; LeDoux, 1996), disgust-related avoidance is theorized to have aided by distancing humans from potential contaminants (Keltner & Haidt, 2001; Matchett & Davey, 1991).

The Disease-Avoidance Model of Disgust

The aforementioned characteristic facial expression of disgust is strongly connected to the disease-avoidance model of phobias. In other words, disgust is presumed to protect individuals from ingesting potentially dangerous substances with noxious odors or tastes. Thus, the function of the disgust facial expression is to reduce the amount of offensive odor coming in through the nostrils and to expel the possibly hazardous contents of the mouth after something distasteful has been eaten, or to serve as a barrier to ingestion in the first place. In addition to the facial expression, neuro-vegetative components have also been identified as part of the disgust reaction, specifically, an increase in saliva production and the tendency to vomit (Angyal, 1941). The extra saliva serves to dilute the offensive taste in the mouth, and the nausea and vomiting function to avoid the ingestion of offensive objects. Physiologically, disgust is associated with parasympathetic nervous system activation. Recently, Stark, Walter, Schienle, and Vaitl (2005) found that participants experienced a decrease in heart rate and an increase in skin conductance response while viewing disgusting pictures. Thus, Tomkins (1982) described disgust as an "innate defensive response" (p. 377).

Disease Avoidance and Animal Phobias

Matchett and Davey (1991) proposed that there was a connection between disgust and animal phobia, known as the disease-avoidance model. These researchers suggested that fear of some animals is mediated by disgust sensitivity, as opposed to being mediated by the threat of being attacked or physically injured. In other words, individuals fear and avoid relatively harmless animals because these creatures are theoretically connected to disease and contamination, and therefore, evoke feelings of disgust (e.g., rats, cockroaches, and spiders).

As evidence, Matchett and Davey found that measures of disgust sensitivity and contamination were significantly correlated with measures of fear for "fear-relevant" (but typically harmless) animals (e.g., rats, cockroaches, and spiders), and "disgust-relevant" animals (e.g., slugs, maggots, and frogs). These measures of disgust and contamination were not significantly correlated with fear of the predatory animals that are likely to physically harm a person (e.g., lions, tigers, and bears).

Webb and Davey (1992) utilized an experimental design to further explore the role of disgust sensitivity in some animal phobias. After completing self-report measures of fear for several types of animals (i.e., fear-relevant, disgust-relevant, and predatory animals, as described above), participants were subjected to one of three different experimental conditions. Participants viewed one of the following: a fear-inducing video depicting extreme violence, a disgust-inducing video of bloody surgery in a hospital, or a neutral video of outdoor landscapes. The participants' animal fears were re-assessed after viewing the video, and for each experimental condition, pairwise comparisons were conducted for change in fear scores between the different types of animals. The results indicated

that the violent material significantly increased fear of predatory animals only, while exposure to the disgusting video led to a significant increase in fear of the fear-relevant and disgust-relevant animals only.

Ware, Jain, Burgess, and Davey (1994) confirmed through factor analysis that animal fears can be divided into two distinct categories, which they labeled Fear-relevant and Predatory. Ware et al. also found a significant correlation between disgust sensitivity, and fear-relevant animal phobias only with no such correlation between disgust and predatory animal fears. Furthermore, individual differences in disgust sensitivity accounted for a significant amount of variance in fear of animals in the fear-relevant category (e.g., snakes, bats, and spiders).

Disease Avoidance and Disgust Elicitors

Curtis and Biran (2001) have also proposed a disease-avoidance theory of disgust, based on extensive qualitative research on disgust elicitors in several different cultures, including Africa, India, the Netherlands, the United Kingdom, and Greece. They concluded that hygiene-related behaviors across cultures were consistently motivated by avoidance of contact with disease-causing pathogens. Extrapolating from their hygiene-related research, Curtis and Biran asked people in these different countries about objects that elicited disgust, and found that these disgust elicitors fell into five categories, including (1) bodily excretions and body parts, (2) decayed and spoiled food, (3) particular animals and insects, (4) certain categories of "other people," and (5) violations of morality and social norms. These categories, in their opinion, provide support for the role of disgust as a defense against the spread of infectious disease. The disgust elicitors in the first three categories clearly have the potential to harbor disease. However, the last two are more loosely related. According to Curtis and Biran, avoidance of contact with disgusting "other" people (e.g., "Americans," as one respondent indicated in Greece) may prevent exposure to pathogens to which a person may not be immune. These authors also proposed that avoidance of immoral people and acts "may serve to promote the avoidance of social rather than physical parasites" (p. 29). This theory adds partial support to the theory that disgust functions to drive people away from potential sources of infection.

Disease Avoidance and Children

With the exception of facial expressions, most accepted indicators of disgust (i.e., aversions to body products) appear to be absent in very young children, not developing until about 5 years of age (Rozin & Fallon, 1987). Although Darwin (1998) noted that he "never saw disgust more plainly than on the face of one of [his] infants at the age of 5 months, when, for the first time…a piece of ripe cherry was put into his mouth," he qualified this observation by adding that he "doubt[ed] whether the child felt real disgust" (p. 261). While the characteristic facial expression may be the same, there seems to be a difference between the distaste expressed by an infant, and the "real" disgust, endowed with meaning, that adults experience.

Although there is ample support for the disease avoidance model of disgust in adults, there is little evidence that the same theory applies to children. It has been shown in several experimental studies (Rozin et al., 1986; Stein, Ottenberg, & Roulet, 1958) that very young children react positively to typical disgusting odors, such as synthetic sweat and feces. Furthermore, children are even willing to taste objects that would be rejected by most adults, such as realistic looking dog excrement made from peanut butter and stinking cheese. Although children begin to reject food at around age five, Rozin and Fallon (1987) suggested that children do not yet refuse food based on disgust as it relates to contamination. They proposed that the relationship between food rejection and disgust emerges around age eight, as cognitive skills develop that allow children to make a connection between an object being introduced to a substance and then removed, leaving trace amounts behind (e.g., the concept that a bug briefly dipped into a cup of juice may leave

"germs" behind). Furthermore, in a study of 38 monozygotic (MZ) and 34 same-sex dizygotic (DZ) twin pairs, Rozin and Millman (1987) found that although the siblings were similar in their food preferences and beliefs about disgust and contamination, there was not a significant genetic contribution to these variables. Similarities in food preference and disgust sensitivity were therefore contributed to the shared family environment.

Development of Disgust

Evaluative conditioning (EC; de Houwer, Thomas, & Baeyens, 2001) has been proposed as a mechanism for the acquisition of disgust (Schienle, Stark, & Vaitl, 2001). EC is the process by which individuals learn to like or dislike an object based on its pairing with a positive or negative stimulus and a verbally mediated label (de Houwer et al., 2001). Oaten et al. (2009) recently reviewed the empirical evidence supporting the disease avoidance model of disgust, and concluded that it is likely that disease-related disgust develops in childhood through EC via the pairing of disease-related events with disgust reactions by their parents (e.g., parental facial expressions and verbal cues). For example, when a child drops food on the floor, the parent may throw away the food, and react with disgust by giving certain facial and vocal responses that are observed and learned by the child. In support of this theory, Repacholi (1998) found that young infants ranging from 14- to 18- months-old showed aversion to items toward which an adult had responded with disgust (i.e., made a disgust face and said, "Eww! I've found something! Eww! I can see it! Eww!," p. 1019).

Assessing Disgust

Disgust sensitivity is most often measured by self-report. As the conceptualization of disgust has changed over time, the content of the self-report measures has also changed accordingly. An early self-report assessment was the Disgust Sensitivity Questionnaire (DSQ; Rozin, Fallon, & Mandell, 1984), a measure of disgust that addresses only one specific aspect of disgust sensitivity, food contamination. There is a simplified version of the DSQ (Muris, Merckelbach, Schmidt, & Tierney, 1999) for administration to children. This simplified DSQ is comprised of 18 items that ask how disgusting they would find it to eat particular contaminated food items (e.g., "How disgusting would you find it to eat your favorite soup from a soup bowl, after it had been stirred by a thoroughly washed fly swatter?," "How disgusting would you find it to drink your favorite lemonade, when a nontoxic leaf from a houseplant falls into your glass and goes to the bottom?," and "How disgusting would you find it to eat your favorite cookie, after a bite had been taken by a waiter in a restaurant?" (Muris, van der Heiden, & Rassin, 2008, p. 137). Each item is rated on a five-point Likert scale ranging from 1 (i.e., "not at all disgusting") to 5 (i.e., "very much disgusting"), and the scores for all 18 items are summed to yield a total score ranging from 18 to 90, with higher scores indicating increased disgust sensitivity. In a study of the connection between spider phobia and disgust sensitivity with young girls, de Jong et al. (1997) added two items to the original DSQ to assess spiders' disgust-evoking status (i.e., "How much would you like to eat your favorite chocolate bar after a spider has walked across the bar when it is still wrapped in its package?" and "How much would you like to eat your favorite chocolate bar after a spider has walked across the unpacked bar?," p. 560).

A more comprehensive and widely used measure is the Disgust Scale (DS; Haidt et al., 1994). The DS consists of 32 items measuring disgust sensitivity among seven domains of disgust elicitors: Food, Animals, Body Products, Sex, Envelope Violations, Death, and Hygiene. There is an additional eighth scale, Sympathetic Magic, which measures respondents' attitudes about objects that resemble or have had brief contact with disgust elicitors from the seven domains. Each subscale of the DS is composed of four items. The first two items are answered true or false (scored 0 or 1), and the last two items are assessed on a 3-point Likert-scale ranging from 0 ("Not disgusting at all") to 1 ("Very disgusting").

Three of the true/false items are reverse-scored (i.e., Items 1, 4, and 10). The alpha coefficient for the DS is 0.84, and the alpha coefficient for the eight subscales range from 0.34 to 0.60: Food $\alpha = 0.34$; Sympathetic Magic $\alpha = 0.44$; Hygiene $\alpha = 0.46$; Body Products $\alpha = 0.55$; Animals $\alpha = 0.47$; Body Envelope Violations $\alpha = 0.60$; Sex $\alpha = 0.51$; Death $\alpha = 0.59$ (Haidt et al., 1994). The reliabilities of the individual subscales are quite low; thus, scores on individual subscales should be interpreted with caution. This scale has not yet been adopted for use with children.

In general, research on the role of disgust sensitivity in psychopathology among children and adolescents has largely relied on the DSQ. Recently Muris, van der Heiden, et al. (2008) measured disgust sensitivity with both the DSQ and the DS; some modifications to the DS were made before administering the scale to children. These authors reported that they simplified some items, and replaced "too offensive formulations" (e.g., "You see a man with his intestines exposed after an accident" was changed into "You see a man with an injured face after an accident") (p. 136). Muris et al. also removed the Sex domain from the scale because they deemed that these items were inappropriate for children. Lastly, they changed the response scale for the last 16 items into a Likert-scale with four, rather than three, options: "not at all disgusting," "somewhat disgusting," "disgusting," and "very disgusting."

Beyond using the typical paper-and pencil approach to measure disgust sensitivity, other methods have been used, including observation of facial expressions (Ekman & Friesen, 1986), neuroimaging techniques (Schienle, Schäfer, Stark, Walter, & Vaitl, 2005), psychophysiological measures (Stark et al., 2005), and behavioral tasks (Klieger & Siejak, 1997; Tsao & McKay, 2004). These alternative means of measuring disgust sensitivity have not only added to the expanding literature on disgust sensitivity, but also served as a means of validating self-report measures. Rozin, Haidt, McCauley, Dunlop, and Ashmore (1999) demonstrated that scores on the DS predicted behavior on a series of behavioral tasks designed to evaluate disgust in a large sample of undergraduate students. Rozin et al. found that performance on the behavioral tasks correlated with the score on the DS for participants who took the DS 2 months prior to the behavioral tasks, as well as for participants who took the DS immediately following the experiment.

In a sample of children, Muris, van der Heiden, et al. (2008) included a behavioral measure of disgust sensitivity in addition to the DSQ and DS by asking the children to select "defiled candy" (p. 135) as a reward for their participation in the task. Children were asked to choose whether they would like either "five pieces of fresh chocolate, ten pieces of chocolate that had passed the best-before date, or 15 pieces that had been dropped on the floor" (p. 137). The authors conducted a pilot investigation of their behavioral task with a sample of 114 children and asked them to rate their level of disgust for each of the three conditions from 1 ("not at all disgusting") to 5 ("very disgusting") and found that ratings for condition 1 were low ($M = 1.34$, $SD = 0.74$) but ratings for condition 2 and 3 were each significantly higher ($M = 3.68$, $SD = 1.16$ and $M = 3.48$, $SD = 1.21$, respectively).

The Role of Disgust in Psychological Disorders

Although disgust was referred to as the "forgotten emotion of psychiatry" a decade ago (Phillips et al., 1998), it has recently emerged as an increasingly important variable in psychological research (Olatunji & McKay, 2007, 2009). Foremost, trait disgust has been proposed as a central variable in the etiology and maintenance of some anxiety disorders, including contamination-related OCD, animal phobias, and BII phobia, all of which are discussed in detail below. Anxiety disorders have primarily been conceptualized as being phenomenologically and etiologically related emotional responses associated with overdeveloped and overgeneralized danger perceptions that result in anxious arousal (Barlow, 2002; Barlow, Allen, & Choate, 2004; Cisler et al., 2009). However, the literature investigating the relationship between disgust and anxiety disorders is quickly mounting,

and the results have begun to provide a more comprehensive perspective on factors involved in avoidance. Indeed, disgust sensitivity has been conceptualized as a dispositional trait that increases the likelihood of an individual developing avoidance reactions (McNally, 2002).

In a review of 41 studies examining the emotional responding towards disorder-relevant stimuli, Cisler et al. (2009) demonstrated that spider phobia, BII phobia, and contamination-related OCD are all characterized by fear *and* disgust. The authors of this study investigated fear and disgust across four separate response domains believed to differentiate between these emotions: heart rate, cognitive appraisals, facial expression, and neural substrates. Several additional lines of research have examined disgust's relationship with small animal phobia, BII phobia, and contamination-related OCD and, taken together, suggest that disgust may be implicated in the pathogenesis and maintenance of these conditions (Olantunji et al., 2010). First, self-report measures of disgust propensity[1] have repeatedly been associated with self-report measures of these conditions (e.g., Olantanji & Cisler, 2009). Second, research has demonstrated that persons with elevated spider fears, BII phobia, and contamination fears report feelings of disgust when exposed to associated stimuli (e.g., Deacon & Olatunji, 2007; Sawchuk et al., 2002; Tolin, Lohr, Sawchuk, & Lee, 1997). Third, self-reported disgust is related to avoidance of spiders, BII-related stimuli, and contamination-related stimuli (e.g., Deacon & Olatunji, 2007; Olatunji, Connolly, & David, 2008; Tsao & McKay, 2004; Woody, McLean, & Klassen, 2005). Fourth, studies have indicated that disgust plays a critical role in the cognitive biases exhibited by small animal, BII, and contamination-fearful individuals (e.g., Huijding & de Jong, 2007; Sawchuk, Lohr, Lee, & Tolin, 1999; Teachman, Gregg, & Woody, 2001; Tolin, Worhunsky, & Maltby, 2004).

These data suggest that disgust may function as a maintenance factor in contamination-related OCD, animal phobias, and BII phobia (Muris, 2006). Although speculative, the pattern of findings described above suggests several avenues by which this may occur. In accordance with Mowrer's two-factor model (1960), disgust-related avoidance is likely to minimize exposure to the avoided stimuli and, consequently, deprive an individual of the opportunity to incorporate corrective information into his or her maladaptive disgust- or fear-related schemata (Muris, 2006). Thus, a child who actively avoids spiders would, theoretically, minimize his or her opportunities to learn, for example, that he or she will not be overwhelmed with disgust or panic when a spider is encountered. Second, as avoidance functions to minimize aversive emotional states (Barlow, 2002; Barlow et al., 2004), this method of coping is likely to be negatively reinforced (Mowrer, 1960). Third, the cognitive biases associated with disgust (e.g., sympathetic magic, primary and secondary disgust-related appraisals, and attentional, perceptual, and memory biases) may promote the persistence of these dysfunctional schemata and indirectly promote the utilization of avoidance.

In contrast to the disgust state, the propensity to experience disgust (i.e., trait disgust) appears to be a specific, genetically-based vulnerability factor to the development of contamination-related OCD, animal phobias, and BII phobia (Muris, 2006). More specifically, on the basis of the results of mediational studies, Olantunji et al. (2010) suggest that disgust propensity may mediate the relationship between general vulnerabilities (e.g., negative affectivity, contamination-related cognitions, contamination fear) and the aforementioned anxiety disorders. In other words, mediational studies suggest that these higher-order factors contribute to the development of spider phobia, BII phobia, and contamination-related OCD via one's proclivity to experience disgust. According to the authors (Olantunji et al., 2010): (a) disgust propensity may play a role in these conditions via interpretation biases, attentional biases, or dread of contagion, (b) anxiety sensitivity and difficulties in general emotional

[1] Otherwise known as *disgust sensitivity*, *disgust propensity* is a trait-level construct reflecting the tendency to experience state disgust upon exposure to disgust elicitors (see Olantanji & Cisler, 2009).

regulation may potentiate the relationship between disgust propensity and contamination and spider fears, and (c) parental disgust propensity may be implicated in the development of spider phobia and, pending further research, BII phobia and contamination-related OCD.

Animal Phobias

Although there is ample evidence from research with adults for a disgust conceptualization of animal phobias (e.g., Matchett & Davey's (1991) disease-avoidance model), there have been far fewer studies with pediatric samples. In a sample of school children aged 8–13 years in the Netherlands, Muris et al. (1999) found that disgust sensitivity as measured by the DSQ was significantly correlated with animal phobias, even when controlling for trait anxiety ($r = 0.14$). More recently, Muris, ven der Heiden, et al. (2008) also found that DS and DSQ scores were both significantly correlated with small animal phobias (mean $r = 0.42$) and spider phobia (mean $r = 0.36$) for boys and girls aged 9–13 years. Furthermore, these researchers found that the DS Animals subscale in particular was specifically related to small animal and spider phobia. In a behavioral test, in which children were asked to select from clean or contaminated candy as a reward, the results were significantly correlated with small animal and spider phobia for girls only.

Muris, Mayer, Huijding, and Konings (2008) demonstrated that fear of an unknown animal can be experimentally induced in children by providing disgust-related information about the animal. In this study, Muris et al. provided disgust-related information (e.g., "When a cuscus/quokka has to urinate or to relive himself, he just does it in the hole where he also sleeps," p. 139) and cleanliness-related information (e.g., "The cuscus/quokka lives in a hole which smells nice. This is because he decorates his bed with petals and flowers," p. 139) to Dutch school children about unknown Australian marsupials. The results indicated that disgust-related information induced both higher levels of disgust and fear in relation to these animals, while the cleanliness-related information decreased disgust and fear towards the animal. This is compelling evidence that disgust-related information increases fear of unknown animals.

With regard to disgust sensitivity and small animal phobias, research has primarily focused on spider phobia in particular (de Jong et al., 1997; de Jong & Muris, 2002). With a sample of 22 spider-phobic girls, de Jong et al. (1997) found that not only was disgust sensitivity significantly correlated with fear of spiders, but also ratings of disgust decreased along with fear after successful treatment. Specifically, the authors found that spider-phobic girls had had higher disgust sensitivity and found spiders in particular more disgusting than did nonphobic controls. Additionally, they found that disgust associated specifically with spiders was reduced through treatment using eye movement desensitization and reprocessing (EMDR) as well as in vivo exposure. However, the level of disgust sensitivity, as measured by the DSQ (Rozin et al., 1984), remained unaffected by treatment targeting the spider phobia.

In a follow-up study, de Jong and Muris (2002) compared a sample of 18 spider phobic girls to a group of 18 nonphobic girls on their ratings of disgust sensitivity as well as their ratings of the subjective likelihood of a spider to enter their private living space, spiders' tendency to approach and make physical contact, and the subjective probability of spiders doing physical harm. The results indicated that spider phobic girls reported significantly higher levels of disgust sensitivity, and found spiders more disgusting than nonphobic girls. Notably, phobic girls in this study reported higher ratings concerning spiders' tendency to enter their living space and approach and make contact with them. The authors hypothesize the combination of increased disgust sensitivity and cognitions related to increased likelihood of making physical contact leads to the development of spider phobia. It is interesting to note that the results indicated that the critical variable in distinguishing between the phobic and nonphobic girls in regression analyses was the perceived ability of spiders to contaminate a chocolate bar (i.e., response to the items: "How much would you like to eat your favorite chocolate bar after a spider has walked across the bar when it is still wrapped

in its package?" and "How much would you like to eat your favorite chocolate bar after a spider has walked across the unpacked bar?" (de Jong et al., 1997, p. 560). Cognitions regarding the likelihood for a spider to approach and make contact had no additional predictive value in this study, which is strong evidence that spider phobia is most closely related to disgust sensitivity.

Obsessive Compulsive Disorder

In addition to phobias, a growing body of research has indicated there is a relationship between disgust sensitivity and OCD. Fear of contamination has been identified as one of the most common obsessive concerns among people who suffer with OCD (Foa & Kozak, 1995; Foa et al., 1995), and this preoccupation with avoiding contamination points to a plausible relationship between disgust sensitivity and OCD. Tolin et al. (2006) suggested that disgust may uniquely contribute to contamination-based OCD because feelings of disgust lead to phobic avoidance of certain stimuli that are relieved through compulsive behavior, and the behavior is sustained through negative reinforcement.

There is ample empirical research linking disgust sensitivity and OCD symptoms in adult samples (Mancini, Gragnani, & D'Olimpio, 2001; Schienle, Stark, Walter, & Vaitl, 2003; Thorpe, Patel, & Simonds, 2003). In particular, research has suggested that disgust sensitivity appears to be most strongly associated with washing and checking symptoms in OCD. Muris et al. (2000) found that obsessive-compulsive symptoms, especially cleaning concerns, were significantly related to disgust. Olatunji, Sawchuk, Arrindell, and Lohr (2005) also found that disgust sensitivity was a predictor of high levels of contamination fear.

Recently, Moretz and McKay (2008) investigated the relationship between OCD contamination symptoms, trait anxiety, and disgust sensitivity in a large sample of undergraduate students ($N=740$). Using structural equation modeling, disgust sensitivity, as measured by the DS, was directly and positively associated with contamination fear and washing rituals. The relationship between disgust sensitivity, and contamination and washing, and OCD symptoms was neither fully nor partially mediated by trait anxiety, which indicates that contamination-based OCD symptoms may be better conceptualized as resulting from increased disgust rather than fear.

To date, there has been very little research on the connection between OCD and disgust sensitivity in pediatric samples. In a sample of school children aged 8–13 years in the Netherlands, Muris et al. (1999) found that disgust sensitivity as measured by the DSQ was significantly correlated with OCD symptoms ($r=0.30$), but this correlation lost significance when trait anxiety was held constant. More recently, in another nonclinical sample, Muris, van der Heiden, et al. (2008) found that DS and DSQ scores were both significantly correlated with OCD symptoms for boys aged 9–13 years. For girls in the sample, DS score was significantly correlated with OCD symptoms, but the DSQ score was not significantly correlated. Furthermore, these researchers found that the DS Hygiene subscale in particular was specifically related to OCD symptoms. In a behavioral test of disgust sensitivity, there was a significant correlation between disgust sensitivity and OCD symptoms for boys only. These preliminary results are similar to findings in adult populations, and indicate a link between disgust sensitivity and OCD, but there is a clear need for more research utilizing clinical pediatric samples.

Blood-Injection-Injury Phobia

Discomfort upon exposure to blood, injury, and needles is a common phenomenon in childhood and adolescence. Research indicates that between one-quarter and one-half of children experience mild BII fears (Lapouse & Monk, 1959; Marks, 1988). For approximately 3% of children and adolescents, however, BII fears are severe and debilitating enough to warrant a clinical diagnosis (Marks, 1988; Miller, Barrett, & Hampe, 1974). Research has revealed that BII phobia is closely related to disgust (de Jong & Merckelbach, 1998; Olatunji et al., 2005; Page, 1994, 2003; Sawchuk et al., 2002; Tolin et al., 1997).

Disgust reactions (i.e., state disgust) are believed to be centrally involved in BII phobia-related fainting (Page, 1994, 2003; Page & Tan, 2009). Upon presentation of BII stimuli, individuals exhibit a biphasic response characterized by an initial surge in sympathetic nervous system activity, rapidly followed by a drop in blood pressure and heart rate. If the drop in blood pressure is precipitous enough to impede cerebral blood flow, fainting and, to a lesser extent, seizures can occur (Bienvenu & Eaten, 1998; Graham, Kabler, & Lunsford, 1961; Marks, 1988; Page, 1994, 2003). Fear is likely responsible for the initial increase of sympathetic nervous system activity (Olatunji, Connolly, et al., 2008; Page, 1994, 2003; Thyer & Curtis, 1985); the mechanism responsible for the shift into the latter phase of the diphasic response is hypothesized to be state disgust (Page, 1994, 2003; Page & Tan, 2009).

While the incidence of fainting among BII phobic children has not been reported, a significant minority of adolescents faint in response to BII stimuli (Kleinknecht & Lenz, 1989), and fainting in response to presentation of a "noxious" or "emotional" stimulus has been documented in children and adolescents (Driscoll, Jacobsen, Porter, & Wollan, 1997). These findings, in conjunction with the early age of onset of BII phobia (Bienvenu & Eaten, 1998; Marks, 1988; Ost, 1992), current etiological theories of BII phobia (Olatunji, Connolly, et al., 2008; Olatunji, Williams, et al., 2006; Page, 1994; Page & Tan, 2009), and modern adaptionist conceptualizations of fainting in response to BII-related stimuli (Bracha, 2004), suggest that fainting may directly influence the etiology and maintenance of the disorder in children.

Trait disgust has also been moderately to strongly correlated with BII fear, BII fainting, and BII avoidance (e.g., de Jong & Merckelbach, 1998; Muris et al., 1999; Muris, van der Heiden, et al., 2008; Olatunji, Connolly, & David, 2008; Olatunji, Sawchuk, de Jong, & Lohr, 2006; Olatunji, Williams, et al., 2006; Page, 2003; Schienle et al., 2001). For example, Muris et al. (1999) examined the relationship between trait disgust and BII phobia symptoms in non-clinical children and found that trait disgust was moderately correlated with BII phobia symptoms, even after controlling for levels of trait anxiety. In a more recent study, Muris, van der Heiden, et al. (2008) found significant positive correlations between trait disgust and symptoms of BII phobia, which were not attenuated when controlling for neuroticism (i.e., the tendency to experience negative affect).

Finally, disgust-related cognitive processes are also speculated to be involved in the pathogenesis and maintenance of BII phobia (Olantunji et al., 2010; Page & Tan, 2009). As described above, the cognitive processing of disgust-related information is often biased by the laws of contagion and similarity (i.e., law of sympathetic magic; Rozin & Fallon, 1987; Teachman, 2006), pathological disgust reactions are characterized by disgust-related primary and secondary appraisals (Teachman, 2006), and disgust may be associated with unique attentional, perceptual, and memory biases (Williams et al., 2009). Unfortunately, only limited research has investigated the relationships between these cognitive phenomena and BII phobia. Future research should attempt to continue to elucidate these associations and to further determine the extent to which these constructs are involved in childhood BII phobia specifically.

A Preliminary Model of Disgust in Childhood Anxiety Disorders

The available evidence suggests that disgust plays a role in several different anxiety problems that manifest in childhood. In the light of the research conducted, illustrating a connection between avoidance and disgust, and the basic research on the development of disgust-related aversions, a preliminary model may be considered to guide future research.

Development of Disgust

As discussed earlier, infants show the capacity to express disgust reactions. However, perhaps more than other emotional states, disgust for specific objects is taught by caregivers and other

environmental sources (Sawchuk, 2009). The most basic learning for disgust involves adverse reactions to food-related stimuli that would be deemed unpalatable, either due to risks of ingesting toxins for similar appearing foods (e.g., eating candy shaped like feces) or for culturally specific reasons (e.g., proscribing consumption of uncooked vegetables in some Chinese cultures). The underlying basis for how disgust is acquired has recently focused on EC, as discussed earlier (de Houwer et al., 2001). To summarize, the act of labeling an object, in conjunction with the modeled reactions of caregivers, produces a powerful learning experience that consolidates the emotional reaction and leaves it resistant to extinction.

It is interesting to note that disgust is unique in this regard. Other emotional states associated with psychopathological conditions do not show this kind of unambiguous direct connection between parental modeling and learning. For example, recent evidence suggests that many phobias arise without any direct experience with the phobic stimulus, and that in some instances, conditions for which learning theory would predict the onset of phobias, instead show substantial approach behavior for the same stimulus (detailed in Menzies & Clarke, 1995).

While the parental modeling approach appears to effectively instruct children on disgust for food and objects resembling disgust-related stimuli, this only accounts for one facet of disgust. Recent research has suggested that the seven disgust elicitors comprise three larger categories, namely core (which includes food and body products), animal reminder (such as body envelope violations and sex), and contamination (prominently featuring sympathetic magic). These domains, identified in psychometric evaluations of the DS (Olatunji et al., 2007) have unique behavioral, psychophysiological, and self-report correlates when examined with undergraduate and community samples (Olatunji, Haidt, McKay, & David, 2008). How these disparate forms of disgust develop is not clear, although each has been found in multicultural evaluations (Olatunji et al., 2009).

Sawchuk (2009) suggests that older children and adolescents develop more sophisticated appraisal processing skills that, in conjunction with normal neural development, allows for greater distinctions among potentially disgust-evoking stimuli and situations that would pose risks for contamination and other harm. Accordingly, sympathetic magic, and its associated laws of similarity and contagion, have their roots in parental instruction, but gain greater prominence in more elaborate situational appraisal that comes with cognitive development.

Internal Evaluation and Appraisal

As children develop greater appraisal processing skills, anxiety can be conferred by increased internal monitoring. Anxiety sensitivity has been shown to be a potent explanatory construct for a wide range of anxiety states (Taylor, 1999). However, anxiety sensitivity derives from a broader expectancy model (Reiss, 1991). Whereas disgust is taught for a wide range of stimuli, experienced disgust has specific physiological consequences (i.e., nausea, lightheadedness, reduced blood pressure). According to Reiss, self-monitoring of internal states, particularly when monitoring for increased risk, is a constitutional attribute. Anxiety sensitivity can be reliably assessed in children, and has been shown to predict several childhood anxiety disorders (Silverman & Weems, 1999). Recently, it has been proposed that a similar construct for disgust related to internal monitoring could predict avoidance reactions and anxiety states that are closely tied to disgust (Olantunji et al., 2010).

Summary and Future Directions

The research summarized here illustrates that disgust has recently been shown to play a prominent role in a wide range of anxiety problems. The vast majority of this research has focused on adult undergraduate, community, and clinical samples. While relatively little attention has been devoted to the role of disgust in childhood anxiety disorders, the early findings appear to suggest that there is a connection similar to that seen in adults. We propose

here a preliminary model that would account for the development of disgust reactions in conjunction with anxiety problems. The model depends primarily on basic learning of disgust in conjunction with a proneness to monitor internal states, and appraise changes due to disgust in a manner similar to that for anxiety sensitivity and monitoring for potential harm. As disgust is resistant to extinction due to its roots in EC, interventions other than exposure may be warranted in order to alleviate these reactions as part of a comprehensive approach to treating childhood anxiety disorders.

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Emotion Regulation in Childhood Anxiety

12

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Theoretical Foundations of Emotion Regulation in Anxiety Disorders

The field of psychology is in the midst of an "emotion revolution," reflecting the emerging role of emotion theory in clinical research and practice (Samoilov & Goldfried, 2000; Southam-Gerow & Kendall, 2002). Although many researchers have commended this trend, there is also an ongoing call for more clinical research that is founded on emotion theory and expands our understanding of the relations between the development of psychopathology, including anxiety disorders (ADs), and various emotional constructs (Hannesdottir & Ollendick, 2007; Suveg, Southam-Gerow, Goodman, & Kendall, 2007). Emotion regulation is one such construct.

Emotion regulation (ER) is defined as "the extrinsic and intrinsic processes responsible for monitoring, evaluating, and modifying emotional reactions, especially their intensive and temporal features, to accomplish one's goals" (Thompson, 1994, p. 27–28). More simply stated, ER involves an awareness of an emotional experience, the ability to appraise the context surrounding the emotional experience, and the modification of the expression of the emotion to the social context demands. Emotion regulation is not solely emotional suppression. It is a dynamic and complex process that involves controlling mechanisms such as exaggeration, substitution, and neutralization in addition to inhibition (Zeman, Shipman, & Penza-Clyve, 2001). Emotion regulation is intimately linked with both emotion understanding and emotion awareness; people need to be aware of their own and others' emotions, and have an understanding of the social implications of given emotions in various contexts in order to engage in adaptive regulation strategies (Campos, Mumme, Kermoian, & Campos, 1994; Saarni, 1999).

Emotion dysregulation, or maladaptive methods of managing emotional experiences in a given social context, has implications for both intrapersonal (e.g., low self-efficacy about one's ability to manage emotions) and interpersonal (e.g., difficulties relating to others) functioning (Thompson, 1994). Thus, ER is posited to play a role in many forms of psychopathology (Bradley, 2001; Cicchetti, Ackerman, & Izard, 1995; Cole, Michel, & Teti, 1994). Although emotion dysregulation is not specific to ADs, there are certain patterns of emotional arousal and inefficient emotion management that are associated with childhood ADs, as opposed to other types of internalizing difficulties (Suveg, Hoffman, Zeman, & Thomassin, 2009). Individual differences in children's ER result from elements both internal and external to the child (Calkins, 1994). Cognitive, biological, and environmental factors are linked to children's emotional development and are subsequently associated with the link between ER and ADs in youth. Understanding the dynamic contexts

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_12,

surrounding children's development is an essential component of using an ER framework.

Biological Foundations of Emotion Regulation in Anxiety

Neurobiological and genetic factors are pivotal in considering the development of ER because their influence is present from birth. Although there is no single genetic marker for ADs, there are abnormalities in neurobiological systems and patterns of reactivity that are associated with anxiety (e.g., Gordon & Hen, 2004). Specifically, several major neurobiological systems are associated with the elicitation, experience, and regulation of emotions (e.g., amygdala, prefrontal cortex, vagal tone), and a growing body of literature has linked anxiety with abnormalities in such substrates (Banks, Eddy, Angstadt, Nathan, & Phan, 2007; Santucci et al., 2008; Thomas et al., 2001).

The amygdala plays an essential role in emotion management and arousal (Banks et al., 2007; Davis, 1998), and children with ADs have been shown to exhibit greater amygdala responses to fearful stimuli than non-anxious children (Thomas et al., 2001). Frontal cortical regions of the brain are involved in modulating amygdala activity, and are also highly involved in ER activity (Banks et al., 2007). For instance, right frontal lobe asymmetry is associated with behavioral inhibition (a temperamental style discussed below) and reticence (Fox, Henderson, Rubin, Calkins, & Schmidt, 2001). Animal and human studies suggest that there may be a distinct fear circuitry system in the brain connecting the amygdala and ventral prefrontal cortex that serves as a neural basis for ADs (Amaral, 2003; Amaral et al., 2003; Gross & Hen, 2004). Miller, Taber, Gabbard, and Hurley (2005) discuss the proposed components of this fear circuitry system. Sensory input first reaches the thalamus. The thalamus then activates the amygdala through either direct or indirect pathways, depending on the nature and significance of the emotionally-salient stimuli, and the imminence of perceived danger. If this transmission occurs through indirect pathways, other regions such as the prefrontal cortex serve to modulate the information to obtain an accurate appraisal of its significance before it reaches the amygdala. The amygdala, in turn, then activates other regions of the brain that are associated with fear, such as the hypothalamus (which manages hormone release, such as in fight or flight responses) and brainstem (Miller et al., 2005). Thus, the amygdala-prefrontal cortex connections are central in producing a fear response (see Chapter 5, this volume, for a more thorough explanation of this fear circuitry system). This fear circuitry system has been associated with changes in social-threat perception. For instance, a study of adolescents with and without ADs found that there was greater amygdala and ventral prefrontal cortex activation in anxious youth than non-anxious youth when faced with undesired social evaluations (Guyer et al., 2008). Vagal tone, a measure of the balance between the sympathetic and parasympathetic nervous systems, is another psychophysiological marker for both ER and ADs, such that lower vagal tone (i.e., heart rate variability) is associated with ER deficits and difficulties managing emotionally arousing situations (El-Sheikh, Harger, & Whitson, 2001; Santucci et al., 2008). Neurobiological factors alone are not sufficient to explain why some youth develop ADs and others do not. Rather, it is the interplay of these factors with other temperamental, cognitive, and environmental influences that helps us understand what increases and decreases a child's vulnerability to developing an AD (Vasey & Dadds, 2001).

The tendency to respond in particular ways to environmental situations and challenges is believed to be, at least in part, temperamental (Calkins, 1994). Temperament, or innate reactivity to environmental changes, involves biological, emotional, and behavioral processes (Fox & Calkins, 2003). Behavioral inhibition has been identified as a risk factor for the development of ADs in childhood (Biederman et al., 2001; Degnan & Fox, 2007; Gar, Hudson, & Rapee, 2005). In toddlerhood, behavioral inhibition, or a tendency towards negative reactivity to novel stimuli, often involves withdrawal behavior and reticence to approach new people, places, or situations (Kagan, 1984; Kagan, Reznick, Snidman, & Gibbons, 1988). Research has documented a high degree of heterotypic continuity in the developmental trajectories of children with this

temperamental trait, often with a pattern of negative reactivity as an infant, inhibited behavior as a toddler, and hesitance in social situations as a school-aged child (Fox, Henderson, Marshall, Nichols, & Ghera, 2005). An important finding to this line of research is that not all children initially classified as inhibited remain inhibited across time (Gladstone, Parker, Mitchell, Wilhelm, & Malhi, 2005; Schwartz, Snidman, & Kagan, 1999). Research suggests that it is children who exhibit very extreme inhibition that maintain their classification years later.

Discontinuities in this trajectory (e.g., behaviorally inhibited toddlers who show little social reticence or anxiety in adolescence) have led researchers to investigate the factors or processes that might account for such resilience (Degnan & Fox, 2007). In a longitudinal study examining trajectories of anxiety symptoms, Feng, Shaw, and Silk (2008) followed boys longitudinally from ages 2–10 years. Multiple child anxiety risk factors were examined (e.g., attachment style, parenting), along with child shyness, which they conceptualized as a discrete form of behavioral inhibition reflecting reticence in social situations. Trajectory analyses indicated that shy temperament was associated with initial levels of anxiety in early childhood, but weakly related to anxiety in middle childhood. In contrast, maternal negative control was related to increases in anxiety over time. Various explanations for the findings were offered but collectively, the results potentially suggested that early temperamental risk factors for anxiety could be moderated by parenting factors over time. An overly controlling and negative family context may preclude youth from developing a repertoire of effective ER strategies and the self-efficacy needed to enact them.

Cognitive Foundations of Emotion Regulation in Anxiety

Emotional development is closely related to cognitive development, such that children's understanding of their own and others' emotions tends to develop in a simultaneous manner. For example, children's ability to understand their own and others' emotions tends to improve noticeably throughout early childhood (Denham, 1998). By the time children reach elementary school, most have developed a basic foundation of emotion understanding, and they start demonstrating increases in empathy and more complex emotional appraisal (Saarni, 1989). By middle childhood, children tend to be relatively efficient and consistent in their emotional predictions, justifications, and manipulations (Brown & Dunn, 1992). Thus, as children mature, increasing ER abilities often mirror increasing cognitive abilities. Though youth with ADs do not evidence deficits in intellectual functioning, they exhibit several cognitive processing issues that are related to ER deficits (e.g., see Amstadter, 2008).

A number of studies have captured cognitive processing difficulties related to ER that are common in anxious children. Research suggests that anxious children attend more to threatening information and experience heightened sensitivity to negative emotions when compared with their less anxious peers. For example, one study using a non-referred sample found that children *high* in test-anxiety had an attentional bias *towards* emotionally threatening stimuli when compared with their less test-anxious peers (Vasey, El-Hag, & Daleiden, 1996). Further, children *low* in test-anxiety showed an attentional shift *away* from emotionally threatening stimuli; although this finding was only true for boys. This was examined by measuring visual attention in terms of latency to detect dot-probes after the presentation of emotionally-threatening (e.g., injury) and neutral (e.g., apple) words. Research capturing an attentional shift in anxious youth *towards* threatening stimuli is consistent with research suggesting that ER abilities are affected by how children process information (Garber, Braafladt, & Zeman, 1991). However, some limitations exist regarding the examination of attentional bias towards threat in AD youth, as the majority of research utilizes a modified Stroop-task or a probe-detection task, and results have varied somewhat depending on the methodology used (Vasey & Dadds, 2001). Additionally, attentional biases may be difficult to assess and detect in younger children, and results may vary depending on whether the words are concern-relevant to the youth (Vasey & Dadds, 2001).

Another cognitive factor that may contribute to anxious youths' poor ER is lower self-efficacy.

Several studies reported that anxious children have lower self-efficacy in multiple domains than non-anxious children (Muris, 2002; Suveg & Zeman, 2004). Lower self-efficacy results in increased doubts regarding their ability to control their emotional experiences and responses in arousing situations (Suveg & Zeman, 2004; Weems, Silverman, Rapee, & Pina, 2003). Anxious youth also engage in fewer problem-solving strategies when managing their emotions than non-anxious youth (Suveg et al., 2008). Collectively, a focus on threatening stimuli, high arousal, low self-efficacy, and less problem-solving likely leads youth with ADs to avoid or give up in emotionally challenging situations, and reinforces their cognitions regarding their abilities to handle future emotionally challenging situations (Bradley, 2000). Many features of ADs can be conceptualized as maladaptive attempts to regulate undesirable emotions (Campbell-Sills & Barlow, 2007). Avoidance, for example, may serve as a method to regulate emotional arousal by simply evading it altogether. Although avoidance is effective in the short-term by producing immediate reductions in anxiety, it prevents the child from learning to regulate emotional arousal and achieving a sense of mastery over the anxiety-provoking event. Counterproductively, this avoidance will serve to maintain a child's fears and may hinder him or her broadly, primarily through restricting social, academic, and other opportunities. These negative emotions may facilitate further negative emotions, which will likely worsen the child's overall symptoms. Distraction techniques may also work similarly, as they temporarily allow an individual to avoid engaging in an emotional experience, therefore concurrently preventing them from using cognitive restructuring to restructure an intrusive worry thought.

Attempts at emotional inhibition may also serve to increase a youth's arousal. Thought suppression, the deliberate effort to suppress or inhibit a thought in an attempt to neutralize any anxiety or discomfort that is associated with it (Wegner, Schneider, Carter, & White, 1987), is one maladaptive ER strategy suggested to be commonly used by youth with obsessive-compulsive disorder (OCD) (Tolin, Abramowitz, Przeworski, & Foa, 2002). For example, a youth with OCD experiencing a distressing thought regarding stealing money from his or her parents would likely experience intense negative emotions (e.g., shame), and might attempt to engage in thought suppression efforts. Janeck and Calamari (1999) suggest that thought suppression may be a volitional response strategy that individuals with OCD will use as an avoidance behavior or coping mechanism against their obsessional thoughts, thus serving as an attempt at ER. Nonetheless, several studies have noted the paradoxical increase in obsessive thoughts that often occurs following these suppression efforts (Tolin et al., 2002; Wegner et al., 1987), so such efforts would likely maintain a youth's anxiety. Overall, it seems that youth with anxiety engage in several counterproductive strategies to regulate their emotions. These maladaptive ER strategies often result in the exacerbation and maintenance of their unwanted emotion (Campbell-Sills & Barlow, 2007).

Environmental Foundations of Emotion Regulation in Anxiety

Environmental influences are also considered in the dynamic transaction of factors that may predispose or protect a child from developing an AD. In particular, several factors have been implicated in the delineation of the link between children's ER and anxiety (e.g., children's opportunities to observe and practice ER skills, children's opportunities to master early control experiences, parental responses to children's anxiety; see Vasey & Dadds, 2001). Parental emotion socialization is often considered to be at the core of these external influences (Saarni, 1999).

Parental emotion socialization influences children's ability to regulate their emotions through direct (e.g., instruction) and indirect (e.g., modeling) pathways (Eisenberg, Cumberland, & Spinrad, 1998). Parents often serve a foundational role in monitoring children's exposure to emotional experiences, acting as filters of children's emotional environments. Although these early familial experiences contribute to many facets of development (e.g., social, psychological; Saarni,

1999), there are many influences, both internal (e.g., temperament) and external (e.g., parental psychopathology), that have been associated with problems in these socialization processes (Cassano, Perry-Parrish, & Zeman, 2007; Suveg, Zeman, Flannery-Schroeder, & Cassano, 2005).

Research suggests that parents of anxious youth engage in certain socialization behaviors that may contribute to their child's anxiety (McLeod, Wood, & Weisz, 2007). For instance, parents of anxious children may be more likely to be suffering from anxiety and other forms of psychopathology. They in turn may model anxious or avoidant behaviors, and may engage in over-controlling and intrusive behaviors (Connell & Goodman, 2002; Dadds, Marrett, & Rapee, 1996; Siqueland, Kendall, & Steinberg, 1996). Further, parents of anxious children may show low levels of emotional expressivity and engage in maladaptive socialization techniques (e.g., high levels of negativity and intrusiveness) when they do share emotional experiences with their child (Hudson & Rapee, 2001). For instance, one study used an emotion discussion task to examine emotion socialization in families and found that mothers of children with ADs spoke less frequently, used fewer positive emotion words, and discouraged their child's emotional discussion more than mothers of youth without ADs (Suveg et al., 2005). Similarly, a later study on emotion socialization in youth with ADs included fathers and found that parental socialization behaviors varied based on the sex of their child (Suveg et al., 2008). Specifically, there was less explanatory discussion about emotions by fathers whose children had an AD. These fathers also showed more negative and less positive affect when interacting with their anxious sons than did fathers whose sons did not have an AD. These and similar studies highlight the important role of parental emotion socialization and suggest several mechanisms of socialization that may go awry in families with anxious youth. Parents who are less accepting of youth emotional displays may reinforce a child's inhibition of emotion, thus leading to increased arousal and fewer opportunities to learn successful coping strategies. Youth who are not given such opportunities to process emotionally arousing situations are less likely to acquire emotion-related skills (Suveg et al., 2008). As youth with ADs often have anxious parents (Last, Phillips, & Statfeld, 1987), anxious parents may also model poor ER skills or shield their child from emotionally-arousing situations, thus providing them with fewer opportunities to develop ER skills (Hannesdottir & Ollendick, 2007). Given that parents serve as primary socialization agents, AD youth who experience maladaptive emotion socialization are likely to be at a disadvantage relative to their non-clinical peers in terms of emotion learning. However, it is important to note that these processes are likely bidirectional. Child factors (e.g., temperament) could elicit a negative reaction from a parent, while an anxious parent could model emotion dysregulation for their child. Thus, it is likely that several parent and child factors interact to result in emotion dysregulation in youth with ADs.

When considering the clinical presentation of ER in youth with anxiety, ER deficits could likely vary by disorder. Scarce research, however, has examined differences in ER that are specific to the particular type of AD in youth. As several studies have linked ER difficulties and social competence (Eisenberg, Fabes, Guthrie, & Reiser, 2000), youth with social anxiety might have particular difficulty managing their negative emotions in social situations. Socially-phobic youth have also been found to have significantly poorer affect recognition skills when compared with non-clinical youth (Simonian, Beidel, Turner, Berkes, & Long, 2001), suggesting that affect recognition skills would likely be helpful in social skills training with socially-phobic youth. As youth with panic disorder are particularly fearful of the physiological symptoms of anxiety, they may have low self-efficacy regarding their ability to manage emotionally-arousing situations (Hannesdottir & Ollendick, 2007). Recent research utilizing an adult population also suggests an ER model of trichotillomania (Diefenbach, Tolin, Meunier, & Worhunsky, 2008), suggesting that hair pulling may be used to modulate both high arousal (e.g., anxiety) and low-arousal (e.g., boredom). Thus, youth with trichotillomania may notice an immediate reduction in emotional arousal after hair-pulling, serving to reinforce maladaptive ER strategies.

Research examining the existence of sex differences in the presentation of ER in anxious youth is also rather limited. Suveg and Zeman (2004) found that both girls with and without ADs reported less adaptive emotion coping than boys. This finding could be due to girls being more socialized to disclose their emotional difficulties when compared with boys. Sparse research suggests that boys exhibit greater difficulty with the use of display rules (i.e., one form of ER strategy) than girls (Davis, 1995; Saarni, 1984), though this research did not utilize youth with ADs. Another study suggests that children's ER decisions may vary according to sex, with males being less likely to report expressing sadness and pain (Zeman & Garber, 1996). One study using a community sample reported that girls displayed less emotional self-efficacy when compared with boys (Muris, 2001), which could certainly be a consideration in the implementation of treatment. Researchers have instead focused on sex differences in parental emotion socialization strategies and gender-stereotyping. In general, emotion expression tends to be encouraged in girls and discouraged in boys, though some emotions may be considered more acceptable if expressed by one sex versus another (i.e., anger expression in boys; Suveg et al., 2008). Additionally, some studies have suggested that child ER strategies may vary between cultures (e.g., appropriateness of emotional expression, ways in which physiological arousal is reported; Mesquita & Karasawa, 2002; Raval, Martini, & Raval, 2007), so clinicians should be aware of these differences when considering the clinical presentation of ER in youth with anxiety (Ehrenreich, Fairholme, Buzzella, Ellard, & Barlow, 2007). Are these normative patterns of emotion socialization also evidenced in families of youth with ADs? If not, how are the socialization practices different and what are the implications for youth emotional functioning? Future work should examine sex and cultural differences in ER skills in youth with ADs. See Fig. 12.1 for an illustrative conceptualization of the various

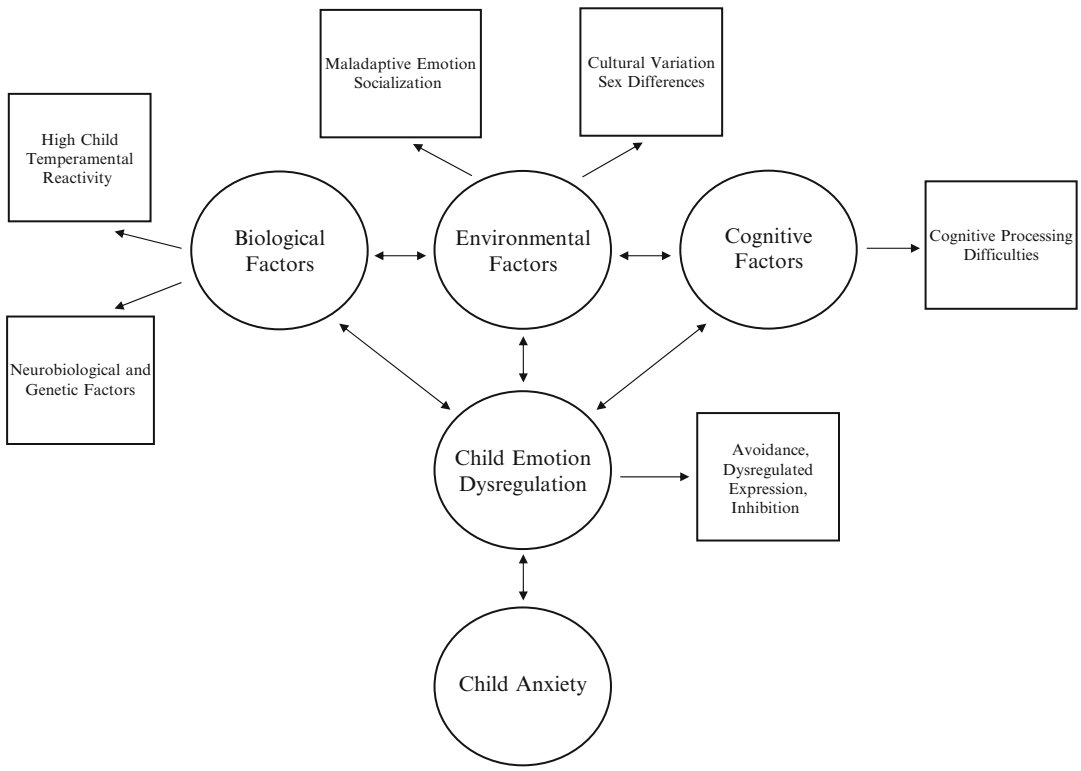

Fig. 12.1 Illustrative model depicting several of the major variables involved in child emotion dysregulation and anxiety disorders

pathways associated with the development of ER in youth ADs. The figure, which was adapted from Suveg, Morelen, Brewer, and Thomassin (2010), is not exhaustive and highlights only some of the potential variables involved in ER in youth with ADs.

Assessment of Emotion Regulation in Childhood Anxiety

Research in the area of ER assessment has recently received considerable attention, particularly with samples of youth. Despite recent advances, we encounter debates in the child ER literature regarding discrepancies between child and parent reports of ER abilities (Kazdin, 1989, 1994; Offord, Boyle, Racine, & Szatmari, 1996). These discrepant data have proven difficult to integrate, and leave researchers questioning who is a better reporter of child emotional experiences. As a result, various researchers have called for multi-informant reports of ER (Kazdin, 1994; Kazdin & Weisz, 2003; Larsen & Prizmic-Larsen, 2006). Despite this, a review of the child ER literature reveals that as many as 44% of the published studies employed only one method of assessment (Zeman, Klimes-Dougan, Cassano, & Adrian, 2007). The discrepancy between the call for multi-informant methods and the implementation of such methods suggests that this area of research is in need of development. Rather than serve as an exhaustive review, the purpose of the following section is to illustrate various methodologies and examples of instruments developed to assess ER in youth, many of which have been utilized with samples of youth with ADs.

Self-Report

Various developmental issues arise when asking youth to report on their emotional experiences. For example, youth may not possess the self-awareness necessary to make such reports. Kazdin and Weisz (2003) suggest that youth below the age of five cannot accurately report on their experiences. Younger children also exhibit dichotomous thinking and therefore may have difficulty with the rating scales associated with the measures. These limitations are especially salient when assessing ER in children below school-age years. When assessing ER in older children, however, researchers argue that youth *can* reliably report on their emotional experiences because they are less likely to fall victim to the limitations listed above (e.g., Ialongo, Edelsohn, & Kellam, 2001; Laurent et al., 1999). Obtaining ER data from youth themselves is necessary given that emotional experiences are not always expressed outwardly; thus, only youth may be aware of and able to report on their internal emotional experiences.

Children's Emotion Management Scales (CEMS anger, sadness, and worry scales; Zeman et al., 2001; Zeman, Cassano, Suveg, & Shipman, 2010) are one of the few psychometrically studied measures of ER in youth. The CEMS assess ways in which youth manage anger, sadness, and worry. Each measure includes three subscales: (a) Inhibition, suppression of emotional expression (e.g., "I get sad inside but I don't show it."); (b) Dysregulated Expression, children's culturally inappropriate emotional expression (e.g., "I do things like slam doors when I'm mad."); and (c) Emotion Regulation Coping, children's adaptive methods of emotion management (e.g., "I keep myself from losing control of my worried feelings."). Initial reliability and validity data for the scales are acceptable ($a = 0.62–0.77$) and the scales demonstrate good test-retest reliability (Zeman et al., 2001). Initial data support the use of a Worry scale with a similar three-factor structure (Zeman et al., 2010).

How I Feel (HIF; Walden, Harris, & Catron, 2003) is a 30-item self-report measure of emotional arousal and control over the past three months. The measure can be characterized by three factors: the frequency and intensity of (a) negative emotions (e.g., "I was mad very often.") and (b) positive emotions (e.g., "When I felt happy, my happy feelings were very powerful."), and (c) negative and positive emotion control (e.g., "I was in control of how often I felt scared."). This instrument exhibits good internal consistency ($a = 0.84–0.90$) and concurrent validity (Walden et al., 2003).

The *Emotion Expression Scale for Children* (EESC; Penza-Clyve & Zeman, 2002) is a 16-item self-report measure that assesses youth's ability to identify and willingness to communicate

their emotions on a 5-point Likert scale (1 = *not at all true*; 5 = *extremely true*). The instrument is comprised of two subscales: Poor Awareness, which measures difficulty in labeling internal emotional experiences (e.g., "I often do not know how I am feeling."), and Expressive Reluctance, that assesses lack of motivation or willingness to express negative emotions (e.g., "I prefer to keep my feelings to myself."). The EESC has high internal consistency ($a = 0.81–0.83$) with adequate test-retest reliability (0.56–0.59; Penza-Clyve & Zeman, 2002).

The *Cognitive Emotion Regulation Questionnaire* (CERQ; ages 12 and older; Garnefski, Kraaij, & Spinhoven, 2001) and the *Cognitive Emotion Regulation Questionnaire – kids version* (CERQ-k; ages 9–11; Garnefski, Rieffe, Jellesma, Terwogt, & Kraaij, 2007) consist of 36 items measured on a 5-point Likert scale (1 = *almost never*; 5 = *almost always*). The CERQ and CERQ-k measure nine cognitive ER strategies (e.g., self-blame, catastrophizing, positive reappraisal) that children and adolescents may use after the experience of negative life events. Preliminary evidence has demonstrated reliability ($a = 0.68–0.83$ for CERQ; $a = 0.62–0.79$ for CERQ-k) for these scales (Garnefski et al., 2001, 2007), but further studies will be necessary to establish the psychometric properties of these measures.

Additional self-report measures may be used as screeners to assess global emotional functioning in youth. For example, the *Positive and Negative Affect Scale for Children* (PANAS-C; Laurent et al., 1999) contains subscales that examine positive and negative affect. Although the PANAS-C does not directly measure ER in youth, the measure has been shown to have convergent and divergent validity with respect to symptoms of anxiety and depression (Laurent et al., 1999). Projective measures have also been used to assess for general emotionality in youth (e.g., Thematic Apperception Test).

Parent and Teacher Reports

In order to address potential limitations stemming from developmental issues associated with youth reporting on emotion regulation processes, investigators have stressed the need for multi-informant reports. Consequently, several instruments have been developed for such purposes. As listed below, these measures are to be completed by individuals that have had extensive interactions with the child (e.g., parents, caregivers, teachers).

The *Emotion Regulation Checklist* (ERC; Shields & Cicchetti, 1997) is a commonly used parent-report measure that assesses perceptions of their child's ER abilities. This measure yields two subscales: Emotion Regulation, which assesses appropriate emotional expression, empathy, and emotional self-awareness (e.g., "Can modulate excitement in emotionally arousing situations"), and Lability/Negativity that assesses inflexibility, lability, and dysregulated affect (e.g., "Exhibits wide mood swings," "Is easily frustrated"). Reliability coefficients are high for the overall scale (0.89) and for the two subscales (Lability/Negativity = 0.96, Emotion Regulation = 0.83; Shields & Cicchetti, 1997). The ERC can also be used with teachers.

Other measures such as the *Behavior Rating Inventory of Executive Function* (BRIEF; Gioia, Schultz, & Corley, 2000) and the *Behavior Assessment System for Children* (BASC; Reynolds & Kamphaus, 1992) contain more global subscales related to emotion processes. The BRIEF, for example, assesses youths' ability to control their emotional experiences. The BASC contains two subscales that assess emotional functioning (emotional self-control, negative emotionality). Though these measures do not directly measure ER abilities, they may be used as screening measures to better understand a youth's general emotional functioning.

Interview Instruments

The *Kusche Affective Interview-Revised* (KAI-R; Kusche, Greenberg, & Beilke, 1988) is a semi-structured interview that assesses emotional development in youth. Several components of emotional functioning are examined including the ability to discuss emotion-related experiences (e.g., "Tell me about a time when you felt sad."),

recognition of emotions in self and others (e.g., "How do you know when other people are feeling jealous?"), and understanding of how emotional experiences can change (e.g., "Suppose you were feeling upset, could your feelings change?" and if so, "Tell me what would happen."). Responses to these items are recorded verbatim and later coded for developmental level of response. Interrater agreement is good (0.79–1.0; Cook, Greenberg, & Kusche, 1994), and internal validity has been established as well (Cook et al., 1994; Greenberg, Kusche, Cook, & Quamma, 1995).

Behavioral Observation Methodology

Self- and parent-report of emotional functioning in youth give rise to several limitations. With respect to self-report, for example, developmental level plays a crucial role in whether youth can accurately report on their emotional state (Kazdin & Weisz, 2003). In fact, a controversy in the field of emotion assessment questions whether children possess the metacognitive ability to examine the subjective experience of emotion. As a result, several paradigms and coding schemes have been developed to assess emotional functioning in youth. Despite great variability in paradigms, the field often considers behavioral observation methods as the "gold standard" for assessment in youth.

Behavioral observation paradigms are developed to elicit a low to moderate level of emotional arousal within the child (e.g., disappointing gift; Saarni, 1984). The disappointing gift paradigm, for example, creates positive expectations within the child of receiving a desired reward. When this gift violates the youth's expectations, children are then expected to appropriately modulate their emotions and follow certain display rules. A set of behavioral observations is examined to assess ER processes exhibited by the child. Distinct coding techniques such as microanalytic coding and global coding have been suggested for facial expressions, tone of voice, emotions expressed, and intensity of emotion (Zeman et al., 2007).

Other research has utilized emotion discussions as a method of examining both emotional functioning in youth as well as socialization processes. One typical paradigm has youth talk about times when they felt particular emotions. The discussions are coded for variables such as the strategy that the youth implemented when feeling the emotion and their affect during the discussion. Research using this paradigm with both typical and anxious populations has yielded interesting results (Hudson, Comer, & Kendall, 2008; Suveg et al., 2005, 2008).

Electronic Diaries

Assessment of emotion and ER specifically is plagued by the transitory nature of emotional states. The use of diaries for data collection originated to address several limitations obstructing the acquisition of ecologically valid data and allows the researcher to collect data on momentary emotional experiences. Preliminary data suggests that electronic diaries may be a feasible method of assessment in child and adolescent populations. A study examining changes in adolescents' everyday moods and their perceptions regarding the impact of the September 11th terrorist attacks indicated that anxiety measured by electronic diaries versus paper measures was an independent predictor of post-traumatic distress (Whalen, Henker, King, Jamner, & Levine, 2004). Using a community sample of youth, Suveg, Payne, Thomassin, and Jacob (2010) found a high number of missing data points and some technical difficulties associated with using the electronic diaries. However, the data available provided useful information regarding the youth's functioning.

Neuroscience Methodology

Researchers have implicated several systems in emotion processing (e.g., cortisol levels, parasympathetic activation, vagal tone, cortico-limbic system and the amygdala; Gottman, Katz, & Hooven, 1996; Ochsner, Bunge, Gross, & Gabrieli, 2002). More recently, research has implicated the ventrolateral prefrontal cortex (VLPFC) in ER processes. As Taylor, Lerner,

Sage, Lehman, & Seeman (2004) comment, the amygdala activates a set of responses that, in turn, are modulated via the VLPFC. Research has shown that the right VLPFC (RVLPFC) is activated during labeling of negative emotion (Hariri, Bookheimer, & Mazziotta, 2000; Lieberman, Hariri, Jarcho, Eisenberger, & Bookheimer, 2005). They therefore specified that increased activity in the RVLPFC of this neural region coupled with low activation of the amygdala may be associated with emotion dysregulation. To examine this hypothesis, Taylor, Eisenberger, Saxbe, Lehman, and Lieberman (2006) examined amygdala reactivity to fearful and angry faces, and RVLPFC reactivity to labeling those emotions using functional magnetic resonance imaging in a sample characterized by family stress. They concluded that participants from risky families (i.e., families in which youth were exposed to harsh, conflict-ridden, or neglectful parenting) exhibited such a pattern, suggesting atypical neural responses to affective stimuli. Although significant advances have been made in the field of affective neuroscience, this area is still blossoming and appropriate experimental designs for clinical application have not yet been developed.

Overall, the literature on assessment of ER requires the continued use of multi-method data collection (i.e., obtaining parallel child-, parent-, and teacher-report measures) to help increase our understanding of emotion assessment reliability and validity for youth. Further research is needed to develop and validate measures that allow us to accurately capture emotional variability across contexts, and the moment-to-moment changes in emotion regulatory strategies (Ehrenreich et al., 2007).

Emotion Regulation Considerations in the Treatment of Childhood Anxiety

Research on the role of ER in the treatment of child ADs and general psychopathology is becoming more prevalent (see Ehrenreich et al., 2007; Hannesdottir & Ollendick, 2007; Suveg et al., 2007). Given the salience of ER difficulties in many forms of child psychopathology (American Psychiatric Association, 2000; Mullin & Hinshaw, 2007; Suveg & Zeman, 2004), the consideration of ER seems particularly relevant to the treatment of youth ADs. Though cognitive-behavioral therapy (CBT) remains the only evidence-based psychological treatment for ADs in youth, researchers are increasingly trying to incorporate ER components into the modification of current treatments as well as the development of new treatment approaches. Several of these potential treatment options are discussed below.

Cognitive-Behavioral Therapy

CBT is considered "probably efficacious" (see Chaps. 19–25) for the treatment of ADs in youth (Ollendick & King, 1998; Silverman, Pina, & Viswesvaran, 2008). Most CBT programs focus on modifying the cognitive (e.g., maladaptive thinking patterns) and behavioral (e.g., avoidance) components of anxiety. Some CBT programs, however, also incorporate emotion regulatory components. Many components of typical CBT programs serve to target emotion dysregulation. For example, relaxation training is often used to help reduce a child's physiological response to anxiety (e.g., Coping Cat; Kendall, 1994). Relaxation may serve as an ER strategy because it allows the youth to modify their physiological response to anxiety and decrease arousal (Hannesdottir & Ollendick, 2007). Cognitive restructuring may also change a child's affect though changing maladaptive thinking patterns (e.g., increasing self-efficacy for emotion regulatory abilities) (Hannesdottir & Ollendick, 2007).

A study by Suveg, Sood, Comer, and Kendall (2009) sought to examine ER and more specific emotional functioning following CBT for youth with ADs. Given that anxious youth have difficulty managing emotions in addition to worry (e.g., anger, sadness; Suveg & Zeman, 2004); Suveg, Sood, et al. (2009) examined changes in emotion awareness along with worry, anger, and sadness regulation. Thirty-seven youth, aged 7–17 years, diagnosed with either GAD, Separation Anxiety Disorder, and/or Social Phobia completed 16 CBT sessions. Youth demonstrated significant improvements in anxiety, self-efficacy, emotion

awareness, and worry regulation skills, though these gains did not generalize to either anger or sadness regulation. Results suggest that CBT for youth with ADs may facilitate broad emotion identification skills, yet does not adequately teach youth how to regulate emotional experiences beyond the experience of anxiety (Suveg, Sood, et al. (2009). The findings are meaningful because they suggest that at least some maintaining factors associated with childhood anxiety are not addressed in typical CBT protocols.

Recently Suveg, Kendall, Comer, and Robin (2006) developed an emotion-focused CBT program (ECBT) for youth with ADs. ECBT addresses all of the empirically-based components of traditional CBT, yet also includes an additional component to address the emotion-related deficits identified in youth with ADs (Southam-Gerow & Kendall, 2000; Suveg & Zeman, 2004). According to Suveg et al. (2006), "The fundamental difference between individual CBT and ECBT is the systematic integration of emotion-related concepts in ECBT in an effort to facilitate the development of both emotion understanding and emotion regulation skills, beyond the experience of anxiety" (p. 80–81). During the first phase of ECBT treatment, youth learn about different emotions (e.g., anxiety, anger, guilt, happiness), focusing on how to recognize the emotion in oneself and others. The second half of treatment, exposure treatment, utilizes exposures to anxiety-provoking scenarios, as well as exposures to situations that provoke other emotions (e.g., anger) that the child has difficulty regulating. Children are then coached on how to manage these emotion-provoking experiences. Suveg et al. (2006) conducted a multiple-baseline study using ECBT for six anxious youth with principal diagnoses of Generalized Anxiety Disorder, Separation Anxiety Disorder, or Social Phobia. After completion of a 16-session treatment, most youth exhibited improvements in anxiety and overall adjustment, their ability to identify emotional states, ability to use emotion language to discuss emotion-related experiences, and ability to understand ER strategies such as hiding and changing emotions. Though this study provided initial support for ECBT, it will be important to compare ECBT to other treatment approaches (e.g., CBT) to identify whether one treatment may be more beneficial for youth with particular characteristics.

Clinical Implications

Though in its infancy, research documenting ER deficits in anxious youth has direct implications for both assessment and treatment. Clinicians should assess emotional functioning when conducting an assessment of youth with anxiety. In particular, clinicians should identify the *functional* role of a child's emotions and ER strategies in order to understand how they are used to regulate the child's internal and external environment (Ehrenreich et al., 2007). Then, treatment could include skills to build emotional competence in youth, such as the development of emotional awareness and a "toolbox" of ER and coping strategies (Suveg, Hoffman, et al., 2009). Emotion regulation strategies could help anxious youth manage their arousal before it becomes overwhelming and interfering. Furthermore, CBT primarily focuses on anxiety and worry and does not necessarily target other emotions. By learning to differentiate between and identify emotions and situations which elicit certain emotions, youth will be better equipped to regulate them correctly, instead of feeling emotionally-aroused and unsure of how to ameliorate themselves (Hannesdottir & Ollendick, 2007). Therapists may use methods of parent training to guide parents in serving as "emotion coaches" (Lagacé-Séguin & Coplan, 2005, p. 615) to encourage appropriate expression and discussion of emotions within the family. Given the presence of maladaptive parental emotion socialization often present in families of youth with ADs (Suveg et al., 2008), these discussions may be especially pertinent and may facilitate the development of better ER strategies (Hannesdottir & Ollendick, 2007).

Summary and Future Directions

Research has identified various ways in which emotion dysregulation may be involved in the etiology and maintenance of ADs in youth; however, longitudinal research will be necessary to

delineate whether ER difficulties contribute to the development of ADs and/or exist as a result of these disorders. Future research should address the role of various socialization influences (e.g., peers, teachers) on the ER strategies in youth with anxiety, as well as whether ER strategies vary by age, gender, culture, or specific type of AD in youth. The development of reliable and developmentally-appropriate assessment tools remains limited, so continued work in this area is necessary. Preliminary treatment findings suggest that anxiety-disordered youth benefit from the inclusion of ER components in treatment. Overall, continued work in this area will improve our understanding of ER in AD youth, as well as facilitate the development and refinement of developmentally-appropriate intervention programs for youth.

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Emergent Personality Disorders Among Adolescents with Anxiety Disorders

13

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Introduction

Since the introduction of well-defined diagnostic criteria in the Third Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III; APA, 1980), there has been a steady increase in the amount of research devoted to the study of personality disorder (PD), focusing initially and predominantly on adult populations. As currently defined, "A PD is an enduring pattern of inner experience and behavior that deviates markedly from the expectations of the individual's culture, is pervasive and inflexible, has an onset in adolescence or early adulthood, is stable over time, and leads to distress or impairment (APA, 2000; p. 685)." Research activity in the field of adolescent PD has also increased substantially in recent years, although there have been concerns about diagnosing PD among adolescents (Silk, 2008). Epidemiological research has suggested that although there are noteworthy differences in the phenomenology, assessment, and treatment of PD symptoms among adolescents and adults, the prevalence, comorbidity, and sequelae of PD may tend to be broadly similar in comparable adolescent and adult populations.

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This chapter begins with a summary of research findings pertinent to the clinical presentation of emergent PD that may cooccur with anxiety disorders during adolescence, and a discussion of factors associated with the development of personality and anxiety disorders. Assessment instruments including structured diagnostic interviews, clinician-administered rating procedures, and questionnaires used to assess maladaptive personality traits in a dimensional manner are presented. The chapter concludes with a description of therapeutic interventions that have been found to be useful in treating adolescents with PD.

Clinical Presentation

In clinical and nonclinical populations, youths with emergent PD tend to experience higher levels of impairment or distress, and tend to have more severe and chronic symptoms than do youths without PD (Daley, Hammen, Davila, & Burge, 1998; Johnson, Hyler, Skodol, Bornstein, & Sherman, 1995; Johnson et al., 1999; Johnson, Cohen, Smailes, et al., 2000; Levy et al., 1999; Westen et al., 1990). In a variety of clinical populations, patients with anxiety disorders and cooccurring PD have been found to have lower levels of functioning, more persistent anxiety symptoms, and poorer long-term outcomes than those without PD (Sanderson, Wetzler, Beck, & Betz, 1993; Skodol et al., 1995).

D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_13, © Springer Science+Business Media, LLC 2011

Most youths deal with a number of challenging developmental and psychosocial transitions between childhood and adolescence, both internally (e.g., changes in self-perception) and externally (e.g., changes in social roles). These transitions may be associated with the development of mild, moderate, or severe anxiety symptoms, and/or maladaptive personality traits. During the transition to adolescence, the development of self-consciousness, increased social comparisons, and the need for peer acceptance can collide with social stressors, such as exclusion and shame, to produce maladaptive outcomes in some children (Thomaes, Bushman, Stegge, & Olthof, 2008). Factors including unpopularity with peers, few extracurricular activities, and few positive relationships with adults during childhood may be associated with risk for the development of PD symptoms (Rettew et al., 2003).

Clinical Features of Specific Personality Disorders

Avoidant PD is defined, in the DSM-IV-TR (APA, 2000), as "a pervasive pattern of social inhibition, feelings of inadequacy, and hypersensitivity to negative evaluation." Antisocial PD, diagnosed only among individuals who are at least 18 years in age, is defined as "a pervasive pattern of disregard for and violation of the rights of others, occurring since age 15, and a history of conduct disorder by age 15." Borderline PD is defined as "a pervasive pattern of instability of interpersonal relationships, self-image, and affects and marked impulsivity." Dependent PD is defined as "a pervasive and excessive need to be taken care of that leads to submissive and clinging behavior and fears of separation." Histrionic PD is defined as "a pervasive pattern of excessive emotionality and attention seeking." Narcissistic PD is defined as "a pervasive pattern of grandiosity, need for admiration, and lack of empathy." Obsessive–compulsive PD is defined as "a pervasive pattern of preoccupation with orderliness, perfectionism, and mental and interpersonal control, at the expense of flexibility, openness, and efficiency." Paranoid PD is defined as "a pervasive distrust and suspiciousness of others such that their motives are interpreted as malevolent." Schizoid PD is defined as "a pervasive pattern of detachment from social relationships and a restricted range of expression of emotions in interpersonal settings." Schizotypal PD is defined as "a pervasive pattern of social and interpersonal deficits marked by acute discomfort with, and reduced capacity for, close relationships as well as by cognitive or perceptual distortions and eccentricities of behavior."

Comorbidity Between Anxiety and Personality Disorders

Potential comorbidity between anxiety and personality disorders is an important clinical consideration, because maladaptive personality traits tend to be associated with treatment complications, persistent anxiety symptoms, and poor outcomes (Brandes & Beinvenu, 2006; Skodol et al., 1995). Moreover, cooccurring disorders are often associated in a pathoplastic manner, with one disorder influencing the course, manifestation, and outcomes of the other. Such pathoplasticity frequently complicates treatment, but, in some cases, a cooccurring condition may be associated with reduced symptom expression. For example, there have been findings suggesting that anxiety disorders may have a protective or dampening effect in youths with antisocial characteristics (Tackett, 2006).

Studies in adolescent and adult populations have suggested that some types of anxiety disorders may be differentially associated with specific PDs. For example, McGlashan et al. (2000) have reported associations between social phobia and avoidant PD, and between OCD and obsessive–compulsive PD. Skodol et al. (1995) reported that among patients with anxiety disorders, OCD was associated with obsessive–compulsive and avoidant PDs; that panic disorder was associated with borderline, avoidant, and dependent PDs; and that social phobia was associated with avoidant and obsessive–compulsive PDs.

Studies of maladaptive traits, such as behavioral inhibition and emotional dysregulation, have also findings that are informative about the potential

associations between anxiety and personality disorders among youths. Behavioral inhibition, a temperament characteristic that may be evident during early childhood, has been found to predict childhood and adolescent anxiety disorders, and may also be associated with the development of Cluster C PD traits (see Tackett, 2006). Research has suggested that delinquent adolescents with high levels of emotional dysregulation and inhibitedness may tend to have difficulties with social withdrawal and anxious–depressive symptoms (Krischer, Sevecke, Lehmkuhl, & Pukrop, 2007).

Longitudinal Associations Between Anxiety and Personality Disorders

Research has suggested that anxiety disorders during childhood may contribute to elevated risk for DSM-IV Cluster A and C PDs (Goodwin, Brook, & Cohen, 2005), and that PDs during adolescence may be associated with elevated risk for subsequent anxiety disorders (Johnson, Cohen, Kasen, & Brook, 2006). Borderline and schizotypal PD traits were associated with risk for agoraphobia, generalized anxiety disorder (GAD), obsessive–compulsive disorder (OCD), panic disorder, and social anxiety disorder. Dependent PD traits were associated with risk for agoraphobia, OCD, panic disorder, and social anxiety disorder. Histrionic PD traits were associated with risk for GAD and OCD; schizoid PD traits were associated with risk for panic disorder; and avoidant PD traits were associated with risk for OCD and social anxiety disorder (Johnson et al., 2006).

Factors Associated with the Development of Personality and Anxiety Disorders

Childhood Adversities and Development of Personality Disorders

Numerous studies have provided findings suggesting that childhood maltreatment, problematic parenting, parental loss, and adversities may contribute to the development of PD and maladaptive personality traits during adolescence (e.g., Cohen, Brown, & Smailes, 2001; Johnson, Cohen, Brown, Smailes, & Bernstein, 1999; Johnson et al., 2001; Johnson, Cohen, Chen, Kasen, & Brook, 2006). Low parental affection has been found to be associated with elevated risk for offspring antisocial, avoidant, borderline, depressive, paranoid, schizoid, and schizotypal PDs, and aversive parental behavior has been found to be associated with elevated risk for offspring borderline, paranoid, passive–aggressive, and schizotypal PDs (Johnson, Cohen, Chen, Kasen, & Brook, 2006).

Specific types of maltreatment or problems associated with upbringing may be differentially associated with risk for the development of specific types of PD traits. Among the significant associations in the research literature are findings suggesting that childhood abuse and emotional neglect may contribute to the development of avoidant PD (Johnson et al., 2005). In addition, individuals with avoidant PD have reported higher levels of parental shaming and intolerance, and childhood feelings of guilt (Stravynski, Elie, & Franche, 1989), and histrionic patients have reported high levels of parental control and low familial cohesion (Baker et al., 1996). Maternal inconsistency and over-involvement have been found to predict offspring borderline and histrionic PDs, respectively (Bezirganian et al., 1993). Childhood physical and emotional abuses have been found to be associated with risk for dependent and obsessive–compulsive PDs, respectively (Johnson et al., 2005). High levels of parental control and over-protectiveness, along with low levels of family expressiveness have also been associated with dependent PD (Johnson et al., 2005).

Overprotective, authoritarian parenting may foster dependency by reducing opportunities for autonomous learning experiences and thereby preventing the child from developing a trans-situational sense of mastery (Bornstein, 1992). Such children may develop a self-concept dominated by themes of powerlessness and incompetence, as well as persistent fears of abandonment and negative evaluations by others. In this regard,

it is notable that dependent PD often cooccurs with anxiety disorders (Brandes & Beinvenu, 2006; Grant et al., 2005).

Attachment Difficulties

Attachment theorists have hypothesized that interruptions and disturbances in relationships with attachment figures during early childhood may contribute to the development of maladaptive attachment styles, which often persist into adolescence or adulthood (Bowlby, 1973, 1977, 1982). Bowlby observed a strong causal relationship between the quality of child–parent experiences and later ability to form emotional relationships, noting that difficulties in emotional capacity often manifest as neurotic symptoms (e.g., anxiety) and maladaptive personality traits (e.g., interpersonal avoidance). Research has supported the inference that insecure attachment style is associated with an elevated likelihood of PD (Tackett & Krueger, 2005).

Fossati et al. (2003) found that avoidant, depressive, paranoid, and schizotypal PDs were associated with avoidant attachment styles, and that dependent, histrionic, and borderline PDs were associated with anxious attachment styles. West et al. (1994) reported that dependent and schizoid PD were associated with showed that preoccupied (i.e., enmeshed) and dismissing (i.e., detached) attachment styles, respectively.

Difficulties in Psychosocial Development

Erikson's theory of psychosocial development (Erikson, 1963, 1968, 1980) provides a particularly useful framework for understanding how difficulties in relationships with caregivers and significant others may lead to difficulties with anxiety, and the development of maladaptive personality traits. Erikson (1963) hypothesized that there are eight major developmental stages during the human life span, each of which is characterized by a normative psychosocial "crisis." Each of these crises can potentially arise at any point in life as a function of psychosocial forces or "hazards of existence" (Erikson, 1963, p. 274).

Erikson hypothesized that positive relationships with primary caregivers during childhood contribute to the child's capacity to develop a sense of basic trust, which forms the basis for his or her capacity to venture forth in the world (autonomy), take risks (initiative), and develop a cohesive sense of self (identity). Interpersonal experiences during childhood that disrupt this basic developmental sequence tend to be anxiety provoking and to create conditions for the development of maladaptive traits. For example, caregivers who invalidate the child's emotional reactions to the world or are insensitive to the child's emotional states run the risk of undermining the communicative function of emotion, which may lead to the child's inability to trust his or her emotional experience of the world (Linehan, 1993). This basic sense of relational mistrust, if it becomes persistent during childhood, increases the likelihood of feelings of shame, doubt, guilt, inhibition, reluctance to take risks, and identity difficulties during adolescence.

Erikson (1963; 1968; 1980) theorized that the process of identity development is the key developmental milestone during adolescence, and that the adolescent struggle for identity is the most prominent of the normative developmental crises. Identity consolidation during adolescence enables the developing youth to develop a sense of continuity with the past, meaning in the present, and direction for the future (Marcia, 1994). As such, identity consolidation forms the cornerstone of well being and the basis of self-esteem. Successful identity achievement eventuates in a clear sense of self, well-defined beliefs and values, and a place in the community. Failure to achieve an identity may be associated with feelings of anxiety, depression, and with a wide range of maladaptive personality traits (e.g., identity disturbances associated with borderline PD). Disruptions in the process of identity consolidation may, thus, contribute to the emergence of PDs and anxiety disorders during adolescence (Brandes & Beinvenu, 2006; Grant et al., 2005; Johnson, 1993; Lenzenweger et al., 2007).

Identity Diffusion, Object Relations, and Personality Disorders

Kernberg (1984; 1996) has set forth a theory of PD development that elaborated upon the mental representations associated with basic mistrust during early childhood, and the processes leading to identity diffusion. Kernberg's theory emphasizes the role of core impairments in the conceptions of self and significant others, or "object relations." According to Kernberg (2005), problematic interactions with significant others during childhood tend to be split into those that are ideal and pleasurable, as opposed to those that are painful, perceived as persecutory, and subsequently avoided. Ideal and painful memories are kept separate, according to object relations theory, until the maturing child can realistically integrate the two categories. Identity diffusion is hypothesized to occur when this split between idealized and painful representations of self and others persists through adolescence (Kernberg, 2005). Research has suggested that many adolescents with identity diffusion may have persistent object-relational difficulties attributable to childhood adversities including excessive frustration during infancy, childhood maltreatment, and family turmoil (Akhtar, 1992). Identity diffusion and severe interpersonal difficulties during adolescence have been found to be associated with PD symptoms (Crawford et al., 2004; Johnson, 1993; Wilkinson-Ryan & Westen, 2000).

Assessment and Diagnosis of Emergent Personality Disorders

Special Considerations for Assessment of Personality Disorders in Children and Adolescents

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; Fourth Edition, Text Revision), several diagnostic considerations should be used in assessing PDs among children and adolescents (APA, 2000). First, PDs are not to be diagnosed unless a youth has maladaptive personality traits that deviate markedly from cultural expectations and are "…pervasive, persistent, and unlikely to be limited to a particular developmental stage or an episode of an Axis I disorder (APA, 2000; p. 687)." Second, the features of a PD must have been present for at least 1 year. Third, antisocial PD cannot be diagnosed in individuals under 18 years of age, and may only be diagnosed in individuals who have a history of conduct disorder with an onset by age 15 years. Moreover, it should be noted that some personality traits that may be regarded as being pathological when expressed during adulthood are considered relatively normal during adolescence (e.g., affective lability, impulsivity). Only those traits that deviate markedly from cultural expectations are to be considered symptomatic of a PD.

Diagnostic Instruments Used for the Assessment of Personality Disorders

Several diagnostic interviews and questionnaires are available for the assessment of PD during childhood or adolescence (see McCloskey, Kane, Morera, Gipe, & McLaughlin, 2007).

The Structured Clinical Interview for DSM-IV Personality Disorders (SCID-II; First, Spitzer, Gibbon, & Williams, 1995) is a two-stage diagnostic system that includes a screening questionnaire and a semistructured clinical interview. During the SCID-II interview, clinicians determine whether affirmative responses on the questionnaire indicate the presence of PD symptoms. Research has supported the reliability and validity of the SCID-II (Ekselius et al., 1994; Jacobsberg et al., 1995; O'Boyle & Self, 1990; Skodol et al., 1991). SCID-II items have been used, in epidemiological research, to assess adolescent PD symptoms (e.g., Bernstein et al., 1993).

The Structured Interview for DSM-IV Personality Disorders (SIDP-IV; Pfohl et al., 1997) is a semistructured diagnostic interview, available in two different versions, one with items grouped by diagnosis and the other with items grouped topically. Research has supported the

reliability and validity of the SIDP-IV in adult and adolescent populations (Brent, Zelenak, Bukstein, & Brown, 1990; Pfohl et al., 1997).

The International Personality Disorder Examination (IPDE; Loranger, 1994) is a two-part instrument used for the clinical assessment of PDs. The first section is a 77-item screening questionnaire. The second component is a 99-item semistructured interview, which takes approximately 3 h to administer. A modified version of the IPDE has been used with individuals as young as 15 years (Lenzenweger, 2008; Lenzenweger et al., 2007). Research has supported the reliability and validity of the IPDE (Loranger et al., 1994).

The Personality Disorder Interview-IV (PDI-IV; Widiger et al., 1995) is a semistructured interview. Manualized administration of the PDI-IV usually takes 90–120 min. The PDI-IV items may be administered thematically or by diagnostic criteria. The thematic format assesses attitudes toward self and others, security of comfort with others, friendships and relationships, conflict and disagreements, work and leisure, social norms, mood, appearance and perception. Research has supported the reliability and validity of the PDI-IV (Widiger et al., 1995).

The Diagnostic Interview for DSM-IV Personality Disorders (DIPD-IV; Zanarini et al., 1996) is a 108-item semistructured clinical interview. The DIPD-IV takes approximately 90 min to administer. Research has supported the inter-rater reliability of the DIPD-IV (Zanarini et al., 2000).

The Personality Diagnostic Questionare-4th Edition (PDQ-4+; Hyler, 1994) includes a 100-item self-report questionnaire and a clinician-administered clinical significance scale (CSS) assessing impairment, duration, and timing of traits identified based on questionnaire responses. Research has supported the inter-item and test–retest reliability of the PDQ-4+; (Hyler et al., 1989; Trull, 1993). Although the PDQ-4+ has a high false-positive rate, research has supported its use as a screening instrument (e.g., Davidson et al., 2001), and PDQ-4+ items have been used for research in adolescent populations (e.g., Johnson et al., 1995).

Dimensional Assessment of Maladaptive Personality Traits

Consistent with recent developments in the assessment of PD symptoms in adult populations, considerable attention has been devoted, in recent years, to the dimensional assessment of maladaptive personality traits in children and adolescence (Tackett, Balsis, Oltmanns, & Krueger, 2009). Dimensional approaches may be more informative than categorical diagnoses, and data regarding adaptive and maladaptive traits can be integrated readily within a dimensional framework (see Cicchetti & Rogosch, 1996; Mulder, 2008; Silk, 2008). Historically, adult trait models have frequently been applied to younger age groups. However, in recent years, efforts have been made to develop age-specific personality models for children and adolescents (Tackett, 2006). Middle childhood and early adolescence may be a critical period for the development of PD, given the changing nature of social relationships during these years (Tackett et al., 2009).

The Shedler-Westen Assessment Procedure-200 for Adolescents (SWAP-200-A; Westen, Shedler, Durrett, Glass, & Martens, 2003) is a Q-sort instrument, designed for the dimensional assessment of DSM-IV PD symptoms. The SWAP-200-A is a set of 200 descriptive statements, printed on cards, which clinicians rank–order based on their observations. The SWAP-200-A has been found to be a promising tool for assessing adolescent PD traits (Westen & Shedler, 2005).

The Dimensional Assessment of Personality Pathology-Basic Questionnaire for Adolescents (DAPP-BQ-A; Tromp & Koot, 2008), a 290-item questionnaire, is an age-appropriate version of the Dimensional Assessment of Personality Pathology-Basic Questionnaire (DAPP-BQ; Livesley et al., 1992). Research has supported the reliability of the DAPP-BQ (e.g., Livesley et al., 1998) and the DAPP-BQ-A (Tromp & Koot, 2008).

The Dimensional Personality Symptom Item pool (DIPSI; DeClercq, De Fruyt, & Widiger, 2009), developed for the dimensional assessment of adolescent personality characteristics, assesses 27 lower-order facets and 4 higher-order factors

(i.e., disagreeableness, emotional instability, introversion, and compulsivity). The three latter factors are particularly pertinent to childhood anxiety disorders and cluster C PD symptoms. The emotional instability facets include reflecting anxiety, insecure attachment, ineffective stress coping, dependency, and inflexibility. The introversion domain facets include shyness and withdrawn tendencies. The compulsivity facets include perfectionism, extreme order, and extreme achievement striving associated with early manifestations of obsessive–compulsive PD.

Reliability and Validity of Personality Disorder Assessment in Adolescent Populations

Numerous studies have demonstrated that when different clinicians conduct independent ratings of PD diagnostic interviews, in adolescent samples, inter-rater agreement has ranged from moderate to high (Becker et al., 2002; Brent et al., 1990; Daley et al., 1999; Grilo et al., 1998; Guzder et al., 1996; Lenzenweger, 1999; Ludolph et al., 1990; Westen & Muderrisoglu, 2003). Research has indicated that PD traits tend to be moderately stable during adolescence (e.g., Barasch et al., 1985; Bernstein et al., 1993; Daley et al., 1999; Johnson, Cohen, Kasen, et al., 2000; Korenblum et al., 1987; 1990; Lenzenweger, 1999). Similar findings regarding the temporal stability of PD diagnoses and traits have been obtained from adult samples when similar retest intervals and assessment procedures have been used (e.g., Johnson et al., 1997; Johnson, Cohen, Kasen, et al., 2000; Loranger et al., 1994; McDavid & Pilkonis, 1996; Trull et al., 1998).

Support for the concurrent, construct, and predictive validity of adolescent PD diagnoses has been provided by research indicating that adolescent PDs are associated with significant impairment and distress, maladaptive personality traits, and elevated risk for Axis I disorders, interpersonal aggression, suicide, and other adverse outcomes (Bernstein et al., 1993; Brent et al., 1993, 1994, 1990; Daley et al., 1998, 1999; Grilo et al., 1997; Guzder et al., 1996; Johnson, 1993; Johnson et al., 1995; Johnson et al., 1999; Johnson, Cohen, Smailes, et al., 2000; Levy et al., 1999; Pinto et al., 1996; Westen et al., 1990). Risk factors for borderline PD during childhood have been found to be similar to those associated with borderline PD during adulthood (Guzder et al., 1996). Adolescents with borderline PD have been found to have self-concept disturbances that are not accounted for by depressive traits (Pinto et al., 1996). Evidence of familial aggregation of PDs has been reported (Johnson et al., 1995), and PD traits have been found to have similar correlates in adolescent and adult samples (DeClercq & De Fruyt, 2003).

Prevalence of Personality Disorders Among Youths in the Community

The available evidence indicates that PDs may tend to be approximately as prevalent among adolescents as they are among adults in the general population. Estimates of the prevalence of DSM-III-R and DSM-IV PDs among adolescents in community and primary care settings, based on diagnostic interviews, have ranged from 6 to 17%, (Bernstein et al., 1993; Daley et al., 1999; Johnson et al., 1999; Lenzenweger et al., 1997; Zaider et al., 2000). The median of these PD prevalence estimates is approximately 11%. In comparison, it has been estimated that approximately 10% of the adults in the general population are likely to have a current PD (Oldham, 1994; Weissman, 1993). Moreover, evidence from clinical studies has indicated that when similar assessment procedures are administered, the prevalence of PDs among adolescent inpatients is nearly identical to the prevalence of PDs among adult inpatients (Becker et al., 2002; Grilo et al., 1998).

Treatment of Personality Disorder Symptoms in Youths with Anxiety Disorders

A number of therapeutic modalities have been developed for the treatment of PD symptoms in children, adolescents, and adults (see Freeman &

Reinecke, 2007; Kernberg, Weiner, & Bardenstein, 2000; Oldham, Skodol, & Bender, 2005). Detailed information regarding issues such as level of care, cross-cultural and gender issues, and the assessment and management of suicidality and behavior problems in patients with PD is presented in the *Handbook of Personality Disorders* (Oldham, Skodol, & Bender, 2005).

Cognitive Therapy

A variety of cognitive approaches, including cognitive therapy (CT; Beck et al., 1990), cognitive-behavioral therapy (Hayward et al., 2000), and schema therapy (Young & Klosko, 2005) have been developed for the treatment of PD. Cognitive therapies for PD focus on helping patients learn how to modify problematic thoughts and behaviors and to develop improved coping skills. Client misperceptions of the therapist are addressed directly and corrected to preserve the therapeutic alliance. Schema-focused therapy addresses the interaction of core psychological themes (e.g., experiences of abandonment or abuse) and maladaptive coping styles (e.g., surrender, avoidance, overcompensation). Cognitive therapy for PD and other disorders may be appropriate for youths who are 11 years of age or older, and capable of abstract thought (Ronen, 2007). Cognitive-behavioral therapy, which includes affective education, cognitive restructuring, and practicing, has been found to be an effective treatment for youths with a wide range of disorders, including social anxiety disorders and schizoid spectrum disorders (e.g., Hayward et al., 2000; Atwood, 2007). Schema-focused therapy has been found to be an effective treatment for patients with avoidant PD (Coon, 1994), and research has supported the efficacy of CT in the treatment of PD (Pretzer, 2004).

Dialectical Behavior Therapy

Dialectical behavior therapy (DBT) is a structured treatment approach that combines cognitive-behavioral interventions with mindfulness meditation practices. DBT was originally developed as a treatment for individuals with Borderline PD and a history of self-injurious behavior, but has been used in recent years to treat both adolescents and adults with a variety of other psychiatric conditions (Koerner & Dimeff, 2000). DBT treatment is organized into stages, addressing the following: (1) self-harmful and suicidal behaviors; (2) behaviors that could lead to termination of treatment; (3) behaviors interfering with quality of life (substance abuse, high-risk sexual behavior, extreme financial difficulties, criminal behavior, unemployment, housing difficulties); and (4) life skills training. Treatment goals, agreed upon by therapists and clients, are defined behaviorally. Emphasis is placed upon maintaining clear communication, appropriately validating clients' thoughts, perceptions, and feelings, and a strong therapeutic alliance. DBT therapists verbalize belief in the client's inherent capacity to improve and overcome difficulties. Therapeutic validation is intended to enhance the therapeutic relationship, facilitate behavior change, and help the client to learn to self-validate (Swales, Heard, Williams, & Mark, 2000; Linehan, 1993).

DBT has been found to be particularly effective when individual psychotherapy, group skills training, and telephone consultations are employed concurrently. In individual sessions, the therapist and client typically set an agenda of behaviors to target at the beginning of each session. Diary cards, which clients complete throughout the course of a week, are used for setting the session agenda. "Problem-solving" is a core strategy of treatment and consists of behavioral and solution analyses in individual sessions. When conducting a behavioral analysis, the client and therapist collaboratively break down all the links in the "chain" between triggers and consequent thoughts, feelings, and behaviors. Solution analysis seeks to identify the choice points at which the client could handle situations more adaptively in the future. Clients are actively encouraged to make a commitment to try to attempt more adaptive strategies when future choice points occur.

Skills training is a central focus of DBT treatment, aimed at increasing adaptive behaviors

while simultaneously reducing maladaptive behaviors. A basic assumption of DBT is that clients engage in dysfunctional behaviors because they lack the skills to deal with difficult situations. Four skill modules are taught in the context of a group modality and include core mindfulness, distress tolerance, emotion-regulation, and interpersonal effectiveness skills. The skill modules target four characteristic problem areas, which include confusion about self, impulsivity, emotional instability, and interpersonal problems. Telephone "coaching" between outpatient therapy sessions is offered to assist clients in generalizing skills to their outside lives. Phone coaching additionally provides an avenue for clients to repair and enhance the therapeutic relationship (Swales, Heard, Williams, & Mark, 2000; Linehan, 1993).

Modifications of DBT in working with adolescents include involvement of caregivers, strategies to enhance motivation, attention and engagement, and length of treatment. Teaching skills to caregivers can foster skill generalization and decrease caregivers' involvement in conflict within the home environment. Multifamily skills training groups, including youths and their caregivers, can help caregivers to learn behavioral skills alongside teens. Family sessions often include family behavioral analyses of problematic behaviors and directly target ineffective use of contingency management and invalidation (e.g., communications of nonacceptance and/or expressed belief that teens' behavior is manipulative). Role-play and experiential exercises are used in skills groups with teams to facilitate engagement. Between-session assignments may be referred to as "practice exercises" as opposed to "homework" to decrease negative connotations associated with school. With adolescents, the duration of treatment may be shortened to maximize engagement, because teens may exhibit less entrenched personality problems than adults.

DBT has been found to be effective in treating adults with borderline PD (Linehan, Armstrong, Suarez, Allmon, & Heard, 1991; Linehan, Heard, & Armstrong, 1993). Several studies have yielded findings supporting the efficacy of DBT in adolescent populations (Desmond, 2008; Katz, Cox, Gunasekara, & Miller, 2004; Rathus & Miller, 2002; Miller, Wyman, Huppert, Glassman, & Rathus, 2000). Research has suggested that the combination of DBT and family therapy may be especially useful in treating adolescents (Miller, Glinski, Woodberry, Mitchell, & Indik, 2002).

Psychodynamic Psychotherapy

A number of psychodynamic models including ego psychology, object relations theory, and attachment theory are relevant to the treatment of PD (Yeomans, Clarkin, & Levy, 2005). In therapy approaches based on self-psychology, therapeutic empathy is used in a nondirective manner to activate the innate potential of the patient. Client resistance is empathized with, rather than interpreted. Transference-focused psychotherapy (TFP), which is based on object-relations theory, is a more directive, manualized approach, involving a highly engaged therapeutic relationship and therapist interpretation (Kernberg et al., 1989). Attachment-based treatment focuses on helping the patient to develop a more secure attachment style in the context of the therapeutic relationship (Travis, Binder, Bliwise, & Horne-Moyer, 2001). Expressive-supportive psychotherapy emphasizes the expression of feelings in a supportive environment.

Research has suggested that psychodynamic therapy may be effective for older children and adolescents with emotional disorders, although interpretation of unconscious conflict may be of limited value with severely disturbed youths (e.g., Fonagy & Target, 1996). According to Bleiberg (2001), the principal goal of effective psychodynamic therapy with youths is to promote reflective functioning. In adult populations, expressive-supportive psychodynamic therapy has been found to be effective in the treatment of obsessive–compulsive and avoidant PDs (Barber, Morse, Kraukauer, Chittams, & Crits-Christoph, 1997). Brief dynamic therapy has been found to be effective in mixed Axis II samples (Winston et al., 1994), and therapy based on self-psychology has been found to be helpful in treating patients with borderline PD (Stevenson & Meares,

1992). In addition, time-limited dynamic psychotherapy has been found to promote the development of a more secure attachment style (Travis et al., 2001).

Mentalization-Based Treatment

Based on attachment theory, mentalization-based treatment (MBT) is a psychodynamic therapy that seeks to enhance individuals' capacity to understand their thoughts and feelings in the context of attachment relationships. MBT is based on the premise that disruptions in mentalization (i.e., "reflective function") occur as a consequence of disruptions in attachment during infancy and early childhood, resulting in problems including anxiety, depression, and cluster B PD symptoms. MBT, which includes individual, group, and family sessions, promotes the capacity for mentalization, and works with youths and family members to transform problematic attachments and coercive cycles into healing and sustaining relationships (Bateman & Fonagy, 2004). Group sessions are used to assist clients in practicing mentalization skills. Research has found MBT to be effective in improving functioning and in reducing impairment, suicidality, and psychiatric service utilization (Bateman & Fonagy, 2004, 2008; O'Malley, 2003).

Cognitive Analytic Therapy

Cognitive analytic therapy (CAT) is an approach that synthesizes elements of psychodynamic and cognitive therapy. Dysfunctional patterns of interpersonal behavior are hypothesized, by CAT therapists, to be based on problematic attempts to elicit response from others, referred to as reciprocal role procedures (RRPs) (Ryle, 2001). These RRPS (e.g., patterns of interaction such as "caring-cared for" and "rejecting-rejected") are derived from early interactions, or ongoing interactions in the case of children, with caretakers and peers. During the course of therapy, the CAT clinician generates diagrams depicting how RRPs tend to be enacted by the patient, and how others tend to reciprocate. These diagrams are used to help patients understand the nature and interpersonal consequences of their RRPs. Research has suggested that CAT may be an effective treatment for adolescents with borderline PD symptoms (Chanen et al., 2008).

Family Therapy, Parent Training, and Multimodal Treatment Approaches

In addition to providing individual treatment, it is often essential to address contextual factors that may contribute to youths' anxiety and personality problems. Children and adolescents' symptoms may result, in part, from problems in the family home environment, such as marital difficulties, family conflict, or parental impairment (Bleiberg, 2001; Framo, 1970; Magnavita, 2007). Family therapy, marital therapy, and/or provision of health or social services to other family members may play an important role in providing adequate treatment to youths with anxiety and personality disorders. In some cases, it may be helpful to provide services assisting parents in optimal child-rearing skills and enhancing caregiver competence (Bleiberg, 2001; Brestan & Eyberg, 1998). Parent training programs using videotaped modeling in a group format and manualized parent training protocols based on operant behavior principles have been found to be effective interventions (Brestan & Eyberg, 1998). Multisystemic therapy that addresses all areas of an individual's life in a comprehensive manner has been found to be efficacious with high-risk youths (Brestan & Eyberg, 1998). School-based family interventions (Dishion & Kavanagh, 2000) and multimodal interventions including family and individual therapy with home visits (Brotman et al., 2008) can reduce problem behaviors and improve parenting for youths who are at high risk for adverse mental health outcomes. Social skill training has been found to be helpful in addressing skill deficits in individuals with PD (Lieberman, DeRisi, & Mueser, 1989; Sperry, 2003). For example, cognitive therapy, combined with social skills training in a group format, has been found to be particularly effective for the

treatment of avoidant PD (Alden, 1989). Group therapy, combined with multifamily skills training, has been found to be effective in treating suicidal adolescents (Rathus & Miller, 2002).

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Temperament and Anxiety Disorders

14

Elizabeth C. Winter and O. Joseph Bienvenu

Epidemiology of Anxiety Disorders in Children and Adolescents

Psychiatric illness is highly prevalent among children and adolescents. For example, Costello, Mustillo, Erkanli, Keeler, and Angold (2003) psychiatrically evaluated over one thousand children aged 9 to 13 years yearly until age 16 years. The 3-month prevalence of any disorder was 13%. However, over the course of the study, 31% of girls and 42% of boys had at least one psychiatric disorder meeting DSM-IV criteria. In children and adolescents in the general population, anxiety disorders are particularly common, with a lifetime prevalence of 29% (Costello, Egger, & Angold, 2005). The median age of onset for anxiety disorders (11 years old) is earlier than that for other mental illnesses (Kessler et al., 2007). The age of onset varies for specific disorders. For example, in the National Comorbidity Survey Replication, median ages of onset in years were as follows: 7 for specific phobia and separation anxiety disorder, 13 for social phobia, 19 for obsessive compulsive disorder, 20 for agoraphobia without panic, 23 for post-traumatic stress disorder, 24 for panic disorder, and 31 for generalized anxiety disorder (GAD) (Kessler et al., 2005).

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Unfortunately, despite the pervasiveness of these disorders, less than one-third of children receive treatment. For example, Chavira, Stein, Bailey, and Stein (2004) reported that, of children with a diagnosis of any anxiety disorder, only 31% received medication or psychotherapy, compared with 40% of children with major depression or 79% of children with attention deficit/hyperactivity disorder. Lack of treatment for mental illness is not unique to the United States. The WHO World Mental Health Survey Consortium's report (2004) found that 36–50% of people with major mental illness in developed countries – and a staggering 76–85% in less developed countries – received no mental health treatment in the preceding year. Anxiety disorders can be debilitating and generate significant burden for the sufferers and their families. Clearly more work needs to be done to identify children who either are at risk for developing anxiety or have already developed symptoms of anxiety, so that they benefit from prevention or early intervention (Bienvenu & Ginsburg, 2007). As outlined in this chapter, temperamental traits are promising as easy-to-measure risk factors, markers of risk, or correlates of anxiety disorders.

Temperament vs. Personality Traits

Bates (1987) described temperament as the individual differences in how one responds behaviorally to emotions or environmental stimuli. This definition is similar to that of other temperament theorists (Goldsmith et al., 1987). These

D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_14, © Springer Science+Business Media, LLC 2011

differences are generally considered to appear early in life and remain somewhat stable over time. The fact that temperament appears early in life, before infants have much opportunity to interact with their environments, suggests that temperament traits are at least partly genetically determined (Cloninger, Svrakic, & Przybeck, 1993). Twin studies confirm the substantial heritability of temperament (DiLalla & Jones, 2000; Goldsmith & Lemery, 2000; McCartney, Harris, & Bernieri, 1990; Plomin, Owen, & McGuffin, 1994).

There is some debate regarding the difference between temperament and personality (McCrae et al., 2000). According to Cloninger, personality grows out of the combination of temperament, or behavioral predisposition, and character, defined as the goals and values developed through environmental interaction (Cloninger et al., 1993). Alternatively, Kagan posits that the relationship between temperament and personality is more direct, with temperament as the substrate upon which the environment acts to produce personality over time (Kagan, 1997).

Researchers have developed the convention of using temperament to describe dimensional traits in children and personality to describe dimensional traits in adults. Numerous prospective studies have shown significant correlations between temperament and personality traits. Hagekull and Bohlin (1998) demonstrated that early levels of activity and sociability positively correlated with later extraversion, and that early negative emotionality correlated with later neuroticism. Similarly, Caspi et al. (2003) found that temperamentally under-controlled toddlers showed higher levels of negative emotion as adults. Notably, there is little concrete evidence to differentiate temperament from personality, and it is possible that the distinction between them is more terminological than actual.

Temperament is usually measured via questionnaire administered to a child's parents or teacher, or by standardized observation in the laboratory (Rettew & McKee, 2005). Personality, on the other hand, is generally assessed via self-report. The partitioning of temperament and personality may be due, in part, to the discontinuity of the evaluation methods used in children and adults. Further exploration of the distinction between temperament and personality is beyond the scope of this chapter, however, and we will confine ourselves to the term temperament to minimize confusion.

Nomenclatures of Temperament

The temperament field was revolutionized by the work of Thomas and Chess (1977). Thomas and Chess delineated nine temperamental dimensions based on parent interviews about their infants' behaviors: (1) activity level – the motor component of behavior and its diurnal fluctuation; (2) rhythmicity – the predictability of a behavior or reaction over time; (3) approach or withdrawal – the initial response to a new stimulus; (4) adaptability – the ease with which a child was able to change his behaviors in order to shift the situation in a desired direction; (5) threshold of responsiveness – the intensity of stimulus required to provoke any response; (6) intensity of reaction, in either direction; (7) quality of mood; (8) distractability – the ease with which a child's attention could be diverted from the current stimulus; and (9) attention span and persistence – the length of time an activity was pursued and continued in the face of distraction or obstacles. Later work by the pair condensed the model into three fundamental types. The "easy temperament" referred to reliably positive approach responses to new stimuli, high adaptability to change, and a typically positive mood of mild to moderate intensity. The "difficult temperament" referred to poor rhythmicity, withdrawal responses to new stimuli, poor adaptability and intense, negative moods. Finally, the "slow to warm up temperament" was conceptualized as a combination of negative responses to new stimuli with slow adaptability despite repeated contact (Chess & Thomas, 1986).

Unfortunately, the nine dimensions of Chess and Thomas proved unwieldy, and factor analysis did not find strong support for nine independent factors. Some of the dimensions were highly intercorrelated and could be subsumed into one

factor, while others did not emerge at all (Prior, 1992; Shiner & Caspi, 2003). The original nine dimensions were eventually combined into three traits, activity level (impulsivity, novelty seeking), negative emotionality (related to the concept of the difficult temperament, approach/withdrawal, and social inhibition), and attention span/persistence (related to a dimension called effortful control or conscientiousness).

Buss and Plomin (1975) hypothesized a model of temperament similar to the eventual condensation of Thomas and Chess' dimensions. Temperament, as construed by Buss and Plomin, represents broad, early appearing (from the first year of life), heritable, stable characteristics of infants and children that presumably form the basis for adult personality development. The authors published a questionnaire called the EASI, which was meant to measure four relatively independent aspects of temperament: Emotionality (E) (specifically refers to *negative* emotionality), Activity (A), Sociability (S), and Impulsivity (I). In their work with the EASI, Buss and Plomin concluded that Emotionality, Activity, and Sociability met their criteria for temperament traits. However, the data on Impulsivity were inconclusive for two main reasons (Buss & Plomin, 1975): (1) Impulsivity as construed in the EASI did not appear to be a psychometrically distinct or singular construct and (2) the data on heritability of Impulsivity was equivocal at the time. Because of these difficulties, in their subsequent development of an instrument to measure temperament (the EAS), the authors dropped their measure of impulsivity (Buss & Plomin, 1984). Since then, several investigators have noted that "impulsivity" can be usefully broken down into cohesive elements that are heritable (reviewed in Buss, 1995). Support for both negative and positive emotionality as traits includes the fact that these are relatively stable over time (Lonigan, Phillips, & Hooe, 2003). Comparison of the EAS model with Costa and McCrae's five-factor model (Costa & McCrae, 1992) revealed that emotionality was strongly correlated with neuroticism, and that extraversion was correlated with activity and sociability (Muris & Ollendick, 2005). We would expect the latter traits to be correlated with positive emotionality, as well (as in extraversion).

A third model of childhood temperament involves behavioral inhibition to the unfamiliar. Kagan, Reznick, and Snidman (1988) defined behavioral inhibition as an overwhelming propensity toward withdrawal and reluctance to interact when presented with unfamiliar people, objects, or situations, similar to Thomas and Chess' "slow to warm up temperament." Importantly, behavioral inhibition differs from shyness because it includes nonsocial as well as social reticence. Behavioral inhibition is evident in 10–15% of children and is moderately stable from early childhood through early adulthood (Kagan, Snidman, Zentner, & Peterson, 1999; Kagan, 1994; Caspi & Silva, 1995), with a heritability coefficient of 0.4–0.6 in twin and adoption studies (Smoller & Tsuang, 1998). It would not be surprising to find that behavioral inhibition correlates positively with neuroticism (negative emotionality) and negatively with extraversion, though, to our knowledge, this has not been tested (Bienvenu & Stein, 2003; Bienvenu, Hettema, Neale, Prescott, & Kendler, 2007).

Emotionality, activity, sociability, and behavioral inhibition are all traits that determine an individual's reactions to stimuli, whether the stimulus is internally or externally generated. Most researchers agree that temperament not only is made up of reactive traits but also requires a self-regulatory component. In 1989, Rothbart introduced the concept of effortful control, or the ability to voluntarily maintain or shift attention as well as the ability to inhibit or activate behaviors that will lead to a more positive outcome in the long term, even if this requires unpleasantness in the short term (Rothbart, 1989; Posner & Rothbart, 2000). In 2001, Rothbart et al. performed factor analysis on 15 temperament characteristics and described three broad dimensions: negative affectivity (similar to emotionality), extraversion/surgency (a combination of activity and sociability), and effortful control (Rothbart, Ahadi, Hershey, & Fisher, 2001). Effortful control is similar to conscientiousness (sometimes termed constraint) in the five-factor model of temperament/personality. Conscientiousness refers to a person's capacity

for behavioral and cognitive control, including responsibility, attentiveness, carefulness, persistence, orderliness, and planfulness (Caspi, Roberts, & Shiner, 2005).

Temperament and Anxiety Disorders

Numerous cross-sectional studies in children (Huey & Weisz, 1997; Ehrler, Evans, & McGhee, 1999; Muris, Winands, & Horselenberg, 2003) and adults (Brandes & Bienvenu, 2006; Bienvenu, Brown, et al., 2001; Bienvenu, Nestadt, et al., 2001; Bienvenu et al., 2004) document strong relationships between temperament traits like negative emotionality (neuroticism) and anxiety disorders. Nevertheless, it would be a mistake to assume that anxiety disorders are identical to extremes of temperament. Not only do these constructs differ but empirically they show incomplete overlap. For example, Fig. 14.1 shows the distribution of neuroticism and extraversion (factor T-scores) in persons with and without lifetime agoraphobia or GAD in the Hopkins Epidemiology of Personality Disorders study (Bienvenu et al., 2004). Those with agoraphobia tended to be high in neuroticism and low in extraversion, though a few persons with agoraphobia were neither, and many subjects who were high in neuroticism and low in extraversion did not have agoraphobia. Similarly, many, but not all, persons with GAD were high in neuroticism, and many persons who were high in neuroticism did not have GAD.

A potentially important question is *how* temperament traits relate to anxiety disorders. In the next four subsections, we will review the evidence for four ways in which temperament and illnesses such as anxiety disorders may relate: the vulnerability model, the complication model, the pathoplastic model, and the common cause model. These theoretical models are illustrated schematically in Fig. 14.2.

The Vulnerability Model

The vulnerability model avers that temperament traits predispose persons to develop psychopathology. Prospective studies of Thomas and Chess' (1977) nine temperamental factors revealed that extremes were positively correlated with psychopathology (Maziade et al., 1985; Maziade, Caron, Côté, Boutin, & Thivierge,

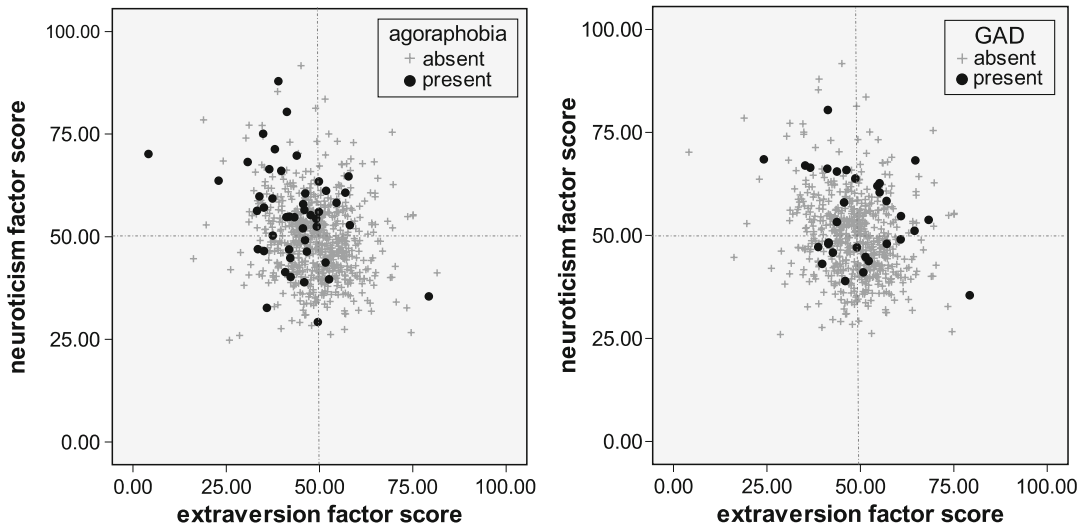

Fig. 14.1 Distribution of neuroticism and extraversion factor T-scores in persons with and without lifetime agoraphobia or generalized anxiety disorder (GAD) in the Hopkins Epidemiology of Personality Disorders Study (Bienvenu et al., 2004). Factor T-scores have a mean of 50 and a standard deviation of 10. Here, scores were standardized to external population norms (Costa & McCrae, 1992)

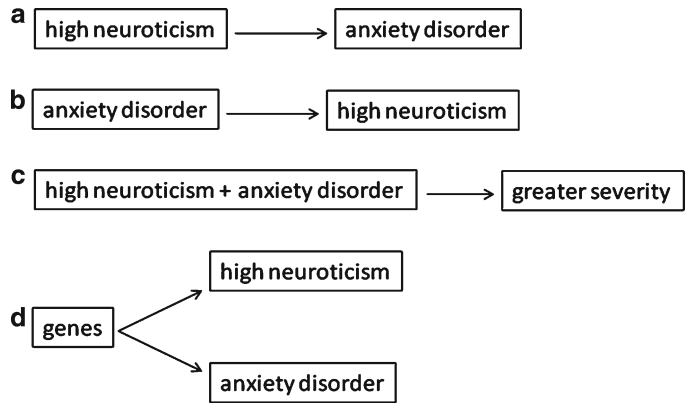

Fig. 14.2 Theoretical models of relationships between temperamental traits (e.g., neuroticism) and anxiety disorders. In model **a**, the vulnerability model, a person's temperamental traits predispose to the development of an anxiety disorder. In model **b**, the *complication* model, the onset of an anxiety disorder influences a person's temperament measure acutely (state-trait confounding) or causes a permanent change in temperament (scar effect). In model **c**, the *pathoplastic* model, temperamental traits modify the manifestation, severity, and/or course of an anxiety disorder. In model **d**, the *common cause* model, a genetic or environmental factor influences temperament as well as anxiety disorder development

1990; Guerin, Gottfried, & Thomas, 1997). Caspi, Henry, McGhee, Moffitt, and Silva (1995) noted that withdrawal at age three (presumably related to neuroticism and introversion) predicted internalizing symptoms in middle childhood and early adolescence. Using the same sample (the Dunedin birth cohort), Craske, Poulton, Tsao, and Plotkin (2001) showed that emotional reactivity at age three predicted panic disorder and agoraphobia at age 21 in males. Many studies have shown that early childhood behavioral inhibition is a predictor of later internalizing psychopathology (e.g., Biederman et al., 1993; Schwartz, Snidman, & Kagan, 1999), particularly social phobia (Biederman et al., 2001; Hirshfeld-Becker et al., 2007), though it is also worth noting that early childhood behavioral inhibition is negatively associated with disruptive behavior disorders (i.e., from the perspective of later psychopathology, behavioral inhibition appears to be both a risk factor for anxiety disorders and a protective factor for disruptive behavior disorders).

It is also worth noting that variation in psychiatric outcome might be explained by moderating factors, including environmental factors. For example, Maziade et al. (1985) found that, in children described as having difficult temperaments at age 7 years, psychiatric disorders at age 12 years were more frequent among those with dysfunctional families. Another potential moderating factor from the temperament realm is effortful control/conscientiousness. Empirical studies suggest that high negative affectivity is especially predictive of anxiety in the context of low effortful control. Lonigan, Vasey, Phillips, and Hazen (2004) noted that anxious children with high negative affectivity had attentional bias toward punishment cues during a timed task. When subjects were given sufficient time to shift attention, however, only the group with high negative affectivity and low effortful control gave prolonged attention to the punishment cues. The group with high negative affectivity and high effortful control did not differ from nonanxious children. The interaction between high negative affectivity and low effortful control on anxiety symptoms has been replicated in several recent studies (Lonigan & Vasey, 2009; Muris, 2006; Oldehinkel, Hartman, Ferdinand, Verhulst, & Ormel, 2007).

The Complication Model

The complication model involves acute (state-trait confounding) or chronic (scar) effects of psychopathology on temperament. Unfortunately, there are few empirical studies of this model, and such studies would optimally include premorbid

temperament assessments (i.e., before anxiety disorder onset). Nevertheless, the Children in the Community study provided evidence that childhood- or adolescent-onset anxiety disorders are associated with later onset of personality disorders from the "anxious" and "odd" clusters – by young adulthood (Kasen, Cohen, Skodol, Johnson, & Brook, 1999).

The Pathoplastic Model

In the pathoplastic model, temperament traits are observed to affect the manifestation, severity, and/or course of anxiety disorders. As in the complication model, such studies would optimally include premorbid temperament assessments. One study by Schwartz et al. (1999) found that, among 13-year olds with social anxiety, teens who were behaviorally inhibited as toddlers had significantly greater levels of impairment than teens who had not been inhibited. Interestingly, boys with high levels of inhibition appear to develop less severe and more easily treated conduct disorder (Kerr, Trembaly, Pagani, & Vitaro, 1997).

The Common Cause Model

In the common cause model, temperament and anxiety disorders are thought to have overlapping genetic and/or environmental causes. Many family studies provide evidence for such effects. For example, several studies show that adults with anxiety disorders like panic disorder are more likely to have children who are behaviorally inhibited; the reverse is also true, i.e., there is a higher prevalence of anxiety disorders among parents of children with behavioral inhibition than among parents of children who are not behaviorally inhibited (Biederman et al., 1990; Rosenbaum et al., 1991, 1992). Similarly, siblings and parents of children with anxiety have higher emotionality scores than normal subjects (Kelvin, Goodyer, & Altham, 1996; Masi et al., 2003), and preschoolers who are described as shy by their mothers and teachers have mothers with higher prevalences of social phobia than children who are not shy (Cooper & Eke, 1999). Interestingly, Mufson, Nomura, and Warner (2002) found that the offspring of parents with a single psychiatric disorder had significantly higher levels of adaptability and approachability than the offspring of parents with multiple comorbid diagnoses.

Twin studies provide evidence that genes that influence temperament also influence risk for anxiety disorders. For example, genes that influence negative emotionality/neuroticism also appear to influence some anxiety symptoms (Goldsmith & Lemery, 2000) and syndromes (Hettema, Neale, Myers, Prescott, & Kendler, 2006). Further genetic influences on neuroticism and extraversion appear to overlap completely with those that cause social phobia and agoraphobia (Bienvenu et al., 2007).

Notably, these models of temperament/anxiety disorder relations are not mutually exclusive, though existing studies, to our knowledge, do not attempt to integrate the models. For example, it may be that genes influence temperament directly and that temperament traits are true risk factors for psychopathology (as opposed to just markers of genetic risk). Results from longitudinal twin studies, however, suggest that this is not the case in the relationship between neuroticism and major depression (Kendler, Neale, Kessler, Heath, & Eaves, 1993; Fanous, Neale, Aggen, & Kendler, 2007). That is, neuroticism appears to be a marker of genetic risk for depression, but not a direct causal factor. In contrast results from these studies do suggest a direct causal effect of major depressive episodes on higher neuroticism scores, including both state-trait confounding and short-term scar effects (Kendler et al., 1993; Fanous et al., 2007).

Temperament Traits as Markers for Early Intervention

Anxiety disorders represent a significant burden to patients and their families. Ideally, it would be best to prevent anxiety disorders from developing, and attention to temperament may provide a

gateway for intervention. The Institute of Medicine defines prevention as being indicated, selective, or universal (Mrazek & Haggerty, 1994). Indicated prevention targets people who have already developed symptoms of illness, selective prevention aims to help people at risk for developing illness, and universal prevention is directed at an entire population regardless of whether or not an individual within the group is at risk. As we have reviewed, temperament traits appear to be risk factors, or at least markers of risk, for anxiety disorders. Thus, temperament measures may be useful in identifying at-risk youth for indicated or selective prevention programs.

Rapee's group in Sydney, Australia, designed a program to target behaviorally inhibited children through parental education in order to reduce parental anxiety as well as modeling, instructing, or promoting vicarious learning of avoidant behaviors. Those in the intervention group had a significant decrease in behavioral inhibition and anxiety disorders at 6- or 12-month follow-up (Rapee, 2002; Rapee, Kennedy, Ingram, Edwards, & Sweeney, 2005; Kennedy, Rapee, & Edwards, 2009). Overall, this success of this program indicates that there is a role for indicated or selective prevention based on measures of temperament. Further study may illuminate additional temperament targets and interventions that will have similar success.

Summary

Anxiety disorders are common and begin early in life. Temperament traits like high neuroticism (negative emotionality), introversion (low extraversion), and low effortful control (conscientiousness) are strongly associated with anxiety disorders. Though these aspects of mental life are not identical, temperament traits appear to be at least markers of risk for anxiety disorders. Thus, temperament is an excellent candidate to select at-risk youths for preventive interventions.

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Parenting and Child Anxiety Disorders

15

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What role does parenting play in the development, maintenance, and amelioration of child anxiety? In this chapter, we address this question by reviewing the current state of knowledge regarding the nature and direction of the relationship between parenting and child anxiety. Numerous theoretical models outline the role that various parenting practices may play in the development, maintenance, and amelioration of childhood anxiety. These models vary in terms of their precision and specificity. Traditional models of childhood anxiety focused primarily on broad parenting dimensions of acceptance and psychological control (see Gerlsma, Emmelkamp, & Arrindell, 1990; Masia & Morris, 1998; Rapee, 1997). However, these broad parenting dimensions have fallen out of favor in recent years as meta-analyses have demonstrated that these dimensions explain little of the variance in child anxiety (McLeod, Wood, & Weisz, 2007; van der Bruggen, Stams, & Bogels, 2008). Consequently, experts have issued calls for a move toward a more precise study of the parenting–child anxiety linkage (McLeod et al., 2007; Wood, McLeod, Sigman, Hwang, & Chu, 2003). In response, the field has adopted a more microscopic approach with greater theoretical specificity that focuses upon particular salient parenting practices that may influence children's acquisition of fear.

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An important emphasis of the movement toward greater theoretical specificity is the focus upon the mechanisms linking parenting and child anxiety. Increasingly, theories are specifying the underlying processes hypothesized to link parenting to child anxiety such as cognitive sets, attentional biases, and associative learning. Furthermore, key components of these theories are being evaluated using experimental designs. Indeed, studies that use experimental research paradigms are beginning to shed light upon the nature and direction of the parenting–child anxiety relation. Together, specifying and testing the underlying processes represents an important advance for the field that will have both theoretical and clinical implications.

In this chapter, we provide a general overview of the literature, describe emerging theories, and review experimental studies. General models positing a link between the broad parenting dimensions and variations in childhood anxiety have been more extensively examined than the emerging theories. The literature focused upon the more general models is therefore considered first by reviewing the most recent meta-analyses. We then consider the literature published since the meta-analyses. Our review of the recent literature focuses upon new theories of the parenting–anxiety link as well as the studies that have emerged in the past decade evaluating these refined contemporary models. We finish the chapter with a discussion of avenues for future research intended to build upon and extend the existing research.

D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_15, © Springer Science+Business Media, LLC 2011

Traditional Dimensions of Parenting Hypothesized to Affect Child Anxiety

Traditional models of childhood anxiety focused primarily on broad parenting dimensions of acceptance versus rejection and psychological granting of autonomy versus psychological control (see Gerlsma et al., 1990; Masia & Morris, 1998; Rapee, 1997; Wood et al., 2003). Both these broad categories represent bipolar parenting dimensions, with positive parenting practices (e.g., acceptance) at one end of the continuum and negative parenting practices (e.g., rejection) at the other end. The first parenting dimension, *rejection*, involves low levels of parental warmth, approval, and responsiveness (i.e., coldness, disapproval, and unresponsiveness) (e.g., Clark & Ladd, 2000; Maccoby, 1992). The second parenting category, *control*, involves excessive parental regulation of children's activities and routines, encouragement of children's dependence on parents, and instruction to children on how to think or feel (e.g., Barber, 1996; Steinberg, Elmer, & Mounts, 1989). Theoretical models posit that variations in these broad parenting dimensions are at least partially responsible for variations in childhood anxiety (DiBartolo & Helt, 2007; Fox, Henderson, Marshall, Nichols, & Ghera, 2005; Hudson & Rapee, 2001; Rapee, 2001; Wood, 2006a). The terms *rejection* and *control* will be used throughout the rest of this paper to refer to these broad parenting categories.

Estimating the Strength of the General Relationship Between Parenting and Child Anxiety

The bulk of the parenting and child anxiety research has focused upon the broad dimensions of parental rejection and control (see Ballash, Leyfer, Buckley, & Woodruff-Borden, 2006; Dibartolo & Helt, 2007; McLeod et al., 2007; Wood et al., 2003). Recent comprehensive literature reviews have synthesized the literature and assessed the strength of the association between parenting and childhood anxiety. We therefore start our review by summarizing the findings from two recent meta-analytic reviews (McLeod et al., 2007; van der Bruggen et al., 2008).

A recent meta-analysis synthesized the available literature, focusing upon the relation between the broad parenting dimensions and variations in childhood anxiety (McLeod et al., 2007). In all, 47 studies published from 1960 to 2002 were included in the meta-analysis. The findings indicated that parenting accounted for only 4% of the variance in child anxiety ($d=0.43$), which meets criteria for a small effect (Cohen, 1988). Parental control evidenced a slightly stronger relation with child anxiety ($d=0.52$) compared to parental rejection ($d=0.41$). Further, moderator analyses revealed that the strength of the association differed significantly across parental sub-dimensions – the association ranged from $d=0.12$ (parental warmth) representing a small effect, to $d=0.93$ (autonomy granting) representing a large effect. These findings suggest that efforts to tease apart the traditional parenting dimensions of parental rejection and control may benefit the field. Moderator analyses also revealed that three methodological factors explained some variability of the effects, with somewhat stronger effects emerging for studies comparing diagnosed and non-diagnosed youth, for studies using observers to report upon parenting, and for studies with higher quality measurement of parenting practices (i.e., observation methods). Finally, this review highlighted an important limitation in the field. That is, the direction of effects linking parenting to child anxiety had not been established since most studies utilized cross-sectional designs and descriptive methods.

Another recent meta-analysis extended these findings by focusing upon the strength of the association between child and parent anxiety and parental control (van der Bruggen et al., 2008). The review identified 23 studies published from 1989 to 2006 that evaluated the relation between parental anxiety and parental control ($N=11$) or the relation between child anxiety and parental control ($N=17$). The findings indicated that child anxiety and parental control were moderately associated ($d=0.58$), which is consistent with

past reviews (see McLeod et al., 2007). However, there was not a significant association between parental anxiety and parental control ($d = 0.08$). These findings suggest that parental anxiety may not translate into higher levels of control, despite conventional wisdom and recent models of anxiogenesis (e.g., Rapee, 2001).

The meta-analytic findings suggest that parenting explains little of the variance in child anxiety. These findings challenge the traditional models that assert parenting plays a pivotal role in the development, maintenance, and amelioration of child anxiety (e.g., Parker, 1983). However, some simply state these findings suggest that the field needs to move beyond the traditional, poorly specified theoretical models. Proponents of the latter perspective argue that more precisely defined models that specify the putative mechanisms (e.g., modeling; opportunities for extinction; self-appraisal and self-efficacy) underlying the relationship between particular types of parenting and child anxiety will help advance the field (Fisak & Grills-Taquechel, 2007; Fox et al., 2005; Hadwin, Garner, & Perez-Olivas, 2006; Rapee, 2001; Wood, McLeod, Piacentini, & Sigman, 2009).

In recent years, calls for greater theoretical specificity and sharper definitions and measurement of parenting have increased. In the following section, we review efforts to address these calls. We start by reviewing new theories focused upon specific parenting behaviors posited to play a pivotal role in the development, maintenance, and amelioration of child anxiety. Then, we examine recent findings from longitudinal and experimental studies that have attempted to test the connection between these particular parenting practices and patterns of childhood anxiety.

Updating the Literature Review

As noted, calls for researchers to address the gaps in the field have recently increased. Wood and colleagues (2003) called for (a) further specification of theories and (b) clarification of the direction of effects linking parenting to child anxiety. To gauge efforts to heed these calls, we conducted a literature search to identify studies that were not included in the most recent comprehensive meta-analysis (i.e., McLeod et al., 2007). The search covered from April 2004 up to February 2008 and included the following 12 anxiety-related key terms used by McLeod and colleagues (2007): *Internaliz-*, *Anxi-*, *Fear-*, *Obsessive, Compulsive, OCD, Panic, Phobi-*, *Worr-*, *Inhibit-*, *Shy-*, and *Somat-*. These key terms were crossed with the following parenting-related key terms: *Father-*, *Maternal, Mother-*, *Parent-*, *Paternal, Rearing,* and *Socializ-*. Relevant literature reviews (e.g., Ballash et al., 2006; Dibartolo & Helt, 2007; Field, Cartwright-Hatton, Reynolds, & Creswell, 2008; Fisak & Grills-Taquechel, 2007; Ginsburg, Siqueland, Masia-Warner, & Hedtke, 2004; Hadwin et al., 2006; Tiwari et al., 2008; van der Bruggen et al., 2008) were used to initiate reference trails. We included studies in our review that met the following criteria: (1) The study included a measure of the parenting of one parent in relation to a target child, or separate measures of both parents in relation to the target child; (2) The study either included a measure of anxiety (e.g., self-report) or the child participants were diagnosed with an anxiety disorder (e.g., separation anxiety disorder); (3) The association between parenting and childhood anxiety was tested statistically (e.g., correlation); and (4) The reported mean age of the child participants was below 19 years.

These steps produced a pool of 25 studies (14 cross-sectional, 1 longitudinal, 6 experimental, and 4 interventions) that met criteria. A review of these studies indicates that researchers have made notable efforts to address key gaps in the field. Researchers have adopted a more microscopic focus on the parenting practices that influence children's acquisition of fear. In particular, two parenting behaviors, parental intrusiveness and parental modeling of anxious behaviors, have gained increased theoretical and empirical attention in recent years. Next, we define these parenting behaviors and specify the theoretical models linking these behaviors to the development, maintenance, and amelioration of child anxiety. Then we review the recent empirical literature that has addressed gaps in the field by utilizing

longitudinal and experimental designs to help clarify the direction of effects linking parenting and child anxiety.

Contemporary Theoretical Models: Specific Parenting Dimensions

In recent years, researchers have moved beyond the traditional definitions of parenting to more specific parenting behaviors. This work has primarily focused upon parental intrusiveness and parental modeling of anxious behavior. This level of specificity represents an important shift for the field.

Parental Intrusiveness

Parental intrusiveness is considered a subdimension of parental control (Ispa et al., 2004; McLeod et al., 2007). Parents who act intrusively tend to take over tasks that children are (or could be) doing independently and impose an immature level of functioning on their children (e.g., Carlson & Harwood, 2003; Egeland, Pianta, & O'Brien, 1993; Ispa et al., 2004; Wood, 2006a). When defining parental intrusiveness, it is important to consider both the parent's behavior and the developmental level of the child since parent–child interactions that are commonplace for certain age groups can become atypical later in childhood. For example, among school-aged children (i.e., 6–11-year olds), parental intrusiveness can manifest in at least three domains: unnecessary assistance with children's activities and daily routines (e.g., scholastic tasks, dressing), infantilizing behavior (e.g., using baby words, excessive affection), and invasions of privacy (e.g., when parents open doors without knocking) (Hudson & Rapee, 2001; Wood, 2006a; Wood, Kiff, Jacobs, Ifekwunigwe, & Piacentini, 2007). It is also important to distinguish intrusive parental behavior from helpful responsiveness. Responsiveness involves providing support to children who evidently need help in a task – a positive parental behavior (e.g., Maccoby, 1992), whereas intrusiveness involves taking over tasks in which children could function independently. Intrusiveness therefore needs to be defined in relation to appropriate expectations about a child's capabilities.

Parental intrusiveness may affect the development and maintenance of childhood anxiety by influencing children's self-efficacy and perceived control. Intrusive parental behavior can affect children's self-efficacy (i.e., perceptions of agency and competence with regard to specific tasks; Bandura, 1997). Research has consistently demonstrated that an association between self-efficacy and anxiety regulation exists (e.g., Muris, 2002) and this linkage is explicitly hypothesized and explained in Bandura's social cognitive theory (e.g., Bandura, 1997). Similarly, children's perceived control (i.e., perceptions that one can directly influence opportunities for positive and negative reinforcement) is another process that can be affected by intrusiveness (Chorpita, 2001; Chorpita & Barlow, 1998). It is hypothesized that parents may contribute to the development of cognitive vulnerabilities – undermining self-efficacy and/or lowering perceived control – and, in turn, elevating a child's risk for anxiety when they routinely take over tasks that the child could do for himself/herself (i.e., act intrusively; Chorpita, 2001; Krohne & Hock, 1991). Thus, intrusive parental behavior is hypothesized to contribute to the development of cognitive vulnerabilities that may affect the development and maintenance of child anxiety.

Parental intrusiveness may also affect childhood anxiety by influencing children's opportunities for extinction particularly for children with a high baseline level of fears or a slow extinction curve (e.g., Rubin, Hastings, Stewart, Henderson, & Chen, 1997; Wood et al., 2009). Extinction plays a key role in the amelioration of fear and anxiety wherein repeated exposure to a feared (but benign) stimulus leads to a reduction in the strength of the fear response (Rachman, 1977). Parents who act intrusively are posited to interfere with extinction by preventing the child from actually confronting feared stimuli or by enabling the child to escape anxiety when the naturally occurring exposure is initiated (Fox et al., 2005; Rapee, 2001). For example, the parents of a child

who freezes when he/she is faced with unfamiliar peers in social situations (a common symptom of social anxiety disorder in middle childhood) like church might rub the child's shoulders, hold his/her hand, and remain very close to him/her in an attempt to reduce the child's negative affect. Though potentially effective as a short-term emotion regulation strategy, such parental behavior may unintentionally prevent the child's fear from extinguishing by keeping the child from experiencing the situation independently (and learning there is nothing to be afraid of). Instead, this response may induce dependence on the parents for external emotion regulation (e.g., "I only feel comfortable around new kids when mom and dad are there to calm me down"). Conversely, parents who exhibit low intrusiveness and grant autonomy (i.e., encouraging the child to interact with peers; refraining from physical or verbal comforting) may promote extinction. Though a high level of intrusiveness may contribute to the *maintenance* of a child anxiety disorder, a corollary hypothesis is that reducing intrusiveness may contribute to the amelioration of children's anxiety symptoms, making intrusiveness a potential change mechanism in children's anxiety trajectories (Wood, Piacentini, Southam-Gerow, Chu, & Sigman, 2006).

Parental Modeling of Anxious Behavior

In recent years, research has increasingly focused upon parental modeling of anxious behavior. Parental modeling of anxious behavior entails describing problems to children as irresolvable or dangerous, encouraging (rewarding) children to view problems in a catastrophic manner, and extinguishing via punishment children's expressions of coping thoughts and problem-solving strategies (Capps & Ochs, 1995; Whaley, Pinto, & Sigman, 1999). Modeling is neither necessary nor sufficient to the development of anxiety. However, modeling may increase risk for fear acquisition or interact with other factors to increase risk for the development of anxiety (Fisak & Grills-Taquechel, 2007). Children predisposed to developing an anxiety disorder may be particularly susceptible to environmental influences, such as modeling (Rapee, 2002). For example, a shy child who consistently watches his/her anxious parent avoid social events may be less likely to initiate play-dates and attend social events himself/herself. Children of observably anxious parents may come to believe that there is no way of coping effectively with problems and are not likely to develop strategies that can help reduce fear and anxiety (Barrett, Duffy, Dadds, & Rapee, 1996; Capps & Ochs, 1995; Whaley et al., 1999).

Two prominent theories are used to explain the causal relation between parental modeling and child anxiety: (a) Bandura's social learning theory (Bandura, 1997) and (b) Rachman's theory of the pathways to anxiety (Rachman, 1977). The social learning theory posits that children acquire fears through observation and replication of parental anxious behaviors (e.g., visual signs of anxiety, verbal expression of anxiety, or behavioral avoidance). Similarly, Rachman's theory suggests that vicarious acquisition represents one of three pathways through which child anxiety may develop (the other two being conditioning and transmission of information). The three-pathway model was an extension of the prevailing theory at the time – fear acquisition through conditioning. Rachman added vicarious acquisition and transmission of information due to evidence that conditioning alone does not provide a comprehensive explanation of fear development. Such evidence included the fact that fears can emerge suddenly or gradually, differences exist in susceptibility to acquisition, fears can be acquired indirectly (even if the person has never been exposed to the stimuli), and some stimuli are more commonly feared than others. Rachman associates more mild and common fears with indirect pathways (e.g., vicarious acquisition) and intense fears with direct acquisition (e.g., conditioning). Together, Bandura and Rachman's theories posit that modeling promotes the development of child anxiety. Specifically, modeling serves to deliver threat information regarding specific stimuli that influence the creation of cognitive biases and promote avoidance of the stimuli (Field, 2006). Thus, parental modeling

is hypothesized to generate cognitive and attentional biases that help contribute to the development, maintenance, and amelioration of child anxiety.

In sum, researchers have recently begun to move beyond the traditional models of parenting. Increased attention upon parental intrusiveness and parental modeling of anxious behavior represents a notable advance for the field as these theories carefully specify how parenting contributes to the development, maintenance, and amelioration of child anxiety. In the following sections, we review the empirical studies completed in recent years that have helped advance understanding of the relation between parenting and child anxiety.

Recent Studies of Parenting and Child Anxiety

Cross-Sectional Studies

In this section, we focus upon the 14 studies completed since 2004 that utilized a cross-sectional design. An in-depth review of these studies is beyond the scope of this chapter since many findings replicate those reported in the recent meta-analyses (McLeod et al., 2007; van der Bruggen et al., 2008). However, we highlight several important trends in the literature.

A few studies have examined the relation between parenting and child anxiety among different ethnic and cultural groups. In the past, most studies have primarily utilized Caucasian samples, which have limited the ability to generalize findings to different ethnic and/or cultural groups (Wood et al., 2003). Two recent studies addressed this limitation. Luis, Varela, and Moore (2008) examined whether parental control and rejection were associated with child anxiety in European American, Mexican American, and Mexican families. Using observational methods to assess parental behaviors, Luis and colleagues found that high parental control was associated with child anxiety in the European American and Mexican American families, but not the Mexican families. These findings suggest that contextual and cultural factors may influence the nature and strength of the relation between parenting and child anxiety. In another study, Muris et al. (2006) investigated the relation between perceived parental behavior and child anxiety in a large South African sample ($N=701$) of children and adolescents from black, white, and mixed racial backgrounds. Overall, the relations between perceived parental behavior and child anxiety across the ethnic/cultural groups were similar, except that the relation between anxious rearing and child anxiety was stronger for Caucasian youth ($r=0.37$) than for black youth ($r=0.19$). Together, these studies raise important questions and suggest that cultural factors may influence the strength of the association between parenting and child anxiety. Clearly, more research among different ethnic and cultural groups is needed.

A handful of studies have moved toward greater theoretical specificity. One example of this trend is a shift toward examining the relation between parenting behaviors and specific clusters of anxiety symptoms. To date, two studies have evaluated the relation between perceived parenting and symptoms of generalized anxiety disorder (see Brown & Whiteside, 2008; Hale, Engels, & Meeus, 2005). Both studies found that perceived parental rejection evidenced a stronger relation with symptoms of generalized anxiety disorder than did parental control, which runs counter to past meta-analytic findings (see McLeod et al., 2007). These findings suggest that specific parental behaviors may be differentially associated with specific anxiety disorders (e.g., generalized anxiety disorder versus social anxiety or specific phobia). However, these findings require replication since youth reported on both the parenting and symptom measures.

Two studies have investigated the specific linkage between parental intrusiveness and children's separation anxiety (as compared to other types of anxiety) (Wood, 2006a; Wood et al., 2007). In a clinical sample of children with various kinds of anxiety disorders, a measure of parental intrusiveness based upon a composite of child, parent, and observer ratings was linked specifically with separation anxiety. These ratings were not linked to generalized anxiety, social anxiety, or physical symptoms (Wood, 2006a).

However, there was relatively little evidence that child- and parent-reported intrusiveness was differentially linked with child- and parent-reported separation anxiety as compared to other types of anxiety in a typically developing elementary school sample (Wood et al., 2007). All told, the field is moving toward testing the specificity of linkages of particular types of parenting with particular anxiety syndromes. The mixed evidence thus far hints at the possibility that more refinements of methodology could reveal more robust evidence of patterns of differential associations.

Some studies have also begun to investigate whether specific cognitive factors (e.g., threat interpretations, cognitive distortions) mediate the relation between parenting and child anxiety. Studies have found support for this association (Creswell & O'Connor, 2006; Gallagher & Cartwright-Hatton, 2008). Creswell and O'Connor (2006) found a positive relation between the number of threat interpretations made by mothers and children when presented with an ambiguous task, and this effect was partially mediated via the mother's expectations for how her child would interpret the task. Gallagher and Cartwright-Hatton (2008) found that a negative cognitive style (e.g., cognitive distortions) mediated the relation between parental behavior and child anxiety. Together these findings provide evidence that specific cognitive factors may mediate the relation between parenting and child anxiety.

Experimental and Longitudinal Tests of Contemporary Theoretical Models

Until recently, the literature was limited in what it could tell us about the direction of effects linking parenting and childhood anxiety (McLeod et al., 2007; Wood et al., 2003). No study had (a) tested parental behavior as a *causal* influence on childhood anxiety, (b) ruled out the possibility that childhood anxiety causally affects parenting behavior, or (c) ruled out that a third variable (i.e., common genes) affects both parenting behavior and childhood anxiety systematically (or that there is an additive or multiplicative combination of more than one of these possibilities). Thus, the causal mechanisms that produce the linkage between parental behavior and child anxiety were not established.

Given that current theoretical models posit that parenting plays a role in the development, maintenance, and amelioration of childhood anxiety, the field needs to employ methodologies that can help clarify what role, if any, parenting behaviors play in *causing*, *sustaining*, or *reducing* childhood anxiety. Two types of studies are needed to address the issue of causality. First, longitudinal studies that utilize repeated measures of parenting behavior and childhood anxiety at theoretically meaningful time intervals can test for the sequencing order implicit in the causal models noted above. Second, experimental methods can be employed to directly evaluate the effects of manipulating parenting behavior on childhood anxiety, and vice versa. In the following section, we review recent studies that fall into both categories.

Our literature review identified one longitudinal study conducted since 2004 that addresses the parenting–anxiety linkage. Feng, Shaw, and Silk (2008) examined the developmental trajectories of anxiety symptoms in 290 boys aged from 2 to 10 years. A group-based analysis revealed that the development of anxiety symptoms could be categorized into four distinct trajectories based upon yearly ratings of anxiety symptoms: low, low increasing, high declining, and high increasing. Parenting was measured with an observational paradigm. Temperament (i.e., a largely biological factor) accounted for initial levels of anxiety, whereas higher early maternal control (i.e., an environmental factor) was associated with the low increasing and high increasing developmental trajectories. Notably, the high increasing group had the greatest chance of meeting diagnostic criteria for an anxiety disorder between age 9 and 11 years. These findings support developmental psychopathology models that posit there are multiple pathways through which children develop anxiety symptoms. However, they also support the hypothesis that parenting may play a role in the development of child anxiety, since parenting was related to increases in child anxiety over time. Lastly, from a clinical standpoint, these

findings suggest that early efforts to decrease parental over-control may play an important role in preventing the onset of anxiety disorders.

In a recent study, de Wilde and Rapee (2008) used an experimental design to examine the influence of maternal controlling behaviors upon child-state anxiety. The mothers of 26 children aged 7–13 years were randomly assigned to either an overly controlling or minimally controlling condition toward their child while he/she was preparing a speech. Children whose mothers acted in an overly controlling manner reported experiencing more state anxiety compared to children whose mothers acted in a minimally controlling manner. This pilot study is one of the first to suggest that parental behaviors exert a causal influence upon child anxiety.

A growing body of literature is using a social referencing paradigm to examine the early influences of parental anxious modeling on infants. Social referencing refers to an infant's use of cues from parents to interpret unfamiliar people and events (Feinman, 1992). Infants use their interpretation of their parent's emotional response as a guide to their own behavior. Social referencing processes have been evaluated using semi-naturalistic (see Murray et al., 2007) and experimental designs (see de Rosnay, Cooper, Tsigaras, & Murray, 2006), with findings consistently revealing infants mimicking their mother's affective response to unfamiliar stimuli. It is speculated that the parent's behavior and emotional response is not only mimicked in the moment, but the child may also develop schemas about different aspects of the environment based on continuous and consistent observation of parental fearful behaviors. For example, an infant who regularly observes a parent respond fearfully to strangers may develop a generalized schema about all strangers being harmful. These schemas highlight the potential early environmental influences (e.g., social processes in infancy) on the later development of anxiety disorders (de Rosnay et al., 2006; Egliston & Rapee, 2007). Additionally, children who are exposed to signs of parental anxiety when around unfamiliar stimuli adopt distinctive patterns of interpersonal responsiveness, such that they respond similarly to their parents in interpersonal situations (Murray et al., 2007). This line of research suggests that parental modeling of anxious behavior may begin to influence a child's cognitive schemas and behaviors at a very young age.

We now turn to another area of experimental research that has systematically evaluated the theories linking parental modeling to child anxiety. In general, these studies entail (a) obtaining a baseline rating of the child's emotional response to a novel stimulus, (b) manipulating the child's exposure to maternal affective responses or verbal information linked to the stimulus (e.g., negative, positive, neutral), (c) rating the child's subsequent emotional response to that stimulus, and (d) re-evaluating the child's emotional response in a short-term follow-up. Despite variations in the designs, findings consistently suggested that mother's responses toward the novel stimuli or verbal information regarding the stimuli subsequently predicted the child's fear and behavior.

Egliston and Rapee (2007) found that the infants whose mothers modeled positive affect showed an increase in positive affect toward the stimulus from baseline, suggesting that maternal positive response interferes with fear learning that was subsequently modeled by the experimenter. Findings are consistent with the social referencing framework, such that infants as young as 12 months use affective signals of familiar adults to regulate their own behavior. One caveat to these findings is that there was only an effect for positive and not negative modeling. However, the fact that negative affect was modeled by an experimenter rather than a familiar adult may have reduced the magnitude of the effect.

Dubi, Rapee, Emerton, & Schniering (2008) addressed this limitation with a similar design, such that mothers were randomly assigned to respond positively or negatively to novel stimuli. Consistent with other studies, results revealed that children whose mothers reacted negatively were more fearful and avoidant toward the stimuli. However, contrary to previous findings in which fearful modeling effects persisted (Gerull & Rapee, 2002) or effects persisted for positive modeling (Egliston & Rapee, 2007), the effects of the conditioned fear response were short lived. Dubi and colleagues suggest that learning through

observation is a weak pathway to develop fear relative to verbal information or conditioning. Indeed, the authors concluded that modeling may be more effective in teaching children true dangers about the world than irrational fears. The authors also suggest that the findings may have been confounded by verbal information provided by the mother rather than indirect observation.

To assess the effects of information on fear response, Field, Ball, Kawycz, and Moore (2007) developed a computerized experimental paradigm using unfamiliar animals. Based upon the general experimental model described above for testing fear acquisition, novel animals were presented on a computer screen accompanied by positive, negative, or no information. The child's fear of the animals was then assessed and compared to their baseline ratings. Field and colleagues found that punitive parenting style moderated the relation between threat information and children's self-reported fear beliefs about novel stimuli. This is consistent with Field and colleague's (2008) theory of the intergenerational transmission of anxiety in which anxious parents provide the child with an unusual set of learning experiences, such as exaggerating threat aspects of information. Unlike previously discussed studies, however, positive information did not function as a moderator. Field and colleagues suggest that threat information contributes to anxiety because it primes children to pay particular attention to it when encountering novel stimuli. Field and Lawson (2008) used the same paradigm to examine the accuracy of the associative strength between the animals and outcome based on verbal information presented (e.g., fearful, positive, neutral). They found that the associative strength was highest when associative learning was consistent with verbal information, required the longest learning time without any information, and was overestimated when associative learning trials were inconsistent with verbal information. These results provide preliminary evidence that specific parenting behaviors interact with one of Rachman's (1977) pathways to fear (verbal information) and suggest that specific learning processes may mediate the relation between parenting and child anxiety.

These experimental studies represent a significant step forward for the field. Most notably, these studies test causal pathways that may contribute to the development and maintenance of child anxiety. One design strength worth noting is the inclusion of a condition in which children were exposed to the stimulus alone without parental manipulation (Egliston & Rapee, 2007). Findings demonstrated that modeling influences a child's emotional response beyond mere exposure to the stimulus, implying that exposure plus modeling may produce stronger effects in intervention than exposure alone. Given that positive modeling and information promoted positive outcomes that interfered with fear development, such techniques may be effective targets for prevention and intervention. A limitation noted by nearly all authors includes a controlled lab setting, which may not simulate a child's natural environment. Future research should therefore focus on controlled experiments in natural settings. Furthermore, the retention of modeling effects beyond the experimental session needs to be further explored. Although follow-up observations were conducted, they were within the confines of the experimental session. One study also hypothesized that toddlers who had access to touch the object may have learned by direct experience that object is harmless (Dubi et al., 2008). This represents a methodological problem in social referencing literature, such that physical touch has been inconsistently regulated across studies. Future research should compare social referencing to direct physical contact as a source of learning to tease apart these two different mechanisms. Several other questions remain unanswered: Is the mother the only influential model? How important is developmental level in the acquisition of fear through modeling? Is modeling truly accounting for the variation in development of anxiety disorders or does it more accurately explain the transmission of brief and specific threat from mother to child?

A final issue that warrants further attention is the interaction between temperament and environmental factors. Dubi and colleagues (2007) found that a behaviorally inhibited temperament did not influence instrumental learning

of approach/avoidance behaviors. This suggests that the interaction between temperament and environmental factors (i.e., modeling) may not be as pronounced as previously hypothesized. However, the authors did note a restricted range of temperaments, such that there were few behaviorally inhibited children, which may have accounted for these findings. Conversely, de Rosnay and colleagues (2006) found that temperamental fearfulness moderated the effect of observed maternal anxiety on avoidance behavior, such that high-fear toddlers were affected more by mothers exhibiting socially anxious behaviors than low-fear toddlers, and only high-fear children were more avoidant in the maternal socially anxious condition than the non-anxious one. This is especially important to explore given that these experimental studies consisted of non-clinical samples. Because anxiety moderates the effect of verbal threat information on avoidance behaviors and attentional biases (Field, 2006), results may differ for children with clinical levels of anxiety or children who are temperamentally predisposed to anxiety (Field & Lawson, 2008).

Testing Models with Intervention Studies

Intervention designs can help clarify the causal relation between parenting and child anxiety as well as help elucidate the change processes in treatment that account for observed outcomes. Although randomized controlled trials (RCTs) cannot provide information about whether parenting behaviors (e.g., intrusiveness) initially cause child anxiety problems, they do represent a rigorous method to test if these parenting practices *maintain* (or, if altered, *ameliorate*) children's anxieties (cf. Cowan & Cowan, 2002). Several studies have experimentally documented an influence of parenting practices on changes in children's internalizing or externalizing behavior using intervention or prevention designs (Brody et al., 2006; Tein, Sandler, MacKinnon, & Wolchik, 2004); a small number have also recently done so for childhood anxiety (Silverman, Kurtines, Jaccard, & Pina, 2009; Wood et al., 2009).

Since interventions for child anxiety disorders are reviewed elsewhere in this book, we consider this literature only briefly and then explore how interventions have been used to evaluate the effects of parenting practices on child anxiety disorders. A typical child-focused cognitive behavioral (CCBT) program involves anxiety management skills training (e.g., psychoeducation, relaxation, cognitive skills) and exposure interventions. CCBT programs have been found to reduce child anxiety at immediate post-treatment relative to wait list control groups (Kendall, 1994; Kendall, Flannery-Schroeder, Panichelli-Mindel, & Southam-Gerow, 1997). Moreover, studies have found that the benefits of CCBT programs are maintained at 1-year (e.g., Flannery-Schroeder, Choudary, & Kendall, 2005; Kendall, 1994; Kendall et al., 1997), 3.35-year (Kendall & Southam-Gerow, 1996) and 7-year (Kendall, Safford, Flannery-Schroeder, & Webb, 2004) follow-ups.

Family-focused CBT (FCBT) programs can be used to examine the effect of manipulating parenting on child anxiety. These programs have been found to reduce child anxiety at immediate post-treatment and 1-year and longer follow-up periods when compared to wait list control groups (e.g., Barrett, 1998; Barrett et al., 1996). Moreover, two studies have compared the relative efficacy of individually administered (as compared to group therapy) FCBT and CCBT programs (Barrett et al., 1996, Wood et al., 2006, 2009). Both trials found that youths in FCBT had lower rates of anxiety disorders and fewer parent-reported anxiety symptoms at post-treatment and follow-up than youths in CCBT. This difference did not hold at a 6-year follow-up (Barrett, Duffy, Dadds, & Rapee, 2001). Furthermore, the majority of FCBT programs have been conducted in group-therapy format and have not differed in treatment effects from CCBT (Barmish & Kendall, 2005). It has been suggested that parental involvement in CBT may be particularly important for child outcomes under specific conditions (Barmish & Kendall, 2005; Kendall & Ollendick, 2004). One relevant parameter includes the extent to which interventions target parental behavior that maintains

child anxiety (Barmish & Kendall, 2005; Barrett et al., 1996).

Silverman and colleagues (2009) used an intervention design to evaluate the directionality of effects linking parenting and child anxiety. A total of 119 youth diagnosed with anxiety disorders were randomly assigned to CCBT with minimal parent involvement or CCBT with active parent involvement (CBT/P). The CBT/P condition was designed to target (a) positive and negative parental behaviors, (b) parent–child conflict, and (c) parental anxiety. A few important findings relevant to understanding the nature and direction of the parenting–child anxiety linkage emerged from this study.

First, there were no significant differences between the CBT and CBT/P at post-treatment suggesting that parental involvement in treatment did not have a notable impact upon youth anxiety outcomes. Second, the findings suggest that there may be a reciprocal relation between parenting and child anxiety. In fact, the findings suggest that child anxiety may influence parental behavior. At post-treatment, there were no differences between the CCBT and CBT/P conditions at the level of parent–child conflict, positive and negative parental behaviors, or parental anxiety. Thus, both child-focused and parent-focused interventions led to similar reductions in parent–child conflict, improvements in parenting behaviors, and reductions in parental anxiety. These findings therefore challenge the traditional assumption that parenting causally influences child anxiety.

Altogether, these findings have important clinical implications. Several large clinical trials have demonstrated that parental involvement in CBT has not produced a meaningful impact upon youth anxiety outcomes. Moreover, Silverman and colleagues (2009) demonstrated that key parent-level factors hypothesized to be causally related to the maintenance of child anxiety (e.g., level of parent–child conflict, specific parental behavior) changed in the CCBT condition. This study therefore does not support the incremental validity of adding family involvement to CBT for child anxiety. However, although these findings indicate that adding family involvement does not produce superior results, there may be specific circumstances in which FCBT may enhance clinical outcomes.

Wood and colleagues (2006a, b, 2009) randomly assigned 35 children (6–13-years old) to 12–16 sessions of FCBT or CCBT and followed up with them one year after treatment was completed. FCBT focused specifically on reducing parental intrusiveness and increasing autonomy granting, and incorporated traditional CCBT elements delivered in the family context. Blinded diagnostician ratings as well as parent reports of anxiety favored FCBT over CCBT at both post-treatment and follow-up, as did composite ratings of intrusiveness using a multifaceted measure described above in the discussion of Wood (2006a). Child ratings of anxiety symptoms did not differ between groups.

Reductions in parental intrusiveness at post-intervention played a mediating role linking the family intervention (FCBT) with superior child anxiety outcomes at 1-year follow-up. Interestingly, children's age group moderated the association between intrusiveness and anxiety, suggesting that developmental processes influence the relation between parental behavior and child anxiety trajectories. Early adolescents (10–13-year olds) experienced more improvement in anxiety at the 1-year follow-up if their parents had decreased in intrusiveness at post-intervention. However, the same pattern was not observed for younger children (6–9-year olds). To date, few models of the influence of parenting behavior on children's regulation of anxiety have proposed that children of different developmental stages might react differently to specific parenting behaviors. Yet these findings suggest that a child's developmental level may play a role in determining the impact (for good or ill) of specific parental behaviors on children's well-being.

Social cognitive theory provides an explanation of these findings that takes into account the observed developmental differences. This theory posits that individuals have an ongoing need for mastery experiences throughout development to promote self-efficacy and potentiate optimal functioning (Bandura, 1997). Often there is a confluence of the need for mastery experiences

and the particular objectives or tasks requiring mastery that arise at specific stages of development (some of which are culturally defined and others intrinsically motivated). For example, Bandura (1997) notes the developmental advantages to infants of having parents who facilitate mastery experiences in interactions with the physical environment (e.g., helping infants experience cause-and-effect relations as they touch objects to promote a sense of control). It is plausible that the transition to early adolescence is a developmental period marked by a confluence between the child's general need for mastery experiences and a culturally defined need for children to achieve autonomy from their parents. Such a confluence might explain the beneficial effect of reduced parental intrusiveness (and corresponding increased autonomy) for adolescent (but not child) anxiety problems that were found in this study.

According to this formulation, early adolescents may have a particular need for mastery experiences in self-help tasks which, if absent, would reduce their sense of autonomy. Steinberg (1990) has written, "The second decade of a child's life – and, in particular, the first few years of this decade – is a critical time for the realignment and redefinition of family ties" (p. 255). He and other investigators view increased autonomy in adolescence as a catalyst that promotes positive growth in the cognitive, emotional, and social spheres, with parents playing a key role in this transformation by encouraging independence of functioning and volitional behavior (Allen, Hauser, Bell, & O'Connor, 1994; Soenens et al., 2007). The areas emphasized in the intrusiveness measure used in the Wood and colleagues (2009) study (e.g., daily routines and private self-help activities) may be particularly salient domains for autonomous functioning from an early adolescent's perspective. Choices that parents make about how they respond to the capacities of pre-teens and early teens for independent functioning in this domain naturally set limits on how autonomous their children are able to act and, by extension, how efficacious they feel.

Social comparison processes may make independence in private self-help skills particularly salient to early adolescents as compared to younger children. In terms of base rates, it is atypical to receive parental help with activities such as bathing and dressing for early adolescents, but more typical for younger children (Wood et al., 2007). A common reason for pre-adolescent and early adolescent teasing is the victim acting "babyish" and immature (Fine, 1992); variants of such teases used in mass media portrayals of young adolescents include the expression, "Does your mommy help you with that?" Teases are often a guide to expected behavior (cf. Keltner, Capps, Kring, Young, & Heerey, 2001); early adolescents who are still receiving frequent unneeded assistance from parents in activities of daily living may feel a sense of deviance from these expectations, particularly given the low base rates of such assistance in this age group. Through the process of social comparison, deviance from social norms is often linked with negative self-perceptions and anxiety (e.g., Hedley & Young, 2006; Irons & Gilbert, 2005). It may be that an intervention like FCBT that reverses this deviance by promoting independence in the self-help domain can reduce the anxiety previously associated with the norm-violating behavioral pattern (e.g., being dressed by a parent).

These findings also raise some interesting questions regarding how to account for developmental processes when assessing intrusive parenting. Traditionally, intrusive parenting has been measured the same way across the age range from middle childhood to early adolescence (e.g., Hudson & Rapee, 2001; Wood, 2006a). However, the Wood and colleagues' (2009) findings raise the question of whether researchers should employ different scoring criteria or assessment methods for older versus younger children. Decisions on altering scoring criteria according to the child's age group are likely to vary with the research question being addressed. When differences between age groups in the domain of intrusiveness are of interest, the most unequivocal findings are likely to come from a measure that is scored identically irrespective of the child's age,

so that the scoring method is not confounded with age group. However, when main effects of intrusiveness are of primary interest, it may be useful to consider whether behaviors that are counted as "intrusive" at one age group should also be considered "intrusive" for the other age groups. One important question is when particular parental behaviors become "intrusive" relative to a child's development level and cultural background.

The Silverman and colleagues (2009) and Wood et al. (2009) articles offer examples of intervention research on evidence-based treatments used to examine aspects of theories that have proposed causal linkages between parental anxiety, parenting, and childhood anxiety. While by no means answering completely the core questions in the field about the primary causal and maintaining factors underlying childhood anxiety, both studies offer clues while also exemplifying the different types of methodologies that may be brought to bear on these questions.

Summary and Future Directions

The parenting–child anxiety field is currently making exciting progress. Among the notable accomplishments are greater specificity of theoretical models and the correspondingly precise tests of these models with improving instrumentation (e.g., for measuring parenting practices with more than marginal validity and reliability) and innovative methods. Exemplars of the latter include the use of repeated-measures longitudinal designs using developmentally attuned data-reduction strategies such as latent class analysis to examine the unfolding role of early parenting practices on developmental trajectories of anxiety over childhood; laboratory-based experimental designs that manipulate anxiety modeling, verbal threat information, or parenting strategies to determine the resulting impact on children's anxiety; and intervention studies explicitly designed to test theories about parental transmission or maintenance of children's anxiety. Although many questions remain, the recent research in this area continues to point toward a potential role for parenting practices as one factor of many within the multifactorial, and likely reciprocal, set of dynamics that lead toward or away from child anxiety disorders.

The field may benefit from an increasing breadth of experimental and intervention studies designed to address potential limitations that can be drawn from extant studies. As with all laboratory-based studies, the newly emerging studies on experimental manipulations of parenting in the laboratory would benefit from replication or extension into naturalistic settings. The strengths of the effect of experimental manipulations over time are important to establish in order to assess whether the laboratory effects are analogous or homologous with the development of stable clinical anxiety. Additional experimental studies looking more closely at the effects of particular types of parenting in particular situations would also be quite informative (cf. Wood et al., 2003). The emergence of experimentalism within the discipline may foreshadow a series of studies that could narrow down the contexts, for example, in which parental intrusiveness exerts its expected effects on self-efficacy and state anxiety in adolescents (e.g., only when an audience is present; if the adolescent believes that peers could find out; if the adolescent is primed by information promoting the desire for autonomy in a specific situation). It is, of course, important for experimental studies to examine the other direction of effects, namely, that higher child anxiety may elicit intrusiveness or other parenting practices under certain conditions. A reciprocal influence between parent and child has become a standard element in many conceptual models (e.g., Rapee, 2001) and could be usefully explored within these kinds of experimental designs. In short, an exciting era is upon us in the field of parenting and childhood anxiety. As ongoing studies continue to accrue more information with causal implications, it is likely that extant treatments may be further refined and improved through a more precise focus on putative underlying processes and change mechanisms.

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Part IV

Psychological and Pharmacological Treatments of Child/Adolescent Anxiety Disorders

Specific Phobias

16

Thompson E. Davis III and Thomas H. Ollendick

Introduction

Specific phobias are intense fears of certain, circumscribed objects, animals, situations, or environments. Previously referred to as "simple" phobias in earlier versions of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-III-R*; American Psychiatric Association, 1987), the name now better reflects the complexity and severity of the disorder than its previous "simple" moniker. While not as severe as other more pervasive anxiety disorders (e.g., generalized anxiety disorder, obsessive–compulsive disorder), a specific phobia can be a serious impediment to a growing child's successful development and maturation and can carry significant long-term psychological and social effects, usually into adulthood (Davis, 2009; Davis, Ollendick, & Öst, 2009).

Fear, like many other emotions, is important, normal, and highly adaptive (Davis, 2009). The experience of fear often keeps us safe and is healthy – e.g., we look both ways before crossing the street and we exercise appropriate caution around new and strange dogs. The complexity of fear roughly coincides with increasing cognitive-developmental gains and could be viewed as a sign of cognitive maturation. Early concrete thinking is associated with fears of concrete stimuli (e.g., dogs or bees) while later gains in abstract and social thought lead to fears of more abstract and intangible targets (e.g., the "boogeyman" or public embarrassment; cf. Davis, 2009; Gullone, 2000; Muris, Merkelbach, Meesters, & van den Brand, 2002). For example, more concrete animal fears typically have an onset around 7 years of age, followed by increasingly abstract situational and social fears in the early to late teenage years (Davis, Munson, & Tarcza, 2009; Öst, 1987a). While these fears typically arise and subside, presumably alleviated by increased instruction and exposure to the feared stimulus, not all childhood fears are just a "phase" or transitory in nature (Ollendick, Davis, & Sirbu, 2009).

Phenomenology

Some fears persist despite the best efforts of parents and physicians, and are abnormal in the frequency with which they occur, the intensity with which they are experienced, and the distress and avoidance they cause. In order to be diagnosed with this kind of problematic fear, a child must have the fear for at least 6 months with accompanying problematic avoidance or distress, along with a host of physiological symptoms (APA, 2000). When these enduring symptoms occur, a child may be said to have a "specific phobia" and it can be further classified into one of several types: animal (i.e., both animals and insects), natural environment (e.g., the dark or heights),

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_16, © Springer Science+Business Media, LLC 2011

blood injection injury (e.g., receiving an injection or seeing blood from a scrape), situational (e.g., small enclosed spaces or flying in an airplane), or other (e.g., loud noises, clowns, costumed characters, and additional fears that do not fit neatly into the previous types; APA, 2000).

Broadly, what those having a specific phobia are experiencing is the unusually strong, integrated, potentiated, and pathological emotional response of a neural fear network of memories and prepotent responses (Davis & Ollendick, 2005; Lang, 1979; note: this is different than neural circuitry – for a review please see Chap. 5). Essentially, from an information-processing model, a specific phobia is a psychopathological combination of psychophysiology, behavior, and cognition. With exposure to cues associated with the feared stimulus, children with specific phobias typically experience activation of the autonomic nervous system (e.g., increased heart rate), usually attempt to engage in avoidance behavior (e.g., running away), and think catastrophic thoughts (e.g., the dog is going to bite me, the lightning will strike our house and burn it down; Davis & Ollendick, 2005). When all three components of the emotional response appear, synchronous responding occurs; however, desynchronous or partial responses can occur as well (i.e., incomplete or partial activation of the fear network resulting in a partial response or only a response in one or two components; Hodgson & Rachman, 1974; Rachman & Hodgson, 1974). Given this, a clinician's treatment goal is to alter this fear network of memories and prepotent responses (e.g., learning histories, conditioning experiences, feared stimulus characteristics) and through therapy create new, adaptive, memories which will compete with the previous psychopathological information (Bouton, 2004; Davis, 2009). A daunting task, indeed – and to make things more difficult this type of corrective learning experience tends to be context specific, so clinicians must plan for treatment generalization to combat the spontaneous recovery of fear (Bouton, 2004).

Several developmental adaptations to the typical diagnostic criteria must also be considered. Evidence-based practitioners of clinical child and adolescent psychology must also concern themselves with developmental psychopathology, including what developmental trajectory a given child may be on and to what degree a child's presentation may or may not be developmentally appropriate (Davis, 2009). Children may not be able to definitively articulate their fears or related cognitions and may not realize the fear they experience or their response upon exposure is extreme (Davis et al., 2009; APA, 2000). A child may become clingy, cry, or possibly even aggressive when exposure is forced or escape prevented (APA, 2000). Finally, to avoid misdiagnosing the typical developmental progression of fears traversed by children as a clinically significant specific phobia, a child must also have the fear for at least 6 months.

Unfortunately, to date relatively little research has been focused on the phenomenology of specific phobias specifically in children and adolescents. From what is known, it appears that specific phobias strike children from a variety of racial, ethnic, and socioeconomic backgrounds (Ollendick, Raishevich, Davis, Sirbu, & Öst, 2010). It also appears that animal- and natural environment type specific phobias are the most common (Last, Perrin, Hersen, & Kazdin, 1992; Milne et al., 1995; Ollendick, Öst et al., 2009; Ollendick et al., 2010; Silverman et al., 1999), with specific phobias of dogs, insects, heights, the dark, and storms being common. In addition, children with specific phobias have been found to differ by type too. For example, Ollendick et al. (2010) found that children with natural environment phobias were more severely impaired than those with animal phobias in their somatic and anxious symptoms, depressive symptoms, and life satisfaction (i.e., a measure of quality of life), and on the Child Behavior Checklist (CBCL) (Achenbach, 1991) they were rated as being more withdrawn, having more somatic complaints, being more anxious/depressed, and as having more social problems than those children with animal phobias. Even so, no differences emerged between the two groups of children for socioeconomic variables, demographic variables, family variables, severity of the specific phobias themselves, or on ratings of coping or dangerousness of their respective feared stimuli (Ollendick et al., 2010).

Comorbidity also appears to be the rule for children with specific phobias rather than the exception in both community and clinical samples. The rates for comorbidity tend to vary greatly with approximately half of all children with specific phobias having another comorbid specific phobia in community samples (25% may have another disorder; Costello, Egger, & Angold, 2004). This rate is comparable to clinical samples, although the rates vary considerably. For example Öst, Svensson, Hellstrom, and Lindwall (2001) found 42% of children were comorbid with at least one other disorder, Last et al. (1992) found 50% were comorbid, Silverman et al. (1999) found 72% were comorbid, and Ollendick, Öst, et al. (2009) found 95% of a United States sample were comorbid – half of those comorbid with at least another specific phobia. Typically, across studies comorbidity appears to be other specific phobias or other anxiety disorders; however, other comorbid internalizing and externalizing disorders have been observed (Ollendick et al., 2010). The most common comorbid diagnoses across studies appear to be other specific phobias, and then, in varying order depending on the studies, generalized anxiety disorder, social phobia, separation anxiety disorder, attention-deficit/hyperactivity disorder, and major depression (Ollendick, Öst et al., 2009; Ollendick et al., 2010; Öst et al., 2001). To date, only one study has reported on comorbidity differences by type of specific phobia: Ollendick et al. (2010) found higher rates of generalized anxiety disorder and separation anxiety disorder in children having a natural environment type phobia compared to an animal type phobia.

Epidemiology

Overall, anxiety disorders have been found to be the most commonly occurring group of psychological disorders, and of the anxiety disorders specific phobia is the most prevalent with a 12-month prevalence rate of 8.7% and a lifetime prevalence rate of 12.5% (Kessler, Berglund, et al., 2005; Kessler, Chiu, Demler, & Walters, 2005). In children, approximately 5% of community samples and 10% of clinical samples have fears persistent and intense enough to be deemed specific phobias (Ollendick, Hagopian, & King, 1997). Higher rates have been reported, however, with some studies suggesting 17.6% of parent-reported childhood fears are severe enough to constitute specific phobias (Muris & Merkelbach, 2000) and 22.8% of child-reported fears severe enough to be viewed as phobic disorders (Muris, Merkelbach, Mayer, & Prins, 2000). In addition, while the mean age of onset has been suggested to be 9–10 years of age (Stinson et al., 2007), there is also wide variability reported in the literature depending on the type of fear, ranging in emergence from childhood to early adulthood (Öst, 1987a). Unfortunately, the toll exacted by specific phobia on the health care system and those with the fear has been great with those having specific phobias accessing medical care at higher rates than those with obsessive–compulsive disorder, and second only to panic disorder (Deacon, Lickel, & Abramowitz, 2008). Even so, fewer than 10% of adults ever seek treatment for specific phobia, and most have had their fear an average of 20 years, presumably because of the degree of accommodation in daily life and overall avoidance (Stinson et al., 2007). Still, others are simply unaware that effective treatments exist for these disorders.

Etiology

The exact causes of specific phobias are still not well understood to this day; likely there are myriad causes which can act either alone or in combination to bring about a fear intense enough to be a specific phobia depending on the unique characteristics of the individual (Davis, 2009). Four common pathways are recognized, however, and grouped into three associative accounts (classical conditioning, modeling, transmission of negative information) and one other pathway (the nonassociative account; Poulton & Menzies, 2002; Rachman, 1977, 2002). Classically conditioned phobias are acquired through direct contact with the stimulus (e.g., a snake bites a child). Phobias acquired through modeling involve seeing another individual act afraid (e.g., a parent acts very afraid of snakes in front of the child).

The transmission of negative information serves to impart fear through the retelling of scary stories, catastrophic beliefs about exposure to the stimulus, and the like (e.g., a parent tells a child to only play inside their yard because there are snakes everywhere and they will bite you). Finally, the nonassociative account attempts to capture those fears which seem to have more of a biological or genetic foundation (Rachman, 2002), though often individuals who have difficulty recalling the exact origin of their fear are relegated to this category (e.g., "I don't know; I've always been afraid of snakes."). Even so, an additional factor is necessary as many individuals experience associative events and do not develop a specific phobia (e.g., many people have been bitten by snakes or dogs but do not subsequently develop a phobia). While any one path may cause a specific phobia on its own, it is likely that associative experiences increase over time until they interact with an individual's own unique nonassociative vulnerability (cf. Ollendick & King, 1991; Ollendick, King, & Muris, 2002). As a result, the answer may be more aptly summarized as it is simply a matter of determining how much associative experience is necessary for an individual to develop a specific phobia given his or her unique inborn diatheses and competing corrective experiences (Marks, 2002).

Evidence-Based Assessment

With the rise of evidence-based practice, and empirically supported treatment in particular, a detailed and thorough assessment phase prior to commencing treatment has become essential to the adequate provision of clinical services. While a thorough description of the assessment process for child anxiety is beyond the scope of this chapter (see Ollendick, Davis, & Muris, 2004 and Silverman & Ollendick, 2005 for reviews), a clinician attempting to choose an evidence-based treatment option should carefully consider the assessments used in the studies upon which the evidence is built, so that an accurate and compatible diagnosis can be made (i.e., using the same assessment techniques as the evidence to know if a patient does have a disorder similar to that in a particular randomized trial and therefore may be amenable to that treatment). In addition, a comprehensive assessment should include procedures and instruments that allow for a detailed diagnostic assessment of childhood disorders (including comorbid conditions) and it should include an examination of the components of the phobic response (i.e., psychophysiology, behavior, and cognition; Davis & Ollendick, 2005; Ollendick, Davis, et al., 2009). The assessment should ideally be multimethod and multiinformant: use a variety of techniques and respondents to be sure an accurate diagnostic picture emerges of the child across many different situations. Instruments and interviews typically recommended for this type of assessment include the Anxiety Disorders Interview Schedule for *DSM-IV* Child/Parent version (ADIS-IV-C/P; diagnostic interview; Silverman & Albano, 1996), the Multidimensional Anxiety Scale for Children (MASC; anxiety self-report measure; March, Parker, Sullivan, Stallings, & Conners, 1997), the Fear Survey Schedule for Children-Revised (FSSC-R; fear self-report measure; Ollendick, 1983), and the CBCL (broadband parent report measure; Achenbach, 1991) among others. Phobia specific questionnaires can be considered for inclusion as well (e.g., questionnaires about particular stimuli like spiders). Behavioral avoidance tasks (BATs) should be considered for inclusion by clinicians because of the unique psychophysiological, behavioral, and cognitive information they offer (Davis et al., 2009; Ollendick, Davis, et al., 2009). While these behavioral avoidance paradigms may be difficult to arrange (e.g., getting, storing, and caring for stimuli or arranging for offsite visits), especially for private practitioners with limited resources, help, and space, the incorporation of BATs into the assessment process has been strongly encouraged as it provides valuable information about how the child will respond during an actual encounter with the stimulus or situation (Davis et al., 2009). Ideally, a comprehensive pretreatment assessment will provide enough information to determine a diagnosis of specific phobia, identify any comorbid diagnoses which may require additional treatment or need to be considered during treatment

for the phobia (e.g., separation anxiety disorder in addition to a specific phobia of the dark), and plan the steps of a gradual, hierarchical exposure (typically in vivo).

Treatment

Empirically Supported Treatments

Currently, clinicians seeking to treat child and adolescent fears have a variety of well-researched techniques available in their clinical armamentarium. These options have come from decades of study leading to the identification of several singular, stand-alone treatments for child anxiety and fear (e.g., behavior therapy; BT), as well as an increasing trend toward combined treatments (e.g., cognitive behavioral therapy; CBT). Consequently, "innovation in treating child phobias in recent years has come less from reinventing the wheel than from engineering how the wheels can move together to be more efficient; newer treatment alternatives have typically represented innovative ways of combining older, established techniques into a single therapy" (Davis et al., 2009, p. 295). Following a brief review of the established treatments for child-specific phobia, an emphasis will be placed on the newer, empirically supported, intensive CBT called "One-Session Treatment" (OST; cf. Davis et al., 2009; Ollendick, Öst, et al., 2009; Öst, 1987b, 1989; Zlomke & Davis, 2008).

Currently, there are four major types of empirically supported treatment for child specific phobia: systematic desensitization (SD), reinforced practice (RP) (also called contingency management), modeling and participant modeling (PM), and CBT (Davis, 2009; Davis & Ollendick, 2005). Given this, it is no surprise then that the most widely used treatment techniques for children with anxiety have been exposure, relaxation, cognitive restructuring, modeling, child psychoeducation, and reinforcement (Chorpita & Daleiden, 2009). Evidence for these treatments has been categorized in a number of different ways, but the most commonly used criteria are those put forth by Division 12 of the American Psychological Association Task Force, with the resulting designations of treatments being well-established (i.e., the most support), probably efficacious (i.e., some support), or experimental (i.e., either no support or not yet researched; Task Force, 1995). For the following treatment descriptions, an evidence-based approach will be taken with designations presented using a strict interpretation of Task Force criteria based on children diagnosed with specific phobia (i.e., Davis, 2009) and a more broad interpretation based on the inclusion of children with diagnoses but also with undiagnosed yet problematic fears (i.e., Davis & Ollendick, 2005). This broader evidence-based interpretation (i.e., Davis & Ollendick, 2005) comes from many of the studies used to support the empirical status of phobia interventions neglecting Task Force criterion IV: to clearly specify the characteristics of client samples. As a result, the most common deficiency has been the use of nonclinical samples or combined anxiety disorder samples as evidence for the empirical support of a treatment with a particular clinical disorder. For example, Davis (2009) writes, "Menzies and Clarke (1993) was used to suggest probably efficacious status for 'exposure' (cf. Chambless et al., 1998) for 'water phobia' (Menzies & Clarke, 1993), but also did so using arguably analog participants who on average at pretreatment could at least proceed down to about neck depth in a pool, if not further with hesitation" (p. 213). As a result, the review by Davis (2009) is based on studies using well-described, children diagnosed with specific phobias, and Ollendick and Davis (2004) present more of a sum of all of the evidence for treatments to that date – whether studies strictly meet empirically supported treatment criteria or not.

Systematic Desensitization (SD)

SD is one of the earliest and most influential child treatments for specific phobia, though its underlying theory and use have been increasingly criticized in recent years (Davis, 2009; Ollendick, Davis, et al., 2009). According to Wolpe (1958), SD works through a process of

reciprocal inhibition – the notion that one cannot experience two competing emotions simultaneously. The goal, then, is to work toward extinguishing the classically conditioned fear response by weakening the ability of the conditioned stimulus to elicit the conditioned response (e.g., a dog no longer elicits a fear response). A necessary component, then, becomes exposure to the feared stimulus while an emotion other than fear is experienced. This is accomplished by carefully constructing a graduated fear hierarchy with the child's input and then inducing an incompatible emotion in the child during each step of the exposure. Wolpe (1958) recommends any appetitive behavior – for example humor or eating – but progressive muscle relaxation (PMR) has come to be the primary technique of choice. Treatment progresses by initially developing the graduated fear hierarchy and then instructing the child in PMR until mastery is achieved. Several scripts for PMR exist (e.g., see Ollendick & Cerny, 1981), but they all involve training the child to progress through various muscle groups briefly tensing and relaxing them (Ollendick et al., 2004). Perhaps not surprisingly, this approach has been used less frequently with young children who may have difficulties both with mastering PMR and in formulating graduated fear hierarchies. For older children and adolescents, after the hierarchy as been determined and PMR has been mastered, treatment proceeds by relaxing the child and then gradually exposing the child to increasingly more difficult steps in the hierarchy either imaginally or in vivo. Importantly, for this treatment to be effective the child should not actually experience undue or high levels of fear, but rather the associative strength of the conditioned stimulus and response should be weakened by not feeling overly afraid during exposure (Davis, 2009; Davis & Ollendick, 2005). To this end, clinicians frequently use a prearranged signal to indicate when a child is beginning to become afraid and the intensity of the exposure is subsequently reduced (Ollendick & Cerny, 1981).

While initially one of the treatments of choice for specific phobia, enthusiasm for SD in research has waned over the past several decades as the field has moved toward fewer distractions from exposure (e.g., relaxation training). In addition, research into extinction has led to an understanding of exposure as creating a competing, context-specific type of learning as opposed to the original counterconditioning hypothesis (i.e., competing learned responses are created as opposed to the previous belief that the fearful response was "unlearned;" Bouton, 2004). In addition, SD and RP (another treatment procedure) have frequently been confused by researchers and practitioners in the literature. Even so, SD has enough early research to merit probably efficacious empirical status for alleviating fears, though its effects have surprisingly not been robust for psychophysiological changes (Davis & Ollendick, 2005). For children diagnosed with specific phobias, SD is still considered experimental (Davis, 2009).

Reinforced Practice (RP)

Based upon operant conditioning principles, a clinician using RP attempts to reinforce successive steps toward feared stimuli, thereby overcoming avoidance behavior (Davis & Ollendick, 2005). RP requires the clinician again devise a detailed fear hierarchy, but also conduct a functional assessment to determine the maintaining functions of the avoidance (including any secondary gain) and a reinforcer survey to create an array of reinforcers to apply contingently upon the completion of a step in the hierarchy. This treatment progresses by successively reinforcing approach behavior during in vivo exposure. Once successful approach behavior is shaped for a step, various steps can be chained if appropriate, and the schedule of reinforcement is thinned with the overall goal being to fade it out all together (Davis & Ollendick, 2005; Ollendick, Davis, et al., 2009). As a result, the technique makes use of reinforcement, shaping, extinction, and verbal feedback regarding performance (Davis & Ollendick, 2005). RP has been found to be successful when used as one component of a behavioral approach (cf. Silverman et al., 1999), and as such, has merited well-established support for the treatment of fears (Davis & Ollendick, 2005).

Care in the implementation of RP and SD needs to be taken, however, based on when the

competing response or reinforcer is delivered (Davis, 2009). As SD can make use of other competing appetitive behaviors (e.g., eating, humor – anything inducing a response that competes with fear), it has frequently been confused with RP or ignored all together in the literature as "distraction" and the like (cf. Davis, 2009; Ollendick, Davis, et al., 2009). The critical issue is when the item to be used during treatment is delivered – if an item is delivered in preparation for and during an exposure to "distract" or "calm" the child, then the clinician is actually conducting SD; if an item is delivered contingent upon completion of an exposure, then the clinician is conducting RP. The difference is actually very important, both theoretically and practically. If a clinician is using SD, then the key is for the child not to experience fear; if, however, RP is the goal, then the clinician does want the child to feel manageable amounts of fear and allow extinction of the avoidance behavior to occur. At present, an empirical investigation of the mix of the two treatments has not been undertaken.

Modeling and Participant Modeling (PM)

Modeling is based on social learning theory with treatment progressing by having a model (usually the clinician) demonstrate the successful completion of steps in the fear hierarchy to the child (Davis & Ollendick, 2005). Originally called contact desensitization (Ritter, 1965, 1968), PM carries this procedure further by actually incorporating the child into the exposure by having the clinician successfully model the completion of a particular step in the fear hierarchy and then involve the child in completing the modeled step (Davis, 2009; Davis & Ollendick, 2005; Ollendick, Davis, et al., 2009). The child can be incorporated using a number of techniques depending upon the child's ability to negotiate the step: the clinician may simply provide verbal instruction on the completion of the step or may go as far as to engage in physical contact ranging from simply standing beside the child while holding hands to using hand-over-hand assistance in close proximity to the feared stimulus to help the child voluntarily complete the step (i.e., as opposed to compulsory hand-over-hand procedures seen in three-step prompting; Miltenberger, 2001). It is in this way that PM has the additional benefits of skill building (e.g., how to approach and pet a dog if a child has never done that before) and breaking down larger, more intimidating fear hierarchy steps into several smaller, more manageable steps (e.g., having to pet a dog becomes slowly watching a clinician pet a dog followed by having the clinician slowly move the child's hand down their own until the child can independently complete the step).

While PM has not been evaluated using a strict interpretation of the Task Force (1995) guidelines (cf. Davis, 2009), an evidence-based evaluation has suggested it is well-established for the treatment of fears in children (Davis & Ollendick, 2005). Finally, given descriptions of its use in the literature, PM has frequently been misconstrued as only being viable for animal type phobias. However, it is inaccurate to believe PM can only be used with animal type phobias (Davis et al., 2009; Zlomke & Davis, 2008). In actuality, PM has been used as a component in other treatments (e.g., CBT) in situational and natural environment type phobias as well. For example, in these situations PM may simply involve modeling leaning against a railing while looking down (e.g., exposure for heights) followed by a hand on the child's shoulder while he or she leans over the railing and looks down.

Cognitive–Behavioral Therapy

CBT is a combination treatment that employs graduated hierarchical exposure along with any or all of a number of the preceding behavioral techniques and cognitive techniques to address behavioral avoidance as well as catastrophic cognitions, attentional biases, cognitive distortions, and maladaptive automatic thoughts (Beck, 1993; Beck & Clark, 1997; Davis & Ollendick, 2005; Kendall, 1993). As a result, CBT makes use of behavioral interventions such as reinforcement, relaxation, and modeling, and also incorporates techniques

to identify and counter cognitive biases and distortions which have theoretically come to be part of stable, pathological psychological structures which direct avoidance behavior and biased or catastrophic thought (i.e., schemas; Beck, 1993; Davis & Ollendick, 2005; Kendall, 1993). Using either strict criteria (Davis, 2009) or more of an evidence-based approach (Davis & Ollendick, 2005), CBT has been found to be probably efficacious for the treatment of children diagnosed with specific phobias or with problematic fears. Using the more evidence-based criteria set (i.e., Davis & Ollendick, 2005), CBT has been found to be superior to a control group (Kanfer, Karoly, & Newman, 1975) and a waitlist group (Graziano & Mooney, 1980), and has been found equivalent to RP (Silverman et al., 1999).

One-Session Treatment

Recently, there has been significant interest in the use of one variant of CBT for specific phobia: OST (Davis et al., 2009; Öst, 1987b, 1989; Zlomke & Davis, 2008). OST is a unique combination of several of the probably efficacious and well-established child anxiety treatments previously discussed into a single, massed 3-h session of in vivo exposure (Davis et al., 2009; Zlomke & Davis, 2008). Excitement over OST has led to its being described as one of the best CBTs to learn and an excellent initial foray for new clinicians into the world of CBT (Albano, 2009). Further, OST has been deemed an empirically supported treatment and the use of OST with children has merited probably efficacious status given the studies completed to date (Davis, 2009; Zlomke & Davis, 2008). The efficacy of OST is supported by two randomized clinical trials (Ollendick, Öst, et al., 2009; Öst et al., 2001), two crossover studies (Muris, Merckelbach, Holdrinet, & Sijsenaar, 1998; Muris, Merckelbach, van Haaften, & Mayer, 1997), and one case study with a child who also had pervasive developmental disorder-not otherwise specified (PDD-NOS) and severe behaviors (Davis, Kurtz, Gardner, & Carman, 2007). Briefly, OST has been found superior to a waitlist condition (Ollendick, Öst, et al., 2009; Öst et al., 2001), superior to an attentional/placebo or educational support condition (Muris et al., 1998; Ollendick, Öst, et al., 2009), and superior to eye-movement desensitization and reprocessing (EMDR; Muris et al., 1997, 1998). OST has also been demonstrated to successfully treat phobias of water and heights in a developmentally delayed boy using a multiple baseline design (Davis et al., 2007). In addition, large effect sizes have been found for pre- to post-treatment differences on subjective units of distress (SUDS; $d = 1.91$), BATs ($d = 1.40$), and self-report instruments of fear ($d = 1.43$) for children receiving OST (Zlomke & Davis, 2008). For a more detailed review of the evidence-based status of OST, please see the review by Zlomke and Davis (2008). It is toward a more detailed discussion of the use of this promising exposure-based CBT to which we now turn.

Overall Description: OST is a 3-h, massed cognitive–behavioral intervention during which a child is gradually exposed to increasingly more fear-evoking stimuli or situations (Davis et al., 2009; Zlomke & Davis, 2008). The treatment session incorporates several empirically supported treatment components while progressing at a pace jointly determined by the clinician and child. As a result, OST makes use of graduated hierarchical exposure, PM, cognitive challenges, reinforcement, psychoeducation, and skills training (Davis et al., 2009; Zlomke & Davis, 2008). This combination treatment has also been found to be exceeding well tolerated by children, with the large majority of children being satisfied with the outcome (82.1%) and reporting treatment occurred at a good pace (89.3%) and with no children reporting treatment progressed too quickly (Svensson, Larsson, & Öst, 2002).

A successful OST session has its beginnings in the assessment of the child's specific phobia. An important part of the assessment process is a functional assessment of the child's phobia during which the fear hierarchy is created, maintaining variables are explored, and catastrophic cognitions are elicited from the child and cataloged by the clinician (for a detailed description of the functional assessment see Davis et al., 2009). This functional assessment portion typically requires 45 min to complete and can be supplemented by additional information or confirmation from

parents or caregivers at the conclusion of the assessment (Davis et al.). At the conclusion of the functional assessment, the clinician also provides the rationale for the upcoming exposure session and attempts to assess the child's motivation for treatment. Briefly, the rationale includes a description of the exposures to come, termed "behavioral experiments," reassurances that nothing will be done to the child without first discussing it with the child, and that the goal is not to shock, surprise, or further traumatize the child, but rather the clinician and child will act as a team working together to overcome the child's fear (Davis et al.). An informal assessment of the child's motivation is also important as the clinician explains that the child will have to experience some fear during the behavioral experiments (ideally a mild to moderate amount), but that it is the clinician's responsibility to ensure these are exposures that the child is able to handle and that if the child remains in the situation instead of avoiding it that the fear will subside or at least be greatly reduced (Davis et al.). Ideally, the functional assessment session is conducted far enough in advance to allow for the necessary preparations for the exposure session (e.g., arranging for relevant stimuli or situations; Davis et al.).

Treatment Components and Implementation: OST proceeds at an irregular pace over 3 h of exposure and sessions can vary from child to child – even when the same phobia is involved (Davis et al., 2009). Unfortunately, there is no standard formula for structuring an OST session, other than generally proceeding at the child's pace – with frequent clinician encouragement – and attempting to make the session as engaging and fun as possible (successful sessions with younger children may even take the form of a turn-taking game suggesting behavioral experiments and then attempting them). Initially, it can seem unwieldy for the clinician to have to incorporate cognitive challenges, PM, psychoeducation, skills training, and reinforcement at the same time; however, exposure (i.e., behavioral experiments) sets the stage for using the various other techniques as necessary to assist with allaying fear or educating the child (Davis et al., 2009). Behavioral experiments generally progress in a three-step fashion: first, the clinician and/or child suggest and discuss a possible exposure; second, the clinician models the proposed experiment; third, the child attempts the modeled step, with the assistance of the therapist, and success or failure is discussed (Davis et al., 2009; Zlomke & Davis, 2008). The other components of OST simply act as tools in a clinician's toolkit to address different pitfalls, distortions, or deficits during treatment (Davis et al., 2009). After agreeing on a behavioral experiment, information on the catastrophic cognitions obtained from the functional assessment are used to prompt the child as to what he or she predicts will happen (e.g., "do you think the dog is going to bite you if you get closer?") and then to discuss what really did transpire following the experiment (Davis et al., 2009). Reinforcement is used throughout to reinforce attempts, praise success, and encourage further discussion; while psychoeducation about the feared stimulus or situation (e.g., how to tell a "mean" dog from a "nice" dog) serves to remedy lulls in session progress while waiting for fear to habituate during a step while at the same time keeping the session focused on exposure to the stimulus (Davis et al., 2009; Zlomke & Davis, 2008). Finally, PM can be used to break down seemingly large steps into smaller, more manageable steps while also enhancing clinician support for the encounter (e.g., actually touching a dog may be a roadblock and PM allows that large step to be further broken into touching the clinician while the clinician touches the dog and so forth). Further, PM allows the clinician to remediate any skill deficits through active instruction in interacting with stimulus or situation (e.g., how to approach and pet a dog without intimidating or scaring it; Davis et al., 2009). As a result, within the broader framework of the behavioral experiments, OST flexibly incorporates these various other treatment components fluidly (see Table 16.1 for a partial dog phobia treatment step-by-step description).

Potential Impediments to Treatment Success

A number of factors may unfortunately contribute to treatment failure or backsliding following gains. Several of these issues will be briefly discussed

Table 16.1 Hypothetical example of the progression of treatment for a child with a dog phobia

First dog (approximately 1–1.5 h of the massed session)
Talk about dogs; introduce idea of bringing a dog into the room; negotiate details of first exposure and assess the child's predictions of what will happen
A small dog is brought into the room (e.g., a West Highland Terrier) leashed by an assistant who holds the leash close and tight at the opposite end of the room from the child and clinician. The clinician praises progress and encourages the child to watch the dog. They discuss how the dog's behavior is similar or dissimilar to expectations and cognitions discussed earlier
The clinician suggests moving closer. The child declines and details are discussed. The interim is used to discuss educational elements regarding dogs (e.g., Do you know how to tell a mean dog from a nice dog? How can we tell if that is a mean or nice dog?). The clinician again suggests moving closer. The child and clinician move three feet closer to the dog and discuss/challenge cognitions and predictions
The clinician again suggests moving closer; however, before details can be negotiated the child simply begins moving forward and the therapist replies, "I'll just stop when you do then; you're doing great!" The child and clinician move four more feet closer to the dog and discuss/challenge cognitions and predictions
The child agrees to allow the dog two more feet of freedom on its retractable leash
The child agrees to allow the clinician to touch the dog. Predictions of what will happen are assessed before and discussed following
The clinician uses participant modeling (PM) to have the child in closer proximity while the clinician pets the dog
The clinician shapes the response with praise and PM until the child is independently petting the leashed dog
The child realizes how close she is to the dog's teeth and recoils slightly
The clinician assesses the catastrophic thought (i.e., "it will bite me"), asks the child for a prediction of what will happen if she pets the dog's head, and with permission demonstrates how the dog dislikes having the clinician's hand in its mouth. The child is then encouraged to do the same and performance is discussed
Etc
Similar procedures would occur with the second and third dogs (a medium and large dog, respectively) taking up the remaining 1.5 h or until sufficient behavioral experiments have been conducted and over learned until the child exhibits little or no fear

Note: treatment occurs at an uneven pace and differs considerably from child to child, even for the same phobic stimulus. This example was constructed with the catastrophic fear being associated with the size of the dog and it knocking the child over and biting him or her. Reproduced with permission from Davis et al. (2009)

below; for a more thorough review of CBT for refractory cases of specific phobia see Ollendick, Davis, et al. (2009). In the three larger scale trials of CBT for specific phobia in children to date (Ollendick, Öst et al., 2009; Öst et al., 2001; Silverman et al., 1999 which also targeted other anxiety disorders than specific phobias), a mixed picture of treatment response appears. Across all three trials, age does not seem to be related to treatment outcome, and in the two studies examining it, diagnostic comorbidity did not seem to impact the results (Ollendick, Davis, et al., 2009). In the two OST trials, girls were found to respond better to treatment, and Öst et al. (2001) found better outcomes for animal type phobias. Child and parental self-report of depression and anxiety were found to be related to treatment failure for Silverman et al. (1999); however, the other studies do not report either differences for or data on these variables (Ollendick, Davis, et al., 2009). Though unexamined in these trials, anecdotally, family variables that were initially etiological may also continue to play a role by hampering treatment. For example, two recent refractory cases familiar to the authors have involved separate boys with specific phobias of dogs who responded quite well to treatment (i.e., both were able to interact with dogs of various sizes on and off of leashes by the end of treatment), but also had mothers who reported significant specific phobias of dogs as well. Both children, interestingly, astutely noted during the functional assessment that a significant component to their fear was the modeling and negative information provided by their mothers.

Unfortunately, neither mother was willing to undergo treatment of her own phobia of dogs and in each case the child's progress was noted by clinicians to suffer.

Subsequently, the issue becomes what to do in instances when treatment is not completely effective or other obstacles to treatment success arise. Overall, a four-stage procedure is recommended for treating children's specific phobias and addressing refractory cases (Ollendick, Davis, et al., 2009; see Fig. 16.1). First, and following an initial assessment, one of the preceding evidence-based treatments should be selected and implemented. If, following implementation, only a partial response is achieved from that intervention, a variety of options exist for supplementing the treatment during stage two including additional assessment, increasing treatment frequency or intensity, and/or addressing other impediments to treatment or comorbid conditions. After at least two attempts to administer the selected evidence-based intervention, stage three may be reached in which another evidence-based treatment should be considered and administered. Following success at any of these stages, one should also look toward the maintenance and generalization of treatment gains (i.e., stage four; Ollendick, Davis, et al., 2009).

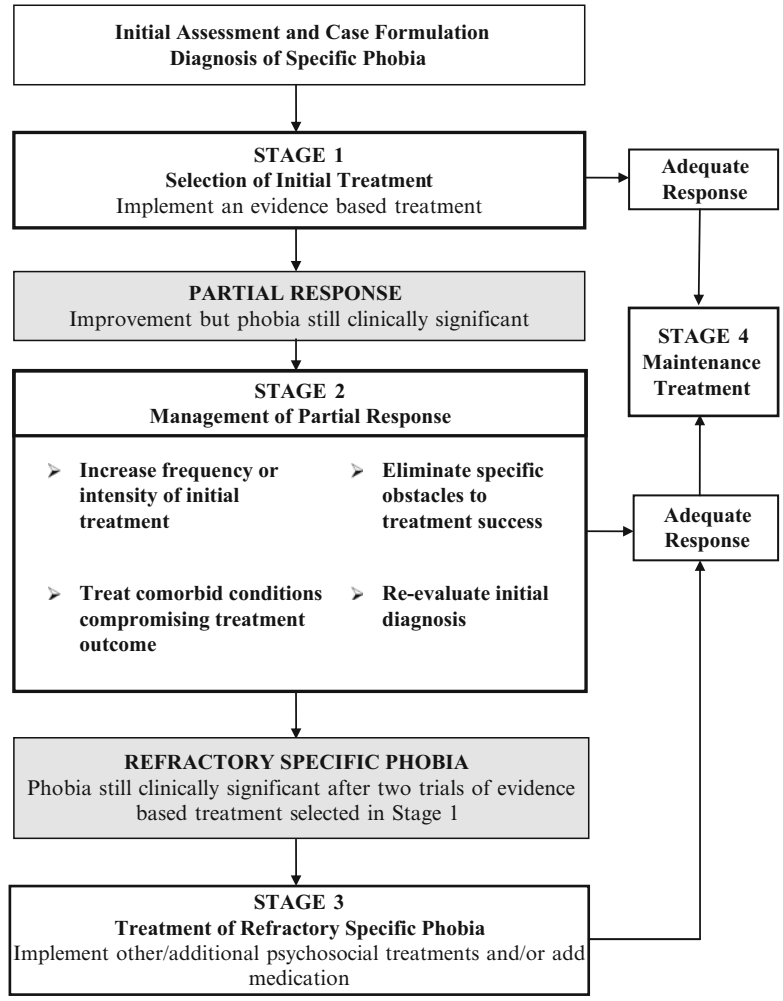

Fig. 16.1 Treatment algorithm for children with specific phobia (adapted from Ginsburg & Walkup, 2004, and Ollendick & March, 2004). Reproduced with permission from Ollendick et al. (2009)

Summary

Anxiety disorders can impair children in numerous ways from hampering the attainment of developmentally appropriate milestones (Davis, 2009), to impairing the development of social skills and socialization (Davis et al., in press), to even impacting intellectual ability (Davis, Ollendick, & Nebel-Schwalm, 2008). In as much as specific phobia is the most prevalent anxiety disorder (cf. Kessler, Berglund, et al., 2005; Kessler, Chiu, et al., 2005), the disorder tends to begin in childhood (Stinson et al., 2007), and if left untreated symptoms tend to persist for decades (Stinson et al., 2007) and exact a toll on the health care utilization (cf., Deacon et al., 2008), it is surprising that with so many brief, efficacious therapies for child specific phobia that few take advantage of treatment. There are likely many reasons only 10% of those with specific phobia seek treatment (Stinson et al., 2007); however, in part this disservice is likely due to continued difficulty with the dissemination of evidence-based practices to the community of practitioners and the public at large (Ollendick & Davis, 2004). Even so, clinicians currently have a variety of evidence-based treatments at their disposal which have very good support: SD, RP, PM, and CBT. In particular, OST seems a unique and promising choice given its seeming resistance to interference from comorbid conditions, success across a broad age range and, at least tentatively, across developmental capabilities (i.e., Davis et al., 2007), and its relatively streamlined, brief, and cost-effective format (Albano, 2009; Davis et al., 2009; Zlomke & Davis, 2008). As a result, OST may be an initial quick and successful experience with CBT for children and families while teaching many of the techniques for other CBT procedures to be used with comorbid conditions.

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Separation Anxiety Disorder

17

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Diagnosis and Classification

According to the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition, text revision (DSM-IV-TR; American Psychiatric Association [APA], 2000), the central feature of separation anxiety disorder (SAD) is unrealistic and excessive anxiety upon separation or anticipation of separation from major attachment figures. SAD is the only anxiety disorder based on specific child criteria as well as having a childhood onset. DSM-IV-TR requires evidence of at least three (of eight) separation-related symptoms that cause (1) significant interference in social and academic functioning and (2) continuous disturbance for at least 1 month. These impairment criteria are important since separation anxiety is typical and can be developmentally appropriate in young children (Hanna, Fischer, & Fluent, 2006).

Key symptoms of SAD include excessive worry about potential harm to oneself and/or major attachment figures as well as somatic complaints. Common worries include getting kidnapped, being abandoned, and becoming ill. Frequently reported somatic complaints include stomachaches, headaches, nausea, and vomiting.

Most somatic complaints and/or worries are in response to anticipated separations. In addition, children frequently avoid situations that lead to separation from primary caregivers. Common situations include refusing to attend school, sleeping alone at night, or visiting with a friend. Oppositional behaviors (e.g., temper tantrums, screaming, pleading, and threats) often result when avoidance is inevitable (see Eisen, Brien, Bowers, & Strudler, 2001; Eisen & Schaefer, 2005).

Distinction from School Refusal Behavior

As many as 75% of children with SAD experience some form of school refusal behavior (Kearney, 2008). For this reason, it is important to distinguish SAD from this behavioral problem. First, school refusal behavior is often a consequence of SAD. This is especially true when the school refusal is acute or mild in nature. Chronic school refusal, on the other hand, is more characteristic of older children and adolescents, and is associated with severe problems such as depression or agoraphobia. School refusal is also associated with other anxiety disorders such as specific phobias, social and generalized anxieties, and panic attacks. When this occurs, examination of the context of the symptoms can help to distinguish SAD from school refusal behavior.

For example, children with specific phobias may fear situations related to school attendance. In this case, the child's anxiety is related to specific school issues, such as a teacher or the school setting, rather than any experience of separation from major attachment figures. Children with social anxiety may avoid school because of a fear

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_17,

of embarrassment in performance-based situations, such as taking a test or giving an oral presentation. Once again, the anxiety experienced is directly related to the social situation rather than any discomfort associated with the absence of the caregiver.

School refusal behavior can be related to generalized anxiety disorder (GAD) or a mood disorder. By definition, GAD is chronic in nature, lacks situational specificity, and typically occurs when the attachment figure is present. Children with GAD worry about a wide range of areas, but especially minor events such as doing poorly on a test. Children with GAD are also more likely to experience fatigue, muscle tension, irritability, and sleep problems (Chorpita, Tracey, Brown, Collica, & Barlow, 1997). When depressive symptoms emerge, problematic school attendance, poor peer relations, and academic problems are likely to be key factors (Kearney, 2008).

Finally, panic attacks may also be observed in children with SAD and/or school refusal behavior. Panic disorder (PD), however, involves recurrent panic attacks that are uncued in nature, as well as a fear of having additional attacks (APA, 2000). Common symptoms associated with panic attacks include pounding heart, nausea, shortness of breath, and shakiness (Kearney, Albano, Eisen, Allen, & Barlow, 1997).

However, regarding SAD or school refusal behavior, the panic symptoms experienced are more related to the context in which they occur, such as anticipating separation from a major attachment figure and/or a feared catastrophic outcome in the school setting. Careful assessment is necessary to distinguish the function(s) that maintain school refusal behavior (see Kearney, 2007).

Relation to Homesickness

For most youngsters, spending time away from home (e.g., summer camp) is a positive experience. Mild homesickness is observed in 80–90% of children and is considered a normal part of development (Thurber, 1999). Severe homesickness (5–10%), however, is frequently associated with anxiety, depression, social and behavior problems (Thurber & Patterson, 2007). Although the features of SAD and homesickness may overlap (e.g., somatic complaints), homesickness can be distinguished from SAD on several grounds.

For example, SAD is primarily about preseparations from people (e.g., caregivers, safe persons), whereas homesickness is primarily about post-separations from home-related attachment objects (e.g., house, cooking) and persons. In addition, SAD typically involves anticipatory anxiety, whereas homesickness involves both anxiety and consequential depression. Youngsters with homesickness are more likely to experience elevated levels of negative emotion both prior to and subsequent to separations (Thurber & Patterson, 2007).

For youngsters on the verge of attending day camp (with planned overnights) or sleep away camp, features of both separation anxiety and homesickness should be integrated into the treatment process. Doing so will help foster coping skills, independence, and enhance the security of attachment with caregivers.

Epidemiology

SAD is the most common childhood anxiety disorder with typical onset around 7–12 years of age (Allen, Rapee, & Sandberg, 2008; Compton, Nelson, & March, 2000; Keller et al., 1992). Lifetime prevalence of childhood SAD in the general population is 4.1% (Shear, Jin, Ruscio, Walters, & Kessler, 2006). Prevalence estimates from a clinically anxious pediatric population are substantially greater. For example, Hammerness et al. (2008) reported that SAD accounted for 49% of admissions.

Prevalence rates of childhood SAD have been shown to vary by gender. SAD is more commonly observed in girls (6.8%) than boys (3.2%) (e.g., Foley et al., 2008). In addition, prevalence rates for SAD appear to vary across age. For children under 14 years, the rate of occurrence for SAD was 6.5%. In adolescents aged 14–16 years, however, prevalence rates were 2.9% (Foley et al., 2008). Finally, SAD also has a lower age of onset than most other childhood anxiety disorders. For instance, the mean age of onset for SAD is

8.59 years as compared to 11.37, 13.70, and 14.28 years for GAD, obsessive–compulsive disorder (OCD), and social anxiety disorder (SOC), respectively (Bacow, Pincus, Ehrenreich, & Brody, 2009).

Comorbidity

A large body of research has demonstrated high rates of psychiatric comorbidity in children with anxiety disorders (Chase & Eyberg, 2008; Franco, Saavedra, & Silverman, 2006; Kendall, Brady, & Verduin, 2001; Shear et al., 2006). Anxious youth rarely present for treatment with a single disorder. In children with SAD, 79% had at least one comorbid disorder, and 54% had two or more comorbid disorders, the most common being other anxiety disorders (Kendall et al., 2001).

High rates of comorbidity between SAD and PD have been reported, especially at the symptom level. For example, comorbid separation anxiety has been reported to be as high as 73% in youth with panic attacks (Masi, Favilla, Mucci, & Millepiedi, 2000). Studies have also supported the link between childhood separation anxiety and adult panic (Battaglia et al., 2009; Lewinsohn, Holm-DeNoma, Small, Seeley, & Joiner, 2008). Alternatively, other studies (e.g., Aschenbrand, Kendall, Webb, Safford, & Flannery-Schroeder, 2003) have failed to support this connection. Thus, the precise relationship between separation anxiety and adult panic warrants further investigation.

Given that both GAD and OCD are associated with worry and somatic complaints, it is not surprising that both disorders are frequently comorbid with SAD. GAD co-occurs with SAD approximately one-third of the time (Kendall et al., 2001). Obsessive–compulsive disorder co-occurs with SAD as much as 24–34% of the time (Geller, Biederman, Griffin, Jones, & Lefkowitz, 1996; Valleni-Basile et al., 1994). The combination of OCD and SAD is associated with an earlier onset of PD (Goldwin, Lipsitz, Chapman, Fyer, & Manuzza, 2001).

The association of anxiety and depression in children is well established (Brady & Kendall, 1992; Suveg et al., 2009). As such, it is not surprising that comorbid separation anxiety and depression are common in children and adolescents. As many as one-third of children with SAD develop a depressive disorder (Shear et al., 2006). Typically, comorbid depression results when SAD becomes debilitating and/or interferes with at least two spheres of functioning (e.g., school, peers, or family) (Eisen & Schaefer, 2005).

Finally, disruptive behavior disorders are also likely to co-exist with SAD (Hammerness et al., 2008). Attention-deficit hyperactivity disorder (21.7%), oppositional-defiant disorder (19.6%), and conduct disorder (21.4%) were found to be the most frequently occurring externalizing disorders comorbid with SAD (Shear et al., 2006).

Developmental Course

The onset of separation-anxious symptoms can be acute or insidious. Symptoms may stem from genuine fearfulness associated with anticipated harm to the child and/or major caregiver, significant life stressors, or seemingly innocuous events (e.g., stomachache or nightmare) that become overgeneralized.

The frequency and intensity of the child's symptoms are often maintained by parental accommodation (Eisen, Raleigh, & Neuhoff, 2008). For example, when a parent allows a child to miss school, presumably for "feeling sick," or to sleep in the parental bed due to a nightmare, avoidance of such anxiety-provoking situations may strengthen the child's initial symptoms. Parental accommodation may also occur in the form of overprotection (Eisen, Engler, & Geyer, 1998; Eisen & Engler, 2006). For instance, at times, parents may restrict a child's participation in potentially anxiety-provoking situations, such as playing contact sports or attending a relative's funeral. However, when excessive restrictions occur, the stage is set for a child's SAD to adversely school performance, peer relations/extracurricular activities, and family life (see Eisen & Schaefer, 2005).

Separation-anxious symptoms can be chronic in nature but more typically undergo alternating periods of remission and exacerbation. In general,

younger children tend to experience fewer and less distressing symptoms, whereas older children and adolescents experience greater avoidance levels and frequent somatic complaints (Last, 1991). However, recent data suggest an opposite trend (Hale, Raaijmakers, Muris, Van Hoof, & Meeus, 2008), where separation-anxious symptoms were stronger in children, and ultimately, decreased with age. Further research is necessary to examine the nature of developmental trajectories in separation-anxious youth.

Although most youth are able to successfully negotiate SAD, evidence suggests that separation-anxious symptoms may linger into adulthood or serve as a general risk factor for anxiety, panic or depressive symptoms (Lewinsohn et al., 2008). Approximately one-third of individuals experience childhood separation-anxious symptoms that persist into adulthood (Shear et al., 2006). SAD in young adulthood is associated with adjustment problems, tension, worry, and somatic complaints (Ollendick, Lease, & Cooper, 1993).

An Emphasis on Symptom Dimensions

Given the highly comorbid nature of anxiety disorders in general, and SAD in particular, support is emerging for classifying these disorders based on the frequency and intensity of symptoms (Ferdinand, van Lang, Ormel, & Verhulst, 2006; Hirshfeld-Becker, Micco, Simoes, & Henin, 2008).

Recently, Eisen and colleagues (Eisen & Engler, 2006; Eisen, Pincus, Hashim, Cheron, & Santucci, 2008; Eisen & Schaefer, 2005) proposed a conceptual framework that examines separation anxiety based on core symptom dimensions and seeking safety behaviors. The symptom dimensions include fear of being alone, fear of abandonment, fear of physical illness, and worry about calamitous events. The first two dimensions address the avoidance component of separation anxiety. Children that fear being alone frequently avoid being alone somewhere in their house such as a bedroom, bathroom, or finished basement. Naturally, being alone during the day is typically easier than at night. In our own work (Hajinlian et al., 2003), 50% of a large sample of youth experiencing internalizing and/or externalizing disorders reported being afraid to sleep alone at night.

Although a fear of being alone is our most common referral, fear of abandonment is most predictive (83%) of SAD (Hajinlian, Mesnik, & Eisen, 2005). Children that fear abandonment may express reluctance or refusal to be "dropped off" specific places like school, an extracurricular activity, or play date unless promised close proximity or complete access to the major attachment figure. Excessive avoidance may lead to social isolation.

The third and fourth symptom dimensions, i.e., a fear of physical illness and worry about calamitous events, capture the maintenance component of separation anxiety. Somatic complaints such as headaches, stomachaches, and nausea are common in youth with anxiety disorders in general and SAD in particular (e.g., Last, 1991).

Typically, somatic complaints occur in response to anticipated separations. At times, the somatic complaints may serve an attention-getting function or be utilized in an effort to postpone separation (see Eisen & Schaefer, 2005 for a full explication). However, it is not so much the experience of somatic complaints that is daunting, but the fear of their implications. For instance, most youth can tolerate the periodic experience of feeling nauseous. But it is the fear of becoming ill that the nausea triggers, that leads to avoidance behaviors. Although the youngster's fear may be limited to one or two somatic sensations (e.g., vomiting, choking), this fear is very similar to the process of interoceptive avoidance that is characteristic of adults with PD (Barlow, 2002).

While a fear of physical illness often maintains a fear of being alone, worry about calamitous events is more likely to be associated with a fear of abandonment. Children with abandonment fears worry about getting dropped off places because of fear of not getting "picked up." This worry is triggered by catastrophic outcomes possibly occurring to the major attachment figure, such as being killed in a car accident. For this reason, unless promised close proximity to the

caregiver, children may avoid a wide variety of situations.

Given the insecure nature of separation-anxious symptoms, it is not surprising that children seek safe persons, places, objects, or actions during anticipated separations. Safety signals help individuals feel more secure and restore control in anxiety-provoking situations (Barlow, 2002).

Safety signals are frequently present across the dimensions of separation anxiety. For example, being with safe persons such as a best friend or nurse, having access to safe objects such as a blankie or water bottle, or engaging in safe (distracting) activities such as watching television or playing video games can help children be alone or be dropped off places without the major attachment figure.

What is important to keep in mind, however, is that excessive reliance on safety signals may strengthen anxiety (through avoidance) and ultimately result in a limited range of social and emotional functioning. Thus, the gradual elimination of unhealthy safety signals and the learning of new coping strategies are the key goals in facilitating positive treatment outcomes in youth with separation anxiety.

Separation Anxiety Subtypes

In order to facilitate individualized case formulation and treatment, separation anxiety subtypes (please refer to Table 17.1) were developed based on symptom dimensions and specific safety needs (see Eisen & Engler, 2006; Eisen, Pincus et al., 2008; Eisen, Raleigh, et al., 2008; Eisen & Schaefer, 2005). For example, the "follower" refers to a child with a fear of being alone during the day (somewhere in the house when others are present) that is maintained by a fear of physical illness. The safety need that emerges is a "medical monitor," i.e., someone to stay nearby just in case illness develops. The "visitor" is afraid to be alone at night and that fear is maintained by worry about calamitous events. The chief worry is that someone will break into the house. The safety need that emerges is a "security guard," i.e., someone to remain alert at night for signs of a break-in.

The subtypes that capture the fear of abandonment include the "misfortune teller" and the "timekeeper." The misfortune teller's fear of abandonment is maintained by a fear of physical illness. The safety need that emerges is a "lifeguard," i.e., someone who can remain nearby such as a nurse, coach, or friend that can prevent or minimize the likelihood of illness occurring. Finally, the timekeeper's fear of abandonment is maintained by worry about parental safety. The safety need that emerges is a "parental bodyguard," i.e., a need for constant access to the major caregiver's whereabouts or promises to stay at home.

This framework makes sense given the high prevalence of separation-anxious symptoms, and the findings that sub-clinical problems (i.e., less than three diagnostic symptoms) are often associated

Table 17.1 Separation anxiety subtypes and safety needs

Separation anxiety subtype	Safety needs
Follower Fear of being alone during the day, maintained by a fear of physical illness	Medical monitor Someone to stay nearby just in case illness develops
Visitor Fear of being alone at night, maintained by worry about calamitous events (intruder)	Security guard Someone to remain alert at night for signs of a break-in
Misfortune teller Fear of being abandoned, maintained by a fear of physical illness	Lifeguard Someone who can remain nearby to protect/from physical illness (panic)
Timekeeper Fear of being abandoned, maintained by worry about calamitous events (parental safety)	Parental bodyguard Child needs constant access to parent's whereabouts by sight, sound, or parental promises

with significant psychosocial impairment (2005, Foley et al., 2008; Hajinlian et al., 2003).

Assessment

In this section, we review widely used empirical assessment methods to assess childhood anxiety in general and separation anxiety in particular. As a first step, it is important to gather developmental history in general (e.g., pregnancy and birth, motor development, toilet training, speech/language, school, and medical histories) and any relevant information that may be associated with a child's heightened sensitivity to developing and/or maintaining separation anxiety (e.g., adverse events associated with separations from caregivers). A comprehensive assessment consists of structured interviews, child self-report measures, parent-completed measures, teacher reports, and behavioral observations.

Structured Clinical Interviews

A number of structured interviews (child and parent versions) are available to assess child behavioral and emotional disorders. Each of the following interview schedules possesses adequate psychometric properties (see Silverman, 1991) and include: Diagnostic Interview Schedule for Children (DISC; Costello, Edelbrock, Dulcan, Kalas, & Klaric, 1984), Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS; Puig-Antich & Chambers, 1978), Diagnostic Interview Schedule for Children and Adolescents (DICA; Herjanic & Reich, 1982), Interview Schedule for Children (ISC; Last, Strauss, & Francis, 1987) Child and Adolescent Psychiatric Assessment (CAPA; Angold & Costello, 2000), Child Assessment Schedule (CAS; Hodges, Kline, Stern, Cytryn, & McKnew, 1982), and the Anxiety Disorders Interview Schedule for DSM-IV (ADIS-DSM-IV-C/P; Silverman & Albano, 1996; Silverman, Saavedra, & Pina, 2001).

When assessing anxiety and related problems, however, we employ the ADIS-DSM-IV-C/P since it provides the most comprehensive coverage of DSM-IV anxiety disorders. More importantly, the section on SAD covers not only anxiety symptoms but also etiology, developmental precursors, and a functional analysis of the disorder. Finally, the ADIS-DSM-IV-C/P also permits differential diagnosis for the majority of other child behavior and emotional disorders.

Child Self-Report Measures

Child self-report measures are useful for identifying salient characteristics of anxiety disorders. Of particular use for identifying features of separation anxiety include:

Multidimensional Anxiety Scale for Children (MASC; March, Parker, Sullivan, Stallings, & Connors, 1997), Child Anxiety Sensitivity Index (CASI; Silverman, Fleisig, Rabian, & Peterson, 1991), Revised Children's Manifest Anxiety Scale (RCMAS; Reynolds & Richman, 1978), State-Trait Anxiety Inventory for Children (STAIC; Spielberger, 1973), and the Fear Survey Schedule for Children-revised (FSSC-R: Ollendick, 1983).

Multidimensional Anxiety Scale for Children contains 45 items, possesses strong psychometric properties, and includes a separation anxiety subscale (e.g., "I keep the light on at night"). In addition to corroborating a diagnosis of SAD, the MASC is also helpful for identifying social anxiety and somatic complaints.

Child Anxiety Sensitivity Index contains 18 items, possesses strong psychometric properties, and measures how aversive children view the experience of physical sensations (e.g., "It scares me when I feel like I am going to throw up"). Elevated scores on the CASI are helpful for identifying separation-anxious youth with a proneness to panic (Kearney et al., 1997).

Revised Children's Manifest Anxiety Scale contains 37 items, possesses strong psychometric properties, and yields four subscales including Worry/Oversensitivity, Physiological, Concentration, and Lying. The RCMAS includes a number of separation-related items such as "It is hard for me to get to sleep at night", "Often I feel sick to

my stomach", "I wake up scared some of the time", "I worry when I go to bed at night" and "I often worry about something bad happening to me." Elevated scores on the RCMAS are useful for distinguishing youth with GAD from SAD (Eisen et al., 2008).

State-Trait Anxiety Inventory for Children contains two 20-item scales that measure state (variable) and trait (stable or chronic) anxiety. Both scales possess strong psychometric properties (Spielberger, 1973) and contain relevant items for assessing SAD. For example, "I worry about school" and "I worry about my parents." Like the RCMAS, elevated trait anxiety scores are helpful for distinguishing SAD from GAD.

Fear Survey Schedule for Children-Revised contains 80 items, possesses strong psychometric properties, and measures general fearfulness. Separation-related items include "Having to go to school," "Being alone," and "Being left at home with a sitter." Like the RCMAS, the FSSC-R is useful for distinguishing youth with GAD from youth with separation anxiety and/or school refusal behavior (Last, Francis, & Strauss, 1989).

Until recently, separation anxiety was assessed solely at the level of the symptom.

However, Eisen and colleagues developed the *Separation Anxiety Assessment Scale-Child and Parent Versions* (SAAS-C/P; Eisen, Hahn, Hajinlian, Winder, & Pincus, 2005). The SAAS-C goes beyond assessing separation anxiety at the level of the symptom, by providing a conceptual framework that permits individualized case formulation and treatment planning (see Eisen & Schaefer, 2005 to obtain a copy of the scale and permission for use, and Eisen, Pincus et al., 2008; Eisen, Raleigh, et al., 2008 for guidance in treating related anxiety disorders).

The SAAS-C is a 34-item empirically derived self-report measure designed to assess the key dimensions of separation anxiety including a fear of being alone (e.g., "How often are you afraid to sleep alone at night?"), fear of abandonment (e.g., "How often are you afraid to go on a play date at a new friend's house?"), fear of physical illness (e.g., "How often are you afraid to go to school if you feel sick?"), and worry about calamitous events (e.g., "How often do you worry that bad things will happen to you?"). The SAAS-C also contains a nine-item safety signal index that assesses a child's dependence on safe persons, places, objects, and actions (e.g., "How often do you need your mom or dad to stay with you when you go on a play date?"). The frequency of symptoms is scored on a 1 (Never) to 4 (All the time) scale. Preliminary data support the psychometric properties of the scale (Hahn et al., 2003; Hajinlian et al., 2003, 2005; Hashim, Alex, & Eisen, 2006).

Parent Measures

Given that discrepancies often emerge between child and parent reports, parent-completed measures should be included in the assessment process. As a first step, the SAAS-P should be administered to parents. The SAAS-P is similar to the child version regarding both the content and structure of the questions.

In order to assess a broad range of internalizing and externalizing behavior problems, the *Child Behavior Checklist* (CBCL; Achenbach, 1991a) and/or the *Connors Rating Scale-Parent Version Revised* (CRS-PVR; Conners, 1997) should be administered. The CBCL contains 118 items and measures a broad range of internalizing and externalizing behavior problems. The CBCL also contains separate age and gender profiles, possesses strong psychometric properties, and relies on a national normative base. Relevant subscales for assessing separation anxiety include withdrawn, somatic complaints, and anxious/depressed. The CRS-PVR is an excellent measure to consider if there are time constraints (short form), and Attention-Deficit-Hyperactivity Disorder (ADHD) is a suspected comorbid disorder. Regarding separation anxiety, relevant subscales include psychosomatic, anxious-shy, and perfectionism.

Given the role that family dynamics often plays in the development and maintenance of anxiety in general, and separation anxiety in particular (Cobham, Dadds, & Spence, 1998; Eisen et al., 2008; Ginsburg & Schlossberg, 2002), an examination of the family environment is an integral part of the assessment process. Two key measures

include the *Family Environment Scale* (FES; Moos & Moos, 1986) and the *Family Adaptability and Cohesion Evaluation Scales-III* (FACES-III; Olsen, McCubbin, Barnes, et al., 1985).

Both measures possess strong psychometric properties and can be used to assess the family environments of anxious youth. The FES contains ten subscales. Relevant subscales for assessing separation anxiety include independence, cohesion, expressiveness, and control. The FACES-III addresses the degree to which families are enmeshed, disengaged, separated, or neglected.

Similarly, parent self-reports also afford a more complete clinical picture to emerge. Measures of parental anxiety, such as the *Beck Anxiety Inventory* (BAI; Beck, 1990) and the *Fear Questionnaire* (Marks & Mathews, 1979) as well as depression, e.g., *Beck Depression Inventory-II* (Beck, Steer, & Brown, 1996) are helpful for determining the impact that parental psychopathology may have on family-based treatment outcome (Barrett, Rapee, Dadds, & Ryan, 1996; Siqueland, Kendall, & Steinberg, 1996).

In addition to child, parent, and family measures, teacher reports are useful to consider, especially if the child's separation anxiety occurs in the school setting. Teacher measures can help clarify the relationship between a child's academic performance and anxious apprehension. The most widely used teacher measure is the *Teacher Report Form* (TRF; Achenbach, 1991b). The TRF possesses strong psychometric properties, contains a national normative base, and covers both internalizing and externalizing behavior problems. Collaboration among the clinician, school, and family helps identify anxiety-related issues and monitors a child's continued progress.

Finally, if possible, conducting behavioral observations can help circumvent potential biases associated with child, parent, family, and teacher measures. More importantly, behavioral observations can be measured during exposure-based assignments. In the clinic setting, for instance, children with SAD can be instructed to spend increasingly greater amounts of time alone (e.g., sitting in the waiting area). As a child develops its coping skills, exposures should become more anxiety provoking. For example, a parent can be encouraged to spontaneously run an errand and leave the child with the therapist. At home, parents can monitor behavioral observations as they arrange for their child (under guidance of therapist) to remain alone in a variety of situations while varying the timing (day vs. night), duration, and predictability of the exposures (see Eisen & Schaefer, 2005).

Evidence-Based Treatment

In this section, we provide an overview of cognitive–behavioral, family-based, and pharmacological treatment methods. There is a paucity of controlled empirical studies specifically devoted to investigating cognitive–behavioral interventions for SAD. However, a number of large-scale studies have included separation-anxious youth in their treatment programs.

Cognitive–Behavioral Treatment Methods

A recent meta-analysis of CBT treatment for anxious youth suggested that both individual and group versions of CBT are effective forms of therapy (Ishikawa, Okajima, Matsuoka, & Sakano, 2007). Given that group-based CBT can provide time and cost-effective care, emerging studies are integrating group elements into their treatment programs for anxious youth.

For example, Waters, Ford, Wharton, and Cobham (2009) examined the efficacy of group CBT for 80 children (60 by time of post-treatment), aged 4–8 years. Though a group treatment style was utilized, the actual purpose of the study was to compare CBT with parent only as the focus of treatment, to CBT in which both the parent and child were treated. Children with primary diagnoses of SAD, GAD, Specific Phobia (SP), or SOC were included in the study. Thirty-eight families were assigned to the Parent+Child condition (GAD=22.58%, SAD=19.35%, SOC=12.90%, SP=45.16%; 84% with at least one anxiety disorder), 31 were assigned to the Parent Only condition (GAD=10.52%, SAD=26.31%, SOC=23.68%,

SP=39.47%; 87% with at least one anxiety disorder), and 11 were assigned to a waitlist condition (GAD=27.27%, SAD=9.09%, SOC=27.27%, SP=36.36%; 82% with at least one anxiety disorder).

Treatment for children (P+C condition) consisted of ten 60-min sessions. Child treatment modules included psycho-education about anxiety and its physiological correlates, relaxation training, exposure, problem solving and social skills training, and replacing negative self-statements with calming/coping self-talk. Parent treatment content included psycho-education about anxiety, strategies for anxiety management, and tips on improving the parent–child relationship, learning skills taught in child treatment and how to best reinforce them, and training in communication and problem-solving skills. The Parent Only condition treatment was identical to the parent component of the P+C condition. Booster sessions were held 8 weeks after treatment to review skills and monitor progress.

Both Parent+Child and Parent Only conditions were effective in comparison to the waitlist control group. Seventy-four percent of children in the P+C group no longer met criteria for their primary anxiety diagnoses at post-treatment, and 61% no longer met criteria for any anxiety disorder diagnosis. Eighty-four percent of the Parent Only condition children no longer qualified for diagnoses of their primary anxiety disorders, while 60% no longer met any anxiety disorder diagnosis. Treatment gains for both groups were maintained at 6- and 12-month follow-up. Regarding the Waitlist condition, only 18% no longer met criteria for their primary diagnoses and 9% for any anxiety disorder diagnosis.

Overall, Parent Only CBT treatment, particularly in groups, has the potential to provide highly cost-effective and accessible care, as it essentially teaches the parents of anxious youth to become lay therapists. Parent Only CBT may be especially useful for young children with anxiety disorders, who may not readily grasp the more cognitive-based components of the therapy.

Parental involvement in treatment of child anxiety disorders can be extremely beneficial, as it generalizes elements of therapy to the home environment. For SAD in particular, family involvement can be integral to treatment gains. Families can become active participants in behavioral experiments (e.g., graded exposure to feared situations) involving separation from loved ones, as well as invaluable sources of information with regard to how separation-anxious behaviors are being maintained. This process is extremely important, since in many cases, parents inadvertently reinforce the anxious behaviors of their child (see McLean, Miller, McLean, Chodkiewicz, & Whittal, 2006; Pincus, Santucci, Ehrenreich, & Eyberg, 2008).

For this reason, Eisen and colleagues (Eisen & Engler, 2006; Eisen & Schaefer, 2005; Eisen et al., 2008) developed a 10-week integrated parent training (PT) program specifically designed for youngsters with separation anxiety. The program trains parents to implement cognitive–behavioral treatment strategies (relaxation training, cognitive therapy, contingency management, exposure) to their children at home. A preliminary study examined the program's efficacy (Eisen et al., 2008).

Six families with children aged 7–10 years with primary diagnoses of SAD were recruited. Ten weekly sessions were held with parents. The first two sessions focused on educating parents about the nature of separation anxiety. Sessions three through six involved skill building (e.g., progressive muscle relaxation, challenging anxious cognitive distortions). Sessions seven through nine allowed parents to practice newly learned skills (e.g., in vivo exposure outside of the sessions). The final sessions addressed issues of relapse prevention and stressed the need for continued practice and consistency. Weekly homework was assigned to reinforce content of the sessions.

In general, PT produced remarkable changes in parenting competence, stress and anxiety, and perceptions of child symptom severity. These changes translated to major reductions in children's somatic complaints and SAD symptoms. In fact, five of six child participants no longer met DSM-IV criteria for SAD. It is not surprising that family-based treatment programs are proliferating given the success of parental involvement in the treatment of childhood anxiety in general and SAD in particular.

Family-Based Treatment

Family-based treatment modalities for child anxiety stress the importance of family interactions in the development and maintenance of the child's symptoms. For example, Attachment-Based Family Therapy (ABFT) promotes child autonomy and individuation from parents through altering parenting factors, such as overprotection and parent–child communication style (Siqueland, Rynn, & Diamond, 2005).

In a preliminary investigation, Siqueland et al. (2005) compared ABFT to traditional CBT for adolescents aged 12–17 years. Eleven adolescents with primary diagnoses of GAD, SAD, or social phobia and their families were randomly assigned to either ABFT/CBT or CBT treatment. In the CBT condition, typical CBT components were utilized in 16 sessions (e.g., relaxation training, cognitive restructuring, exposure). The first eight sessions of the ABFT/CBT condition involved traditional CBT components. The remaining sessions, however, revolved around the family's beliefs, behaviors, and interactions, and the development of a flexible attachment style between parent and child. Treatment promoted open communication in families and facilitated opportunities for the adolescents to express themselves and develop strong self-identities.

At post-treatment, four of six adolescents in the CBT group no longer met diagnostic criteria for an anxiety disorder. By comparison, two of five in the ABFT/CBT group no longer met diagnostic criteria. At 6-month follow-up, none of the participants in the CBT condition met diagnostic criteria, while four of five did not in the ABFT/CBT group. Despite the limited sample size, ABFT shows promise and warrants further investigation as a potential treatment for separation-anxious youth.

Recently, Suveg et al. (2009) compared individual CBT to CBT with family involvement (FCBT), and Family-Based Education, Support, and Attention (FESA). FESA involved providing families with therapeutic support and attention during sessions, as well as education about child anxiety.

Participants consisted of 161 children, aged 7–14 years, with primary diagnoses of SAD ($n=47$), SP ($n=63$), and GAD ($n=88$) that were randomly assigned to one of the conditions. All treatments involved 16 weekly hour-long sessions. Individual CBT was conducted solely with the child, while both children and parents were the focus of treatment for FESA and FCBT. The first eight sessions of both CBT conditions involved psycho-education and skills training. The latter half included practicing skills and exposure tasks. All 16 sessions of FESA were devoted to education (not skills related), and supportive attention to child anxiety symptoms and family interactions.

Improvements in reported symptoms, functioning, and social competence were comparable across groups at post-treatment and 1-year follow-up. The results not only support the efficacy of CBT in both individual and family modalities but also indicate the utility of family education and therapeutic alliance with family members in treating child anxiety.

Family-based treatment programs are becoming increasingly innovative in helping anxious youth manage anxiety disorders. For example, Khanna and Kendall (2008) are in the process of developing and evaluating "Camp Cope-a-Lot: The Coping Cat CD-ROM", an interactive computer program meant to supplement face-to-face CBT treatment for children aged 7–13 years with SAD, GAD, and specific phobias. The Coping Cat CD-ROM program includes six computer-based independent sessions. These are meant to be accompanied by six in-person exposure sessions, two of which involve parent coaching. With the aid of the computer program and manual, the service provider does not necessarily need to be experienced in delivery of CBT, which could greatly broaden access to empirically supported treatment.

Computer sessions focus on education about feelings and anxiety, as well as anxiety management tools (e.g., exposure, shaping, social reward, and role-playing). The program should be completed in 12 weeks, with the child advancing one "level" per week. Preliminary findings suggest that this computer-assisted treatment may be effective. A clinical trial is currently underway to compare its efficacy to traditional CBT and

Education, Support, and Attention therapy (ESA). A similar computer program is also in development for adolescents ("Cool Teens;" see Cunningham, Rapee, & Lyneham, 2006). This innovative use of technology may increase the ease, access, and portability of treatment, as well as tapping into a new way of engaging anxious youth in therapy children in therapy.

Another novel implementation of family-based CBT involves a week-long summer-based treatment program for separation-anxious youth (Santucci, Ehrenreich, Trosper, Bennett, & Pincus, 2009). In their study, five girls, aged 8–11 years, with a primary diagnosis of SAD were recruited. At baseline, parents and children developed a Fear and Avoidance Hierarchy of the child's top ten feared situations. Items on the hierarchy were rated at baseline and throughout treatment. Components of treatment included psycho-education, identification, and management of somatic symptoms of anxiety, cognitive restructuring, problem-solving skills, and relapse prevention. Three 60-min parent coaching sessions were also incorporated, emphasizing parenting factors related to separation anxiety (e.g., encouraging child autonomy).

During the week, parental presence was gradually decreased, and rewards were given to the children for successful separation from their parents. Sessions began in the morning and afternoon, working up to an evening meeting, and finally culminating in a sleepover at the end of the week. Following the sleepover, parents rejoined their children to review skills, such as in vivo exposure in the home, and to discuss relapse prevention.

At post-treatment and 2-month follow-up, none of the participants met criteria for SAD, and all showed reduced fear and avoidance of items on their hierarchies. According to post-treatment ADIS-C/P scores, there was even some generalization of treatment to non-separation-related anxiety symptoms. Treatment satisfaction was high.

Though preliminary, the studies by Khanna and Kendall and Santucci and colleagues present new treatment delivery options for anxious youth that demonstrate promise. Both interventions address the time constraints that are so often impediments to accessing effective treatment for families. More importantly, these treatment methods allow for the dissemination of CBT across multiple settings, not necessarily restricting treatment to a clinic environment.

Pharmacological Treatment Methods

Significant progress has been made in establishing the safety and efficacy of psychopharmacological treatments for pediatric anxiety disorders (Gleason et al., 2007; Reinblatt & Riddle, 2007; Vitiello, 2007; Walkup, Albano, & Piacentini, et al., 2008). Although clinical research has demonstrated the safety and efficacy of medication, there are currently no pharmacological treatments approved by the Food and Drug Administration (FDA) for the treatment of non-OCD anxiety disorders in children and adolescents. Selective serotonin reuptake inhibiters (SSRIs) such as fluoxetine, sertraline, and fluvoxemine are the most commonly prescribed medication for GAD, SOC, and SAD in children and are considered to be an efficacious treatment modality for anxiety disorders (Keeton & Ginsburg, 2008; Reinblatt & Riddle, 2007; Walkup et al., 2008)

Recently, a large-scale NIMH-funded study indicated that CBT alone, sertraline alone (Zoloft), and their combination are effective therapies for children and adolescents aged 7–17 years, diagnosed with primary anxiety disorders (i.e., SAD, $n=16$; SOC, $n=55$; GAD, $n=33$; SAD with comorbid SOC, $n=33$; SAD with comorbid GAD, $n=30$; SOC with comorbid GAD, $n=137$) (Walkup et al., 2008). Participants were randomly assigned to combination therapy, sertraline only, CBT only, or placebo conditions.

The CBT treatment condition entailed 14 60-min sessions, which included reviews and ratings of anxiety symptoms, evaluating response to treatment, training in anxiety management, and exposure to anxiety-provoking situations. Though customized based on patient age and the duration of the study, session content was based on the Coping Cat program (Kendall & Hedtke, 2006a; Kendall & Hedtke, 2006b). The CBT condition also involved two parent only training and

education sessions, as well as weekly parent check-ins. The pharmacotherapy conditions (sertraline only or placebo) involved eight 30- to 60-min sessions in which anxiety symptoms and response to treatment were discussed. Dosage began at 25 mg, and was adjusted up to 200 mg by week 8. A matching dose of either sertraline or placebo was given, depending on assigned condition.

All active treatments produced improvement. For example, at 12 weeks, 80.7% of participants in the combination therapy condition reported that they were "very much improved," compared to 59.7% for CBT only, 54.9% for sertraline only, and 23.7% for the placebo condition. Combination therapy was superior to all other conditions, though all active treatments were more effective than placebo. Adverse reactions (e.g., hospitalization, suicidal/homicidal ideation) were minimal for all treatment conditions. In addition, participants in the CBT condition reported fewer side effects (e.g., restlessness, fatigue, insomnia) than the sertraline group. Given that all active treatments were shown to be effective, treatment recommendations for child anxiety disorders should consider the unique needs of the family (e.g., costs and time available).

Concluding Remarks

Despite SAD's unique status as the only anxiety disorder in DSM-IV-TR based solely on child criteria, the empirical treatment literature is not as well developed as for other anxiety and related disorders. In this chapter, we reviewed empirically supported assessment and treatment interventions for youth experiencing SAD. While recent large-scale treatment outcome studies have supported the efficacy for cognitive–behavioral interventions for anxiety disorders in general and SAD in particular, further research is necessary for clinical researchers to develop prescriptive treatment strategies (e.g., Chorpita, 2006; Eisen & Silverman, 1998).

Toward this aim, we presented a conceptual framework that affords individualized case formulation and treatment planning for youth experiencing separation anxiety and related problems (see Eisen, 2008; Eisen & Schaefer, 2005; Eisen et al., 2008).

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Generalized Anxiety Disorder

18

Carl F. Weems and R. Enrique Varela

The Treatment of Generalized Anxiety Disorder in Youth

This chapter reviews the literature on the treatment of Generalized Anxiety Disorder (GAD) in youth. We first discuss what GAD is, present key phenomenology, and make assessment recommendations. We next review the extant empirical data on treatment efficacy drawing heavily upon conclusions from several recent meta-analyses and focus on cognitive behavioral therapy (CBT) techniques and procedures as they have the most empirical support (Chambless & Ollendick, 2001; Silverman, Pina, & Viswesvaran, 2008). In this treatment study review, we focus on findings in terms of GAD treatment specifically. However, most, if not all, treatment studies to date have included other anxiety disorders in the samples, for example, separation anxiety disorder (SAD) and social anxiety disorder, and so specific conclusions about GAD are limited by that fact. We make conclusions about the general efficacy of CBT for GAD and then draw conclusions about treatment efficacy in terms of format (e.g., group vs. individual), and discuss any differential effects for ethnicity, age, and sex as well as other predictors of outcome that have been reported. We conclude the chapter with some "hands on" advice – how does one actually do CBT for GAD, with some suggestions for developmental modifications to the "how to" for younger children.

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Generalized Anxiety Disorder: Key Features

The Diagnostic and Statistical Manual of Mental Disorders-IV (American Psychiatric Association APA, 2000) provides criteria to make an anxiety disorder diagnosis and differential diagnostic criteria that distinguishes among the anxiety disorders. GAD is characterized by persistent and excessive worry about a number of events or activities. While worry can be normal (Borkovec, Shadick, & Hopkins, 1991; Mathews, 1990), the worries experienced in GAD interfere with the child's life preventing him/her from, for example, going to or doing well in school and interfering with friendships, etc. Children may worry about their school performance, their social relationships, and their health or the health of others. These children may seek constant reassurance and approval from others to help alleviate their worry. Most specifically impairing for youth with GAD appears to be the intensity of their worries (Weems, Silverman, & La Greca, 2000). These worries may disrupt family routines (e.g., bedtime, going to school, travel).

To be diagnosed with GAD according to DSM-IV criteria (APA, 2000), a child must exhibit excessive anxiety and worry for more days than not for at least 6 months and the child must find it difficult to control the worry. At least one of the following physical symptoms must

D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_18,

accompany the anxiety or worry: restlessness, being easily fatigued, difficulty concentrating, irritability, muscle tension or sleep disturbance. The focus of the anxiety and worry is not confined to features of another Axis 1 disorder (e.g., worry is not about a Panic Attack) and the anxiety, worry, or physical symptoms must cause significant distress or impairment in at least one important area of functioning (APA, 2000).

Clinically, worry has been and continues to be a central component of the DSM definition of GAD in children. Specifically, in DSM-IIIR (American Psychiatric Association, 1987), worry was a major clinical feature of Overanxious Disorder (OAD). Whereas the subsequent version, DSM-IV (American Psychiatric Association, 1994) eliminated OAD and subsumed it under GAD, worry nevertheless remains a major clinical feature of GAD in youth (Perrin & Last, 1997; Weems et al., 2000). Youth with GAD also have more somatic symptoms such as restlessness, stomachaches, blushing, palpitations, and muscle tension than youth with other anxiety disorders (Ginsburg, Riddle, & Davies, 2006), and research suggests youth with GAD may also have relatively more sleep problems (Alfano, Ginsburg, & Kingery, 2007).

Like all the anxiety disorders, GAD is highly cormorbid with other anxiety disorders in samples of clinic-referred anxious youth (e.g., Weems, Hammond-Laurence, Silverman, & Ginsburg, 1998) and also in general population samples (see Costello, Egger, & Angold, 2004). GAD may also be cormorbid with other disorders. Across studies, anxiety disorder comorbidity estimates with ADHD have ranged from 0 to 21%, with conduct disorder and oppositional defiant disorder from 3 to 13%, and with depression from 1 to 20% (Costello et al., 2004). Developmentally, GAD symptoms are most likely to become prominent around age 10–12 years but can be evident in children as young as 6 years (Costello et al., 2004; Weems, 2008).

Assessment

We suggest using a multimethod (e.g., parent and child reports) multitrait (e.g., DSM-based diagnostic interview and worry checklist) assessment (Weems & Stickle, 2005) to identify if treatment is warranted. In our work, we have used the Anxiety Disorders Interview Schedule for DSM-IV: Child and Parent Versions [(ADIS for DSM-IV: C/P; Silverman & Albano, 1996) and its previous edition (ADIS for DSM-III-R C/P; Silverman & Nelles, 1988)] to make diagnostic decisions. The ADIS has been the subject of several reliability and validity studies (e.g., Silverman & Nelles, 1988; Rapee et al., 1994) each demonstrating good estimates of reliability and validity for childhood anxiety disorders. Most recently, Silverman, Saavedra, and Pina (2001) found the ADIS for DSM-IV to have kappas ranging from 0.80 to 0.92 for 2- to 3-week test–retest reliability for SAD, social phobia (SoP), specific phobia (SP), and GAD. The ADIS has also been used in most randomized treatment studies for GAD and related anxiety disorders in youth (see Silverman et al., 2008).

In addition to a diagnostic interview, we suggest assessing children's worries with a checklist or worry interview. For example, Perrin and Last (1997) developed a 31-item worry scale based on DSM-III-R criteria for OAD, avoidant disorder (AD), SAD, and social phobia. Chorpita, Tracey, Brown, Colluca, and Barlow (1997) have adapted the Penn State Worry Questionnaire for use with children (PSWQ-C). Using a community sample ($n = 199$), Chorpita et al. (1997) examined the psychometric properties of this 16-item instrument and found good internal consistency as well as convergent and discriminant validity. Vasey, Crnic, and Carter (1994) have developed a vignette-based interview strategy to provide a developmental examination of the process of children's worries. Case vignettes were used to provide a context for assessing children's ability to conceive of threatening possibilities and the frequency of worrisome thoughts for each of three hypothetical vignettes is computed.

We have used the Worry Interview for Children (WIC; Silverman, La Greca, & Wasserstein, 1995) in our research (Weems et al., 2000). The WIC is a semi-structured interview and was designed to assess children's worries in 14 areas: School, Performance, Classmates, Friends, War, Disasters, Money, Health, Future Events, Personal Harm, Little Things, Appearance, Family, and Other worries not covered by previous categories.

For each worry reported, the child is asked to rate how much (i.e., intensity) they worried about the item on a five-point scale (0 = none, 1 = a little bit, 2 = some, 3 = a lot, 4 = very very much). Further, children are asked to rate how often (i.e., frequency) they worried about the item (0 = none, 1 = some, 2 = a lot). The interview has good reliability and validity. For example, test–retest reliability of the WIC for the total number of worries ($r = 0.75$) and the total number of areas of worry ($r = 0.78$) has been reported (Silverman et al., 1995). The interview scores discriminate anxious children from nonanxious children and youth with GAD from those with other anxiety disorders (see Silverman et al., 1995; Weems et al., 2000).

Cognitive Behavioral Therapy for GAD in Youth

CBT is a psychosocial treatment that emphasizes the role of cognitions and behavioral learning in the development, maintenance, and amelioration of emotional problems. CBT has several characteristics from the cognitive tradition (e.g., Beck, 1976) as well as from the behavioral tradition (Skinner, 1953; Wolpe, 1958). CBT is time limited and the typical number of sessions children receive varies from around 10 to 16. While CBT is conceptualized as a collaborative effort between the therapist and the client, it is relatively more structured and therapist directed than other therapies (e.g., client-centered therapy, play therapy, psychoanalysis). CBT is based on an educational model with the goal being to help clients unlearn their unwanted reactions and to learn new ways of reacting. Homework is also a central feature of CBT for childhood anxiety disorders.

Cognitive therapy is based on the idea that our thoughts influence our feelings and behaviors and has its roots in the work of Aaron Beck and others in the cognitive tradition (Beck, 1976; Lang, 1977). Behavior therapy or behavior modification is the treatment of behavioral and emotional disorders through the reinforcement of desired behavior and suppression of undesirable behavior. The behavioral techniques have their roots in the experimental work of Ivan Pavlov (respondent tradition) and B. F. Skinner (operant tradition) as well as the applied work of Joseph Wolpe and Nathan Azrin (see Kazdin, 1978, 2001). Contingency management and reinforcement strategies, for example, follow from the operant conditioning paradigm while systematic desensitization follows from the respondent paradigm. These traditions (cognitive and behavioral) have been largely integrated in current CBT treatment manuals for childhood anxiety (Barrett, 1998; Kendall, 1994; Silverman, Kurtines, Ginsburg, Weems, Lumpkin, et al., 1999; Silverman, Kurtines, Ginsburg, Weems, Rabian, et al., 1999). Specific techniques are discussed further below and are outlined in Table 18.1.

Anxiety disorders such as GAD in childhood and adolescence are highly prevalent and can cause intense psychosocial impairment (Langley, Bergman, McCracken, & Piacentini, 2004; Silverman & Treffers, 2001). For example, children with GAD often have difficulty studying for and taking tests, poor school attendance, intense somatic symptoms, and school refusal (Pina, Silverman, Alfano, & Saavedra, 2002; Weems et al., 2000). As noted, the literature also shows that children diagnosed with GAD experience more sleep-related problems (Alfano et al., 2007) and somatic symptoms (Ginsburg et al., 2006) than clinically anxious youth without GAD.

The field has advanced with demonstrated efficacy of cognitive behavioral and pharmacological strategies in the treatment of childhood anxiety and phobic disorders (see Albano & Kendall, 2002; Creswell & Cartwright-Hatton, 2007; Kendall, 1994; Ollendick & King, 1998; Silverman et al., 2008; for a review of pharmacological interventions see Walkup, Labellarte, & Ginsburg, 2002). Central to CBT interventions for anxiety problems are exposure-based anxiety-reduction strategies (i.e., relaxation training consisting of progressive muscle relaxation and deep breathing paired with gradual approach to fearful stimuli followed by positive reinforcement of progress through praise or tangible reinforcers). Also central to CBT are cognitive self-control training strategies (see Silverman & Kurtines, 1996). The latter involve teaching children to self-observe, self-talk (identify and modify), self-evaluate, and self-reward (see also Kendall, 1994).

Table 18.1 Common techniques used in CBT for childhood anxiety disorders

Technique	Description	Example use for GAD
Graduated exposure	The basic idea is that you cannot run from your problems/fears, you must face them head on	This means confronting the worry (i.e., fully processing the worry or worry-provoking stimulus). Worry hierarchy is developed and therapist helps client face from least intense to most intense
Relaxation training	Training in progressive muscle relaxation and deep breathing	When worries arise client is instructed to do relaxation exercises
Systematic desensitization	Relaxation training paired with exposures along a hierarchy	Condition a relaxed response to worries or worry-provoking stimuli by pairing "relaxation" with increasing levels (or hierarchy) of the worries or worry-provoking stimulus
Self-monitoring	Systematic observation and recording of target behaviors	Client keeps a daily record of worries and the things that prompted the intense worry
Cognitive modification-challenging irrational beliefs	Often termed "cognitive restructuring" (Aaron Beck) An array of strategies utilized to identify and restructure maladaptive and distorted cognitions	Identification of the cognitive causes of the worries in GAD and teaching of positive self-talk, challenging beliefs and worry schemas. Socratic method of challenging irrational beliefs Empirical demonstrations of the fallacy of the belief with the use of mini experiments and exposure hierarchy
Contingency management	Designed to facilitate child graduated exposure by using behavioral contingency management procedures. Specific principles and procedures positive reinforcement, shaping, extinction, and contingency contracting	Contracts are written between the parent and child that details the child exposure task (i.e., the step on the hierarchy) as well as the details of the reward that the parent would give to the child (i.e., an item on the reward list) as a consequence for successful completion of the exposure task
Modeling	The therapist acts out appropriate reactions to different situations	The client models the therapist's positive solutions to the worries

Review of Outcome Studies

The number of studies examining the efficacy of psychosocial treatments for anxiety disorders in childhood has grown substantially in the past 20 years. In 1998, Ollendick and King reviewed the anxiety treatment literature and found only four studies using randomized control designs. More recent reviews of the literature indicate that there are at least 23 well-designed studies demonstrating the efficacy of CBT that have been conducted since Ollendick and King conducted their review with 19 of these studies including children with GAD diagnoses (see Barrett & Farrell, 2007; Silverman et al., 2008).

The majority of treatment studies that have included children with GAD have employed individual or group treatment formats (ICBT, GCBT) with some also including a Parent component. Several of these studies have included only a small number of youth whose primary diagnosis was GAD or OAD (e.g., Bogels & Siqueland, 2006; Heyne et al., 2002; King et al., 1998; Nauta, Scholing, Emmelkamp, & Minderaa, 2003; Öst, Svensson, Hellström, & Lindwall, 2001; Wood, Piacentini, Southam-Gerow, Chu, & Sigman, 2006). Although no study has focused solely on the treatment of GAD, several have included a relatively large number of youth diagnosed with GAD. In the following sections, we review this literature with a focus on studies in which a large portion of the youth participants had a primary diagnosis of GAD or OAD.

Individual Format: Kendall (1994) reported the first large-scale clinical trial in which individual child-focused cognitive behavioral treatment (ICBT; $n = 27$; aged 9–13 years) was found to be

efficacious relative to a waitlist control condition ($n=20$) using a randomized design and employing multimethod assessment and diagnostic interviews (e.g., structured interviews, multisource assessment). Primary diagnoses in the sample were OAD ($n=30$), SAD ($n=8$), and AD ($n=9$). Sixty-four percent of the children in the treatment group no longer met criteria for an anxiety disorder after treatment, whereas only one child in the control condition no longer met criteria for a diagnosis after the wait period. Analyses of treatment effects by diagnosis indicated no differential treatment effects for children diagnosed with OAD vs. other diagnoses.

In a similar study using a randomized design and employing a multimethod assessment, Kendall et al. (1997) replicated his initial findings on ICBT with a larger sample ($n=94$) of 9–13-year-old children with a primary diagnosis of anxiety; OAD ($n=55$), SAD ($n=22$), AD ($n=17$). Participants were randomly assigned to a 16-week cognitive behavioral treatment or an 8-week waiting-list (WL) control condition. Assessments occurred pretreatment, mid-treatment, posttreatment and at 1-year follow-up. Results indicated that per parent ADIS interview 71.28% of the treated children no longer had their primary diagnosis as primary at the end of treatment and 53.19% no longer met criteria for their primary anxiety disorder at posttreatment based on either parent or child ADIS interviews. Gains were maintained at 1-year follow-up for most dependent variables. By comparison, only two of the children in the waitlist condition no longer met criteria for their primary anxiety disorders at the end of the waitlist period. Kendall et al. (1997) also examined treatment effects by diagnosis. They concluded that there were no overall differences in treatment effects among OAD, SAD, and AD. However, there were significant Diagnoses by Trials interactions in predicting the mother report STAIC-P and the CBCL internalizing scale with simple main effects tests revealing reductions only for the OAD and SAD groups. Another interaction in predicting TRF Internalizing scale scores was also significant with reductions in scores only for the OAD group.

Barrett, Dadds, and Rapee (1996) examined the efficacy of the CBT approach developed by Kendall and colleagues with an Australian sample of clinically anxious 7–14-year-old children; OAD ($n=30$), SAD ($n=30$), SoP ($n=19$). The children were randomly assigned to one of three 12-week conditions: CBT ($n=28$), CBT plus a parent component referred to as FAM (CBT + FAM) ($n=25$), or a WL condition ($n=26$; treated after the waitlist period); 69.8% of the children ($n=37$) in the treatment conditions no longer met criteria for an anxiety disorder following treatment compared to 26% of the children ($n=6$) in the WL condition after the waiting period. There was also a difference between the treatment conditions with 84% of the children in the CBT+FAM condition no longer meeting criteria compared to 57% of the children in CBT alone condition. This difference was no longer significant at a 6-month follow-up, but was significant again at a 1-year follow-up with 70.3% of the children in the CBT group no longer meeting criteria for an anxiety disorder compared to 95.6% of the children in the CBT+FAM group. Barrett et al. did not find significant differences in treatment outcome by type of pretreatment diagnosis (GAD, OAD, SoP).

Dadds, Heard, and Rapee (1992) had also demonstrated that CBT+FAM ($n=7$) was superior to a waitlist condition ($n=7$) in a relatively small sample of 7–14-year-old anxious youth; OAD ($n=10$), SAD ($n=4$), with five of the seven children in the treatment condition no longer meeting criteria for an anxiety disorder diagnosis at posttreatment. All seven children in the waitlist condition continued to meet criteria for an anxiety disorder at end of the treatment period. Treatment effects by diagnosis were not reported.

Two other studies have examined the efficacy of ICBT in comparison to group cognitive behavioral treatment (GCBT) (Flannery-Schroeder & Kendall, 2000; Manassis et al., 2002). Flannery-Schroeder and Kendall randomly assigned 8–14-year-old anxious children to one of three conditions: 18-week ICBT ($n=13$), 18-week GBCT ($n=12$), or 9-week waitlist (WL) ($n=12$; treated after the waitlist period). Primary diagnoses were GAD ($n=21$), SAD ($n=11$), and SoP ($n=5$). The group treatment was developed based on Kendall's earlier ICBT work (see Flannery-Schroeder & Kendall, 2000). Results showed that

73% of the children in the ICBT group and 50% of the children in the GCBT group did not meet criteria posttreatment for their primary anxiety disorder. Only 8% of the children in the WL condition did not meet criteria for their primary anxiety disorder at posttreatment. Differences between the two treatment conditions and the WL condition were significant but the two treatment conditions were not significant from each other. In addition, 64% of children in the ICBT group and 50% of children in the GBCT group no longer met criteria for any anxiety disorder following treatment. At 3-month follow-up, 79% of children in ICBT and 53% of children in GBCT did not meet criteria for their primary diagnosis and 50% of children in ICBT and 53% in the GBCT did not meet criteria for any anxiety disorder (GAD, SAD, SoP). Treatment effects by diagnosis were not reported.

Manassis et al. (2002) randomly assigned 78 clinically anxious 8–12-year-old children to a 12-session ICBT ($n=41$) condition or a 12-session GCBT ($n=37$) condition. In both conditions, parents received a parent training program. Primary diagnoses were GAD (60.3%), SAD (25.6%), simple phobia (SP) (6.4%), SoP (6.4%), and Panic Disorder (1.3%). Both conditions were shown to lead to significant improvements in parent and child report measures, and only clinician ratings varied by treatment group with clinicians rating the ICBT group as showing more gains than the GCBT. Independent of treatment condition, children with GAD showed more gains as reported by mothers than children with other diagnoses.

In sum, ICBT has been shown efficacious to waitlist controls in a number of well-designed randomized control studies with samples consisting of a large portion of youth diagnosed with GAD/OAD. In addition, where ICBT was compared with GCBT, there were no consistent differences, but when differences were found, these favored ICBT. Similarly, when outcomes were compared by diagnosis, there appear to be fairly inconsistent results. However, when differential gains were found, these tended to be relatively better results for youth whose primary diagnosis was GAD/OAD.

Group Format: A group format has also shown efficacy for the treatment of GAD. Barrett (1998) was the first to demonstrate that group cognitive behavioral treatment (GCBT; $n=23$, GCBT + FAM; n = 17) was efficacious relative to a waitlist control condition ($n=20$) (age 7–14 years). Primary diagnoses were: OAD ($n=30$), SAD ($n=26$), and SoP ($n=4$). The percentage of children who were improved (i.e., no longer met DSM-III-R criteria for any anxiety disorder) was significantly greater for children in GCBT (55.9%) and GBTC+FAM (70.7%) than for children in the waitlist control condition (25.2%). There was no significant difference between the two treatment groups. Treatment effects by diagnosis were not reported.

Silverman, Kurtines, Ginsburg, Weems, Lumpkin, et al. (1999) also used a randomized clinical trial to evaluate the efficacy of group cognitive behavior therapy (GCBT) vs. a waitlist control condition to treat GAD ($n=8$; or 22% of the completers in the sample had GAD); OAD ($n=17$; 46% of the sample); or SoP ($n=12$; 32% of the sample). Results indicated that GCBT was efficacious in producing and maintaining treatment gains (youth in GCBT showed substantial improvement on all the main outcome measures. These gains were maintained at 3-, 6- and 12-month follow-up and youth in the waitlist control condition did not show improvements from the pre- to the post-wait). In particular, using the ADIS-C/P diagnoses, 64% (16/25) of the participants in GCBT were recovered at posttreatment (i.e., no longer met primary diagnoses); 12.5% (2/16) in the waitlist condition were recovered at post-wait. Although there was no differential effect for type of primary anxiety diagnosis, comorbid child depression and parent depressive symptoms were associated with less favorable outcomes (see Berman, Weems, Silverman, and Kurtines, 2000). We review additional predictors of efficacy in the next section.

Predictors of Treatment Outcome

Of the ICBT and GBCT studies targeting GAD reviewed above, most examined potential moderating effects of some key demographic and related

variables on treatment outcomes. No moderating effects were found for gender (Silverman, Kurtines, Ginsburg, Weems, Lumpkin, et al., 1999; Silverman, Kurtines, Ginsburg, Weems, Rabian, et al., 1999; Manassis et al., 2002), or age and comorbid status (Silverman, Kurtines, Ginsburg, Weems, Lumpkin, et al., 1999; Silverman, Kurtines, Ginsburg, Weems, Rabian, et al., 1999; Kendall et al., 1997). Only one study found main effects for treatment outcomes based on gender and age (Barrett et al., 1996). Specifically, for females, the CBT+FAM condition was more effective than the CBT alone condition at the end of treatment and at 1-year follow-up. Younger children (7–10 years) had higher rates of diagnosis-free participants at posttreatment and at 1-year follow-up in the CBT+FAM condition compared to young children in the CBT alone condition. The older children (11–14 years) did not show differences in treatment effects across outcomes.

Of the studies reviewed, only Silverman, Kurtines, Ginsburg, Weems, Lumpkin, et al. (1999) and Silverman, Kurtines, Ginsburg, Weems, Rabian, et al. (1999) included a sufficient number of ethnic minorities, mostly Hispanic/Latino ($n=26$), to examine moderating effects of ethnicity on treatment outcomes. They found that ethnicity did not moderate treatment effects. Two subsequent studies combined the two samples from the Silverman, Kurtines, Ginsburg, Weems, Lumpkin, et al. (1999) and Silverman, Kurtines, Ginsburg, Weems, Rabian, et al. (1999) and re-analyzed those data to examine the equivalence of treatment effects across Hispanic/Latino and white Non-Latino youth (Pina, Silverman, Fuentes, Kurtines, & Weems, 2003) and to identify potential moderating effects of ethnicity, other child individual characteristics, and parent mental health in treatment outcomes (Berman et al., 2000). Although the samples for these two studies include children with a large portion of other anxiety disorders in addition to GAD, we review them considering the scarcity of research in this area with ethnic minorities.

Pina et al. (2003) examined the efficacy of exposure-based cognitive treatments on 6–16-year-old Hispanic/Latino youth ($n=52$) and European American youth ($n=79$). Primary diagnoses for the Hispanic/Latino youth were GAD/OAD ($n=10$), SAD ($n=4$), SoP ($n=10$), SP ($n=23$), and other ($n=5$). Primary diagnoses for the European American youth were GAD/OAD ($n=15$), SAD ($n=4$), SoP ($n=7$), SP ($n=46$), and other ($n=7$). Results indicated that 84% of Hispanic/Latino youth and 83.9% of the European American youth no longer met criteria for their primary diagnosis at posttreatment and these percentages were statistically equivalent. Treatment effects were also equivalent between the two cultural groups in clinically significant improvement and child- and parent-completed questionnaires. Treatment gains over time (3-, 6-, and 12-month follow-ups) were also generally equivalent across the two groups in most measures, with one exception. The European American youth reported more gains over time through use of the Revised Children's Manifest Anxiety Scale (RCMAS; Reynolds & Richmond, 1978).

One other study has focused on ethnicity in the treatment of GAD using GCBT. Ginsburg and Drake (2002) randomly assigned 12 African American 14–17-year-old adolescents to a GBCT condition ($n=6$; four completed) or an attention and support (AS) condition ($n=6$; five completed). Primary diagnoses of completers were GAD ($n=5$), SoP ($n=2$), and SP ($n=2$). The GBCT protocol was 10 weeks and was based on the work of Silverman, Kurtines, Ginsburg, Weems, Lumpkin, et al. (1999) and Silverman, Kurtines, Ginsburg, Weems, Rabian, et al. (1999). At posttreatment, three of the four youth in the GCBT condition no longer met criteria for their primary diagnosis and one of the five youth in the AS condition no longer met criteria for their primary diagnosis.

Berman et al. (2000) examined a number of potential moderators of treatment outcomes of exposure-based CBT with data from the Silverman, Kurtines, Ginsburg, Weems, Lumpkin, et al. (1999) and Silverman, Kurtines, Ginsburg, Weems, Rabian, et al. (1999) studies. They found that comorbid diagnoses of depression (assessed through the ADIS, C/P), depressive symptoms (measured with the Children's Depression Inventory, CDI; Kovacs, 1981), and trait anxiety (measured with the State Trait

Anxiety Inventory for Children – Trait Version, STAIC; Spielberger, 1973) at pretreatment were associated with treatment failure, defined as not having "recovered" (i.e., no longer meeting criteria for the DSM diagnostic criteria for the primary and targeted phobic or anxiety disorder). Parents' global severity ratings on the Symptom Checklist – 90 (SCL – 90; Derogatis, 1983), parents' symptom scores on the obsessive–compulsive, psychoticism, depression, hostility, and paranoia subscales of the SCL-90, parents' self-rating of depression (measured with the Beck Depression Inventory, BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), and parent self-ratings of anxiety (assessed with the Fear Questionnaire; Marks & Matthews, 1979) at pretreatment were also associated with treatment failure as defined above. Age, income, and primary anxiety diagnosis were not predictors of success or failure in therapy.

In addition, children's scores on the STAIC and parents' global severity score on the SCL-90 and scores on the depression, hostility, obsessive–compulsive, and paranoia subscale of the SCL-90 at pretreatment were associated with poor outcomes gauged by a lack of a drop of four points or more on a eight-point clinicians' severity scale. Children's scores on the CDI and STAIC and parents' scores on each of the subscales of the SCL-90 predicted post-treatment clinicians' ratings of symptom severity (i.e., more than 5% of variance in severity ratings explained) for those involved in individual treatment, whereas only the children's scores on the RCMAS and Externalizing subscale of the CBCL were predictive of severity ratings for those in group treatment (i.e., more than 5% of variance explained). SCL-90 global severity rating, and scores on the depression, hostility, somatization, paranoia, obsessive–compulsive, and psychoticism subscales of the SCL-90 predicted clinician's ratings (i.e., more than 5% of variance explained) of symptom severity at posttreatment for children under 12 years old. For adolescents (12 years or older), CDI scores and parents' scores on the Internalizing scale of the CBCL and parents' score on the RCMAS were predictive of severity ratings (i.e., more than 5% of variance explained).

Southam-Gerow, Kendall, and Weersing (2001) also examined potential effects of a number of child, parent, and environmental characteristics on treatment outcomes, specifically good treatment response (i.e., not meeting criteria for any anxiety disorder based on ADIS -P) vs. poor treatment response (i.e., meets criteria for one anxiety disorder immediately after treatment ($n = 135$) or at 1-year follow-up ($n = 107$) based on ADIS-P). They combined the samples from the Kendall (1994) and Kendall et al. (1997) studies and re-analyzed those data (85% of total *N* for their analyses) in combination with new data collected in the same anxiety clinic (15% of total *N* for their analyses). Pretreatment primary diagnoses were OAD or GAD (59%), SAD (24%), SoP or AD (17%). They found that higher scores on the withdrawn subscale of the CBCL and higher scores on the Anxious/Depressed subscale of the Teacher Report Form (Achenbach, 1991) were associated with poor treatment response immediately following treatment and at 1-year follow-up. In addition, being older was associated with poor treatment response immediately following treatment and mother depression (measured by the BDI) was associated with poor response to treatment at 1-year follow-up. Ethnicity, gender, family income, family composition, and a measure of therapeutic relationship did not have an effect on treatment outcome.

In all, the available literature indicates little or no differential effects of ICBT and GCBT for GAD based on demographic variables (i.e., gender, family income, and ethnicity) and primary anxiety diagnosis, but other variables appear to affect treatment outcomes. Specifically, comorbid depression, severity of anxiety symptoms, and parental psychopathology each have tended to be associated with poorer outcomes. In addition, although effective across ages, CBT-based treatments may be even more effective for younger children with GAD. Additional attention to moderators and mediators of efficacy is needed in the next generation of outcome studies.

Practical Suggestions for Implementing CBT for Youth with GAD

For clinicians new to the treatment of anxiety in youth, we would suggest using one of the excellent guides for professionals (e.g., Silverman & Kurtines, 1996) and parents (reviewed in Weems, 2005). For example, the text *Treating Anxious Children and Adolescents* by Rapee, Wignall, Hudson, and Schniering (2000) was designed for professionals and presents their insights that they have gained from years of research and clinical work at their anxiety disorders research center and clinic. The goal of the text is to provide mental health professionals with understandable and detailed suggestions for conducting effective treatment procedures. Although not a treatment manual, the book provides sample treatment programs designed for different clinical contexts (i.e., the authors' typical program, a managed care setting, and an extended treatment setting) with illustrative case studies. Rapee, Spence, Cobham, and Wignall (2000) is a companion book for parents.

Table 18.1 delineated some of the common techniques used in CBT for GAD. In the following we provide some specific suggestions for doing treatment for youth with GAD. While CBT is directive we always take time to develop rapport with the child and their family and part of this work is done during the assessment process. Participants in our intervention work with anxiety disorders, including GAD, first learn about anxiety in general. To do this the therapist presents a cognitive and behavioral conceptualization of anxiety (see Silverman & Kurtines, 1996 for more detailed instructions). It is explained to client and his or her mother and father that when we are afraid or anxious, fear or anxiety is evident in three main ways: (1) body reactions, such as heart beating fast, (2) cognitions (e.g., talking to oneself, such as "I might fail"), and (3) behaviors, in particular, we avoid the feared object or event. We also explain that worry is natural because it helps us to plan for the future and anticipate future danger; however, when it gets too intense, it can interfere with our ability to do well in school or prevent us from doing the things we would like to do.

The therapist also takes time to explain the importance of exposure or approach behavior. With GAD it can be more difficult to help the client conceptualize this in terms of worry. "How am I supposed to approach my worry?" youth and parents may wonder. We explain that we will approach the things that make us worry (school, tests) and confront the worries. For a child who worries about crime or world events, this means talking about the specific concerns and processing the worry fully. Often worries are maintained by a superficial contemplation of the true dangers involved.

In initial sessions, youth are given an overview of the treatment and the therapist tries to create the sense that therapy is a joint effort between the counselor and the youth to help them worry less and to help them, so that the worry no longer interferes with their life. The overall rationale might be explained as being able to worry appropriately and so the emphasis is on mastery but not perfection (i.e., no worry at all is an unreasonable goal). The joint effort is facilitated by using the first session to develop a therapeutic alliance (i.e., emphasis in the initial sessions should also focus on empathetic understanding of the goals and desires of the client (both child and family).

The therapist also tries to foster a sense of universality about worry and youths develop a worry hierarchy in the initial session. Use of a worry interview can facilitate the ranking of the various worries from least fear provoking/interfering/intense to most fear provoking/interfering/intense. Later in treatment, the therapist will utilize various techniques (e.g., relaxation training) and client education (contingency management) to help the client face increasingly intense worries along the hierarchy.

We next begin to teach relaxation techniques. After the child has mastered the relaxation techniques (with in session and homework assignments), the relaxation techniques are then practiced during imagined exposure to the initial or lower-level hierarchy items. The goal of these sessions is to create a context where youth can practice their relaxation skills while "facing" or approaching items on the stimulus hierarchy. We find that homework assignments are facilitated by parental involvement, and depending on the age of the child

we often include parents in the therapy sessions (i.e., with younger children parents tend to spend more time in the session). In addition, we often hold a "parents only" time at the end of each session when the procedures are taught to parents.

In addition to pairing exposures with relaxation, we use contingency management procedures. This includes positive reinforcement, shaping, extinction, contingency contracting, following through, and consistency. In particular, performance of in-session and out-of session exposures along the fear hierarchy is facilitated by the use of contingency management. Specifically, contracts are written between the parent and child that details the child exposure task (i.e., the step on the hierarchy) as well as the details of the reward that the parent would give to the child (i.e., an item on the reward list) as a consequence for successful completion of the exposure task.

Sessions then begin to focus on hierarchy exposure tasks (i.e., gradual exposure to items on the hierarchy combined with relaxation and contingency contracting), with self-efficacy building (i.e., therapist praise at success along the hierarchy and self-praise at successes), and continued relaxation training practice. We introduce the concept of self-evaluation as deciding whether or not one is satisfied with his/her accomplishments. Sports examples are used to help youth learn the concept of shaping (or gradual learning). For example, it might be explained that it would not be reasonable to expect to hit a three-point shot in basketball every time one shoots a basket or even in every game.

Youth are helped to make a list of possible rewards that the youth might receive (e.g., get to go to the park with mom; extra play time after school; points toward a tangible reward). An emphasis on verbal self-rewards is part of our work with older youth and children who are particularly motivated. Examples might include: "I'm really proud of myself," "I really handled that well," "I can handle it if I try," "Good going," and/or "Great Job!" The importance of believing in one's self is emphasized as well. The therapist explains how we should reward or praise ourselves for even partial successes (shaping). That is, we will praise ourselves for partial successes as well, not just for the "three-point shot." The focus is on the idea that no one does everything perfectly and not doing something 100% perfectly should not mean that you should not praise yourself.

We next begin cognitive modification work. Some therapies do this cognitive training before exposures are begun (Kendall, 1994). This may be more appropriate for older youth who can understand the abstract issues involved. We have found that the exposures often provide concrete examples, so that children understand the cognitive component better. Thus, doing the cognitive work as exposures progress is one developmental modification to CBT that therapists may wish to try. Cognitive modification is also often termed "cognitive restructuring" (Beck, 1976) and is really a vast array of strategies utilized to identify and help restructure maladaptive and distorted cognitions. Such strategies include the identification of negative thoughts, images, and beliefs and the teaching of positive self-talk, self-observation, challenging beliefs and schemas, and self-evaluation. Common negative thoughts in anxious youth and their definitions with GAD-related examples are presented in Table 18.2 (see also Weems, Costa, Watts, Taylor, & Cannon, 2007).

Cognitive modification strategies might include challenging the above irrational or erroneous beliefs by demonstrating the logical fallacy of the belief or by empirical demonstrations of the fallacy of the belief. For example, we use mini experiments and the exposure hierarchy to demonstrate that the result a child expects from the worry (e.g., social ridicule) does not always happen. However, the period from childhood to adolescence is characterized by changes in the way a child is able to process information (e.g., young children are often not conscious – or as conscious – of their threat evaluative thoughts and are often unable to articulate their cognitive experience in a way that lends itself to easy identification of their anxiety-related cognitions). Trying to identify anxious cognitions such as catastrophizing or attempting to have the child monitor castastrophizing thoughts in such cases will often prove unhelpful to the therapeutic process.

In our work with younger children (see e.g., Weems & Carrión, 2003), we start from a "teaching

Table 18.2 Common negative thoughts experienced by anxious youth

Negative cognition	Definition	GAD-related examples
Catastrophizing	Expecting the worst possible outcome of an event or situation	Worries that if it rains there will be a flood. News story about crime means robbers are going to break into the house at night
Overgeneralizing	Believing that a single negative outcome is representative of or will occur in all similar future events	One difficult test results in worries that school will always be awful
Personalizing	Attributing control over the outcome of negative events to internal causes	A team loss results in persistent worries that "the team lost the game because of me"
Selective abstraction	Focusing on only the negative aspects of an event	Worries that she/he ruined the whole recital/game because of one little mistake
Anxiety sensitivity	The beliefs that anxiety-related sensations (such as heart beat awareness, increased heart rate, trembling, shortness of breath) have severe negative social, psychological, or physical consequences	A racing heart rate leads to worries that they have heart problems

adaptive cognitions" framework. That is, the focus is simply on teaching verbal (cognitive) statements that are adaptive. In the case of children with GAD, the idea is teaching statements that counteract avoidance and promote facing your worries. For example, the therapist might ask the child with GAD, "What can you say when you worry about what will happen when you have to leave Mommy to go to school? How about, 'Mommy will be back later today', or 'I will have fun in school today' or 'I am a big girl/boy now I can go to school by myself." Framing the cognitive session in this way changes the focus from identification and modification to directly teaching adaptive self-statements.

Summary

This chapter reviewed the literature on the treatment of GAD in youth. Worry is a central feature of the DSM definition of GAD in youth and so in addition to a careful diagnostic assessment, we suggest a comprehensive assessment of the child's worries. The extant empirical data on treatment efficacy suggest that CBT techniques and procedures have excellent empirical support (Silverman et al., 2008). While the treatment studies to date have included other anxiety disorders in the samples evaluated, we concluded that GAD can be effectively treated with CBT. Moreover, treatment efficacy does not appear to vary by format (e.g., group vs. individual), ethnicity, and gender. However, there is some evidence to suggest that comorbid depression and parental mental health may decrease efficacy. We concluded the chapter by providing some hands on suggestions in the implementation of CBT for GAD in youth based on our intervention experience.

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Selective Mutism

19

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Selective mutism is a persistent and debilitating condition in which a child fails to speak in public situations where speaking is expected. Children with selective mutism often speak well in familiar situations such as home but do not speak to people in public situations such as parks, shopping malls, restaurants, and school. Failure to speak must last at least 1 month. A diagnosis of selective mutism does not generally apply to youths with a communication disorder such as stuttering or to youths who lack comfort or knowledge with the primary language spoken in public situations (American Psychiatric Association, 2000). Selective mutism thus does not generally apply to new immigrants or to youths whose parents are non-English speakers, though prevalence of selective mutism among established immigrants may be elevated compared with the general population (Elizur & Perednik, 2003; Krysanski, 2003; Vecchio & Kearney, 2007).

Selective mutism affects 0.2–2.0% of children, with girls slightly more affected than boys (Bergman, Piacentini, & McCracken, 2002). The disorder commonly begins during preschool years but treatment is often delayed by parents or others who believe the problem is temporary (Chavira, Stein, Bailey, & Stein, 2004; Kumpulainen, 2002). Selective mutism may have a chronic course for some children and can produce significant problems with respect to peer rejection, incomplete verbal academic tasks or standardized tests, or inadequate language or social skills (Cohan, Price, & Stein, 2006; Cunningham, McHolm, & Boyle, 2006; Remschmidt, Poller, Herpertz-Dahlmann, Hennighausen, & Gutenbrunner, 2001; Steinhausen, Wachter, Laimbock, & Metzke, 2006). Family functioning in this population has not been found to be substantially different than controls, though youths with selective mutism have been found to be more noncompliant than controls (Cunningham, McHolm, Boyle, & Patel, 2004).

The conceptualization of selective mutism has been the subject of intense debate. Many researchers have linked selective mutism to social anxiety disorder or an extreme form of social anxiety (e.g., Kristensen, 2000; Sharp, Sherman, & Gross, 2007). Others have found children with selective mutism to display characteristics of oppositionality, developmental disorder, depression, and trauma-based reactions (Arie et al., 2007; Kristensen, 2000; Kristensen & Oerbeck, 2006; Manassis et al., 2003; Yeganeh, Beidel, & Turner, 2006). A latent profile analysis of 130 children with selective mutism revealed the following three main groups: anxious-mildly oppositional, anxious-communication delayed, and exclusively anxious. Social anxiety was characteristic of all groups (Cohan et al., 2008). Vecchio and Kearney (2005) found comorbidity rates among youths with selective mutism to be particularly strong

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_19, © Springer Science+Business Media, LLC 2011

for social anxiety disorder (100.0%), separation anxiety disorder (40.0%), specific phobia (20.0%), and encopresis (13.3%).

Psychosocial treatments for youths with selective mutism have been generally geared toward reducing anxiety and oppositional behavior and developing language, but considerable eclecticism and poor control are evident across many studies (Viana, Beidel, & Rabian, 2009). A primary goal of treatment for selective mutism is to increase the audibility and frequency of speech, especially in public situations such as school (Sharkey & McNicholas, 2008). Major treatment components for this population are outlined next prior to a description of empirical studies that support their effectiveness.

Primary Psychosocial Treatment Components for Selective Mutism

The most common and empirically supported treatment components for selective mutism are behavioral in nature. These components include exposure-based practices that are integrated with stimulus fading, self-modeling, and shaping and prompting. Supplementary procedures are also described, including negative reinforcement/escape, social skills and language training, family therapy, and anxiety management techniques. Parent-based contingency management procedures are also important to facilitate a child's more audible and frequent speech and reduce nonverbal compensatory behaviors. These treatment components are typically used in conjunction with one another in various settings and with various people such as parents, school officials, and peers. Pharmacological treatment has been utilized for this population as well and is described in a later section.

Exposure-Based Practices

A common strategy for treating selective mutism is to have a child practice saying words in increasingly difficult or anxiety-provoking situations. Such exposure-based practice mirrors what is commonly done for children with social anxiety disorder and usually involves a hierarchy of speaking situations (Rye & Ullman, 1999). A typical hierarchy for a child with selective mutism might include speaking to a therapist in the child's home, speaking to a therapist and others in a clinic setting, speaking to a therapist and others in community situations, and speaking to a therapist and others at school. Community situations may include convenience stores, shopping malls, pet stores, and parks, among other areas. School-related situations may include classrooms, hallways, offices, playgrounds, and special classes such as music. Expectations for speaking in school can also involve peers, teachers, administrators, and other personnel.

Exposure-based practices can also involve hierarchies that range from mouthing words to whispering to barely audible speech to low-volume speech to full-volume speech. A child may begin each stage of her hierarchy at baseline functioning (e.g., whispering) and gradually increase audibility and frequency of speech until full volume is reached. A child is generally not asked to attempt the next level until sufficient proficiency is demonstrated at the current level. For example, a child may need considerable practice speaking to a therapist and staff members in a therapeutic setting before advancing to more difficult community settings.

Early stages of exposure-based practice can be quite difficult, especially in cases where a child has rarely spoken outside the home. Therapists will often play games with a child early in the treatment process to build rapport and model appropriate speech. Later sessions may involve deliberate game-related errors on the therapist's part to encourage speech to correct the error. Nonverbal compensatory behaviors shown by the child, such as pointing or nodding, can be ignored at this stage as well in favor of audible speech. Children at this stage are encouraged to say any word they choose in any manner, even whispering, to secure a reward or correct a mistake. Expectations are later altered to increase the number of words spoken and verbal responses to others, develop sentences, and enhance voice volume. Stages of exposure-based practice typically involve stimulus fading and shaping and prompting as well.

Stimulus Fading

Stimulus fading involves systematically increasing the difficulty of an exposure by fading in new stimuli such as peers or teachers. Stimulus fading is commonly used in school-related exposures because a child's lack of speech there is often intransigent. A child may be initially asked to speak to his therapist in an empty classroom and eventually read books aloud or give a short oral presentation there. Once the child is comfortable with this scenario and speech is audible and proficient, a new stimulus is introduced. For example, a teacher may sit at her desk several feet away as the child reads aloud or speaks. Over time, a therapist may ask individual classmates to join the small group and then systematically add to their numbers until the child can speak and read aloud to her entire class. Stimulus fading may occur as well in therapeutic and community settings.

Stimulus fading is used in conjunction with ongoing rewards and prompts for speech. Reinforcement from others in the child's natural environment is important to dispel notions about the negative consequences of speech and to increase future social behavior. Stimulus fading in a school setting must sometimes be accompanied by educating peers and teachers about the importance of encouraging independent speech from the child and ignoring or downplaying nonverbal compensatory behaviors.

Self-Modeling

Self-modeling for selective mutism involves audiotaping or videotaping a child as he speaks clearly and well in a comfortable situation such as home. Parents are typically asked to complete this task in a comfortable setting such as a child's bedroom so he speaks freely and clearly. The recording is then replayed in a low-frequency speaking situation such as a therapist's office and with the child and others such as family members present. This process may be accompanied by anxiety management techniques (see later section) if the child is particularly distressed by the procedure. Self-modeling may be distinguished from exposure-based practice in that the procedure is specifically designed to maximize observer identification and increase self-efficacy (Kehle, Madaus, Baratta, & Bray, 1998).

During this process, the therapist and family members provide ample reinforcement to the child for the clarity, volume, and beauty of her voice. The child is essentially viewing oneself as a model for appropriate and audible speech, which will hopefully translate into generalization to the therapeutic and other settings. The process is also aimed at rewarding speech, easing discomfort, and helping the child recognize that no negative consequences will result from speaking in a public place. Self-modeling is sometimes referred to as audio/video feedforward (Blum et al., 1998).

Shaping and Prompting

Therapists commonly used shaping and prompting during the treatment process for youths with selective mutism. Shaping refers to reinforcing successive approximations of a desired response, in this case audible and frequent speech. Therapists may initially reward vocalizations on a child's part, such as laughter or humming, using verbal praise or tangible rewards such as stickers. A therapist will then try to shape vocalizations into verbalizations, a process that may intersect with language training (see later section). Therapists frequently prompt speech during the shaping process, usually prodding the child to use words to communicate, speak more articulately and loudly, establish eye contact, and extend the duration of speech. The child is continually encouraged as well to express speech in common situations such as greeting or thanking someone.

Negative Reinforcement/Escape

Another behavioral technique for selective mutism is to maintain a child in a therapeutic or other setting for an extended period of time, sometimes several hours, until he speaks one word and is

then allowed to leave. Speaking thus allows the child to escape a boring and potentially stressful situation. Although effective for some children, the technique is not well-tested, and many clinicians do not generally employ the strategy unless they are confident that it would work in an intransigent case (Cunningham, Cataldo, Mallion, & Keyes, 1983). The feasibility of this approach for regular clinical practice is questionable as well. Punitive measures have also been discussed in the literature but typically aggravate anxiety in this population and are not recommended (Dow, Sonies, Scheib, Moss, & Leonard, 1995).

Social Skills Training

Because many children have not spoken publicly for lengthy periods of time, social skill and friendship development may be arrested to some degree. Some youths with selective mutism will benefit from formal social skills training to build basic skills such as establishing and maintaining eye contact, starting and maintaining conversations effectively, and developing friendships. Many children with selective mutism do have friends at school, albeit in nonverbal fashion, so encouraging speech in these relationships is a top priority. Skills training may be extended as well to social-academic tasks such as asking or answering a question in class, responding to instructions on a standardized test, or participating in music or other specialty classes. Group therapy may be particularly useful for this population but this approach has not been extensively tested.

Language Training

Some children with selective mutism will benefit from language training, especially those who are younger or demonstrate some developmental delay in speech. Though not widely tested, some researchers integrate phonics training into various aspects of exposure-based practice (Mendlowitz & Monga, 2007). Such training may initially involve asking a child to use gestures to imitate sounds and then introduce other sounds for basic three-phoneme words such as "cat." This process can mimic what occurs in exposure-based practice by having a child advance from mouthing to whispering to low-volume speech to regular-volume speech. Other researchers endorse collaborations with speech therapists at a child's school to build articulate language and generalize speech.

Managing Physical Aspects of Anxiety

Some researchers have utilized techniques to help children with selective mutism quell physical feelings of anxiety in speaking-related situations (Suveg, Comer, Furr, & Kendall, 2006). For example, muscle relaxation training involves teaching a child to tense and release different muscle groups when preparing to speak before or to others. Breathing retraining involves teaching a child to breathe in slowly through her nose and exhale slowly through her mouth. Both techniques are portable and can be taught with little or no verbalization from the child. As such, the techniques are commonly used early in treatment.

Parent-Based Contingency Management

Contingency management, which includes establishing rewards and disincentives for a child's behavior, is sometimes used to support exposure-based practices. Parents are encouraged to replicate exposures completed during a therapy session and provide ample reinforcement for appropriate speech. A response cost component can be added to these exposures as well. For example, parents may take children to an ice cream parlor and issue the rule that children who speak clearly to the clerk receive ice cream and that those who do not receive no ice cream. In this instance, a natural reinforcer or disincentive is provided for speaking or not speaking, respectively.

Parents are also encouraged to take advantage of natural situations to facilitate speech in their child. For example, a child with selective mutism may be asked to answer the telephone, say hello

to someone in a store, or ask for help in a library. Contingency management is often utilized during the shaping process, so parents can reward gradual increases in speech audibility and frequency during natural exposures as well.

Parent-based contingency management can apply as well to reducing compensatory behaviors such as pointing or gesturing. Parents can be encouraged to ignore compensatory behaviors or instruct a child to use audible words to communicate. Parents may also be asked to discourage their child's use of clinging or hiding to avoid social contact, practice social or language skills as appropriate, and work with school personnel such as teachers or speech pathologists to ensure that a child's speech is continually encouraged and developed in classroom and related settings.

Family Therapy

Some researchers have adopted a family systems perspective to conceptualize selective mutism. Interventions in this regard include educating family members about selective mutism, exploring family patterns of communication, addressing enmeshed or overcontrolling parent–child relationships, and reducing family member pressure on a child to speak. Little evidence is available to support a family systems approach to selective mutism, but many therapists likely utilize these strategies in conjunction with contingency management techniques (Cohan, Chavira, & Stein, 2006).

Empirical Support for Psychosocial Treatments for Selective Mutism

The psychosocial treatment outcome literature regarding selective mutism has been historically dominated by case or otherwise uncontrolled studies (Viana et al., 2009). However, a comprehensive, historical review of 114 studies up to 2002 revealed that behavioral approaches were rated as most effective (Stone, Kratochwill, Sladeczek, & Serlin, 2002). Biological (see later section), family systems, psychodynamic, combined, and other (e.g., cognitive, play) approaches were rated as significantly less effective than behavioral approaches. Since 2002, treatment outcome studies have tended toward more controlled procedures and sophisticated assessment methodologies and are emphasized here.

Vecchio and Kearney (2009) employed an alternating treatment design for nine children with selective mutism aged 4–9 years. The design followed an ABBABAAB format with Treatment A as child-focused, exposure-based practice and Treatment B as parent-focused contingency management. Child-focused, exposure-based practice (Treatment A) involved shaping, modeling, prompting, and in vivo exposure regarding a hierarchy of speech-based situations. These situations included playing games with verbal input, reading aloud, giving short oral reports, asking and answering questions, engaging in short conversations, and ordering food. Speech-based situations at school included reading and speaking to a therapist in an empty classroom and then gradually speaking and reading more before a larger group of peers and a teacher. Shaping during these exposures concentrated on vocalizations with mouth closed and then open, mouthed words without verbalization, whispered single words and then sentences, and sentences with progressively increased audibility toward a final goal of normal spontaneous communication. Anxiety reduction techniques such as breathing retraining were utilized during this treatment condition as well.

Parent-focused contingency management (Treatment B) involved establishing a consequence system for speaking and failure to speak in public places. Rewards and punishments surrounded privileges or loss of privileges such as later/early bedtime, toys, and television time. Social reinforcement was emphasized in later sessions. This treatment condition also involved establishing routines so a child would have increased opportunities to speak in public, such as asking a child to greet someone or taking a child to recreational activities that required some social interaction. Parents were also instructed to ignore compensatory behaviors and issue brief, clear commands to their children. Teachers were asked

to engage in similar contingency management procedures in later sessions.

Dependent measures focused on daily recordings of anxiety ratings and number of words spoken. Measures were completed by children, parents, and teachers. Children received 8–32 treatment sessions split equally across the two treatment conditions. At posttreatment and 3-month follow-up, eight of nine children met criteria for positive end-state functioning. One child met criteria for selective mutism at posttreatment and 3-month follow-up based on parent but not child reports from a structured diagnostic interview. However, this child was speaking more often in public and with greater ease during many social situations by the end of treatment.

Effectiveness of both treatment conditions was compared by pooling data across children, thus comparing all sessions of child-focused treatment vs. parent-focused treatment. Children demonstrated significantly greater speech for the child-focused, exposure-based treatment compared with the parent-focused, contingency management approach, though both treatments were effective. Treatment in general produced a large effect size based on child report (0.83), a moderate effect size based on parent report (0.41), and a small effect size (0.25) based on teacher report. Parents also reacted to exposure-based practice more positively than contingency management in ratings following treatment.

Some researchers have also examined single cases with controlled procedures. Beare, Torgerson, and Creviston (2008) utilized an A-B-B´ multiple baseline design across settings to treat a 12-year-old boy with selective mutism. Settings included a resource room, study room, and mainstream classroom. Number of verbal replies to prompts and rate of words said aloud per minute were the dependent variables. Treatment involved stimulus fading, prompting, reinforcement, and social skills training. Prompts to speak in class were gradually reduced over time. The procedures resulted in substantial improvements in verbal responses and words per minute. For example, words said per minute increased from a mean of 0.1 at baseline to 3.5 at end of treatment in the mainstream classroom.

Others have examined cases of selective mutism in recent years using uncontrolled but innovative procedures. For example, Fisak, Oliveros, and Ehrenreich (2006) used social effectiveness therapy for children, a manualized behavioral treatment program for social anxiety, as well as parent training to address selective mutism in a 10-year-old boy. A multimodal assessment indicated that the boy's mutism was designed to avoid anxiety feelings in speech-related situations and was partly a function of poor social skills. Treatment focused on social skills training surrounding behaviors such as establishing eye contact, asking questions, greeting others, and giving a short speech. Voice volume and words spoken were met with positive reinforcement, and social skills were practiced in gradually more public situations such as school. Parent training focused on appropriate verbal reinforcement of the child's spoken behavior and use of social skills. Treatment was successful in producing a substantially increased number of verbalizations over 22 sessions.

Jackson, Allen, Boothe, Nava, and Coates (2005) treated a 6-year-old boy with selective mutism via a multidimensional approach. This approach involved play therapy, rewards for vocalizations and later verbalizations, self-modeling, relaxation training, prompting, and parent training to refrain from rewarding nonverbal requests. Treatment over 25 sessions resulted in extensive speech at school. Baskind (2007) also successfully treated an 8-year-old boy with selective mutism by encouraging the child to speak to his mother and cousin in school.

O'Reilly et al. (2008) used a social-problem solving intervention to treat selective mutism in two sisters along a multiple baseline design. The intervention included a rationale for learning to speak audibly in class, practicing five questions about an upcoming math or other lesson in class, modeling and role playing social rules and appropriate responses, practicing speech in class, and evaluating one's response. Practice over 21 observation sessions resulted in substantial increases in audible responses to teacher questions. Others have treated youths with selective mutism history within the context of a large-scale

trial of treatment for social anxiety disorder that emphasized social skills training (Garcia-Lopez et al., 2006).

Special Populations and Practices

Others have examined treatment of selective mutism in special populations. For example, Vecchio and Kearney (2007) treated a 10-year-old Hispanic girl with selective mutism, whose father spoke limited English and whose mother spoke no English. One therapist served as the primary therapist and a cotherapist served as translator and treatment facilitator. Early treatment sessions focused on playing games, encouraging the child to speak verbally, and ignoring attempts to communicate nonverbally. This led to brief conversations with the therapists and later exposures in community-based settings such as a pizza restaurant. Final exposures included school-related situations and even a brief discussion with a television reporter. At the end of treatment, the girl was speaking audibly to others at school and was able to invite friends to her house.

Facon, Sahiri, and Riviere (2008) employed a changing criterion design to test treatment of severe selective mutism in a 12-year-old Moroccan boy with mental retardation. The authors utilized shaping and stimulus fading in the form of gradually increasing the number of people in a speaking situation, number of questions asked of the child, and number of sessions conducted in the child's classroom. Praise and tokens for greater audibility of speech were provided as well, and an innovative strategy was to place a hand-held sound level meter near the child's mouth. The criterion changing design was linked to levels of decibel loudness set by the therapist. Over 85 sessions, the child's speech volume increased from a baseline phase mean of 43 decibels to a maintenance phase range of 72–76 decibels.

Others have applied interventions to youths with selective mutism in innovative ways. Sharkey, McNicholas, Barry, Begley, and Ahern (2008) examined a group therapy approach to treat five youths with selective mutism over an 8-week period. Groups were conducted for parents and children. The parent group involved education about selective mutism, strategies for managing lack of speech in public places, anxiety reduction techniques, and methods of encouraging confident speech in their children. The child group involved education about social anxiety via storytelling, relaxation exercises, and exposure-based practice along a hierarchy of social situations. Homework assignments were part of each group as well. Posttreatment results revealed substantial reductions in functional impairment, anxiety, and separation anxiety for the children. Clinician ratings of confident speaking increased significantly as well.

Fung, Manassis, Kenny, and Fiksenbaum (2002) also reported an innovative use of an internet-based treatment program for a 7-year-old with selective mutism. The program focused on psychoeducation, recognizing symptoms of anxiety, using specific social skills, and practicing anxiety management techniques over 14 weekly sessions. Homework assignments were provided via e-mail. Anxiety, global functioning, and selective mutism were reportedly improved by posttreatment. A summary of these studies and their treatment components is in Table 19.1.

Empirical Support for Pharmacological Treatments for Selective Mutism

Pharmacological treatment outcome study for selective mutism remains in a fairly nascent stage, but some investigations have provided important information. The predominant medications used by psychiatrists for selective mutism have been antidepressants, particularly phenelzine, fluoxetine, sertraline, fluvoxamine, citalopram, and paroxetine (Carlson, Kratochwill, & Johnston, 1994; Kearney & Vecchio, 2007). Black and Uhde (1994) conducted a double-blind, placebo-controlled study of fluoxetine for 16 youths with selective mutism over 12 weeks. Ratings of selective mutism, anxiety, and social anxiety improved significantly in both fluoxetine- and placebo-treated groups, though youths in both

Table 19.1 Summary of recent treatment studies for selective mutism

Authors	Study components and outcome
Vecchio and Kearney (2009)	Child-focused exposure-based practice and parent-based contingency management; seven girls and two boys with a mean age of 6.6 years; four European-Americans, two biracial, two Asian-American, one Hispanic; eight of nine participants no longer met criteria for selective mutism
Beare et al. (2008)	Stimulus fading, prompting, reinforcement, and social skills training; one boy aged 12 years; participant increased verbal communication in three different settings
Fisak et al. (2006)	Social effectiveness therapy and contingency management; one boy aged 10 years, Hispanic; participant communicated well in multiple settings including school
Jackson et al. (2005)	Play therapy, rewards for speech, self-modeling, relaxation training, prompting, and contingency management; one boy aged 6 years; participant displayed a substantial increase in verbal behaviors across therapy, public, and school situations
O'Reilly et al. (2008)	Social problem-solving skills training; two girls aged 5 and 7 years in Ireland; participants displayed a substantial increase in percentage of verbal opportunities performed correctly in classroom situations
Vecchio and Kearney (2007)	Prompting and exposure-based practice; one girl aged 10 years; Hispanic; participant displayed a substantial increase in verbal behaviors across therapy, public, and school situations
Facon et al. (2008)	Shaping, stimulus fading, and reinforcement for speech; one boy aged 12 years born in Morocco; participant displayed a substantial increase in production of words and speech loudness
Sharkey et al. (2008)	Group therapy, anxiety reduction, psychoeducation, and exposure-based practice; four girls and one boys with a mean age of 6.1 years in Ireland; participants displayed significant improvements in measures of confident speaking and anxiety
Fung et al. (2002)	Internet-based treatment of psychoeducation, anxiety management, and social skills development; one boy aged 7 years; participant displayed improvements in speaking to teachers and anxiety ratings

groups were also defined as "very symptomatic" at the end of treatment. Parent ratings of mutism and global change did improve more significantly for the fluoxetine group than the placebo group. Others have found more substantive reductions in anxiety and mutism following a 9-week open trial of fluoxetine (Dummit, Klein, Tancer, Asche, & Martin, 1996).

Manassis and Tannock (2008) treated 17 youths with selective mutism that lasted at least one school year. Ten children were treated with selective serotonin reuptake inhibitors (fluoxetine or sertraline) and seven children received unspecified psychotherapy as well as speech therapy. Treatment assignment was based on parental preference. Outcome was assessed after 6–8 months but revealed that 16 of the 17 children still met criteria for selective mutism. However, the medicated group did show greater improvement regarding speech outside the family than the unmedicated group.

Other medications, such as anxiolytics and neuroleptics, have been less commonly used. Uncontrolled studies reveal a moderate effect for reducing selective mutism, though side effects and adverse food and drug interactions are of substantial concern in young children with the disorder (Carlson, Mitchell, & Segool, 2008; Kumpulainen, 2002). Medication for selective mutism may decrease physical arousal but does not appear to enhance social or related skills necessary for full symptom improvement (Viana et al., 2009). Medication in conjunction with behavioral techniques may be most applicable to severe cases of selective mutism (Manassis, 2009).

Prognostic Indicators of Treatment Outcome

The treatment outcome literature for selective mutism remains relatively sparse, and large-scale investigations are lacking. As such, little empirical information is available regarding prognostic indicators of treatment outcome. However, researchers have discussed complications regarding treatment in several publications reviewed earlier. Major complications are summarized here.

One important complication for this population is parental reaction to a child's mutism. Parents often delay treatment for selective mutism, believing that the problem is due to simple shyness and will eventually remit spontaneously. In addition, many children with selective mutism are never referred for treatment. If parents do refer a child with selective mutism for treatment, other complications could arise. Parents of children with selective mutism are sometimes quiet and reserved themselves, so therapists may find the task of conveying the importance of a child's speech in different social situations to be difficult. Some parents of this population resist exposure-based practices as well, so a careful explanation of treatment rationale is important. Parents of this population sometimes allow for compensatory behavior, "baby" talk, and avoidance of social and speaking-related situations. Such allowances should be discouraged (Baskind, 2007; Fisak et al., 2006).

Some families are isolated as well and choose to shelter their child from extracurricular and other social activities. In these cases, social skills training and integrating a child into peer groups may be necessary. Therapists may also choose to incorporate siblings and friends into the treatment process to generalize speech and reduce social isolation. During this process, parents should be encouraged to maintain consistency with respect to expectations of speech and disciplinary style for all children in the family.

Another common complication for selective mutism treatment occurs in cases of bilingual children whose parents rarely speak English at home. A child may thus be more reluctant to speak English at school, withdraw from social situations there, or have difficulty understanding the teacher or others. In these cases, we encourage parents to speak English at home to a greater degree. Home visits, use of interpreters, and collaboration with multilingual school personnel are also important in these cases (Vecchio & Kearney, 2007). Cultural factors, such as a parent's belief that a child should obey directives without use of rewards, must be considered as well (Fisak et al., 2006).

Another complication for treating selective mutism is the lack of cooperation from school officials. Successful treatment of selective mutism typically requires extensive in-school exposure sessions. If teachers or other school personnel resist exposure-based practices, then full remission of selective mutism is unlikely. We encourage therapists to develop a close working relationship with school officials very early in the treatment process to determine what techniques will be most feasible. Ongoing daily assessment of a child's speaking behavior and subsequent consequences at school and home will be imperative as well.

Other unfortunate aspects of treatment for selective mutism are its intensity and duration, which can be unpalatable for many clinicians. Treatment for this population often involves lengthy sessions and frequent out-of-office exposures, which can be taxing and costly. Most outcome studies have occurred in specialized, university-based clinical settings, so researchers will need to design protocols that are amenable to everyday clinical practice and school settings. Exposure-based practices are likely an indispensible aspect of treating selective mutism, but many exposures can be designed and implemented by school officials and parents (see Kearney, 2010; McHolm, Cunningham, & Vanier, 2005).

Atypical Presentations of Selective Mutism

As mentioned earlier, social anxiety is a dominant characteristic of many cases of selective mutism. Several atypical presentations of selective

mutism have been historically described in the literature, however. Some cases of selective mutism clearly involve a willful, stubborn, manipulative, or oppositional component where a child refuses to speak even if not fearful. Recall that Cohan et al. (2008) found that one subtype of youths with selective mutism was anxious-mildly oppositional. In these cases, parent- and teacher-based contingency management practices will likely be important adjuncts to exposure-based practices. In addition, clinicians are encouraged to identify what factors may be maintaining a child's mutism, including avoidance of directives from others or to secure attention or sensory feedback from others.

Another atypical presentation of selective mutism involves overlap with a sometimes undefined speech or language problem or other developmental delay. Some children with selective mutism are quite inarticulate or have great difficulty grasping basic speech concepts even when more willing to speak. We recommend nonverbal tests of intelligence and receptive vocabulary ability in these cases as well as adjunct language and phoneme training. Close collaboration with a school-based speech pathologist and school psychologist will be necessary as well. A child's academic placement should also be reviewed so curriculum can be tailored to the child's educational and speech-related needs.

Other cases of selective mutism have been described in the literature as related to depression or trauma (Anstendig, 1999; Steinhausen & Juzi, 1996). Depressive symptoms may be linked to the social anxiety that pervades much of this population. Given that some youths with selective mutism have responded to antidepressant medication, the presence of depression in some cases should not be discounted. Traumatic experiences in children may or may not be directly linked to selective mutism, but aspects of posttraumatic stress disorder in young children do include social withdrawal and less verbal expression (Kearney, Wechsler, Kaur, & Lemos-Miller, 2010). Clinicians are thus encouraged to assess for recent history of trauma as well as school-based threats and other contextual factors that may lead to poor verbal expression.

Pathway for Treatment

Many researchers of selective mutism have gravitated toward behavioral techniques to address audibility and frequency of speech, but no consensus protocol exists. Keen, Fonseca, and Wintgens (2008) attempted to address this gap by soliciting opinions about management of selective mutism from a range of professionals in Europe, North America, and Australia. Participants ranked agreement to various statements surrounding selective mutism before rating a second series of revised statements. Key principles were then designed for a care pathway regarding selective mutism.

One key principle was that a range of professionals in and outside a school setting should receive training to identify important features of selective mutism. More specifically, school-based personnel such as speech and language pathologists and school and educational psychologists should have extensive training regarding selective mutism and its symptoms. These personnel could also advise teachers and others and confirm whether a true case of selective mutism exists. We have found in our own experience that coordination between a therapist and school officials is often critical to the successful resolution of a mutism case. Support groups for parents were also recommended.

Keen et al. (2008) also found that most professionals strongly recommended that children with selective mutism receive early intervention following a multidisciplinary assessment approach. Assessment should concentrate not only on mutism behaviors but also on comorbid problems such as developmental or linguistic problems that must be addressed. Concerns about English as a second language, family function, and behavior disorder should also be fully considered during the assessment process. In addition, parents must be fully integrated into the assessment and intervention process, and parents and school officials must develop a close collaborative relationship.

The key target for intervention for youths with selective mutism is improving social function by increasing observable verbal behaviors in a range

of locations and with different people. Nonverbal communication may need to be developed first in more difficult cases. Daily assessment of verbal frequency and audibility is recommended. In more severe cases, especially those involving high levels of anxiety, medication could be considered as an adjunct to a behavioral approach.

Summary

Selective mutism is a potentially debilitating and severe disorder that is finally receiving increased attention from researchers. Although large-scale studies of treatment outcome remain needed, evidence indicates that behavioral interventions are perhaps most useful for this population. Future research will have to concentrate on more refined and clinically palatable procedures, well-defined outcome measures, and older youths with selective mutism. The degree to which comorbid problems intersect with selective mutism, especially communication disorders or developmental delay, must be examined more closely as well. A comprehensive theory of selective mutism that connects etiology, symptomatology, assessment, and treatment also remains lacking and should be prioritized. Researchers have unlocked many secrets regarding selective mutism in recent years, so the future for many children with this disorder is substantially brighter now than in the past.

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Social Anxiety

20

Tracy L. Morris and Chelsea M. Ale

Transitory shyness is particularly common among very young children and a large segment of the population will experience symptoms of social anxiety at some point across the lifespan. Fortunately, such episodes pass without major incident for most individuals. For others, the experience of social anxiety is pervasive and leads to substantive distress and impairment. Social anxiety disorder (also known as social phobia) is defined as a "marked and persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others" (American Psychiatric Association, 2000, p. 456). The classic symptom constellation includes heightened physiologic reactivity (e.g., increased heart rate and muscle tension), cognitions reflecting negative evaluation (e.g., "Everyone is looking at how stupid I am"), and overt escape and avoidance and avoidance behaviors (e.g., school refusal, reticence to speak), although primary response modes vary considerably across individuals. As school is children's primary social venue, it is not surprising that the school context is a significant source of distress for children and adolescents with social anxiety disorder (Essau, Conradt, & Petermann, 1999; Strauss & Last, 1993). As children often do not have the freedom to avoid school and other feared social situations, parents and teachers may misinterpret clinging and crying as oppositional behavior rather than as a symptom of social anxiety, and as such appropriate intervention is delayed or denied. For those for whom more covert cognitive or physiologic modes predominate, parents may be unaware of their child's distress until the condition becomes quite severe and comorbid conditions such as depression and substance abuse begin to wreak havoc.

Epidemiology

Lifetime prevalence estimates for social anxiety disorder range have ranged from 2.4 to 13.3% depending on the sampling procedures and methods of assessment employed (Chavira, Stein, Bailey, & Stein, 2004; Kessler et al., 1994; Schneier, Johnson, Hornig, Liebowitz, & Weissman, 1992). Within community samples, higher rates of social anxiety symptoms have been found for girls (Epkins, 2002; Morris & Masia, 1998), but distribution of social anxiety across men and women in clinic samples has been reported as approximately equal (Last, Perrin, Hersen, & Kazdin, 1992; Turner & Beidel, 1989).

Early work in the area of social phobia frequently cited the mean age of onset as early- to mid-adolescence (Öst, 1987; Turner, Beidel, Dancu, & Keys, 1986), despite common reports from adults seeking treatment that they had experienced for as long as they could remember. It is possible that the increased social demands and

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_20, © Springer Science+Business Media, LLC 2011

capacity for self-awareness that occur during adolescence may result in symptoms of shyness crossing the threshold into social anxiety disorder during this developmental stage. It also may be the case that ages of onset estimates have not been entirely accurate due to the relatively limited research on the expression of social anxiety in young children, which in turn may be due to the paucity of developmentally appropriate assessment measures (see Morris, Hirshfeld-Becker, Henin, & Storch, 2004).

Social anxiety disorder is frequently comorbid with other psychiatric conditions, particularly generalized anxiety disorder and depression (Beidel, Turner, & Morris, 1999; Chavira et al., 2004; Schneier et al., 1992). Children and adolescents who experience extreme levels of social anxiety have lower levels of peer group acceptance and fewer close friendships (Greco & Morris, 2005; La Greca & Lopez, 1998; Morris, 2001), which may help set the stage for a downward spiral leading to depression. Adolescents may turn to alcohol and other substances in attempt to self-medicate and feel less inhibited in social situations – and their subsequently more socially gregarious behavior is reinforced by peers which in turn leads to increased substance use (see Essau et al., 1999; Kushner, Sher, & Beitman, 1990). Social anxiety disorder is likely to be a chronic condition in the absence of direct intervention (Yonkers, Dyck, & Keller, 2001).

Causal Factors

As with most psychiatric disorders, no single causal path has been identified for social anxiety disorder. Rather, multiple authors have provided explanatory models for the development of social anxiety in which the interaction of multiple factors is paramount (e.g., Morris, 2001; Rapee, 2001). Primary proposed risk factors include genetic predisposition, physiologic reactivity, parenting style, and peer socialization. High familial loadings have been found for social anxiety disorder (Fyer, Mannuzza, Chapman, Liebowitz, & Klein, 1993). Behavioral inhibition (a tendency to approach new situations with restraint, avoidance, and distress) is thought to have an inherited biological component and higher rates of social anxiety disorder have been found among children previously classified as behaviorally inhibited (see Hirshfeld-Becker et al., 2008, for review).

A growing literature base has implicated the role of parenting in the development and maintenance of anxiety disorders in general, and social anxiety disorder in particular (see Hudson & Rapee, 2001, and Masia & Morris, 1998, for more extended discussion). Children and adults with social anxiety have described their parents as engaging in overcontrolling behavior and restricting social interaction (Anhalt & Morris, 2008; Greco & Morris, 2002; Rapee & Melville, 1997). Laboratory investigations have found parents of socially anxious children to demonstrate more controlling and rejecting behavior toward their children during joint interaction tasks than parents of nonanxious children (Greco & Morris, 2002; Hummel & Gross, 2001; Rork & Morris, 2009). Parents of anxious children have been found to model threat interpretations to ambiguous cues and to provide and reinforce avoidant solutions in response to hypothetical social scenarios (Barrett, Rapee, Dadds, & Ryan, 1996; Barrett, Shortt, & Healy, 2002; Dadds, Barrett, & Rapee, 1996).

Outside the home, the quality of children's peer relationships has been found to be associated with social anxiety, though it is often difficult to ascertain whether lowered peer acceptance is a cause or consequence of anxiety-related behavior (Erath, Flanagan, & Bierman, 2007; Greco & Morris, 2005; La Greca et al., 1988; La Greca & Lopez, 1998; Morris, 2001; Storch, Masia-Warner, Crisp, & Klein, 2005). Some research has suggested that children and adolescents who are socially anxious underestimate their own level of social skill, and focus – to their detriment – on perceived errors in social behavior (Chansky & Kendall, 1997; Higa & Daleiden, 2008; Inderbitzen-Nolan, Anderson, & Johnson, 2007; Vasey, Daleiden, Williams, & Brown, 1995).

Assessment of Social Anxiety in Children and Adolescents

Proper assessment is necessary not only for purposes of diagnostic classification but in order to generate useful targets of change for inclusion

in treatment plans – and to adequately evaluate treatment outcome. When evaluating children and adolescents, it is important to obtain information from multiple sources. Due to the covert nature of many aspects of social anxiety, parents should not be considered the gold standard for all information about their children. Consideration must be given to the context in which behaviors occur. For instance, teachers and peers may be the most appropriate sources of information regarding a child's performance in school and interactions with peers. As a multi-contextual assessment strategy will help guide case conceptualization and treatment planning, the most commonly employed methods for the assessment of social anxiety in children and adolescents are presented briefly below.

Anxiety Disorders Interview Schedule for DSM-IV Child Version (ADIS-C/P; Silverman & Albano, 1996). The ADIS-C/P provides thorough coverage of anxiety disorder symptom clusters and also screens for the presence of affective and disruptive behavior disorders. The social phobia section of the ADIS-C/P asks the child (and parents – who are interviewed separately from the child) to provide fear, avoidance, and interference ratings across 13 social and performance situations. Intensity ratings are included to assess the extent to which social fears interfere with daily functioning.

Self-report measures: Self-report questionnaires are integral to the assessment of children over 8 years of age. The most extensively validated and widely used self-report measures of social anxiety are the Social Anxiety Scale for Children-Revised, the Social Anxiety Scale for Adolescents, and the Social Phobia and Anxiety Inventory for Children (SPAI-C).

The Social Anxiety Scale for Children-Revised (SASC-R; La Greca & Stone, 1993) is a 22-item measure comprised of three factors: fear of negative evaluation, social avoidance and distress with new or unfamiliar peers, and more generalized social avoidance and distress. The Social Anxiety Scale for Adolescents (SAS-A; La Greca & Lopez, 1998) parallels that of the SASC-R. Scores on the SASC-R and SAS-A have been found to correlate with peer sociometric data and measures of self-esteem. Recent research conducted by Reijntjes, Dekovic, and Telch (2007) found SASC-R scores were predictive of negative response biases and lower approach behavior among children playing a videogame task with peer confederates.

The SPAI-C (Beidel, Turner, & Morris, 1995) consists of 26 multi-part items assessing overt behavior, thoughts, and physiologic responses across a range of potentially fear-inducing situations. Beidel, Turner, Hamlin, and Morris (2000) have provided data on the external and discriminative validity of the measure. The SPAI-C has been shown to correlate with independent observer ratings of anxiety and effectiveness during behavioral performance tasks, as well as with children's ratings of their own anxiety and distress. Importantly, the measure has been able to successfully discriminate children with social anxiety disorder from normal controls and those with other anxiety disorders. Psychometric properties of the SPAI-C also have been established with cross-cultural samples (e.g., Aune, Stiles, & Svarva, 2008).

Several investigations have examined the association of the SPAI-C and SASC-R and have found that the measures appear to assess overlapping, but not identical constructs (Epkins, 2002; Morris & Masia, 1998). General findings have been that the SPAI-C has greater specificity and selectivity for diagnoses of social anxiety disorder. However, as the SASC-R typically takes less time to administer than the SPAI-C, the SASC-R may be preferable in large-scale screening investigations.

Behavioral observation and performance tasks: Direct observation of behavior is a critical component of the assessment of social anxiety and associated social skills. Observation of children in the natural setting (e.g., school classroom or on the playground during recess) may be particularly enlightening if one is able to move beyond clinic walls. However, relevant analog or role-play tasks may readily be conducted within office confines.

Peer report: Peer nominations or ratings of social status may be particularly useful in gauging generalization of treatment effects. Classic sociometric nomination procedures categorize children along two dimensions: social preference (how much a

child is liked or disliked by his or her peers) and social impact (the child's visibility within the peer group; see Coie, Dodge, & Coppotelli, 1982). Due to the effort required to obtain peer reports within school settings, such data typically are included only in the context of extended research investigations and seldom systematically collected by clinicians engaged in routine treatment.

Psychological Treatment of Social Anxiety

Theoretical Models Underlying Behavioral and Cognitive Behavioral Treatment

Current empirically supported treatments for social anxiety have their roots in the historical work on classical conditioning and operant learning conducted by John Watson and B.F. Skinner. Watson's case study of "Little Albert" (Watson & Rayner, 1920) illustrated how fear and anxiety may develop through the pairing of aversive and neutral stimuli, which may then rapidly extend to other associated stimuli. Accordingly, the classical conditioning paradigm has been put forth as one explanation for the acquisition and generalization of the heightened physiological arousal experienced by children with anxiety disorders.

In his work on operant conditioning, Skinner emphasized that behavior is learned as a function of its consequences (Skinner, 1953). Anxiety-related responding (e.g., avoidance) will increase if followed by a pleasurable event (positive reinforcement) or the removal of an aversive stimulus (negative reinforcement). All children experience normal, developmentally appropriate fears which are relatively limited and decrease over time (King, Muris, & Ollendick, 2005). Young children may whine, cry, or engage in oppositional behavior in attempt to escape or avoid a feared stimulus or situation. In an attempt to comfort their distressed child, parents may inadvertently reinforce inappropriate fearful or avoidant behavior, which may then lead to more persistent expression of fear and anxiety. In the case of social anxiety, parents who allow their child to refuse to participate in social activities with same-age peers, or to stay home from school in order to avoid the distress of an oral spelling bee, are strengthening the child's avoidance behavior and limiting contact with contingencies that ultimately will serve to reduce the anxiety response.

Clearly, both classical and respondent approaches have a place in furthering our understanding of anxiety. Mowrer (1947, 1960) proposed a two-factor learning theory that serves to integrate the two paradigms. To summarize, upon exposure to an aversive event the child responds with increased physiological reactivity and subjective distress. This uncomfortable physiological arousal then becomes associated with previously neutral stimuli present at the time (including external environmental stimuli and internal cognitive cues that may serve as reminders of the aversive event). As this state of heightened physiological arousal is aversive for the child, escape from associated stimuli is negatively reinforced through reduction of arousal – increasing the likelihood of subsequent avoidance behavior. In a vicious cycle, extended avoidance further reduces the likelihood that the child will develop the necessary skills to manage arousal and anxiety in the future.

Following the early behavioral work on conditioning and learning, later theorists such as Albert Ellis and Aaron Beck sought to provide more focus on cognitive factors underlying anxiety. The basic premise of most cognitive models is that anxiety stems from a response bias in which an individual overestimates the probability of threat in their environment and underestimates their ability to cope with the situation (Beck, 1976; Ellis & Harper, 1975). Children with social anxiety may engage in self-talk emphasizing negative evaluation and embarrassment (e.g., "What if I mess and they all laugh at me?").

While at first glance behavioral and cognitive perspectives on the development and maintenance of anxiety disorders may appear in conflict, many contemporary theorists have noted that it is not necessary to treat cognitions as a distinct class in that the same principles of learning apply to cognitions as to physiological and overt behavioral responding. The more relevant question really lies with which approach to treatment will

be most effective for which individuals. As such, it is important to more carefully consider the therapeutic mechanisms by which the components of various psychological treatments for social anxiety exert their effects.

Behavioral and Cognitive Behavioral Treatment Components

Behavioral and cognitive behavioral approaches to the treatment of social anxiety in children and adolescents have received strong empirical support. As most treatment programs have included one or more of the following components, these frequently implemented techniques will be covered briefly before the research findings from specific treatment packages are reviewed.

Exposure therapy: Ample empirical evidence suggests that exposure may be the key component in the successful treatment of anxiety disorders. Exposure-based treatments are based on the extinction paradigm within classical conditioning. Essentially this involves having the child face the feared stimulus or situation for a sufficient period of time for anxious physiological arousal to diminish. Through repeated presentation of feared stimuli in the absence of any real adverse consequence, the child comes to master their own anxiety.

Exposure-based techniques include flooding, graduated exposure, and systematic desensitization. Flooding involves sustained exposure to fear stimuli (in vivo or imaginally), whereas graduated exposure refers to progressive in vivo exposure to feared stimuli. While flooding has been used with particular success in the treatment of adult PTSD, it is less frequently employed in the treatment of social anxiety in children and adolescents – in part due to the generalized complexity of social stimuli central to social anxiety and to the perception that graduated exposure is less stressful for child clients. Due to its efficacy and relative ease of administration, graduated exposure has become a standard component of many treatment protocols for social anxiety.

In contrast to flooding and graduated exposure techniques, systematic desensitization requires that the child first masters relaxation training. Once the child is in a relaxed state, the therapist presents items from the child's fear hierarchy. There is no strong empirical evidence to suggest that the inclusion of relaxation training yields any incremental gain to the success of exposure in the treatment of social anxiety, and some theorists would contend that use of relaxation or distraction strategies actually may impede the process of extinction. However, some therapists may find that the process of relaxation training may help establish rapport which in turn may foster cooperation among extremely fearful children during subsequent exposure sessions.

Contingency management: Contingency management entails the provision of specific consequences for the child engaging in specific target behaviors. This typically involves working closely with the child's parents (and possibly teachers) to develop contracts outlining the manner in which reinforcement will be delivered for the performance of specific behaviors. Contracts often include a response cost in which points or privileges may be lost for failure to meet a specified goal. For example, a contract targeting social interaction may state: "If Alex joins a group activity with his peers during recess on three of five school days, the family will go to a movie of his choice on Saturday afternoon. In addition, if Alex tries to avoid attending school on any day, he will forfeit his allotted television time for two days." Contingency management contracts can be particularly useful in providing a system of reinforcement for the completion of between-session homework assignments employed in conjunction with graduated exposure treatment plans.

Social skills training (SST): Social skills deficits commonly have been implicated in the presentation of social anxiety in children and adolescents (Beidel et al., 1999; Spence, Donovan, & Brechman-Toussaint, 1999). Children who manifest extreme shyness and social avoidance from a very early age may miss out on opportunities to learn age appropriate social skills. Real or perceived social skills deficits may then lead to heightened anxiety in social situations. SST programs

generally include coaching, modeling, and social problem-solving components. Common skills covered in such programs include peer group entry and exit strategies, conversational skills, assertiveness, and developing and maintaining friendships. SST components have been included in several of the empirically supported treatments for social anxiety discussed later in this chapter.

Peer modeling and peer-pairing: Peer relationships are central to social and emotional development. Interaction with peers provides a crucial context for the learning of social skills and emotion regulation. Children who are isolated from their peers are at increased risk for chronic social anxiety and other forms of psychopathology. Consequently, the incorporation of peers in the treatment of social anxiety may be of important benefit. Peer–helper interventions involve the selection and training of socially skilled peers who model desired social behavior and administer reinforcement to the target child. In contrast, peer-pairing interventions merely provide strategic opportunities for the target child to engage in joint activities with a more socially skilled peer (with no formal training required of the peer). One advantage of peer-pairing is that it is relatively easy to implement within activities occurring in the child's natural environment, thus allowing for enhanced generalization. Notably, simple peer-pairing interventions have been shown to increase positive social interaction and sociometric status among peers (e.g., Morris, Messer, & Gross, 1995).

Cognitive Restructuring

The term cognitive restructuring encompasses a variety of techniques intended to alter maladaptive thinking patterns, increase the frequency of positive self-talk, and enhance self-concept. Cognitive restructuring techniques require that the client have sufficient metacognitive and logical reasoning skills to engage in formal problem solving. As such, cognitive restructuring techniques are not likely to be effective with very young children. In the treatment of adolescents with social anxiety, cognitive restructuring often is employed to target irrational self-statements tied to fear of negative evaluation ("I'm nobody. I want to ask Erika to the prom but I know she will say no … then everyone will make fun of me ... and no one will ever go out with me").

Cognitive restructuring typically is combined with modeling and reinforced practice, and as such is rarely implemented as a purely cognitive procedure. Empirical findings have been mixed regarding the incremental utility of using exposure and cognitive restructuring in combination. With respect to treatment outcome, the benefits of cognitive restructuring tend to be more pronounced for self-report data than for direct measures of behavioral change (e.g., observation and behavioral performance tasks). In related research, Parr and Cartwright-Hatton (2009) conducted a study of 36 adolescents with social anxiety in which one group was provided video feedback following a speech task and the other group was not. Individuals in both groups were then required to engage in second speech task and re-rate their own performance. Two same-aged peers also independently watched the speech videos and rated the performances. Adolescents who received video feedback reappraised their performance more positively, reported less anticipatory anxiety prior to the second speech, and greater expectations for success prior to the second speech than those who did not receive video feedback. However, there was no change in peer ratings of performance from the first speech to the second speech for either group.

Multi-Component Programs for the Treatment of Social Anxiety

Cognitive behavioral group treatment for adolescents (CGBT-A): CGBT-A initially was designed as a 16-week treatment program consisting of psychoeducation, skill building, cognitive restructuring, and exposure to socially distressing or fearful situations. In an uncontrolled pilot investigation, Albano, Marten, Holt, Heimberg, and Barlow (1995) reported 3- and 12-month follow-up data for five adolescents diagnosed with social phobia, four of whom were reported as diagnosis free at both follow-up evaluations. In a subsequent investigation by Hayward et al. (2000),

35 adolescent girls were assigned to CGBT-A or waitlist control conditions. Significantly fewer adolescents in the treatment condition met diagnostic criteria for social phobia following intervention. However, no differences between groups were found at 1-year follow-up.

More recently Herbert et al. (2009) have reported results from a randomized controlled trial comparing three forms of treatment: (a) a 12-week group treatment program (G-CBT) reported as similar to that of CBGT-A, (b) individual CBT, and (c) group psychoeducational supportive therapy. Large effect sizes were yielded for all three treatments. Treatment condition was not related to symptom reduction as measured by self-reports (SPAI-C, SAS-C) or clinician severity ratings (CGI-S). At treatment completion, there were no significant group differences on treatment responder criteria (with recovery rates of 16–29%). However, at the 3-month follow-up assessment, greater treatment response (54%) was observed for adolescents who completed the course of G-CBT. Significant limitations of the study include the relatively small initial sample size (23–26 per group), a 29% treatment drop-out rate, and further attrition of 27% for the final assessment (follow-up data were obtained for only 13 adolescents in the G-CBT group).

Social effectiveness therapy for children (SET-C): Beidel, Turner, and Morris (2000) published the first randomized controlled trial of behavioral treatment for social phobia in pre-adolescent children. In contrast to "cognitive behavioral" treatment programs such as CGBT-A, SET-C does not include a cognitive restructuring component. SET-C is a 12-week behavioral intervention that incorporates parent education, group SST, peer generalization, and individual graduated in vivo exposure components. Instruction, modeling, behavior rehearsal, feedback, and social reinforcement are used to teach and reinforce appropriate social behavior. A unique and essential component of SET-C is the use of peer interaction experiences (age-appropriate group recreational activities with peer facilitators) to assist in the generalization of social skills to situations outside the clinic. Sixty-seven children (aged 8–12 years) were randomized to SET-C or an active treatment for improving test taking and study skills. Children in the SET-C group demonstrated statistically and clinically significant improvements across multiple domains (including self-reported anxiety, independently observed social skills, and adaptive functioning in daily situations) and gains were maintained 6 months posttreatment. Notably, 67% of children who participated in the SET-C program no longer met diagnostic criteria for social phobia following treatment compared to only 5% of those receiving the active control treatment.

Extensive follow-up data have been reported for SET-C. Beidel, Turner, Young, and Paulson (2005) provided results of a 3-year follow-up assessment that included 90% of children who completed the original controlled trial of SET-C. Seventy-two percent of these children (now aged 11–18 years) no longer met criteria for social anxiety disorder, a significant increase from the 62% who were diagnosis free at the end of treatment. No participants had sought additional intervention following the completion of SET-C, thereby supporting the durability of treatment gains. At 5-year follow-up, 25 SET-C completers (now aged 13–20) were reassessed and compared to a matched nonclinical sample to determine long-term treatment effects (Beidel, Turner, & Young, 2006). None of the individuals had sought pharmacological or psychological treatment after completing SET-C, yet 80% no longer met criteria for social anxiety disorder (a recovery rate that continued to climb from posttreatment through extended follow-up). Comparing treatment responders to the matched nonclinical controls, there were no differences in self-report, parent report, or observation of social skill – thus demonstrating meaningful and lasting change for these formerly socially anxious children.

Baer and Garland (2005) conducted a pilot investigation in which they substantially modified the SET-C protocol to create a simplified treatment for use in community psychiatric clinics. Twelve adolescents with social phobia were assigned to treatment or wait-list control groups. Active treatment consisted of 12 sessions led by three co-therapists. The 90-min sessions were split into two parts: (a) social skills and (b) behavioral exposures. In contrast to SET-C, the program did not include peer generalization sessions, did

not make use of a behavioral reward system, and implemented behavioral exposures in a group format rather than the individual therapist directed exposure component of SET-C. In further contrast, one session included cognitive restructuring strategies. Participants were encouraged to find peer or family "coaches" who could help with exposure practice in the natural environment, but this aspect was not structured with the therapists. Peer volunteers from a local high school assisted in a limited number of in-session group exposure activities. Following intervention, 36% of adolescents in the treatment group no longer qualified for a diagnosis of social phobia, while no members of the waitlist group demonstrated such improvement. Although reported effect sizes were smaller than those obtained with the SET-C, the authors note that this modified treatment may be more easily transported to community settings.

School-based intervention: Masia et al. (2005) reported results for 42 adolescents with social anxiety disorder who were randomized within their schools to Skills for Academic and Social Success (SASS) or a wait-list control condition. SASS, based in part on the SET-C and CGBT-A programs, consisted of 12 in-school sessions including psychoeducation, cognitive restructuring, SST, exposure, and relapse prevention; two individual problem-solving meetings; four unstructured social events; two psychoeducational parent meetings; and two brief psychoeducational teacher meetings. At treatment completion, 67% of adolescents completing SASS no longer met criteria for social anxiety disorder, compared with only 6% in the wait-list control condition.

In further work with the SASS (Masia-Warner, Fisher, Shrout, Rathor, & Klein, 2007), 36 adolescents diagnosed with social anxiety disorder were randomized to 12 weeks of SASS or an attention control condition termed Educational Supportive Group Function (ESGF). ESGF included psychoeducation and general relaxation skills, but did not include SST, cognitive restructuring, exposure, or peer generalization components. SASS proved superior to ESGF (59 vs. 0% diagnosis free) with symptom improvement maintained at 6-month follow-up.

Cognitive behavioral treatment plus parental involvement: Given the mounting evidence that parents may play a role in the development and maintenance of anxious behavior, including parents in the treatment process may be prudent. Spence, Donovan, and Brechman-Toussaint (2000) investigated the effectiveness of a cognitive behavioral treatment (CBT) program with or without parental involvement. Fifty children diagnosed with social phobia (aged 7–14 years) were randomly assigned to CBT, CBT plus parental involvement (CBT-PI), or a wait-list control condition. CBT components included SST, relaxation, cognitive restructuring, and graduated exposure. The parent involvement component was designed to help parents model and reinforce the social skills taught in CBT, ignore anxious and avoidant behavior, encourage their child's participation in social activities, and provide contingencies for homework completion. Parents participated in a 30-min weekly training session and also observed the children's group sessions behind a one-way mirror. The CBT and CBT-PI interventions both included 12 weekly group sessions and two booster sessions (at 3- and 6-month posttreatment). Based on parent report, children in both active treatment groups demonstrated improvement in social skills. However, significant differences were not found for either treatment with respect to children's total number of peer interactions or independent observer ratings of assertiveness. While CBT and CBT-PI both resulted in a decrease in social anxiety symptoms, neither yielded significant change in social behavior, thus perhaps providing support for the inclusion of peers in effort to enhance generalization to the child's natural social environment.

Pharmacological Treatment of Social Anxiety

At present, the most widely prescribed pharmacologic agents for the treatment of social anxiety in children and adolescents are the class of drugs known as selective serotonin reuptake inhibitors (SSRIs). Several open-label or uncontrolled have been conducted in recent years. Isolan et al.

(2007) treated twenty children and adolescents (aged 10–17) with escitalopram (Lexapro). After 12 weeks of treatment, 65% of the intent-to-treat sample met treatment response criteria and showed significant improvement on self-report and parent-report measures. Mrakotsky and colleagues (2008) conducted an open-label pilot trial of mirtazapine (Remeron) with 18 children and adolescents diagnosed with social anxiety disorder (aged 8–17 years). A significant decrease in social anxiety symptom severity and impairment was observed after 8 weeks of treatment. Notable weight gain was observed ($M = 3.27$ kg) and four participants experienced additional side-effects (e.g., moderate sleepiness, moderate headaches, and increased depressive symptoms).

Wagner et al. (2004) conducted a large multicenter randomized placebo-controlled trial of paroxetine (Paxil) among 322 children and adolescents with social anxiety disorder (aged 8–17 years). Following 16 weeks of treatment, clinician-rated improvement was significantly greater for paroxetine (48%) than placebo (15%). Adverse side-effects were relatively infrequent and included insomnia (14.1 vs. 5.8%), decreased appetite (8.0 vs. 3.2%), and vomiting (6.7 vs. 1.9%).

March, Entusah, Rynn, Albano, and Tourian (2007) conducted a randomized controlled trial of venlafaxine (Effexor) versus placebo among 293 children and adolescents with social anxiety disorder (aged 8–17 years) who were treated across 48 academic and community clinics. Drop-out rate was 35% for venlafaxine versus 27% for placebo control. After 16 weeks, treatment response to venlafaxine was significantly larger than placebo as determined by self-report (SAS-C/A) and clinician ratings (CGI-Improvement). Notably, there were three reported cases of treatment-emergent suicidal ideation in the venlafaxine condition, with none occurring in the placebo condition.

Comparison of CBT and Pharmacologic Treatments

Segool and Carlson (2008) present the results of a meta-analysis in which they reviewed seven CBT trials and seven SSRI trials conducted between 1994 and 2004 for children and adolescents (aged 6–19 years) with social anxiety disorder. All evaluated CBT studies included cognitive restructuring and exposure, and the majority included psychoeducation and social skill training components. It should be noted that the authors excluded results from SET-C trials on the basis that SET-C is a behavioral intervention that does not include cognitive restructuring. Studies ranged in duration from 3 to 16 weeks. All CBT and SSRI treatments yielded moderate to large effect sizes (0.59–2.92) for reduction of social anxiety symptoms and overall impairment, with slightly larger effects for SSRIs. Gains in social competence were somewhat (but not significantly) higher for CBT than SSRI. The authors noted major limitations in drawing conclusions across studies, in part due to the lack of universally applied assessment measures.

As the Segool and Carlson meta-analysis excluded SET-C, it is important to note the findings of recent research directly comparing SET-C with SSRI treatment (Beidel et al., 2007). Children and adolescents with social anxiety disorder (aged 7–17 years) were randomized to 12 weeks of pill placebo, fluoxetine (Prozac), or SET-C. Participants in the placebo and fluoxetine conditions attended a 60-min weekly medication management and supportive counseling session by a psychiatrist. Following treatment, significantly more participants (79%) in the SET-C condition met treatment responder criteria and no longer carried a diagnosis of social anxiety disorder than those in the fluoxetine or placebo conditions (36.4 and 6.3%, respectively). With respect to improvement in social skills, SET-C resulted in significantly greater gains than either fluoxetine or placebo, which did not differ significantly from one another. Treatment gains were maintained at 1-year follow-up.

Although the empirical research base primarily has investigated the use of psychological or pharmacologic treatments in isolation from one another, clinicians and health care providers have long stressed the notion that pharmacologic treatments will be enhanced if behavioral or cognitive behavioral treatments are implemented in conjunction (see Chavira & Stein, 2002). Although not

specific to social anxiety disorder, a randomized control trial of sertraline, cognitive behavior therapy, or combined treatment (sertraline + cognitive behavior therapy) conducted with 488 children (aged 7–17 years) diagnosed with generalized anxiety disorder, separation anxiety disorder, or social anxiety disorder, found that while both sertraline and cognitive behavior therapy were superior to placebo, response rates were highest for the combined treatment (Walkup et al., 2008). Medication may reduce the physiological arousal that accompanies anxiety in relatively short order, but behavioral and cognitive behavioral interventions are more likely to result in acquisition of skills (e.g., social competence) that will generalize across settings, leading to greater maintenance and enhancement of treatment gains over the long term. More research is needed on potential differential efficacy by response modality. Another area in need of further study is that of the potential benefit of sequentially phased treatment – for instance, might initial medication be helpful in lowering arousal in severe cases to the point at which the child may be more receptive to subsequent exposure and skills-based treatments? Anecdotal reports of such strategies abound, but at present there is scant empirical data to support or refute such a practice.

Summary

Strong empirical support is available for several multi-component programs for the treatment of social anxiety disorder in children and adolescents. Several SSRIs also have proved useful in ameliorating the condition, although the one study, which directly compared an SSRI (fluozetine) with behavioral treatment (SET-C), demonstrated differential superiority for the behavioral intervention. More research is needed on the use of combined behavioral and pharmacologic treatment. The literature is rapidly expanding with respect to our knowledge of potential risk factors in the development of anxiety (particularly in terms of parenting) and this information is furthering the development of treatment targets and applications. The inclusion of parents and peers in the provision of treatment is an especially exciting trend as it reflects increasing developmental sensitivity to social world of children and adolescents. As social anxiety is a relatively early onset and chronic condition, future efforts should be directed toward early intervention studies and dissemination of treatments beyond specialized academic centers. No doubt, front line clinicians will have much to offer as we work toward cost-effective treatments that may be delivered through school, home, and clinic settings to the large numbers of children and adolescents who are currently underserved.

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Pediatric Posttraumatic Stress Disorder

21

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Across the world, as many as 80% of children experience traumatic events including physical abuse, sexual abuse, domestic violence, community violence, and war/conflict/terrorism (United Nations, 2006). Although prevalence rates vary across studies, more than 30% of children experience one or more traumatic events by late adolescence (Copeland, Keeler, Angold, & Costello, 2007). Complexity of trauma experiences has been associated with diverse short- and long-term negative mental health outcomes, including posttraumatic stress disorder (PTSD), other anxiety disorders, depression, risky behaviors (e.g., substance use), and disruptive behavior problems (Silverman et al., 2008). In one longitudinal study, those exposed to trauma had almost double the rates of comorbid psychiatric disorders and PTSD as nontrauma-exposed children (Copeland et al., 2007). Exposure to violence also can result in greater vulnerability to social, emotional, and biological impairments over the course of the life time (e.g., Pervanidou, 2008). Taken together, these findings underscore the need for intervention for children and adolescents who have been exposed to trauma.

This chapter examines treatment outcome studies of psychosocial and pharmacological treatments of PTSD in youth. The following sections include theoretical and practical arguments for cognitive behavioral therapy (CBT). A number of specific treatment considerations, including developmental and cultural factors, are discussed. Factors related to treatment outcome are also mentioned. Research concerning pharmacological interventions is presented. Clinical implications and research recommendations are presented.

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Child and Adolescent Models of PTSD Development

Several models of PTSD in youth (see Meiser-Stedman, 2002 for full review) have been proposed to explain the range of children's trauma responses. Pynoos, Steinberg, and Piacentini (1999) describe four groups of moderators of PTSD development in children: proximal trauma reminders (e.g., internal/external cues), proximal secondary stressors (e.g., changes to family variables), ecological variables (school, peer factors), and individual factors (e.g., genetic vulnerability). Chiefly, they suggest trauma-specific and environmental (i.e., secondary) factors are key to the development of PTSD. Other models have emphasized additional etiological factors including parent reaction in younger children, cognitions, exposure severity, gender, and family functioning (Dyregrov & Yule, 2006). Salmon and Bryant (2002) argue that developmental issues (e.g., language, emotion development) need to be incorporated into current information-processing (e.g., fear networks; Foa & Kozak, 1986) and cognitive

D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_21, © Springer Science+Business Media, LLC 2011

theories, explicating the ways in which these issues influence treatment modules focused on integrating traumatic experiences. Lastly, van der Kolk (2005) and others have focused on the influence of early attachment theories and chronic trauma exposure on the development of complex trauma reactions. Specifically, van der Kolk (2005) found older adolescents and adults who experience multiple traumas experience symptomatology beyond that captured by a DSM-IV-TR diagnosis of PTSD (American Psychiatric Association, 2000), including problems with affect regulation, impulse control, attention/memory, interpersonal relationships, self-perception, somatization, and systems of meaning. Research examining the treatment of PTSD in youth has focused primarily on the following orientations: cognitive behavioral, eye movement desensitization and reprocessing (EMDR), and psychodynamic psychotherapies.

Using Trauma-Specific Cognitive Behavioral Therapy to Treat PTSD in Youth

Description of Trauma-Specific Cognitive Behavioral Therapy

Exposure therapy (conducted gradually or via flooding) and cognitive restructuring are the core elements of trauma-specific cognitive behavioral therapy (TS-CBT; Brown & Campbell, 2009). Exposure to the traumatic memory and associated fear network alters the memory such that threat cues are re-evaluated in the absence of aversive consequences and in a setting that allows for habituation (Foa, Steketee, & Rothbaum, 1989). Additional emotions (e.g., shame or anger) are addressed through direct confrontation of conflicts, misattributions, and expectations (i.e., cognitive restructuring; Resick & Schnicke, 1992). The discussion of the trauma also allows for elaboration and integration of the memory into the person's existing memory system (Ehlers & Clark, 2000). Parent involvement in TS-CBT is used to support participation in and responses to exposure and cognitive restructuring, as well as manage trauma-related externalizing behavior problems (Cohen, Mannarino, Berliner, & Deblinger, 2000). Bouchard, Mendlowitz, Coles, and Franklin (2004) outline fundamental principles to guide the use of exposure in children and adolescents, briefly addressing developmental considerations. Likewise, Cohen, Deblinger, Mannarino, and de Arellano (2001) provide recommendations for cultural adaptations.

As a result of the increased awareness of the prevalence of trauma and subsequent PTSD symptoms in youth, the treatment outcome literature has grown significantly over the past decade. Reviews published in the past 5 years (Chaffin & Friedrick, 2004; Feeny, Foa, Treadwell, & March, 2004; Nikulina et al., 2008; Saunders, Berliner, & Hanson, 2004; Silverman et al., 2008; Taylor & Chemtob, 2004) have summarized the studies to date, including 14 randomized clinical trials (RCTs) on the treatment of PTSD in youth. Recent literature searches yielded four additional RCTs (Ahmad, Larsson, & Sundelin-Wahlsten, 2007; Cohen, Mannarino, Perel, & Staron, 2007; Layne et al., 2008; Tol et al., 2008). Researchers (e.g., Silverman et al., 2008) have classified the treatments according to Chambless and Hollon's (1998) criteria and found superiority of two forms of TS-CBT. Trauma-Focused Cognitive Behavioral Treatment (TF-CBT; Cohen & Mannarino, 1996a) was designated as "well-established," and Cognitive Behavioral Intervention for Trauma in Schools (C-BITS, Stein et al., 2003) was designated as "probably efficacious." Huey and Polo (2008) found both TF-CBT and C-BITS to be efficacious psychosocial treatments for trauma-exposed ethnic minority youth. Other treatments (e.g., Resilient Peer Treatment, Fantuzzo, Manz, Atkins, & Myers, 2005; Fantuzzo et al., 1996; Cognitive Processing Therapy, Ahrens & Rexford, 2002; Child-Parent Psychotherapy, Lieberman & Van Horn, 2005; Lieberman, Van Horn, & Ippen, 2005) were found to be "possibly efficacious or experimental." The following is a brief review of studies examining the efficacy of psychosocial treatments for reducing children's posttraumatic stress symptoms.

Efficacy of Trauma-Specific Cognitive Behavioral Therapy

Many empirically sound research studies, including a meta-analysis, a multi-site study, and numerous RCTs, have demonstrated the efficaciousness of TS-CBTs. In their meta-analysis of evidence-based treatments of trauma, Silverman et al. (2008) included randomized studies with comparison conditions, multi-source assessments, manualized treatments, and clearly described statistical analyses. The authors contend that TS-CBT protocols have the strongest evidence as a treatment of PTSD in children, with comparable results using individual and group formats. Of the 21 studies included, approximately half (11) targeted sexual abuse, six targeted community violence, four targeted single incident traumas (i.e., major hurricane, marital violence, motor vehicle accident, and a mix of single incident traumas), and three targeted physical abuse. Notably, they reported statistically significant treatment effects only for CBT interventions ($d = 0.50$). Although variations in content were present across therapies, TS-CBTs typically included exposure therapy, cognitive restructuring, and affective (e.g., anger management) and behavioral (e.g., problem-solving) skill-building components. Half of the TS-CBT protocols included parent involvement, in parallel parenting sessions and/or joint parent–child sessions. Parenting sessions consisted of a combination of behavioral management strategies (i.e., parent training), sharing of the narrative, and/or clarification (accepting responsibility for role in abuse). Lastly, interventions included safety planning with children and caregivers, ongoing safety assessment, stress and crisis management, and future planning (Vickerman & Margolin, 2007).

The most comprehensive examinations of TS-CBT have been conducted by Drs. Cohen, Deblinger, Mannarino, and Steer, the developers of TF-CBT. In a series of multi-site studies with over 300 participants from urban and rural settings, Cohen and colleagues compared TF-CBT to Child-Centered Therapy and Nondirective Supportive Treatment. Trauma Focused Cognitive Behavior Therapy (vs. Child-Centered Therapy) showed statistically significant improvements in child sexual abuse-related PTSD as well as child depressive symptoms and behavioral problems (Cohen, Deblinger, Mannarino, & Steer, 2004; Cohen, Mannarino, & Knudsen, 2005). Critical child sexual abuse-related cognitions related to interpersonal trust and shame also significantly improved. Both TF-CBT and Nondirective Supportive Treatment were found to demonstrate similar reductions in youth's PTSD symptoms at post-treatment and 6-month follow-up, with only TF-CBT evidencing significant improvements for PTSD symptoms at 12-month follow-up. Children (aged 8–15 years) in these samples reported multiple traumas and were more racially/ethnically diverse than those in earlier studies.

Making a Practical Argument for CBT

Despite the strong empirical support for CBT, getting families and therapists to engage in the treatment approach can be a challenge due to barriers to mental health, including language differences, lack of available transportation, lack of insurance coverage, long waiting lists, fear of stigmatization, low acculturation, delay in seeking treatment until patients are in crisis, and use of alternatives to therapies (e.g., church, family, friends; Brown, Albrecht, McQuaid, Munoz-Silva, & Silva, 2004). Thus, it is essential that therapists and clients be provided an acceptable rationale for treatment. Often, this is an ongoing process, with a rationale provided for the overall model and each component.

There are both scientific and clinical arguments for the utility and feasibility of trauma-specific CBT with children (Addis & Carpenter, 2000; Verduyn & Calam, 1999). In CBT, attention is given to a diversity of symptoms using a model that addresses cognitive, physiological, and behavioral responses to trauma cues. Thus, the diversity of children's responses to trauma exposure (e.g., PTSD symptoms, maladaptive cognitions, behavior problems) is addressed

within a single treatment modality. Because trauma survivors often experience perceived uncontrollability and unpredictability, psychoeducation (i.e., rationales for each treatment component) is provided. For example, prior to relaxation training, the therapist describes the flight or fight reaction, with an explanation of the way in which relaxation reduces anxiety by decreasing muscle tension. In addition to the client's mastery of coping skills, the collaborative work serves as experiential learning that empowers the patient, re-establishing a sense of control. The "evidence-gathering" aspect of cognitive restructuring also functions as an experiential exercise. Additionally, coping skills are portable techniques that can be used in multiple settings in which children's symptoms arise (e.g., classroom, home, car), increasing generalizability of therapeutic gains.

Cognitive behavior therapy protocols for children (e.g., TF-CBT) have outlined strategies to adapt the coping skills based on the client's developmental level. For example, the fight or flight response might be explained to younger children via a story (e.g., "A caveman who sees a bear in the bushes while gathering berries might jump, run away, or stay to defend himself. His muscles have to be tense to help him do these things"; Brown, 2002). The relaxation technique used with preschoolers is a simple, two-step procedure (e.g., acting like a "tin soldier," then a "wet noodle"), whereas teenagers learn progressive muscle relaxation. Because children are accustomed to didactic interactions, the psychoeducational framework of CBT is familiar to them.

Lastly, children exposed to trauma are socioeconomically, racially, and ethnically diverse. Given the finding that ethnic minority youth may be particularly vulnerable to emotional problems following a trauma (e.g., Santos et al., 2008), the feasibility of CBT with diverse populations is critical. In a review of treatments for ethnic minority youth, Huey and Polo (2008) critique the literature, stating that few tests of cultural adaptations have been conducted, but note that TF-CBT is "probably efficacious" and CBITS is "possibly efficacious" with ethnic minority youth. Accordingly, the active, directive, and structured nature of CBT appears to be effective and acceptable with diverse ethnic groups (Verduyn & Calam, 1999). Adaptations of evidence-based treatments to include culturally responsive elements have been proposed and included in some studies, though none directly tested for cultural effects; still preliminary correlation data provide some evidence for its beneficial effects (Huey & Polo, 2008), arguing for the continuation of integrating cultural constructs into treatment as needed.

Using EMDR and Other Short-Term Interventions to Treat PTSD in Youth

EMDR (EMDR Institute, Inc., 2004) and other short-term therapies have been examined in the treatment of sexually abused youth, with comparisons to waitlist control, CBT, and nonspecific group therapy. EMDR, historically considered as a behavior therapy, is currently described as a structured "comprehensive, integrative" therapy that includes elements from "psychodynamic, cognitive behavioral, interpersonal, experiential and body-centered therapies" (EMDR Institute, Inc.). Descriptively, EMDR consists of graduated imaginal exposure sessions with simultaneous visual tracking of therapist hand movements; however, there is considerable debate on the mechanisms underlying the effectiveness of EMDR (e.g., Lee, Taylor, & Drummond, 2006). The one study using psychodynamic therapy for traumatized youth involved a manualized individual psychoanalytic treatment with a list of unspecified topics (Trowell et al., 2002).

EMDR has been examined in the treatment of PTSD subsequent to sexual abuse and exposure to war. In a small sample ($N = 14$) of sexually abused Iranian girls, Jaberghaderi, Greenwald, Rubin, Zand, and Dolatabadi (2004) compared CBT and EMDR using child and parent report of PTSD symptoms. The authors describe the CBT treatment as being similar to TF-CBT (e.g., Deblinger, Lippmann, & Steer, 1996). They found statistically significant improvements on parent-reported PTSD symptoms for both conditions, and on child-reported PTSD symptoms only for those receiving EMDR. EMDR was found to be superior to a waitlist control in a randomized trial with

33 youth (aged 6–16 years) meeting criteria for PTSD (Ahmad et al., 2007). Participants endorsed a range of traumatic experiences, with sexual abuse and other forms of maltreatment as the most frequent. The small and mixed trauma samples and associated limited statistical power of these studies result in limited generalizability of the efficacy of EMDR to other sexually abused children.

Two RCTs have been conducted to examine the efficacy of EMDR for children exposed to war. Chemtob, Nakashima, and Hamada (2002) examined 4-week protocols designed to address trauma themes via play, art, or talk therapy. Using a randomized lagged-groups design, children aged 6–12 years were assigned to one of three treatment waves of this protocol provided as group vs. individual therapy (six conditions). PTSD symptoms decreased for children in treatment (vs. waiting list) with no differences between the active treatments; attrition rates were higher for individual (vs. group) therapy. Chemtob, Nakashima, and Carlson (2002) followed this study with an investigation of EMDR (three sessions) for 32 of the children who continued to meet PTSD criteria 1 year after the earlier study, again using a randomized lagged-groups design in two treatment waves. Children in both waves of EMDR showed significant decreases in symptoms of clinician-rated PTSD that were maintained at 6-month follow-up assessment. Although both of these studies are limited by the lack of a therapy placebo, lack of self-report of PTSD, and small samples, they provide evidence for the value of short-term EMDR and psychodynamic interventions for disaster-related PTSD.

Psychodynamic Psychotherapy

Only one known study examining psychodynamic therapy in the treatment of PTSD in youth has been published. Trowell et al. (2002) randomly assigned sexually abused girls to individual psychodynamic therapy (30 weeks) or "group psychotherapeutic and psychoeducational therapy" (18 weeks). They found significant improvements for both groups, with psychodynamic therapy evidencing greater improvements on PTSD symptoms.

The studies of the above interventions for PTSD in youth lend preliminary support for EMDR following maltreatment and war, and psychodynamic therapy following sexual abuse. Limits of the reviewed studies include lack of follow-up, small samples, and limited range in ethnicity, different formats (individual vs. group; Trowell et al., 2002), different lengths of treatment (Trowell et al., 2002), lack of independent investigators, and absence of comparison to other active treatments (Ahmad et al., 2007). Additional randomized trials of EMDR, particularly in comparison to TS-CBT, are warranted.

Summary of Psychosocial Treatments for PTSD

In sum, CBT and EMDR may be efficacious for PTSD in youth. Silverman et al. (2008) and others have established the superiority of TS-CBT. The robustness of this conclusion is strengthened by emerging literature with larger sample sizes, multi-informant assessment, and diverse samples. The data suggest the importance of focusing directly on the traumatic event and including both children and their caregivers (Friedrich, 1996). One of the key components of TS-CBT is exposure, argued to be similar in procedures and outcome to EMDR (Lee et al., 2006). Although gains have been made to the literature in identifying efficacious treatments for youth, more research is needed to better assess and treat developmentally specific trauma sequelae, determine long-term effects of treatment, and show effectiveness of these treatments among diverse ethnic groups and settings. The state of the literature is reviewed below in the context of these important issues, highlighting the strengths and gaps.

Critical Issues in Treating PTSD in Youth

Developmental Considerations

Although research is emerging, investigations consistently have documented the relation between developmental stage and clinical presentation of

PTSD, illustrating key differences in traumatic stress reactions among preschoolers, children and adolescents (Kendall-Tacket, Meyers Williams, & Finkelhor, 1993; Saul, Grant, & Carter, 2008; Scheeringa, 2008). Common symptoms in preschoolers include anxiety, nightmares, aggression, and PTSD symptoms, whereas school-aged children tend to present with behavioral problems and more repetitive play (Dyregrov & Yule, 2006). Large national studies focusing on adolescents have reported evidence in support of an alternative model of symptom presentation with clusters of arousal, avoidance, intrusion, and numbing (e.g., Saul et al., 2008).

Collectively, these findings highlight the need for the integration of developmentally relevant clinical patterns into the treatment. The vast majority of the aforementioned treatment outcome research has focused on school-aged children (between the ages of 8 and 15). The following highlights the studies that have focused on preschoolers and adolescents.

Treatment of Preschoolers

It is noteworthy that research has focused on specific traumas with specific age groups. The majority of research involving preschoolers has focused on sexual abuse and domestic violence; no RCT has been conducted with preschoolers who have PTSD subsequent to experiencing physical abuse, community violence, disaster, or war/terrorism.

Treatment of Adolescents

Few studies have been published on the treatment of adolescents with PTSD. No randomized trial has been published on the treatment for abuse-related PTSD in adolescents. This may be due to the perception that adolescents are difficult to engage and more likely to drop out of treatment (e.g., Copeland, 2006; Stevens, Kelleher, Ward-Estes, & Hayes, 2006), and in turn, are understudied. Teenagers account for 51% of all reported sexual abuse, with approximately 1.8 million adolescent victims of sexual assault (Kilpatrick et al., 1998). Additionally, adolescent women experience sexual assault at rates higher than any other age group, with 33% of sexual assaults occurring when the victim is between the ages of 12 and 17 (U.S. Department of Justice, 2000), resulting in serious mental health consequences including PTSD (e.g., Dyregrov & Yule, 2006). Also given that 20% of child physical abuse reports in U.S. are for adolescents (Administration for Children Services, 2006) and 10% of adolescents report physically abusive punishment each year (Brown, Swenson, Saunders, Kilpatrick, & Watner, 2009), treatment outcome studies for teenagers are necessary. Recent studies focusing on outcomes in adolescent victims of physical abuse have documented internalizing and externalizing symptoms (e.g., Bourassa, 2007), substance use (Hamburger, Leeb, & Swahn, 2008), and social isolation (Elliott, Cunningham, Linder, Colangelo, & Gross, 2005), underscoring the need to provide developmentally appropriate treatment for this group.

Two ongoing studies of TS-CBT are evaluating interventions for adolescents exposed to interpersonal violence, Skills Training in Affect Regulation (STAIR; Cloitre, Heffernan, Cohen, & Alexander, 2001), and Structured Psychotherapy for Adolescents Responding to Chronic Stress (SPARCS; DeRosa et al., 2006), respectively. STAIR includes elements of TS-CBT (e.g., psychoeducation, behavioral and cognitive coping skills, processing of trauma narrative) and adds components to address affect dysregulation (e.g., acceptance) and behavioral problems (e.g., interpersonal skill building). Preliminary findings in a randomized trial (Cloitre & Carr, 2005) suggest that STAIR is associated with reductions in PTSD, depression, and behavioral problems; it is rated "supported and acceptable" by the National Child Trauma Stress Network (NCTSN). Similarly SPARCS includes components of TS-CBT, affect regulation and interpersonal skill-building approaches; key therapeutic components draw from principles of dialectical behavior therapy (DBT; Miller, Rathus, & Linehan, 2007). Pilot data (NCTSN, 2008a) indicate significant improvement in PTSD symptoms, behavioral dysfunction, and interpersonal relationships. Strengths include a specific focus on adolescents and use with ethnically diverse groups including African American, Latino, Native American and refugee/immigrant

populations (NCTSN, 2008a). Neither treatment program includes caregivers in assessment and treatment, a significant limitation.

Although quasi-experimental studies (e.g., Goenjian et al., 1997) and one RCT (Layne et al., 2008) have provided preliminary support for school-based group CBT interventions in reducing PTSD symptoms following community violence, disaster, and war, findings have been inconsistent on the reductions of symptoms and problems particularly associated with teenagers (e.g., emotion dysregulation, peer conflicts). Lack of parent-report measures as well as follow-up data precludes clear interpretation of results. RCTs of TF-CBT which have included youths up to 15 years of age also provide support for the use of TS-CBTs with adolescents, but may not explicitly focus on adolescent developmental needs.

Trauma Type

As previously noted, approximately a third of children and adolescents are exposed to one or more traumatic event by late adolescence (Copeland et al., 2007), with rates varying across trauma types and samples. Moreover, exposure to trauma has been associated with diverse negative psychological outcomes (e.g., depression, PTSD, disruptive behavior problems; Silverman et al., 2008). The current state of the literature is reviewed with respect to trauma type, primarily focusing on the treatment of PTSD.

Sexual Abuse/Assault

The majority of the investigations conducted to date have been of CBT for victims of child sexual abuse with the most commonly investigated treatment being TF-CBT (e.g., Cohen et al., 2005). In the first RCT examining TF-CBT, Deblinger et al. (1996) compared the efficacy of CBT in treating full or partial PTSD as a function of treatment participants (i.e., child sexual abuse victim and/or nonoffending caregivers) in a predominantly Caucasian sample of 90 children (aged 7–13 years) and their caregivers. Children who received CBT evidenced greater reductions in PTSD symptoms than those in the control sample. Moreover, these PTSD symptom reductions were maintained 24 months post-treatment (Deblinger, Steer, & Lippman, 1999). In another investigation of 32 school-aged sexually abused girls (aged 8–13) of predominantly African-American background, Celano, Hazzard, Webb, and McCall (1996) compared an 8-week protocol, Recovery From Abuse Program (RAP) to treatment as usual (TAU) and found reductions in PTSD symptoms for both groups and improvements for caregiver-related outcomes (e.g., self-blame) for RAP only. RAP sessions included psychoeducation, discussion of trauma-specific cognitions, "traumatic sexualization," coping and assertiveness skills, and safety planning. Although the abuse was discussed in each session, no structured exposure was described and that omission may have contributed to limited group differences.

The aforementioned recent randomized trials (Cohen et al., 2004, 2005) have demonstrated the efficacy of TF-CBT in treating child sexual abuse-related PTSD in children and young adolescents (aged 8–15 years). TF-CBT has been found to be superior to waitlist control, supportive psychotherapy, and routine community care in reducing PTSD symptoms (Cohen et al., 2004, 2005; Cohen & Mannarino, 1998; Deblinger et al., 1996; King et al., 2000). Of note, study samples in Cohen et al.'s studies also reported physical abuse (26%) and witnessing domestic violence (58%), suggesting that TS-CBTs are effective with multiply traumatized children.

No studies have examined treatment of PTSD symptoms among sexually abused preschoolers. In an RCT with 67 sexually abused children and caregivers, Cohen and Mannarino (1996a) found TS-CBT to be superior to nondirective supportive therapy in reducing emotional symptoms, sexualized behaviors, and externalizing behaviors in children. These gains were maintained at 1-year follow-up assessments (Cohen & Mannarino, 1996b). The focus of treatment on other trauma sequelae (e.g., sexualized behaviors, externalizing behaviors) may be in part due to lack of a developmentally appropriate DSM diagnosis of PTSD for preschoolers.

Child Physical Abuse

Research examining the treatment of youth with PTSD subsequent to physical abuse is limited. In a preliminary study, Swenson and Brown (1999) examined the efficacy of CBT to address sequelae specific to school-aged child physical abuse victims and reported its effectiveness at decreasing trauma symptoms. An early RCT (Kolko, 1996b) that compared parent and child CBT and Abuse-Focused CBT (AF-CBT; Kolko, 1996a) to TAU found improvements for both active treatments on children's internalizing and externalizing symptoms and parenting-related variables. Despite the strength of this investigation (e.g., repeated assessments of numerous areas of functioning), this study provides little guidance regarding the treatment of PTSD because only two participants (of 47) met criteria for the disorder at pretreatment. Other studies focusing on treatment of physical abuse present with similar limitations as they do not assess PTSD symptoms (e.g., Fantuzzo et al., 2005; Runyon, Deblinger, & Steer, 2010).

Domestic Violence

Younger children, mostly under the age of 5, are the age group most likely to be exposed to domestic violence (Fantuzzo, Boruch, Beriama, Atkins, & Marcus, 1997). National reports have also found that children living in such households are at increased risk for physical abuse and/or injury (National Center for Children Exposed to Domestic Violence, 2006). As such, treatments focusing on physical abuse often address domestic violence as well. Vickerman and Margolin (2007) review treatments for youth exposed to family violence, concluding that TF-CBT (Cohen et al., 2004) and AF-CBT (Kolko, 1996a) are deemed to be well supported to treat PTSD and/or externalizing behavior problems. The Kids' Club (Graham-Bermann, 1992) is a group psychoeducational program for children (aged 6–13) and their parents with treatment components focusing on emotion identification, coping skills, cognitive restructuring, and safety planning. The Kids Club was found to be effective in reducing PTSD symptoms compared to waiting list control (Vickerman & Margolin, 2007).

Lieberman et al. (2005) developed an intervention, Child-Parent Psychotherapy, based on CBT and psychodynamic theories consisting of weekly individual joint sessions guided by free play. The intervention focused on changing maladaptive behaviors, reinforcing developmentally appropriate social interactions, and helping the mother and child to create a joint narrative of the traumatic event. Analyses supported that the intervention significantly reduced child PTSD symptoms and behavior problems for 75 preschoolers exposed to domestic violence in an RCT comparing treatment to routine community care (Lieberman et al., 2005). Improvements in behavioral problems were maintained at 6-month follow-up assessment but no information was provided about PTSD (Lieberman, Van Horn, & Ippen, 2006).

Community Violence

Most treatment outcome studies focusing on treatment of PTSD subsequent to community violence have been with children (Seiger, Rojas-Vilches, McKinney, & Renk, 2004) focusing on early intervention/prevention and in school settings, with two RCTs that included adolescents. Wolfe et al. (1996) developed a group intervention, The Youth Relationships Project, for at-risk teens with histories of exposure to violence. The intervention involves psychoeducation and skills training specific to community violence, with particular focus on adolescent issues related to healthy relationships (e.g., dating violence, conflict resolution). Wolfe et al. (2003) conducted an RCT with 158 adolescents, aged 14–16 years, to evaluate the intervention vs. no-treatment control group and reported a general decrease in PTSD symptoms for participants in the active treatment. Smith et al. (2007) evaluated the efficacy of individual TS-CBT vs. a waitlist control group in children and adolescents (aged 8–18 years old) who met full criteria for PTSD after experiencing single incident traumas, including community violence and interpersonal violence. Participants who received CBT evidenced statistically significant improvements in PTSD symptoms at post-treatment and 6-month follow-up evaluations.

War

Two studies have demonstrated the efficaciousness of CBT in treating PTSD in youth exposed to war. Tol et al. (2008) found CBT to be an efficacious

treatment for youth exposed to war. Tol et al. conducted a large school-based randomized trial with 495 children aged 7–15 years (80% aged 9–11 years) exposed to political violence in Indonesia. Children were assigned to a 15-week manualized treatment (including CBT techniques, trauma-specific elements, and cooperative play) or a waiting list. Therapy was conducted with groups of approximately 15 youth in the classroom setting. Results of the study demonstrated moderate reductions in PTSD symptoms for girls (vs. boys) enrolled in the active treatment (vs. waitlist) that were retained at the 6-month follow-up assessment; neither condition evidenced change in other outcome variables (e.g., depression). Strengths of the study are inclusion of a large non-Caucasian sample and successful implementation of a CBT program in a low-resource community setting.

In a RCT, Layne et al. (2008) examined the effectiveness of a two-tiered school-based CBT group intervention program with 127 adolescents exposed to war-related trauma and bereavement in Bosnia. Adolescents reporting PTSD symptoms were randomized to a classroom-based psychoeducation/skills intervention (active treatment comparison) or comparison plus 17-session manual-based group therapy that included trauma and grief components. Significant reductions at post-treatment and 4-month follow-up assessments were demonstrated for both treatment conditions, whereas improvements in grief reactions were present for only the second group. Findings from these studies suggest that although trauma-based treatments are effective in reducing PTSD symptoms, specific components to address other sequelae (e.g., grief) may be warranted. The authors also suggest the need to integrate psychosocial interventions with poverty reduction and conflict resolution to address chronic stressors.

Multiply Traumatized Youth

Research on youth exposed to chronic stressors has documented complex stress reactions. Experts (e.g., van der Kolk, Roth, Pelcovitz, Sunday, & Spinazzola, 2005) argue for the expansion of the PTSD diagnosis to include dysregulation in affective, behavioral, and relational domains, and refer to as Disorders of Extreme Stress Not Otherwise Specified, Developmental Trauma Disorder, or Complex PTSD. Studies have shown that preschoolers, children, and adolescents who experience multiple traumas present with more complex symptomatology (e.g., Finkelhor, Ormrod, & Turner, 2007; Green et al., 2000; Hall, 1999). Given that the large majority of traumatized youth are exposed to multiple forms of trauma (Dyregrov & Yule, 2006), it is important for treatment to include assessment and treatment of PTSD and other trauma sequelae.

Cultural Considerations

Although there have been many recommendations to address cultural constructs in the treatment of PTSD in youth, research support has been inconsistent. In an empirical review, Cohen et al. (2001) concluded that findings have been mixed with some studies reporting differential symptom severity patterns for minority ethnic groups and others finding no differences. For example, in a large sample of adolescent and adult trauma survivors, aged 14 years and older ($N=269$), Santos et al. (2008) reported participants of non-Caucasian ethnic/racial groups endorsed greater levels of posttraumatic distress. More research is needed to identify critical constructs and assess their relative importance among ethnic groups.

Treatment Modality

Several studies indicate that TS-CBT presented via a group format is an efficacious treatment modality. Avinger and Jones (2007) reviewed ten outcome studies of group therapy for female adolescents, aged 11–18 years, with a history of child sexual abuse or sexual assault. Two studies used TF-CBT models (Cohen & Mannarino, 1997; Sinclair et al., 1995); two used multidimensional models that included sharing of abuse stories, coping skills, "general psychotherapy," and psychoeducation; and the rest used Rogerian and/or unspecified models. Limitations include variations in length of treatments, small sample size, no

follow-up assessments, lack of multiple reporters on symptoms (e.g., caregiver report), and lack of comparison groups (only four studies included controls), precluding any definitive conclusions. Despite the limitations, only the studies using TF-CBT and multidimensional models demonstrated reductions in PTSD, with both approaches including an element of gradual exposure. All group modalities demonstrated significant improvements in self-esteem and anxiety, suggesting that group therapies in general provide an outlet for peer support.

Stein et al. (2003) evaluated C-BITS for 126 children in the sixth grade exposed to community violence. C-BITS is a TS-CBT for children between the ages of 10–15 and is delivered in a group format, often in schools (NCTSN, 2008b). Children were randomized to 10-week group C-BITS vs. waiting list and those receiving C-BITS evidenced significantly greater reductions in PTSD symptoms. Kataoka et al. (2003) compared an 8-week manualized individual treatment based on C-BITS for community violence to a waiting list with 198 Latino immigrant children. PTSD symptoms decreased from pre- to post-treatment and at follow-up for C-BITS only. Both treatments lacked comparison to another active treatment, but established the utility of the intervention for different formats and ethnic minority children, warranting replication.

Participants of Treatment

In their meta-analysis, Silverman et al. (2008) found that the inclusion of parents (vs. only children) was correlated with more effective treatment of child anxiety and depression, but not PTSD symptoms. Deblinger et al. (1999) reported similar results and also found that parent involvement was related to improvements in other outcome variables (e.g., child trauma-related cognitions, parenting skills). King et al. (2000) compared child CBT, family CBT, and a waitlist control condition in 37 sexually abused youth (5–17 years) and showed statistically significant reductions on children's PTSD symptoms for both CBT conditions but not the waitlist. These improvements were maintained at the 12-week follow-up assessment. Family CBT group evidenced additional benefit in decreasing fear at 3-month follow-up.

Factors Related to Treatment Outcome

Few studies have explored mediators and moderators of psychosocial treatment of PTSD in youth. Studies have examined other trauma-related outcomes such as externalizing and internalizing symptoms that are often comorbid with PTSD (Silverman et al., 2008). These studies can inform future investigations focusing on PTSD. Researchers have identified trauma characteristics (e.g., severity), family variables (cohesion, parental responses), and treatment format (parent/child only, or both) as treatment outcome predictors. Study findings also have noted developmental differences in the relative importance of factors. Silverman et al. (2008) examined the mediators and moderators of treatment of trauma and found that type of treatment (CBT), trauma type (sexual abuse), and parental involvement (vs. control) were all moderators of children's responses to treatment (i.e., reductions in anxiety, depressive and/or PTSD symptoms).

Implications of Research on the Efficacy of CBT

Reviewing the present state of psychosocial treatments for PTSD suggests several implications. First, it is apparent that including parents in the treatment of children who have experienced traumatic experiences is an important component in interventions aimed at PTSD symptoms. The results of several studies indicate that including parents in treatment improves children's response to treatment (e.g., Deblinger et al., 1996). Second, it is clear that additional research examining treatments for children with PTSD is necessary for several reasons. The majority of research is conducted on children with sexual abuse histories and research examining other traumas (e.g., physical abuse, natural disasters, witnessing domestic violence, community violence) is less

developed. Second, most studies focus on children and younger adolescents, whereas little research has examined the treatment of older adolescents (i.e., 14–18 years) with PTSD. Third, several treatments have shown promise, but cannot yet be considered efficacious given design limitations (e.g., EMDR and short-term psychodynamic therapies); therefore, future research must examine these treatments in longitudinal and methodologically sound experimental designs (e.g., RCTs). Lastly, research focusing on cultural adaptations of treatment and correlates of outcome in diverse groups is lacking.

Psychopharmacological Treatments for PTSD in Youth

A literature review on the use of pharmacotherapy in children and adolescents for the treatment of PTSD indicates that the research on this subject is limited and consists mostly of open trials and case studies. At this time, the U.S. Food and Drug Administration has not approved any medications for the treatment of pediatric PTSD, and has approved sertraline and paroxetine for the treatment of PTSD in adults (National Institute of Mental Health, 2009). As such, pharmacological interventions are off-label and primarily considered to be adjunctive to psychosocial treatments to control severe and debilitating symptoms and/or treat comorbid conditions (Cohen & Mannarino, 2000; Perrin, Smith, & Yule, 2000; Pynoos, & Nader, 1993). Below is a review of the studies that can inform choice of a medication for treatment of PTSD symptoms.

Psychopharmacological Interventions

Initial studies on the efficacy of psychopharmacological interventions focused on the treatment of nightmares and other re-experiencing symptoms. Extending from studies with veterans that demonstrated reduction of explosive behavior and nightmares, Famularo, Kinscherff, and Fenton (1988) conducted an ABA design study examining the use of propranolol in the treatment of acute PTSD in 11 children (aged 6–12 years) receiving concomitant psychotherapy. No information was provided on the types or numbers of traumas experienced. Starting dosage of propranolol was 0.8 mg/kg/day in three divided doses and was gradually increased to a maximum of 2.5 mg/kg/day over a 2-week period. The medication was administered for 4 weeks and then tapered over the fifth week. Mild adverse side effects were reported included sedation, mildly lowered blood pressure/pulse. Results showed a significant pre–post improvement on PTSD severity but also a tendency toward relapse after medication discontinuation, suggesting that propranolol was beneficial in the treatment of acute PTSD only during its use.

Other medications were evaluated in later research on the treatment of re-experiencing symptoms. Loof, Grimley, Kuller, Martin, and Shonfeld (1995) examined the use of carbamazepine with a mixed gender sample of 28 youth (aged 8–17 years) with a diagnosis of PTSD during hospitalization in a state hospital. Participants had histories of chronic sexual abuse, and reported a range of re-experiencing symptoms (e.g., intrusive thoughts, flashbacks, nightmares). Unlike Famularo et al.'s (1988) sample, more than half of the current participants met criteria for comorbid conditions for which additional medications were added to the treatment. The starting dosage of carbamazepine was 100 mg bid and was titrated up every 4–7 days. Carbamazepine was dosed (300–1,200 mg/day) to a serum level of 10.0–11.5 μg/ml, until PTSD symptoms remitted. Serum carbamazapine levels were measured every 2 months following symptom remission. No adverse drug reactions to the carbamazepine were reported. Eight patients presented with comorbid ADHD or depression for which methylphenidate/clonidine or antidepressants were added, respectively. The authors found that 22 out of the 28 patients became asymptomatic, and the remaining six were significantly improved. However, no information was provided regarding the type of PTSD symptoms that remitted or follow-up assessments.

Two early investigations examined the use of clonidine in the treatment of nightmares in children with mixed results. In a single case study

of a 7-year-old girl (history of physical abuse and exposure to domestic violence) diagnosed with chronic PTSD (symptom duration of 10 months), Horrigan (1996) reported the introduction of clonidine 0.05 mg qhs subsequent to 3 months of psychotherapy focusing on her history of maltreatment. Clonidine was initially effective in reducing the nightmares but discontinued due to breakthrough nightmares and a course of guanfacine 0.50 mg qhs was initiated. At the end of treatment, the patient reported no nightmares for the subsequent 7 weeks. In an open trial (Harmon & Riggs, 1996), the investigators reported success with clonidine for symptoms of aggression, hyperarousal, and sleep disturbances for seven preschool children (aged 3–6 years) with histories of severe maltreatment, diagnosed with PTSD, and receiving psychosocial treatment at a day hospital. Starting dosage of clonidine was 0.05 mg qam and if well tolerated, a second dose of 0.05 mg qhs was added. Two of the children also were being treated with imipramine for depression and one was taking clonidine at the time of admission. Most children experienced transient sedation for the first week and an average drop in blood pressure of less than 10% from baseline levels with no other reported side effects. To avoid the initial sedating effects, the clonidine was patch administered and was found to be well tolerated. Still, two participants developed temporary local irritation: one continued to pull off his patch and one developed a severe poststreptococcal glomerulonephritis with hypertension due to an abrupt discontinuation of the patch. Target symptoms, assessed weekly, were rated as "moderately" to "greatly improved" by both teachers and physicians. Although this study did not use standardized symptom-assessment scales and results were based on subjective clinical impressions, clonidine was deemed to be effective in reducing symptoms of aggression, hyperarousal, and sleep disturbances in children with PTSD.

While earlier research focused on a single PTSD symptom cluster, recent studies of psychopharmacological treatments have examined the efficacy of medications for all three clusters of PTSD. Based on the adult literature on the use of SSRIs, Seedat, Lockhat, Kaminer, Zungu-Dirwayi, and Stein (2001) conducted a 12-week open trial on the use of citalopram in eight adolescents (mean age = 14.8 years) with PTSD. Study participants were diagnosed with moderate to severe PTSD of which six of the adolescents also met criteria for mild major depression and one met criteria for panic disorder. Participants were given 20 mg of citalopram and administered a diagnostic measure of PTSD every 2 weeks for 12 weeks. Mild adverse effects were reported, the most common being sweating, nausea, headache, and fatigue. Seven participants completed the study and evidenced 38% reduction in PTSD symptoms.

To further examine the utility of citalopram, Seedat et al. (2002) expanded the sample to include children, adolescents, and adults with PTSD. The authors conducted an 8-week trial that compared 24 children and adolescents whose ages ranged from 10 to 18 years (mean = 14.3 years) to 14 adults (mean = 33.5 years). The sample from the 2001 study was included in the group of children/adolescents. Of the youth, 14 experienced sexual assault, eight witnessed violence or death, one was a perpetrator of violence (accidentally stabbed his brother), and one experienced physical assault. Assessments were conducted biweekly and included age-appropriate diagnostic interviews and PTSD symptom scales. Mean duration of PTSD symptoms was 10.96 months in children and 38.4 months in adults. Patients previously treated with citalopram were excluded as well as those who reported comorbid mood and anxiety disorders preceding the diagnosis of PTSD. Twelve children met criteria for a depressive disorder and one adolescent met criteria for panic disorder. There was a 2-week washout period for all subjects. During this trial, concomitant pharmacotherapy or psychotherapy was not permitted; however, supportive counseling was provided by the treating clinician. Participants were prescribed 20–40 mg/day of citalopram (mean dose = 20 mg). Most side effects were mild and self-remitting (e.g., drowsiness, headache, nausea, sweating, insomnia, dizziness, tremor, increased appetite), but two children withdrew due to more serious adverse effects (i.e., nose bleed, skin rash). Of the youth

participants, 16 were responders, defined as a score of 1 or 2 (much or very much improved) on a measure of PTSD administered at the conclusion of the study. Five participants were minimally improved, and three were minimally worse on the PTSD symptom measure. Overall, there was a 54% reduction in PTSD severity scores for youth. Duration of symptoms, mode of onset, and comorbidity did not impact treatment outcome. Collectively, these findings lend support to the use of citalopram for children and adolescents with comorbid conditions.

The most recent studies in children and adolescents have continued to focus on all PTSD symptoms and extended to other samples, including the incarcerated population as they tend to have high rates of PTSD. Stathis, Martin, and McKenna (2005) conducted a 6-week case series study of the use of quetiapine in treating PTSD, an atypical antipsychotic that has been effective in treating psychotic symptoms in adolescents and adults. Participants were six adolescent males, aged 15–17 years incarcerated in a juvenile detention center and who did not meet criteria for conduct disorder. No information on trauma history was provided. Starting dose of quetiapine was 25–50 mg at night and was titrated up to 100 mg at night, or until a clinical response was observed. All six adolescents successfully completed the study period and elected to continue taking quetiapine afterward. After 6 weeks, participants demonstrated a significant decrease in PTSD symptoms as well as symptoms of dissociation, anxiety, depression, and anger. No daytime sleepiness was reported and although nighttime sedation (side effect) was reported by all participants, it was viewed positively because of its assistance with sleep. Significant weight gain was reported over the 6-week period. No other persistent adverse effects were reported. Results of this study provide evidence for the use of atypical antipsychotic medications in treating incarcerated adolescents with PTSD. More information is needed on the use of these mediations with specific trauma types.

Continuing the examination of incarcerated adolescents, Steiner, Saxena, Carrion, Khanzode, Silverman, and Chang (2007) examined data from a randomized control trial conducted by Steiner, Petersen, Saxena, Ford, and Matthews (2003) on the efficacy of divalproex sodium (DVP), an anticonvulsant frequently used as a mood stabilizer. DVP was chosen based on evidence for its success in treating adolescents with a variety of disorders and for its lack of adverse side effects. The original sample (2003) consisted of 71 incarcerated male youth with conduct disorder. Participants in the original sample ranged in age from 14 to 18 years (mean = 15.9 years). There was a 1- week washout period prior to enrollment. Participants were randomized into one of two dosing conditions, a federal requirement. In the high-dose condition, participants received 50–1,500 mg/day of DVP, with a modal oral dose of 1,000 mg/day and were gradually titrated up to therapeutic plasma levels between 50 and 120 mg/ml. In the low-dose condition, participants received up to 250 mg/day of DVP with a modal oral dose 125 mg/day. Both groups received a starting dose of 125 mg/day. DVP was well tolerated by all participants and side effects were generally mild, consisting of sleepiness and gastrointestinal upset, and generally resolved in 3–4 weeks. No serious side effects were reported. Twelve participants in the 2003 study met criteria for PTSD, and were evenly divided between dose conditions; this subsample was re-examined by Steiner et al. (2007). Mean blood level was 71.5 mg/ml (±12.4) in the high-dose condition and 15.6 mg/ml (±3.55) in the low-dose condition. At the end of the trial, participants in the high-dose compared to the low-dose group reported significantly less PTSD symptom severity, greater improvement in core PTSD symptoms, and fewer core PTSD symptoms. The results of this study provide preliminary evidence for the use of psychopharmacological treatments in incarcerated youth with PTSD and comorbid conduct disorder.

Combined Treatment

Only one study to date has examined the benefits of medication to that of psychosocial treatment. Cohen et al. (2007) randomized 24 sexually

abused youth and their primary caretakers to TF-CBT plus sertraline or TF-CBT plus placebo. Sertraline was started at 25 mg/day with instructions to increase dose to 50 mg/day. At week 3, PTSD symptoms were assessed and if improvements were observed, the current dose was maintained. For participants whose symptoms did not improve significantly and/or whose side effects were not judged to be severe, dose titration was continued to a maximum of 200 mg/day. No differences between groups were found for PTSD symptoms (i.e., both groups evidenced improvements). Further, the investigators note that their sample was not representative of treatment seekers as many families refused to consider pharmacological treatments. Study limitations included small sample size that indicates a need for a larger trial to assess the potential benefits of adding sertraline.

Clinical Implications of Research on Pharmacological Treatments

In summary, the current body of research on the use of medication as treatment for PTSD continues to expand with encouraging results. Initial studies focused on treating a single symptom, nightmares, and have advanced to the treatment of cluster of symptoms, and finally to all clusters of PTSD symptoms. Most recently, studies are strengthened by larger sample sizes and the use of medications without serious adverse side effects. The prevalence of medications without serious side effects significantly increases the utility and acceptability of pharmacological treatments. In clinical practice, children with PTSD are generally considered for medication treatment when other psychotherapeutic interventions produce less than ideal results and can be a useful addition in treating children with some of the more debilitating symptoms (Donnelly & Amaya-Jackson, 2002). Based on the two open studies employing SSRIs in children with PTSD (Seedat et al., 2001, 2002) that have demonstrated significant improvements in symptomatology with mild side effects, SSRIs (vs. other medication options) should be considered as a first-line medication, especially in patients with comorbid depression (Donnelly & Amaya-Jackson, 2002; Putnam & Hulsmann, 2002). However, there is preliminary evidence suggesting that SSRIs in conjunction with TF-CBT do not improve PTSD symptoms more than TF-CBT alone (Cohen et al., 2007). More rigorous research is needed to investigate the benefits of SSRIs, therapy, and combination treatment. Based on conclusions from earlier studies, other classes of medication also can be considered when focusing on particular symptoms (e.g., nightmares, hyperarousal). There is also some evidence for the use of atypical antipsychotics as pharmacological treatments in adolescents with PTSD in juvenile detention centers (Stathis et al., 2005) and anticonvulsants for adolescents with comorbid PTSD and conduct disorder (Steiner et al., 2007). Limitations of the studies reviewed include small sample sizes, failure to specify trauma type and frequency, lack of specification of PTSD symptom type, and failure to discuss follow-up assessments. These issues should be addressed in future research.

In addition to the potential added benefits of pharmacotherapy in treating PTSD in children, several considerations are necessary. One, choice of medication can be complicated by the presence of comorbid conditions (e.g., depression, anxiety) that frequently occur in children with trauma experiences (e.g., Silverman et al., 2008). For instance, Geller et al. (2003) examined the use of SSRIs in the treatment of pediatric OCD, reporting a reduced response due to comorbidity. Similar studies of comorbid PTSD are necessary to determine whether the use of SSRIs for comorbid conditions results in increased or reduced response. Additionally, based on a review of controlled clinical trials of antidepressants, the FDA has issued a "black box" warning in the use of SSRIs with youth due to a potential increased risk of suicidal ideation and/or attempted suicide (NIMH, 2009), though also noting that potential benefits for depression and anxiety disorders likely outweigh the risks. When beginning treatment with any psychopharmacologic agent, it is imperative that elements of informed consent be addressed, particularly focusing on issues related to the onset of action of agents, especially when discussing

SSRIs that are associated with delayed onset. This can help caregivers establish realistic expectations and avoid premature frustration and discontinuation of potentially useful medications.

A more complicated issue is that of duration of treatment for children and adolescents with PTSD. There is a dearth of systematic research, making it difficult for physicians to rely solely on research to guide their treatment planning. Based on past research on the efficacy of medications in the treatment of PTSD, Putnam and Hulsmann (2002) suggest that responders with acute forms of PTSD should continue the agent for at least 6 months following remission, while continued treatment for periods of 12 months or more is indicated for those with chronic forms of the disorder. Finally, the clinician may ultimately wish to yield to the established psychosocial treatment practice for this particular condition (Cohen & Mannarino, 2000).

Conclusions and Research Recommendations

The literature reviewed in this chapter clearly demonstrates the efficacy of CBT-based psychosocial treatments, specifically TS-CBT, in the treatment of PTSD symptoms for youth who have experienced a range of traumas. Fewer studies have focused on traumas other than child sexual abuse and have varied in their assessments of PTSD symptoms but also provide support for the use of CBT. Still, subsets of youth remain symptomatic or are excluded due to severe psychopathology. Recently, researchers have described theoretical frameworks of the development of complex trauma/PTSD reactions (Cook et al., 2005), conducted empirical investigations to document the prevalence and nature of complex PTSD (van der Kolk et al., 2005), and provided neurological assessment methods for children and adolescents (Gabowitz, Zucker, & Cook, 2008). Researchers have also theorized treatment considerations for clinicians when treating complex PTSD (e.g., Amaya-Jackson & deRosa, 2007; Gleiser, Ford, & Fosha, 2008) that warrant empirical investigations. Further research on mediators and moderators also can enhance our understanding of treatment mechanisms and help tailor treatments for these groups. Studies on medication have yielded promising results for SSRIs. Only one study has examined the effects of combined psychosocial and pharmacological treatments limiting any conclusions for its utility. Medication may be more effective in addressing certain symptom clusters and/or severity of symptoms. Studies combining interventions and examining the relative effects of the respective treatment's components may be the most informative.

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Obsessive–Compulsive Disorder

22

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Obsessive–compulsive disorder (OCD) is a neuropsychiatric disorder characterized by the presence of both obsessions and compulsions (American Psychiatric Association, 2000), and is expressed in approximately 2–4% of children (Esser, Schmidt, & Woerner, 1990; Flament et al., 1988; Maggini et al., 2003; Thomsen 1993). On the one hand, obsessions are composed of recurrent and persistent thoughts, impulses, and/or images that are experienced as intrusive and unwanted by the individual, with the most common including thoughts of contamination and images of violence (Leonard, Ale, Freeman, Garcia, & Ng, 2005; March & Leonard, 1996; Storch et al., 2009). Compulsions, on the other hand, are repetitive behaviors or mental acts that the individual feels compelled to perform (Carter & Pollock, 2000; Leonard et al., 2005; March & Leonard, 1996; Riddle et al., 1990), with the most common being excessive washing of the hands and a repetitive checking or touching of objects (Storch et al., 2009). In most cases, obsessions and compulsions are present together, and may relate in a meaningful way (e.g., obsessive thoughts about hygiene paired with compulsive hand-washing); however, neither a dual nor a meaningful presentation of obsessions and compulsions is required for a diagnosis of OCD (Carter & Pollock, 2000; Keeley, Storch, Dhungana, & Geffken, 2007). OCD is diagnosed when at least one obsession or compulsion is present and causes significant interference to the child's life. In this context, significant interference is defined by the loss of 1 or more hours per day to an obsession or compulsion (American Psychiatric Association, 2000). In general, OCD is chronic and debilitating in its effects: without treatment only 10% of diagnosed children experience a remission; 10% experience a worsening of symptoms (and/or associated impairments) over time; and the other 80% experience a fairly stable, unremitting course (Hollander & Evers, 2004; Keeley et al., 2007).

OCD frequently leads to a wide range of functional impairments (e.g., Piacentini, Bergman, Keller, & McCracken, 2003; Sukhodolsky et al., 2005). In a study by Piacentini and colleagues (2003), 85–88% of children experienced a significant problem in at least one of the three functioning domains – home/family, school/academic, and social – and close to half (44–46%) evidenced at least one significant problem in each domain. Parents and children asserted that there were significant problems in home/family functioning in 66 and 48% of the cases, respectively; school/academic functioning in 47 and 44% of the cases, respectively; and social functioning in 33 and 19% of the cases, respectively (Piacentini et al., 2003; for further studies on family impairment see also Allsopp & Verduyn, 1990; Cooper, 1996; Storch et al., 2007; Toro, Cervera, Osejo, & Salamero, 1992). Furthermore, the number of significant impairment

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_22, © Springer Science+Business Media, LLC 2011

items (across parents and children) correlated positively with clinician-rated OCD symptom severity (Piacentini et al., 2003; see also Masellis, Rector, & Richter, 2003).

OCD onset in childhood differs from later presentations. For instance, there is a relatively stronger familial trend (Chabane et al., 2005; do Rosario-Campos et al., 2005; Hanna, Himle, Curtis, & Gillespie, 2005); children with OCD are slightly more likely to be male (e.g., Jaisoorya, Reddy, & Srinath, 2003; Mancebo et al., 2008); and earlier onset is associated with a more variable comorbidity presentation. In general, as many as two-thirds of youth with OCD have at least one additional psychiatric diagnosis (Storch et al., 2008). In addition to comorbidities with anxiety and mood disorders (both common in later presentations), pediatric onset of OCD is associated with tics (40–60%), attention deficit hyperactivity disorder (ADHD; 30%), and disruptive behavior (20–50%) (e.g., Geller, Biederman, Griffin, & Jones, 1996; Geller et al., 2003c; Sukhodolsky et al., 2005). The presence of comorbid diagnoses is associated with increased impairments in socialization, academics, and family functioning (Masi et al., 2006; Sukhodolsky et al., 2005). Moreover, Sukhodolsky and colleagues (2005) found evidence of greater internalizing difficulties among those children (aged 7–18 years) who had comorbid OCD and ADHD ($n = 43$) when compared with those with OCD alone ($n = 56$). In an investigation of 75 children aged 7–18 years, Storch and colleagues (2007) found that those with nonanxiety comorbid diagnoses exhibited greater severity of OCD symptoms – most notably compulsions. Comorbid conditions are also associated with poorer treatment response. For instance, Storch and colleagues (2007) found that pediatric OCD patients with nonanxiety comorbidities (vs. either no comorbidities or anxiety comorbidities only) exhibited significantly less reduction in OCD symptoms after a 14-session cognitive-behavioral protocol. Storch et al. (2008) also showed that certain comorbidities, namely disruptive behavior disorders, major depression, and ADHD, were associated with attenuated CBT response and/or remission rates. Geller and colleagues (2003a, c) found less frequent response to paroxetine among those youth with comorbid ADHD, tics, and oppositional defiant disorder (response rates of 56, 53, and 39%, respectively, when compared with 71% among the sample ($n = 193$) of children with OCD as a whole). Together, these findings suggest the clinical relevance of comorbidity profiles in pediatric OCD, and the utility of establishing a treatment hierarchy that addresses the potential for impeding factors (e.g., attention deficits, disruptive behavior).

Etiology

Biological Factors

The extant literature offers a number of hypotheses regarding OCD etiology – primarily, biological, genetic, behavioral, and cognitive models. The biological model is informed by various metabolic and structural abnormalities noted in OCD. For instance, untreated individuals evidence abnormalities in metabolism are most reliably recorded as increased activity of the orbitofrontal cortex (OFC) and basal ganglia (Breiter et al., 1996; Busatto et al., 2000; Hollander & Evers, 2004; Schwartz, Stoessel, Baxter, Martin, & Phelps, 1996), with metabolic activity of the OFC and basal ganglia positively related to OCD symptom severity (Baxter et al., 1987; Rauch et al., 1994; Swedo, Leonard, & Rapoport, 1992). As well, orbital frontal cortex and basal ganglia volumes are abnormally small among those with OCD (pretreatment) when compared with that of controls (Aylward et al., 1996; Gilbert et al., 2000; Rauch et al., 1997; Rosenberg & Keshavan, 1998; Rosenberg et al., 1997; Szeszko et al., 1999). Together, metabolic and structural findings of corticostriatal abnormalities that are positively related to, and change with, symptom severity have provided support for a "striatal topography" model of OCD. In the general population, unconscious and conscious processing is delegated to the striatum and frontal lobes, respectively (Rauch et al., 1997; Rosenberg et al., 1997; Schultz et al., 1999). In OCD, the "striatal topography" model posits that striatal dysfunction necessitates frontal lobe involvement in the processing of typically unconscious thoughts (Hollander & Evers, 2004; Kang et al., 2004; Kuelz, Hohagen, &

Voderholzer, 2004; Leonard et al., 2005; Rauch et al., 2001). Ineffective frontal lobe "overriding" of striatal motor or cognitive programs might explain the perseverative behaviors and obsessive thoughts characteristic of OCD (Cavedini et al., 2002; Kuelz et al., 2004; Nielen, Veltman, de-Jong, Mulder, & den-Boer, 2002; Schultz et al., 1999) – with the OFC, in particular, implicated in the regulation and maintenance of cognitive sets and impulse/behavioral control (Carter & Pollock, 2000; Henry, 2006; Sachdev & Malhi, 2005).

Research has consistently shown the importance of genetic factors in OCD etiology (e.g., Pauls, 2008; van Grootheest, Cath, Beekman, & Boomsma, 2005). Although the precise mechanism of influence remains in question (Pauls, 2008), the serotonergic and dopaminergic systems have most reliably been implicated. Of interest, animal models of compulsive behavior have variably offered support for the critical role of both systems in OCD presentation (e.g., Campbell et al., 1999; Joel & Doljansky, 2003; Joel, Doljansky & Schiller 2005; Tsaltas et al., 2005). In addition, the unparalleled efficacy of serotonin reuptake inhibitors in the pharmacological treatment of OCD (e.g., Goodman, Price, Rasmussen, Delgado et al., 1989; Goodman, Price, Rasmussen, Heninger & Charney, 1989) has implicated both the serotonergic system and – due to serotonin–dopamine interaction and presumed secondary effects on dopamine release – the dopaminergic system (Westenberg, Fineberg, & Denys, 2007). To date, evidence for either mechanism remains circumstantial.

Cognitive-Behavioral Factors

From a behavioral perspective, the pathophysiology of OCD is commonly conceptualized as the product of both classical and operant conditioning – specifically, a clinical application of Mowrer's (1939, 1960) two-factor theory of fear. According to this fusion approach, fear that is classically conditioned in turn produces ritual performance or avoidance behavior. A negative reinforcement loop is henceforth instilled, as rituals and/or avoidance diminish the fear sensation. In OCD, a neutral stimulus (e.g., a door knob) becomes associated with an unconditioned stimulus (e.g., the thought of becoming sick) and, itself, becomes a conditioned stimulus – thus eliciting distress even in the absence of the previously associated thought. Ritual engagement (e.g., washing hands after touching a door knob) or avoidance behaviors (e.g., using clothing to create a barrier between one's skin and door knobs) results in the following: (1) a diminishing of distress; and (2) the implementation of a negative reinforcement loop, as the individual becomes more likely to rely upon rituals and/or avoidance when confronted with the conditioned stimulus (e.g., a door knob) in the future.

Research has also uncovered a number of cognitive misappraisals associated with OCD. Before proceeding, it is important to note that much of the research on cognitive misappraisals is with adult samples. It is speculated that these same factors play a role in child and adolescent manifestations of OCD, but this has not yet been substantiated. It has been suggested elsewhere (Abramowitz, Taylor, & McKay, 2007) that the beliefs associated with OCD follow a developmental trajectory. Cognitive theorists propose that thought content does not distinguish those with OCD from those without; rather, misappraisals of typical thoughts are believed to elicit distress and, subsequently, necessitate reliance upon compulsions. First, those with OCD exhibit an inflated responsibility for harm (Freeston, Rheaume, & Ladouceur, 1996; Rachman, Thordarson, Shafran, & Woody, 1995; Salkovskis, 1985), perceiving centralized control over the safety of their loved ones (Foa, Sacks, Tolin, Prezworski, & Amir, 2002). For instance, a typical individual who wonders if she extinguished candles may step back into a room to check, but then proceed with other activities. An individual with OCD who experiences the same thought might check repeatedly, fueled by an inflated sense of responsibility over others' well-being. Second, those with OCD presume controllability over their thoughts (Salkovskis, 1989). Although the content of obsessions and typical thoughts are not believed to differ reliably (e.g., Rachman & de Silva, 1978), individuals with OCD may be unique in expecting the ability to override or eliminate their appearance. Third, those with OCD overestimate the threat associated with their thoughts (Foa & Kozak,

1986; Salkovskis, 1985). For instance, after coming in contact with a person exhibiting symptoms of a cold, a typical individual may experience transitory concerns of catching the cold herself. In contrast, an individual with OCD might take the thought to its catastrophic end, believing that she will become severely ill after the aforementioned contact. Fourth, those with OCD express an atypical intolerance of uncertainty (Guidano & Liotti, 1983; Kozak, Foa, & McCarthy, 1987). The distinction might be best evidenced through a return to the previous example of candles that may or may not have been extinguished. On the one hand, a typical individual might never be certain that the candles had been extinguished, and he finds the uncertainty manageable and can proceed with his planned activities. On the other hand, an individual with OCD may find this sense of uncertainty unbearable, and find the need to check over and over again. Fifth, those with OCD tend to overestimate the anxiety they will feel if they do not perform compulsions (i.e., if they allow bothersome thoughts to proceed in the absence of ritual performance or avoidance behaviors; Freeston, Rheaume, & Ladouceur, 1996), making them unlikely to spontaneously extinguish these protective behaviors on their own. Finally, those with OCD tend to underestimate their coping ability (Guidano & Liotti, 1983). As with previously addressed misappraisals, an underestimation of one's coping ability makes adaptive learning improbable; rather than confront the possibility of feared consequences, the individual finds himself stuck in a maladaptive cycle of thoughts and behaviors.

Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus

In addition to the biological, genetic, behavioral, and cognitive explanations for the etiology of OCD, the extant literature suggests that in a subset of cases OCD may result from an autoimmune reaction (Hoekstra & Minderaa, 2005; see also Chap. 36 this volume) that causes basal ganglia dysfunction (Moretti, Pasquini, Mandarelli, Tarsitani, & Biondi, 2008) – particularly in the caudate nucleus and putamen (Snider & Swedo, 2004). Cases of abrupt onset in association with group A beta-hemolytic streptococcus have been increasingly categorized among "pediatric autoimmune neuropsychiatric disorders associated with streptococcus" (PANDAS), since the term's inception by Swedo and colleagues (1998). More recent study has suggested additional characteristics unique to the PANDAS phenotype, including strictly prepubertal onset, notably episodic course and severity of symptoms (Murphy & Pichichero, 2002), and associated neurological abnormalities (e.g., frequent urination, deterioration in handwriting, and hyperactivity; Swedo, Garvey, Snider, Hamilton, & Leonard, 2001). One study (Giedd, Rapoport, Garvey, Perlmutter, & Swedo, 2000) compared 34 children who were thought to have PANDAS-related OCD or tics with 84 matched controls. They found that average sizes of the caudate, putamen, and globus pallidus, but not of the thalamus or total cerebrum, were significantly greater in the PANDAS group. The authors concluded that the results were consistent with the hypothesis of an autoimmune response to streptococcal infection. In contrast, in a recent study, Schrag and colleagues (2009) compared 255 patients recently diagnosed with OCD or tics and matched them to 4,519 controls. They found that the patients with OCD or tics were no more likely than controls to have had strep infections in the 2 years prior to diagnosis. This finding does not confirm those of earlier (and smaller) studies that have found an association between strep an OCD/tics. However, the authors do acknowledge the possibility of a weak association that was not detected in their study. The PANDAS classification remains controversial (Gilbert & Kurlan, 2009; Kurlan, 2004; Swedo & Grant, 2005); continued investigation will be critical to determine the potential for infection-induced OCD onset.

Assessment of OCD

Unstructured clinical interviews, structured interviews, self-report measures, clinician rating scales, and parent and teacher report measures

have all been used to gather information related to OCD in children (see Merlo, Storch, Murphy, Goodman, & Geffken, 2005, for a review). Examples of structured interviews are the Diagnostic Interview Schedule for Children (Shaffer et al., 1993), the Kiddie-Schedule for Affective Disorders and Schizophrenia (Kaufman, Birmaher, Brent, Rao, & Ryan, 1997), and the Anxiety Disorders Interview Schedule for DSM-IV: Child Version (Silverman & Albano, 1996). Schniering, Hudson, and Rapee (2000) conclude that although children are often reliable about their overall level of anxiety symptoms, they may not be very accurate when reporting individual symptom and their report may not always correspond to the parent report. Indeed, this has been the case in pediatric OCD where some youth may under-report symptoms and associated impairment relative to their parent (e.g., Piacentini et al., 2003).

A particularly useful instrument in the assessment of OCD in children is the Children's Yale-Brown Obsessive–Compulsive Scale (CY-BOCS; Scahill et al., 1997). The CY-BOCS is a clinician-rated semi-structured interview, which assesses OCD symptoms for the previous week. The CY-BOCS provides scores for the severity of obsessions, severity of compulsions, and an overall severity score. The instrument has shown excellent internal consistency: Scahill and colleagues (1997) reported the Cronbach's alpha coefficient to be 0.87, and Storch and colleagues (2004) reported it as 0.90. In addition, the CY-BOCS has shown good interrater reliability (Scahill et al., 1997), convergent and discriminant validity (Scahill et al., 1997; Storch et al., 2004), and treatment sensitivity (POTS, 2004).

Although there are many strengths of clinician-rated measures, disadvantages include a longer length of administration and training requirements for the person administering the instrument. Accordingly, self-report measures of OCD symptoms may hold relevance, particularly in settings where it is not feasible to administer a clinician-rated measure. The following self-report measures may be appropriate for assessing OCD-related symptoms.

Childhood Obsessive–Compulsive Impact Scale (*COIS;* Piacentini & Jaffer, 1999). The COIS is 53-item measure designed to assess OCD-related impairment in the domains of school, home, and social situations. The COIS has both a parent and child version. In addition, the measure has four items that assess overall impairment in each domain as well as globally. The COIS has demonstrated good internal consistency and construct validity (Piacentini et al., 2003), and be treatment sensitive (e.g., Piacentini et al., 2002). Piacentini, Peris, Bergman, Chang & Jaffer (2008) recently published a revised version of the instrument, the COIS-R. They found a four-factor structure for the parent report version (Daily Living Skills, School, Social, Family/Activities) and a three-factor structure for the youth-report form (School, Social, Activities). Overall, both measures had good internal consistency, concurrent validity, and test–retest reliability. Like the COIS, the COIS-R appears to be a good measure of domain-specific impairment in youth with OCD.

Children's Florida Obsessive–Compulsive Inventory (*C-FOCI;* Storch et al., 2009). The C-FOCI is a self-report measure composed of a 17-item symptom checklist and a 5-item severity scale. The authors reported that in two studies, one with a clinical sample of OCD patients and the other with a nonclinical sample of 191 nonclinical adolescents, the C-FOCI showed adequate internal consistency and construct validity. The measure is brief to administer and requires no training; the authors provide evidence that the C-FOCI may be valid for administration over the internet.

Obsessive–Compulsive Inventory-Child Version (*OCI-CV;* Foa et al., 2010). The OCI-CV is a 21-item self-report measure of OCD symptoms for use in youth aged 7–17 years. The OCI-CV is an adaptation of the Obsessive–Compulsive Inventory for adults (OCI). The OCI-CV provides symptom severity scores across six areas of OCD (washing, obsessing, hoarding, ordering, checking, and neutralizing.). The authors report that the measure has good internal consistency, test-retest reliability, and sensitivity to treatment.

Children's Obsessional–Compulsive Inventory (*CHOCI;* Shafran et al., 2003). The CHOCI is a self-report measure that assesses the presence of obsessions and compulsions. In addition to the symptom checklist, it also has separate severity ratings for both obsessions and compulsions and an overall impairment rating. Shafran and colleagues (2003) developed and tested the instrument with 42 youth with OCD, along with a nonclinical sample of 46 schoolchildren. They reported that the CHOCHI showed good internal consistency, good criterion validity, and was able to discriminate between the clinical and nonclinical sample. It also significantly correlated with the CY-BOCS. Thus, the CHOCHI may be an efficient instrument for the screening of OCD symptoms in youth.

Leyton Obsessional Inventory-Child Version (*LOI-CV*; Berg, Whitaker, Davies, Flament, & Rapoport, 1988). The LOI-CV is a 20-item self report composed of a symptom checklist and an impairment scale. The authors report that the instrument has demonstrated good validity and internal consistency (Cronbach's alpha = 0.81). In addition, the LOI-CV has demonstrated good test-retest reliability at 5 weeks (Berg, Rapoport, & Flament, 1986) and concurrent validity (Rapoport & Mikkelson, 1980). However, the positive predictive power has been reported as low (18%; Flament et al., 1988), which may limit the use of the instrument.

In addition to OCD specific instruments, self-report measures of anxiety, such as the State-Trait Anxiety Inventory for Children (Hodges, 1990) and the Multidimensional Anxiety Scale for Children (March, Parker, Sullivan, Stallings and Conners 1997), have been used for assessing non-OCD anxiety symptoms in children. Self-report instruments such as these are cost-effective and efficient for screening for anxiety in children. In general, it appears that self-report instruments are able to distinguish between children who are anxious from nonanxious children. However, they are typically poor in distinguishing between children anxiety disorder and other psychiatric disorders and in identifying a specific anxiety disorder (Schniering et al., 2000). Therefore, it is recommended that self-report instruments be used only for screening purposes and not for diagnosing OCD in children. In summary, the use of a through clinical interview (structured or unstructured), along with an OCD-specific instrument such as the CY-BOCS, be used to assess obsessive–compulsive symptom severity in children.

Treatment

Cognitive-Behavioral Therapy

Nature of CBT. Cognitive-behavioral treatment for children with OCD has several components and usually involves the family. Initially, the child and the parents (or other caregivers) are provided with psychoeducation, in which they learn about the symptoms of OCD and how they manifest themselves in the child. They also learn about the reinforcing nature of ritual engagement; that is, rituals reduce anxiety temporarily but make future ritual engagement more likely by virtue of negative reinforcement. In addition, child and the parents learn to recognize symptoms of OCD, label, and externalize symptoms, and then challenge them through a variety of cognitive strategies (e.g., externalizing OCD, "bossing back" symptoms, Socratic thinking).

During exposure and ritual prevention (ERP), the child is intentionally and systematically exposed to situations that trigger OCD-related anxiety without engaging in rituals or compulsions. By being exposed to anxiety-provoking stimuli and not engaging in compulsions, the child habituates to anxiety associated with the obsessional trigger. This process is then repeated, with increasing level of intensity, until the particular stimuli no longer elicits anxiety. For instance, a child with contamination-related OCD may be asked to touch "dirty" things, such as doorknobs or surfaces and resist the compulsion to wash hands. Once the child's anxiety habituates to these exposures, they may be asked to shake hands, touch faucets in bathrooms, etc. Finally, the child may progress to being able to touch toilet seats, flush handles, garbage cans, etc., without cleaning

hands afterwards. The final component of treatment includes relapse prevention where the child is taught ways to maintain treatment gains. For an example of a widely used treatment manual, please see March and Mulle, 1998.

Empirical Support for CBT. There is considerable evidence that CBT with ERP is the most effective form of psychotherapy for treatment of OCD; and, it is superior as a monotherapy to antidepressant medication (Abramowitz, Whiteside and Deacon 2005; POTS, 2004). In an open trial of cognitive-behavioral therapy with 15 children and adolescents, March, Mulle, and Herbel (1994) developed a treatment protocol, which was effective in improving OCD symptoms. Of the 15 patients, 9 achieved a symptom reduction of at least 50%; 6 achieved remission. Treatment gains were maintained up to 18 months posttreatment. Most of the patients were also taking antidepressant medication, but CBT along with booster sessions allowed several to discontinue medication. In their treatment, the authors emphasized patient and parental compliance, exportability of the treatment, empirical evaluation of treatment outcome. Franklin and colleagues (1998), in an open trial of CBT for OCD, found that 12 of 14 children and adolescents had a symptoms reduction of at least 50%. They achieved a mean symptom reduction of 67% posttreatment and 62% at follow-up (average follow-up interval was 9 months). Piacentini, Bergman, Jacobs, McCracken, and Kretchman (2002), in an open trial, found that 79% had a positive response to CBT. Interestingly, the response rate did not differ between those receiving CBT only and those who were also taking medication. In addition, Benazon, Ager, and Rosenberg (2002), in a 12-week open trial of CBT with 16 children and youth aged 8–17 years, found that 10 children had at least 50% reduction in OCD symptoms.

Several controlled trials have also shown the efficacy of CBT for improving OCD symptoms. In one of the first controlled trials, de Haan, Hoogduin, Buitelaar, and Keijsers (1998) examined the relative efficacy of 12-weeks of ERP and clomipramine in 22 individuals between ages 8 and 18 years. Although both types of treatment led to significant improvement, ERP was more effective in reducing the severity of OCD symptoms (evaluated by CY-BOCS scores) compared with clomipramine (60 vs. 33%). Barrett, Healy-Farrell, and March (2004) conducted a controlled trial with 77 children with OCD, who were randomized to individual family-based CBT, group family-based CBT, or a waitlist control condition. They found that 88% of the children in the individual condition and 76% of children in the group condition responded positively to treatment. There was no positive response in the control group.

A large scale multi-site investigation, the Pediatric OCD Treatment Study (POTS, 2004), has also provided significant evidence for the efficacy of CBT and antidepressant for pediatric OCD. In that study 112 youth between ages 7 and 17 years were randomized to CBT, sertraline (trade name Zoloft, an SSRI), a combination of CBT and sertraline, or pill placebo. All three treatment conditions led to a significant reduction in OCD symptoms. The most improvement was achieved in the combined CBT and sertraline condition. With combined treatment, 54% achieved symptom remission, compared with 39% in the CBT group and 21% in the sertraline group; CBT was superior to sertraline in this regard. Based on these results, the authors recommended that youth with OCD should be treated with CBT combined with an SSRI or with CBT alone. Storch et al. (2007) randomized 40 children to receive 14 sessions of treatment either weekly or daily. At posttreatment, 75% in the intensive group and 50% in the weekly group met remission criteria; 90% in the intensive group and 65% in the weekly group responded positively to treatment. Most maintained gains at the 3 month follow-up period.

Family Involvement in CBT. Like many psychiatric disorders, OCD causes significant distress not only to the patient, but also to family members, who often play a significant part by accommodating the OCD symptoms of the patient (Calvocoressi et al., 1995). When patients with OCD engage in avoidance, or ritualistic and com-

pulsive behavior, they frequently disrupt the normal of the family. In attempt to reduce the patient's anxiety, avoid conflict, and minimize disruption, family members often make significant changes to their own behavior in an attempt to accommodate symptoms. Accommodation by family members can take the form of one or more behaviors: offering reassurance, refraining from saying or doing things that may initiate symptoms, helping the patient avoid anxiety-provoking situations or participate in rituals, helping the patient make decisions, allowing the patient to avoid responsibilities, or changing family routines around the patients OCD symptoms (Calvocoressi et al., 1995).

Studies with relatives of pediatric OCD patients generally have reported a high level of family accommodation (e.g., Calvocoressi et al., 1995; Peris et al., 2008). In a study with 57 children and adolescents and their parents, Storch et al. (2007)) found that family accommodation was directly correlated with parents' ratings of child impairment. Additionally, Amir, Freshman, Foa, & (2000) found that family accommodation was positively correlated with OCD symptom severity posttreatment, even when controlling for pretreatment scores. In other words, family accommodation of OCD symptoms predicted poorer treatment outcome. And, Peris and colleagues (2008) found that parental involvement in rituals was positively correlated with their child's OCD severity.

In general, support has been found for the idea of family involvement in cognitive-behavioral treatment (Storch et al., 2007; Barrett et al., 2004; Foa & Wilson, 1991; Steketee, 1993). Barrett and colleagues, as noted earlier, found that parent training sessions were an important aspect of treatment. In addition, parents and other relatives of OCD patients may be able to significantly improve treatment outcome by reducing how much they accommodate the patient's OCD symptoms. Storch et al. (2007), in a study of 40 children and adolescents, used a family-based format for delivering treatment. Parents served as facilitators in generalizing treatment gains and completing homework, and reducing family accommodation of OCD symptoms. They reported that family-based treatment was very successful in reducing OCD symptoms. Freeman and colleagues (2003), in a review of family-based treatment of early onset OCD, identified the need for treatment that involves, and is acceptable to, the family. They also offer a treatment model that is specifically applicable to young children. In addition, Freeman et al. (2008) conducted a study with 42 young children (ages 5–8 years), who were randomized to either family-based CBT or family-based relaxation training. Treatment was adapted to the family context and developmental needs of the children. They found that in the sample of CBT completers, 69% achieved clinical remission, when compared with 20% in the relaxation group. Overall, it appears that involving the family in treatment of OCD for children and adolescents may be particularly important.

Format of Treatment. Treatment of OCD is sometimes available in various formats, such as traditional weekly session or intensive (i.e., daily) sessions. Storch and colleagues (2007) compared the effectiveness of these approaches to treatment. They randomized 40 children to receive 14 sessions of treatment either weekly or daily. They found that at the end of 3 months posttreatment, both groups had similar (and largely positive) outcomes. Thus, both weekly and intensive treatment formats as effective options for children who require treatment for OCD. An intensive format may be especially beneficial for children who do not have access to a provider who is specialized in OCD treatment in their community. In addition, Franklin and colleagues (1998) also found that intensive and weekly treatment formats were both effective in reducing OCD symptoms substantially. Currently, POTS-II (Freeman et al., 2009) is being conducted to investigate the effectiveness of a single-doctor approach, where the physician managing medication also provides a less intense version of CBT, compared with a dual-doctor approach, which includes a highly trained CBT specialist providing a full course of CBT and a psychiatrist managing medications. At this point, no data are available from this study.

There is also some evidence that a group format may be effective for treatment of OCD in children and adolescents. Barrett and colleagues (2004) conducted a study with 77 children and adolescents, randomized to family-based

group CBT, family-based individual CBT, and a waitlist control group. They found that both treatment groups improved, whereas the waitlist group did not. Moreover, there was no significant difference in the level of improvement between the group and individual conditions. Thus, for some children, group treatment for OCD may be a reasonable option.

Pharmacologic Treatment

The use of pharmacological agents in treating OCD in adult populations has long been considered to be a relatively safe and effective treatment option, and the efficacy of using these agents to treat OCD in pediatric populations, though less robust, has begun to produce similar results (Geller et al., 2004). This efficacy has been demonstrated in several controlled trials using SRIs (Stewart et al., 2004). Geller and colleagues (2003b) conducted a metaanalysis on randomized controlled trials of serotonin reuptake inhibitors in pediatric OCD populations. The metaanalysis was composed of 12 studies that included 1,044 participants. The studies examined the efficacy of four SSRIs (paroxetine, fluoxetine, fluvoxamine, and sertraline) and clomipramine, a nonselective serotonergic agent. The following dependent outcome measures were used in the analysis: CY-BOCS, NIMH Global OCD Scale, LOI-CV, and the CGI of severity. Two types of outcome scores (change and posttreatment) were derived from these measures. The results of the investigation revealed that serotonergic agents have been highly efficacious and significantly superior to placebo in treating pediatric OCD. Although the four SSRIs examined in the studies were comparably effective, clomipramine (Anafranil), a tricyclic antidepressant, demonstrated superiority in reducing obsessive–compulsive symptoms. Despite this finding, caution is advised when considering this option. Clomipramine should not be recommended as a first option in treating pediatric OCD because of the high risk profile, requirement of electrocardiogram and blood level monitoring, and frequency of adverse side effects experienced by patients being treated with this medication. SSRIs that do not carry such precautionary measures should therefore be considered as first-line agents.

More recently, Geller et al. (2004) conducted a prospective randomized, multicenter, double-blind, placebo-controlled trial to assess the safety and efficacy of paroxetine in pediatric OCD patients. Participants in the study consisted of 207 patients who ranged in age from 7 to 17 and met diagnostic criteria for OCD. They were randomized to treatment (10–50 mg paroxetine daily) or placebo for 10 weeks. The CY-BOCS administered at baseline data and again at week-10 termination. Safety was assessed at each visit, through physical exams, monitoring of vital signs, clinical laboratory tests, and electrocardiograms. Results demonstrated that it is a safe and effective pharmacologic treatment option for OCD that is generally well-tolerated in pediatric patients (Geller et al., 2004).

Safety and Tolerability. Although SSRI medications may have some side effects among pediatric patients (Goodman, Murphy, & Storch, 2007), SSRIs are generally well-tolerated and considered safe (Murphy, Segerra, Storch, & Goodman, 2008). In the last decade, some concerns related to an increased risk of suicide following the use of an SSRI have been reported (Goodman et al., 2007). As a result, the FDA has adopted a "black box" warning and stressed the importance of close monitoring of pediatric patients with whom SSRI treatment has been initiated. Overall, the evidence suggests that SRI medications are safe and effective for the treatment of OCD in pediatric patients. Currently, there are four medications approved by the U.S. Food and Drug Administration for use in pediatric patients with OCD: clomipramine (a tricyclic antidrepressant) for ages 10 and above, and three SSRIs: fluoxetine for ages seven and above; fluvoxamine for ages eight and above; and sertraline for ages six and above (POTS, 2004; Geller et al., 2003b).

In some cases, serotonin-based medication treatment for OCD can be augmented by other medications, such as an antipsychotic. Although the addition of antipsychotic medications in treating

refractory OCD has recently been documented in the adult OCD literature (McDougle, Epperson, Pelton, Wasylink, & Price, 2000, McDougle et al., 1994), the pediatric literature on augmentation is sparse. In fact, augmentation in applied practice today is characterized by off-label use that is extrapolated from the adult literature. However, some studies have produced promising results. Thomsen (2004), for example, examined the adverse effects and clinical utility of risperidone as augmentation to SSRI treatment in treatment-resistant adolescents with severe OCD. This open-label risperidone augmentation trial produced significant reductions in OCD symptoms for patients at 12-weeks as measured by the CY-BOCS/Y-BOCS. This preliminary finding suggests that augmentation with risperidone may be effective in treatment-resistant cases. Although antipsychotic augmentation in OCD patients is becoming increasingly more common, this strategy is still novel and available data suggest that side effects associated with atypical antipsychotics are common in adults (Correll & Carlson, 2006). Therefore, caution is especially advised when treating pediatric patients for whom considerably less data are available.

Impact of Comorbidity on Treatment

Given the substantial rate of comorbidity in pediatric patients with OCD, it is important to address the effect of that comorbidity on treatment. In a study with 335 pediatric OCD patients, Geller and colleagues (2004) found that 58% had a comorbid diagnosis. Their findings showed that a comorbid illness reduced treatment response to paroxetine in significantly increased relapse risk after discontinuation of paroxetine. The authors also make the point that because of the relatively high comorbidity in pediatric OCD patients, studies that tend to exclude comorbid diagnoses may be limited in their generalizability to the overall OCD pediatric population.

Storch and colleagues (2008), in a study with 96 children and adolescents with OCD, found that CBT found that those with a comorbid disruptive behavior disorder (i.e., oppositional defiant disorder) had significantly poorer treatment response and lower remission rates. About 57% of those with comorbid DBD were treatment responders, when compared with 75% of the overall sample. In addition, 24% of those with disruptive behavior achieved OCD symptom remission, compared with 59% of the overall sample. In a case study with a 10-year old female, Lehmkuhl and colleagues (2009) report the successful treatment of OCD and comorbid disruptive behavior. The treatment was sequential, consisting of parent training for managing disruptive behavior, followed by CBT for OCD. The authors suggest that assessment in children with suspected OCD include assessment of disruptive behavior, and that addressing the disruptive behavior prior to conducting CBT for OCD may improve treatment outcome. Overall, it seems that assessing for and treating, either sequentially or concurrently, comorbid conditions in pediatric patients can not only enhance overall functioning, but also improve response to OCD treatment.

Conclusions and Future Directions

The discussion of the literature presented here suggests that OCD in children, while complex, can be treated using either cognitive-behavior therapy, pharmacotherapy, or a combination of these. Although this is generally accurate, there are a substantial number of cases where this does not apply. First, in adults OCD typically presents with adequate insight into the senselessness of symptoms, while it is not a requirement to make the diagnosis in children. This single difference in the diagnosis can lead to significant barriers to treatment, beginning with the application of CBT approaches that rely on deliberate exposure to feared stimuli. In adults who have limited or poor insight yet meet criteria for OCD, this is a serious limitation to treatment (Neziroglu, Pinto, Yaryura-Tobias and McKay 2004; Neziroglu, Stevens, Yaryura-Tobias and McKay 2001). The degree that insight is established, and the difficulties this may pose in therapy, warrants additional investigation. Clinicians in this instance may need to

rely more heavily on parental involvement since there could then be indirect measures taken to eliminate symptom accommodation and increase compliance.

Comorbidity warrants further investigation as a complicating factor in treatment. In adult OCD, comorbidity, particularly of other anxiety disorders, has been associated with poorer outcome (McKay, et al., 2004). This has been far less investigated in children, but early evidence suggests that it is likewise problematic for treatment delivery. Aside from simply comorbidity, the nature of the presenting symptoms themselves often creates difficulty in treatment outcome. For example, OCD is associated with some symptoms that, during exposure based treatment, has conceptually little time between exposure and feared outcome (i.e., contamination fear). These experiences provide rapid corrective feedback. On the contrary, some symptoms have an extremely long latency between exposure and feared outcome (i.e., fears of postmortem eternal damnation). We have discussed elsewhere how these variations in symptom presentations can limit treatment, or draw upon the full extent of clinical acumen for creatively approaching these problems in a productive manner (McKay, Storch, Nelson, Morales, & Moretz, 2009).

An additional important area that requires investigation is the degree that specific obsessive–compulsive beliefs play a role in childhood manifestations of the disorder. The cognitive model has become a dominant approach for treatment conceptualization (Wilhelm & Steketee, 2006). Part of the appeal of this model is the reduced role of exposure-based interventions. Many clinicians are uncomfortable with the application of exposure approaches, with a number of disparate, and unfounded, reasons. Even among cognitive behavioral psychologists, there are concerns with exposure because of (a) symptom substitution, (b) litigation risk, or (c) insufficient information about the relation between safety signals and treatment outcome. Each of these assumptions may be effectively challenged on the science behind them, yet clinicians cling to these concerns and often avoid applying exposure procedures despite the fecundity of data supporting the approach. First, symptom substitution, which is a concept that persists from the psychodynamic model, posits that direct removal of a presenting symptom will lead to its emergence in another form. This hydraulic perspective on cognitive functioning has no empirical support (Tryon 2008) despite its centrality to psychodynamic theory. The concern over increased litigation risk when using exposure is also unfounded, and when applied properly has no increased legal potential than any other direct service delivery approach (Richard & Gloster, 2007). Finally, the limited understanding about safety signals arises from an assumption that clients must have a "safe base." This also has been shown to be false, particularly in the case of anxiety disorders. Indeed, it appears that the opposite is true, and that the persistence of safety cues diminishes treatment outcome (McKay, 2010).

In closing, it appears there is much reason to be hopeful regarding the conceptualization and treatment of childhood OCD. Effective psychological and pharmacological approaches are available, and the dissemination of these approaches has become increasingly widespread. What was once considered a difficult condition to treat is routinely handled effectively for the wide range of symptoms.

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Pharmacological Treatment for Phobias and Anxiety Disorders

23

Michael H. Bloch and Joseph F. McGuire

Anxiety disorders in childhood are quite common, affecting between 6 and 20% of all children (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003). Anxiety disorders can adversely impact social and academic functioning as well as self-esteem (Mendlowicz & Stein, 2000). Children with anxiety disorders grow up to having greater rates of depression, new anxiety disorders, substance abuse, educational underachievement, and suicide attempts than the general population (Achenbach, Howell, McConaughy, & Stanger, 1995; Ferdinand, Verhulst, & Wiznitzer, 1995; Pine, Cohen, Gurley, Brook, & Ma, 1998; Woodward & Fergusson, 2001).

Early recognition of, and intervention for, childhood anxiety disorders has the potential to reduce the impact of these disorders on childhood social and academic function (Connolly & Bernstein, 2007). Early treatment may also reduce the adverse adulthood outcomes with childhood anxiety disorders. Psychotherapeutic interventions have demonstrated efficacy for all childhood anxiety disorders. Pharmacological interventions have demonstrated efficacy for all childhood anxiety disorders excluding post-traumatic stress disorder (PTSD). In recent randomized controlled trials of pediatric anxiety disorders, combination therapy with both medication and cognitive behavioral therapy (CBT) has been demonstrated superior to either treatment alone (POTS, 2004; Walkup et al., 2008). Table 23.1 lists situations in which pharmacological treatment is recommended.

The focus of this chapter is to discuss the pharmacological treatment of anxiety disorders. Evaluation, diagnosis, and psychotherapeutic treatment of these conditions will only be briefly discussed as these issues have been discussed in preceding chapters. We will discuss pharmacological treatment of obsessive–compulsive disorder (OCD), PTSD, and other anxiety disorders (i.e., separation anxiety disorder (SAD), selective mutism, social phobia, generalized anxiety disorder, and specific phobia). We will then provide in-depth discussion about the following: (1) the risks and benefits of various pharmacological agents commonly used to treat pediatric anxiety; and (2) situations in which pharmacological treatments are recommended for pediatric anxiety disorders.

Pediatric Anxiety Disorder Nosology

Pediatric anxiety disorders excluding OCD and PTSD have been commonly grouped together in pharmacological trials. These childhood anxiety disorders have been grouped together because (1) there exists a large degree of symptom overlap between the conditions – children with symptoms of one anxiety disorder often have symptoms of some of the others; and (2) there is a high degree of comorbidity between the conditions (Reinblatt &

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_23,

Table 23.1 Clinical situations in which pharmacological treatment for pediatric anxiety disorders is advisable

Clinical cases in which referral for pharmacological intervention is recommended
Child has marked or severe symptoms of an anxiety disorder
Impairment makes participation in psychotherapy difficult
Evidence-based psychotherapeutic unavailable
History of inadequate response to adequate psychotherapy trial
Family preference
Comorbid conditions such as depression, attention deficit hyperactivity disorder (ADHD), or substance use disorder that requires medical treatment

Table 23.2 Clinical characteristics of pediatric anxiety disorders

Separation anxiety disorder (SAD) – excessive concern and distress when separated from attachment figures that occurs after age 6 years
Generalized anxiety disorder (GAD) – excessive worry about everyday things such as schoolwork, health, safety, and world events
Social phobia (SoP) – excessive concern and fear in certain social settings such as discomfort with peers, talking in class, attending parties and starting conversation
Selective mutism – persistent fear to speak or read aloud in certain situations despite speaking in others
Panic disorder – recurrent episodes of intense fear that occur out of the blue
Obsessive-compulsive disorder (OCD) – characterized by obsessions – intrusive, bothersome thoughts, images and impulses and compulsions repetitive actions that need to be performed in a stereotyped way to relieve anxiety. Common OCD symptoms include cleaning/contamination, need for symmetry, fear of harm associated with checking, and hoarding
Post-traumatic stress disorder (PTSD) – requires previous exposure to a traumatic event at least 1 month prior to diagnosis. The child must (1) reexperience the event (i.e., nightmares, flashbacks, distress with recollection), (2) display avoidance (i.e., avoid reminders of event (thoughts, places, feelings or conversations) and/or display restricted range of affect, feelings of detachment, sense of forshortened future or amnesia regarding event) and (3) display hyperarousal (i.e., insomnia, irritability, hypervigilence, exaggerated startle or poor concentration)

Walkup, 2005). Approximately 60% of children with a non-OCD anxiety disorder meet criteria for at least two other anxiety disorders (Kashani & Orvaschel, 1990). Table 23.2 offers a brief description of diagnostic criteria for pediatric anxiety disorders as the diagnostic criteria for each of these disorders have been described in greater depth in previous chapters.

Pediatric OCD

Evaluation and Assessment

OCD is characterized by the presence of obsessions (unwanted and intrusive thoughts, images, or impulses) and/or compulsions (repetitive behavioral or mental rituals) (*Diagnostic and statistical manual of mental disorders: DSM-IV-TR*, 2000). Since obsessions and compulsions are usually recognized by the child as nonsensical, inappropriate, or unreasonable, they are often both kept hidden from both parents and therapists. When this takes place, especially in younger children, parental observation of compulsive behaviors (i.e., repeated checking of locks, washing or cleaning objects, hoarding) or physical signs of compulsive behaviors (i.e., chapped hands or ulcerations from excessive washing) can be the only definite signs of the disorder. Since the vast majority of OCD patients have insight into their condition, a detailed clinical history of obsessive and compulsive behaviors from the child and his parents is sufficient to make a diagnosis of OCD. Getting a detailed history of specific OCD symptoms is also crucial to developing a successful treatment plan.

Although defining features of OCD, recurrent thoughts, images, and impulses similar to the obsessions also characterize many other mental disorders. For instance, in major depressive episodes, it is not uncommon for patients to have persistent thoughts

about unpleasant circumstances, personal worthlessness, or about possible alternative actions. These ruminative thoughts of depression can be distinguished from OCD by the fact that they are a mood-congruent aspect of depression, ego-syntonic compared with obsessions of OCD which are ego-dystonic. There is a high comorbidity between depression and OCD, and thus it is common for both ruminative thoughts of depression and OCD to present in the same individual.

Aside from major depressive episodes, the symptoms of other anxiety disorders can also mimic the symptoms of OCD. Generalized anxiety disorder is characterized by excessive worry, but such worries can be distinguished from obsessions by the fact that the person experiences them as excessive concerns about real-life circumstances, whereas obsessions in OCD are generally experienced as excessive but unreasonable. Obsessions of OCD must also be distinguished from mental disorders where individuals have excessive worries about their appearance (body dysmorphic disorder, anorexia, and bulimia), a specific situation or circumstance (specific phobia), or of serious illness due to misinterpretation of normal bodily signals (hypochondrias).

In children, OCD obsessions concerning the fear of harm coming to self or others must be distinguished from those typical of SAD. These two conditions can often be distinguished by the observation that obsessions of OCD are usually accompanied by stereotyped and specific compulsive rituals (i.e., specific checking behavior, counting) whereas of SAD the compulsive actions are less stereotyped. Furthermore, the presence of other OCD symptoms besides fear of harm can aid in diagnostic clarification.

The repetitive stereotypies of children with autism spectrum disorders, mental retardation, and pervasive developmental disorders can resemble the compulsions of OCD. However, these stereotypies can usually be easily distinguished from OCD, based on the child's accompanying symptoms as well as the fact that stereotypies are usually experienced as soothing or pleasurable whereas compulsions are ego-dystonic. Stereotypies can often be present in children with normal socialization skills, cognitive ability, and developmental trajectory. In these cases, an early-onset of symptoms (at less than 2 years of age) and an increase in movements with excitement can be used additionally to distinguish these two conditions. Complex tics in children with Tourette syndrome can also mimic the compulsions of OCD. Complex tics are usually preceded by a physical urge, noted in the literature as a premonitory urge, whereas compulsions are preceded by anxiety or a specific obsession. The high comorbidity between tic disorders and OCD often makes this distinction difficult or arbitrary. Getting a detailed history about comorbid tics is particularly important in patients with OCD because it may be a mediator of pharmacological treatment response.

The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) is the standard clinical rating scale used to assess symptom severity in adults with OCD (Goodman, Price, Rasmussen, Mazure, Delgado, et al., 1989; Goodman, Price, Rasmussen, Mazure, Fleischmann, et al., 1989). The Y-BOCS is a 10-item ordinal scale (0–4) that rates the severity separately for both obsessions and compulsions of OCD, according to the time occupied, degree of interference, subjective distress, internal resistance, and degree of control. The children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) is an identically designed scale for use in children with OCD (Scahill et al., 1997). CY-BOCS and Y-BOCS scales differ only according to the accompanying symptom screening checklist with the CY-BOCS being more developmentally appropriate for children. Both scales have been validated for use in their representative patient populations and are sensitive to changes in symptom severity with treatment. Both measures rate OCD symptoms on a scale that ranges from 0 (no symptoms) to 40 (severe OCD), with a score less than 8 considered as subclinical symptoms, over 16 as clinically significant, and over 24 as moderate–severe OCD. Generally a reduction in Y-BOCS score of 25 or 35% with a final Y-BOCS rating of less than 16 is considered the criteria for response to treatment (Pallanti et al., 2002). The Y-BOCS rating scale takes approximately 5 min to complete once the patient has completed the initial symptom checklist and serves as a good measure to assess symptom fluctuation in a clinical setting.

First-Line Pharmacological Treatment

Selective serotonin reuptake inhibitor (SSRI) pharmacotherapy is the pharmacological treatment of choice in the treatment of pediatric-OCD. Six randomized, placebo-controlled trials have all demonstrated superior effect of SSRI pharmacotherapy compared with placebo (Barbanti, & Fabbrini, 2004; Geller, Biederman, Stewart, Mullin, Farrell, et al., 2003; Geller et al., 2001; Liebowitz et al., 2002; March et al., 1998; Riddle et al., 2001). Table 23.3 demonstrates the characteristics and results of double-blind placebo-controlled trials of SSRI in pediatric OCD. Effect size for SSRI pharmacotherapy ranged from 0.32 to 0.67 in these trials. Differences in response rates and efficacy between trials is just as likely related to differences in trial design, study population, and dose titration schedule when compared with differences in pharmacological agent utilized. Aside from differences in effect sizes between trials, there is no evidence from pharmacological trials in both children and adults that any one SSRI is more effective than any other. The number needed to treat (NNT) is the number of children that need to be treated with an intervention for one child to respond who would not have responded to placebo treatment. NNT for SSRI intervention in pediatric-OCD ranged from 2.8 to 8.1.

Predictors of Treatment Response

The presence of increased comorbidity, most specifically comorbid tics and externalizing disorders are associated with poor response to SSRIs (Geller, Biederman, Stewart, Mullin, Martin, et al., 2003). Pediatric-onset OCD with comorbid tics may be associated with improved long-term outcome – OC symptoms that are more likely to remit during adolescence (Bloch et al., 2009). Treatment-refractory OCD with comorbid tics appears equally responsive to CBT and more responsive to antipsychotic augmentation than OCD without comorbid tics (Bloch et al., 2006).

PTSD

Evaluation and Assessment

Roughly one and four children experience a significant traumatic event before reaching adulthood (Costello, Erkanli, Fairbank, & Angold, 2002). Traumatic events may include child abuse, domestic violence, vehicular accidents, traumatic injury to self or significant others, medical trauma, war and disasters. Although a majority of individuals experiencing a life-threatening event manifest posttraumatic symptoms immediately, only about 30% will manifest symptoms past the first month (Aaron, Zaglul, & Emery, 1999; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995; Rothbaum, Kozak, Foa, & Whitaker, 2001).

In addition to the presence of a known trauma, individuals with PTSD must manifest (1) reexperiencing symptoms, (2) hyperarousal, and (3) avoidance. Reexperiencing symptoms typically include flashbacks, nightmares, and other intrusive recollections of traumatic events. Avoidance typically involves avoidance of reminders of the trauma including talking about it, amnesia to important aspects of the traumatic event, decreased interest in activities, and a sense of detachment or estrangement. Hyperarousal symptoms include insomnia, irritability, angry outbursts, hypervigilence, poor concentration, and increased startle response. Acute PTSD is diagnosed if individuals demonstrate symptomatology 1–3 after a traumatic event. Chronic PTSD is diagnosed when PTSD symptoms endure beyond 3 months. Either acute stress disorder or adjustment disorder is diagnosed when individuals express posttraumatic symptomatology within the first month after a trauma (*Diagnostic and statistical manual of mental disorders: DSM-IV-TR*, 2000). Several structured diagnostic instruments such as the Clinician's Assessment of PTSD Child and Adolescent Version (CAPS-CA) and the PTSD Semi-Structured Interview and Observational Record for Infants and Young Children (PTSD-SSI) exist to aid clinicians in the diagnosis of PTSD (Nader et al., 1996; Scheeringa, Zeanah, Myers, & Putnam, 2003).

Table 23.3 Randomized, placebo-controlled trials of pharmacological interventions for non-OCD pediatric anxiety disorders

					Dosage (mg/day)				Response Rate (CGI <3)			
Study	Drug	*N*	Disorders	Length (weeks)	Range	Mean	Rating scale	Effect Size	Drug (%)	Placebo (%)	Number needed to treat (NNT)	Time of significant response (weeks)
RUPP (2001)	Fluvoxamine	128	SoP, SAD, GAD	8	50–300	2.9/kg	PARS	1.11	76[a]	29[a]	2.1[a]	3
Rynn, Siqueland, and Rickels (2001)	Sertraline	22	GAD	9	25–50		HAM-A	1.93	91	9	1.2	4
Birmaher et al. (2003)	Fluoxetine	74	SoP, SAD, GAD	12	20	20	PARS	0.41	61	35	3.8	9
Wagner et al. (2004)	Paroxetine	322	SoP	16	10–50	33	LSAS-CA	0.52	78	38	2.6	3
Beidel et al. (2007)	Fluoxetine	65	SoP	12	10–40		SPAI-C	0.35	36	6	3.3	4
Walkup et al. (2008)[a]	Sertraline	488	SoP, SAD, GAD	12	25–200	146	PARS	0.45	55	24	3.2	4
Rynn (2007)	Venlafaxine ER	320	GAD	8	37.5–225		PARS	0.48	69	48	4.8	2
March, Entusah, Rynn, Albano, and Tourian (2007)	Venlafaxine ER	293	SoP	16	37.5–225	142	SAS	0.46	56	37	5.3	Baseline

[a]Based on CGI <4

SoP Social phobia; *SAD* separation anxiety disorder; *GAD* generalized anxiety disorder; *CGI-I* Clinical Global Improvement, *PARS* Pediatric Anxiety Rating Scale; *LSAS-CA* Liebowitz Social Anxiety Scale; *HAM-A* Hamilton Anxiety Scale; *SPAI-C* Social Phobia and Anxiety Inventory for Children; *SAS* Social Anxiety Scale

The UCLA PTSD Reaction Index is a useful self-report tool from diagnosing and assessing severity of PTSD in older children (Steinberg, Brymer, Decker, & Pynoos, 2004).

Assessment and diagnosis of PTSD is particularly difficult in children. Diagnosing PTSD requires compelling evidence of the occurrence of a traumatic event, yet avoidance of talking about the event is a core feature of PTSD (Practice parameter for the assessment and treatment of children and adolescents with posttraumatic stress disorder, 2010). Parental denial of the child's traumatic exposure often occurs because they are unaware, suffering from the effects of PTSD themselves or a perpetrator of the events. Sometimes compelling evidence of trauma can be documented in the absence of child or parent report if there exists other reliable eyewitness report (i.e., police accident report), physical evidence (i.e., physical trauma or presence of sexually transmitted disease), or a forensic evaluation suggestive of trauma (practice parameter for the assessment and treatment of children and adolescents with posttraumatic stress disorder).

Children exhibiting symptoms of PTSD or significant psychopathology in general should be routinely asked about traumatic experience. Screening should include inquiring about maltreatment, acute injuries, disasters, witness violence to loved ones, and physical and sexual abuse. The Juvenile Victimization Questionnaire (JVQ) is a tool that can aid clinicians in screening for developmental trauma (Finkelhor, Hamby, Ormrod, & Turner, 2005). For children suffering from PTSD initial assessment should also examine the severity and functional impairment caused by PTSD. The most important aspect of initial treatment is to minimize and remove children from situations of repeated trauma.

First-Line Pharmacological Treatments

Trauma-Focused psychotherapies are the treatments of choice for childhood PTSD. Among trauma-based psychotherapies, trauma-focused cognitive behavioral therapy (TF-CBT) has the most empirical support. TF-CBT has been demonstrated to be superior to supportive therapy in four randomized placebo-controlled trials in children (Cohen, Deblinger, Mannarino, & Steer, 2004; Lieberman, Van Horn, & Ippen, 2005; Najavits, Gallop, & Weiss, 2006; Trowell et al., 2002). TF-CBT helps children work on the following: (1) coping skills, (2) expression and identification of feelings, and (3) gradual exposure, whereby children are assisted in developing their own trauma narrative. Typically TF-CBT also includes psychoeducation about PTSD and involves the inclusion of the caregiver in a developmentally appropriate manner. Inclusion of the caregiver typically comes through conjoint child–parent sessions in which the child shares their trauma narrative and other family issues surrounding the trauma are addressed (Cohen, Mannarino, & Deblinger, 2006). Eye movement desensitization therapy and reprossessing (EMDR) is a therapy that also has strong evidence of efficacy in adult PTSD but well-controlled trials in childhood PTSD are lacking (Ahmad, Larsson, & Sundelin-Wahlsten, 2007). The psychotherapeutic treatments for PTSD are explored in much greater depth in other sections of this book.

In contrast to the evidence supporting TF-CBT in children, there are no positive, randomized, placebo-controlled trials for any pharmacological treatments of PTSD in children. SSRIs have demonstrated efficacy for several randomized, placebo-controlled trials for adult PTSD (Brady, Pearlstein, & Asnis, 2000; Connor, Sutherland, Tupler, Malik, & Davidson, 1999; van der Kolk et al., 1994). SSRIs in adults have been demonstrated to reduce PTSD symptoms in all three PTSD symptom clusters. Uncontrolled trials of SSRIs in children have shown significant improvement over time with SSRI pharmacotherapy However, a subsequent, currently unpublished, double-blind, placebo-controlled trial in 67 children with PTSD failed to demonstrate a benefit of sertraline over placebo (Robb, Cueva, Sporn, Yang, & Vanderburg, 2008). A second trial examined the addition of sertraline or placebo to TF-CBT in 24 children with sexual-abuse related PTSD (Cohen, Mannarino, Perel,

& Staron, 2007). Although this trial was severely underpowered to detect the marginal treatment effect of sertraline beyond TF-CBT, this trial still did not demonstrate a significant benefit of sertraline compared with placebo. These trials emphasize the need for appropriately powered placebo-controlled SSRI trials for PTSD, especially since these agents are already commonly prescribed for the condition.

Uncontrolled trials in children have suggested the possible efficacy of the alpha-2 antagonists (clonidine or guanfacine) and beta-blockers (propranolol) in the treatment of the hyperarousal symptoms of PTSD in children; however, data from controlled trials are lacking (Harmon & Riggs, 1996; Horrigan, 1996). Uncontrolled trials in children and placebo-controlled trials in adults support the use of antipsychotic-augmentation to SSRIs in the treatment of refractory PTSD (Reich, Winternitz, Hennen, Watts, & Stanculescu, 2004; Stathis, Martin, & McKenna, 2005; Stein, Kline, & Matloff, 2002). The evidence supporting the pharmacological treatments for PTSD in children lags far behind that of trauma-focused psychotherapies. Currently, it is recommended to use pharmacotherapy for symptomatic relief in children with PTSD, who cannot tolerate or do not respond to evidence-based therapies. Pharmacotherapy for PTSD should not be used in lieu of evidence-based psychotherapies (Practice parameter for the assessment and treatment of children and adolescents with posttraumatic stress disorder, 2010).

Predictors of Treatment Response

Given the paucity of placebo-controlled medication trials for childhood PTSD, there is no data regarding moderators and mediators of treatment response. However, after following a significant trauma, lack of social supports, female gender, the presence of preexisting psychopathology, parental psychopathology, past trauma exposure, multiple traumas, and greater exposure to the index trauma were all risk factors for the subsequent development of PTSD (Pine & Cohen, 2002).

Pediatric Anxiety Disorders Excluding OCD and PTSD

Evaluation and Assessment

All children presenting for psychiatric attention deserve screening for anxiety disorders, given their high prevalence in pediatric populations. Screening instruments such as the Multidimensional Anxiety Scale for Children (MASC) are useful for formally assessing anxiety symptoms in children (March, Parker, Sullivan, Stallings, & Conners, 1997). Children tend to be more aware of the inner tension caused by anxiety, whereas parents and teachers are often better reporters of academic and social impact of anxiety (Connolly & Bernstein, 2007).

Children presenting for evaluation of anxiety disorders often present with somatic symptoms (i.e., headaches or stomach aches). Part of the initial psychiatric evaluation should involve consultation with the child's pediatrician and confirmation that their somatic complaints sufficiently evaluated. As demonstrated in Table 23.4, there are multiple medications, substances, and medical conditions that can mimic some symptoms of anxiety disorders. A thorough past medical and medication history can bring to light many of these conditions.

Symptoms of many psychiatric conditions can mimic anxiety disorders. Children with anxiety disorders also have a high rate of comorbidity with other psychiatric conditions such as mood disorders, substance abuse, and attention deficit hyperactivity disorder (ADHD). Symptoms of many other psychiatric conditions can mimic those of anxiety disorders (Table 23.4). Therefore, a thorough screening for other psychiatric conditions is warranted.

First-Line Pharmacological Treatment

Evidence of Efficacy

SSRIs are the pharmacological treatment of choice for pediatric anxiety disorders, not including PTSD. The eight randomized, placebo-controlled trials that have been conducted in pediatric anxiety

Table 23.4 Differential diagnosis for anxiety disorders in children

Condition	Common symptoms with anxiety disorders	Confused conditions
Psychiatric disorders		
ADHD	Restlessness and inattention	GAD
Asperger's disorder	Social awkwardness and withdrawal, social skill deficits, repetitive behaviors and adherences to routines	SoP, OCD
Learning disabilities	Persistent worry about school performance	School refusal, SAD
Psychotic disorder	Restlessness and social withdrawal	GAD, SoP
Bipolar disorder	Restlessness, irritability and insomnia	GAD
Depression	Somatic complaints, poor concentration, insomnia	GAD
Medical conditions		
Hyperthyroidism	Sweating, emotional lability, poor attention, heart palpitations	Panic disorder
Asthma	Shortness of breath, chest tightness	Panic disorder
Seizure	Panic, lightheadedness, numbness, Deja Vu	Panic disorder
Lead intoxication	Reduced cognitive abilities, inattention, irritability	GAD
Hypoglycemia	Poor concentration, nervousness, sweating, heart palpitations	Panic disorder
Cardiac arrhythmias	Heart palpitations, dizziness, lightheadedness	Panic disorder
Prescription medications		
Antipsychotics	Akathisia, obsessive-compulsive symptoms, dysphobia	GAD, OCD
Psychostimulants	Insomnia, irritability, heart palpitations, nervousness	GAD, panic disorder
Selective serotonin reuptake inhibitor (SSRI)	Insomnia, akathisia, discontinuation syndrome	
Steroids	Insomnia, euphoria, anxiety	
Antiasthmatics	Heart palpitations, insomnia, nervousness	Panic disorder
OTC medications		
Diet pills	Insomnia, dry mouth, nervousness, heart palpitations	GAD, panic disorder
Cold medications	restlessness, insomnia, anxiety, heart palpitations	Panic disorder
Caffeine	Insomnia, restlessness, heart palpitations	Panic disorder
Substance abuse	Alcohol, marijuana, cocaine, psychostimulants	

disorders have all demonstrated significantly greater improvement with SSRI pharmacotherapy compared with placebo (Beidel et al., 2007; Birmaher et al., 2003; Rynn et al., 2001; The Research Unit on Pediatric Psychopharmacology Anxiety Study Group, 2001; Wagner et al., 2004; Walkup et al., 2008). The effect sizes (*d*) of SSRIs in these trials ranged from 0.35 to 1.93. The NNT for these interventions ranged from 1.2 to 3.3. Table 23.5 documents the characteristics and results of double-blind placebo-controlled trials in pediatric non-OCD anxiety disorders. Despite noticeable differences in effect sizes between trials, there is no evidence from pharmacological trials in both children and adults that any one SSRI is more effective than any other. Differences in response rates and efficacy between trials is just as likely related to differences in trial design, study population, and dose titration schedule when compared with differences in pharmacological agent utilized. A recent randomized, controlled-trial compared CBT, SSRI pharmacotherapy with sertraline and their combination to placebo (Walkup et al.). All three treatment conditions were superior to placebo with statistically comparable response rates between CBT and sertraline treatment. Combination treatment with both sertraline and CBT was superior to treatment with either treatment alone suggesting that first-line treatments for non-OCD anxiety disorders are complimentary.

Table 23.5 Randomized, placebo-controlled trials of pharmacological interventions for pediatric OCD

Study	Drug	*N*	Length (weeks)	Dosage (mg/day) Range	Dosage (mg/day) Mean	Effect size (CY-BOCS)	Response rate (CGI <3) Drug (%)	Response rate (CGI <3) Placebo (%)	NNT	Time of significant response (weeks)
March et al. (1998)	Sertraline	187	12	25–200	167	0.42	42	26	6.3	3
Geller et al. (2001)	Fluoxetine	103	13	10–60	25	0.50	55	19	2.8	7
Riddle et al. (2001)	Fluvoxamine	120	10	25–200	165	0.32	30	18	8.1	1
Liebowitz et al. (2002)	Fluoxetine	43	8	20–80	65	0.67	57	27	3.3	16
POTS (2004)	Sertraline	112	12	25–200	170	0.67	39[a]	21[a]	5.9[a]	4
Geller (2004)	Paroxetine	207	10	10–50	23	0.51	47	33	7.4	2

[a]Response rates and NNT based on a CY-BOCS <10 at endpoint
CGI-I Clinical Global Impression-Improvement; *CY-BOCS* Children Yale-Brown Obsessive Compulsive Scale

Predictors of Treatment Response

Given the relative paucity of randomized clinical trials in the field of pediatric anxiety disorders, there are few reliable predictors of clinical response to SSRI pharmacotherapy. Across anxiety disorders, increased severity of initial symptoms is associated with poor response (Geller, Biederman, Stewart, Mullin, Martin, et al., 2003). In non-OCD anxiety disorders, the presence of social phobia has been associated with poor pharmacological treatment response (The Research Unit on Pediatric Psychopharmacology Anxiety Study Group, 2001).

Pharmacological Treatments for Pediatric Anxiety Disorders

First-Line Pharmacological Treatment

Selective Serotonin Reuptake Inhibitors

As discussed previously, SSRIs are a first-line treatment for all pediatric anxiety disorders with the exception of PTSD. The benefits of SSRI in the treatment of anxiety disorders appear to be additive with those associated with evidence-based psychotherapy. This section will summarize the dosing, onset of action, duration of treatment, and side-effects of SSRI pharmacotherapy.

Dosing

Table 23.6 demonstrates typical starting and target dose ranges of SSRIs used to treat children and adults with anxiety disorders. In children, there exist no fixed-dose studies, which are used to evaluate the relative efficacy of different doses of medications. In adulthood OCD, recent meta-analysis has demonstrated that higher doses of SSRI pharmacotherapy are more effective than lower dose treatment. This contrasts with the SSRI efficacy dose curves in adult depression, where low and high-dose SSRI treatment has been demonstrated to have similar efficacy (Bloch, McGuire, Landeros-Weisenberger, Leckman, & Pittenger, 2010; Bollini, Pampallona, Tibaldi, Kupelnick, & Munizza, 1999). In adulthood, OCD higher doses of SSRI pharmacotherapy were associated with a significantly higher rate of drop-out due to side-effects when compared with low-dose treatment. No such metaanalysis of fixed-dosed SSRI trials has occurred for the treatment of PTSD or other anxiety disorders.

On the basis of this evidence and clinical experience, we have developed two SSRI dosing strategies based on illness severity, family preference, and side-effect history with medications. In children with severe anxiety symptoms (especially OCD) causing significant impairment and distress, who does not have a family history of bipolar disorder and no previous history of

Table 23.6 Evidence-based pharmacological interventions for pediatric anxiety disorders

	Starting dose		Target dose	
Medication	Children	Adults	Children	Adults
SSRIs				
Fluoxetine	5–10	20	10–80	40–80
Fluvoxamine	12.5–25	50	50–300	100–300
Sertraline	12.5–25	50	50–200	150–250
Paroxetine	5–10	10–20	10–60	20–60
Citalopram	5–10	20	10–60	20–60
Escitalopram	2.5–5	10	5–30	20–40
SNRIs				
Venlafaxine (ER)	37.5	37.5–75	75–225	150–300
TCAs				
Clomipramine	12.5–25	25	50–200	100–250

side-effects with SSRI pharmacotherapy, we generally aggressively increase the dose of SSRI medication (i.e., for fluoxetine starting at 10–20 mg for children and increasing by similar increments to a target dose of 60–80 mg). If side-effects occur, we will generally slow-down or stop titration and possibly decrease medication dosage. In cases where disease severity or impairment is moderate, if there is a family history of bipolar disorder or previous side-effects to medications, we will slowly titrate up to the minimum target dose (i.e., 20 mg of fluoxetine) and then wait until 1–2 months after reaching the target dose to evaluate treatment efficacy. If the child does not improve sufficiently, we will then titrate toward the maximum dose of that agent. Medications with liquid-dosing formulations or smaller tablet increments are easier to tolerate up more slowly. Fixed-dose trials in pediatric anxiety disorders are needed to provide appropriate evidence behind these treatment recommendations.

Onset of Effects

Tables 23.3 and 23.5 demonstrate the time at which SSRI pharmacotherapy demonstrates statistically significant improvement compared with placebo. In both OCD and non-OCD pediatric anxiety disorders, SSRI pharmacotherapy takes between 2 and 9 weeks to statistically distinguish itself from placebo In anxiety disorders, it is typical to see some response to pharmacotherapy around a month after initiating treatment but the full treatment benefits are not realized for 2–3 months. Thus the decision about whether to change an SSRI medication due to lack of efficacy is not advisable until at least 2 months after the initiation of treatment. Changing between SSRIs may be advisable before 2 months if a child experiences significant side-effects prior to the minimal target dose.

Side Effects

SSRIs are generally well tolerated in children compared with other medications used to treat child psychiatric conditions. Gastrointestinal disturbance, headache, fatigue, and sleep disturbances are common side-effects of SSRI medications (affect approximately 10% of patients). These side-effects are often ephemeral and typically occur at the initiation of treatment or at an increase in dose. With continued treatment at the same dose, these side-effects often disappear. Sexual side-effects such as decreased libido or decreased sexual performance are frequent dose-related side-effects of SSRIs and are a frequent reason for medication noncompliance in teenagers. Sexual side-effects are not permanent with SSRIs and can be improved with either a dose reduction or discontinuation of the medication.

Behavioral activation and suicidal ideation are more severe but less common side-effects of SSRIs. In 2004, the Food and Drug Administration issued a "black-box warning" stating that these

medications were associated with an increased risk of suicide. This warning was based on a metaanalysis of 24 placebo-controlled trials in children with depression, anxiety disorders, and ADHD (Hammad, 2004). The metaanalysis found a 2% increase in the risk of suicidal ideation with treatment with SSRI. There were no completed suicides that occurred in any of these trials. Growing epidemiologic evidence since the issuing of this warning suggests that there has been an increase in the number of suicide attempts and completions since the decreasing in prescribing that concurrently occurred. OCD and non-OCD anxiety disorders appear to have a decreased risk of suicidal ideation compared with children treated for depression (Bridge et al., 2007). This decreased risk along with the greater demonstrated efficacy of SSRIs in treating pediatric anxiety disorders makes the risk benefit profile of SSRIs in treating these conditions particularly favorable. Based on this warning, the FDA currently advises clinicians to see a child weekly for 4 weeks after starting SSRIs and monthly thereafter (Hammad, 2004).

Behavioral activation is a syndrome associated with SSRI use, which is characterized by hyperactivity, giddiness, insomnia, and agitation. These symptoms can sometimes involve mania, irritability, and aggression. Typically this behavioral activation occurs within days or weeks of initiating SSRI treatment or after increasing their dosage (Goodman, Murphy, & Storch, 2007). Behavioral activation is relatively uncommon in children treated with SSRIs and may be more frequently associated with tricyclic antidepressants (Martin et al., 2004).

Duration of Treatment

There exists a complete absence of any long-term discontinuation studies in pediatric OCD or non-OCD anxiety disorder. Long-term discontinuation studies in adulthood OCD strongly support continued treatment with SSRI for a minimum duration of 1 year in treatment responders (Greist et al., 2003). Data from a recent metaanalysis of double-blind discontinuation studies suggest that the risk of relapse nearly doubles for individuals taking placebo as opposed to SSRI when the discontinuation begins prior to 1 year of SSRI treatment (Fineberg, Pampaloni, Pallanti, Ipser, & Stein, 2007). The absolute risk of relapse in adulthood OCD is well over 50% within 6 months in individuals blindly treated with placebo (Hollander et al., 2003). Data regarding the relapse rate of discontinuing SSRIs after more than 1 year of treatment is absent in both adults and children with OCD and non-OCD anxiety disorders.

Based on the available evidence, it is currently suggested to continue SSRIs for at least 1 year in children who respond to pharmacological treatment (Connolly & Bernstein, 2007). The decision to discontinue SSRIs should be based on the following: (1) child's level of current symptom severity, (2) level of current side effects on medications, (3) degree of original symptom response to pharmacotherapy, and (4) the family's attitude toward medication. It is currently not recommended to discontinue SSRIs in a child with significant residual symptoms despite receiving first-line treatments and had an initial response to pharmacotherapy. When discontinuation of medication occurs it should be done during a period of low stress for the child and after a long period of symptom stability. During the course of SSRI discontinuation most medications need to tapered slowly to prevent a discontinuation syndrome. Discontinuation symptoms upon abrupt withdrawal of an SSRI, clomipramine, or venlafaxine can include flu-like symptoms, increased anxiety, panic attacks agitation, insomnia, poor concentration, and suicidal ideations. These discontinuation symptoms can last several weeks. Therefore, it is advised that discontinuation of an SSRI be done with a well-trained physician to monitor for both relapse and discontinuation symptoms and that SSRI doses be tapered slowly over several weeks.

Alternative Pharmacological Treatments for Treatment-Refractory Anxiety Disorders

Clomipramine

Clomipramine, a tricyclic antidepressant, was the first medication with demonstrated efficacy in treating OCD. Clomipramine has demonstrated efficacy in multiple double-blind trials and appears

at least as effective as SSRIs in the treatment of pediatric anxiety disorders (Geller, Biederman, Stewart, Mullin, Martin, et al., 2003). Clomipramine is currently not widely utilized as a first-line treatment because of its poor tolerability compared with SSRIs. Common side effects with clomipramine include dry mouth, sedation, and weight gain. Increased seizure risk and cardiovascular events, mainly hypotension and arrhythmias, are serious side-effects associated with clomipramine. The cardiovascular events necessitate EKG monitoring during treatment. Behavioral activation may also be associated with clomipramine use. In children with OCD, clomipramine treatment is generally limited to monotherapy for children who have not experienced symptom relief with multiple adequate SSRI trials or in low-doses as a pharmacological agent to augment SSRI pharmacotherapy in treatment-refractory OCD.

Venlafaxine

Venlafaxine, a serotonin norepinephrine reuptake inhibitor, is also commonly used as a pharmacological agent for monotherapy in children who have not responded to SSRI treatment for OCD. Venlafaxine also has demonstrated efficacy in double-blind trials of pediatric social phobia (March et al., 2007). Common side-effects of venlafaxine include nervousness, headache, dizziness, and insomnia. Venlafaxine has a fairly significant discontinuation syndrome when discontinued abruptly.

Antipsychotic Augmentation

Low-dose antipsychotic augmentation with either typical (i.e., haloperidol) or atypical antipsychotics (i.e., risperidone) appears to have modest benefit as an augmentation agent for treatment refractory adult OCD (Bloch et al., 2006). Antipsychotic augmentation may improve OCD symptoms significantly in roughly one in four adults with treatment-refractory OCD (Bloch et al.). Case series have suggested similar efficacy in children. Antipsychotic augmentation appears particularly effective in children with comorbid tics (Bloch et al.).

Anxiolytics

Anxiolytics such as antihistamines, diphenydramine and hydroxyzine, and benzodiazepines are used by many clinicians to treat anxiety or for bedtime sedation in children. These medications often cause anticholinergic side effects most significantly confusion or delirium. Although these medications may have short-term effects, there is no evidence of long-term efficacy in children (Graae, Milner, Rizzotto, & Klein, 1994; Simeon et al., 1992). These medications are thus not recommended for long-term treatment of pediatric anxiety disorders.

Psychotherapy

CBT has been demonstrated to be an effective treatment for OCD refractory to treatment with multiple SSRIs (Simpson, 2008 #716). Even if a child does not respond to CBT treatment with one therapist at one particular point in development, it is quite reasonable to revisit another trial of CBT periodically.

Conclusion

Pharmacotherapy with SSRIs alone or in combination with CBT benefits a substantial proportion of children with pediatric anxiety disorders. Combination therapy with both SSRIs and CBT is more effective than either treatment alone for most anxiety disorders. The full clinical benefit of SSRI pharmacotherapy is often realized after 4–8 weeks of treatment, so patience by the clinician and family is needed. Higher doses are often needed to obtain the full clinical benefit of SSRIs, especially in OCD. SSRIs are generally well-tolerated but the association of increased suicidal ideation and behavioral activation with their use requires regular monitoring at the initiation of

treatment. With discontinuation of SSRIs, there appears to be a high rate of relapse especially when medications are discontinued abruptly. A substantial proportion of children with anxiety disorders will have significant residual symptoms despite treatment with the available first-line interventions. Further research is needed to identify additional pharmacological and behavioral treatments for refractory pediatric anxiety disorders and to identify predictors of treatment response to first-line interventions.

Acknowledgments The authors acknowledge the National Institute of Mental Health support of the Yale Child Study Center Research Training Program (MHB), NARSAD (MHB), Trichotillomania Learning Center (MHB), the National Institutes of Health Loan Repayment Program (MHB), and the APIRE/Eli Lilly Psychiatric Research Fellowship (MHB).

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Pharmacologic Approaches to Medication-Resistant Anxiety in Children and Adolescents

24

Justine Larson, Susan DosReis, Marisa Matthys, and Mark Riddle

Anxiety disorders are extremely common in the pediatric population, with prevalence estimates ranging from 12 to 20% (Achenbach, Howell, McConaughy, & Stanger, 1995; Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; US Surgeon General, 1999). In the last 10 years, important advances in the psychopharmacologic treatment of childhood anxiety disorders include the increasing evidence of the efficacy of selective serotonin reuptake inhibitors (SSRIs) (Birmaher et al., 2003; Research Unit on Pediatric Psychopharmacology Anxiety Study Group, 2001; Rynn, Siqueland, & Rickels, 2001; Walkup et al., 2008). The major pediatric anxiety disorders can be divided into the following four main groups: (1) generalized anxiety disorder (GAD), separation anxiety disorder (SAD), social phobia (SoP), and specific phobia, which are often considered together and is the most common group of childhood anxiety disorders; (2) panic disorder with and without agoraphobia is less common in children, and is considered separately; (3) acute stress disorder and posttraumatic stress disorder (PTSD); and (4) obsessive–compulsive disorder (OCD). Selective mutism has also been included as a childhood anxiety disorder as it may be a form of SoP (Black & Uhde, 1994).

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Anxiety disorders cause significant morbidity in children in multiple arenas, including home, school, and with peers (Ialongo, Edelsohn, Werthamer-Larsson, Crockett, & Kellam, 1995; Langley, Bergman, McCracken, & Piacentini, 2004; Messer & Beidel, 1994). There is increasing evidence of the efficacy of SSRIs (Birmaher et al., 2003; Research Unit on Pediatric Psychopharmacology Anxiety Study Group, 2001; Rynn et al., 2001; Walkup et al., 2008). Although a full discussion of the data supporting the use of SSRIs in pediatric anxiety is beyond the scope of this chapter, there are a number of major studies that are worth briefly summarizing. For example, the Childhood Anxiety Multimodal Study (CAMS, 2008) randomized 488 children between the ages of 7 and 17 years with diagnoses of SAD, GAD, or SoP to CBT, sertraline (up to 200 mg/daily), combined CBT and sertraline, or placebo. The study found that 80% of children on combined CBT and sertraline were very much or much improved from baseline, 60% on CBT alone were very much or much improved, and 55% on sertraline alone were very much or much improved. All three groups were improved compared with those on placebo, 24% of whom improved (Walkup et al., 2008). Similarly, the Research Units for Pediatric Psychopharmacology (Research Unit on Pediatric Psychopharmacology Anxiety Study Group, 2001) Anxiety Study group randomized 128 children and adolescents with SAD, SoP, or GAD to fluvoxamine or placebo after a 3-week

D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_24,

lead-in supportive therapy. In this study, 76% of the active treatment group vs. 29% in the placebo group responded. Other studies have demonstrated similar response rates to SSRIs (Birmaher et al., 2003)For OCD, the Pediatric OCD Treatment Study Team (POTS, 2004) was a randomized, controlled 12-week study in a sample of 112 OCD patients ages 7–17 years old who were randomized to cognitive-behavioral therapy (CBT) alone, sertraline alone, or combined sertraline and CBT. Combined treatment was found to be superior to both CBT alone and sertraline alone, both of which were superior to placebo.

More research is required to support the use of SSRIs in pediatric panic disorder (Masi, 2006). However, early data do show that SSRIs may have an impact, and SSRIs are frequently recommended for first-line treatment in this relatively rare disorder (Birmaher, Birmaher, & Ollendick, 2004). In a chart review of 18 children and adolescents with panic disorder, paroxetine treatment was shown to be safe and effective (Masi et al., 2001). An open-label study by Renaud et al. (1999) demonstrated safety and effectiveness of SSRIs in children and adolescents with panic disorder. Like pediatric panic disorder, more research is required to determine efficacy of pediatric PTSD, although preliminary results are promising. In an 8-week open treatment trial, the use of citalopram in children/adolescents and adults with PTSD resulted in improvement in PTSD symptoms including reexperiencing, avoidance/numbing, and hyperarousal (Seedat et al., 2002). For both pediatric PTSD and panic disorder, more randomized controlled data are required, although SSRIs may have an important utility and are generally recommended as first-line treatment for these disorders (Masi, 2006; Seedat, Seedat, & Stein, 2001). Despite the significant advances in efficacious psychopharmacologic treatments for OCD and non-OCD childhood anxiety disorders, there remains a sizeable portion of children who continue to experience ongoing anxiety symptoms even if they have received an adequate dose and duration of an SSRI. Treating those children who do not respond to first-line agents can be a significant challenge to the clinician for multiple reasons. By the time children and families arrive at the office, they may be demoralized and discouraged. Families may have received conflicting information regarding their diagnosis and may be confused about whom to trust. The patients themselves often have complex problems, with multiple comorbidities and psychosocial risk factors, which may influence the selection of a second-line psychopharmacologic treatment. Finally, there is very little scientific research to offer clinicians guidance on alternative treatments for children who are resistant to first-line psychopharmacologic medications for childhood anxiety disorder. This chapter discusses children who present with “medication-resistant” anxiety, and factors to consider in the evaluation and treatment of these cases.

It is also important to note the significant advances made in psychotherapeutic approaches to anxiety treatment (Compton et al., 2004). Although this chapter focuses on the psychopharmacologic treatment of medication-resistant children and adolescents with anxiety disorders, psychotherapeutic options including CBT (Compton et al., 2004), psychodynamic therapy (Milrod, Busch, Shapiro, Leon, & Aronson, 2005), and family therapies (Bernstein, Layne, Egan, & Tennison, 2005) can play an important role for this patient population. Generally, CBT has the most empirical support for the treatment of pediatric anxiety. A review of controlled studies in CBT by Compton et al. (2002) supports CBT as the most promising psychosocial intervention in reducing the symptoms of childhood anxiety disorders for extended periods of time. Family therapy and psychodynamic therapies are supported by clinical experience and some research, although ongoing research is required to better understand how they can be useful in the treatment of pediatric anxiety. Psychotherapies should be considered as part of the treatment plan, both as stand alone as well as adjunctive treatments. Though more research is needed in combined CBT and pharmacotherapy for the treatment of childhood anxiety, combined treatment is advised for children who have undergone unsuccessful treatments (Keeton & Ginsburg, 2008).

Evaluating "Medication-Resistant" Pediatric Anxiety

Definition

For the purposes of this chapter, the term *medication-resistant* pediatric anxiety will be defined as those cases for which an adequate trial in both dose and duration of an SSRI has resulted in either a partial or a nonresponse. Although there is no universally accepted definition of medication-resistance, a number of studies have used this definition to describe medication-resistant or treatment-refractory patients (Dell'osso, Mundo, Marazziti, & Altamura, 2008; McDougle, Goodman, Leckman, & Lee, 1994). Other published studies have used definitions ranging from cases that have failed all available treatments to cases that have failed multiple SSRI trials (Dell'osso et al., 2008; Fineberg et al., 2006).

Dosing and Treatment Duration

Unfortunately, there are no specific parameters regarding dosing in pediatrics (Seidel & Walkup, 2006). Generally, starting at a low dose and increasing according to tolerability, treatment response, and side effects is recommended (Labellarte, Ginsburg, Walkup, & Riddle, 1999). It is also not clear how long treatment with an SSRI should occur to achieve maximum benefit, although the general consensus regarding an adequate trial is 8–12 weeks. There is some limited research in the adult literature to suggest that patients may improve over longer periods while treated with SSRIs. For example, in a study of adults with treatment-refractory PTSD, 54% of those patients who had not responded to sertraline in the first 12 weeks responded between 12 and 24 weeks of ongoing treatment (Londborg et al., 2001). In addition, an open label SSRI extension study suggests that longer term treatment with sertraline in pediatric OCD may have utility (Cook et al., 2001). Children and adolescents with OCD who participated in a placebo controlled 12-week trial of sertraline (March et al., 1998) were eligible to participate in an open label 52-week trial of sertraline, and results of the open label study showed significant improvements in children/adolescents regardless of whether they received placebo or sertraline, and regardless of response status in the previous 12-week trial. Thus, some children who do not respond after a 12-week trial of sertraline may show improvements over a longer course of treatment, and children who do show an acute response after 12 weeks may display additional improvements if treatment is continued. More research is required to determine the appropriateness of longer treatment durations for pediatric patients, although limited data suggests that longer duration of treatment may result in ongoing improvement for some patients.

Reevaluation

In evaluating patients with medication-resistant anxiety, it is first important to revisit the diagnostic formulation, and to consider the possibility of missed or inaccurate diagnoses (see Table 24.1). There are a number of conditions that may mimic anxiety symptoms, including ADHD (see Chap. 12), learning disabilities, language disorders, oppositional defiant disorder, mood disorders, and pervasive developmental disorders (see Chap. 33). For example, patients who experience a feeling of restlessness or jitteriness may be experiencing either anxiety symptoms or ADHD symptoms. Similarly, patients who may appear inattentive can be suffering from ADHD or may be preoccupied with anxious thoughts. It is also important to consider medical conditions that can present with anxiety-like symptoms, such as thyroid problems, asthma, seizure disorders, and lead intoxication. Other less common medical diagnoses to consider include pheochromocytoma (catecholamine-producing tumor of the adrenal medulla), variations in blood sugar, CNS lesions, and cardiac arrhythmias. Ingestions can also result in anxiety-like symptoms, as is the case with caffeine, marijuana, and other substances. Lastly, certain prescription and nonprescription drugs can elicit anxiety-like symptoms.

Table 24.1 Disorders that mimic anxiety

	Medical conditions		Medications		
Psychiatric disorders	Common	Less common	Prescription drugs	Nonprescription drugs	Substances
ADHD Psychotic disorders Oppositional defiant disorder Mood disorders (bipolar disorder, depression) Pervasive developmental disorders (Asperger's disorders Language disorders	Hyperthyroidism Migraine Asthma Seizure disorders Lead intoxication	Pheochromocytoma Hypoglycemia CNS disorder (delirium, brain tumors) Cardiac arrhythmias	Antiasthmatics Sympathomimetics Steroids SSRIs Antipsychotics Haloperidol Pimozide Atypical antipsychotics	Diet pills Antihistamines Cold medicines	Caffeine Marijuana

Comorbidities

It is important to assess for any comorbid disorders or complicating factors and ensure that these are addressed. Anxiety disorders have high rates of comorbidities in the pediatric population, including depression (Lewinsohn, Zinbarg, Seeley, Lewinsohn, & Sack, 1997), ADHD (Kendall, Brady, & Verduin, 2001), substance abuse (Schuckit & Hesselbrock, 1994), learning disorders (Manassis & Monga, 2001), and language disorders (Manassis & Monga, 2001). Many patients will require a treatment plan that simultaneously addresses multiple comorbidities. At other times, adequately addressing one problem will impact the symptoms of another. For example, a patient with ADHD who is also experiencing anxiety symptoms with school work and in social situations may experience an improvement in his anxiety once adequately treated for ADHD, and thus becomes able to organize schoolwork and behave less impulsively in social situations. Other comorbidities may complicate treatment response (Manassis & Monga, 2001). For example, comorbid major depression is associated with greater severity of anxiety symptoms, older age, high levels social anxiety, and may be an indicator of poor prognosis (Manassis & Menna, 1999). Adequate treatment of the comorbidity may allow for the anxious child to respond to treatments that he or she had not responded to previously. For example, an adolescent who is using marijuana may continue to have significant anxiety symptoms despite treatment with an SSRI. Addressing the substance use is imperative in order for the patient to fully benefit from psychiatric treatment.

Complicating Factors

In addition to comorbidities, other complicating factors may impact treatment response. These include parent–child relationship factors, secondary gain from anxious behaviors, noncompliance with treatment, intraparental conflict, and other family factors. Individual therapy may not attend to maladaptive relationships, parenting skills, and family dynamics, and these problematic entities can significantly hinder a child's ability to develop his own coping strategies, independence, and willingness to engage in the treatment process (Connolly & Bernstein, 2007). Secondary gain from anxious behaviors can occur in a child who has long suffered from anxiety symptoms. In some cases, the patient may begin to experience benefits from his condition, such as increased parental attention, successful avoidance of undesirable activities, or other secondary gains, causing the treatment response to be slowed by the unwillingness to move forward. In other situations, the child's symptoms may be playing a role in maintaining a family dynamic that is serving another purpose, such as "uniting" two parents that might otherwise be disagreeing. Addressing these complicating factors, through behavioral interventions,

family therapy, individual therapy, or other interventions, may result in better response to medication.

Medication History

A detailed psychopharmacologic medication history including previous dosages of medications, duration of treatment, and any adverse effects of these medications should be obtained. Other considerations should be over-the-counter products and herbal preparations, and the possible side effects of these as a cause of anxiety symptoms. Steroids, asthma medications, SSRIs, and antihistamines are examples of medications that may in fact worsen anxiety symptoms.

Patients who present as "treatment-resistant" may, upon further questioning, have had the SSRI discontinued due to adverse effects, rather than due to lack of efficacy of treatment. Although SSRIs are generally well-tolerated in children and adolescents, common side effects include gastrointestinal distress, headache, insomnia, and akathisia. However, the clinician should be aware that children with anxiety disorders may be more highly attuned to somatic symptoms, gastrointestinal symptoms, and other adverse effects that may be attributed to the medication. A full exploration of the timing of symptoms, the nature of these symptoms, and whether these symptoms existed before initiation with an SSRI is important.

Disinhibition, or behavioral activation, resulting from SSRIs is another common adverse effect in the pediatric population (Carlson & Mick, 2003; Reinblatt, DosReis, Walkup, & Riddle, 2009). However, disinhibition secondary to SSRIs is not always easy to distinguish from baseline symptoms of oppositionality, aggression, or hyperactivity. Certain populations of children, such as those with ADHD, PDD, and younger children, may be more prone to disinhibtion secondary to SSRIs (Carlson & Mick, 2003). This may make the identification of true, SSRI-induced disinhibition even more challenging, as these populations are more likely to have symptoms of higher levels of activity and decreased impulse control at baseline. Another phenomenon that can be misattributed to drug-induced disinhibition is the celebratory behavior of patients who have been anxious and who are no longer being inhibited by anxiety (Seidel & Walkup, 2006). Again, a full description of the behavior and the setting in which the behavior occurred can help differentiate these phenomena from a treatment-resistant patient. Occasionally, the clinician will be in the position of having a partial or vague history regarding possible drug-induced disinhibition. A careful weighing of the risks and benefits of treatment options is required. Psychotherapeutic options should be considered. In severe cases of anxiety that are not responsive to psychotherapy, it is important for the clinician to engage in an open discussion of the risks of rechallenging with an SSRI vs. the risks associated with ongoing anxiety symptoms. The relative strength of the evidence supporting the use of SSRIs in childhood anxiety disorders, combined with less adequate safety data regarding the use of other medications, should be carefully weighed against the severity of the patient's symptoms and current functioning.

Nonresponse Prevalence Estimates

It is unclear how many children with anxiety will be partial or nonresponders to treatment with SSRIs. Some limited information regarding number of responders and nonresponders can be gleaned from recent trials. For example, the Childhood Anxiety Multimodal Study (CAMS, 2008) randomized 488 children between the ages of 7 and 17 years with diagnoses of SAD, GAD, or SoP to CBT, sertraline (up to 200 mg/daily), combined CBT and sertraline, or placebo. As described earlier, the study found that 80% of children on combined CBT and sertraline were very much or much improved from baseline, 60% on CBT alone were very much or much improved, and 55% on sertraline alone were very much or much improved. All three groups were improved compared with those on placebo, 24% of whom improved (Walkup et al., 2008). Even with the excellent clinical response of those children treated with both sertraline and CBT, then, there

remains 20% of children receiving both treatments who did not demonstrate significant improvement and who continued to have significant anxiety symptoms. Similarly, the Research Units for Pediatric Psychopharmacology (Research Unit on Pediatric Psychopharmacology Anxiety Study Group, 2001) Anxiety Study group randomized 128 children and adolescents with SAD, SoP, or GAD to fluvoxamine or placebo after a 3-week lead-in supportive therapy. In this study, 76% of the active treatment group vs. 29% in the placebo group responded. Despite the impressive results, 24% of children did not respond adequately to fluvoxamine. Other studies have demonstrated similar response rates to SSRIs (Birmaher et al., 2003).

Similar response rates have been demonstrated for OCD. The POTS trial randomly assigned 112 patients ages 7 through 17 with OCD to three groups: CBT alone, sertraline alone, or combined CBT and sertraline. Combined treatment was superior to CBT alone and sertraline alone. In the combined treatment group, 53.6% experienced clinical remission, while clinical remission rates for CBT alone, sertraline alone, and placebo were 39.3, 21.4, and 3.6%, respectively. Thus, 46.4% of children with pediatric OCD had not obtained remission despite receiving combined treatment (POTS, 2004). Other randomized controlled trials in pediatric OCD have shown the acute effectiveness of SSRIs including sertraline (March et al., 1998), fluvoxamine (Riddle et al., 2001), and fluoxetine (Geller et al., 2001). In the study by March et al. (1998), 42% of patients receiving sertraline were very much or much improved compared with 26% receiving placebo (March et al., 1998). Likewise results by Riddle et al. (2001) showed a 42% response rate in patients taking fluvoxamine and a 26% response rate in patients receiving placebo (Riddle et al., 2001). Geller et al. (2001) showed a response rate of 49% in the fluoxetine treatment group and that of 25% in the placebo group (Geller et al., 2001).

It is important to note that different studies have used different definitions of response, with some studies using a categorical approach, and others using a percentage cut point. Although response rates are reasonably high, the ultimate goal of treatment is complete remission of symptoms. Clinically, even when a patient "responds" to treatment, ongoing symptoms may significantly impact his functioning and quality of life. In addition, the response rates in the literature base may underestimate the response rates of the general population. Many of these studies excluded participants with nonanxiety related comorbidities and therefore may not be entirely reflective of a clinical sample of anxiety patients. Therefore, nonresponse or partial response is likely to be in the range of 30–50% in clinical samples, and it is important to consider that for individual patient remission of symptoms, rather than "response," is the goal of treatment.

Predictors of Response

Response rates may also differ across diagnostic and other categories, although more research regarding what predicts treatment response is required. In the RUPP Anxiety study, increased symptom severity and SoP predicted less medication treatment response (Research Unit on Pediatric Psychopharmacology Anxiety Study Group, 2001). Geller (2003) examined the effects of psychiatric comorbidity on response and relapse to paroxetine treatment in the pediatric OCD population. Children with comorbid ADHD, TD, or ODD had significantly lower response rates as well as greater rates of relapse (Geller et al., 2003). It has also been noted that pediatric OCD patients with nonanxiety comorbidities are less likely than patients with anxiety comorbidities or OCD alone to respond to CBT (Storch et al., 2008).

Specific Treatment Strategies

Although data specifically addressing psychopharmacologic options for patients who have not responded or who are unable to tolerate SSRIs is sparse, the literature examining medication-resistant children and adolescents with depression may have some utility, but the degree to which information from the depression literature can be extrapolated to the anxiety literature is not clear. There is evidence

to suggest that SSRIs may have different response rates in pediatric MDD and anxiety (Bridge et al., 2007), which indicates that SSRIs may behave differently in the two disorders. Similarly, adult studies for treatment-refractory anxiety may also be helpful in informing possible areas for future research in the pediatric population, but, again, extrapolating medication treatment studied in adults to children should be approached very cautiously. Medications can behave differently in children than in adults, and may have a different impact on the developing brain (Vitiello, 2006). Furthermore, the adult literature for treatment-refractory anxiety is in itself limited; there is a paucity of randomized trials for treatment-refractory anxiety, and most of the information available is from open-label or retrospective reports, with one exception being OCD and atypical antipsychotics (Pollack et al., 2008). Currently, there are no FDA-approved medications for treatment-refractory anxiety in adults.

Single-Agent Medication Treatment for Medication-Resistant Anxiety

Switching SSRIs

There are no controlled studies examining SSRI switches for partial or nonresponsive pediatric patients with anxiety disorders. In one open treatment trial during the 6 months following the 8-week phase of the RUPP Anxiety trial (Research Unit on Pediatric Psychopharmacology Anxiety Study Group, 2001), those who did not respond to fluvoxamine were changed to fluoxetine. Of these 14 individuals, 10 (74%) improved significantly after switching to fluoxetine. This technique has also been recommended in the treatment of pediatric depression (Emslie & Mayes, 2001; Hughes, Budd, & Greenaway, 1999). In the TORDIA Randomized Controlled Trial (Brent et al., 2008), the first large trial for treatment-refractory depression in adolescents, a clinical sample of 334 adolescent patients ages 12–18 with major depressive disorder who had not responded to a 2-month trial of an SSRI (paroxetine, citalopram, or fluoxetine, doses 20–40 mg) were randomized to 12 weeks of either: (1) a switch to another SSRI; (2) a switch to a different SSRI plus CBT; (3) a switch to venlafaxine (doses 150–225 mg), or (4) a switch to venlafaxine plus CBT. The study found that the group that was switched to another SSRI plus CBT had the highest rate of response. In addition, the study found that switching to an SSRI was as efficacious as switching to venlafaxine, with fewer adverse effects.

There is also little data available to determine which SSRI is more efficacious than another in pediatric anxiety. A metaanalysis compared 12 new-generation antidepressants (buproprion, citalopram, duloxetine, escitalopram, fluoxetine, fluvoxamine, milnacipram, mirtazapine, paroxetine, reboxetine, sertraline, and venlafaxine) by examining 117 randomized controlled trials for treatment of adults with depression (Cipriani et al., 2009). Mirtazapine, escitalopram, venalfaxine, and sertraline were more efficacious than the other agents. Escitalopram and sertraline showed the highest profile of acceptability, with fewer discontinuations than with the other options. Although this metaanalysis was only conducted examining adults with depression, it is one of the first large analyses comparing antidepressant agents.

Given the lack of specific guidelines regarding which SSRIs are more effective for pediatric anxiety, the decision regarding which SSRI to prescribe should be made according to a number of factors. The clinician may first consider the SSRIs which have NIMH-supported data associated with them. These include sertraline (Walkup et al., 2008), fluvoxamine (Research Unit on Pediatric Psychopharmacology Anxiety Study Group, 2001), and fluoxetine (Birmaher et al., 2003). Regarding Federal Drug Administration approval (FDA), none of the SSRIs are FDA-approved for pediatric anxiety, with the exception of fluoxetine, sertraline, and fluvoxamine for OCD. Another factor to consider is the pharmokinetics of the various SSRIs in children. In children and adolescents, the half-life of paroxetine, when compared with the other SSRIs, has significant variability between subjects, making dosage decisions less straightforward (Findling et al., 1999). When considering compliance issues, fluoxetine may be of some advantage given the long half-life of its metabolite.

such as weight changes, nausea, increases in blood pressure, and others make switching to an alternate SSRI a preferable treatment option for most children.

Tricyclic Antidepressants

The use of tricyclic antidepressants (TCAs) has fallen out of favor due to concerns regarding the risk of sudden cardiac death (Reinblatt & Riddle, 2007) and other side effects. The data for the use of TCAs for non-OCD anxiety disorders have been mixed (Bernstein, Garfinkel, & Borchardt, 1990; Hughes, Preskorn, Wrona, Hassanein, & Tucker, 1990; Klein, Koplewicz, & Kanner, 1992). The evidence base for the use of tricyclics for pediatric anxiety disorders is summarized elsewhere (Walkup et al., 2002). Clomipramine, a tricyclic with serotonergic properties, has been demonstrated to be useful in the treatment of pediatric OCD (DeVeaugh-Geiss et al., 1992; Flament et al., 1985; Leonard et al., 1989). In cases where SSRIs cannot be used or have limited efficacy, TCAs could be considered, particularly for pediatric OCD. It should be noted that clomipramine has significant anticholinergic side effects and, at higher doses, poses risk of cardiotoxicity. Electrocardiogram and plasma trough levels should be monitored. There are no specific parameters for plasma trough levels of clomipramine in children; however, it has been recommended that adult plasma trough levels of clomipramine, combined with its metabolite demethylclomipramine, should be maintained below 500 μg/L (Fineberg et al., 2006).

In adults with treatment-refractory OCD, several studies have evaluated the effects of clomipramine delivered intravenously (Fallon et al., 1998). One double-blind placebo-controlled study of IV clomipramine in adults refractory to oral clomipramine also demonstrated effectiveness (Fallon et al., 1998). Other short-duration trials against oral clomipramine have failed to show a benefit of intravenous administration (Koran et al., 2006). The use of intravenous clomipramine in children is logistically problematic. For the majority of patients and families, it is likely not justified given the mixed data in pediatric anxiety, although further exploration of its use is warranted.

Other Agents

Other agents including buspirone and benzodiazepines have not been studied in pediatric medication-resistant anxiety. At this point, there are insufficient data to recommend these agents for use in children who are treatment-refractory to an SSRI. Several reviews of possible new approaches to treatment for refractory anxiety disorders are available for adults (Bystritsky, 2006; Pollack et al., 2008). New potential molecular targets for drug development, such as substance P antagonists, NMDA receptor antagonists, and neurosteroid modulators of the GABA system have been suggested (Pollack et al., 2008) but are in early stages of development.

Augmentation of SSRIs

Although the use of multiple medications is becoming increasingly common, polypharmacy should be approached cautiously in the pediatric population (Wilens, Spencer, Biederman, & Wozniak, 1995). There are no randomized trials for SSRI augmentation in treatment-resistant pediatric anxiety or depression. Clinical observations have shown improved response of medication-resistant anxiety with the use of more than one psychopharmacologic agent.

Augmentation with Tricyclics

Tricyclics have also been used with SSRIs for treatment-resistant anxiety. This should be done carefully because of the risk of drug–drug interactions. Several of the SSRIs, such as fluvoxamine, may have potent inhibitory effects on the cytochromic p450 metabolism of tricyclics.

An SSRI that blocks the cytochrome p450 metabolism of clomipramine increases the ratio of the substrate clomipramine relative to its metabolite, desmethylclomipramine. Theoretically, this could be of therapeutic value because it makes the substrate more available to act on serotonin receptors. The metabolite, desmethylclomipramine, is the cause of many noradrenergic side effects but does not act on serotonin receptors itself. In adults with treatment-refractory OCD, there have been favorable reports of the use of tricyclics to augment SSRIs (Szegedi, Wetzel, Leal, Hartter, & Hiemke, 1996), although in some cases this resulted in EKG changes. Serum levels as well as EKGs should be followed very closely to avoid the risk of cardiotoxicity. Given the cardiotoxic risks of elevated TCA levels in combination with SSRIs that inhibit their metabolism, this approach should be used only in inpatient settings and as a last resort.

Neuroleptics

In the adult literature, the strongest evidence for augmentation involves the use of neuroleptics, although this is based on relatively few placebo-controlled trials. Most data comes from open-label studies, case reports, and controlled trials suggesting the benefit of using atypical antipsychotics as an augmenting agent in refractory OCD. Typical neuroleptics are not widely used because of concerns about tardive dykinesia and other extra pyramidal side effects (Pollack et al., 2006), although recently there has been revitalized interest in their use due to findings from the CATIE trial that their efficacy and side effect profile may be similar to that of atypical for schizophrenia (Lieberman et al., 2005). In treatment refractory OCD, placebo-controlled studies have shown benefits with the use of haloperidol (McDougle et al., 1994), risperidone (Brawman-Mintzer, Knapp, & Nietert, 2005; McDougle, Epperson, Pelton, Wasylink, & Price, 2000), and quetiapine (Atmaca, Kuloglu, Tezcan, & Gecici, 2002; Simon et al., 2008) in combination with SSRIs. There is little evidence for other treatment-refractory non-OCD anxiety disorders. Several double-blind placebo-controlled trials examine augmentation of SSRIs with neuroleptics in adults with treatment-refractory GAD, utilizing olanzapine (Pollack et al., 2006) and risperidone (Brawman-Mintzer et al., 2005). Another open-label study of quetiapine augmentation of paroxetine CR for adults with treatment-refractory GAD showed negative results (Simon et al., 2008). Likewise, a controlled trial in augmentation with olanzapine in fluoxetine-resistant OCD patients showed that olanzapine addition had no significant advantage over placebo (Shapira et al., 2004). One controlled study examining neuroleptic augmentation of SSRIs for adult PTSD (Stein, Kline, & Matloff, 2002) showed some benefit. The data in the adult literature for neuroleptic augmentation in treatment-refractory anxiety are somewhat limited, but show promise.

The literature examining the use of augmentation of SSRIs in treatment-resistant anxiety in children is sparse. One open-label case series examined the use of risperidone augmentation in four treatment-refractory pediatric OCD patients, and demonstrated a reduction in obsessive–compulsive symptoms. One case report on an adolescent who did not respond to combined CBT and sertraline suggests that aripiprazole augmentation of CBT in adolescent treatment-refractory OCD may be of some benefit (Storch et al, 2007). Additional research is required to determine the efficacy of neuroleptics used to augment SSRIs for pediatric anxiety. The risks of adverse effects in children, including extrapyramidal side effects, weight gain, changes in lipid metabolism, and sedation makes antipsychotic use in children challenging, and a practice that should be exercised conservatively.

Benzodiazepines

The use of benzodiazepines either alone or combined with an SSRI has been suggested only when patients' anxiety symptoms are preventing them from reaching their treatment goals (Masi, 2006). Their use should be approached cautiously

and as a last resort given the mixed results of its efficacy in childhood anxiety disorders (Bernstein et al., 1990; Grae, Milner, Rizzotto, & Klein, 1994; Simeon, Ferguson, Knott, & Roberts, 1992). In addition, there is a risk of dependency (Riddle et al., 1999) and other adverse effects such as sedation and disinhibition. Despite these concerns, there may be some benefit in certain cases from *short-term* use of benzodiazepines.

Other Agents

The use of other adjunctive agents, including NSRIs, buproprion, MAOI's, buspirone, clonidine, and antihypertensives, has not been studied in the pediatric population. Augmentation of SSRIs with NSRIs has been suggested in the use of treatment-refractory anxiety (Bystritsky, 2006), although data to support its use is limited. In adults, augmentation with beta-blockers for SSRI-resistant anxiety has shown mixed results (Hirschmann et al., 2000; Stein, Sareen, Hami, & Chao, 2001). Case reports and case series in the adult population have also shown some possible utility for adjunctive treatment with anticonvulsants such as valproic acid (Ontiveros & Fontaine, 1992), gabapentin (Brannon, Labbate, & Huber, 2000), and tiagabine (Zwanzger et al., 2001). One 8-week open trial examined the efficacy of SSRI augmentation with buspirone for patients with SoP. The data suggested that buspirone augmentation of SSRIs in SoP may be an effective treatment for partial responders to SSRIs alone; however, double-blind controlled trials are needed to assess the efficacy of this treatment of SoP (Van Ameringen, Mancini, & Wilson, 1996). Although potentially promising, without further investigation these data have limited applicability in children.

Treatment Recommendations

Although more research is required, several recommendations can be made for the pediatric patient with medication-resistant anxiety (see Fig. 24.1). First-line treatment includes an SSRI. Second-line treatment involves changing to an alternate SSRI. Third-line treatment might include changing to venlafaxine, or augmenting SSRI treatment with a neuroleptic or tricyclic. Obtaining a second opinion may be useful if third-line treatments are being considered. In the rare case where fourth-line treatment proves necessary, consultation should be sought and all treatment options should be approached cautiously. Possible fourth-line treatments include intravenous clomipramine; SSRI augmentation with venlafaxine, buproprion, benzodiazepine, although more research is required to determine the efficacy of these interventions. Psychotherapy, especially CBT, should be considered at all steps in the treatment process.

Summary

The treatment of medication-resistant pediatric anxiety represents a particular challenge. Generally, when a patient presents with medication-resistant anxiety, the diagnosis should be revisited and the patient should be assessed for any comorbidities. Complicating factors, such as secondary gains for anxious behaviors, family-related factors, or other issues should be assessed. Psychosocial approaches such as cognitive behavior therapies, family therapy, and psychodynamic approaches should be considered. SSRIs are the first-line treatment choice in pediatric anxiety. Therefore, the patient and family should be carefully questioned regarding previous SSRI dose and duration. The reason for previous discontinuation, if applicable, should be explored. If the patient has had a previous trial of adequate dose and duration of an SSRI, or was intolerant to the SSRI, a trial of an alternate SSRI should be considered. As a third choice, venlafaxine or augmentation of an SSRI with a neuroleptic or TCA could be considered. If this fails, obtaining a consultation with an anxiety expert is recommended. Overall, more research is required to better understand the efficacy and safety of the various treatment options of pediatric medication-resistant anxiety.

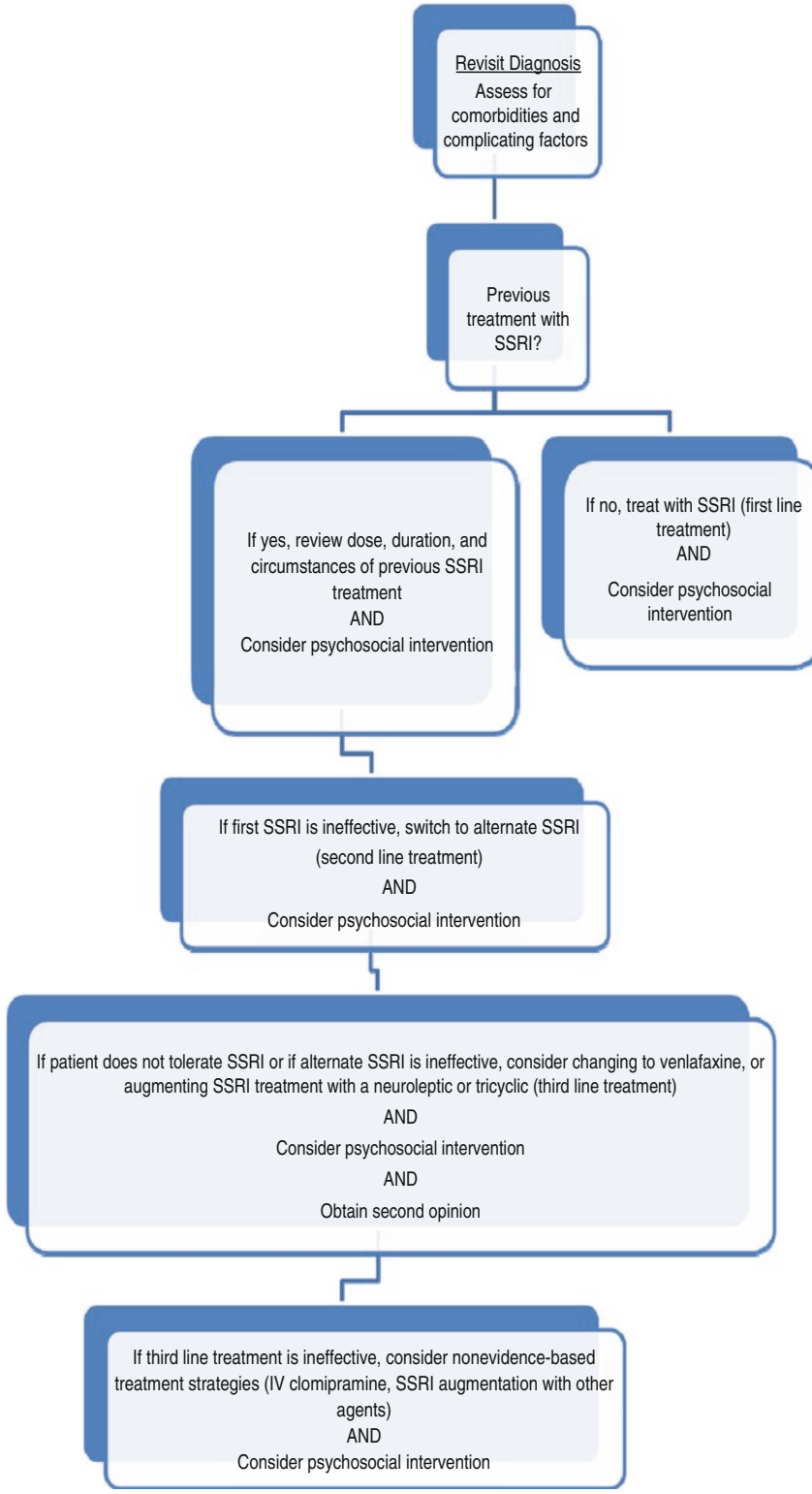

Fig. 24.1 Flowchart of treatment of medication-resistant anxiety disorders

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Psychopharmacological Treatment of Anxiety in Adolescents with Comorbid Substance Abuse

25

Marco A. Grados

Pharmacological treatments of anxiety in adolescents generally follow the same guidelines as that of the treatment of anxiety in adults. To provide a working framework that considers the dual diagnosis of anxiety disorder and substance abuse, a biological perspective on anxiety and substance abuse as conditioned responses with pathophysiologic commonalities is presented. Then, biological commonalities are formulated as an opportunity to consider current and future treatment approaches to adolescents with dual diagnosis.

Phenomenology of Anxiety Disorders and Substance Abuse

Anxiety and substance abuse coexist more frequently than expected by chance in both the general population and clinical samples (Castle, 2008). As that occurs when psychiatric conditions are comorbid, in dual diagnosis patients, it is not always possible, or even heuristic, to determine which disorder is "primary" and which is "secondary." However, the notion that substance abuse is a "secondary" disorder is generally prevalent (Kushner, Sher, & Beitman, 1990). Rather, as will be seen below, common biological pathways may be predisposing patients to both conditions. Often the "primary" disorder is considered as the one that appears first, yet this presentation may develop as a function of environmental exposures or triggers rather than clinical or biological predominance.

From an epidemiologic perspective, approximately one-quarter of the population will have an anxiety disorder or substance-use disorder; however, if either disorder is present then psychiatric comorbidity is common in up to 75% of affected individuals (Kessler et al., 1996). Further, specificity is present for anxiety and substance use disorder comorbidity: if either generalized anxiety disorder or panic disorder is present, then the risk ratio for substance dependence is 3.8, and only slightly lower for social phobia (2.6), specific phobia (2.5), or agoraphobia (2.9). The highest comorbidity is for posttraumatic stress disorder (PTSD), with PTSD patients having a 4.0 excess risk for substance dependence (Regier et al., 1990). Conversely, treatment-seeking samples of substance abuse cohorts have very high rates of diagnosed anxiety disorders. In summary, although it is biologically plausible that substance abuse, including alcohol abuse, may uncover susceptibilities to anxiety disorders as evidenced by experiments showing that alcohol cues activate brain regions associated with negative affect (Feldstein, Filbey, Chandler, & Hutchison 2009), it is also observed that alcohol and substance abuse diminish the threshold for anxiety expression

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_25,

(Feldstein et al., 2009). For example, protein kinase C epsilon, ethanol, and corticotropin releasing factor (CRF) interact to alter GABAergic inhibition in the central and basolateral amygdalar nuclei. Up to 50% of individuals seeking treatment for substance dependence have a comorbid anxiety disorder (Kushner et al., 1990), with implications for treatment as well as recovery. Individuals with comorbid alcohol abuse and anxiety disorders are at higher risk for relapse after alcohol treatment with social phobia predicting any relapse and panic disorder predicting relapse into dependence (Kushner et al., 2005). Other studies have reaffirmed the importance of taking into consideration comorbid depressive and anxiety disorders when treating individuals for substance abuse, with a significant impact on long-term disability (Bovasso, 2001). Further, there is some epidemiologic support for a common "factor" underlying both psychiatric and substance abuse morbidity. In a study of over 5,000 respondents to a questionnaire on depressive, anxiety, alcohol, and drug abuse disorders, there was significant familial aggregation among disorders. That is, if the proband had one of the disorders, then relatives were more likely to have the other disorders even if the relative did not have the original proband disorder (Kendler, Davis, & Kessler, 1997). However, more contemporary evidence is now available to support biologic commonalities among psychiatric and substance abuse disorders as discussed below.

Pathophysiology of Anxiety Disorders and Substance Abuse

Anxiety disorders and substance abuse can be framed in the context of conditioned responses, anxious, or appetitive, respectively, which lack developed emotional regulation mechanisms. Anxiety, an exaggerated fear response, may be conceptualized as a conditioned response, which builds on an inborn reactivity to threatening stimuli, captured under the concept of fear conditioning. Key brain areas underlying fear conditioning include the amygdala and insula. For example, subjects with social and specific phobias and healthy subjects undergoing fear conditioning have consistently shown greater amygdala and insula activity associated with negative emotional responses compared with matched comparison subjects (Etkin & Wager, 2007). Substance abuse, operationalized as drug-seeking behaviors, can also be conceptually framed as a conditioned response or learned behavior. Rat studies support the notion that, as conditioned responses, both anxiety and drug-seeking are subsumed by initiation in prelimbic cortex circuitry and suppression circuitry in infralimbic cortex (Peters, Kalivas, & Quirk, 2009). In this physiologic framework, the infralimbic rat brain region is analogous to human ventral prefrontal cortex (Brodmann Areas 10–13, Brodmann Area 25), which is involved in emotional regulation and ultimately responsible for suppression of conditioned responding (Peters, LaLumiere, & Kalivas, 2008a). Extinction memory, a process that involves the suppression of conditioned responses, serves to regulate the emotional response to learned behaviors. Stimulation of the infralimbic area in rats, both electrophysiologically (Milad & Quirk, 2002) and pharmacologically (Sierra-Mercado, Corcoran, Lebron-Milad, & Quirk 2006), is associated with stronger extinction memory. The same stimulation is now associated with enhanced regulation of emotional responses to learned behaviors, aiding behavioral extinction. For example, in Sierra-Mercado et al. (2006) study, tetrodoxin inactivated the ventromedial prefrontal cortex in rats prior to extinction, which led to impaired recall of extinction the next day. These data suggest that active extinction-related neuroplasticity in targeted brain areas plays a role in fear inhibition. These same areas could then subsume learned behaviors for anxiety conditioning and the inability to regulate emotional responses in drug-seeking behaviors. The amygdala, in particular, is thought to be involved in all stages of fear learning but prefrontal areas are specific to the extinction phase (Delgado, Olsson, & Phelps, 2006). In particular, long-term potentiation (LTP) maintenance in the medial prefrontal cortex is associated with maintenance of extinction learning, preventing a return of a fear response after administration of the conditioned fear-inducing stimulus in mice (Herry &

Garcia, 2002). Using a similar paradigm, it has been proposed that extinction failure in the appetitive domain can lead to relapse in addiction. Studies now show that by using inhibition of selected brain nuclei with GABA agonists, suppression of cocaine-seeking produced by previous extinction training requires activity in the rat infralimbic cortex (Peters et al. 2008b). By activating this same brain region with glutamate-based AMPA receptor stimulation, reinstatement of cocaine drug-seeking was suppressed in these animals (Peters et al., 2008b). As noted earlier, the infralimbic cortex also subsumes extinction learning in anxiety-based paradigms. In contrast to anxiety-based circuitry, in drug addiction, the connection of the infralimbic cortex to the nucleus accumbens (NA) shell plays a critical role. Inhibition of the NA shell can induce cocaine seeking in extinguished rats (Sesack, Deutch, Roth, & Bunney, 1989).

Principles of Treatment of Anxiety Disorders and Substance Abuse

In concert with the parallel pathophysiology of anxiety and substance abuse, based on plausible common biological substrates for conditioned learning, there are similarly possible common approaches to conceptualizing interventions that aim to provoke extinction memory or suppression of conditioned responses in anxiety and drug addiction. The amygdala plays a role in modulating anxiety extinction memory, via the lateral nucleus (LA), the afferent arm of the amygdala receiving input from the cortex and thalamus. The LA dissipates its neuronal firing in cell experiments if the unconditioned stimulus (US), for example, an electric shock following a sound (CS; conditioned stimulus) is no longer delivered after the CS (Quirk, Repa, & LeDoux, 1995). An important goal of clinical intervention in anxiety disorders is to facilitate extinction of fear responses. Any adjuvants to extinction learning would enhance the therapeutic process. Facilitation of neuroplasticity in the amygdala for learning of extinction responses would thus be germane to anxiety treatments (Myers & Davis, 2002). In this vein, the use of d-cycloserine (DCS), a partial glutamate agonist, has been used to facilitate extinction learning and has proven to even prevent learned fear after reinstatement of the UCS (Ledgerwood, Richardson, & Cranney, 2004). It is of interest that DCS has been effective when used acutely shortly before (Walker, Ressler, Lu, & Davis, 2002) or immediately after (Ledgerwood, Richardson, & Cranney, 2005) extinction sessions; more chronic use of DCS can have a blunting effect on the beneficial effects of immediate DCS (Quartermain, Mower, Rafferty, Herting, & Lanthorn, 1994).

The management of stress, in turn, has been linked to improving outcomes in relapse prevention in substance abuse (Goeders, 2003). A physiologic connection has been made between exposure to stress, modifications of the HPA axis and abstinence cravings. In animals, exposure to electric footshock increases subsequent reinforcing efficacy of heroin (Shaham & Stewart, 1994) and morphine (Will, Watkins, & Maier, 1998). Thus, it is not surprising that the acquisition of amphetamine and cocaine self-administration is enhanced in rats exposed to tail pinch (Piazza, Deminiere, le Moal, & Simon, 1990), social defeat (Kabbaj et al., 2001), or neonatal isolation (Kosten, Miserendino, & Kehoe, 2000), all stress-inducing environmental conditions. By activating the hypothalamic-pituitary-adrenal (HPA) axis, it is plausible that anxiety disorders generate a persistent internal milieu that is analogous to the effects of outward adverse environmental stressors. Additionally, anxiety disorders precipitated by environmental stressors may similarly mediate the effects of the adverse environment and perpetuate its effect. In both cases, environmental stressors, anxiety disorders, and substance abuse serve to self-perpetuate a cycle of relapse and barriers to effective treatment. Given that childhood anxiety disorders are precursors to later mental health vulnerabilities, early intervention in anxiety disorders could plausibly address a critical link in the longitudinal acquisition of comorbid conditions in different environmental contexts.

Given the plausible etiological connections between stress, anxiety, and substance abuse, it is not surprising that, in particular, PTSD has been

associated with substance abuse. Psychopathologically, PTSD is a multidetermined event, mediated by the environmental exposure in vulnerable individuals. Females with a history of affective disorders are at higher risk for PTSD, while males with a history of anxiety disorders are similarly at higher risk (Bromet, Sonnega, & Kessler, 1998). In turn, individuals who are engaged in substance abuse are at increased risk for exposure to trauma (Cottler, Compton, Mager, Spitznagel, & Janca 1992). In this complex interaction among anxiety, PTSD, substance abuse, and exposure to trauma, it appears that anxiety disorders mostly precede PTSD but that subsequent occurrence of PTSD or multiple traumas does not increase the occurrence of other anxiety disorders; therefore, non-PTSD anxiety disorders appear to act primarily as predisposing factors for both PTSD and substance abuse. In a comprehensive study of 1,420 children followed longitudinally, traumatic events were fairly common and did not frequently result in PTSD; however, multiple traumas or prior anxiety disorders were associated with PTSD development (Copeland, Keeler, Angold, & Costello, 2007). In another study of 1,140 children in South Africa, a clear relationship was found between cumulative trauma and incidence of PTSD symptoms and depression but not of anxiety disorders (Suliman et al., 2009). In particular, the subgroup of children who are poly-victimized (Finkelhor, Ormrod, & Turner, 2009) are thus at high risk for both PTSD and substance abuse. Childhood abuse is associated with a persistent sensitization of the HPA axis in adulthood, and in children, a similar sensitization has been detected in social anxiety patients with a history of childhood abuse (Elzinga, Spinhoven, Berretty, de Jong, & Roelofs, 2009).

In light of the plausible influence of pediatric anxiety disorders on the development of substance abuse, an epidemiologic perspective would strongly support the early treatment of anxiety, especially in vulnerable children (i.e., positive family of substance abuse, exposure to trauma). Although much research is sorely needed to establish reciprocal etiological pathways between anxiety disorders and substance abuse, there is sufficient evidence to recommend the early detection and treatment of anxiety in childhood as a component of a general strategy to prevent distal substance abuse, depression, and PTSD outcomes. In particular, it is known that early life anxiety disorders predispose to adult anxiety disorders (Kim-Cohen et al., 2003), which are in turn highly comorbid with alcohol abuse (Saraceno, Munafo, Heron, Craddock, & van den Bree, 2009).

Pharmacology in Anxiety Disorders and Substance Abuse: Current and Novel Approaches

Although psychosocial treatments for substance abuse are a primary intervention to break the cycle of drug use and drug seeking, the current focus will be on the *phamarcological* treatment of anxiety disorders in the context of substance abuse in adolescents. Most trials of antianxiety agents do not include individuals with substance abuse, as this is almost universally an exclusion criterion in efficacy trials. Therefore, informed but empirical clinical decision-making needs to guide treatment approaches, given the paucity of controlled data in dual diagnosis populations, especially adolescents. In adults, alcohol-related depression has shown a good response to SSRI treatment (Lejoyeux, 1996). And in general, given the wide spectrum of anxiety disorders that respond to SSRIs, this medication class remains the treatment of choice for anxiety in the context of comorbidity, including substance abuse (Dunner, 2001). As evidenced by studies in adults, SSRIs can also be helpful in the context of alcoholism comorbid with PTSD (Brady, Sonne, & Roberts, 1995) as well as social anxiety (Randall et al., 2001). SSRIs are also generally safe in the context of medical complications from substance abuse, such as liver dysfunction (see Table 25.1).

Buspirone (Buspar) has been used to control anxiety symptoms in alcohol abuse with reduced anxiety and drinking associated with its use (Kranzler et al., 1994). A similar positive experience was obtained with the use of buspirone in methadone patients (McRae, Sonne, Brady, Durkalski, & Palesch, 2004). By extension, these

Table 25.1 Sample pharmacologic approaches to treatment of comorbid anxiety and substance abuse

Drug	Use	Side effects	Comments
Conventional pharmacological approaches			
SSRIs[a] (Fluoxetine 20–40 mg/day or equivalent; single dose)	Ethanol abuse Drug abuse	Insomnia, headaches, GI upset, sexual dysfunction	Broad spectrum use for anxiety and depressive disorders associated with dual diagnosis
Buspirone (Buspar) (15–60 mg/day; divided doses)	Ethanol abuse or opioid abuse	Dizziness, nausea, headache, nervousness, lightheadedness	Anxiolytic properties useful in ethanol/opioid abuse
Novel pharmacological approaches			
Gabapentin (Neurontin) (300–1,800 mg/day; divided doses)	Ethanol abuse Cocaine abuse	Back pain; diplopia or blurry vision; clumsiness; constipation; diarrhea; dizziness; drowsiness; dry mouth; nausea; stomach upset; tiredness; vomiting; weight gain	Animal studies suggest specific effect in ethanol-dependence; may also decrease withdrawal-associated anxiety from ethanol and cocaine
N-acetylcysteine (200–1,200 mg/day)	Cocaine abuse	Nausea, vomiting, headache, rash, dry mouth, dizziness, or abdominal pain (cramps, diarrhea), depletion heavy metals and vitamins	Pretreatment with *N*-acetylcysteine prevents cocaine-induced changes in nucleus accumbens

[a]Selective serotonin reuptake inhibitors: fluoxetine (Prozac); sertraline (Zoloft); fluvoxamine (Luvox); escitalopram (Lexapro); citalopram (Celexa); paroxetine (Paxil)

approaches may be reasonable in adolescent populations that require pharmacological management of anxiety disorders in the context of alcohol abuse or opioid dependence.

Novel approaches to the pharmacologic treatment of drug dependence focus on reducing cravings for the drug, making use of glutamate-GABA brain homeostasis modulation. Gabapentin (Neurontin), a nonbenzodiazepine anticonvulsant GABA analog, modulates transmission in the central amygdala (CeA) via GABA-B receptors (Roberto et al., 2008). Ethanol also modulates GABAergic transmission in the pre and postsynapse in the CeA, but apparently via GABA-A receptors (Roberto, Madamba, Moore, Tallent, & Siggins, 2003). More importantly, when ethanol-dependent rats, which developed an increase in baseline GABA transmission, were administered gabapentin, excess GABA transmission was attenuated. Gabapentin produced a different effect in nondependent rats (i.e., an increase in GABA transmission) (Roberto et al., 2008). Thus, gabapentin may have a specific use in the context of ethanol dependence separate from that in nondual diagnosis patient. Further, in experimental animals, anxiety-related withdrawal was attenuated with gapabentin, which suggests that relief of anxiety via GABA mechanisms may attenuate alcohol consumption. Gabapentin is thus a promising drug for treating alcohol abuse via its anxiolytic properties (Clemens & Vendruscolo, 2008). Earlier, gabapentin had been used to treat cocaine craving in 30 cocaine-dependent subjects. In an 8-week, open-label trial of 1,200 mg/day of gabapentin, there was a very significant reduction in craving and use of cocaine in the treated group (Myrick, Henderson, Brady, & Malcolm, 2001).

Future approaches to the treatment of anxiety may focus on the modulation of glutamate NMDA receptors. In this context, drugs that are NMDA receptor antagonists will block, and drugs that are NMDA receptor agonists will facilitate extinction and reconsolidation of fear memories. CNS glutamate modulators are glycine and d-serine (agonists), felbamate (antagonist), d-cycloserine (partial agonist). Ketamine, amantadine, memantine, and dextrometorphan are glutamate ion channel blocker antagonists; however, multiple other effects of each of these drugs on various receptors make them a very heterogeneous drug category. Studies are underway to test the promise for this novel approach in anxiety disorders, which affects learning rather than fear mechanisms

directly (Amaral & Roesler, 2008). Glutamate homeostasis is proposed to play a role in addictions, manifesting as a failure of the prefrontal brain areas to control drug-seeking behaviors, leading to proposed glutamate-based therapies for addiction treatment (Kalivas, 2009). For example, *N*-acetylcysteine could activate the cystine–glutamate exchange by restoring nonsynaptic glutamate release and the ability to induce neuronal LTP and long-term depression (LTD): this process can enhance extinction learning and decrease drug-cravings in the case of cocaine (Madayag et al., 2007).

Conclusions and Future Directions

At present, based on sound clinical judgment, empirical treatments will need to guide the pharmacological management of anxiety comorbid with substance abuse given the notable dearth of controlled trials in dual diagnosis clinical populations. Hopefully, as effectiveness studies get underway with a renewed interest and support of funding agencies for "real world" outcomes, more data will be available to direct clinician interventions in this challenging group of patients. As discussed earlier, pathophysiologic studies provide initial evidence for putative common mechanisms for anxiety and substance abuse disorders. If these observations are supported by future research, there will be a notable opportunity to develop pharmacological treatments that take advantage of shared biological mechanisms, mostly focused on the CNS glutamate-GABA homeostatic system.

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Combined Psychological and Pharmacological Treatment of Pediatric Anxiety Disorders

26

Hunna J. Watson

Combined Psychological and Pharmacological Treatment of Pediatric Anxiety Disorders

The identification of efficacious psychological and psychiatric therapies is arguably one of the most significant achievements in the pediatric anxiety disorders field. Controlled trials have supported the usefulness of psychological and pharmacological monotherapies for pediatric obsessive–compulsive disorder, social anxiety disorder, panic disorder, agoraphobia, generalized anxiety disorder, specific phobia, posttraumatic stress disorder, and separation anxiety disorder (Compton et al., 2004; Feeney, Foa, Treadwell, & March, 2004; In-Albon & Schneider, 2007; Reinblatt & Riddle, 2007; Seidel & Walkup, 2006; Watson & Rees, 2008). Clinical practice guidelines, developed from a synthesis of research evidence and expert opinion, have recommended cognitive-behavioral therapy (CBT) as the first line psychotherapy and treatment of choice (American Academy of Child and Adolescent Psychiatry (AACAP), 2007; Canadian Psychiatric Association (CPA), 2006). The selective serotonin reuptake inhibitors (SSRIs) are the recommended first-line pharmacological agents for pediatric anxiety disorders. Second or third-line pharmacotherapy alternatives include noradrenergic antidepressants (tricyclic antidepressants (TCAs), venlafaxine), benzodiazepines, and buspirone.

Despite the significant progress that has been made in identifying efficacious interventions, there is no "holy grail" of pediatric anxiety treatment. A systematic review of CBT reported that the average remission rate at treatment completion was 56% for CBT-treated youth and 35% for controls (Cartwright-Hatton, Roberts, Chitsabesan, Fothergill, & Harrington, 2004). The remission rate for pharmacotherapy is less clear given the relative dearth of controlled studies, but appears to be equal to or less than that of CBT, particularly in the case of pediatric obsessive–compulsive disorder. In a randomized controlled trial (RCT) among youth with generalized anxiety disorder, social anxiety disorder, or separation anxiety disorder, approximately three-fifths of youth receiving monotherapy CBT or sertraline achieved global improvement in symptoms (Walkup et al., 2008). A RCT among youth with obsessive–compulsive disorder indicated that 39% of youth treated with CBT achieved remission at endpoint, compared with 21% treated with the SSRI

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_26, © Springer Science+Business Media, LLC 2011

sertraline and 4% that received placebo (Pediatric OCD Treatment Study Team (POTS), 2004). In another RCT for pediatric obsessive–compulsive disorder, 67% of those treated with CBT were classed as responders at posttreatment compared with 50% treated with the TCA clomipramine (de Haan, Hoogduin, Buitelaar, & Keijsers, 1998). Clearly, a significant proportion of youth treated with CBT or pharmacological monotherapy do not improve or remit within a reasonable time-frame.

Given that psychiatric conditions are caused and maintained by a complex interaction of biological, psychological, and sociocultural factors, it is not surprising that researchers and clinicians have sought to treat pediatric anxiety disorders with an armory of treatment approaches. Published reports indicate that a wide variety of treatment combinations have been utilized to manage pediatric anxiety. CBT programs have been combined with SSRIs, TCAs, atypical antipsychotics, atypical neuroleptics, and parent/family anxiety management training (e.g., Barrett, Dadds, & Rapee, 1996; Barrett, 1998; Bernstein et al., 2000; Cobham, Dadds, & Spence, 1998; Eisen, Raleigh, & Neuhoff, 2008; Neziroglu, Yaryura-Tobias, Walz, & McKay, 2000; POTS, 2004; Storch, Lehmkuhl, Geffken, Touchton, & Murphy, 2008; Walkup et al., 2008). SSRI treatment has been combined with benzodiazepines, anxiolytics, atypical antipsychotics, and buspirone (e.g., Alessi & Bos, 1991; Leonard et al., 1994; Storch, Lehmkuhl, et al., 2008; Thomsen & Mikkelson, 1999). TCAs have been combined with benzodiazepines (e.g., Ballenger, Carek, Steele, & Cornish-McTighe, 1989) and benzodiazepines have been combined with mood stabilizers (e.g., Wilens, Spencer, Biederman, Wozniak, & Connor, 1995).

Despite few efficacy studies of combined treatment, data from naturalistic settings suggest that a high proportion of children with anxiety problems access a combination of psychotherapeutic and pharmacological interventions (Bernstein, Hektner, Borchardt, & McMillan, 2001). Moreover, clinical practice guidelines endorse a combined treatment approach as a treatment strategy (AACAP, 1998, 2007), but provide only tenuous guidance as to whom this approach might benefit, the degree of benefit to be expected, and other relevant issues. Assumedly, the availability of a combined approach is proliferating as the number of evidence-based monotherapies grows, treatment protocols become published, and practitioners become trained or increasingly skilled in treatment methods. Evidently, the interest in a combined treatment approach, coupled with the lack of understanding about the utility or applicability of this treatment strategy, suggest that this is a salient and topical subject matter that would benefit from a detailed consideration.

What is Combined Treatment?

By definition, "combined treatment" refers to the use of two or more treatments, administered concurrently or sequentially, to treat a particular indication, whereby each treatment comprises an effective stand-alone treatment. In some instances, both of the interventions are considered central to the treatment strategy; in others, one treatment may be viewed as central and another as adjunctive. The term "combined treatment" is not usually inclusive of occasions in which the same treatment modality is combined. For instance, the use of CBT in combination with a TCA constitutes an instance of combined treatment, whereas the concurrent use of two TCAs does not. In recent clinical and research literature, combined treatment is interchangeably referred to as "multimodal treatment".

Should Treatment Approaches be Combined?

To have an informed perspective of combined treatment for pediatric anxiety disorders, it is essential to be aware of the rationales that have been presented in favor of and in opposition to a combined treatment approach for this specific population. Various rationales will be presented in the following sections, informed by the extant literature. The rationales that are introduced are grounded in large part in theoretical and clinical

reasoning or adult research, rather than firm empirical evidence from pediatric samples, because of the inchoate nature of this avenue of investigation.

First and foremost, clinicians seeking to implement treatment for pediatric anxiety disorders are advised to consult existing clinical practice guidelines (AACAP, 2007; CPA, 2006).

What is the Rationale for Combining Treatments?

Generally-speaking, monotherapeutic treatment applications can be differentiated according to whether they stem from a biological or psychological theoretical explanatory model. A biological model has predominantly underpinned pharmacological interventions, while psychological models have informed psychotherapeutic treatments. Yet, it is *both* biological and psychological mechanisms that underlie anxiety disorder etiology and maintenance, and not one specific set operating in isolation. Studies of fear and anxiety in animal and human samples have provided evidence for dysregulation in the serotonergic, dopaminergic, and GABA-ergic neurotransmission systems; and open and controlled trials of serotonergic and noradrenergic pharmacotherapies have provided indirect support for neurobiological mediators of pathological anxiety (Sallee & March, 2000). Cognitive and behavioral models, which describe how aberrant cognitive processing of threat-related information and the use of escape and avoidance behaviors perpetuate anxiety, have likewise garnered empirical support. By conjecture, a combined treatment approach could confer a superior treatment effect by activating a wider variety of anxiety-modulating mechanisms. Potentially, this effect could be additive, in that the benefit equates to the sum of the effects of the individual treatments, or synergistic, in that the combination produces an even greater effect. A synergistic effect could occur if the treatment combination targets complementary mechanisms that interact. For instance, pharmacotherapy may more selectively target somatic symptoms and CBT may more readily target cognitive and behavioral symptoms. Together, these mechanisms may interact to produce a benefit that is greater than the sum of each treatment administered singly.

A second rationale for combining active treatments concerns the finding that children with a primary anxiety diagnosis have a high rate of comorbidity, most commonly mood and other anxiety disorders (Bernstein, Borchardt, & Perwien, 1996). It is important to consider comorbidity in the overall treatment strategy, because comorbidity can potentially attenuate treatment response during the acute treatment phase. For instance, depression is known to negatively impact upon essential prerequisites for psychotherapeutic interventions, such as motivation, memory functioning, and cognitive performance (Mohanty & Heller, 2002). Presumably, a combined treatment approach could benefit related psychopathology (i.e., anxiety, depression) to a greater extent than a monotherapeutic approach, because of the likely enhanced potency afforded through the greater array of biological and psychological mechanisms targeted. The assumption that comorbidity attenuates treatment response has not garnered much empirical investigation among youth with anxiety disorders. With respect to comorbid internalizing diagnoses or symptomatology, four studies have reported that comorbidity does not impair response to CBT (Kendall et al., 1997; Kendall, Brady, & Verduin, 2001; Rapee, 2003; Storch, Merlo, et al., 2008). Conversely, one of these studies found that major depressive disorder, but not the internalizing diagnoses of generalized anxiety disorder, social anxiety disorder, and panic disorder, was associated with a significantly lower remission rate at posttreatment (Storch, Merlo, et al., 2008). In the adult anxiety field, more research has been conducted, with some studies supporting (e.g., Hansen, Vogel, Stiles, & Götestam, 2007; van Balkom et al., 2008) and others failing to support (e.g., Joormann, Kosfelder, & Schulte, 2005; Marom, Gilboa-Schechtman, Aderka, Weizman & Hermesh, 2009; Kampman, Keijers, Hoogduin, & Hendriks, 2008; Lesser et al., 1988) an impact of comorbid anxiety or depression on CBT or pharmacotherapy outcome. Mixed findings have

occurred even among studies that have addressed the same primary diagnosis. At present, the relationship between comorbidity and treatment outcome is unclear, yet clinical lore suggests the potential for comorbidity to negatively impact upon treatment response. Ultimately, greater improvement in comorbidity during the acute phase of combined treatment may confer a greater treatment response for symptomatology specific to the primary diagnosis.

There is evidence to show that comorbidity severity is differentially related to relapse and maintenance of treatment gains for the primary anxiety diagnosis. This may be another reason why practitioners might consider using a combined treatment approach among patients with comorbidity. Marom and colleagues (2009) reported that adults with social anxiety disorder with or without comorbid major depressive disorder demonstrated an equivalent response to CBT at posttreatment; however, notable differences in outcome occurred at 1-year follow-up in favor of the patients without comorbidity. The patients who had a diagnosis of major depressive disorder at intake experienced an exacerbation of symptoms at follow-up, whereas those who had not been diagnosed with major depressive disorder maintained their gains. Although there is some evidence from adult research that monotherapy alone can help with both primary and comorbid diagnostic treatment response to a clinically significant degree (Marom et al., 2009; Tsao, Lewin, & Craske, 1998), some research has suggested that this may not always occur. Depression severity may remain high even after CBT monotherapy has effectively reduced anxiety disorder symptomatology (Joormann et al., 2005). A fruitful avenue for future research would be to conduct post-hoc analyses on adult or child RCT data to determine the relative impact of monotherapy and combined treatment on diagnostic and symptomatology comorbidity, and the impact of comorbid diagnoses or symptomatology on remission rates after acute treatment and on relapse rates at follow-up.

Although CBT is generally regarded as the first-line treatment approach for pediatric anxiety disorders, CBT has a notably slower onset of action compared with that of pharmacological agents. Rapid symptom relief may be required in instances where the anxiety disorder is associated with a great deal of functional impairment, for social and environmental reasons, or when the symptoms are impacting upon the child's physical safety. For example, a child with separation anxiety disorder may initiate school refusal, which may not only impair academic learning, but also presents a significant management issue for a working parent who for financial or employer-related reasons is unable to take work leave. On rare occasions, a child with severe obsessive–compulsive disorder characterized by contamination concerns may present with a refusal to eat. In these and other circumstances, it may be desirable and necessary to augment CBT with a pharmacological agent to accelerate treatment response. Combination therapy for pediatric anxiety disorders appears to produce a faster rate of improvement during the acute treatment phase compared with monotherapy with CBT or pharmacotherapy (Walkup et al., 2008).

A patient with a debilitating level of anxiety may be unwilling to engage in exposure therapy or even psychotherapy more generally. For this particular subset of patients, even the demands of attending the physical location of a treatment service may offset a genuine desire to obtain help. Consider the case of a young girl with obsessive–compulsive disorder, whose mother inquired about enrolling her in a group CBT program. The girl's severe anxiety and contamination concerns had become increasingly debilitating, to the point where she was largely home-bound. She refused to use bathrooms outside her home, and was managing only small trips away from her home with the aid of an apparatus to urinate in, a behavior that was associated with feelings of embarrassment and shame. The mother reported that she had discussed the program with her daughter, and although her daughter desired to obtain help, the daughter reported that it would be too distressing for her to be away from home for the time it would take to attend the treatment center. In some cases, sequencing and augmenting antidepressant or anxiolytic medication may be imperative to enable a patient to initiate psychotherapy.

Some patients encounter intolerable anxiety and emotional discomfort during exposure tasks, which can translate into an unwillingness to engage in therapy. This may occur even when the best-intentioned therapist has devised a graded exposure plan with gentle lower-hierarchy exercises. Adjunctive treatment with benzodiazepines or other pharmacotherapy may reduce somatic arousal sufficiently to facilitate confrontation of anxiety-provoking stimuli (Hafner & Marks, 1976; Marks, Viswanathan, Lipsedge, & Gardner, 1972).

Earlier it was stated that depressive symptoms frequently cooccur with pediatric anxiety disorders (Seligman & Ollendick, 1998). There has been a justifiable degree of concern over claims that pharmacological agents increase the risk of treatment-emergent suicidal ideation and attempts in young people with depression. On the basis of data from the Treatment of Adolescent Depression Study (TADS; Emslie et al., 2006; March et al., 2004), Compton and colleagues (2007) suggested that in instances where pharmacological treatment is indicated it may be beneficial to combine pharmacological treatment with CBT to reduce risk. Although a heightened risk for treatment-emergent suicide-related events with pharmacological monotherapy has not been observed in two large-scale multicentre RCTs for pediatric anxiety disorders (Walkup et al., 2008; POTS, 2004), there is presently insufficient data to fully investigate this issue. The very low base-rate of treatment-emergent suicide-related events significantly impairs the statistical power required for comparisons (Tsang, Colley, & Lynd, 2009). Despite this, many youth with anxiety disorders present with depression comorbidity (Seligman & Ollendick, 1998).

Another rationale for combining CBT and pharmacotherapy might relate to capitalizing on particular individual strengths of each treatment approach and mitigating relative weaknesses. In terms of relative strengths, CBT is generally considered to be more effective, treatment may enhance self-efficacy for symptom management, and gains are more likely to be maintained after treatment completion. Pharmacotherapy has a faster onset of action, is more widely available, can be administered in primary care settings, and time to treatment commencement is usually shorter. Relative weaknesses of CBT are that exposure procedures can evoke discomfort and a minimum threshold of anxiety tolerance is required to enable participation, while a weakness of pharmacological treatment is that it is associated with a higher risk of relapse upon completion (i.e., medication withdrawal). Combining the treatment approaches may garner particular benefits not afforded by monotherapy and may extenuate the weaknesses of each approach.

Finally, it is worth noting that neither treatment alone is sufficient to achieve remission in all cases, and combining treatment modalities may potentially represent another means with which to optimize treatment response and recovery.

What is the Rationale for not Combining Treatments?

There has been discussion around the potential pitfalls that may be associated with combining CBT and pharmacotherapy in anxiety disorder treatment (e.g., Westra, Stewart, & Conrad, 2002). These have been elucidated more fully in work produced within the adult anxiety disorder field, where it has been proposed that medication augmentation can disrupt the effectiveness of CBT.

The combined treatment approach that has incited the most debate is the augmentation of CBT with benzodiazepine treatment. Outcomes from adult treatment trials examining combined CBT and benzodiazepines have yielded mixed findings. Marks et al. (1993) found that the risk of relapse among a large sample of patients with panic disorder was significantly increased among those treated with time-limited CBT and benzodiazepines compared with those who received CBT alone. Other studies among patients with panic disorder and agoraphobia without panic have confirmed more positive outcomes after CBT among non-benzodiazepine-treated patients compared with benzodiazepine-treated patients (Echeburua, De Corral, Garcia Bajos, & Borda, 1993; Otto, Pollack, & Sabatino, 1996; Westra et al., 2002). Alternatively, some studies have indicated that CBT combined with benzodiazepines

yields clinical benefit (Johnston & Gath, 1973; Marks et al., 1972; Riley et al., 1995).

CBT is an empirically-supported treatment of choice for many childhood anxiety disorders, and exposure therapy is a key component of CBT (Albano & Kendall, 2002). A central feature of exposure therapy is that anxiety must be sufficiently elevated to facilitate habituation to anxiety-provoking stimuli and to provide opportunities for adaptive cognitive reprocessing. Anxiolytic agents, particularly benzodiazepines, may reduce the degree of somatic and physiological arousal during exposure tasks (Riley et al., 1995), which could possibly translate to a reduced response to exposure-based treatment.

Benzodiazepines may interfere with learning and memory recall and therefore may not be a suitable augmentation strategy for CBT. Findings from animal research have suggested that learning achieved in one particular environmental or interoceptive context may not generalize to other distinct contexts, a phenomenon known as "state-dependent learning" (Otto, Smits, & Reese, 2005). If during combined treatment the medication-induced state operates as a context for learning, coding, and retrieving information, then discontinuation of medication could "undo" helpful cognitive changes brought about by CBT and strengthen preexisting catastrophic cognitions (Westra & Stewart, 1998). State-dependent learning effects have been documented in several studies of benzodiazepines and learning and recall (Jensen, Hutchings, & Poulsen, 1989). Benzodiazepines act on the same receptor sites as alcohol, a known context for state-dependent learning effects (Knight & Longmore, 1994). Recently, Morisette, Spiegel, and Barlow (2008) conducted a within-subjects experimental study to determine whether concurrent benzodiazepine use attenuated exposure benefit as a function of state-dependent learning effects. Four social anxiety disorder subjects were observed in four treatment conditions of benzodiazepine, beta-blocker, pill placebo, or no-pill. Subjects rated their subjective units of distress (SUDs) during exposure exercises on three occasions within each treatment condition: at baseline, after pill ingestion, and absorption (or the equivalent time frame for the no-pill condition), and after a 48-hour drug washout. During the benzodiazepine condition, two patients' SUDs ratings increased after benzodiazepine withdrawal and plateaued for the other two patients, indicating that state-dependent learning effects attenuated exposure gains. During pill placebo and no pill conditions, SUDs continued to decrease from the second to the third exposure sessions. In the beta-blocker condition, negligible changes in SUDs ratings occurred between the second and third exposure sessions for three patients and one patient experienced a small decrease. Although the study was based on a very small sample, the findings indicate that benzodiazepines may interfere with CBT treatment, though the effect appears to be inconsistent.

An aim of CBT is to remediate unhelpful cognitive processing biases that perpetuate anxiety, such as the fear of anxiety-related internal physical sensations and environmental stimuli and, more broadly, the appraisal of ambiguous stimuli as threatening and dangerous (Barlow, 2002; Beck, Emery & Greenberg, 1985). Benzodiazepines, when used concurrently with CBT, may increase selective attention to threat cues and reinforce the belief that anxiety-related stimuli are dangerous (Stewart, Westra, Thompson, & Conrad, 2000). Hypervigilance to internal sensations and the processing of ambiguous information in a threat-related manner are core maintaining mechanisms in cognitive accounts of anxiety, and they are also targets of treatment in CBT for anxiety disorders (Barlow, 2002). Presumably, interference arising through benzodiazepine use would most likely affect those on a PRN ("as needed") dosing schedule. These individuals may rely on internal sensations or situational anxiogenic stimuli as cues to self-dispense medication, thereby strengthening anxiety-maintaining cognitive schemata, such as the belief that these stimuli are dangerous and that they must be avoided at all costs (Stewart et al., 2000). The adjunctive use of benzodiazepine treatment may inhibit improvement in fear of anxiety-related symptoms. Westra et al. (2002) found that PRN benzodiazepine use over the course of CBT for panic disorder with agoraphobia was associated with a smaller change in fear of anxiety-related symptoms, such as somatic sensations and cognitive dyscontrol, relative to

unmedicated and regular benzodiazepine users. This occurrence is problematic because this construct of "fear of fear" has been shown empirically to be a mechanism of change in CBT for panic disorder (Smits, Powers, Cho, & Telch, 2004). Interestingly, this same effect emerged in a RCT that involved benzodiazepine augmentation of SSRI, rather than CBT, treatment (Simon et al., 2004). The rate of improvement in fear of anxiety-related symptoms among adults with panic disorder was lower for those who remained on benzodiazepines throughout SSRI treatment, in comparison with those who underwent benzodiazepine tapering or who received placebo treatment. Studies have reported that benzodiazepines may have no effect on unhelpful cognitive biases related to threat processing (e.g., Golombok et al., 1991) and others have found that they may actually worsen these biases (e.g., Stewart et al., 2000), suggesting the potential for benzodiazepine treatment to interfere with CBT treatment procedures. A controlled study among patients with generalized anxiety disorder suggested that SSRI treatment does not increase selective attention to threat or worsen unhelpful cognitive processing biases (Mogg, Baldwin, Brodrick, & Bradley, 2004). In fact, this study showed that treatment with SSRI monotherapy improved subjects' ability to interpret ambiguous stimuli in a non-threat related manner.

There are additional potential problems associated with using benzodiazepines as an augmenting strategy for youth with anxiety disorders. First, the evidence for clinical benefit of benzodiazepines alone or in combination is lacking. Although benzodiazepines have been recommended as an adjunctive short-term treatment with SSRIs (AACAP, 2007), this recommendation is mainly derived from the findings of particular adult treatment trials that have shown that use can be associated with clinically significant benefit (Labellarte, Ginsburg, Walkup, & Riddle, 1999). In pediatric samples, small-sample placebo-controlled trials have not discerned an efficacious treatment effect for patients with generalized anxiety disorder, avoidant disorder (i.e., social anxiety disorder), separation anxiety disorder, and school refusal with anxiety (Bernstein, Garfinkel, & Borchardt, 1990; Graae, Milner, Rizzotto, & Klein, 1994; Simeon et al., 1992). Second, benzodiazepine use is accompanied by a risk of tolerance, dependence, and abuse, and therefore, is contraindicated for youth with a personal or family history of drug abuse (AACAP, 2007).

Patients undergoing CBT who use concurrent anti-anxiety medication may attribute their symptom improvement to the medication and deny contribution of their own actions. This may undermine the development of self-efficacy to manage anxiety symptoms and it may encourage an external, rather than an internal, locus of control, which may heighten risk of relapse following acute treatment. Self-efficacy, generally-speaking, is more greatly enhanced in CBT or CBT-augmented interventions compared with medication monotherapy or placebo and predicts outcome in CBT for anxiety disorders (e.g., Casey, Newcombe, and Oei, 2005; Gaudiano & Herbert, 2007; O'Connor et al., 2006). In a controlled trial among adults who were treated with CBT in combination with the benzodiazepine alprazolam or placebo, patients who attributed improvement to medication were more likely to relapse, conversely, patients who attributed improvement to personal effort and internal factors were better able to maintain their gains (Başoğlu, Marks, Killiç, Brewin, & Swinson, 1994). Medication alone or in combination with CBT may interfere with the development of self-efficacy for symptom management, which may constitute a mediator of symptom change.

Medication may interfere with CBT for anxiety disorders by becoming a "safety aid" to the patient, in that patients may become prone to attributing safety and anxiety reduction to the medication. This is particularly likely if the patient is using the medication on a PRN schedule (common with benzodiazepine use), and the medication is taken in anticipation of or in response to anxiogenic stimuli or internal sensations. Safety-behavior utilization is theorized to be a critical maintaining mechanism of anxiety disorders (Salkovskis, 1991). Medication as "safety aid" can prevent disconfirmation of maladaptive interpretive biases that maintain anxiety, a core mechanism of change in cognitive-behavioral

interventions. The use of medication in response to anxiogenic stimuli or internal sensations reaffirms these stimuli as dangerous, directly contradicting CBT treatment objectives. For instance, exposure for panic disorder involves intentional exposure to anxiety-related physical and somatic sensations and is designed to teach patients not to fear these sensations. Removing the opportunity to engage in adaptive cognitive processing and habituation may potentially weaken the impact of cognitive-behavioral interventions. In support of this premise, one study showed that exposure plus reduced safety behaviors was superior to exposure without reduced safety behaviors in reducing within-situation anxiety and anxiety-perpetuating cognitions (Wells et al., 1995). A placebo-controlled study suggested that it is the perceived availability of safety aids, with or without actual use of these aids, which detracts from exposure therapy (Powers, Smits, & Telch, 2004). Medication may potentially interfere with CBT by becoming a "safety aid," which can reinforce neutral ambiguous stimuli as dangerous and circumvent therapeutic cognitive change.

Concurrent pharmacotherapy may result in a relatively rapid improvement in anxiety symptomatology, which may reduce patient and family motivation to engage in and comply with CBT procedures. Child-related distress and functional impairment from anxiety symptomatology often enhances patient motivation to engage in CBT. Likewise, family-related impairment in functioning may enhance parental motivation to support CBT, tangibly (e.g., transporting child to appointments, treatment costs) and therapeutically (e.g., encouraging completion of homework exercises, participation in family-based protocols). Given that CBT is usually associated with a more efficacious treatment outcome at posttreatment and follow-up compared with medication monotherapy, it may be that concurrent treatment could endanger outcome if an early impact of medication reduced motivation to participate in CBT.

Treatment with CBT and concurrent pharmacotherapy invites greater risk compared with treatment with CBT alone, which is the existing treatment of choice. Pharmacotherapy is typically accompanied by mild to clinically significant side effects. In extreme cases, antidepressants such as the TCA imipramine have resulted in sudden death (Varley, 2000). In recent years, there has been alarm and controversy over the claim that SSRIs can increase risk of treatment-emergent suicidal ideation and events in pediatric populations. The Food and Drug Administration (FDA) requested in 2004 that pharmaceutical manufacturers place a "black box" label on antidepressant packaging warning of the increased risk of suicide-related events that may accompany SSRI use in youth. Generally-speaking, very little is known about the hazards and long-term impact of anxiogenic pharmacotherapies in this population. Given that we have efficacious psychotherapeutic interventions for pediatric anxiety, it has been argued that practitioners should not expose children needlessly to the potential risks of psychoactive medications (Stein & Seedat, 2004). However, the potential risks of a combined treatment approach must be balanced against the potential risks of continuing with an ineffective clinical or treatment strategy; severe, nonremitting anxiety by itself carries the putative risk of long-term psychological, social, academic, and occupational impairment (Stein & Seedat, 2004).

Does the Evidence Indicate that Combined Treatment for Pediatric Anxiety Disorders Is More Effective than an Active Monotherapy?

RCTs that have examined the use of combined treatment for pediatric anxiety indications, including diagnoses, syndromes, or symptoms, are arguably the strongest data source to inform clinicians of the comparative effectiveness of combined treatment. RCTs optimize treatment and subject characteristics to provide a best estimate of the true effect of an intervention upon a particular indication. Control is exerted over extraneous factors, treatment is often delivered by clinicians trained in the treatment model and protocol, control subjects help to illuminate the unique impact

of treatment, and exclusion criteria can effectively remove patient characteristics that might "cloud" or attenuate treatment response. These and other characteristics are all key features of high quality study methodology, and are most typically adopted in RCT treatment studies as opposed to non-RCT treatment studies. The method, treatment regimens, inclusion and exclusion criteria, and findings of RCTs that have examined combined treatment for pediatric anxiety indications are described next. For convenience, pertinent information from each study is summarized in Table 26.1. The methodological quality of these studies according to satisfaction of specific quality indicators is summarized in Table 26.2.

Obsessive–Compulsive Disorder

In a trial by Neziroglu and colleagues (2000), 10 youth aged 10–17 years with a diagnosis of obsessive–compulsive disorder who had not demonstrated a sufficient response to behavior therapy (BT) were randomly assigned to fluvoxamine monotherapy or fluvoxamine combined with BT. Diagnoses were assigned according to *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV; American Psychiatric Association (APA), 1994). Eligibility for study entry was based on age, diagnosis, and previous BT failure, and no exclusion criteria. Participants were assessed at baseline and at weeks 10, 43, 52, and 2-year follow-up.

Participants in both treatment conditions were treated with fluvoxamine from baseline to 1 year, and at week 11, youth in the combined group commenced a 20 session program of BT. BT consisted of graded exposure and response prevention. Fluvoxamine was administered at 50 mg per day and titrated to a maximum of 200 mg per day at increments of 50 mg per week. All patients reached maximal dosing that was held constant during the maintenance phase (up to 1 year), and no serious side effects were observed to warrant downward adjustment.

At all assessment points, improvement in both groups was observed, though more consistently in the combined treatment group. Outcome was determined through the index of reliable change, which depicts whether an individual has improved beyond that which could be attributed to the unreliability, or measurement error, of the symptom measure. Relative to baseline scores, three of five youth in the fluvoxamine monotherapy condition achieved a reliable improvement in obsessive–compulsive disorder symptoms at week 10; three were reliably improved at week 43; three were reliably improved and two were reliably deteriorated at week 52; and at 2-year follow-up, two of three contactable youth were reliably improved. In the combined condition, five of five children were reliably improved at weeks 10, 43, 53, and 2-year follow-up. Of those in the full sample who made reliable improvements from baseline, many also made reliable improvements between assessment points. In a Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS; Scahill et al., 1997), score of 10 or less at posttreatment has been used as an indicator of remission and appears to be clinically meaningful (POTS, 2004; Stewart, Ceranoglu, O'Hanley, & Gellar, 2005). On the basis of the published raw score data, no patient was remitted by week 10 or 43; one in the monotherapy condition was remitted at week 52; and four of five in the combined condition and two of three contactable in the monotherapy condition were remitted at 2 years. The Hedges *g* effect size of combined treatment compared with monotherapy was 0.63 (medium) at week 43 and 1.03 (large) at week 52, as indicated by CY-BOCS scores. Overall, the results indicated that combined treatment may be more useful than fluvoxamine monotherapy for patients with obsessive–compulsive disorder who have not initially responded to BT monotherapy, though the robustness of the findings are compromised by a very small sample size.

The POTS Team (2004) compared CBT, sertraline, combined CBT and sertraline, and pill placebo among 112 youth aged 7–17 with a primary diagnosis of obsessive–compulsive disorder. Diagnosis was established using a standardized, established diagnostic interview based on *DSM-IV* criteria. The trial was conducted across three sites and treatment lasted 12 weeks. Study inclusion criteria comprised a primary

Table 26.1 RCTs with combined BT/CBT-medication arms for pediatric anxiety indications – study characteristics and findings

Study	Treatment	Main indication and demographics	Outcome assessments	Findings in relation to combined treatment ("greater than" [>] indicates a superior treatment effect)[a]	Effect size (Hedges *g*)[b]
Gittelman-Klein and Klein (1973)	1. BT + IMI 2. BT + Placebo	ScP; *N* = 35; 6–14 years	A. Mother rating of school attendance B. Psychiatrist rating of global improvement C. Mother rating of global improvement D. Child rating of global improvement	*6 weeks* A: BT + IMI > BT + Placebo B: BT + IMI > BT + Placebo C: BT + IMI > BT + Placebo D: BT + IMI > BT + Placebo	*6 weeks* A: 1 vs. 2 = 0.73
Bernstein et al. (2000, 2001)	1. CBT + IMI 2. CBT + Placebo	ScP + AD + DD; *N* = 63; 12–18 years	A. RCMAS B. ARC-R C. School attendance D. BDI E. CDRS-R	*8 weeks* A: CBT + IMI = CBT + Placebo B: CBT + IMI = CBT + Placebo C: CBT + IMI > CBT + Placebo D: CBT + IMI = CBT + Placebo E: CBT + IMI > CBT + Placebo *52 weeks* E: CBT + IMI = CBT + Placebo	*8 weeks* A: 1 vs. 2 = 0.74 B: 1 vs. 2 = 0.60 C: 1 vs. 2 = 1.25 D: 1 vs. 2 = 0.42 E: 1 vs. 2 = 0.82
Neziroglu et al. (2000)	1. FLV + BT 2. FLV	OCD; *N* = 10; 10–17 years	A. CY-BOCS B. NIMH-GOCS C. CGI-S D. CGI-I	*10 weeks* A: FLV + BT: 5/5 reliably improved FLV: 3/5 reliably improved, 2/5 unchanged *42 weeks* A: FLV + BT: 5/5 reliably improved FLV: 3/5 reliably improved; 2/5 unchanged *52 weeks* A: FLV + BT: 5/5 reliably improved FLV: 3/5 reliably improved; 1/5 unchanged; 1/5 reliably deteriorated *2 years* A: FLV + BT: 5/5 reliably improved FLV: 2/3 reliably improved , 1/3 unchanged	*10 weeks*[d] A: 1 vs. 2 = 0.20 B: 1 vs. 2 = –0.07 C: 1 vs. 2 = –0.21 D: 1 vs. 2 = 0.52 *42 weeks*[c] A: 1 vs. 2 = 0.57 B: 1 vs. 2 = 0.00 C: 1 vs. 2 = 0.31 D: 1 vs. 2 = 0.41 *52 weeks*[c] A: 1 vs. 2 = 0.92 B: 1 vs. 2 = 0.14 C: 1 vs. 2 = 1.02 D: 1 vs. 2 = 1.31 *2 years*[d] A: 1 vs. 2 = –0.11 B: 1 vs. 2 = –0.03 C: 1 vs. 2 = –0.05 D: 1 vs. 2 = 0.49

POTS (2004)	1. CBT + SER 2. CBT 3. SER 4. Placebo	OCD; *N* = 112; 7–17 years	A. CY-BOCS	*12 weeks* A: CBT + SER > CBT = SER > Placebo	*12 weeks* A: 1 vs. 4 = 1.44 A: 2 vs. 4 = 0.97 A: 3 vs. 4 = 0.67 A: 1 vs. 2 = 0.31 A: 1 vs. 3 = 0.27
Cohen et al. (2007)	1. CBT + SER 2. CBT + Placebo	Sexual abuse-related PTSD symptoms; *N* = 24; 10–17 years	A. PTSD diagnosis B. C-GAS C. CPSS D. MFQ E. SCARED F. CAPS G. CBCL-P H. BDI[e] I. PERQ J. PSQ	*12 weeks* A: Clinical change: CBT + SER: 9/11 with PTSD at pre-tx; 1/11 with PTSD at post-tx; CBT + Placebo: 11/11 with PTSD at pre-tx; 5/11 with PTSD at post-tx B: Statistical analysis: CBT + SER = CBT + Placebo Clinical change: CBT + SER: 11/11 in "clearly impaired" range at pre-tx; 2/11 in "clearly impaired" range at post-tx; CBT + Placebo: 11/11 in "clearly impaired" range at pre-tx; 5/11 in "clearly impaired" range at post-tx C: Statistical analysis: CBT + SER = CBT + Placebo D: Statistical analysis: CBT + SER = CBT + Placebo Clinical change: CBT + SER: 8/11 in "clinical" range at pre-tx; 0/11 in "clinical" range at post-tx; CBT + Placebo: 5/11 in "clinical" range at pre-tx; 0/11 in "clinical" range at post-tx E: Statistical analysis: CBT + SER = CBT + Placebo Clinical change: CBT + SER: 9/11 in "clinical" range at pre-tx; 1/11 in "clinical" range at post-tx; CBT + Placebo: 9/11 in "clinical" range at pre-tx; 4/11 in "clinical" range at post-tx F: Statistical analysis: CBT + SER = CBT + Placebo G: Statistical analysis: CBT + SER = CBT + Placebo	B: 1 vs. 2 = 0.69

(continued)

Table 26.1 (continued)

Study	Treatment	Main indication and demographics	Outcome assessments	Findings in relation to combined treatment ("greater than" [>] indicates a superior treatment effect)[a]	Effect size (Hedges *g*)[b]
				Clinical change: CBT + SER: 8/11 in "clinical" range at pre-tx; 4/11 in "clinical" range at post-tx; CBT + Placebo: 10/11 in "clinical" range at pre-tx; 6/11 in "clinical" range at post-tx H: Statistical analysis: CBT + SER = CBT + Placebo Clinical change: CBT + SER: 7/11 in "non-normal" range at pre-tx; 3/11 in "non-normal" range at post-tx; CBT + Placebo: 7/11 in "non-normal" range at pre-tx; 5/11 in "non-normal" range at post-tx I: Statistical analysis: CBT + SER = CBT + Placebo J: Statistical analysis: CBT + SER = CBT + Placebo	
CAMS (Walkup et al., 2008)	1. CBT + SER 2. CBT 3. SER 4. Placebo	SAD or GAD or SocAD *N* = 488; 7–17 years	A. CGI-I B. PARS C. CGAS D. CGI-S	*12 weeks* A: CBT + SER > CBT = SER > Placebo B: CBT + SER > CBT = SER > Placebo C: CBT + SER > CBT = SER > Placebo D: CBT + SER > CBT = SER > Placebo	*12 weeks* B: 1 vs. 4 = 0.86 B: 1 vs. 2 = 0.57 B: 1 vs. 3 = 0.40 C: 1 vs. 4 = 0.80 C: 1 vs. 2 = 0.46 C: 1 vs. 3 = 0.34 D: 1 vs. 4 = 1.04 D: 1 vs. 2 = 0.69 D: 1 vs. 3 = 0.46

Note: *CBT* cognitive-behavioral therapy; *IMI* imipramine; *FLV* fluvoxamine; *SER* sertraline; *Placebo* pill placebo; *ScP* school phobia; *AD* anxiety disorder; *DD* depressive disorder; *OCD* obsessive-compulsive disorder; *SAD* separation anxiety disorder; *GAD* generalized anxiety disorder; *PTSD* post-traumatic stress disorder; *SocAD* social anxiety disorder; *RCMAS* Revised Children's Manifest Anxiety Scale; *ARC-R* Anxiety Rating for Children Revised; *BDI* Beck Depression Inventory II; *CDRS-R* Children's Depression Rating Scale-Revised; *CY-BOCS* Children's Yale-Brown Rating Scale; *NIMH-GOCS* National Institute of Mental Health-Global Obsessive-Compulsive Scale; *CGI-S* Clinical Global Impression-Severity; *CGI-I* Clinical Global Impression-Improvement; *CPSS* Children's PTSD Symptoms Scale; *MFQ* Mood and Feelings Questionnaire; *SCARED* Screen for Children's Anxiety Related Emotional Disorders; *CAPS* Children's Attributions and Perceptions Scale; *CBCL-P* Child Behavior Checklist-Parent Version; *PSQ* Parental Support Questionnaire; *PARS*: Pediatric Anxiety Rating Scale; *CGAS* Children's Global Assessment Scale

[a] In studies with small samples (<30) and poor statistical power, outcomes other than statistical analyses are provided, if reported in the original study

[b] Effect size conventions: small ≥0.3, medium ≥0.5, large ≥0.8; A positive effect size denotes that the combined treatment group performed superior to the comparison group

[c] One patient's CGI-I score from the FLV group not obtained

[d] Three CGI-I scores, two CY-BOCS scores, two NIMH-HOCS scores, and two CGI-S scores from the FLV group not obtained at this assessment point

[e] Administered to parents to assess parent depression symptoms

Table 26.2 RCTs with combined BT/CBT-medication arms for pediatric anxiety indications – methodological strengths

	Gittelman-Klein and Klein (1973)	Bernstein et al. (2000, 2001)	Neziroglu et al. (2000)	POTS (2004)	Cohen et al. (2007)	CAMS (Walkup et al., 2008)
Randomization to treatment	✓	✓	✓	✓	✓	✓
Placebo-only control	×	×	×	✓	×	✓
Medication monotherapy comparator	×	×	✓	✓	×	✓
BT/CBT monotherapy comparator (with/without concurrent placebo-pill)	✓	✓	×	✓	✓	✓
Multi-site design	×	×	×	✓	×	✓
Relatively large sample size/ treatment cell sizes (i.e., cell sizes ≥ 25)	×	✓	×	✓	n/a	✓
Standardized diagnostic criteria	n/a	✓	✓	✓	n/a	✓
Structured, validated interviews to assist with yielding diagnoses/ main indication	×	✓	×	✓	✓	✓
Exclusion criteria	×	✓	×	✓	✓	✓
Evaluators trained in assessment administration	×	✓	×	✓	✓	×
Validated outcome assessments	×	✓	✓	✓	✓	✓
Multi-informant assessment						
Clinician-rated	✓	✓	✓	✓	✓	✓
Parent-rated	✓	×	×	×	✓	×
Child-rated	✓	✓	×	×	✓	×
Structured treatment protocols	×	✓	×	✓	✓	✓
BT/CBT delivered by clinicians trained in the protocol	×	✓	×	✓	×	✓
Regular on-site therapist supervision (and cross-site, if applicable)	×	✓	×	✓	×	✓
BT/CBT adherence checks	×	×	×	×	✓	×
Medication adherence checks	✓[a]	✓[a]	×	✓[b]	×	✓[b]
Subjects blind to medication status (active vs. placebo)						
In the combined treatment group	✓	✓	n/a	×	✓	×
In the medication monotherapy group	n/a	n/a	n/a	✓	n/a	✓
In the placebo only group	n/a	n/a	n/a	✓	n/a	✓
In the BT/CBT + placebo group	✓	✓	n/a	n/a	✓	n/a
Medication management clinician blind to medication status (active vs. placebo)						
In the combined treatment group	✓	✓	n/a	✓	✓	×
In the medication monotherapy group	n/a	n/a	n/a	✓	n/a	✓
In the placebo only group	n/a	n/a	n/a	✓	n/a	✓
In the BT/CBT + placebo group	✓	✓	n/a	n/a	✓	n/a

(continued)

Table 26.2 (continued)

	Gittelman-Klein and Klein (1973)	Bernstein et al. (2000, 2001)	Neziroglu et al. (2000)	POTS (2004)	Cohen et al. (2007)	CAMS (Walkup et al., 2008)
Blinded evaluators at pretreatment	×	×	×	✓	✓	✓
Blinded evaluators at posttreatment	×	✓	×	✓	✓	✓
Interrater reliability checks of clinician-rated assessments and diagnostic interviews at baseline	×	×	×	✓	✓	✓
Interrater reliability checks of clinician-rated assessments at post-treatment	×	×	×	×	✓	✓
Intent-to-treat analysis	×	✓	✓	✓	×	✓
Follow-up data reported on	×	✓	✓	×	×	×

Note: √ = Reported in published study, × = Not carried out or not reported in published study, n/a = not applicable
[a] Blood level monitoring
[b] Medication diaries and pill checks

obsessive–compulsive disorder diagnosis, a CY-BOCS score greater than 16, a National Institute of Mental Health-Global Obsessive–Compulsive Scale (NIMH-GOCS; Insel, Hoover, & Murphy, 1983) score greater than 7, IQ greater than 80, and non-use of antiobsessional medication prior to the start of the study. Youth were excluded from the study if they had a comorbid major depressive or bipolar disorder; a pervasive developmental disorder; psychosis; concurrent treatment with psychotropic medication or psychotherapy external to the study; two previous failed SSRI trials or one failed CBT trial; previous remission from obsessive–compulsive disorder with CBT, sertraline, or their combination; any medical or neurological disorder that contraindicated a study treatment; or if they were pregnant.

The CBT protocol was adapted from a published treatment program (March & Mulle, 1998) and comprised 14 sessions with parent participation in sessions 1, 7, and 11. The program moved through sequential phases of psychoeducation, cognitive therapy, mapping of OCD target symptoms, and graded exposure and response prevention. The sertraline titration schedule was fixed at a starting point of 25 mg per day and was adjusted upward during the first 6 weeks to a maximum of 200 mg per day. Throughout this period, medical management was provided weekly. Between weeks 6 and 12, medical management occurred fortnightly and sertraline dosage could only be adjusted as a function of clinically significant adverse events.

An intent-to-treat analysis revealed that the combined treatment produced a superior outcome to CBT monotherapy, sertraline monotherapy, and pill placebo on the gold standard CY-BOCS measure, as denoted by superior posttreatment scores. According to a remission criterion of 10 or lower on the CY-BOCS, remission rates were 54% for combined treatment, 39% for CBT monotherapy, 21% from sertraline monotherapy, and 4% for pill placebo. The respective drop-out rates were 11% for combined treatment, 11% for CBT alone, 7% for sertraline alone, and 25% for pill placebo. The Hedges *g* effect sizes relative to the placebo condition were 1.44 (large) for combined treatment, 0.97 (large) for CBT monotherapy, and 0.67 (large) for sertraline monotherapy. The treatment effect sizes for combined treatment relative to CBT monotherapy and sertraline monotherapy were 0.31 (small) and 0.27 (small), respectively. Treatment was well-tolerated by all

treatment arms, with no occurrence of serious adverse events, such as manic, hypomanic, or depressive episodes, or suicide attempts.

Although not designed to investigate the effectiveness of combined treatment, it is worth noting outcomes from an RCT by de Haan et al. (1998), who compared BT with clomipramine among children aged 8–18 years with obsessive–compulsive disorder. Following the acute 12-week treatment phase of the trial, five of nine nonresponders (two in BT and three in the clomipramine condition) consented to participate in an open-label extension that involved switching from monotherapy to combined treatment for a further 12 weeks. The mean CY-BOCS score prior to extension was 26.8 (SD = 5.2), which reduced to 18.8 (SD = 5.3) at the end of the extension phase. The small number of participants and the lack of control compromise interpretation of these findings.

Posttraumatic Stress Disorder

Cohen, Mannarino, Perel, and Staron (2007) randomized 24 youth (aged 10–17 years) with sexual abuse-related posttraumatic stress disorder symptoms to a 12-week course of trauma-focused CBT (TF-CBT) combined with either sertraline treatment or pill placebo. Participants met the following study eligibility criteria: (1) contact sexual abuse, as confirmed by Child Protective Services, law enforcement, or an independent forensic investigator; (2) sexual abuse-related posttraumatic stress disorder symptoms (defined as meeting multiple *DSM-IV* criteria assessed by administration of a standardized, validated, clinical interview); and (3) aged between 10 and 17 years. Exclusion criteria were non-English speaking, schizophrenia, psychotic disorder, mental retardation, pervasive developmental disorder, and current use of psychotropic medications. A multi-informant approach to assessment was utilized, including a range of clinician-rated, child-rated, and parent-rated instruments. Assessment of outcome was targeted not just at child posttraumatic stress disorder symptoms, but also child psychosocial functioning more generally, and parent-related outcomes such as depressive symptoms and perceived degree of support for the abused child.

In the initial phase of TF-CBT, psychoeducation about emotional and physiological responses to trauma was provided to promote identification, expression, and normalization of abuse-related responses and feelings. Thereafter, the emphasis shifted to skill-building to manage emotion, and participants were given instruction in relaxation, affect expression and regulation, focused breathing, and cognitive therapy techniques. The next phase involved in vivo exposure to and mastery of trauma reminders, conducted in a graded fashion. In the final phase of therapy, psychoeducation about healthy sexuality, personal safety skills, and relapse prevention activities was delivered. The TF-CBT program was administered in weekly parallel child and parent/caregiver sessions. The medication dosage was titrated upward from a fixed initial dosage of 25 mg per day to a study maximum of 200 mg per day, and the average dosage at endpoint was 150 mg per day.

Cohen and associates had expected to recruit a larger number of participants than that appearing in their final sample; however, recruitment coincided with the release of the FDAs "black box" warning label for SSRIs. Therefore, the statistical power for inferential analysis was low, and reporting of results was supplemented with idiographic data on the clinical meaningfulness of change. An omnibus analysis of outcomes revealed no main effect for treatment group, but a time effect emerged, suggesting that within the full sample improvement occurred from pretreatment to posttreatment. Overall, clinically meaningful changes in symptoms were more likely to be experienced by participants in the combined condition. In terms of posttraumatic stress disorder diagnosis, 82% of children in the TF-CBT + sertraline condition and 100% of children in the TF-CBT + placebo condition met diagnostic criteria at pretreatment. Of these individuals, only 10% of children in the TF-CBT + sertraline condition met diagnostic criteria at posttreatment, compared with 45% in the TF-CBT + placebo condition. Other outcomes are described in Table 26.1. There were no meaningful differences in rates of adverse events between the treatment conditions.

Other Anxiety Disorders

In an early study by Gittelman-Klein and Klein (1973), 35 children with "school phobia" were randomly assigned to "multidiscipline" treatment with either the TCA imipramine or pill placebo for 6 weeks. Children participating in the study were required to be between 6 and 14 years of age and to have "school phobia," defined as school refusal with an apparent cause of separation or other anxiety. No exclusion criteria were utilized for the study. Psychiatrists, mothers, and children rated global improvement in symptomatology at the end of week 6.

The "multidiscipline" treatment program resembled a behavioral therapy program in that children were firmly encouraged to attend school to achieve habituation to anxiety: "in most cases, a family member was advised to accompany the child to school and maintain the child's presence there until there was reduction in the child's anticipatory anxiety" (p. 202). The "exposure" was implemented in a graded fashion, for example, the authors described one boy who was instructed in the first week to get dressed in school clothes on school mornings, though at this point he was not required to attend school. In the second week, the boy was taken to the school grounds on school mornings but was not required to enter the building. This exposure strategy was graduated until the boy was attending classes daily. The imipramine dosage schedule commenced at 25 mg per day and was escalated upward to a maximum of 200 mg at the end of 6 weeks. Patients and families were seen weekly for medical management and "multidiscipline" treatment.

According to psychiatrist ratings, 73% in the combined treatment condition were "much improved" compared with 32% in the monotherapy condition. Mothers' ratings of global improvement likewise favored the combined treatment group, with 87% of children rated as "much improved" compared with 42% in the monotherapy condition. Among children, 100% of those in combined treatment rated themselves as "much improved" compared with 21% in the monotherapy condition. Regular school attendance was achieved by 75% of the combined treatment group and 47% of the monotherapy group. The authors reported a medium treatment effect size of 0.73 for combined treatment compared with monotherapy. Children treated with only "multidiscipline" treatment reported fewer adverse events than those with the combined treatment condition.

Bernstein et al. (2000, 2001) compared CBT and imipramine with CBT and placebo among 63 adolescents who were refusing to attend school and had at least one comorbid anxiety disorder and a comorbid depressive disorder. Diagnoses were established using standardized child and parent interviews and *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Text Revision* (DSM-III-R; APA, 1987) criteria. To be included in the study, subjects needed to have a minimum of 20% days absent from school in the 4 weeks preceding assessment, be aged between 12 and 18 years, postpubertal as confirmed by physical examination, meet diagnostic criteria for an anxiety disorder and major depressive disorder, obtain a minimum score of 5 on the Anxiety subscale of the Anxiety Rating for Children-Revised (ARC-R; Bernstein, Crosby, Perwien, & Borchardt, 1996), and obtain a minimum score of 35 on the Children's Depression Rating Scale-Revised (CDRS-R; Poznanski, Freeman, & Mokros, 1985). Exclusion criteria included a comorbid diagnosis of attention-deficit hyperactivity disorder, conduct disorder, bipolar disorder, eating disorder, alcohol or drug abuse, mental retardation by history, medical disorder that contraindicated imipramine use, history of bipolar disorder in a first-degree relative, use of other psychotropic medications, pregnancy, positive urine toxicology screen, and abnormalities on baseline electrocardiogram (ECG) or blood tests.

The duration of treatment for each treatment condition was 8 weeks. CBT involved weekly sessions that included treatment components of psychoeducation, development of a school reentry plan, cognitive therapy, exposure, and behavioral contracting. The program was adapted from an existing 13-session protocol (Last, Hansen, &

Franko, 1998). Medication management occurred weekly with a psychiatrist. Imipramine dosage was adjusted upward continuously from baseline to achieve a targeted dose of 3 mg/kg per day by the end of week 2. The average dosage was 185 mg per day at week 3 and 247 mg per day at the end of treatment.

At posttreatment, both groups showed significant decreases in anxiety and depressive symptoms, and school attendance increased significantly for the combined group but not the monotherapy group. A significant difference between groups favoring combined treatment was observed on one, but not a second measure of depressive symptoms. Two anxiety symptom measures failed to show a significant difference between the groups. Remission was defined a priori on the basis of three criteria: weekly attendance ≥75% of school hours, a CDRS-R score of ≤35, and an ARC-R score of ≤5. Compared with the monotherapy group, a greater percent of adolescents in the combined group achieved remission of school refusal (54 vs. 17%), anxiety (64 vs. 48%), and depression symptoms (52 vs. 32%). There was no significant difference in the number of dropouts between the combined group and the monotherapy group, with approximately 25% dropping out overall, suggesting that combined treatment had equivalent tolerability to monotherapy with placebo.

At 1 year, 41 children (65%) participated in a follow-up assessment, which involved readministration of the parallel parent and adolescent standardized, structured diagnostic interviews used at pretreatment and psychometric questionnaires (Bernstein et al., 2001). The patients that returned for follow-up were not significantly different from non-followed-up patients in terms of pretreatment demographics and posttreatment anxiety and depressive symptoms, but they did have a better rate of posttreament school attendance. Of the 41 that were followed up, 39 completed parallel parent and adolescent interviews, and 38 had baseline diagnostic data available for comparison. The follow-up diagnostic data revealed no significant differences in prevalence rates of anxiety or depressive diagnosis between the combined treatment and fluvoxamine monotherapy groups. At the follow-up, approximately 64% of patients met criteria for an anxiety disorder and 33% met criteria for major depressive disorder or dysthymia. Of the anxiety disorders, remission was highest for agoraphobia (73%; 11/38 were diagnosed with the disorder at baseline), followed by separation anxiety disorder (71%; 14/38 at baseline), overanxious disorder (60%; 35/38 at baseline), avoidant disorder (50%; 20/38 at baseline), social phobia (50%; 20/38 at baseline), and panic disorder (0%; 1/41 at baseline). The average level of anxiety, as measured by the ARC-R, was in the mild range. Depression severity, as measured by the CDRS-R, was in the mild to moderate range. Depression severity did not differ between the combined and monotherapy groups at follow-up, and relative outcome on the anxiety measure was not reported. It is important to note that two-thirds of the sample received interim treatment, including up to three psychotropic medication trials, outpatient /inpatient treatment, and a variety of psychotherapies, which Bernstein and colleagues (2001) suggested may be an explanation for the lack of differences between the groups at follow-up. Predictors of follow-up outcome on severity measures or in terms of anxiety and depression diagnostic status were examined. Outcomes were not predicted by school attendance at posttreatment, but somatic symptoms on the ARC-R scale were predicted by poor baseline family functioning, and depressive symptoms were predicted by baseline scores on the ARC-R physiological subscale.

The Child-Adolescent Multimodal Study (CAMS; Walkup et al., 2008) is the largest study to date to examine monotherapy vs. combined treatment in youth with anxiety disorders. The study comprised 488 children aged 7–17 years with a primary diagnosis of separation anxiety disorder, generalized anxiety disorder, or social anxiety disorder. The exclusion criteria for the study included an IQ below 80, an unstable medical condition, refusal to attend school due to anxiety, a failed previous response to two SSRIs or one CBT trial, an acute suicide risk, clinical inappropriateness (e.g., bipolar, psychosis history), or pregnant

or sexually active females not using medically accepted birth control. Diagnosis was established using a standardized, structured interview that was based on *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR; APA, 2000) criteria. Youth that were deemed eligible for study entry were randomized to a 12-week course of CBT, sertraline, combined CBT and sertraline, or pill placebo.

The CBT program was adapted from the "Coping Cat" intervention designed by Kendall and colleagues (Kendall & Hedtke, 2006a, b). The program involved 12 individual sessions and two parent sessions with key components of training in anxiety management and exposure to anxiety-provoking situations. Sertraline was administered in a fixed-flexible regimen, initiated at 25 mg per day and adjusted upward to a maximum of 200 mg per day over the first 8 weeks of treatment. Beyond 8 weeks, dosage could only be adjusted upward if the patient was symptomatic and had experienced no or minimal adverse events. The mean sertraline dosage at treatment completion was 134 mg per day for the combined treatment condition and 146 mg per day for the sertraline monotherapy condition.

At posttreatment, combined treatment was superior to CBT and sertraline monotherapies, and all active treatments were superior to pill placebo. On the primary outcome measure, the Pediatric Anxiety Rating Scale (PARS; Research Units on Pediatric Psychopharmacology Anxiety Study Group, 2002), the Hedges *g* effect sizes relative to placebo were 0.86 (large) for combined treatment, 0.45 (small) for sertraline monotherapy, and 0.31 (small) for CBT monotherapy. The effect size of combined treatment was 0.40 (small) compared with sertraline monotherapy and 0.57 (medium) compared with CBT monotherapy. Unfortunately, no data on remission rates was provided; however, the percentage of children responding to treatment as identified by posttreatment scores on the Clinical Global Impression of Improvement scale (Guy, 1976) favored combined treatment. The improvement rates were 81% for combined treatment, 60% for CBT monotherapy, 55% for sertraline monotherapy, and 24% for placebo.

Summary of RCT Evidence

Overall, the findings reported in these RCTs have supported the utility of a combined treatment approach, and provided evidence that combined treatment is associated with greater average improvement compared with placebo control and monotherapy. The studies by Gittelman-Klein and Klein (1973) and Bernstein et al. (2000) showed that anxiety-based school refusal with and without comorbidity was more responsive to combined treatment than to CBT administered with placebo. Neziroglu et al.'s (2000) findings, although based on a small sample, are consistent with the POTS trial findings, and provide tentative evidence for the durability of treatment benefit with combined treatment. Cohen and colleagues (2007) showed superior clinical benefit for combined treatment for posttraumatic stress disorder symptoms compared with monotherapy TF-CBT on multidimensional outcomes. Although these studies are complicated somewhat by small samples and/or complex patient presentations, the findings appear to favor a combined treatment approach relative to a monotherapeutic approach. The strongest level of evidence for combined treatment is in relation to the primary diagnoses of obsessive–compulsive disorder, generalized anxiety disorder, separation anxiety disorder, and social anxiety disorder, and is based upon the POTS and CAMS trial findings. The POTS and CAMS trials are notable for their numerous methodological strengths (as outlined in Table 26.2), including the use of a relatively large number of subjects, primary indications described by standardized diagnostic nomenclature, blind evaluators, and so forth. In the POTS and CAMS trials, the combined treatments showed superior efficacy to CBT monotherapy, SSRI monotherapy, and placebo. In the POTS trial, the remission rate was highest for those treated with combined treatment, and represented over half of the sample after 12 weeks of treatment. All RCTs, where applicable, described few meaningful differences in the rate of adverse events experienced by participants treated with pharmacotherapy alone, in combination, or with placebo or CBT, and there were very few instances of serious adverse events.

Concluding Remarks

The recent small proliferation of controlled research, with combined and monotherapy treatment arms, has allowed practitioners to gain a wealth of knowledge that is crucial to improving the well-being of children and adolescents with anxiety problems. The data to date have suggested that combined treatment is superior to placebo control for particular anxiety disorders, and that combined treatment appears to confer greater treatment benefit than existing active psychotherapeutic and pharmacological monotherapies. In the adult literature, the relative efficacy of monotherapy and combined treatment has been more extensively studied, and a rather different state of affairs has emerged. A combined treatment approach has not been widely supported for adults. In a metaanalysis of ten adult treatment studies, Foa, Franklin, and Moser (2002) found that combined treatment was not superior to BT/CBT monotherapy for obsessive–compulsive disorder, social anxiety disorder, or generalized anxiety disorder. Combined treatment showed superiority to BT/CBT monotherapy for panic disorder at treatment endpoint, but was associated with a greater risk of relapse upon medication discontinuation. The discrepancy between the child and adult literature is intriguing, given that the theoretical models underlying the evidence-based therapies for these populations are equivalent, as are the treatment applications. It will be interesting to reevaluate this issue in the context of forthcoming POTS and CAMS follow-up data – to observe how subjects in each condition perform during the maintenance phase. It may be that combined treatment only shows superiority at completion of the acute treatment phase, and that the relative treatment effects equalize at follow-up, particularly as CBT monotherapy "catches up." This observation would be more consistent with the results of adult trials. Notwithstanding, this discrepancy between bodies of clinical research is interesting and would benefit from further consideration.

The trials summarized in this chapter employed an RCT design, and although this is the gold standard research design, it is not without criticism. Efficacy trials maximize the internal validity of a study by exerting a high level of control over subject and treatment characteristics, enabling the outcome data to approximate the underlying treatment effect distribution. However, a tradeoff occurs in that increases in internal validity proportionately weaken the external validity, or generalizability of study findings. One method of exercising control over confounding factors is through the use of exclusion criteria. In the POTS and CAMS trials, many exclusion criterions were utilized, and the studies' CONSORT flow diagrams suggest that 22%[1] of those interested and able to participate in the POTS trial and 71%[1] of those interested, contactable, and able to participate in the CAMS trial were excluded from study participation. A substantial proportion of children were not included, though admittedly it is not clear how many were not eligible based on failure to meet the trial inclusion criteria (i.e., diagnosis, age) or through satisfying one or more study exclusion criteria. Given that each study had exclusion criteria that are known to pertain to a proportion of the anxiety disorder population (i.e., comorbid depression, acute suicidality, previous failed treatment), practitioners must be mindful of how findings are applied to youth in clinical practice. Caution is necessary in applying study findings to subpopulations not described by study samples, yet this does not provide license to unilaterally dismiss trial findings. If we have insufficient knowledge about what is effective for related but excluded subpopulations, then it may

[1] In the POTS (2004) trial, there were 154 youth screened. Of these, 112 were randomized to treatment, 31 were deemed ineligible, 10 were not interested in participating, and 1 was asymptomatic at baseline. Of those contactable and able to participate in treatment ($n = 143$), 78% ($n = 122$ of 143) were randomized and 22% ($n = 31$ of 143) were deemed ineligible. In the CAMS (2008) trial, 3,066 youth were screened. Of these, 488 were randomized to treatment, 1,223 were deemed ineligible, 817 were not interested in participating, 462 were not contactable, and 73 could not participate for other reasons, and 3 were asymptomatic at baseline. Of those who were contactable and able to participate in treatment ($n = 1711$), 29% ($n = 488$ of 1711) were deemed eligible and were randomized to treatment, and 71% ($n = 1223$ of 1711) were deemed ineligible and were not included in the study.

be that guidance from these trials represents our best estimation of what might be effective for these subpopulations.

There are practical complexities associated with delivering a combined intervention in naturalistic, community settings. It is common for children who receive combined treatment to receive CBT from one care provider and pharmacotherapy from another. Combined treatment is supposed to be integrative, and separate care providers may provide inconsistent treatment rationales and contradictory information. For instance, physicians may encourage patients to take medication in anticipation of or in response to anxiety-provoking situations (e.g., benzodiazepines prescribed on a PRN basis), yet a CBT therapist may conceptualize this medication use as an unhelpful safety aid that circumvents habituation and cognitive reprocessing during exposure. Given that a number of arguments exist as to how medication might interfere with CBT, coupled with an absence of data to negate these criticisms, it may be helpful for care providers to sensitize themselves to salient issues that may enhance or detract from therapeutic outcome. For instance, if benzodiazepines are to be used as an augmentation strategy with CBT, perhaps the most benefit can be derived when a low dose is used, when it is tapered and withdrawn prior to CBT discontinuation, or when it is implemented sequentially prior to CBT. A collaborative, working relationship is arguably the most important component of care when treatment is delivered by multiple care providers. It may be useful to enunciate and promulgate collaborative care models, such as the "blueprint." Craske and colleagues (2002) specified to assist doctors, behavioral health specialists, and psychiatrists within primary care settings to administer combined treatment to patients with panic disorder.

There are many potential avenues for future research into combined treatment for pediatric anxiety. It would be worthwhile to investigate the role of treatment sequencing (i.e., the order in which treatments are used) and newer antidepressant agents, to study predictors of treatment response, to scope a broader array of outcomes (i.e., quality of life, functional impairment, and impact of treatment upon parents and families), and to obtain outcome data from multiple informants (i.e., clinician, child, parents, etc.). An important future research direction is to examine the utility of a combined treatment approach in an "effectiveness" (i.e., naturalistic setting) study design, in order to determine how well the potential benefits of a combined treatment approach can be replicated in real-world clinical settings. As it is unethical to randomize patients in these settings to monotherapy and combined treatment modalities, outcomes could be benchmarked against existing outcomes from RCT data or clinically significant change analysis could be conducted to determine whether patients improve reliably beyond measurement error, and whether posttreatment symptoms fall within a predefined remission range. It would be of great assistance if community-based norms were developed for clinical assessments used in treatment trials (i.e., CY-BOCS, PARS) so that remission and clinically significant change can be more satisfactorily evaluated within forthcoming efficacy and effectiveness studies, and within clinical settings. The reporting of follow-up data from the recent POTS and CAMS clinical trials will be an important step to informing practitioners about the durability of a combined treatment approach and the long-term outcome of this strategy compared with psychotherapy and pharmacological monotherapies. At the level of specific disorders, we do not have a strong understanding of the effectiveness of combined treatment for some diagnoses, for example panic disorder and specific phobia, and within diagnoses, for instance, across different phobias or OCD symptom presentations. These research directions would extend our knowledge of combined treatment for pediatric anxiety disorders.

Summary

Until a recent small proliferation in controlled research at the turn of the century, there had been very little to guide clinicians on the use and effectiveness of combined treatment for pediatric anxiety. Coupled with this were juxtaposing arguments concomitantly opposing and favoring

a combined treatment approach. Opposition has mainly focused on the augmentation of benzodiazepine treatment with CBT treatment. Clinical or theory-based discussion and/or research evidence has suggested that medication treatment may interfere with CBT by blocking treatment processes (e.g., serving as a safety aid, attenuating physiological arousal during exposure, reducing motivation to engage in CBT, negatively affecting learning and recall via drug context effects) and by negatively impacting upon important mediators of symptom change that are associated with remission and recovery (e.g., strengthening unhelpful cognitive biases, lowering self efficacy for symptom management). Conversely, proponents of a combined approach have suggested that CBT outcome may be enhanced by medication augmentation, as this would allow a greater breadth of anxiety-modulating factors to be targeted, enhance the tolerability of exposure therapy, improve comorbidity associated with remission and relapse, and confer greater rapidity of improvement.

To date, six RCTs have included combined treatment arms for pediatric anxiety indications. These studies have supported the efficacy of a combined approach of CBT with SSRI/TCA for specific anxiety problems relative to pill placebo or monotherapy control; furthermore, outcomes have suggested that combined treatment is superior to SSRI/TCA and CBT monotherapy at treatment completion. Follow-up data from the recent larger POTS and CAMS trials are currently unavailable, yet will be crucial to evaluating the durability and relative long-term effectiveness of combined treatment. Notwithstanding, it is clear from existing empirical data and theoretical considerations that combined treatment has a valuable role in the management of pediatric anxiety.

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Part V

Special Populations and Additional Treatment Elements

Parent Training for Childhood Anxiety

27

Adam B. Lewin

Few clinicians would suggest that the parent's role during the treatment of their child's anxiety should be limited to keeping a chair warm in the therapist's waiting room. In fact, etiological models suggest that parenting behaviors impact child anxiety (Hudson & Rapee, 2001). However, the optimal role of parents in the treatment of children with anxiety disorders is unclear. What parent training strategies are helpful for alleviating childhood anxiety? Is parent training a key treatment component or is it ancillary? Are there benefits to parent therapy, e.g., anxiety management training? What is the efficacy of applying nonanxiety specific behavioral parent training approaches, such as those employed for disruptive behavior disorders? Although the answers are far from unambiguous, this chapter will (1) discuss the rationale for parent training and parental involvement in psychotherapy for child anxiety, (2) review research in this developing area, and (3) discuss limitations in the extant research and recommendations for practice and future study.

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Rationale for Parent Inclusion

Insufficient improvement from current interventions. The rationale for parental inclusion in the treatment of childhood anxiety is multifaceted. Despite the efficacy of current first-line treatments for childhood anxiety disorders, namely individual cognitive behavioral therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs), these interventions yield only modest improvement (Eisen, Raleigh, & Neuhoff, 2008). For example, the Child–Adolescent Anxiety Multimodal Study (Walkup et al., 2008) produced only a 59.7% improvement rate in anxiety symptoms following a meticulously-implemented CBT protocol (the Coping Cat protocol; Kendall & Hedtke, 2006). When the outcome of treatment is based on a "diagnosis-free" criterion, results are slightly less encouraging (56.5% diagnosis-free based on metaanalytic techniques) (Cartwright-Hatton, Roberts, Chitsabesan, Fothergill, & Harrington, 2004). Treatment responses may be even lower in community samples where patient presentation is more heterogeneous and implementation of treatment is less standardized (Weisz, Weiss, & Donenberg, 1992). Given that as many as 50% of youth remain symptomatic following an adequate trial of child-focused CBT (in the absence of significant parental participation) (Ginsburg & Schlossberg, 2002; Wood, Piacentini, Southam-Gerow, Chu, & Sigman, 2006), family-based approaches are worthy of consideration.

D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_27, © Springer Science+Business Media, LLC 2011

Family transmission of anxiety. The heritability of anxiety disorders must also be considered when developing and implementing treatment. Anxious children are more likely to have anxious parents – data from family aggregate and genetic studies suggest a range from 60 to 80% (Chorpita & Barlow, 1998; Ginsburg & Schlossberg, 2002; Hudson & Rapee, 2001; Last, Hersen, Kazdin, Francis, & Grubb, 1987; Pauls, 2008; Rutter et al., 1990). For example, Beidel and Turner (1997) examined 129 school-aged children (7–12 years) and found that 33% children of parents with an anxiety disorder met criteria for an anxiety disorder, whereas only 9% of children of normal controls met criteria for an anxiety disorder. Both genetic and environmental (learned) mechanisms are likely involved in multigenerational transmission of anxiety (Hettema, Neale, & Kendler, 2001; Rapee, 1997).

Family-based maintenance of anxiety. Parents may model avoidant behavior as well as anxious thinking patterns (e.g., excessive reassurance, distorted cognitions, though-action fusion) to an impressionable child (Capps & Ochs, 1995; Dadds, Barrett, Rapee, & Ryan, 1996; Eisen et al., 2008; Moore, Whaley, & Sigman, 2004). In a review of the literature, Ginsburg and Schlossberg (2002) suggest that parents of anxious youth (in comparison to parents of nonanxious youth) are more likely to (1) interpret ambiguous situation as worrisome/stressful and (2) are more supportive of avoidance-based coping strategies. Moreover, parents may strengthen (i.e., reinforce) the likelihood of anxiety-related behaviors via escape, avoidance, attention, and accommodation of behaviors (Barrett, Dadds, & Rapee, 1996; Barrett, Duffy, Dadds, & Rapee, 2001; Geffken et al., 2006; Kendall, Hudson, Gosch, Flannery-Schroeder, & Suveg, 2008; Last et al., 1987; Lewin & Piacentini, 2009; Meiser-Stedman, Yule, Dalgleish, Smith, & Glucksman, 2006; Smith et al., 2007; Storch, Geffken, Merlo, Jacob, et al., 2007; Wood, McLeod, Sigman, Hwang, & Chu, 2003).

Parents of anxious youngsters are often overprotective (Last & Strauss, 1990). It is not uncommon for anxious parents to attempt to limit their child's exposure to stressful stimuli, perhaps because they are fearful that the child will lack an ability to cope. However, despite the best of intentions, inadvertent and intentional strategies to mitigate a child's exposure to anxiety may backfire. First, overprotection (among parents of anxious youth) is often accompanied by critical and controlling parental behavior (Cobham, Dadds, & Spence, 1998; Eisen et al., 2008; Hudson & Rapee, 2001; Messer & Beidel, 1994; Siqueland, Kendall, & Steinberg, 1996). At times, parental responses to an anxious child's symptoms may even be harshly antagonistic (Renshaw, Steketee, & Chambless, 2005; Van Noppen, Rasmussen, Eisen, & McCartney, 1991). Second, in comparison with youth without anxiety, anxious youth describe their parents as less supportive, less warm, and as granting less psychological autonomy (Chorpita & Barlow, 1998). Third, the development of psychological autonomy may be hindered by overprotection, control, and punishment of independence (Hudson & Rapee, 2001). For example, when parents reinforce anxious responding and attempt to manage all of the stress in a child's environment, the youngster's development of adaptive behaviors for coping with anxiety may fail to develop (e.g., emotion-focused coping) (Spence, 1994; Strauss, Frame, & Forehand, 1987). Further, children may receive insufficient exposure to learning paradigms involving stressful situations. By shielding a child whenever stress is encountered, parents may communicate a message suggesting that the child is incapable of handling anxiety. Finally, parents of anxious youngsters are more likely to exhibit behaviors that communicate a greater perception of threat in the child's environment (Barrett et al., 1996; Dadds et al., 1996; Spence, Donovan, & Brechman-Toussaint, 2000). In a viscous cycle, parental overprotection and communication-of-environmental-threat may reinforce the child's anxious thoughts and behaviors.

Although longitudinal research suggests that aforementioned parental behaviors maintain child anxiety (Lieb et al., 2000), the relationship between child anxiety and parent anxiety is reciprocal (Bogels & Siqueland, 2006; Chorpita & Burlad, 1998; Kendall et al., 2008) and thus even nonanxious parents may be conditioned to exhibit behaviors associated with the proliferation of child anxiety

(Manassis & Bradley, 1994). In other words, both parents and children contribute to anxiety-maintaining factors, e.g., control, criticism, conflict, and overprotection (Bogels & van Melick, 2004).

Bolstering compliance. CBT for anxiety disorders requires intensive practice in and out of treatment sessions (Kendall & Hedtke, 2006; Lewin et al., 2006; March & Mulle, 1998; Piacentini, Langley, & Roblek, 2007; Silverman, Kurtines, Ginsburg, Weems, Rabian, et al., 1999). Parent endorsement and support for treatment procedures are paramount in compliance with therapeutic procedures outside of session (Hudson & Kendall, 2002). Just as it is unrealistic to expect many children to complete homework from school without some level of parental attention/supervision, one cannot rely on youngsters to engage in CBT exercises (e.g., cognitive logs, exposure/response prevention, routine modifications) without parental assistance. Moreover, the most potent aspect of CBT for child anxiety – exposure – can be terrifying and counterintuitive to a child. In a hierarchical fashion, exposures involve presentation with (in vivo or imaginally) a feared stimuli or situation. Moreover, the child is asked to reframe from using their established (though ultimately fear-maintaining) repertoire of coping strategies (e.g., avoidance, escape, ritualization, and reassurance seeking). Not surprisingly, children are often less-than-excited about participation in therapeutic exposures. When a child is fearful about engaging in therapeutic exercises (and perhaps doubtful of the potential benefit, especially in the initial stages of treatment), it is unrealistic to expect independent engagement in exposure-based practice. Consequently, parental endorsement of the treatment is critical. This is especially important when a child's motivation is low, insight is poor, and expectation for improvement is minimal. Thus, experts may advocate training parents to participate in session and assisting their child to generalize therapeutic procedures to other environments.

In summary, family aggregation (or hereditary predisposition), in combination with several parenting factors, likely plays a significant role in the development and maintenance of child anxiety. Further, modeling and reinforcement of anxious behaviors, overprotection, conflict, and verbal/nonverbal communication (suggesting that the world is unsafe and that the child is ill-equipped to cope) can impede treatment (Nauta, Scholing, Emmelkamp, & Minderaa, 2003; Spence et al., 2000). Moreover, children may lack the initiative and/or their anxiety may be too pervasive for them to participate in therapy independently. Consequently, it is not unlikely that child focused-therapies will be unsuccessful (Thienemann, Moore, & Tompkins, 2006). Accordingly, the addition of parent training and family interventions targeting anxiety-maintaining behaviors may improve outcomes (Ginsburg & Schlossberg, 2002; Lewin, Storch, Adkins, Murphy, & Geffken, 2005; Spence et al., 2000; Thienemann et al., 2006).

Parent Training Approaches for Youth with Anxiety

Despite the nearly universal agreement for the necessity of parent involvement in the treatment of youngsters with anxiety disorders, there is wide variability in approach and application. Ginsburg and Schlossberg (2002) noted that the content of parent-focused interventions typically included psychoeducation, contingency management, and parental inclusion in treatment.

Psychoeducation. Parent psychoeducation is a critical aspect of treatment for anxious youth (Lewin et al., 2006). Although psychoeducation is often disorder-specific, the omnibus goal is to provide a cognitive-behavioral conceptualization for the manifestation and treatment of anxiety (Ginsburg & Schlossberg, 2002). Parental education should highlight the biological etiology of anxiety with a goal of reducing parental self-blame (or child blame) for the development of a child's anxiety. Nevertheless, the role of the child's environment (e.g., the family) in maintaining anxiety must be emphasized. The therapist might explain to the parent that trying to provide comfort and protection, despite being innate parental responses, may actually worsen symptoms in an anxious child. Subsequently, the

therapist should impart knowledge regarding the therapeutic techniques that will be used to extinguish anxiety and augment adaptive coping skills. Additionally, education may focus on the tripartite model (Lang, 1979) to assist parents understand and recognize relations between physiological symptoms, anxious thoughts, and avoidant behaviors. For example, educating a parent that picking up a child (with a stomachache) the day of the child's exam might actually proliferate anxiety.

For psychologically-minded parents, especially in family-systems where coercive cycles (Patterson, 1974) are minimal, psychoeducational aspects of parent training may be sufficient for training the parent to begin to model appropriate behavior and discontinue reinforcement of behavior/overprotection that may perpetuate the child's anxiety. However, at the very least, parent training should attempt to create an anxiety-neutral environment. For parents, psychoeducation may open the first window into the pervasive and debilitating nature of their child's anxiety (Engel, Rodrigue, & Geffken, 1994; Yeh & Weisz, 2001). Further this training can provide the essential "sales pitch" to the parent for treatment; as discussed earlier, the child is unlikely to "buy-in" to treatment without parental endorsement.

Training in therapeutic techniques. Parent training for youth with anxiety disorders often involves instructing a parent to participate with child-focused therapeutic exercises in-and-outside of session (Barrett, Farrell, Pina, Peris, & Piacentini, 2008; Ginsburg & Schlossberg, 2002; Silverman, Pina, & Viswesvaran, 2008; Thienemann et al., 2006). Training ranges from teaching the parent to monitor and assist with therapeutic homework as needed (Kendall & Hedtke, 2006; March & Mulle, 1998), to participation throughout therapy (Lewin & Piacentini, 2009; Smith et al., 2007; Storch, Geffken, Merlo, Mann, et al., 2007) to training as a lay-therapist (Hahlweg, Heinrichs, Kuschel, & Feldmann, 2008; Thienemann et al., 2006). Silverman and colleagues (1999) described a model where the therapist's responsibilities are gradually transferred to the parent. Certain factors may contraindicate parent assumption of therapeutic roles. High parental anxiety, caustic parent–child interactions, poor child motivation, and/or oppositional child behavior dictates concurrent or precursor interventions.

Contingency management. Contingency management techniques are commonly included as part of parent training for child anxiety disorders. Contingency management (often called behavioral parent training) involves teaching parents operant principles: (1) positive reinforcement (e.g., rewarding participation in treatment); (2) negative reinforcement (eliminating escape and avoidance as coping strategies); (3) extinction (ignoring reassurance seeking behavior) and punishment (e.g., removal of privileges or the presentation of a time-out following oppositional behavior). Contingency management techniques can target anxiety specifically or general behaviors (e.g., cooperation, remaining on-task, compliance with assignments). Training should include learning how to identify rewards (that can be used to increase desired behaviors). An emphasis is placed on avoiding power-struggles with the child by (1) being consistent, (2) following-through with contingencies, and (3) refraining from emotionally-reactive responses to the child. Implementing contingency management techniques can dramatically shift family roles (from child-control (or anxiety-mediated control) to parent-control). Despite emotions (e.g., anger, worry, frustration) that a parent or child may be experiencing when delivering/receiving a consequence (e.g., a time-out) or conducting a therapeutic exposure exercise (e.g., withholding reassurance to a child's anxious request), the parent should give the perception of control and level-headedness. The parent should strive to project confidence in the techniques and control over the situation. Parent and child emotional reactions (to potentially major role changes) can be discussed in-session. These techniques are commonly included for most child anxiety disorders including obsessive–compulsive disorder (OCD) and posttraumatic stress disorder (PTSD) (Barrett et al., 1996; Carr, 2004; Dadds, Heard, & Rapee, 1991; Lewin et al., 2006; Smith et al., 2007; Wood et al., 2006).

Additional strategies. Other ancillary parent training approaches may include parent anxiety management, family problem-solving, and communication training (e.g., interventions aimed at improving parent–child interactions). Typically, these strategies do not focus on the specific parenting practices that are hypothesized to contribute to anxiety development and maintenance (Wood et al., 2006). Consequently, these approaches are normally applied only when the characteristics of a particular family dictate their necessity. For example, the therapist might illustrate how a parent's anxious or avoidant behavior may be modeling anxiety. In more severe cases, referral for outside treatment for the parent may be warranted. For example, parents suffering from PTSD are unlikely to be able to assist their child prior to resolving their own symptoms (Carr, 2004). Similarly, families marred by significant conflict may require additional intervention to facilitate their ability to combat anxiety. Targets of training include improving parent–child communication, teaching problem solving skills, increasing positive parental attention, and decreasing blame/conflict. These family therapeutic modules can be added into the anxiety treatment sessions fairly seamlessly (e.g., Wood et al., 2006). However, longstanding psychiatric illness in children, parents, or both may necessitate more intensive prerequisite or concurrent family therapy. If family therapy cannot be implemented (with an extremely caustic family), e.g., because a parent refuses to participate or all the blame is placed on the child, then this is one of the few situations that individual child therapy with minimal parent involvement may be warranted.

Treatment Studies

Studies comparing CBT for child anxiety with and without significant parental components have mixed results (see Table 27.1). Barrett and colleagues (1996) found that although both child-only CBT and CBT + family therapy were superior to a waitlist group, CBT + family (84% diagnosis free) was superior to individual child CBT (57.1%); the differences were maintained at a 1 year follow-up. Similarly, Wood et al. (2006) found that a significantly higher percentage of youth in a family CBT group (78.9%) were rated as very much better (compared with 26.3% among youth receiving CBT without family), although the difference in the percentage of youth who were diagnosis-free at posttreatment (78.9% for family, 52.6% for individual) was not statistically significant. It is noteworthy that the aforementioned trials may have been underpowered to detect differences in two active, robust treatments. Consequently, it would be difficult to detect an additive effect for a parent-training or family component.

Parent training interventions with CBT are almost universally superior to waitlist conditions. In a waitlist comparison trial, CBT with parents was superior to the waitlist group, and 71% of youth were diagnosis free at 1-year follow-up (Bogels & Siqueland, 2006). Using a similar design, an parent–child combined intervention aimed at improving parent–child communication skills and social supports was superior to waitlist (69% diagnosis free vs. 6% after 6–10 sessions) (Shortt, Barrett, & Fox, 2001). In a study of school refusal and anxiety, researchers found that CBT + parent and teacher training were superior to a waitlist condition, based on both anxiety diagnosis and school refusal behavior (King et al., 1998). Studies also support parent training for youth with PTSD in combination with Trauma-Focused CBT or similar parent-inclusive interventions (Deblinger, Lippmann, & Steer, 1996; Deblinger, Steer, & Lippmann, 1999; King et al., 2000). However, family therapy in the absence of a cognitive behavioral intervention may have reduced efficacy (Kolko, 1996; Silverman, Ortiz, et al., 2008).

Both an open trial and a multiple-baseline across subject designed trial found benefits for parent-only skills training (Eisen et al., 2008; Thienemann et al., 2006). However, three studies did not find that CBT with parent involvement outperformed child-focused CBT (Kendall et al., 2008; Nauta et al., 2003; Ost, Svensson, Hellstrom, & Lindwall, 2001). Efficacy for parent training in youth with specific phobias has

Table 27.1 Select controlled parent training trials for child anxiety[a]

Study	Diagnoses	*N*	Ages	Sessions	Conditions	Parent content[b]	Outcome
Barrett et al. (1996)	GAD, SOP	70	7–14	12	Parent and child CBT together; child-only CBT; WL	1,2,3,4,6	Parent + child = child only > WL[c]
Barrett (1998)	GAD, SOP	60	7–14	12, group	Group child-only CBT; group parent and child CBT together; WL	1,2,3,4,6	Parent + child > child only > WL[d]; parent + child = child only > WL[c]
Bernstein, Bernat, Victor, and Layne (2008)	GAD, SOP, SAD	61	7–11	11, group	Group child-only CBT; group child-only CBT + 9 sessions of parent training (without child); no-treatment control	1,2,3	Child only = parent + child > control[d]; parent + child > child only at follow-up[d]
Cobham et al. (1998)	GAD, SP, SOP, SAD	67	7–14	4, group	Child-only CBT; parent and child CBT together	1,2,3,4,6	For children of anxious parents: parent + child > child only[c]; parent + child = child only for non-anxious parents
Kendall et al. (2008)	GAD, SOP; SAD	161	7–14	16	Child-only CBT, parent and child CBT together, family education (control)	1,2,3,4,5	Child only = parent + child > family education[c]
King et al. (2000)	PTSD	36	5–17	20	Child-only CBT, child-only CBT + 20 sessions of parent training (without child), WL	2,6	Child only = child + parent training > WL[e]
Nauta et al. (2003)	GAD, SP, SOP, SAD, PD	79	7–18	12	Child-only CBT, child-only CBT + 7 sessions of parent training (without child), WL	1,2,3	Child only CBT = child + parent training > WL
Spence et al. (2000)	GAD, SP, SOP, SAD	50	7–14	14, group	Group child-only CBT; group parent and child CBT together; WL	1,2,6	Child only = parent + child > WL[c]
Wood et al. (2006)	OCD, GAD, SP, SOP, SAD	40	6–13	12–16	Child-only CBT, parent and child CBT together	1,2,3,4,5	Parent + child > child only[d]

[a] Selected studies must have (a) with/without parent comparison conditions, (b) controlled design, and (c) outcome based on diagnostic status or clinician rating of improvement or clinical symptoms using a well-standardized instrument

[b] Based on review of the study and reviews by Ginsburg and Schlossberg (2002), Silverman, Ortiz, et al. (2008), Silverman, Pina, et al. (2008)

[c] Outcome based on no longer meeting diagnostic criteria

[d] Outcome based on clinician ratings of improvement

[e] Outcome based on clinician-rated symptom decrease for targeted disorder (e.g., PTSD symptoms)

Parent treatment components: *1* psychoeducation; *2* contingency management; *3* parent anxiety management; *4* parent–child problem solving/communication training; *5* in-session training for parents to deliver CBT components; *6* parents trained to model of coping behaviors

GAD Generalized anxiety disorder (or overanxious disorder; DSM-III-R); *SP* specific phobia/simple phobia; *SOP* social phobia/social anxiety disorder; *SAD* separation anxiety disorder; *OCD* obsessive compulsive disorder; *PTSD* post traumatic stress disorder; *CBT* cognitive behavioral therapy; *WL* wait list

also been reported (Dadds, Smith, Webber, & Robinson, 1991).

Several studies examine parental training in the context of group CBT. Outcomes are favorable in comparison to waitlist/no-treatment conditions for youth with separation anxiety disorder (SAD), generalized anxiety disorder (GAD), OCD, and social phobia (SP) (Barrett, Healy-Farrell, & March, 2004; Barrett, 1998; Barrett et al., 1996; Cobham et al., 1998; Silverman, Kurtines, Ginsburg, Weems, Lumpkin, et al., 1999; Spence et al., 2000; Spence, Holmes, March, & Lipp, 2006; Victor, Bernat, Bernstein, & Layne, 2007). Several studies included a comparison of group CBT with and without a formal parent training component. Generally, studies did not find group differences when outcome status was based on diagnostic criteria (e.g., Barrett et al., 2004; Barrett et al., 1996; Spence et al., 2000, 2006). However, Barrett and colleagues (1996) found that group therapy CBT with parents was superior based on clinician ratings of improvement at posttreatment and at 12-month follow-up (see Silverman, Pina, et al., 2008 for a review). Another study found an interaction between treatment conditions (group CBT with and without parent inclusion) and parental anxiety (anxious vs. nonanxious parents) (Cobham et al., 1998). Among youth with nonanxious parents, 82% of youth in the child group CBT no longer met diagnostic criteria, comparable to 80% in the CBT+parents. However, only 39% of youth with anxious parents benefited from CBT alone in comparison with 77% whose parents received anxiety management training. Outcomes from a school-based CBT did not initially differ on the basis of adding parent training sessions (Bernstein et al., 2008). However, child anxiety was lower at 1-year the follow-up among youth whose parent's participated in training.

Only one study compared individual family and group (multi-family) formats of CBT+parent training (Manassis et al., 2002). The authors found that although both conditions yielded improvement, the nongroup format produced greater gains. The benefit of individual family vs. group CBT may be explained because the former can be tailored to the specific needs of the family (Bogels & Siqueland, 2006; Silverman, Pina, et al., 2008).

There is little evidence suggesting that general, nonanxiety specific, parent training approaches benefit youth with anxiety disorders. One study reported an improvement in internalizing symptoms following implementation of a behavioral parent training protocol (Cartwright-Hatton, McNally, White, & Verduyn, 2005). Treatment consisted of teaching labeled-praise, contingency management, and improving general parent–child interactions. However, participants were not evaluated for the presence of an anxiety disorders (evaluation was based on improvement in internalizing symptoms).

Interpretation and Limitations of Research Findings

There is a consensus that parents impact the development and maintenance of childhood anxiety. Additionally, most experts agree that parent involvement is an important aspect of treatment. However, the extant research has produced mixed findings regarding the necessity of parenting interventions for child anxiety disorders. Across studies and specific syndromes, parent training approaches have proved superior to control conditions (e.g., waitlist/no-treatment controls, active psychosocial controls) and, at the very least, equivocal to child-focused treatment without substantial parent involvement. Notably, a number of studies suggest no added benefit (defined by lack of change in diagnostic status and/or lack of clinician-rated symptom improvement) to structured parent training or family therapeutic components.

Despite these results, expert guidelines and consensus support parent inclusion in the treatment of child anxiety (American Academy of Child and Adolescent Psychiatry (AACAP), 1998, 2007; Cartwright-Hatton et al., 2004; Ginsburg & Schlossberg, 2002). Individual child CBT, medication, and their combination are evidence-based interventions (Walkup et al., 2008). However, the fact that youth-centered treatments for anxiety have produced reliably strong outcomes does not negate the possibility that resulting changes in the child's symptoms/behavior impact the family

system, possibly producing reciprocal family/parenting changes. Consequently, the efficacy of individual child treatments does not supersede potential advantages for parental inclusion.

Although few parenting interventions meet criteria for empirically-supported treatments (Chambless & Hollon, 1998; Nathan & Gorman, 2002; Silverman, Pina, et al., 2008), this is due to methodological and procedural variance rather than lack of efficacy. Many approaches have not been fairly tested and external validity of the findings is mostly absent (Weisz, Doss, & Hawley, 2005). For example, to be considered empirically-supported, interventions must be reproduced using controlled designs (Chambless & Ollendick, 2001) – comparing parenting interventions across studies is like comparing oranges to eggplant. Three different research teams may implement similar interventions, but with slightly different manuals and approaches. Even the definition and application of "parent involvement" or "parent training" or "family therapy" in the treatment is highly variable and inconsistently applied. Some studies include only single parent training aspects (e.g., contingency management or psychoeducation), whereas other studies are more comprehensive. Across studies, the content covered in parent sessions varies: for example, parental anxiety management, family problem solving, the training of parents to be lay-therapists, and improving parent–child communication. Nevertheless, the conditions may be labeled identically (e.g., family CBT or parent training; see Silverman, Pina, et al., 2008 for a review). Therapist–parent contact ranges from brief, post-session "check-ins" to participation in the entire session. In some trials, there are consistent, individual parent-training sessions while in others, parents and children are seen concurrently.

Moreover, results from treatment comparison trials must be interpreted in the context of their methodological limitations. For example, most of the aforementioned research involves participants recruited to university-based study centers (Bogels & Siqueland, 2006). Subjects may not be representative of family dysfunction and psychopathology found in referred or community samples (Weisz et al., 1992). Additionally, parenting interventions were not tailored to specific family needs (Manassis et al., 2002). To maximize adherence and treatment success with cognitive-behavioral based therapies for child anxiety, the approaches should be flexible and consider individual family factors and psychosocial stressors (Albano & Kendall, 2002). It is noteworthy that extant research lacks controlled comparisons of child-focused vs. child + parent-focused interventions targeting participants specifically identified on a basis of having family functioning struggles. Given that parent anxiety management benefited child outcomes for youth of anxious parents (but not of nonanxious parents; Cobham et al., 1998), targeted approaches appear warranted.

Dismantling studies is challenging due to several other limitations. Study designs run the gambit from single subject to randomized controlled trials. Additionally, certain studies examine a broad range of anxiety disorders, while others focus on a specific syndrome. Other sample characteristics limit interpretation: many of the extant studies do not include older adolescents or children under age 7, limiting generalizability (Bogels & Siqueland, 2006). Criteria for outcome also vary across studies (e.g., symptom improvement of rating scales, diagnostic remission, clinician-rated improvement scales). Additionally, diagnostic remission may not be sufficiently sensitive to treatment effects (especially in comparing two active treatments; e.g., child-only vs. child + parent components), and many of the best designed randomized controlled trials are opting to use clinician-rated improvement as an alternative (e.g., Storch, Geffken, Merlo, Mann, et al., 2007; Walkup et al., 2008; Wood et al., 2006). Further, raters of improvement and diagnostic-status vary across studies – e.g., child, parent, therapist, vs. independent-observer. Independent evaluators range from undergraduate students to senior psychologists and physicians, limiting generalization across studies. Moreover, given that outcomes are based on parent report (e.g., via a diagnostic interview), the level of parental participation in treatment may influence ratings (Hawley & Weisz, 2005). Comparing group-based treatment to individual family treatments adds to the obfuscation.

On a related note, few studies consider family-based improvement outcomes while evaluating merits of parenting and family-based treatment approaches for child anxiety. Child anxiety occurs within a family system. Although many of the parent-focused approaches in this chapter describe their interventions as family therapy, many of the interventions more accurately depict child-focused procedures with or without some degree of family (or more frequently parental) involvement. In a strict sense, family therapy targets the family system and, depending on the family theoretical approach, family members are seen together, often including multiple parents, siblings, and extended family. The child's anxiety is not the focus of the intervention – the family system that produces symptoms (e.g., child anxiety) is the target. Comprehensive family-based interventions (e.g., Bogels & Siqueland, 2006; Wood et al., 2006) suggest that family therapy may be superior to individual therapy.

However, in many cases, comprehensive family therapy may be an elephant-gun approach to treating a child's anxious symptoms. Although many parents readily endorse that parenting and other family factors may have impacted their child's anxiety, others are steadfast in the "fix-him" approach and are reluctant to accept parent-training, let alone a family-model of treatment. In fact, parents and children often disagree as to the presenting problem (Hawley & Weisz, 2003). Level of family conflict, communication, accommodation, parent anxiety, and parent psychological awareness might dictate the battery, order, and extensiveness of family interventional techniques.

Simply increasing parental inclusion within child sessions may increase therapeutic alliance (Hawley & Weisz, 2005) and consequently improve treatment outcomes. Comparing effect sizes across studies suggests that the substantial in-session inclusion of parents is beneficial. For example, a trial of intensive CBT for OCD, in which parents were included through all sessions yielded a high effect size (ES = 2.62) (Storch, Geffken, Merlo, Mann, et al., 2007) in comparison to child-focused CBT protocols for OCD (with minimal or intermittent parental inclusion is CBT sessions). For example, the Pediatric OCD Treatment Study (2004) reported effect sizes of 0.97, 0.67, and 1.4 for child-focused CBT, sertraline, and CBT + sertraline. Effect sizes for a weekly CBT approach with full-session parental involvement (ES = 1.73; Storch, Geffken, Merlo, Mann, et al., 2007) also exceeded those in POTS, suggesting that the parental involvement (rather that the intensive CBT protocol) component may explain the differences. It is also noteworthy that treatment center site differences brought down the overall effect size in the POTS trial. Similarly, a controlled trial of Trauma Focused CBT for PTSD with significant parental involvement (Smith et al., 2007) produced an effect size of 3.43 (>0.8 is considered a large effect) (Cohen, 1988), larger than comparable studies will less substantial parental inclusion. Although parent contact alone (e.g., education alone; Kendall et al., 2008) is unlikely to be sufficient for treating anxiety, future studies should compare degrees of participation (e.g., parents participate in most/all of every session; parents participate in portions of session; separate parent or family sessions).

Conclusions and Directions for Research and Practice

Even though the degree to which parent training interventions augment benefits from child-focused CBT for child anxiety is unclear, it is the general consensus that family involvement in treatment is necessary (AACAP, 2007). Although findings are mixed, data suggest that parent- and family-based interventions are at least equivalent, if not superior, to child-focused interventions. Overall, the extant literature is limited by significant methodological variability and may underestimate the impact of parent components in the treatment of child anxiety.

A number of research questions remain. First, we lack sufficient analysis of specific parenting and family behaviors that should be considered when deciding the optimal level of family involvement in a child's treatment. Second (and relatedly), future research should evaluate targeted approaches for specific family problems. In other words, clinicians need tools to identify which

families may benefit from which interventions. Third, research should be expanded into community-based samples, generalizing findings outside of recruited and relatively homogenous samples. Fourth, family-based outcomes should be considered. When evaluating the efficacy of parenting and family interventions, diagnostic status may be an insufficient barometer.

There are several considerations when integrating parent training and family approaches into practice. The first series of recommendations focus on assessment. At the onset of treatment, the clinician should assess child and parent attitudes, attributions, and goals for therapy. Additionally, careful screening for significant parental anxiety and family conflict should be conducted. Throughout treatment, the therapist should monitor for accommodation, modeling, overprotective behavior, and reinforcement of anxiety-maintaining behaviors. The second set of considerations includes specific aspects of therapy. First, whenever possible, it might be helpful to meet with the family together. Qualitatively, greater in-session parent participation appears to have advantages (Hawley & Weisz, 2005; Storch et al., 2007). Second, several parent-focused techniques appear helpful, e.g., psychoeducation, training/modeling of therapeutic techniques, and contingency management training. Anxiety management for parents and communication-skills training may benefit particular families. Additional family based interventions may be necessary, depending on the family psychopathology (including individual treatment for parents).

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School-Based Interventions for Anxiety in Youth

28

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Anxiety disorders are a costly problem, accounting for approximately 31% of health care costs in the United States (Rice & Miller, 1993). This expense, in part, is due to the high prevalence of these disorders (Costello & Angold, 1995; Klein & Pine, 2002), and their associated immediate and long-term impairment. Anxiety disorders can cause substantial distress and interfere with school performance, family interactions, and social functioning (Ialongo, Edelsohn, Werthamer-Larsson, Crockett, & Kellam, 1995; Langley, Bergman, McCracken, & Piacentini, 2004). In addition to having an early onset, anxiety disorders are associated with a chronic or fluctuating course into adulthood if left untreated (Achenbach, Howell, McConaughy, & Stanger, 1995; Costello & Angold, 1995; Ferdinand & Verhulst, 1995; Pine, Cohen, Gurley, Brook, & Ma, 1998). Childhood anxiety disorders predict risk for mood and anxiety disorders at later ages (Cole, Peeke, Martin, Truglio, & Seroczynski, 1998; Regier & Robins, 1991), and are associated with suicide attempts and psychiatric hospitalization (Ferdinand & Verhulst, 1995; Klein, 1995; Pine et al., 1998), highlighting the importance of intervening early and effectively.

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Several cognitive-behavioral, manualized treatments have been systematically evaluated and shown to be promising interventions for childhood anxiety (e.g., Beidel, Turner, & Morris, 1998; Kendall, 1991, 1994; Kendall et al., 1997; Kendall, Safford, Flannery-Schroeder, & Webb, 2004; Silverman et al., 1999). Yet, despite the availability of effective treatments, anxiety often goes undetected and untreated (Masia Warner, Fisher, Shrout, Rathor, & Klein, 2007). For example, one study showed that 17% of children in a pediatric primary care setting met criteria for an anxiety disorder, with the lowest rate of reported service use compared to children with other diagnoses (Chavira, Stein, Bailey, & Stein, 2004).

This problem is consistent with a larger literature documenting that the majority of children in the community who would benefit from mental health services do not receive them (Burns et al., 1995; Flisher et al., 1997; Leaf, Alegria, Cohen, & Goodman, 1996; Offord et al., 1987; Verhulst, Van der Ende, Ferdinand, & Kasius, 1997). Many children and families have difficulties accessing adequate mental health care (Essau, Conradt, & Petermann, 1999; Wittchen, Stein, & Kessler, 1999), and fewer than 20% of those who do seek treatment receive efficacious treatments like cognitive behavioral therapy (CBT; Collins, Westra, Dozois, & Burns, 2004; Labellarte, Ginsburg, Walkup, & Riddle, 1999). There is growing recognition that community mental health centers and other standard sites for service delivery are insufficient for ameliorating this situation (Weist, 1999). Waiting lists are often long, no-show and

D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_28, © Springer Science+Business Media, LLC 2011

drop-out rates are high, youngsters are often reluctant to seek services in these settings, and research has been unable to support the effectiveness of community treatment (Weist, 1999; Weisz, Donenberg, Han, & Weiss, 1995). This failure to deliver adequate care to children is a major concern for policymakers, clinicians, and researchers in child psychology and psychiatry.

Rationale for School-Based Intervention

Schools play an important role in addressing the unmet mental health needs of youth by potentially increasing access to care in a cost-effective manner. School-based services offer many advantages over traditional mental health settings. First, schools provide unparalleled access to youth (Adelman & Taylor, 1999; Weist, 1997), representing a single location through which the majority of children can be reached (Anglin, 2003). They also reduce barriers to treatment such as cost and transportation (Catron, Harris, & Weiss, 1998; Wu et al., 1999), possibly increasing compliance and attendance since they are already on location (Armbruster & Lichtman, 1999).

Intervening in schools also provides increased opportunity for early identification and treatment. Educating school personnel and parents to better identify mental health issues and to make appropriate referrals for treatment may prevent the development of secondary dysfunction (Weist, 1999). Furthermore, providing treatment in schools may decrease stigma associated with seeking care at mental health specialty settings (Catron & Weiss, 1994; Weist, 1999). Youth and their families might be more accepting of treatment if it is offered among the many routine services provided by schools.

School-based treatment offers additional advantages beyond increased identification and access to care. Intervention implemented within schools allows for the practice of skills in real-world situations, thereby increasing the likelihood of generalization to the natural environment (Evans, 1999; Evans, Langberg, & Williams, 2003). This advantage may be particularly relevant in the treatment of anxiety disorders since many of the most commonly feared situations occur at school (e.g., approaching peers, initiating conversations, being assertive, using public bathrooms, separating from caregivers, and worrying excessively about grades). The increased accessibility of naturally anxiety-provoking situations and locations, and the availability of teachers and peers, are important resources for engaging children in relevant exposure exercises. For instance, children can complete an exposure to enter into a classroom late, answer questions in class, or initiate conversations with peers. The therapist might even accompany the child during school-based exposure tasks to provide additional coaching or encouragement. In this way, treatment delivered in school can reduce the division between the clinical setting and the naturalistic environment.

There are many advantages of school-based services, but systematic evaluation of their effectiveness has been limited (Adelman & Taylor, 1998; Hoagwood & Erwin, 1997; Leff, Power, Manz, Costigan, & Nabors, 2001; Power, Manz, & Leff, 2003; Rones & Hoagwood, 2000), and schools rarely implement interventions supported by scientific evidence (Rones & Hoagwood, 2000; Walker, 2004). Therefore, an important direction for school-based mental health is to determine the transportability and efficacy of evidence-based programs in school settings. Investigations of school-based interventions targeting anxiety are in their infancy. However, several studies have been conducted that have shown promising results.

School-Based Intervention Outcome Research

The current literature delineates three types of school-based interventions: universal, selective, and indicated. These three types map onto earlier classifications of primary, secondary, and tertiary prevention protocols (Caplan, 1964). Universal intervention programs or primary prevention protocols, provide preventative care for all students. Selective interventions or secondary prevention

programs, are utilized only with those youth who have been identified as being at risk for developing a disorder. The risk factors can be child focused (e.g., some manifest symptoms, but no disorder) or environmental (e.g., parental anxiety disorder or environmental stressors). Indicated interventions or tertiary prevention programs, are implemented only with those youth who meet criteria for a clinical disorder.

Universal Prevention Studies

Three universal prevention programs have been developed to address anxiety in the school setting. One targets anxiety at the preschool level, another is designed for the primary or secondary school level, and the third aims to promote coping in elementary school children routinely exposed to threats of terrorism.

REACH for RESILIENCE

Program Description

The *REACH for RESILIENCE* program is a universal anxiety prevention program aimed at the parents of children aged 3–6, delivered in the preschool setting (Dadds & Roth, 2008). This program includes six biweekly group sessions attended by parents and teachers over a 3-month period. The sessions address the key cognitive-behavioral topics: psychoeducation about stress and anxiety, behavioral management techniques, cognitive restructuring, and problem-solving. The goal of the program is to provide parents with skills to help their children develop positive future expectations, in order to prevent the development of anxiety or depressive disorders. Early sessions focus on using behavioral reinforcement (e.g., verbal encouragement and behavior charts) to promote self-esteem and increase social skills, as well as teaching parents relaxation techniques to help children decrease physiological arousal. Parents are next taught how to identify and challenge anxious cognitions and attribution styles, focusing primarily on reducing pessimistic and catastrophic thinking styles. By the end of treatment, parents have also learned problem-solving strategies, how to instill positive social skills, and how to integrate all of the information provided into a comprehensive approach for addressing their children's emotional needs.

Outcome Studies

A randomized controlled trial of over 500 preschoolers was conducted comparing *REACH* with no intervention. Parents of about 1,600 preschoolers across 25 schools were sent letters inviting them to participate in a longitudinal study (Dadds & Roth, 2008). Randomization occurred by school, with 204 families enrolled in the intervention, and 379 in the no-treatment comparison group. Of those assigned to the intervention, half attended only the first session. The program was implemented at the preschools by an experienced psychologist.

At post-treatment, according to teacher report, children in the intervention scored lower on the and anxious-withdrawn subscales than the comparison group. At 12-month follow-up, children in the intervention group remained less Angry-Aggressive than those in the comparison, but no longer differed on Anxious-withdrawn symptoms. No group differences in parent report were observed. Further analysis was conducted splitting the sample into "low risk" and "at-risk" categories, with at-risk defined as above the 50th percentile on parental stress and child shyness. Participation in at least four sessions significantly increased the likelihood of moving from at-risk to low-risk (61%) compared to the untreated comparison group (49%). The clinical significance of this finding is questionable considering that half of the comparison group improved without intervention. A potential bias is that treatment drop-outs reported significantly lower baseline "stress" and "difficult child" scores on a self-report measure than treatment completers. This may suggest that parents who stayed in the program had children with more significant emotional or behavioral symptoms, making it difficult to form conclusions about the benefits of this program for universal prevention. Clinically, however, this is promising, as it suggests that such parents sought help and found the intervention to be valuable.

FRIENDS

Program Description

The *FRIENDS* program is a school-based universal anxiety prevention program for school-aged youth (Barrett & Turner, 2001) adapted from the *Coping Koala* (Barrett, Dadds, & Rapee, 1996), which was based on the *Coping Cat* (Kendall, 1994). *FRIENDS* is an acronym designed to help children remember the various skills learned during the treatment, which include emotion recognition and regulation, relaxation skills, cognitive awareness and restructuring, problem-solving, and in vivo exposure. The acronym is as follows: F = 10 weekly feeling worried; R = relax and feel good; I = inner thoughts; E = explore plans of action; N = nice work, reward yourself; D = don't forget to practice; S = stay cool. *FRIENDS* consists of 10 weekly sessions, with two booster sessions occurring 1 and 3 months after the final group. In addition, four parent sessions are used to inform parents about the program skills, and to enhance parenting techniques surrounding anxiety management.

Outcome Studies

Two studies (Lowry-Webster, Barrett, & Dadds, 2001; Barrett & Turner, 2001) were conducted evaluating *FRIENDS* with 10–13 year olds in Brisbane, Australia. The first of these compared *FRIENDS*, delivered by trained classroom teachers, to a waiting list control in 7 schools (Lowry-Webster et al., 2001). Randomization occurred by school, rather than at the classroom level. Following recruitment of 594 eligible youth, 531 youth completed the study (with 392 in the intervention, 139 in the waiting list). Self-report measures of anxiety significantly decreased from pre- to post-treatment for both groups, but the magnitude of the change was significantly greater for the intervention group. In addition, of those who were classified as "at-risk" for an anxiety disorder based on high baseline anxiety ratings, only 25% of those in the intervention condition remained at risk at post-treatment when compared to 55% of the wait-list. These findings are promising, however, it should be noted that results are limited to child self-report data; no ratings were provided by parents or teachers. Differences were maintained 1 year following intervention (Lowry-Webster, Barrett, & Lock, 2003). At follow-up, diagnostic interviews were conducted for youth who had scored in the clinically elevated range on baseline depression or anxiety self-report measures, indicating that 85% of treated youth were diagnosis free, compared to only 31% of the waiting list group.

The other study compared *FRIENDS* to usual instruction across 10 schools (Barrett & Turner, 2001). The schools were randomly assigned to teacher-led intervention (TI), psychologist-led intervention (PI), or usual instruction (UI). The study included 253 children in the TI group, 152 in the PI group, and 84 in the UI group. Sessions were conducted weekly during regular school hours. Children in both treatment conditions reported significantly decreased anxiety when compared with UI on two self-report measures of anxiety; no differences were found between the two treatment groups on these measures. In addition, based on elevated pre-treatment child reports of anxiety, 18% of children in each treatment group were identified as "at-risk" compared with 11% of these in UI. At post-treatment, at-risk children in the intervention groups were three times more likely to be considered no longer at-risk than those in UI group. However, these results should be interpreted with caution as these analyses were insufficiently powered given the low number of children at pre-treatment who were classified as at-risk.

FRIENDS was also examined in an open trial in Britain (Stallard, Simpson, Anderson, Hibbert, & Osborn, 2007). Eighty-nine youth aged 9–10 years in three different schools were enrolled in the program. The intervention was delivered by school nurses after a 2-day training with continued monthly group supervision by an experienced psychologist. Assessments were conducted 6 months prior to the start of the intervention, immediately prior to the start of the intervention, and 3 months after intervention completion. Results revealed that overall self-reported anxiety scores were stable during the 6 months prior to the intervention, and then decreased significantly from immediate pre- to post-treatment,

lending additional support for the effectiveness of *FRIENDS*.

A series of separate studies assessed the longitudinal outcomes of *FRIENDS*. Lock and Barrett (2003) evaluated the *FRIENDS* program in seven different schools, with 336 youth in grade 6 (9–10 years of age) and 401 youth in grade 9 (14–16 years of age). The focus of this study was to better understand the long-term (12-month) effects of the intervention when implemented at two different developmental levels. Youth were randomized to either *FRIENDS* or to a monitoring group. Results suggested that the program was successful in reducing anxiety in both age groups, though the younger group showed a significantly greater magnitude of change than the older group. This finding indicates that a preventative intervention for anxiety may be more beneficial for younger children.

A follow-up study was conducted evaluating this same sample at 24- and 36-months post-intervention (Barrett, Farrell, Ollendick, & Dadds, 2006). One school from the initial sample withdrew, leaving 669 students from 6 schools. Consistent with the findings of the previous study, the younger groups assigned to the treatment conditions scored significantly lower on the two self-reported measures of anxiety across both follow-up time points when compared with those in the monitoring group, but the older group was no different than those in the control. In addition, at 36-months post-treatment, only 12% of the intervention group was assessed as being "high risk" (e.g., scoring in the top 10% on an anxiety self-report measure) as compared with 31% in monitoring group.

Overshadowing the Threat of Terrorism

Program Description

The *Overshadowing the Threat of Terrorism* (OTT) program was developed in Israel to help school-aged children cope with the threat and exposure to terrorism (Berger, Pat-Horenczyk, & Gelkopf, 2007). This program includes 8 weekly, 90-min group sessions, which address psychoeducation about stress and trauma, feeling identification, management of somatic symptoms, cognitive restructuring, and enhancing social support. In addition, the program includes skill training using meditative practices, bio-energy exercise, art therapy, and narrative techniques for reprocessing traumatic experiences. Two parent sessions focus on psychoeducation about normative and problematic reactions to terror-related events, and teach parents coping skills such as breathing, mindfulness meditation, and relaxation.

Outcome Studies

A quasi-randomized controlled trial of 142 second to sixth grade students was conducted comparing *OTT* to a waiting list. Randomization occurred by classroom, with five classrooms assigned to receive the intervention immediately ($n = 70$ students), and the other five classrooms waited for the intervention ($n = 72$ students). The program was implemented by teachers after completing five 4-hour training sessions (20 hour). Teachers participated in three 3-hour supervisory sessions during program implementation.

Participants were assessed at baseline and 2 months after completion of the program using self-ratings of postposttraumatic stress disorder (PTSD) symptoms, functional impairment, somatic complaints, and generalized and separation anxiety. Students who received the *OTT* program reported significant reductions on symptoms and impairment when compared to those in the control group. In addition, lower-grade level students (second and third grade) showed greater reductions in PTSD severity, somatic complaints, and separation anxiety compared to their older counterparts (fourth to sixth graders).

Summary of Universal Prevention

Overall, universal prevention has yielded mixed evidence for its short- and long-term benefits, with some promising results particularly for elementary-aged children. Positive aspects of universal prevention are that it tends to be less stigmatizing since all youth are involved, and minimal screening is required. However, it is questionable whether the benefits of universal

prevention outweigh the resources it requires, and thus removes from other academic or extracurricular activities. Additionally, in moderating the content to be applicable for all students, universal prevention interventions may not be as potent as indicated interventions.

Indicated Prevention Programs

The ability to allot resources for only those identified as *at-risk* is an important benefit of selective and indicated interventions. Four indicated programs have been developed to intervene with youth demonstrating anxiety symptoms. Two are modifications of *FRIENDS* for school-age youth. The third, *Cool Kids*, is designed for either school-age or adolescent populations. The fourth was developed to address trauma exposure and symptoms of PTSD.

Queensland Early Intervention and Prevention of Anxiety Project

Program Description

Like *FRIENDS*, this group program was based on the *Coping Koala: Prevention Manual* (Barrett, Dadds, & Holland, 1994), which utilizes the *Coping Cat* FEAR Plan (Kendall, 1994). *F* = feeling good by learning to relax; *E* = expecting good things to happen through positive self-talk; *A* = actions to take in facing up to fear stimuli; and *R* = rewarding oneself for efforts to overcome fear or worry. Children learn about the physiological, cognitive, and behavioral aspects of anxiety and how to counteract them. These skills lead to the development of a plan for graduated exposure to feared stimuli. The intervention is delivered to small groups of children during weekly, 1–2 hour sessions over a 10-week period. Parent sessions are held at weeks 3, 6, and 9 to address parenting techniques, to familiarize parents with the skills the children were learning, and to explore how parents can use the techniques to address their own anxiety.

Outcome Studies

Dadds, Spence, Holland, Barrett, and Laurens (1997) compared this intervention to a wait-list control in 7–14 year-old school children. Children were selected based on self-report scores and teacher nominations. Of the 1,700 youth, 128 were enrolled in the program with 100 meeting diagnostic criteria for one or more anxiety disorders. The intervention was delivered by trained psychologists. There were no significant differences between groups for diagnostic rates or child-rated anxiety immediately following intervention. However, at 6-month follow-up, approximately 25% of the intervention group, compared to 60% of the control, met diagnostic criteria for an anxiety disorder. In addition, although children's reports did not indicate a change in anxiety, both therapists' and parents' ratings of children's anxiety, avoidance, and overall functioning were significantly improved for the intervention group relative to the control. Moreover, a longitudinal follow-up conducted 2 years post-treatment showed lower rates of anxiety disorders in children who participated in the intervention (20%) versus the control (40%) (Dadds et al., 1999).

FRIENDS plus Parent-Training

Program Description

This program is also a modification of *FRIENDS* with the addition of weekly group parent training (Bernstein, Layne, Egan, & Tennison, 2005). The enhanced parent component addresses the impact of the child's anxiety on the family and helps parents to understand how family relationships may maintain anxiety. In addition, parents are taught behavioral strategies to encourage children to face their fears. Finally, parents are instructed how to manage their own anxiety to be a more effective coach and better model for their child. No significant changes were made to the *FRIENDS* child component; one minor change is that the intervention was shortened by one session, though no content was lost.

Outcome Studies

Sixty-one elementary school children aged 7–11 years old with either features or diagnoses of separation, generalized, or social anxiety disorder with mild to moderate symptomatology were randomized to *FRIENDS*, *FRIENDS* with enhanced parent training, both delivered by experienced CBT therapists, or a no-treatment control. Of interest, the intended control group had originally permitted families to access whatever services the school recommended, and provided contact information for a school social worker. However, consistent with the documented low service use in this population, no child in the control group received services, and the comparison became a no-treatment control (Bernstein et al., 2005). Clinician-, child-, and parent-report measures demonstrated significant benefits of both active treatments compared to the no-treatment control. Results were mixed regarding the additional benefits for the inclusion of parent training. It should be noted that the sample was constricted because it excluded severe anxiety, common comorbid disorders (e.g., depression or ADHD), and psychotropic medication usage, raising questions as to the generalizability of the findings.

Cool Kids

Program Description

Unlike *FRIENDS*, which is an adaptation of a treatment protocol, *Cool Kids* was specifically designed to be an indicated intervention (Mifsud & Rapee, 2005). *Cool Kids* consists of eight sessions delivered to small groups of youth during school hours by a trained mental health provider. Separate adolescent and child protocols are available, and the level of parental involvement varies with the age of participants. More specifically, parents may be provided with two information sessions to facilitate parents' understanding of the intervention and to promote involvement or, if more parental assistance is required, weekly parent content is also available. Early sessions include rationale for treatment, psychoeducation about anxiety, identifying and restructuring anxious cognitions, and emotion identification and regulation. By session four, youth are encouraged to begin engaging in graded exposures; these exposures are emphasized throughout the remainder of treatment. In addition to continuing exposures, the remaining sessions teach skills for problem-solving, social interaction, handling bullying or teasing, and increasing assertiveness.

Outcome Study

Cool Kids was evaluated in a sample of 91 children, aged 8–11 years, with notable anxiety symptoms, from 9 schools in a low socioeconomic area. Schools were randomly assigned to either the active intervention or a waiting list. Each intervention group was implemented by a school counselor in conjunction with a community based mental health worker who had attended a 1-day training regarding the intervention. No ongoing supervision was provided by the trainers. Children who participated in the active intervention showed significant improvement immediately after treatment and at 4-month follow-up, based on teacher and child report. Unfortunately, parents did not return enough data for meaningful statistical analyses at either post or follow-up.

UNICEF School-Based Psychosocial Program for War-Exposed Adolescents

Program Description

This treatment was developed within an ecologically-minded framework, given the chronic environmental stressors inherent to living in a country at war. The protocol consists of four modules totaling about 22 sessions. The first module is comprised of six sessions aimed at developing group cohesion, understanding the rationale for treatment, and increasing coping skills such as relaxation, cognitive restructuring, and seeking support from others. The end of this module typically coincides with the winter holidays; as such, the final session focuses on coping with trauma

and grief triggers inherent in the upcoming holiday season. Module two contains 8–10 sessions on narrative exposures that are conducted using written and oral recounts of the trauma experienced by each group member. Module three consists of four sessions focused on grief processing, and the final module consists of three sessions for setting positive life goals.

Outcome Studies

Two uncontrolled studies of this intervention have been conducted. In the first study, 55 students (aged 11–20) from 10 schools throughout Bosnia and Herzegovina participated (Layne et al., 2001). Treatment was delivered in a group format during the school day, with sessions lasting 80–100 min. Groups were led by dyads of trained school counselors. At post-treatment, youth reported decreases in trauma symptoms on a self-report questionnaire, with mean scores below the clinically-distressed range.

The same protocol was tested in a Los Angeles school, where urban environmental stressors often include poverty, crime, and violence. Following the screening of 812 students for trauma-exposure and distress, 26 youth (aged 11–14) were enrolled in the school-based group treatment (Saltzman, Pynoos, Layne, Steinberg, & Aisenberg, 2001). Youth who participated in the group showed statistically significant improvement in trauma symptoms from pre- to post-treatment, though the overall mean scores remained in the clinically-elevated range. However, it should be noted that this sample was quite impaired, with over 50% scoring in the severe to very severe range of self-reported PTSD symptoms. Notably, approximately 75% of those who met criteria for study entry had never been identified as having trauma-related distress or been referred for treatment, again highlighting the lack of identification and treatment of anxious youth.

Summary of Indicated Interventions

Indicated intervention yielded more consistent positive results than universal prevention. One potential explanation is that selective and indicated interventions are often "full strength." That is, the protocols focus on those who are displaying anxiety symptoms, and address specific difficulties rather than offering general skills. All studies used trained CBT therapists to deliver the intervention with the exception of *COOL KIDS*, which employed school and community mental health counselors. The use of specialized clinicians may create obstacles to wider dissemination and sustainability of school programs. Finally, the existing indicated prevention studies are limited by inadequate methodological controls; some trials did not use control groups, while others compared CBT to waiting lists or no-treatment conditions.

Treatment Studies

Three treatments have been developed and evaluated to treat students with anxiety disorders in schools. One program has focused on the treatment social anxiety, another on PTSD, and a third on the treatment of a variety of anxiety disorders.

Skills for Academic and Social Success

Program Description

Skills for Social and Academic Success (*SASS*) (Masia et al., 1999) is a cognitive-behavioral group intervention to treat adolescents with social anxiety disorder in the school setting. *SASS* was based on *Social Effectiveness Therapy for Children* (*SET-C*: Beidel et al., 1998) because of its demonstrated efficacy (Beidel, Turner, & Morris, 2000; Beidel, Turner, Young, & Paulson, 2005), as well as its emphasis on exposure, social skills training, and peer generalization exercises. The protocol was modified for an adolescent population (e.g., developmentally appropriate social skills, addition of training in realistic thinking) and the school environment (e.g., fewer and briefer sessions and incorporation of teachers, parents, and school peers). *SASS* consists of 12 in-school group sessions, two individual meetings, two parent meetings, two teacher meetings, four social events attended by group participants and outgoing school peers, and two booster sessions.

The 12 school sessions include realistic thinking, social skills training, and exposures that are regularly integrated into the school environment and include the assistance of school personnel or school peers (e.g., ordering and returning food in the lunchroom, starting a conversation with the principal). In addition, two individual meetings focus on setting goals and problem-solving treatment obstacles. Sessions occur during the course of the school day, with sessions lasting 40 min, to coincide with a single class period. The parent meetings address psychoeducation about social anxiety and ways to manage children's anxiety and facilitate improvement. Teacher meetings are designed to educate teachers about social anxiety, obtain information about which classroom behaviors to target, and enlist their assistance with classroom exposure exercises (e.g., reading aloud, answering questions in class). Finally, the four social events provide real-world exposures and opportunities for skills generalization. Group members practice social interactions with actual school peers in natural community "hang-outs" (e.g., bowling, laser tag, and school picnic).

Outcome Studies

SASS has been evaluated in a small open trial (Masia, Klein, Storch, & Corda, 2001), a wait-list control trial (Masia Warner et al., 2005), and an attention control trial (Masia Warner et al., 2007). In the wait-list controlled trial, 35 adolescents, aged 14–16 years, from two urban parochial schools were randomized to either *SASS* or a waiting list. Treatment was conducted by a clinical psychologist trained in the intervention. The *SASS* intervention was superior to a waiting list in reducing social anxiety and avoidance as well as enhancing functioning, as noted by blind evaluator, parent, and adolescent ratings. Of the *SASS* group, 94% were classified as responders compared to only 12% of wait-list participants. In addition, 67% of *SASS* participants, versus 6% in the wait-list group, no longer met diagnostic criteria for social phobia at post-assessment.

The second investigation compared *SASS* to a credible attention control in 36 adolescents, aged 14–16, with social anxiety disorder (Masia Warner et al., 2007). The attention control omitted any therapeutic elements considered specific to reversing social anxiety but was matched on other relevant therapy variables. It was designed to match *SASS* in overall structure with the inclusion of the four social events conducted without the outgoing school peers. The content consisted of psychoeducation about social anxiety, relaxation techniques, and support. At post-treatment, *SASS* was superior to the attention control in reducing social anxiety and improving overall functioning. Only 7% in the attention control, versus 82% in *SASS*, were treatment responders. In addition, 59% of the *SASS* group no longer qualified for a diagnosis of social phobia versus 0% of the attention control. *SASS* was also superior to the attention control 6 months beyond the cessation of treatment.

Multi-Modality Trauma Treatment

Program Description

The *multi-modality trauma treatment* (MMTT) was created by combining previously empirically-supported cognitive-behavioral treatments for adult PTSD, childhood anxiety, and externalizing behaviors (March, Amaya-Jackson, Murray, & Schulte, 1998). The *MMTT* is an 18-week school-based intervention delivered in a small group format, with one individual session occurring around the midpoint of the program. The protocol, designed to be delivered by a clinical psychologist, includes emotion recognition, relaxation skills, cognitive awareness and restructuring, the creation of graded hierarchies of exposure, exposure trials, and relapse prevention. Additional PTSD-specific content includes anger management, narrative and imaginal exposures, and trauma-related cognitive distortions. During the individual session, a hierarchy of feared situations is developed, and the first narrative exposure is implemented.

Outcome Studies

The initial evaluation of this treatment used a single-case design, staggering the start date of the program across schools (March et al., 1998). Of 1,800 children screened in Fourth through Ninth

grade across four schools, 17 met diagnostic criteria for PTSD and 14 completed the treatment. Of the 14 completers, 8 (57%) no longer met diagnostic criteria for PTSD following treatment, and 12 (86%) no longer had the diagnosis at 6-month follow-up. Self-reported anxiety symptoms were also significantly decreased at both post-treatment and follow-up compared to baseline.

Baltimore Child Anxiety Treatment Study in the Schools

Program Description

The *Baltimore Child Anxiety Treatment Study* (BCATSS) was developed to tailor child anxiety treatment to an inner city population that is typically underserved (Ginsburg, Becker, Kingery, & Nichols, 2008). Differing from most other school interventions, *BCATSS* is delivered in an individual rather than group format. *BCATSS* consists of 12 sessions conducted during regular school hours. Sessions are approximately 35 minutes in length to coincide with a single class period. The program is designed to be implemented by school psychologists, following a brief training on the manual. A unique feature of the *BCATSS* program is that while the protocol is manualized, it employs a modular approach, which allows the therapist to decide which of the core cognitive-behavioral strategies should be addressed in any given session. The treatment modules include psychoeducation, contingency management, relaxation, exposure, cognitive restructuring, problem-solving, and relapse prevention. A suggested order of the modules is provided in the manual, but adherence to this schedule is not required.

Outcome Studies

In a small open pilot study of nine African-American adolescents with generalized anxiety disorder (GAD), specific phobia, or social anxiety disorder, Ginsburg and Drake (2002) compared school-based cognitive-behavioral treatment to an attention-support control group. Three out of four treatment completers (75%) no longer met criteria for an anxiety disorder at the end of treatment while only one of five youth (20%) in the attention-support control group remitted to nonclinical status. Results supported the feasibility and possible benefits of this approach.

Summary of Treatment Studies

Only five studies have been conducted to examine the feasibility and efficacy of treating students with anxiety disorders in schools, and all employed psychologists. The research suggests that treatment in schools for anxious youth is viable and potentially effective, particularly for social anxiety disorder. The current literature is limited by small sample sizes and with some exceptions, a lack of rigorous controls. Additionally, not enough is known about the ability to intervene in schools with younger children, as most of the research to date focuses on adolescent or older school-age youth.

Implementation Issues

Based on the promising findings of the outcome literature, there is strong justification for continued investigation about how to effectively implement evidence-based treatment in school settings. There are a number of obstacles to implementing and measuring the effectiveness of school-based intervention. These obstacles include incorporating programs into school culture, identifying anxious youth, managing confidentiality, and locating adequate service providers.

School Culture

Successful entry of any novel program into the school system requires an awareness of the school culture and key personnel's attitudes about school-based mental health services. Understandably, academic instruction is the primary mission of schools, and school administrators and parents may question the value of programs that do not directly advance these goals. Therefore, it is important that interventions avoid interfering with academic class instruction. Sessions can be rotated weekly to ensure that students do not miss

the same class repeatedly. Conducting treatments individually allow for more flexibility to schedule sessions during nonacademic periods. Finally, missed group sessions can be made up individually should exams or important class material preclude group attendance.

Another obstacle is that school personnel and parents tend to be wary of research conducted in their schools by outside institutions. It may be helpful to collaborate with community organizations familiar to the schools foster a reciprocal partnership. Researchers may also donate time and resources to school activities such as career day, faculty workshops, honor societies, school mental health education days, and parent meetings, all of which facilitate integration into the school system.

Identification of Anxious Students

A positive feature of universal prevention is that all students are included in the program. Implementation of indicated or treatment protocols requires the identification of anxious youth. Often this requires school-wide screenings since anxiety does not typically get recognized or referred for services. Although these methods seem to be successful for recruiting participants to research studies, they may be burdensome to implement. Other options for identifying anxious students may include sending letters with screening tools to parents, observation of students in various school settings, and teacher nominations. The accuracy of referrals by school personnel may be enhanced by psychoeducation and in-service trainings about anxiety and the benefits of psychosocial interventions (Weissman, Antinoro, & Chu, 2008).

Confidentiality

Identifying students with significant anxiety raises issues regarding confidentiality. Although providing treatment outside of a mental health clinic reduces some concerns about stigma for students and families, it raises others. Students and parents may have concerns that classmates, teachers, and others in the community might learn details about students' anxiety or their participation in an intervention. Anxious youth may be especially sensitive to issues involving possible negative evaluation and stigma.

There are many ways to address concerns regarding confidentiality in the school setting. First, it is important to clarify to families and school personnel what information will be shared with school administrators, teachers, and counselors. For example, school personnel might be informed of which children are participating, and possibly about their general progress, but not about specific diagnostic information or intervention session content. Second, it is important to consider how assessment and treatment materials are distributed, collected, and maintained in order to respect families' privacy. Third, assessment and treatment meetings should be conducted in a private room at the school, preferably in an area with minimal student traffic. Fourth, interventions can be given innocuous names to avoid sounding too "therapy-oriented," and emphasizing the nature of the program (e.g., *SASS, Cool Kids*). They can also be listed among other school groups. Fifth, special attention should be given to how students are called to group sessions, such as providing guidance passes, which students typically receive for various reasons, or having students come directly to sessions at the start of class periods. Finally, group treatment in schools poses another specific type of threat to confidentiality. Members might be hesitant to openly discuss their anxiety because they fear that other group members may break confidentiality and disclose their difficulties to classmates and peers outside the group. Group leaders should carefully discuss the group rules surrounding confidentiality and explain their importance on an ongoing basis.

Service Providers

An important consideration in the effective implementation of school-based mental health services is identifying a skilled and interested party to deliver the treatment. Most school-based

intervention studies have employed specialized CBT therapists funded by research. Obviously, this raises questions as to how to sustain the implementation of these programs in schools. The cost associated with hiring specialized mental health clinicians is often too high for today's underfunded schools. One solution may be to train school personnel such as school psychologists or guidance counselors to deliver interventions. This alternative receives a mixed response. Some school personnel welcome the opportunity to enhance their skills to address issues that they are already routinely expected to handle, while others consider mental health issues outside of their purview and job responsibilities. Incentive in the form of additional pay or decreased responsibilities might help. A larger question is whether services delivered by school personnel will be effective. This is not clear since research suggests that empirical treatments lose potency when transported to practice settings (Weisz et al., 1995).

Summary

Possibly due to the many advantages of school-based services, schools have become a major provider of community mental health to young people (Burns et al., 1995; Costello et al., 1996; Leaf et al., 1996; Zahner & Dasklakis, 1997). An overwhelming majority (70–80%) of youth who receive mental health services obtain them at school (Burns et al., 1995; Hoagwood & Erwin, 1997; Zahner, Pawelkiewicz, DeFrancesco, & Adnopoz, 1992), and the demand for school counselors who can deliver mental health services has substantially increased (Adelman & Taylor, 1998; Hoagwood & Erwin, 1997). School-based intervention is particularly relevant for anxiety because it often goes unrecognized and untreated. In addition, many anxiety provoking situations occur at school, thereby making school a naturalistic setting for intervention delivery, possibly enhancing the generalizability of our treatments. Given the high prevalence of anxiety disorders, and their association with school refusal and underutilization of services, it is especially important to conduct controlled studies of school-based interventions.

Existing literature indicates that school-based intervention for youth with anxiety is promising. Preliminary findings suggest that universal prevention may be most advantageous when implemented in school-age rather than adolescent populations. More consistent positive results have been demonstrated for indicated prevention and treatment programs. Despite the initial obstacles to implementing the programs, school-based intervention appears to be well-received by school personnel, students, and parents (Ginsburg & Drake, 2002; Masia Warner et al., 2005).

Overall, research evaluating school-based programs for anxiety is in its infancy. The majority of studies have used specialized CBT therapists, and thus, it is largely unknown whether professionals with varied backgrounds and little instruction in evidence-based treatment can deliver empirical interventions successfully. Of the existing studies, the majority had no control group or compared CBT to waiting lists or no treatment. Although these studies provide initial support for potential treatment benefits, they fall short of informing on specific efficacy since treatment superiority may be due to nonspecific therapeutic features, such as therapist attention and students' expectations. Credible treatment comparators are essential for demonstrating specific treatment efficacy. Documenting that interventions embedded in the school culture and operations have specific efficacy over standard school programs may justify the training of school staff in evidence-based treatments. In addition, little attention has been directed toward measuring outcomes with clear policy relevance (e.g., attendance, school functioning), which are crucial for guiding the decisions of school administrators regarding future program adoption. Finally, most studies have randomized study conditions across rather than within schools, without examining the possible contextual influences of school (e.g., organizational support and structure and school policies) on outcomes.

Future Directions

An important direction for school-based mental health, therefore, is to determine the transportability and effectiveness of evidence-based programs in school settings. First, questions remain

surrounding the most efficient and cost-effective ways to identify anxious students. In the school-based research, hundreds of students are initially screened to identify relatively small samples of anxious youth. Such a process may be too costly and time consuming for school districts to implement. Future research should investigate the relative utility of various screening methods.

Second, further evaluation is needed regarding the effectiveness of programs delivered by school-based clinicians and counselors. Demonstrating that school-based professionals can deliver a systematic intervention effectively is a crucial first step toward sustainability in schools. It will also provide important information both on the value of training frontline professionals to deliver evidence-based programs and on how to develop the best model for promoting efficacious care for underserved youth with anxiety disorders and other mental health issues.

Third, the existing literature largely neglects the assessment of the cost-effectiveness of school-based interventions. The relative cost-effectiveness of universal compared with indicated prevention or treatment programs is unknown. Universal prevention programs may be more efficient given the high cost of mental health screening. However, if programs that provide services only to those youth who require them result in more clinically significant gains, the benefits of indicated prevention and treatment programs may outweigh the initial cost of detection. In addition, considering anxiety's chronic course, coupled with its high prevalence and low service use, early identification and access to treatment may prevent the cost of longer-term impairment and development of secondary dysfunction (e.g., depression, substance use).

Another strategy to deliver effective intervention while limiting costs may be to utilize innovative technologies. For example, Kendall and Khanna (2008) have developed a CD-ROM version of an evidence-based treatment for youth with anxiety. The children complete many modules on their own, with therapist support necessary for some sections. Should it be proven effective, this program could be easily adapted for a school setting, wherein the children could complete individual sessions during the course of the school day and check in with counselors or school psychologists for the few modules that require therapist supervision. This would ease the burden on school personnel while still ensuring that the youth receive adequate anxiety treatment.

Finally, CBT principles and techniques are transdiagnostic, meaning that the same skills can be applied regardless of the nature of a child's fears. Research should explore the relative effectiveness of protocols targeting specific disorders versus a broader approach that can be applied across anxiety disorders, and the implications for training nonspecialized service providers. It will be important to determine which approach can be successfully transported to school settings and delivered by school personnel.

Although several questions remain unanswered, schools are a promising setting for delivering vital services to anxious youth who might otherwise never gain access to necessary intervention. Continued research in this area will be essential for developing a sustainable model for promoting efficacious care for anxiety in school settings.

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Phobias and Anxiety-Related Problems in Mental Retardation and Developmental Disabilities

29

Dave Dagnan

Young people with intellectual disabilities are at increased risk for anxiety disorders; for example, Dekker and Koot (2003a, b) reported that 22% of a Dutch community sample of 474 7–20 year old young people with intellectual disabilities met DSM-IV criteria for some form of anxiety disorder. This chapter will focus on the literature specific to children and young people with intellectual disabilities, but will make reference to the wider literature where there is good reason to suggest that the general principles identified will apply to this population (e.g. Dagnan & Jahoda, 2006).

The chapter will first consider diagnostic issues and epidemiological studies reporting levels of mental ill-health and anxiety in young people with intellectual disabilities. It will then consider clinical assessment issues and treatments described for young people with intellectual disabilities, with particular emphasis on psychosocial interventions. Whilst there is a growing epidemiological literature in this area, there are relatively few papers discussing assessment and intervention, it will conclude with recommendations for future developments in research and clinical work.

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Diagnostic Issues

Several papers have discussed the difficulties in diagnosing mental ill-health in young people with intellectual disabilities (Dykens, 2000; Tonge, 2007), and have suggested that it may be necessary to modify diagnostic criteria used to identify anxiety in such people (Bailey & Andrews, 2003; Davis, Saeed, & Antonacci, 2008). Dykens (2000) identifies factors that make this diagnosis more complex than for those without intellectual disabilities.

Factors Affecting Diagnosis

Concrete thinking styles. Young people with intellectual disability may have particular difficulty in describing more abstract concepts such as emotions and physiological sensations, and in reflecting on their own behaviour in general (e.g. Masi, Brovedani, Mucci, & Favilla, 2002). This difficulty makes some diagnostic issues particularly complex; for example, diagnosing Obsessive-Compulsive Disorder (OCD) in children and young people with intellectual disabilities, and/or Autistic Spectrum Disorder (ASD) requiring distinguishing stereotyped and rigid behaviours which are core to presentations of ASD, and intellectual disabilities syndromes (Moss, Oliver, Arron, Burbidge, & Berg, 2009) from clear cognitive obsessions and compulsions. Baron-Cohen (1989) argues that "obsession" and "compulsion" are not

D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_29, © Springer Science+Business Media, LLC 2011

present in young people with ASD because it is not clear that observed behaviours are experienced as aversive to the individual. However, authors have reported clear differentiation between stereotyped and anxious behaviours. For example Gothelf et al. (2008) report the prevalence of OCD in 87 young people with intellectual disability in Israel. Using the Children's Yale-Brown Obsessive Compulsive Scale (Scahill et al., 1997), they demonstrate that young people with intellectual disabilities present "classic" obsessions such as those of contamination and compulsions of cleaning, checking and hoarding.

Llimited life experiences, reduced social skills and differences in developmental pathways. Limited life experiences and developmental differences may affect the presentation of symptoms of anxiety. In particular, developmental differences in the area of fear have been noted for young people with intellectual disabilities , that fears that may be developmentally appropriate at a younger age may often persist into adolescence and adult hood (Gullone, 1996).

Functional increases in pre-existing cognitive and behavioural problems. Life events that may be associated with onset of anxiety disorders may also lead to changes in functional relationships of existing behavioural problems, and such changes in behaviour may be misidentified as symptoms of mental ill-health (Sovner, 1986). For example, differentiating between functionally varying responses to auditory and tactile sensitivities and true phobias can be difficult, although Ellis, Ala'i-Rosales, Glenn, Rosales-Ruiz, and Greenspoon (2006) and Koegel, Openden, and Koegel (2004) report the use of a systematic desensitisation procedure to treat hypersensitivity to auditory stimuli and tactile sensitivity, respectively, suggesting that, in some instances, the same intervention will work regardless of the functional origin of the behaviour.

Epidemiology

The prevalence of psychiatric disorders among young people with intellectual disabilities and autism is higher than it is in the general population (Borthwick-Duffy, 1994; Einfeld et al., 2006; Rutter, Tizard, Yule, Graham, & Whitmore, 1976). Emerson (2003) reports a secondary analysis of a large scale (18,415 young people) survey of mental ill-health in 5–16 year olds in the UK. The survey used a structured interview that provided diagnoses against both the DSM-IV and ICD-10. The study identifies a prevalence of mental ill-health of 39% in young people with intellectual disabilities, compared to a prevalence of 8.1% for young people without intellectual disabilities.

Anxiety problems have been reported as one of the most common forms of psychological distress for young people with intellectual disabilities. For example, Dekker and Koot (2003a, b) report that 22% of a Dutch community sample of 474 7–20 year old young people with intellectual disabilities met DSM-IV criteria for some form of anxiety disorder. Gothelf et al. (2008) studied 87 young people with intellectual disabilities in school in Israel; 60.9% of the sample had at least one mental ill-health diagnosis using the "Kiddie-Schedule for Affective Disorders and Schizophrenia" (K-SADS) (Kaufman et al., 1997); of these 44.8% had a diagnosed anxiety disorder, of 8% were diagnosed with separation anxiety, 14% with generalised anxiety disorder, 4% with post-traumatic stress disorder, 1% with panic disorder, 7% with social phobia, 15% with specific phobia and 11.4% with OCD.

Prevalence rates for anxiety in young people with intellectual disabilities are considerably higher than in young people without developmental disabilities. Emerson and Hatton (2007a) report 11.4 % of their sample of young people with intellectual disabilities was identified with anxiety disorder, compared to 3.2% of those without intellectual disabilities. Significant differences in prevalence rates of specific anxiety presentations were found for separation anxiety (2.7% in those with intellectual disabilities and 0.6% in those without), specific phobia (2.0% in those with intellectual disabilities and 0.8% in those without), social phobia (0.9% in those with intellectual disabilities and 0.3% in those without), generalised anxiety disorder (1.6% in those with intellectual disabilities and 0.6% in those without), and other anxiety disorders (4.4% in

those with intellectual disabilities and 0.9% in those without). There were no significant differences in prevalence of anxiety difficulties for panic disorder, agoraphobia, post-traumatic stress disorder or obsessive compulsive disorder.

A number of papers report levels of mental ill-health in young people with ASD ,using populations including young people with and without intellectual disabilities (White, Oswald, Ollendick, & Scahill, 2009; Muris, Steerneman, Merckelbach, Holdrinet, & Meesters, 1998). For example Leyfer et al. (2006) assessed 103 young people with autism of which 32.3% had a full scale IQ score below 70 using the K-SADS (Kaufman et al., 1997) and report a 44.3% prevalence of specific phobia and a 37.3% prevalence of OCD. Studies suggest that young people with autism and intellectual disabilities experience more anxiety than those with intellectual disabilities alone (Bradley, Bolton, & Bryson, 2004; Brereton, Tonge, & Einfeld, 2006). Evans, Canavera, Kleinpeter, Maccubbin, and Taga (2005) reported age and chronologically matched groups of young people with autism, Downs syndrome, intellectual disabilities and normal development. Young people with autism were reported to have more medical phobias than other groups, and fears and phobias were more closely related to problem behaviours, a result that replicated data from Muris et al. (1998).

Understanding Higher Rates of Anxiety

Population factors and measurement issues play a part in the variation in the levels of anxiety disorder reported in epidemiological studies (Dykens, 2000). However, there is a generally a uniform finding of higher levels of disorder. There are several possible reasons for the higher levels of mental ill-health in children with intellectual disabilities (Dagnan & Jahoda, 2006; Dykens, 2000), and possible factors have been identified across the bio-psycho-social continuum, some of which are generally associated with mental ill-health, and some specifically associated with anxiety disorders (Donovan & Spence, 2000). The neuropsychological features of young people with certain disabilities such as Fragile X syndrome, Williams syndrome and Prader–Willi syndrome are specifically associated with anxiety presentations (Dykens, 2003; State, Dykens, Rosner, Martin, & King, 1999; Woodcock, Oliver, & Humphreys, 2009). The stigmatised and disadvantaged lives of many people with disabilities are associated with higher levels of stress (Dykens, 2000; Einfeld et al., 2006). Dagnan and Jahoda (2006) suggest interactions between developmental risk factors and the social context of young people with disabilities that are specifically associated with anxiety. Achievement and educational experiences may affect young people in specific contexts (Wehmeyer & Mithaug, 2006; Zigler & Bennett-Gates, 1999), and the effects of socio-economic factors associated with intellectual disabilities have been identified as critical in explaining variance in levels of mental ill-health (Emerson & Hatton, 2007b).

Assessment

Many papers identify that the assessment of emotional states and functioning in young people with intellectual disabilities requires multi-modal approaches,as the population is likely to find self-report in general and self-report of emotions in particular to be difficult (Dykens, 2000; Hagopian & Jennett, 2008; Rush, Bowman, Eidman, Toole, & Mortenson, 2004). Hagopian and Jennett (2008) suggest a clinical assessment structure for anxiety disorders in adults with intellectual disabilities. King, Ollendick, Gullone, Cummins, and Josephs (1990) and MacNeil, Lopes & Minnes, 2009) suggest a similar structure specific to anxiety in young people with intellectual disabilities, and young people with autism respectively.

Clinical Assessment

Direct observation. The literature on the use of direct observation as a clinical assessment method is considerable (e.g. Paclawskyj, Kurtz, & O'Connor, 2004; Toole, Bowman, Thomason,

Hagopian, & Rush, 2003). Within the context of mental ill-health, there are examples of the reliable observation of mood in people with more severe disabilities as part of the evaluation of psychological interventions (Toole et al., 2003), and there are examples of the comprehensive operationalisation of DSM criteria for direct observation (Sovner & Lowry, 1990). Direct observation of anxious response to stimuli has been reported as part of the assessment of anxious response in most reported intervention studies, although the more structured Behavioural Avoidance Test is not systematically reported (King et al., 1990).

Clinical interviews. There are a number of complexities when interviewing people with intellectual disabilities about their experience of mental ill-health (Findlay & Lyons, 2001; Heal & Sigelman, 1995). However, where possible the young person's perspective on their difficulties should be considered, and many young people with disabilities are able to give essential insights into their difficulties, although developmental age and abilities must always be taken into account (Reynolds, Girling, Coker, & Eastwood, 2006). There are an increasing number of structured self-report measures of anxiety, such as the Beck and Zung anxiety scales, that have been reported to be used with young people with intellectual disabilities (Masi et al., 2002). Scales have also been adapted to assess specific fears in young people with intellectual disabilities (Gullone, 1996; Muris, Merckelbach, & Luijten, 2002). Scales to assess underlying concepts associated with anxiety, such as self-esteem and social comparison (Dagnan & Sandhu, 1999), have been reported for use with young people with intellectual disabilities; for example perceived stigma and self-efficacy has been the focus of a number of studies with this group (Cooney, Jahoda, Gumley, & Knott, 2006; Szivos, 1991), and social comparison, self-esteem, and depression scales have been used with young people with autism (Hedley & Young, 2006).

Interview and assessment of the persons themselves may also include consideration of the potential of the person to engage in intervention. For example, Dagnan & Chadwick (1997) describe assessments of core abilities that might make an adult with intellectual disabilities more able to take advantage of cognitive therapy. Although these assessments have not been reported for young people with intellectual disabilities as part of a plannedintervention,they have been reported for young people without intellectual disabilities, and there is little reason to suppose they would not be a useful form of assessment for this group (Doherr, Reynolds, Wetherly, & Evans, 2005; Reynolds et al., 2006). The assessment process includes assessment of language ability, emotional recognition and expression, abilities to relate events to emotions, and the ability to understand therapy specific concepts such as the cognitive mediation of emotion and behaviour. The results of such assessment may suggest further input to better enable the use of particular therapy, how therapeutic and supportive interventions may be adapted, and offer insights into the formulation of the difficulties experienced by the person.

Interview with caregivers and/or family members. Caregivers and family members may be able to provide information about the developmental history of the problemspresent. It is always important to bear in mind that caregivers will be presenting their perspective of the problem,and that this will often be affected by their own views of the client, and their knowledge of mental ill-health (Rush et al., 2004). Epidemiological and intervention studies often report the use of validated third-party rating scales that can be used with caregivers, to help identify mental ill-health presentations in people with intellectual disabilities. It is difficult to review these comprehensively here, and such assessments are reviewed in other places (e.g. Davis et al., 2008; Masi et al., 2002). In general, scales reported are initially designed for young people without intellectual disabilities, but are reported as easily used with young people with intellectual disabilities. For example Masi et al. (2002) report the use of the Psychopathology Instrument for Mentally Retarded Adults (Achenbach & Ruffle, 2000) and the Child Behavior Checklist (Watson, Aman, & Singh, 1988) which are scales developed for adults and young people without intellectual disabilities respectively. These were used with young people

with intellectual disabilities and the study reports a high degree of concurrence and agreement with self-report scales in this population.

Assessment of the influence of psychosocial factors. Given the dependency of young people with intellectual disabilities, it is important that assessment should also include consideration of the broader psychosocial context of the client (Dagnan, 2007). The assessment of environmental features associated with mental ill-health is underdeveloped. Assessment of this type may include assessment of the beliefs and attitudes of caregivers about the behaviours shown by the young person with intellectual disabilities (Hastings & Brown, 2002), and of the knowledge that caregivers have of mental ill-health presentations (Quigley, Murray, McKenzie, & Elliot, 2001). There is also a beginning literature that suggests that factors such as expressed emotion may be important for young people with intellectual disabilities and mental ill-health (Beck, Daley, Hastings, & Stevenson, 2004; Hastings, Daley, Burns, & Beck, 2006).

Intervention Studies Relating to Young People with Intellectual Disabilities

The psychosocial treatment of anxiety in people with intellectual disabilities has received more attention than many other areas of psychological distress. In general, treatments have been behavioural and physiological in focus,although there are a small number of studies reporting cognitive behavioural approaches (Davis et al., 2008; King et al., 1990). This section will review studies that report interventions with subjects that include young people with intellectual disabilities, and so will report some studies where they are described as young people with ASD.

Behavioural Approaches

A behavioural perspective views anxiety as a disorder of fear association (Davey, 1992). Some of the simplest models of classical conditioning of fear (pairing an unconditioned stimulus with a conditioned stimulus followed by an aversive event) are clinically appealing, and many phobias do appear to have specific conditioning experiences. However, the lack of a clear link between trauma and phobia in all cases suggests that more sophisticated models of how associations are developed are necessary, for example with reference to modelling or developmental sensitivity (Vandenhout & Merckelbach, 1991). Behavioural techniques involving exposure to fear eliciting stimuli are effective components in many anxiety treatments (McNally, 2007).

Intervention studies. Most studies report behavioural interventions to manage anxiety in young people with intellectual disabilities; all behavioural interventions describe exposure as the core component of treatment, and include systematic desensitisation, counter-conditioning, modelling, and/or operant conditioning of appropriate behaviours in the development of adaptive responses to the feared stimuli (King et al., 1990). Behavioural approaches to manage anxiety in people with intellectual disabilities have used relaxation as a means of introducing counter-conditioning of the anxiety associations. Consequently, considerable literature has developed on the use of relaxation for adults with intellectual disabilities (Lindsay, Fee, Michie, & Heap, 1994). Although there is little reason to think that relaxation approaches will not work with young people with intellectual disabilities, there are few studies that have specifically examined the effects and applicability of the approach; although the approach has been included in single case studies of young people with intellectual disabilities and autism (Mullins & Christian, 2001). Many of the published studies of treatment of phobia report use of positive reinforcement for non-anxious behaviour, or use a variety of counter-conditioning approaches such as laughter (Jackson & King, 1982).

There is a relatively long history of intervention for phobia in young people with intellectual disabilities (e.g. Jackson & King, 1982; Kohlenberg, Greenberg, Reymore, & Hass, 1972; Luiselli, 1977, 1978). Jackson (1983) reviewed the use of psychological interventions for phobia, and found, at that time, 15 studies relating to both adults and young people with intellectual disabilities

and autism. These studies used in vivo exposure with reinforcement for contact with the feared stimulus while others used modelling of low fear behaviour. The current chapter will review intervention reports since the review by Jackson.

A number of interventions in this area relate to behaviours that affect medical and dental treatments and interventions as these are relatively common in this population (Muris et al., 1998). Luscre and Center (1996) discuss exposure and counter-conditioning approaches in the treatment of three young people with autism and dental fear. The treatment approach included desensitisation with "guided mastery", video peer modelling and reinforcement of increased exposure to dental environments. Counter conditioning stimuli were selected from stimuli that elicited a positive response from the children during assessment; these included country music, a hand-held mirror, "Play-doh", fruit, songs, and rhymes. The three participants were all able to take part in a substantial subset of components of a dental examination by the end of the intervention.

Hagopian, Crockett, and Keeney (2001) describe the treatment of a 19 year old man with moderate intellectual disability and blood-injury-injection phobia, with the goal of enabling him to consent to having blood taken by a nurse. Treatment was multi-component, consisting of a 10 s differential reinforcement of alternative behaviours procedure which was faded to a 20 s interval. Reinforcement was in the form of tokens that could be traded for preferred activities following the procedure. The young man was initially placed into a restraint "papoose" to enable graduated exposure to the technologies required to take blood. The degree of restraint was increased over four phases as the degree of intrusiveness of the exposed hierarchy of medical treatments increased, subsequently the restraint was faded out while the level of intrusiveness of procedures remained high. At the end of the process the young man was able to sit in a chair in the clinic from which he was free to leave at any time whilst blood was taken. The intervention took place over a period of 6 weeks.

Shabani and Fisher (2006) report a stimulus fading approach combined with positive reinforcement with an 18 year old with autism and intellectual disability and with needle phobia, who had type 2 diabetes and required daily blood samples to be taken to monitor blood glucose levels. The lancet was moved closer to the young person's finger on each trail with access to preferred reinforcement (generally sweet foods) for holding his hand within a hand shape drawn on a poster board on each trial. The intervention lead to the young person's mother being able to draw blood on a daily basis for the duration of the 2 month follow-up.

Other interventions in this area relate to young people with phobias of animals. Newman and Adams (2004) report the case study of a 17 year old boy with moderate intellectual disability with a phobia of dogs using a graded exposure procedure with relaxation as the counter-conditioning stimulus. The young person's mother being used as to modelled appropriate behaviour (in this case study it was noted that the child's mother was also fearful of dogs and that her modelling was likely to be more powerful because of the child's knowledge of her fears).

Davis, Kurtz, Gardner, and Carman (2007) describe the one session treatment of a phobia of water for a 7 year old boy with intellectual disabilities. The treatment used a massed exposure approach with graduated in vivo exposure, participant modelling, cognitive challenges, reinforcement, and other techniques. Both indirect and direct observation measures were utilised to evaluate treatment efficacy. Results suggested the intervention reduced or eliminated behavioural avoidance, specific phobia symptoms, and subjective fear.

Ricciardi, Luiselli, and Camare (2006) report a stimulus fading approach for an 8 year old boy with ASD and intellectual disabilities who had a phobia of "animatronic" toys. The toys were moved a further 1.0 metre towards the child after each successful trial starting at five metres. The target criterion was for the toys to be at arms length from the child. Throughout each trial the child had open access to and was interacting with preferred toys. The intervention took place over 15, 15-min session, and achieved a criterion of the child being able to touch the toys with 100% compliance following a verbal request.

Given the potential for modelling in the aetiology of phobia, a small number of studies have explored the systematic use of parents as mediators of interventions in this area. Matson (1981) describes the treatment of three young people with intellectual disabilities with social phobias, where modelling was provided by the mothers of the young people using prompts which were faded out during the course of the treatment. Love, Matson and West (1990) describe the treatment of two children with ASD and intellectual disabilities who had fears of leaving the house, and of showers and running water where the intervention was delivered by the children's mothers.

Cognitive Therapy Approaches

People with intellectual disabilities have often been seen as unable to benefit from cognitive and other talking therapies, and the volume of published research in cognitive therapy does not match that of other populations. Nevertheless, there is an ongoing history of publication and clinical research in this area (Dagnan & Lindsay, 2004), and there are good reasons to suggest that this type of therapy will be useful for some people with an intellectual disability. For example, many of the cognitive processes that mediate psychological and mental health problems in young people without intellectual disabilities are also present in young people with intellectual disabilities (Cooney et al., 2006; Hedley & Young, 2006), and that some young people with mild intellectual disabilities are well able to work with cognitive material (Suveg, Comer, Furr, & Kendall, 2006). However, in general the outcome literature for cognitive therapy with people with intellectual disabilities is sparse (Dagnan & Lindsay, 2004; Sturmey, 2006).

There are a number of therapeutic approaches for people without intellectual disabilities that can be considered to be "cognitive". Dagnan and Chadwick (1997) identify two distinct approaches to cognitive therapy that have been used with people with intellectual disabilities. The first is based within a "deficit" model that assumes that emotional and behavioural difficulties are due to a lack of cognitive skills and process (Whitman, 1990). The second approach to cognitive therapy for people with intellectual disabilities is concerned with "cognitive distortion," and has developed from a psychotherapeutic tradition. In the clinical models developed by therapists such as Beck, Ward, Shaw, and Emery (1979) and Ellis (1977), unhelpful or irrational emotions and behaviours are considered to be the products of "distorted" cognitions (e.g. beliefs, attributions, inferences, evaluations). Most reported approaches to anxiety management for people with intellectual disabilities have adopted a deficit approach, seeing anxiety management as a skill to be taught or anxiety as a behaviour to be replaced.

Intervention studies. Within a cognitive framework, a number of papers report successful case studies with adults with intellectual disabilities using Beck's cognitive therapy with adults with intellectual disabilities and anxiety disorders (e.g. Lindsay, 1999; Lindsay, Neilson, & Lawrenson, 1997). Several papers report cognitive interventions for young people with intellectual disabilities, although some report interventions with young people with high functioning autism that do not include youth with significant intellectual disabilities (e.g. Chalfant, Rapee, & Carroll, 2007; Ooi et al., 2008; Reaven & Hepburn, 2003; Sze & Wood, 2008; Wood et al., 2009). Although these studies do not report outcomes for young people with intellectual disabilities, they offer useful clinical insights into adaptations to cognitive behavioural intervention protocols. Sze and Wood (2008) describe an established cognitive intervention for anxiety which was adapted for young people with autism. The adaptation included a significant element which addressed some of the core features of autism on the basis that the intervention for anxiety would be more effective if such features were addressed. For example, anxiety over the formation of friendships was addressed with respect to anxiety related behaviours, but then followed up with intervention to enhance social skills to address difficulties associated with autism. The intervention was adapted to include visual aid,s and included support from family members in implementing homework outside of

the therapy sessions. Outcomes indicated substantial improvements in anxiety symptoms, but also a number of improvements in broader aspects of social functioning.

Suveg et al. (2006) report the detailed session plan for adapted cognitive therapy for an 8 year old girl with mild intellectual disabilities,and social and generalised anxiety, who was selectively mute. The early sessions focussed on recognition of emotion and anxiety, subsequent sessions focussed on relaxation, the understanding links between cognition and emotion, and generation of coping statement. Finally a hierarchy of exposure to feared stimuli was generated, and exposure was implemented. At the end of the intervention, she no longer met diagnostic criteria for generalised anxiety disorder, and was no longer selectively mute, although she still met criteria for social phobia. The authors report that the cognitive components of the therapy proved particularly difficult for the girl to grasp, and understanding the role of cognition in her anxiety, and the generation of coping statements was attempted but not fully implemented. There is insufficient data to make generalisable recommendations for the adaptation of therapy for young people with intellectual disabilities, although there are now sufficient studies relating to adults with intellectual disabilities for reviews of adaptations in published literature to be possible (Whitehouse, Tudway, Look, & Kroese, 2006).

There are few reported psychosocial interventions that are neither behavioural nor cognitive-behavioural. One interesting exception is a study by Edelson, Edelson, Kerr, and Grandin (1999), who report the use of "deep pressure" in management of young people with autism and anxiety. The study was a small scale randomisation of 12 young people with profiles that suggest intellectual disabilities. The intervention consisted of 12 20-min sessions over a 6 week period, and demonstrated a marginally significant decrease in anxiety for the treatment group. This study is an example of intervention based upon pragmatic observation of the impact of physical containment on some individuals with autism; the study highlights the potential importance of sensory stimulation, and its management as an adjunct to established treatments for anxiety in young people with autism.

Conclusions

It is clear from an increasing literature that young people with intellectual disabilities experience significantly greater levels of anxiety disorder, than young people without disabilities; the literature offers a quite detailed account of levels of disorder for some presentations. However, the number of studies examining specific presentations is small (e.g. the literature on PTSD consists of one paper at the case study level; Turk, Robbins, & Woodhead, 2005), and there is some inconsistency in reported prevalence rates. Clearly such studies need replication and extension.

There remains a significant gap in the literature with respect to assessments suitable for young people with severe intellectual disabilities where the limits of self-report and the development of well standardised carer reports scales remains to be explored. Given the additional dependency of young people with intellectual disabilities, there is a surprising lack of research into assessments of the supporting environment of young people with intellectual disabilities and mental health presentations. The context of stigma and discrimination that is pervasive in the lives of young people with intellectual disabilities suggests that further work on the assessment and impact of these factors is important.

The psychosocial intervention literature in this area remains limited. Case studies are predominantly in the area of phobias, and for the most part are at the single case or small case series level. It is striking that epidemiological work is identifying a range of distinct presentations that are not reflected in the treatment literature. The effectiveness of behavioural approaches in the treatment of phobia suggests that behavioural interventions should be developed for people with OCD, and generalised anxiety disorders, and that it is likely that such interventions will be based upon the exposure models that have been successful in the treatment of phobia.

There are a small number of studies beginning to examine the cognitive profiles associated with anxiety in young people with intellectual disabilities. However, there are very few cognitive interventions reported for young people with intellectual disability alone; however, there are a small number of well controlled studies reporting cognitive interventions for higher functioning young people with autism. Further research is required to determine the skills that are associated with successful outcomes in cognitive therapy. Individual adaptation should be based upon clear assessment of such skills, which will also enable identification of those young people with intellectual disability who will not be able to participate in verbally based therapies using these approaches, or who may require work in order to acquire the cognitive and emotional skills to be able to participate.

In conclusion whilst anxiety disorders are well recognised in young people with intellectual disabilities, the clinical and research evidence base for assessment and intervention is extremely limited, and whilst reference can be made to wider literatures relating to young people without intellectual disabilities and adults with intellectual disabilities, there is a clear need to develop the research and clinical evidence base in this area.

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Food Neophobia in Children: Misnomer, Anxious Arousal, or Other Emotional Avoidance?

30

Jon Rogove, Jessica Masty, and Dean McKay

> The vital importance of nutrition and the severe risks of poisoning may together account for the strong affective responses associated with eating, and for the ambivalence associated with this process. This conflict… is represented by opposing tendencies to fear and to explore new foods, or to like both familiar and novel foods
>
> (Rozin & Fallon, 1987, p. 27).

Coined the "omnivore's dilemma" (Rozin & Fallon, 1987), this evolutionarily-based mechanism, which is characterized by seemingly conflicting inclinations to ingest and avoid unfamiliar foods, is thought to influence the food preferences and consumption of humans and other omnivorous species (Addessi, Galloway, Visalberghi, & Birch, 2005; Birch, Gunder, Grimm-Thomas, & Laing, 1998; Dovey, Staples, Gibson, & Halford, 2008; Martins & Pliner, 2005; Rozin & Fallon, 1987; Rozin & Vollmecke, 1986). Theoretically, the coexistence of food neophilia (approach to new and unique foods), and food neophobia (avoidance of unfamiliar food items) served to increase the probability that our early ancestors sought and consumed foods that provided adequate nutrition, while avoiding potentially poisonous or toxic plants, animals, and animal products (Dovey et al., 2008; Flight, Leppard, & Cox, 2003; Martins & Pliner, 2005; Milton, 1993; Russell & Worsley, 2008). In humans, the latter, protective mechanism appears to be especially pronounced in early childhood when infants gain the capacity for locomotion, their diets become increasingly omnivorous and varied, and an exclusive milk diet no longer provides adequate nutrition (Addessi et al., 2005; Cooke, Wardle, & Gibson, 2003; Dovey et al., 2008). The impact of food neophobia decreases dramatically in later childhood and, continues to lessen at a more gradual pace in adolescence and adulthood (Dovey et al.).

Defining Food Neophobia

Food neophobia has been operationally defined as the rejection and avoidance of novel foods (Cooke, Carnell, & Wardle, 2006; Dovey et al., 2008; Knaapila et al., 2007; Pliner & Hobden, 1992), and has been conceptualized as both a behavioral process and a personality trait (Pliner & Hobden). In their seminal paper, Pliner and Hobden describe the food neophobia trait as "a continuum along which people can be located in terms of their stable propensity to approach or avoid novel foods" (1992, p. 107). In order to highlight the specificity of the food neophobia construct, several researchers have drawn attention to the distinction between food neophobia and the more general construct, picky eating, which is the general reluctance to consume foods

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_30,

that are appraised as objectionable (Cooke et al., 2006; Dovey et al., 2008; Galloway, Lee, & Birch, 2003; Jacobi, Agras, Bryson, & Hammer, 2003). Thus, food neophobia is considered to be a subtype of picky eating, characterized by unwillingness to consume unfamiliar foodstuffs (Dovey et al., 2008).

Avoidance of unfamiliar foods is an age-old problem, and is a common complaint among parents. They describe their children, who have highly restrictive diets, as "picky eaters." A wide array of explanations have been offered for this pattern of avoidance in children, ranging from increased taste sensitivity in youth (Cowart, 1981) to a more recent conceptualization based on global sensory hyperawareness (Coulthard & Blissett, 2009; Mustonen & Tuorila, 2010), with moderating effects based on mother's food preferences both pre-and post-natally. This has created difficulties in conceptualization of food neophobia in extreme cases, whereby dietary restrictions lead to dietary deficits. Further, parents may inadvertently worsen the problem associated with food neophobia by pressuring children to try unfamiliar foods that they make efforts to avoid. In one recent investigation, Tuorila and Mustonen (2010) conducted an experiment with children who had food aversions (but not dietary deficits associated with the avoidance). A total of 72 children between ages 8 and 11 years were given rating tasks for a range of foods. The most negative ratings were given to foods that the children (a) expressed a reluctance to try even though they had never had those foods, and (b) were nevertheless pressed to try. This suggests that efforts to induce trying of new foods require additional inducements whereby the child ultimately tries the food without undue additional pressure.

While the recently published literature has focused largely on sensory hyper-sensitivity as a predictor, with moderating effects based on parental eating habits, there is limited detailed evaluation of food neophobia and its treatment. The purpose of this chapter is to cover the existing literature, its association with different childhood psychological conditions, and some potentially promising avenues for treatment. As the literature for this problem is limited, we present illustrative cases where different levels of food aversion were present and how treatment was conceptualized. We recognize that this in no way represents a comprehensive means of developing treatment guidelines for mental health practitioners but, instead, suggests potential avenues for further investigation.

Pathological Patterns of Food Neophobia and Associated Consequences

In contradiction to the other diagnostic entities outlined in this volume, comparatively little research has been devoted to investigating the relationship between normative and more maladaptive patterns of food neophobia. Indeed, the phenomenology, etiology, maintenance, and emotional underpinnings of food neophobia are, by and large, not well understood. What is clear, however, is that a large minority of children and adolescents exhibit levels of food neophobia that constrain food selection to a such a degree that diet variety, diversity, and overall quality are negatively impacted (Cooke et al., 2003, 2006; Falciglia, Couch, Gribble, Pabst, & Frank, 2000; Galloway et al., 2003; Russell & Worsley, 2008). Further, picky eating in childhood has been demonstrated to increase the risk of developing extreme levels of anorexic symptoms in adolescence (Marchi & Cohen, 1990).

While the existing research has been limited in scope, investigations have centered on a small subset of genetic sensitivities to bitter taste, in particular the chemical 6-*n*-propylthiouracil (which is also a drug used in the treatment of Grave's disease, which carries an FDA alert regarding risk of serious liver damage and potential life threatening effects associated with its use). Individuals with this specific taste sensitivity are significantly less likely to try novel foods, including those commonly accepted among children (such as American Cheese and whole milk; Keller, Steinmann, Nurse, & Tepper, 2002). Some have observed a gender interaction, in that males consume more fatty protein products (such as animal-based meat products) which leads to

higher weight-to-height ratios, whereas females demonstrate a more global food avoidance, including fatty meat products, leading to lower weight-to-height ratios (Keller & Tepper, 2004).

Dietary restriction. In contrast to the developmentally-appropriate and adaptive pattern described above, a significant minority of children and adolescents exhibit such severe levels of food neophobia that food is restricted to a dysfunctional degree. Russell and Worsley (2008) recently investigated the relationships between food neophobia and food preferences among a sample of preschoolers recruited from the community. The investigators discovered that trait food neophobia was negatively related to children's preferences for all food groups, with substantial correlations between food neophobia and preferences for vegetables, meats, and fruit. Significant negative correlations were also observed between food neophobia and the number of liked food items, the variety of food preferences, and the overall quality of children's preferences.

Falciglia and colleagues (2000) compared the diets of fourth- and fifth-grade students with varying levels of food neophobia. Participants were classified into one of three groups based on their scores on the Food Neophobia Scale (Pliner & Hobden, 1992): (a) food neophobia, (b) average, and (c) food neophilia. Compared to the latter two groups, neophobic children were less likely to meet two thirds of the Recommended Dietary Allowances (RDAs) and Dietary Reference Intakes (DRIs) of vitamin E. The diets of these children were also characterized by a higher intake of saturated fat, less dietary variety, and of poorer overall quality, as measured by the USDA Healthy Eating Index (HEI; United States Department of Agriculture, 1995). As might be expected, neophobic children also consumed fewer unique foods than their neophilic counterparts.

In a survey of the eating behaviors of preschool British children, Cooke et al. (2003) discovered that scores on the Child Food Neophobia Scale (CFNS; Pliner, 1994) were inversely related to frequency of parent-reported consumption of vegetables, fruit, meat, and eggs. Similar findings were ascertained by Cooke and colleagues (2006) in a more detailed analysis of these variables. Consistent with their earlier study (2003), and in accordance with the findings of Russell and Worsley (2008), food neophobia was negatively correlated with consumption of fruit, vegetables, protein foods, and total calories, even after controlling for child age, socio-economic variables, and ethnicity. A comparison of the diets of children with higher and lower levels of neophobia yielded nearly identical results. That is, children with higher neophobia consumed significantly fewer fruits and vegetables, protein foods, and total calories.

Anorexia nervosa. Picky eating in childhood has been demonstrated to increase the risk of extreme anorexic symptoms in adolescence. In a 10-year, longitudinal study of over 800 children, Marchi and Cohen (1990) utilized a logistic regression analysis to identify prospective risks associated with extreme eating disorder symptoms. Among other things, they discovered that (a) pickiness in early and later childhood was a significant risk factor for extreme symptoms of anorexia in adolescence, and (b) picky eating in later childhood and adolescence was predictive of symptoms 2 years later. A word of caution is in order, however. A careful examination of the pickiness construct utilized by Marchi and Cohen reveals a construct that is similar, yet clearly distinct from food neophobia. Therefore, the extent to which of these findings are also true of food neophobia is unclear.

In summary, studies have just begun to uncover the adverse outcomes associated with food neophobia. Although this line of study is merely in the beginning phases, the available research suggests that food neophobia may unfavorably affect diet and eating behaviors, including the variety and overall quality of food preferences and consumption. This is particularly worrisome, as dietary variety and diversity are thought to help ensure that an adequate assortment of necessary nutrients and other essential dietary components are consumed (Falciglia et al., 2000; U.S. Department of Agriculture, 2005). Although less conclusive, research has also indicated that picky eating in childhood may increase the risk of developing anorexic symptoms in adolescence. It remains to be seen if food neophobia poses a similar risk.

Cognitive-Behavioral Approaches for Food Neophobia

This review thus far illustrates that: (a) food neophobia is fairly common; (b) general food aversion is an adaptive response, and reluctance to try novel foods is an effort to protect from ingesting harmful substances; (c) alternatively, consumption of novel foods is also adaptive as it permits ingestion of chemicals associated with a healthy diverse diet; (d) in extreme forms the avoidance mechanism prevents consumption of food, even if it comes with dietary risks; and (e) this proneness to elevated aversive responses to food may be due, in part, to normal developmental factors, inherited components, and parental behavior.

These factors imply several possible lines of intervention, depending on the severity of food avoidance and willingness to engage in activities designed to expand diet choices. In line with cognitive-behavioral approaches to therapy, the most appropriate potential interventions would involve exposure, contingency management, or some combination of these two interventions. In any case, parent training would also be considered crucial for successful treatment. Additionally, it is important to note that most people have specific food likes and dislikes. It is therefore essential that clinicians remain sensitive to the goal of expanding the range of accepted foods while also maintaining that some food aversions may remain regardless of efforts to alleviate them.

Treatment Approach 1: Contingency Management

For mild food aversion that does not rise to the level of impairment (associated with inadequacies in diet), offering contingent rewards for trying new foods can be a viable approach. As noted above, pressure for trying new foods creates negative responses to that class of food (Tuorila & Mustonen, 2010). Therefore, creating inducements for trying classes of foods that may fall outside the range of acceptable foods, but are near to the core feature that is being avoided, may be an acceptable means of increasing the range of foods eaten. This essentially combines the notion of a hierarchy of potentially acceptable foods (ranging from readily acceptable to unquestionably rejected) with providing reinforcement for those food items that would not be readily eaten, but are low on the hierarchy. For example, if a child accepts only chicken nuggets, he may be persuaded to expand his food choices to breaded chicken cutlets (a nearby item, but not as small or as heavily breaded as nuggets).

Setting up the hierarchy may require some ad hoc guesses as to what would constitute acceptable foods. That is, the clinician may need to approximate foods that are not exactly matched to acceptable foods on a trial-and-error basis, to develop a program of contingency management that will be acceptable to the child and viable for the parent or caregiver to implement. Further, the features of new foods that are considered "acceptable" or "unacceptable" can vary, based on several characteristics. Just as fear hierarchies are based on specific parameters (for example, proximity and time in contact; see Wolpe, 1992), food hierarchies may be constructed based on size of food item, texture, and method of preparation. These are just a few possible dimensions on which food hierarchies may be developed. An illustration of this type of hierarchy is presented in Table 30.1. Once a food hierarchy is established, the child should be provided with daily reinforcement for consuming some agreed-upon food listed on the low end of the hierarchy. Once the child becomes proficient at eating low-level preparations of the avoided food, the child should be reinforced for eating preparations that are listed higher on the hierarchy, and so on. Once the hierarchy for a particular preparation is finished, or close to finished, other foods may be approached to expand the range of foods consumed.

Treatment Approach 2: In Vivo and Graduated Exposure

For some children, there is a general willingness to try new foods, but a corresponding problem of lingering aversion arises when the child has a negative gustatory experience. In such instances, exposure (in vivo or graduated) may be attempted, but it would constitute small

Table 30.1 Illustrative hierarchy for developing contingencies to expand food consumption range

	Degree of desirability (0 = not desirable; 10 = highly desirable)
Texture	
Chicken, cooked without skin	0
Chicken, cooked with skin	2
Chicken, boneless, no breading	3
Chicken, boneless, lightly breaded	5
Chicken, boneless, in strips, breaded	7
Chicken nuggets, small, heavily breaded	9
Method of preparation	
Chicken, sautéed	1
Chicken, grilled	3
Chicken, grilled with light breading	4
Chicken, fried with no breading	5
Chicken, fried, lightly breaded	7
Chicken, fried, heavily breaded	9

Note: These are for a child who primarily consumes chicken nuggets but either reluctantly accepts other chicken preparations, or rejects other forms altogether

levels of exposure. That is, in contrast with in vivo exposure approaches for feared situations, where massed exposure to feared stimuli is practiced until there is habituation (for detailed discussion, see Richard & Lauterbach, 2006), it may be more difficult to accomplish true habituation to rejected foods. Indeed, recent analyses have suggested that graduated exposures for food aversion may help children accept new foods (Dovey et al., 2008), but food exposures are unlikely to achieve fear habituation. Instead, the role of food exposures is to expand the range of foods consumed and diminish avoidance, but not necessarily to alter an emotional reaction to different foods.

The hierarchy described in the section related to contingency management would serve the purpose of setting the occasion for an exposure-based approach as well. This can be initiated, developed, and managed in the office, while also being implemented at home by parents and caregivers for enhanced generalization.

The Special Role of Disgust in Food Neophobia

At the beginning, we noted the importance of the omnivore's dilemma in setting the stage for understanding food neophobia. This idea also suggests that disgust plays a critical role in understanding food aversions and neophobia. Disgust is covered elsewhere in this text (Chap. 14), so we will not dwell on it here. Instead, we will center our discussion on the difficulties posed by exposure, with the aim of reducing avoidance. Recent analyses have suggested that direct exposure to disgust requires more time to produce habituation (McKay, 2006). It has also been noted that the conditioning that leads to disgust is more resistant to habituation by its very nature, since it involves evaluative conditioning (de Houwer, Thomas, & Baeyens, 2001). That is, when an object is conditioned to elicit a reaction, the accompanying label attached to it makes it resistant to habituation.

Recent research has suggested that disgust plays an important role in preparing for the development of aversive stimuli in fear conditioning experiments. To illustrate, Muris, Mayer, Huijding, and Konings (2008) found that when children were informed that specific unfamiliar animals were dirty, they were more likely to fear these animals, as compared to children who were told these same animals were clean. Another way in which disgust may operate to increase food avoidance is by observation of the reaction of others to food items. A recent study showed that when adults were presented with facial expressions of disgust in conjunction with food items, the willingness to consume the food was decreased, compared to control participants (Barthomeuf, Rousset, & Droit-Volet, 2009). In light of the attention bias that individuals with contamination fear (Armstrong, Olatunji, Sarawgi, & Simmons, 2010) and unselected non-clinical participants (Cisler, Olatunji, Lohr, & Williams, 2009) show toward disgust stimuli, it is reasonable to suggest that food neophobia may develop, in large part, due to a combination of disgust reactions, the attention bias for minute disgust reactions in others when consuming food, as well as the evaluative

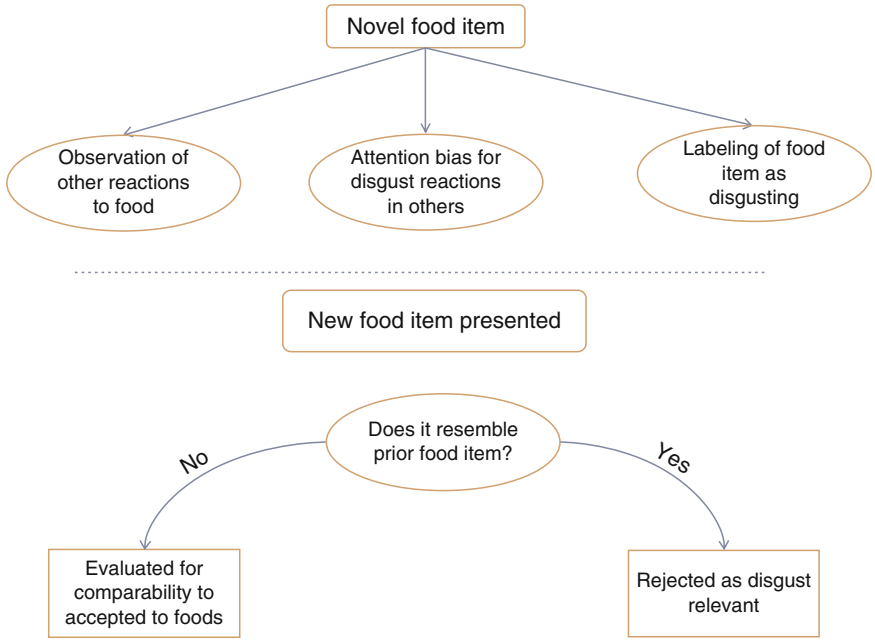


Fig. 30.1 Preliminary cognitive-behavioral model for the development of food neophobia

conditioning process that serves as an etiological mechanism for disgust responses. A preliminary model is illustrated in Fig. 30.1.

Treatment considerations related to disgust: making exposure work. In the light of the difficulty in producing habituation when there is a strong disgust reaction, and the proneness to direct attention to disgust relevant stimuli, applications of both in vivo and graduated exposure procedures requires distraction to allow for adequate tolerability to the stimuli. This method contrasts accepted exposure procedures for fear-based stimuli, where distraction is associated with poorer outcome (Hazlett-Stevens & Craske, 2008). Therefore, we propose applying a set of appealing distractions while setting up exposure for foods that have been labeled disgusting by children with extensive food avoidance. To illustrate, in a case treated by one of the authors of this chapter (DM), a set of strong olfactory distractions were arranged in advance of trying new foods. The child presenting for treatment was a 9-year-old male with an increasingly limited range of acceptable foods due to pronounced disgust reactions. His food avoidance had become so severe that he was losing weight and had difficulty finding acceptable foods at school and at summer day camp. He expressed strong hunger reactions but, at the same time, he was unable to overcome the disgust reaction for a wide range of foods. An illustration of the functional arrangement of relevant stimuli for this boy ("Jake") is presented in Fig. 30.2.

Following assessment, an hierarchy of potentially acceptable, but presently avoided, foods was constructed. In addition, a set of aromatic substances were identified that Jake found appealing. These included an aromatic candle and scented shaving cream, as well as a "taste block" involving a squirt of mouthwash into the mouth immediate prior to tasting new foods (which Jake also deemed acceptable; other possible stimuli include juices or toothpaste). When initiating exposure, the candle was lit, and the shaving cream was wiped just below Jake's nostrils in advance of beginning exposure to low items on the hierarchy. This arrangement is illustrated in Fig. 30.3. Jake responded well to these activities for low items on the hierarchy, and his mother was instructed to

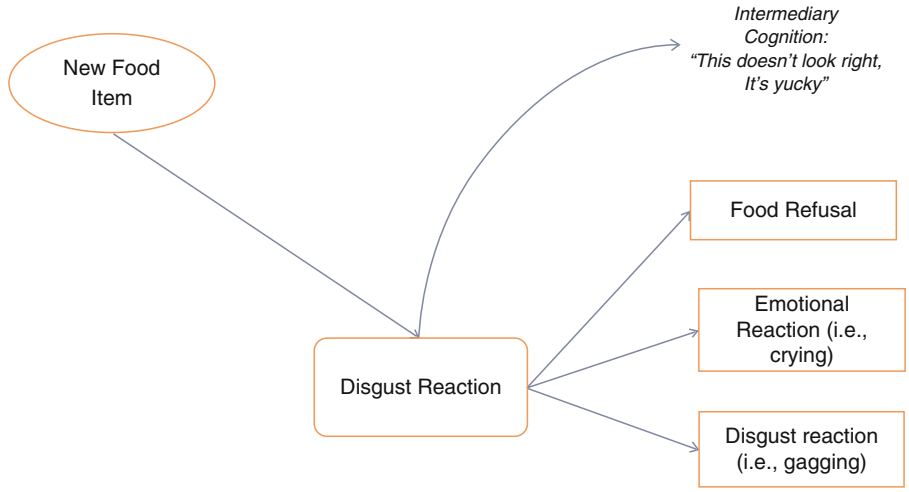


Fig. 30.2 Functional depiction of food refusal maintenance by disgust in "Jake"

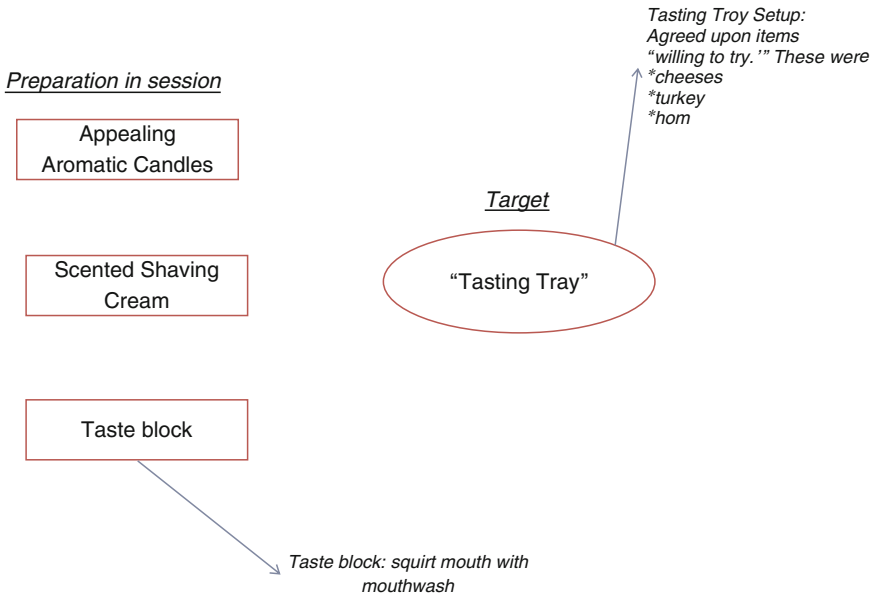
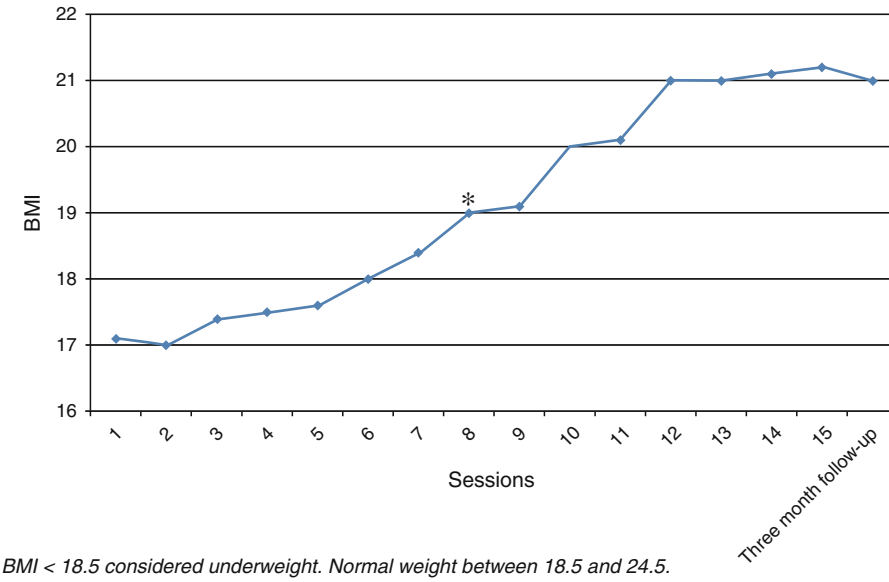


Fig. 30.3 Development of exposure procedures for novel food items for "Jake"

continue this exercise at home. This exercise continued for fifteen sessions, with Jake receiving contingent reinforcement (using a "star chart") for trying new foods on a daily basis, as well as contingent rewards for engaging in treatment on a daily basis with his mother or father. By the end of the treatment, Jake had gained weight and had a body mass index in the normal range. His gains were maintained at 3 month follow-up. His progress is illustrated in Fig. 30.4.



BMI < 18.5 considered underweight. Normal weight between 18.5 and 24.5.
• Reached normal range BMI by session 8 and maintained at follow-up.
• BMI calculated by kg/m²

Fig. 30.4 Treatment outcome for "Jake" following cognitive-behavioral therapy for food neophobia

Conclusions

The literature relating to cognitive-behavior therapy for food neophobia is extremely limited at this point. However, basic research on the correlates and causes of food aversion suggest that several important factors play a role in the problem. First, there are several ways that parents and caregivers, while well-intentioned, worsen food avoidance (such as through pressure on children to consume novel or otherwise rejected foods). Second, some food aversions may be heritable, such as the aversion associated with specific chemicals present in bitter foods. Third, several factors associated with disgust appear to play a prominent role in the development and maintenance of food avoidance.

We have attempted to outline several important features of food aversion towards developing a model for treatment. These components include adjusting exposure-based therapy to account for the special limitations in habituation to disgust, and some potential methods for ensuring success when attempting either in vivo or graduated exposure. While we have been able to demonstrate treatment-related improvements by incorporating an olfactory or gustatory distraction while conducting exposure with a severely food avoidant child, this is by no means to be taken as a set of treatment recommendations. The existing literature is very limited. While some have suggested that exposure could be efficacious (Dovey et al., 2008), there are a wide range of limitations associated with this approach. The most salient concern is how to approach children who are reluctant to engage in treatment at all. In the light of the finding that the potential effectiveness of offering inducements to try new foods is offset by pressure to comply with consumption of new foods, it is highly probable that some efforts at developing exposure procedures would actually worsen food avoidance. Another highly salient consideration is the role of legitimate food taste differences. In highly food avoidant children, this may be difficult to discern but, simultaneously, there are little in the way of guidelines for determining variations in food tastes. We hope that this chapter will set the occasion for additional research on food aversions and neophobia within a cognitive-behavioral context in order that comprehensive treatment guidelines may be developed.

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Social Disability and Impairment in Childhood Anxiety

31

Jordana Muroff and Abigail Ross

Anxiety disorders cause severe impairment and disability with respect to an individual's quality of life and social functioning, especially when untreated (Chavira, Stein, Bailey, & Stein, 2004a). Given the high prevalence of anxiety disorders, it is critical that the resulting impairment is understood, addressed, and prevented when possible. Estimations of lifetime prevalence of anxiety disorders range between 8 and 27% (Costello, Egger, & Angold, 2005a) with age of onset occurring significantly earlier than for all other major mental disorders (Kessler, Chiu, Demler, Merikangas, & Walters, 2005). Rates of childhood anxiety disorders are estimated to be between 6 and 10%, representing the most highly prevalent form of psychopathology in children and adolescents (Briggs-Gowan, Horwitz, Schwab-Stone, Leventhal, & Leaf, 2000; McCracken, Walkup, & Koplewicz, 2002; Merikangas, Nakamura, & Kessler, 2009). Anxiety-related impairment among adults is associated with considerable economic costs related to medical care as well as decreased work productivity (Greenberg et al., 1999). In families with clinically anxious children, societal costs have been estimated to reach 20 times those incurred by families in the general population (Bodden, Dirksen, & Bögels, 2007). Anxiety disorder induced impairment in children includes difficulty in the school environment (Strauss, Lease, Kazdin, Dulcan, & Last, 1989), problematic social interactions (Dweck & Wortman, 1982; Essau, Conradt, & Petermann, 2000), and distress in family life (Bernstein, Borchardt, & Perwien, 1996; Turner, Beidel, & Costello, 1987), that can inhibit the successful completion of discrete developmental tasks (Silverman & Saavedra, 1998). Pediatric anxiety disorders are often unrecognized and undertreated (Chavira, Stein, Bailey, & Stein 2004b; Wren, Scholle, Heo, & Comer, 2003), and may lead to comorbid disorders such as depression or other mental disorders later in life (Kendall & Pimentel 2003; Kovacs, 1996).

Though the manifestation of anxiety-related impairment in children differs from that in adults, systematic examinations of this phenomenon are not reported as extensively in the child and adolescent literature as in the adult literature. Whereas distress and impairment was not required for a DSM-III-R anxiety disorder diagnosis (Cartwright-Hatton, McNicol, & Doubleday, 2006), in the DSM-IV-TR (4th ed. Text revision); an anxiety disorder diagnosis does require "impairment" in conjunction with fulfillment of disorder-specific symptom criteria (American Psychiatric Association [APA], 2000). A clear articulation of what is meant by "impairment," however, has yet to be established with respect to child anxiety disorders. Standards for judging anxiety as "dysfunctional" in nature vary across environmental contexts, cultural values, family attitudes, and developmental

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_31,

stage (Egger & Angold, 2006). For example, parents of very young children may not judge avoidance of being alone, a symptom of separation anxiety, to be "impairing" behavior. Additionally, measures of anxiety-related functional impairment in children are limited and tend to be more focused on symptom severity than domains of disability (Hoagwood, Jensen, Petti, & Burns, 1996).

In this chapter, the concept of impaired functioning is conceptualized as an absence of normal adaptation (or poor performance) with respect to: (1) school performance (related to work completion, attendance, tardiness, and homework completion), (2) a range of developmentally appropriate self-fulfillment activities, including the ability to care for oneself, and (3) interpersonal performance, including family, peer and romantic relationships (Bird et al., 2005). This chapter discusses both the scope and manifestation of anxiety disorder-specific impairment with respect to social functioning in children and adolescents. We conclude with a discussion of impairment related to subthreshold anxiety problems, development, and measurement.

Separation Anxiety Disorder

Separation anxiety disorder (SAD), the only anxiety disorder requiring onset prior to 18 years of age (early onset prior to age 6 years), is characterized by developmentally inappropriate and excessive anxiety concerning real or imagined separation from either the home environment or a primary attachment figure, typically a parent or primary caregiver (APA, 2000). Epidemiological studies indicate the SAD prevalence rate is between 3.5 and 5.4% in children and adolescents (Black, 1995). In contrast to other anxiety disorders, an estimated 50–75% of children with SAD are of low socioeconomic status (Masi, Mucci, & Millepiedi, 2001). Manifestations of SAD include crying, repeated complaints of physical symptoms (e.g., stomachaches, headaches), avoidance of situations requiring separation (e.g., refusal to attend school, to sleep alone, to be left alone in the home, or to play at a peer's house) and increased engagement in safety behaviors (e.g., frequent calls to or from parents) (Jurbergs & Ledley, 2005).

Though the severity of SAD symptomatology ranges from anticipatory discomfort to repeated panic attacks, a diagnosis likely occurs when impairment manifests itself through school refusal or somatic symptoms. Studies indicate that school refusal is reported in approximately 75% of children with SAD (Masi et al., 2001). In a clinical sample of children meeting criteria for either SAD ($n=48$) or school phobia ($n=19$), however, children with SAD were less likely to exhibit school refusal than children with school phobia but more likely to meet criteria for an additional psychiatric diagnosis (Last, Francis, Hersen, Kazdin, & Strauss, 1987). In this sample, more children with SAD were female, prepubertal, and from families with lower socioeconomic backgrounds.

The literature reveals high rates of SAD comorbidity with other psychiatric disorders, especially panic disorder (PD). In addition, several studies of adult populations have confirmed that a history of separation anxiety is present in a significant number of adults with PD and agoraphobia (AG) (Breier, Charney, & Heninger, 1986; Klein, Zitrin, Woerner, & Ross, 1983; Pollock et al., 1996), indicating that separation anxiety may be a precursor to PD onset in adulthood (Mattis & Ollendick, 1997; Ollendick, 1998). The presence of SAD in childhood may represent a risk factor for the development of a number of anxiety disorders later in life, not just PD specifically (Aschenbrand, Kendall, Webb, Safford, & Flannery-Schroeder, 2003; Last, Perrin, Hersen, & Kazdin, 1996; Lipsitz et al., 1994). A diagnosis of SAD may in fact be indicative of early onset PD only in children and adolescents (Doerfler, Toscano, & Connor, 2008; Gittelman & Klein, 1985; Klein, 1980). Though research has yet to determine an algorithm that predicts the exacerbation of SAD to PD (if one exists), Mattis and Ollendick (1997) hypothesize that the combination of a child's temperament, capacity for emotion regulation, and attachment to the primary caregiver likely influence the intensity and duration of the child's responses to separation experiences, and that this combination may ultimately increase the likelihood of developing PD.

Findings from a study comparing a sample of children and adolescents with SAD only ($n=63$), to children and adolescents with comorbid SAD and PD ($n=31$), revealed a later age of onset of SAD and more extensive psychopathology and functional impairment in children and adolescents with comorbid PD and SAD (Doerfler et al., 2008). According to psychiatrist ratings of daily functioning capability, children and adolescents with comorbid SAD and PD were significantly more impaired on measures of global functioning than their counterparts with SAD only. Contrary to the authors' hypothesis, there were no differences between groups in the incidence or prevalence of separation-related events, nor were there any differences in the number of depressive disorder or externalizing disorder diagnoses received (Doerfler et al., 2008). Moreover, children and adolescents in the SAD and PD group averaged 4.2 anxiety disorder diagnoses, whereas children and adolescents in the SAD only group averaged 2.7 anxiety disorder diagnoses. Additionally, parent ratings of children in this sample revealed significantly higher symptom levels on the Child Behavioral Checklist (CBCL; Achenbach, 1991) subscales of internalizing disorders, withdrawn, and thought problems, all of which were clinically significant, in children with comorbid SAD and PD compared to their counterparts with SAD only. Children with both SAD and PD likely experience more impairment with anxiety, self-criticism, and social interactions (Doerfler et al., 2008).

Panic Disorder

PD is characterized by a series of recurrent and unexpected panic attacks. A panic attack is defined as a discrete period of intense fear and discomfort, with a specific symptomatology that develops abruptly and reaches a peak in under 10 minutes and, that occurs and is followed by a persistent concern about experiencing another panic attack (APA, 2000). Prevalence rates of PD in children and adolescents have been reported as high as 10–15% (Alessi, Robbins, & Dilsaver, 1987; Biederman et al., 1997; Masi, Favilla, Mucci, & Millepiedi, 2000) in clinical populations and approximately 0.5–1% in the general population (Essau, Conradt, & Petermann, 1999; Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993). Though PD is less prevalent compared to other psychiatric disorders in the general population, panic attacks occur somewhat more frequently. In one sample of the general population, 18% of adolescents reported the presence of at least one panic attack within a year's time. Slightly more girls than boys reported both panic attacks and PD, with the incidence highest among 14–15 year olds (Essau et al., 2000). Though the age of onset for PD is typically late adolescence or early adulthood (Von Korff, Eaton, & Keyl, 1985; Weissman et al., 1997), some studies of adult populations reveal that as many as 18% of adults with PD indicate initial onset prior to 10 years of age (Von Korff et al., 1985).

Panic attacks are associated with a number of problems, the most frequent being avoiding social situations due to anticipatory fear of another attack and physiological symptoms of palpitations, trembling, nausea, and chills/hot flushes (Essau et al., 2000). In children, the presentation of PD is qualitatively different from that of SAD and generalized anxiety disorder (GAD); children and adolescents typically present with somatic symptoms of palpitations, shortness of breath, sweating, faintness and weakness (Biederman et al., 1997; Bradley & Hood, 1993; Last et al., 1987) as well as chest pain, flushes, trembling, headache and vertigo (Masi, Favilla, Millepiedi, & Mucci, 2000). The cognitive model of panic (Clark, 1996) proposes that cognitive symptoms related to PD differ by age and developmental stage. Fear of dying has been reported in children and young adolescents, whereas cognitive symptoms manifest themselves as fear of going crazy and depersonalization in older adolescents (Masi, Favilla, Millepiedi, et al., 2000). A comprehensive review of the literature indicates that physiological symptoms are reported more frequently than cognitive symptoms in children and adolescents (Ollendick, Mattis, & King, 1994). Nelles and Barlow (1988) posit that the discrepancy in symptom reporting is due to the fact that interpretation of the somatic symptoms is linked to the

course of child development; the catastrophic attributions required for a PD diagnosis are only possible once a child reaches the developmental stage of adolescence, as children lack the cognitive capability to assess the level of "dangerousness" related to physical symptoms. Awareness of early-onset PD, as well as a more precise definition of early signs and possible clinical subtypes may reduce clinical impairment and improve the prognosis of individuals with PD (Masi, Pari, & Millepiedi, 2006). Early onset has been shown to cause severe impairment in adult populations afflicted with the disorder (Weissman, Klerman, Markowitz, & Ouellette, 1989).

Agoraphobia (AG) or phobic avoidance (including avoidance of situations or places related to the panic attack or where escape or obtaining help during an attack is either difficult or embarrassing), may also accompany PD (Masi et al., 2006). There is little research available regarding comorbidity of AG, related avoidance behaviors, and symptom severity in children and adolescents diagnosed with PD (Kearney, Albano, Eisen, Allan, & Barlow, 1997). In one sample of clinically referred children and adolescents, 65% of children meeting criteria for PD also met criteria for PD with AG (Biederman et al., 1997). Findings from another study exploring impairment in children with PD with AG revealed that the most frequently avoided situations were social settings with unfamiliar situations (such as crowds, elevators, and restaurants), but that severity of impairment was not substantial (Kearney et al., 1997). Thus, PD with AG may not result in significant impairment in daily and social functioning in children and adolescents (Kearney et al., 1997).

Even though the prevalence of PD is low in the child and adolescent general population, a significant proportion of children and adolescents diagnosed with PD present with comorbid GAD (Masi et al., 2004), obsessive-compulsive disorder (OCD; Goodwin, Lipsitz, Chapman, Mannuzza, & Fyer, 2001; Masi et al., 2005) and SAD (Alessi & Magen, 1988; Biederman et al., 1997; Bradley & Hood, 1993; Doerfler, Connor, Volungis, & Toscano, 2007; Masi, Favilla, Mucci, et al., 2000). Children with early onset SAD, school refusal, or early "behavioral inhibition to the unfamiliar" (Black & Robbins, 1990; Rosenbaum et al., 1988) are at elevated risk for developing PD. Though a sole PD diagnosis is not as impairing as social anxiety disorder (see below) in children and adolescents with respect to social functioning (Quilty, Van Ameringen, Mancini, Oakman, & Farvolden, 2003), research indicates that children with PD and social anxiety were rated by clinicians as being more severely affected in global impairment than children with other anxiety disorders (Last, Perrin, Hersen, & Kazdin, 1992). If untreated, PD shows the lowest rate of recovery and highest risk of development of new psychiatric/behavioral disorders relative to other anxiety disorders (Last et al., 1996). Comorbid PD and depression has been associated with earlier age of onset of psychiatric illness, an increased duration of current episode of illness, greater intensity of symptoms severity, greater impairment in level of functioning, increased psychopathology, sleep disturbance, and greater levels of objective stress and anger (Dube et al., 1986).

Social Anxiety Disorder

Associated with substantial impairment, social anxiety disorder (also known as social phobia) is characterized by marked and persistent fear of a minimum of one social performance situation in which an individual experiences marked distress, including embarrassment or humiliation upon entering a social situation, fear of possible scrutiny, or an experience of physiological distress that results in interference with daily routines, academic functioning or social relationships (APA, 2000). Depending upon a child's age, marked distress may manifest itself through crying, avoiding social situations (such as school), tantrums, freezing, or panic attacks predisposed by social situations (APA, 2000). With lifetime prevalence rates estimated between 12 and 13%, social anxiety disorder is the most commonly occurring anxiety disorder (Kessler, 2003; Kessler, Berglund, et al., 2005), and one of most prevalent mental disorders in the general population; it ranks third behind substance abuse and depression (Turner, Beidel, & Townsley, 1990).

The onset of social anxiety disorder typically occurs during late childhood or early adolescence. Epidemio-logical studies indicate that over 50% of individuals have retrospectively reported onset by age 13 years (Chavira & Stein, 2002), 75% prior to 16 years and 90% by age 23 (Kessler, Berglund, et al., 2005). The onset of social anxiety disorder prior to 15 years old is especially problematic, as it appears to be associated with an elevated risk of comorbidity with other psychiatric disorders, than is the development of social anxiety disorder later in life (Lecrubier, 1998). Though the course of social anxiety disorder is chronic and debilitating without intervention, the majority of cases appear to go undiagnosed and untreated in pediatric primary care (Chavira, Stein, Bailey, & Stein, 2004b). Findings from a 5-year, prospective longitudinal study of 3,021 community cases exploring the evolution of social anxiety disorder, revealed that the majority of cases of social anxiety disorder had emerged in the early teenage years, and that by 19 years of age either a progressive deterioration in functioning or a persistent course of illness had been established (Narrow, Rae, Robins, & Regier, 2002). Observations of particular cases in this study revealed that social anxieties could be mitigated temporarily through a positive relationship with a partner, but that a subsequent new challenge in life would precipitate the re-presentation of the disorder (Wittchen & Fehm, 2003; Wittchen, Fuetsch, Sonntag, Muller, & Liebowitz, 2000). Further analyses revealed that social anxiety affects most areas of life, particularly education attainment, career/work productivity, and development of functional romantic relationships (Wittchen et al., 2000), also known as romantic competence (Bouchey, 2007).

Children and adolescents with social anxiety tend to endorse the following interpersonal situations as creating significant distress: formal speaking (88.8%), eating in front of others (39.3%), attending parties (27.6%), writing in front of others (27.6%), using public restrooms (24.1%), speaking to authority figures (20.7%), and informal speaking (13%) (Beidel & Morris, 1995). Social anxiety in childhood is associated with impairment most notably in the school domain, manifesting itself through early departures from school, school refusal, acquisition of lower levels of educational training, and academic underachievement (Keller, 2001; Kessler, 2003). Children with social anxiety disorder may have fewer peer relationships, limited involvement in outside activities, and more somatic symptoms, such as headaches and stomachaches, than their counterparts who do not carry the diagnosis (Beidel, Turner, & Morris, 2000; Khalid-Khan, Santibanez, McMicken, & Rynn, 2007). In adolescence and early adulthood, social anxiety disorder has been associated with increased rates of attempted suicide and drug and alcohol dependencies (Keller, 2001; Kessler, 2003; Wittchen & Fehm, 2003). Severe cases of social anxiety disorder may also result in failure to speak in feared social situations, even if normative expressive language development is present, and result in the development of selective mutism (Khalid-Khan et al., 2007), a distinct disorder that interferes with both educational achievement and socialization (Tancer & Klein, 1991).

Of the anxiety disorders, social anxiety may exert the greatest impact upon academic functioning. In the Netherlands, a nonclinical sample of 312 children ages 10–12 was assessed via both teacher and child reports for classroom functioning and symptoms severity (Muris & Meesters, 2002), using the Spence Children's Anxiety Scale (Spence, 1998) and a sociometric ranking procedure that included teacher assessments of learning attitude, quality of the teacher-student relationship, quality of peer relationships, and self-esteem reports. Findings revealed that higher levels of social anxiety symptoms per child-report were associated with increased difficulties in classroom functioning (including general classroom functioning, greater difficulty with peer relations, and lower self-esteem).

A more recent study that conducted follow up diagnostic interviews with 45 school-aged children meeting criteria for an anxiety disorder, revealed that compared to a sample of children carrying a diagnosis of GAD, children with social anxiety disorder feared and avoided a significantly greater amount of social situations, were significantly more likely to have trouble initiating

friendships, and to prefer to spend time alone (rather than with peers) (Bernstein, Bernat, Davis, & Layne, 2008). Moreover, symptom severity was inversely associated with social skills (greater deficits), leadership skills, academic functioning, and directly related to attention difficulties and learning problems in the classroom in the sample diagnosed with social anxiety only. The authors hypothesize that attention problems may occur due to distraction by worries about answering questions in school, fears of reading in front of the class, or fears of talking to peers. Learning problems may be exacerbated by anxiety about asking for help, taking tests, or writing/speaking in front of a class.

These results are consistent with findings in the adult literature indicating that individuals with social anxiety experience a significant impediment to help-seeking behaviors. One study revealed that adults with social anxiety are significantly more likely to report financial barriers, uncertainty over where to seek help, and fear of what others might think/say as barriers to seeking treatment for the disorder (Olfson et al., 2000). The association between symptom severity and school functioning deficits was notable and evident only in the sample of children with social anxiety disorder (Bernstein & Layne, 2006).

The literature reveals high rates of comorbidity with other psychiatric disorders in children diagnosed with social anxiety disorder. In a sample of children ages 7–13 (inclusive) with a primary diagnosis of social phobia, over 60% carried an additional diagnosis; 36% of this sample carried an additional anxiety disorder (Beidel, Turner, & Morris, 1999). In the Bernstein et al. (2008) study sample, 100% of children with social anxiety disorder met criteria for at least one other comorbid psychiatric disorder. Regarding disorder specific comorbidity, other studies reveal that individuals with social anxiety disorder are at significant risk for comorbidity with PD or AG (Sareen & Stein, 2000), major depression (MDD) and ADHD, in addition to GAD and specific phobias (Chavira et al., 2004b). Notably, the generalized subtype of social anxiety disorder was the only anxiety disorder significantly associated with an increased likelihood of MDD in the pediatric primary care study sample of Chavira et al. (2004b). Studies indicate that individuals diagnosed with social phobia who do develop comorbid disorders are at increased risk for both suicidal ideation and attempts (Sareen & Stein, 2000), elevated high school dropout rates (Van Ameringen, Mancini, & Farvolden, 2003), difficulty maintaining employment, and increased social isolation in adulthood (Davidson, 1993).

Finally, of the two subsets of social anxiety disorder, interpersonal anxiety (generalized social anxiety disorder) has been reported to have relatively earlier onset, be more chronic in nature, occur with higher rates of comorbidity with other mental disorders, and is more familial than performance anxiety (nongeneralized social anxiety disorder) (Wittchen, Stein, & Kessler, 1999).

Specific Phobia

Another classification of phobias, specific phobia (previously known as simple phobia in the DSM-III; APA, 1980), is characterized by the presence of marked and persistent fear of particular objects and/or situations (APA, 2000). Though certain fears, such as separation from a primary caregiver, or darkness, are developmentally appropriate at certain ages, specific phobias may be differentiated from normative developmental fears in that a phobic reaction is both disproportionate and excessive, provokes avoidant behaviors, and is maladaptive (Silverman & Rabian, 1994). Four highly prevalent types of specific phobias are identified in the Diagnostic and Statistical Manual of Mental Disorders (4th ed. Text revision [DSM–IV-TR]; APA, 2000): animal, situational, natural environment, blood injection/injury , plus "other" (APA, 2000). Results from a number of studies indicate that the most common phobias of childhood are heights, loud noises, darkness, injections, insects and dogs (King, 1993; Silverman & Rabian, 1994; Strauss & Last, 1993). Though less prevalent than other specific phobias, school phobia may be the most noticeable and result in the most social impairment in a variety of domains; children and adolescents suffering from school phobia may feel unable

perform classroom tasks and experience isolation and alienation from peers. Such perceptions may contribute to prolonged school absence and inhibit completion of developmental tasks (Okuyama, Okada, Kuribayashi, & Kaneko, 1999). In these cases, specific phobia may be difficult to distinguish from SAD.

Though estimates of specific phobia prevalence in the general child and adolescent population range from 2.4 to 3.6% (Kashani, Orvaschel, Rosenberg, & Reid, 1989; McGee et al., 1990), prevalence in clinical samples are estimated to be approximately 20% (Last et al., 1992). Results from a number of studies indicate that specific phobia typically occurs with an early onset, and that children afflicted usually suffer a chronic course of the disease (see Emmelkamp & Scholing, 1997 for a review). Findings from the Epidemiologic Catchment Area Program study indicate that the highest risk for development of specific phobia is between the ages of 10 and 14 years (Burke, Burke, Rae, & Regier, 1991). Other studies reveal that the ages of onset include 7 years old for animal phobia, (Ost, 1987, 1991), between 7 and 9 years for blood injection/injury phobia (Liddell & Lyons, 1978; Ost, 1987, 1991), 11.9 years for natural environment phobia (Liddel & Lyons, 1978), and ranging from 10 to 13 years for other types (Strauss & Last, 1993). Results from a sample of 139 adult phobic patients revealed a differential age of onset depending on the specific phobia; phobias of animals and insects rarely commenced after age five, whereas most phobias of the other varieties (AG), specific situations (heights/thunder), and social situations, started after age 10 (Marks & Gelder, 1966).

Like other anxiety disorders, the anxiety response inherent in specific phobia entails cognitive, behavioral, and physiological components (Flatt & King, 2008). Though physiological (heart palpitations, sweating, etc.) and cognitive (catastrophizing, thoughts of fear, etc.) aspects of the anxiety response mirror those of PD, a number of studies indicate that behavioral responses may also include rigid posture, thumb sucking or crying in addition to avoidance (Barrios & Hartman, 1997; Beidel, Borden, Turner, & Jacob, 1989; King, Ollendick, & Murphy, 1997; Ollendick, Davis, & Muris, 2004; Silverman & Ginsburg, 1995; Silverman & Rabian, 1994). Very few studies have examined the frequency, symptom duration, and associated social impairment of specific phobia in child and adolescent populations. Essau et al. (2000) report that in a clinical population of adolescents meeting criteria for specific phobia, the most frequent phobia reported was blood (39.6%), followed by animals (28%), natural environments (26%), and specific situations (23.7%). Of those with a fear of the natural environment, the most common was fear of height, followed by storms and lightning. Approximately 30% of adolescents in this sample reported fear of a specific situation or object, the most frequently reported of which was blood. Fear of animals, natural environment, and specific situations were all significantly more frequently reported by girls than boys (Essau et al., 2000). Panic symptoms were significantly associated with each phobia during the worst episode, the most frequent of which were that of palpitation, trembling/shaking, and sweating. All cases with any subtype of specific phobia were impaired in school, leisure, and social activities during the worst episode of their disorder (Essau et al., 2000). Results from other studies reveal that specific phobias result in considerable academic difficulties (Ialongo, Edelsohn, Werthamer-Larsson, Crockett, & Kellam, 1995), social and personal distress, such as school attendance and making friends (Braswell & Kendall, 2001; Chansky & Kendall, 1997), and interference in activities of daily living (Ollendick, King, & Muris, 2004).

Generalized Anxiety Disorder

Children presenting with GAD have been characterized as "worriers" and "little adults" due to their excessive, adult-like worries. Though the majority of people with GAD experience their first symptoms in late adolescence, their 20s, or early 30s (Wittchen, Zhao, Kessler, & Eaton, 1994), childhood GAD afflicts approximately 10–15% of the population with a mean age of onset of 8.8 years (Costello, Egger, & Angold, 2005b; Last et al., 1992). In children, a higher

incidence of GAD is reported in girls than in boys (Keeton, Kolos, & Walkup, 2009). Though the disorder is rarely diagnosed in its pure form, it is often co-occurring with social phobia, SAD, depression and ADHD (Masi, Mucci, Favilla, Romano, & Poli, 1999; Verduin & Kendall, 2003). GAD symptoms can impose marked distress and interfere with social, emotional, and educational functioning.

Common themes of worry in children with GAD include perfectionism, punctuality, health and safety of themselves and others, catastrophic world events (e.g., weather disasters, war), family finances, and events in the distant future (e.g., college) (Layne, Bernat, Victor, & Bernstein, 2009). Though children with GAD exhibit age-appropriate worries (e.g., grades, homework, friends), such worries occur more often than in peers their same age. In one nonclinical sample of children ages 8–13, children who met criteria for GAD or overanxious disorder (OAD) endorsed an average of six worries, compared to control children who endorsed an average of only one worry (Muris, Meesters, Merckelbach, Sermon, & Zwakhalen, 1998). In the same study, children meeting criteria for GAD/OAD could also be distinguished from control children due to a higher frequency of their primary worry, a stronger degree of interference in daily functioning, and more difficulty controlling their worry, indicating that frequency and intensity of worry differentiate children with GAD from those carrying other anxiety disorder diagnoses. Other studies revealing that children with GAD endorsed significantly more worries, a greater intensity of worries, and more DSM-IV associated symptoms than anxious children without GAD are consistent with these results (Layne et al., 2009).

Though three (of the six) associated symptoms listed in criterion C of the DSM-IV (i.e., restlessness, fatigue, concentration difficulty, irritability, muscle tension, sleep disturbance) are required for a diagnosis of GAD in adults, only one is required for diagnosis in children (APA, 2000). A number of studies, however, indicate that children diagnosed with GAD commonly endorse more than one symptom. One study revealed that a sample of children with GAD endorsed an average of 3.4 associated symptoms, with restlessness the most common (74%) and muscle tension the least common (29%) (Tracey, Chorpita, Douban, & Barlow, 1997). A subsequent study of 47 children diagnosed with GAD (ages 9–13 years) revealed a consistent pattern of symptom presentation (Kendall & Pimentel, 2003). Both studies revealed that the number of associated symptoms increased with age. A more recent study comparing children with GAD endorsed to anxious children without GAD revealed similar results; children with GAD reported an average of 3.4 associated symptoms, whereas anxious children without GAD reported significantly fewer associated symptoms (Layne et al., 2009). Consistent with previous research, the most common associated symptoms reported by children with GAD included restlessness/trouble relaxing, trouble concentrating, and trouble sleeping, with 67% of children reporting these symptoms.

Though worries of children and adolescents with GAD are characterized by continuous self-doubt, elevated sensitivity to criticism, and chronic need for reassurance (Wagner, 2001), they are more often accompanied by somatic symptoms or physical complaints. Physical complaints were reported in over 70% of subjects in a sample of 58 children diagnosed with GAD (Masi, Favilla, & Romano, 1999). In a subsequent study of 162 clinically referred children, those with anxiety and/or depression reported significantly higher rates of somatic complaints, most often headache, than subjects with other mental disorders (Masi, Favilla, Millepiedi, et al., 2000). Additional research indicates that severity of somatic symptoms may increase with age; older children (ages 12–17 years) with GAD reported more somatic symptoms than younger children (ages 5–11 years), and that somatic symptom incidence was reported more frequently among children with GAD than among those without the diagnosis (Ginsburg, Riddle, & Davies, 2006). Somatic symptoms were significantly associated with anxiety severity, impaired global functioning, avoidance, and interference with family relationships; however, the presence of somatic symptoms was not associated with impaired peer relationships (Ginsburg et al., 2006).

The differential worry content evident in children with GAD has implications for social

functioning. Though results of one study exploring the presentation of GAD in a nonclinical sample of children (7–11 years old), indicate that the most common domain of worry endorsed both by children with GAD (as well as anxious children without GAD), was the health of significant others (55 and 45%, respectively), children with GAD were significantly more likely to worry about their performance and family issues, than were children without GAD diagnosis (Layne et al., 2009). These results are consistent with the characterization that children with GAD are excessively preoccupied with grades, how they are perceived by others, and family matters. Results of another study of school aged children revealed a GAD diagnosis to be positively related to stronger social skills, and negatively related to attention problems, when compared to a sample of children with social anxiety disorder (Bernstein & Layne, 2006). The authors hypothesize that this association may be due to the fact that GAD in children is often characterized by a perfectionism, an overly conscientious work ethic, and an eagerness to please others, especially adults (Bernstein & Layne, 2006).

Like social anxiety disorder, GAD is also highly comorbid with other psychiatric disorders (Layne et al., 2009; Masi et al., 2004). In the study by Layne et al. (2009), only 14% of participants carried GAD as their only diagnosis; 63% of the sample carried comorbid anxiety diagnoses. Masi, Favilla, and Romano (1999) note that co-occurrence with specific phobia, SAD and social anxiety is more often the rule than the exception; several studies reveal that up to 60% of anxious children meet criteria for two of the aforementioned three disorders, and 30% meet criteria for all three (Birmaher et al., 2003; Research Units on Pediatric Psychopharmacology (RUPP) Anxiety Study, 2001). Similarly, in the clinical sample of Masi et al. (2004), the prevalence of a stand-alone GAD diagnosis was 7%; 75% were diagnosed with at least one other anxiety disorder. Though 66% of this sample reported comorbid depression, which is a marked increase from the 4% comorbidity rate reported by Layne et al. (2009), the discrepancy is likely due to fact that the sample in Layne et al.'s (2009) study was a nonclinical population.

Other studies indicate that the type of disorder that coexists with GAD varies with age. Results from one study of children revealed that older children (ages 12–19 years) with GAD more frequently exhibited comorbid MDD or simple phobia, whereas younger children (ages 5–11 years) with GAD more commonly had co-occurring separation anxiety or attention deficit disorders (Strauss, Lease, Last, & Francis, 1988). Older children with GAD also reported significantly higher severity of anxiety and depression symptomatology, and a higher total number of anxiety symptoms on self-report measures, indicating that manifestation of GAD impairment varies by developmental stage (Strauss, Last, Hersen, & Kazdin, 1988). Other research indicates that intensity of symptoms also differentiates children with GAD vs. simple phobia (Weems, Silverman, & La Greca, 2000), but that the most common comorbid disorders are social phobia and SAD (Keeton et al., 2009).

Obsessive-Compulsive Disorder

This next section on childhood anxiety and impairment focuses on OCD, characterized by the presence of recurrent obsessions or compulsions that are distressing, time consuming or debilitating (APA, 2000). The available literature indicates prevalence rates of 2–4% in children and adolescents (Douglass, Moffitt, Dar, McGee, & Silva, 1995; Zohar, 1999). Research indicates that the content of obsessions is similar in general and clinical populations (Freeston & Ladouceur, 1993), and that impairment results from frequency and duration of obsessions rather than content (Valderhaug & Ivarsson, 2005). A review of 70 OCD cases revealed that washing, grooming, and checking rituals, and/or preoccupation with contamination (dirt or germs), danger (to self/others), and the need for exactness, symmetry, order (known as the "just right phenomenon") account for the majority of symptoms among children and adults (Swedo, Rapoport, Leonard, Lenane, & Cheslow, 1989).

The modal onset of pediatric OCD is 10 years of age (Geller et al., 1998); as many as 50% of

adults afflicted with the disorder report symptom development prior to or during adolescence (March, Franklin, Nelson, & Foa, 2001). Though research indicates that early-onset OCD is more frequently familial in nature, afflicts males at a higher rate than females, and is associated with patterns of comorbid disruptive behaviors and specific developmental disorders (Geller et al., 1998), the clinical presentation of OCD in children is very similar to that in adults, affecting a broad range of functional domains (Abramowitz et al., 2003; Hanna, 1995; Piacentini & Bergman, 2000; Rettew, Swedo, Leonard, Lenane, & Rapoport, 1992). Childhood OCD is typically characterized by a chronic yet fluctuating course, and confers heightened risk for later psychiatric and psychosocial morbidity (Bolton, Luckie, & Steinberg, 1995; Hanna, 1995).

Studies of clinical child and adolescent populations reveal that OCD impairment is evident in a range of functional domains. In one study of 151 clinically referred children, the most commonly reported OCD-related problems were concentrating on schoolwork (47%) and doing homework (46%). Almost 90% of children and adolescents in the sample reported at least one significant OCD-related dysfunction, and close to half reported significant OCD-related problems within domains of school, home, and social functioning (Piacentini, Bergman, Keller, & McCracken, 2003). School problems may be related to deficits in implicit procedural learning, which has been found to be impaired in individuals with OCD relative to anxious controls (Goldman et al., 2008). Findings from a study replicating the examination of OCD on psychosocial functioning in a sample of 68 children and adolescents with OCD, revealed profound impairments most markedly at home, but that frequent impairment in the school and social domains was also evident (Valderhaug & Ivarsson, 2005).

Piacentini et al. (2003) also describe how OCD symptoms may manifest in various domains. For example, difficulties with tardiness to school or bedtime routines may be due to compulsions around bathing and dressing. Eating in restaurants and attending public places may be inhibited by contamination concerns. Attention and concentration associated with reading, listening, having a discussion, school and/or job related tasks may be impaired by counting rituals, negative intrusive thoughts, and/or checking and repeating compulsions. The ability for youth to develop friendships and romantic relationships may be hindered by severe OCD symptoms, as well (Piacentini et al., 2003).

Studies have also explored the manifestation of specific OCD symptom impairment with respect to interpersonal relationships. In a sample of 57 youth diagnosed with OCD, results revealed a positive relationship between family accommodation and OCD symptom severity, functional impairment (parent-rated), and both externalizing and internalizing behavior problems (Storch, Geffken, et al. 2007). The authors suggest that the impact upon familial interpersonal relationships may in fact exacerbate the course of OCD-related impairment. While family members may intend to reduce their loved ones' distress and impairment through accommodation, it often has the unintended effect of worsening symptoms, and leading to worse impairment by reinforcing avoidance and interrupting habituation (Steketee & Van Noppen, 2003). "Family accommodation also prevents the child from learning that feared consequences (e.g., getting sick from touching a 'contaminated' object) typically do not occur, and lessens the natural consequences of OCD behavior (e.g., time spent engaging in rituals may interfere with preferred activities)" (Storch, Geffken, et al., 2007, p. 208).

Impairment may also vary by OCD symptom subtype (Baer, 1994; Calamari et al., 1999, 2004). For example, compulsive hoarding is a common subtype of OCD which is associated with significant impairment. In a sample of 80 children and adolescents with OCD, 21 youth who endorsed significant hoarding symptoms reported the presence of poorer insight, greater frequencies of magical thinking obsessions, and ordering/arranging compulsions and higher levels of anxiety, aggression, somatic complaints, and externalizing and internalizing symptoms (Storch, Lack, Merlo, Geffken, et al., 2007), many of which contribute to problematic peer and familial relationships. Higher rates of PD were found in

youth reporting hoarding symptoms than in those who did not, though comorbidity rates of OCD with other disorders did not differ between groups (Storch, Lack, Merlo, Geffken, et al., 2007).

Other studies also indicate that a number of subtypes of childhood OCD exist (Geller et al., 1998; Sobin et al., 2000; Storch, Lack, Merlo, Marien, et al., 2007; Swedo et al., 1997), each of which has developmentally specific traits that change over time (Ivarsson & Valderhaug, 2006). In addition, traumatic life events may also influence and exacerbate obsessive compulsive symptom presentation and subtypes (Cromer et al., 2007a; 2007b). Thus, research on OCD treatment and impairment may consider subtypes, development, and life events (Lewin et al., 2005).

Posttraumatic Stress Disorder

The presentation of posttraumatic stress disorder (PTSD) symptoms is fundamentally different in children than in adults. PTSD is characterized by a series of symptoms that include distressing recollections of a traumatic event (reexperiencing), avoidance of certain stimuli, thoughts or feelings associated with the traumatic event (avoidance/numbing), and hyperarousal following a traumatic event (APA, 2000). Prevalence rates in at-risk child populations range from 23% in children exposed to physical injury (Aaron, Zaglul, & Emery, 1999) to as high as 34% in youth exposed to physical violence (Berman, Kurtines, Silverman, & Serafini, 1996) and 36% in samples of children exposed to physical or sexual abuse (Ackerman, Newton, McPherson, Jones, & Dykman, 1998).

Developmental modifications have been introduced to both criterion A (experience of trauma), and the symptom cluster B criteria (reexperiencing) in the DSM-IV-TR; however developmental modifications to symptom clusters C (avoidance/numbing), and D (hyperarousal) have yet to be established (APA, 2000). Findings from Carrion, Weems, Ray, and Reiss (2002) suggest that developmental modifications to symptom clusters C (Avoidance and Numbing) and D (Hyperarousal) may be necessary to assess functional impairment. Specifically, the evaluation of symptom intensity and their relationship to functional impairment may be more useful in determining a diagnosis of pediatric PTSD, than seeking a threshold number of symptoms.

A number of studies with samples of even younger children who have been traumatized reveal that very young children (ages 4 years and under) can and do exhibit PTSD distinct symptomatology, even when the aforementioned developmental adaptations to the diagnosis have been made (Scheeringa, Peebles, Cook, & Zeanah, 2001; Scheeringa & Zeanah, 2001; Scheeringa, Zeanah, Drell, & Larrieu, 1995). An alternative set of criteria for PTSD for infants and young children has been published in the *Diagnostic Classification:* 0–3 (DC: 0–3; Zero to Three, 1994), which eliminates developmentally inappropriate items (e.g., foreshortened sense of the future, partial amnesia of the event), and incorporates modifications to be less dependent on verbalizations and more dependent on behavioral observations of the children (e.g., an increased frequency of nightmares is sufficient regardless if the child is able to verbalize the content). The DC: 0–3 criteria also contain new items that are more developmentally sensitive to this age group, such as new separation anxiety, new aggression, loss of previously acquired developmental skills (such as toileting and speech), and new fears unrelated to the trauma (such as fear of entering the bathroom alone). In young children, reenactments are more likely to be expressed in play rather than through verbalizations; additionally, flashbacks are less frequently reported than in adults (Terr, 1983; Terr et al., 1999), possibly due to the fact that young children with limited verbal and abstract cognitive capacities cannot yet express their internal experiences (Scheeringa & Zeanah, 2001).

The impact of PTSD symptomatology upon functional and social impairment may be the most severe in nature of all anxiety disorders. In a sample of 384 longitudinal youth studies by Giaconia et al. (1995), 6.3% of the sample met criteria for PTSD by age 18. Those meeting criteria demonstrated widespread impairment cutting across a number of domains, including more overall behavioral-emotional problems, more

interpersonal problems, greater incidence of academic failure, greater frequency and intensity of suicidal behavior, greater frequency of health problems, and increased risk for development of additional disorders. Deficits in many of these domains were also evident in traumatized youth (approximately 40% of the sample) who did not develop PTSD compared with their peers who had not experienced traumas. Other studies reveal that associated psychiatric symptomatology in children exposed to trauma, include depression, anxiety, anticipatory fears, behavioral and affect regulation problems, sleep disturbances, substance abuse, somatic complaints, eating disorders, and learning difficulties (Baker & Shalhoub-Kevorkian, 1999; Kinzie, Sack, Angell, Clarke, & Ben, 1989; Koplewicz et al., 2002; Laor et al., 1997; Pat-Horenczyk, Abramovitz, et al., 2007; Scheeringa, Zeanah, Myers, & Putnam, 2003; Trappler & Friedman, 1996; Zivcic, 1993). Symptoms may remain pervasive and long lasting, and significantly compromise children's development and well-being (Desivilya, Gal, & Ayalon, 1996; Dyregrov, Gjestad, & Raundalen, 2002; Laor et al., 1997). Children with PTSD or partial symptomotology may also experience impairment in attachment, such as boundary problems, social isolation, difficulty attuning to emotional states of others, perspective taking, and impaired ability to enlist others as allies or make friends (Complex Trauma Task Force, 2002). In addition to problems with expressing emotions and affect regulation, children diagnosed with PTSD may experience deficits in the capacity to identify internal emotional experiences, or differentiate among states of arousal, and thus turn to alternative maladaptive coping strategies, including dissociative coping (chronic numbing), avoidance of any experience that may generate a lot of affect (even positive experiences) and/or maladaptive behavioral strategies, such as substance abuse (Complex Trauma Task Force, 2002).

With respect to adolescents, a number of studies have revealed the impact of PTSD upon interpersonal relationships, especially with respect to dating. In a random sample of 402 youth from an active Child Protective Services (CPS) who had begun dating, over 60% of females and nearly half of males (44–49%) reported experiencing some sort of dating violence. PTSD symptomatology significantly mediated the male emotional abuse-perpetration and the female emotional/physical abuse-victimization links (Wekerle et al., 2009). Other studies have revealed gender variation across aspects of the PTSD diagnosis; findings from Pat-Horenczyk, Peled, et al. (2007) revealed that female adolescents reported greater severity of posttraumatic symptoms, whereas boys exhibited greater functional impairment in both social and family domains (Pat-Horenczyk, Abramovitz, et al., 2007), as well as more risk-taking behaviors, even with no gender differences in trauma exposure (Pat-Horenczyk, Abramovitz, et al., 2007).

Discussion and Conclusion

Mixed Anxiety

Currently, the DSM-IV-TR groups anxiety disorders together (except for SAD located in the "child" section). While the previous sections discussed specific anxiety disorders, many studies that attempt to address anxiety-induced impairment collapse all anxiety disorders together into a single category and thus, are unable to isolate disorder-specific aspects of impairment. For example, Strauss, Lahey, Frick, Frame, and Hynd (1988) examined social status among peers of those with anxiety disorders and conduct disorders. Those with anxiety were rated lowest on the social-impact score (based on nominations of like-most and like-least) and were categorized as socially neglected. Low peer popularity among children with anxiety disorders may be due to comorbid depression. Chansky & Kendall (1997) had children with anxiety disorders and nonanxious controls watch a video of confederate children playing a game, with the expectation that they would join the group. They found that children with anxiety disorders reported greater negative social expectations, diminished social self-competence, and elevated levels of social anxiety. These children were also rated as more socially maladjusted than nonanxious controls by their parents and teachers. Others have found that

children with anxiety disorders have more school-related problems, and poorer self-image than their peers without anxiety (Kashani & Orvaschel, 1990). A study examining responses to stories of ambiguous situations revealed that children with generalized, social or separation anxiety experienced more negative thought processes, judge ambiguous situations as more dangerous, and have less confidence in their ability to cope with danger, compared to nonanxious controls (Bogels & Zigterman, 2000). These results are consistent with Mathews' (1990) assertion that anxious individuals selectively attend to threatening information perceived as dangerous and may perceive ambiguous events as more dangerous than do non-anxious individuals. Sleep-related problems have also been associated with anxiety disorders among children and adolescents (Alfano, Ginsburg, & Kingery, 2007).

Anxiety Measures and Impairment

While substantial evidence demonstrates that anxiety impairs children's global functioning, it is critical that there are developmentally sensitive instruments to assess specific areas of impairment. A number of assessment tools for childhood anxiety disorders have been developed (Merlo, Storch, Murphy, Goodman, & Geffken, 2005; Silverman & Ollendick, 2005) such as the Multidimensional Anxiety Scale for Children (MASC; March, Parker, Sullivan, Stallings, & Conners, 1997), The Modified-State-Trait Anxiety Inventory for Children (STAIC-M; Spielberger, 1973), Revised-Children's Manifest Anxiety Scale (RCMAS; Reynolds & Richmond, 1978), Hamilton Anxiety Rating Scale (Clark & Donovan, 1994) and the Fear-Survey Schedule for Children-Revised (FSSC-R; Ollendick, 1983). These anxiety measures tend to focus on symptom severity, differential diagnosis and evaluation of treatment outcomes, with limited attention to impairment, and are not specific to a particular anxiety disorder (Piacentini, 1999).

Several other measures focus on specific areas of impairment. For example, the Child Anxiety Impact Scale – Parent Version (CAIS-P) (Langley, Bergman, McCracken, & Piacentini, 2004) is a parent report instrument assessing the impact of anxiety on the functioning of children and adolescents related to social and home/family domains. The CAIS-P measures anxiety impairment across multiple anxiety disorders; however, several other impairment measures are disorder-specific. The Child OCD Impact Scale (COIS-R, Piacentini et al., 2003; Piacentini & Jaffer, 1999; Piacentini, Peris, Bergman, Chang, & Jaffer, 2007) assesses specific functional impairment among children and adolescents with OCD. The GAD section of the Anxiety Disorders Interview Schedule (ADIS; Silverman, & Albano, (2005)) includes clinician, child and parent impairment ratings based on the child's report of how their GAD worry negatively impacted time with friends, in school and at home (Choudhury, Pimentel, & Kendall, 2003).

To date, only two large scale reviews of social functioning measures for children and adolescents exist. Orvaschel and Walsh (1984) reviewed a total of 31 "adaptive functioning" instruments for use with preschool and school-aged children. Canino, Costello, and Angold (1999) examined 13 measures of "functional impairment" categorized by global impairment, domain-specific measures, and symptom-specific measures. Findings from both reviews underscored the need for the development of more appropriate measures of impairment that differentiate symptom severity from functional impairment in children, as well as clarification with respect to the relationship of anxiety to normative developmental functioning, a child's ability to adapt to varying demands occurring within domains of home, school, community, and interpersonal peer relationships (Hoagwood et al., 1996). Developers of future assessments of functioning related to anxiety may also consider and incorporate the breadth of the domains of impairment relevant to complex trauma, identified by Cook and colleagues, such as problems with perspective taking affecting attachment, difficulties with communicating needs, and wishes influencing affect regulation (see Complex Task Force, 2002).

Another challenging aspect with measuring impairment is concordance between ratings. Evidence suggests that there are sometimes inconsistencies between child-ratings of their anxiety-related impairment and parent-ratings of

their child's anxiety (Choudhury et al., 2003). Parents tended to rate their children's OCD-related functional problems in the home, with family, and at school as more problematic than their children (Piacentini et al., 2003). Meanwhile, children with OCD endorsed several problems more frequently than their parents, such as pleasant activities that demand more attention (e.g., viewing movies, reading) and school or social activities whereby parents are not typically present to observe (e.g., arriving to class punctually, meeting an unfamiliar group of people) (Piacentini et al., 2003). Thus, it seems essential that measures of impairment include a breadth of domains and problems across child and adolescent development, and a number of versions capturing multiple perspectives (e.g., child, caregiver, teacher) in order to more accurately evaluate impairment.

Subthreshold Anxiety

Anxiety-related impairment extends beyond disorder-specific anxiety. While the discussion of impairment has been within the context of specific anxiety disorders, subthreshold levels of anxiety have also been associated with impairment and distress, as well. A longitudinal study investigated the prevalence and outcomes of youth aged 9, 11, and 13 years with psychosocial impairment who did not meet DSM-III-R criteria for any of 29 well-defined disorders, including anxiety disorders (Angold, Costello, Farmer, Burns, & Erkanli, 1999). At Wave 1, 29.6% of the 1,015 subjects with symptomatic impairment and no diagnosis, reported that anxiety-related symptoms contributed primarily to symptomatic impairment (Angold et al., 1999). These results are consistent with past research indicating that individuals with subthreshold conditions in childhood suffer from impairment and increased risk for continuing mental health problems, including disorder development (Angold & Costello, 1996; Gonzales, Magruder, & Keith, 1994; Sherbourne et al., 1994; Spitzer et al., 1995; Valleni-Basile et al., 1996; Williams, Kerber, Mulrow, Medina, & Aguilar, 1995).

Anxiety and Developmental Stages

Subthreshold anxiety symptoms and anxiety disorders are common in adolescence, and cause daily impairment and distress (Ollendick & Hirshfeld-Becker, 2002; Van Oort, Greaves-Lord, Verhulst, Ormel, & Huizink, 2009). Depending on the childs' or adolescents' age and stage of development, specific symptoms may cause impairment in particular domains, and the degree of impairment may increase or diminish. Functional outcomes in elementary school are different from those in high school (Hoagwood et al., 1996). Additionally, a study examining the developmental trajectories of specific anxiety disorders (i.e., separation anxiety, social phobia, GAD, PD, OCD) among a community-based sample of children and adolescents over a 5 year period found that anxiety seems to diminish in early adolescence and then slightly increase during middle (i.e., separation anxiety, social anxiety, GAD) and late adolescence (i.e., panic, OCD), beyond the effects of depression (Van Oort et al., 2009). As noted in the specific sections, there are particular developmental considerations relevant to each of the anxiety disorders with regard to assessment and manifestations of symptoms. Given the substantial evidence that childhood anxiety disorders predict the presence of anxiety and other mental health problems in adolescence and adulthood and the pervasive impairment inherent in such disorders, it is critical to understanding more about the developmental trajectory of anxiety, for purposes of intervention and prevention (Bittner et al., 2007; Bruckl et al., 2007; Ferdinand & Verhulst, 1995; Gregory et al., 2007; Lewinsohn, Holm-Denoma, Small, Seeley, & Joiner, 2008; Pine, Cohen, Gurley, Brook, & Ma, 1998).

Risk and protective factors for anxiety-related distress and impairment also may manifest differently across population subgroups. For example, studies have also found that girls report higher rates of anxiety during adolescence than boys, although this may be in part attributable to higher rates of comorbid depression among girls (Van Oort et al., 2009). There is little research examining whether the predictors of impairment are

the same for males and females. Future research on anxiety-related disability needs to examine what factors predict impairment for children vs. adolescents, and whether differences exist based on environmental stressors, gender, ethnicity, socioecomonomic status, etc. (Layne et al., 2009). Studies that examine environmental/contextual factors (e.g., the mental health of caregivers), developmental issues, and include more diverse samples will provide critical knowledge to better understand childhood anxiety and impairment.

Conclusions

In summary, this chapter provides a review of the literature focused on impairment related to childhood anxiety disorders. While anxiety disorders are highly prevalent and known to be disabling, there is still limited research in the area of impairment, which is due, in part, to the availability of relevant measures. It is essential that development be an important consideration when assessing impairment, as a child's level of functioning is appropriate at specific periods of development, but not others (Hoagwood et al., 1996). Impairment and disability may affect future development, as well. Furthermore, disability and impairment are not only anxiety disorder-specific, but are associated with subthreshold levels of anxiety, as well. Accurate assessment of anxious children and adolescents' functional level and ability to negotiate their environments is critical in order to determine the need for treatment (Hoagwood et al., 1996), prevent possible deterioration and inhibit the development of additional mental health problems.

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Anxiety Disorders in Children with Chronic Health Problems

32

Lara J. Farrell, Caroline Donovan, Cynthia M. Turner, and John R. Walker

In the United States, 10% of all adolescents suffer from a chronic illness (Blum, 1992; Krementz, 1989; Millstein & Litt, 1990). In total, approximately one million children have a chronic illness that affects daily life (Perrin & MacLean, 1988) and another ten million have somewhat less serious physical illnesses (Haggerty, 1984). A chronic illness is defined as "one that lasts for a substantial period of time or that has sequelae that are debilitating for a long period of time" (Perrin, 1985, p. 2). Chronic illnesses are associated with a wide range of sequelae and impairment including pain and discomfort, school absences, activity disruptions, poorer social competence, higher use of medication and health care visits, as well as increased risk for both internalizing and externalizing problems (e.g., Cadman, Boyle, Szatmari, & Offord, 1987; Gortmaker, Walker, Weitzman, & Sobel, 1990; Jackson & Vessey, 2004).

It is well established that comorbidity among medical conditions is common (Dewa & Lin, 2000), and the presence of multiple disorders in clinical samples equates to greater impairment in functioning (Ormel et al., 1994). The co-occurrence of mental disorders with chronic medical conditions is of particular significance, given that the comorbidity of mental and medical conditions has been reported as high within both general population samples (Neeleman, Ormel, & Bijl, 2001) and primary care samples (Berardi et al., 1999), and that these comorbidities lead to excessive impairment and disability (Sullivan, LaCroix, Baum, Grothaus, & Katon, 1997). The presence of a medical condition appears to in fact increase the likelihood of experiencing a mental health problem, with research demonstrating higher rates of both anxiety and mood disorders in samples of people with medical problems compared to the general population (Patten et al., 2005; Scott et al., 2007). Interestingly, recent research has indicated that a great deal of the disability and functional impairment that occurs with chronic health problems, is accounted for more so by anxiety and depression than by features/symptoms of chronic medical conditions (Kessler, Ormel, Demler, & Stang, 2003; Sullivan et al., 1997).

Anxiety disorders are among the most common mental health problem affecting adults (Demyttenaere et al., 2004; Kessler, Chiu, Demler, & Walters, 2005) and children alike (Kendler, Neale, Kessler, Heath, & Eaves, 1992; Mattison, 1992; Pollock, Rosenbaum, Marrs, Miller, & Biederman, 1995), with current estimates indicating as many as 1 in 6 youth experiencing clinical anxiety (Boyd, Kostanski, Gullone, Ollendick, & Shek, 2000). Anxiety disorders during childhood tend to be chronic and unremitting in course

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_32, © Springer Science+Business Media, LLC 2011

(i.e., Aschenbrand, Kendall, Webb, Safford, & Flannery-Schroeder, 2003; Cole, Peeke, Martin, Truglio, & Seroczynski, 1998), and are predictive of other psychiatric disorders later in life (Last, Perrin, Hersen, & Kazdin, 1996; Woodward & Fergusson, 2001); including the development of depression in adolescence and adulthood (Brady & Kendall, 1992; Cole et al., 1998; Orvashel, Lewinsohn, & Seeley, 1995; Pine, Cohen, Gurley, Brook, & Ma, 1998; Pollack et al., 1996; Seligman & Ollendick, 1998), personality psychopathology and suicidality in young adulthood (Brent et al., 1993; Rudd, Joiner, & Rajab, 2004), and an increased risk for substance abuse disorders in late adolescence and adulthood (Christie et al., 1988; Greenbaum, Prange, Freidman, & Silver, 1991; Kessler et al., 1996).

The experience of anxiety and the associated symptoms of excessive worry, physiological arousal, psychosomatic complaints, and avoidance of specific situations (to name a few), not surprisingly causes significant disruption to life for children and youth. Anxious children and youth frequently experience substantial disruption and difficulties in their peer and social relationships (e.g., Chansky & Kendall, 1997; Strauss, Forehand, Smith, & Frame, 1986), in their academic achievement (e.g., Kessler, Foster, Saunders, & Stand, 1995; King & Ollendick, 1989), and often experience concurrent psychosocial difficulties such as immaturity, attention and concentration problems, oversensitivity, low self-esteem, and low social competence (Ialongo, Edelsohn, Werthemar-Larsson, Crockett, & Kellam, 1994; Kashani & Orvaschel, 1990; Kendall, Cantwell, & Kazdin, 1989; Strauss, Frame, & Forehand, 1987).

Research from clinical and community studies suggest that children with anxiety disorders, also frequently present with chronic illnesses and physical conditions, such as asthma (e.g., Feldman, Ortega, McQuaid, & Canino, 2006; Hasler et al., 2005; Ortega et al., 2003), respiratory problems (e.g., Harter, Conway, & Merikangas, 2003; Koltek, Wilkes, & Atkinson, 1993), gastrointestinal (GI) problems (e.g., Campo, Bridge et al., 2004), chronic headaches (e.g., Egger, Costello, Erkanli, & Angold, 1999) and diabetes (e.g., Kovacs, Goldston, Obrosky, & Bonar, 1997). Results from numerous epidemiological studies have highlighted this positive association between the presence of an anxiety disorders diagnosis and self-reported physical disorders (e.g., Goodwin & Stein, 2002; Sareen, Cox, Clara, & Asmundson, 2005). Results from a large study by Scott et al. (2007) using the World Mental Health Surveys data, consisting of results from 19 general surveys collected across 17 countries, revealed that both anxiety and depression independently and comparably related to a wide range of chronic physical conditions. Results further suggested that the presence of *comorbid* anxiety and depression was associated with increased risk for experiencing a number of co-occurring physical medical conditions. Given the profound negative impact that both chronic medical conditions and anxiety disorders have independently on a child's life, the impact of comorbid medical conditions and anxiety disorders is likely to be considerable – for the child and family alike. Research suggests that such comorbidity certainly complicates functioning, as well as disease outcomes, leading to poorer quality of life (Kessler et al., 2003; Sareen et al., 2006; Scott et al., 2007).

A recent study by Chavira, Garland, Daley, and Hough (2008) investigated the impact of medical comorbidity on mental health and functional health outcomes among children with anxiety disorders. This study included a sample of children who were recruited randomly from one of five public health care sectors in San Diego, who had at least one anxiety diagnosis with a physical illness ($N=77$) or without a physical illness ($N=73$), as well as youth with at least one physical illness but no anxiety disorder ($N=438$). Psychiatric diagnoses were assessed with standardized interviews, whilst the child's health, emotional and behavioral functioning were assessed using standardized self-report measures. Results of this study demonstrated that at least half of children with anxiety disorders also had a comorbid physical illness – allergies and asthma being the most common. Furthermore, children with anxiety disorders who had a comorbid physical illness exhibited greater levels of emotional problems, more somatic complaints, and more

school and social functional impairment than anxious children without a physical illness and children with physical illness alone. Parents of children in the comorbid group also reported greater caregiver strain than the other two groups (Chavira et al., 2008). The results of this study provide evidence of the considerable impairment associated with comorbid anxiety and medical problems, and highlight the need to understand the impact of comorbidity on functioning and management regimes.

The nature of the relationship and comorbidity between anxiety disorders and chronic medical conditions is not well understood. The relationship is likely to be reciprocal, in so much as the presence of both anxiety and physical illness will impact on each other in ways that are likely to precipitate and/or exacerbate symptoms of both conditions. There are a number of hypotheses proposed in the literature (e.g., Chavira et al., 2008; Katon, Richardson, Lozano, & McCauley, 2004; Sareen et al., 2006) that may account and explain the higher than expected comorbidity between anxiety and health complaints. First, it may be that the experience of a clinical anxiety disorder leads to increased risk for health/medical complaints,or exacerbation of symptoms through either biological mechanisms (i.e., changes in hormonal systems, autonomic nervous system activity; Sareen et al., 2006), and/or psychological processes, such as biases in symptom perception (e.g., real or perceived bodily symptoms), or deficits in coping/approach behaviors (e.g., self care/seeking assistance); or via a combined effect of biological/psychological processes (e.g., immune deficiency as a result of chronic worry and/or excessive avoidance behaviors). Second, the presence of a medical complaint or condition may precipitate or maintain anxiety and anxiety disorders. For example, the experience of chronic health complaints, reliance on medication/s, and/or frequent hospitalizations may lead to increased fear about safety, and about being away from parents and/or home, leading to increased avoidance of school/separation from parents. Furthermore, the experience of frequent bodily symptoms and pain associated with illness, may lead to increased scanning and hypervigilance regarding bodily symptoms, leading to increased anxiety and panic responses in relation to both normal bodily changes, as well as symptoms of pain and illness. Third, a mediating variable may explain the relationship between these co-occurring conditions, such that an anxiety disorder may precede a substance use disorder, which in turns leads to a physical health condition; or conversely, medication for treatment of a physical complaint may exacerbate anxiety symptoms (Sareen et al., 2006). Finally, common genetic, environmental (e.g., poverty, childhood adversity; Katon et al., 2004; Kessler et al., 2005) and personality factors (Goodwin & Stein, 2002) may explain the co-occurrence of anxiety and medical conditions (see Sareen et al., 2006).

This chapter will focus on three disabling medical conditions of childhood – asthma, GI problems and diabetes – which are each associated with anxiety and anxiety disorders at higher than expected rates. The chapter will review each of these conditions, their association/relationship with childhood anxiety, and implications for management.

Anxiety and Asthma in Children

Asthma is recognized as the most common chronic illness of childhood, with a prevalence of between 7 and 10% (Centers for Disease Control and Prevention, 1998; Weitzman, Gortmaker, Sobol, & Perrin, 1992). Epidemiological research suggests that the prevalence of this disabling condition in childhood is on the rise (Burney, Chinn, & Rona, 1990; Weitzman et al., 1992), and both morbidity and mortality associated with this disease are increasing, particularly in children and youth (Weiss, Gergen, & Wagener, 1993). Whether this documented increase in prevalence and parallel disability are due to better detection of disease, increased public awareness, longer-lasting episodes or a true increase in incidence remains unclear. What is clear,however, is that more children and youth worldwide are suffering from asthma than ever before, with more frequent hospitalizations, increased disability, and more reported deaths as a result of this

chronic illness. Approximately 25% of people with asthma are thought to experience severe symptoms (Pleis & Lethbridge-Çejku, 2006), and generally speaking, asthma accounts for the leading cause of hospitalization among children.

Research examining comorbidity associated with asthma, has found that there is a higher incidence of psychiatric disorders among severely asthmatic children, compared to healthy controls (e.g., Mrazek, Anderson, & Strunk, 1985; Strunk & Mrazek, 1985). This condition in childhood is responsible for more school absenteeism than any other chronic illness (Bloom & Cohen, 2007), therefore having a profoundly negative impact on a child's life across multiple domains including academic, social and psychological adjustment. Greater attention and understanding of emotional disturbances co-occurring with childhood asthma is critical, as the impact of such disorders may exacerbate asthma symptoms, reduce compliance with asthma management, and consequently complicate diagnosis and prognosis.

Asthma in Childhood

Asthma is a chronic respiratory disease, characterized by a reversible inflammatory condition of the bronchial airways. Symptoms associated with this airway obstruction, include chest tightness, coughing, and wheezing (National Heart, Lung, and Blood Institute [NHLB], 2007), and for the majority of children, symptoms are typically episodic, whereby complete reversal of symptoms is the norm until another episode is triggered. The onset of asthma for most patients begins early in life, with etiological models typically describing a complex interplay between genetic risk factors and environmental exposures as predisposing and precipitating factors in the development and maintenance of this disease. It is widely accepted that asthma has a strong genetic component; however, the specific role of genetics in the development of asthma like so many other disorders, remains a complex issue (NHLB, 2007). What is better understood is the role of two major environmental factors as being pivotal in the development, persistence, and possibly severity of asthma: airborne allergens and viral respiratory infections (see NHLB, 2007 for a review).

Various emotions also play a role in the onset of asthma symptoms, such as crying, laughing, or yelling, through the onset of rapid breathing that simultaneously occurs during these emotional states. Not surprisingly, the experience of having an asthma attack is also frequently associated with increased anxiety and fear, which in turn leads to increased heart rate, breathing and hyperventilation in some cases, further exacerbating asthma. The relationship between anxiety and asthma is in fact bi-directional, in that anxiety can also trigger asthmatic reactions. The association between anxiety and asthma is an interesting one, and is indeed one of the most studied of the psychiatric comorbidities of asthma. Asthmatic patients who also experience anxiety have been found to have decreased physical and emotional functioning; poorer control of their asthma symptoms (Lehrer, Feldman, Giardino, Song, & Schmaling, 2002); and greater health care utilization (ten Brinke, Ouwerkerk, Bel, & Spinhoven, 2001), leading these sufferers to be a particularly disabled and high-risk sub-group.

Comorbid Anxiety and Asthma in Children

It is now well established that patients with asthma, especially children, are more likely to experience psychological problems, particularly anxiety disorders (Bussing, Burket, & Kelleher, 1996; Vila, Nollet-Clemencon, de Blic, et al., 1999). There are now numerous studies that have documented the higher than expected prevalence of anxiety in asthmatic children (e.g., Brown, Khan, & Mahadi, 2000; Campbell et al., 1995; Carr, Lehrer, Rausch, & Hochron, 1994; Davis, Russ, & MacDonald, 2002; Goodwin & Pine, 2002; Kolbe, Fergusson, Vamos, & Garrett, 2002; Pollack et al., 1996; Shavitt, Gentil, & Mandetta, 1992), with reported clinical anxiety symptoms or disorders in asthmatic samples ranging from 13% (e.g., Brown et al., 2000) to 52% (Nascimento et al., 2002). Bussing et al. (1996) demonstrated that 43.2% of 37 children with asthma in an

outpatient community clinic met criteria for an anxiety disorder based on clinician interviews, vs. 19.4% of 25 healthy controls. Similarly, Vila, Nollet-Clemencon, de Blic, et al. (1999) and Vila, Nollet-Clemencon, de Blic, Mouren-Simeoni, and Scheinmann (2000) reported more than one third of children with asthma also experienced an anxiety disorder, which was significantly higher than the rates reported in children with diabetes (Vila, Nollet-Clemencon, Vera, et al., 1999), and healthy controls (Vila et al., 2000). A longitudinal study by Craske, Poulton, Tsao, and Plotkin (2001) following children from ages 3 to 21 years also found an earlier experience of asthma predicted the development of agoraphobia and/or panic disorder by ages 18–21 years.

Recently, an Australian longitudinal study examined asthma and anxiety in a cohort of 5,135 children from the Mater University Study of Pregnancy and its outcomes (MUSP; Alati et al., 2005). This study is particularly interesting, in that the analyses of this longitudinal data specifically explored the causal direction of the comorbidity between asthma and anxiety. Asthma symptoms and internalizing behavior were evaluated by maternal reports when the children were 5 and 14 years of age. Consistent with the literature, asthma and internalizing symptoms were significantly associated in cross-sectional analyses at 5 and 14 years. In prospective analyses, after excluding children with asthma at 5 years, internalizing symptoms at age 5 were not associated with the presence of asthma symptoms at 14 years. This study offers strong preliminary evidence for a casual pathway between early asthma experiences, and the development of anxiety symptoms later in life; however, there does not appear to be a causal pathway between early anxiety and later onset of asthma over this time period at least.

Elevated anxiety and depression have been reported to be positively related to asthma severity in children (Mrazek, 1992), suggesting that the experience of having one of these disorders results in increasing symptoms in the other. For children with asthma, who also experience clinical anxiety, there appears to reduced effectiveness of asthma treatments; perhaps through reduced compliance with the treatment regime, or because the emotional state of anxiety itself has a direct effect on autonomic reactions and pulmonary functions, directly affecting asthma symptoms and severity (Miller & Wood, 1997). Increasing our understanding of the relationship between anxiety and asthma would likely lead to improvements in management of both disorders, decreased health care utilization, and better prognosis for those affected.

Treatment Implications for Comorbid Asthma and Anxiety in Children

Psychological factors, particularly anxiety and fear, play a role in the experience, exacerbation and prognosis of asthma in children and youth. To date, there is very little research examining the role of psychological interventions in asthma management; however, interventions that target patients' knowledge, beliefs and behaviors are likely to improve compliance, management and long-term prognosis. Intervention programs typically rely on education delivered in various ways including by health care staff (e.g., Hendricson et al., 1994), peer education (Persky et al., 1999), and innovative approaches using multimedia and computer-based programming (e.g., Bartholomew et al., 2000). Individualized programming based on an assessment of patient functioning, family functioning, psychiatric comorbidity, and levels of motivation and compliance have so far been neglected.

Medical treatment for asthma focuses on four treatment targets; (1) medication to control inflammation and prevent chronic symptoms; (2) medications to treat acute asthma symptoms and attacks as they occur; (3) identification and avoidance of asthma triggers (i.e., environmental – such as allergens or psychological – such as stressors, anxiety, heightened emotional distress); and (4) monitoring of *peak flow*. Measurement of *peak flow* gives an idea of how narrow or obstructed a person's airways are by measuring the maximum (or peak) rate at which they can blow air into a peak flow meter after a deep breath. Peak flow monitoring helps measure how

much, and when, the airways are changing. Research, however, has so far demonstrated that measuring peak flow, while potentially a useful treatment target used to inform assessment and monitor patient symptoms/flare-ups, is rarely practiced by patients (Cote, Cartier, Malo, Rouleau, & Boulet, 1998; Redline, Wright, Kattan, Kercsmar, & Weiss, 1996; Verschelden, Cartier, L'Archeveque, Trudeau, & Malo, 1996) and has not been supported by empirical evidence to improve outcomes over symptoms monitoring (e.g., Charlton, Charlton, Broomfield, & Mullee, 1990; Reeder, Dolce, Duke, Raczynski, & Bailey, 1990; Turner, Taylor, Bennett, & Fitzgerald, 1998). Psychological adjuncts to asthma management that might improve effectiveness of asthma treatment, enhance functioning and quality of life, and reduce associated anxiety and emotional disturbance include; (1) asthma education, (2) symptom perception training, and (3) cognitive-behavioral therapy (CBT).

One of the most important interventions for asthma management is education. The NHLBI's (1997) guidelines emphasize that asthma education plans should include; (a) individualized written action plans for medication management, and instructions for when to seek health care; (b) information regarding basic facts about asthma, and medications used to treat asthma; (c) teaching methods for self-monitoring asthma symptoms, including the use of *peak flow* monitoring; (d) teaching techniques for using inhalers, and how to avoid allergens; (e) devising a daily self-management plan for controlling symptoms; and (f) teaching how to use an asthma diary for self-monitoring and effective self-management. Asthma education has been demonstrated to be cost effective for both children (Greineder, Loane, & Parks, 1999) and adults (Taitel, Kotses, Bernstein, Berstein, & Creer, 1995), to reduce symptoms and improve self-management skills (e.g., Kotses et al., 1995; Vazquez & Buceta, 1993; Wilson et al., 1996), and to increase self-efficacy and locus of control (Tieffenberg, Wood, Alonso, Tossutti, & Vicente, 2000; Wigal et al., 1993).

Symptom perception training is a behavioral treatment focussed on improving the patient's accuracy of perception of airway sensations. Many asthmatic patients fail to effectively discriminate between changes in their airways, or perceive accurate severity of their symptoms, which can lead to near-fatal asthma attacks. A few studies have demonstrated that through biofeedback approaches, patient's perceptions of their airway performance can be improved (e.g., Harver, 1994; Stout, Kotses, & Creer, 1997), although the research in this field remains preliminary. Lehrer et al. (2004) recently evaluated the effectiveness of heart rate variability (HRV) biofeedback as an adjunctive treatment for asthma in a randomized controlled trial. In this controlled study of 94 patients who were treated with HRV biorhythm, results indicated specific treatment effects including reduced asthma severity, less reliance on medication and general improvement in pulmonary function. The researchers concluded that biofeedback therapy may help reduce the use of steroid medication. In children with asthma, one recent study has examined the relationship of anxiety and asthma severity to symptom perception. Chen, Hermann, Rodgers, Oliver-Welker, and Strunk (2006) found that higher trait anxiety was associated with heightened symptom perception (controlling for pulmonary function) at baseline, while greater asthma severity on the other hand, was associated with blunted symptom perception (controlling for pulmonary function). Effective management of asthma relies on accurate perception of symptoms, hence symptom perception training is likely an important adjunct to an asthma intervention program – particularly for those patients with secondary anxiety and/or increased asthma severity. Furthermore, given that both asthma and anxiety are associated with changes in respiratory symptoms, training in *discrimination* between asthma onset and anxiety symptoms is warranted for those patients with comorbid anxiety and asthma to improve self-management of both conditions (see Lehrer, 1998).

CBT may be an effective adjunct to asthma treatment, through addressing treatment-interfering illness representations (Sperry, 2009). Sperry (2009) defines *illness representations* as, "an individual's constellations of perceptions and beliefs about a particular disease – understanding of it and its symptoms, cause, time or illness

duration, impact or consequences, curability, and ability to control it" (Sperry, 2009, p. 109). Illness representations are likely to be associated with treatment compliance, self-management of symptoms, and behavioral responses to environmental and psychological triggers to asthma. Addressing illness representations and symptom perception through CBT approaches may provide improved outcomes for asthma management. In terms of comorbid anxiety symptoms and disorders, CBT is indicated as an evidence-based approach to treatment (see Silverman, Pina, & Viswesvaran, 2008), and may involve education, relaxation training, cognitive therapy targeting unhelpful thinking styles, and behavior therapy targeting exposure to fears and increasing approach behaviors. To the best of the authors' knowledge, there are no published controlled trials of CBT for comorbid asthma and anxiety in children and/or youth.

Sperry (2009) proposes a *combined integrative treatment* approach for asthma, which includes all four of the traditional medical treatment targets (described above), as well as lifestyle modification and psychological adjuncts to treatment described above. This integrative approach to treatment involves four phases of intervention, starting with(1) a thorough biopsychosocial assessment (developing a patient profile and illness profile, screening of psychiatric comorbidities, and developing an asthma symptom diary); (2) intervention planning, based on assessment of illness representations and symptom perceptions, as well as assessment of functional capacity; (3) intervention implementation, including psychoeducation, symptom perception training, relaxation interventions, medication management action plans, and cognitive behavioral therapy to target both asthma treatment compliance and management, as well as psychiatric comorbidities such as anxiety and panic; and finally (4) intervention monitoring, which includes ongoing reviews of asthma symptom diaries, patients medical charts and laboratory tests, and patient progress with regard to compliance, symptom reduction and functionality. An integrative treatment approach such as this is likely to be beneficial in terms of asthma management, anxiety reduction and general improvement in quality of life and functionality. Research is needed to evaluate the efficacy of an integrated treatment approach, such as the protocol proposed by Sperry (2009) and the effectiveness of the specific components of treatment.

There is considerable evidence for an association between pediatric asthma and anxiety, with mounting research indicating poorer outcomes, greater health care utilization, and reduced functioning and quality of life for these patients (Lehrer et al., 2002). Greater understanding of the relationship between these chronic disorders of childhood is sorely needed to inform research, practice and treatment guidelines. Increasing community and practitioner awareness of the higher than expected co-occurrence of these disorders, developing efficient and reliable approaches to *screening*, and forming multi-disciplinary intervention programs for management, is crucial to effectively assisting children and families dealing with comorbid asthma and anxiety.

Functional Gastrointestinal Disorders in Children and Adolescents

The umbrella term of functional gastrointestinal disorders (FGIDs) refers to a variety of conditions which have chronic or recurrent GI symptoms (e.g., abdominal pain, nausea, vomiting, bloating, dyspepsia, diarrhea, constipation) as their main feature (Drossman, 2006). A FGID is diagnosed when the symptoms cannot be attributed to a known physical (anatomical) or physiological (hormonal or other body chemistry) cause.

Research into medically unexplained GI symptoms in childhood has been complicated by the wide variety of terms given to GI conditions, such as recurrent abdominal pain (RAP), childhood irritable bowel syndrome (IBS), functional bowel disorders, and functional abdominal pain (FAP). Historically, these terms have been ambiguous with regard to clinical definitions, and they have often not been mutually exclusive with regard to current classification of symptoms (Varni et al., 2006).

In an effort to provide standardized definitional criteria for classification of childhood FGIDs, available evidence and expert consensus resulted in the Rome II criteria for childhood FGIDs (Rasquin-Weber et al., 1999; Thompson, 2006), and more recently the Rome III criteria (Hyman et al., 2006; Rasquin et al., 2006). These criteria identify 17 FGIDs of childhood. The disorders are classified first by age range, with separate conditions recognized in infants/toddlers to those recognized in children/adolescents aged 4–18 years (Hyman et al., 2006; Rasquin et al., 2006). Within each age group, FGIDs are then classified by area of symptom location (e.g., abdominal, bowel) or symptom pattern (e.g., regurgitation, vomiting, colic, diarrhea, constipation, pain). The Rome III criteria require the presence of GI symptoms at least once per week for at least 2 months in order to make a diagnosis. In addition to symptom presentation, diagnosis requires loss of daily functioning or additional somatic symptoms (e.g., headache, limb pain), or both. The Rome criteria purposefully exclude RAP from its diagnostic classification, because criteria for RAP were considered too general and pediatric patients with RAP often met Rome criteria for other disorders (Varni et al., 2006).

GI disorders in young people are associated with significant functional impairment, including poor school attendance, decreased physical activity, extensive health service utilization, and family disruption (Campo, Jansen-McWilliams, Comer, & Kelleher, 1999; Walker, Garber, & Greene, 1993). Over a longer term, evidence suggests that childhood GI problems are predictive of adult abdominal pain and IBS, as well as anxiety and depressive disorders in adulthood (Campo, Di Lorenzo, & Chiappetta, 2001; Hotopf, Carr, Mayou, Wadsworth, & Wessely, 1998; Mulvaney, Lambert, Garber, & Walker, 2006; Walker & Heflinger, 1998).

Despite the difficulties inherent in labels such as RAP, pain-related disorders appear to be the most frequently studied of the GI conditions of childhood, particularly in relation to psychiatric comorbidity, and abdominal pain is widely considered to be one of the most common reasons for referral to primary care services and gastroenterology clinics (Starfield et al., 1980). Medically unexplained abdominal pain may affect as many as 10–24% of children and adolescents (Garber, Walker, & Zeman, 1991; Hyams, Burke, Davis, Rzepski, & Andrulonis, 1996).

Anxiety in Children with GI Problems

There is increasing evidence to show that young people with GI problems have more symptoms of anxiety and depression than healthy controls (e.g., Egger et al., 1999; Hyams et al., 1996). Garber, Zeman, and Walker (1990) looked at rates of emotional disorders (anxiety or depression) using structured diagnostic interviews in children (8–17 years) with RAP with no identifiable physical cause, compared with children with RAP with an identified organic cause, children with psychiatric disorders, and healthy control children. All children in the RAP group met criteria for at least one DSM-III emotional disorder. The rates of disorder in both groups of children with abdominal pain were significantly higher than that in the healthy control group, and not significantly different to rates found in the psychiatric group. Rates of emotional disorder in RAP children remained even when the somatic symptoms related to RAP were controlled for. Interestingly, mothers of children with RAP reported significantly higher levels of anxiety and depression than mothers of children with organic pain or healthy children.

Similar findings were reported by Dorn et al. (2003). Children with RAP ($N = 15$) were assessed with a structured interview and anxiety disorders were highly prevalent. Fifty percent of the RAP group met diagnostic criteria for a lifetime anxiety disorder. Of note, the majority of these children had not received mental health assistance, and only four young people had received outpatient treatment for a psychological disorder. This is consistent with previous findings that childhood psychiatric/emotional disorders are frequently unrecognized, and that families frequently do not seek mental health services even when they are recommended (Gardner et al., 1999; Horwitz, Leaf, Leventhal, Forsyth, & Speechley, 1992).

Some authors have suggested that approximately 80% of children presenting with RAP in primary care services will meet criteria for an anxiety disorder, and more than 40% will meet criteria for a depressive disorder (e.g., Campo, Bridge et al., 2004).

In addition to anxiety being highly prevalent in children with medically unexplained GI conditions, anxiety symptoms and disorders are also more prevalent in first degree relatives. For example, a number of studies have found that parental anxiety is associated with GI symptoms in childhood and with the persistence of childhood GI symptoms over time (e.g., Garber et al., 1990; Hotopf et al., 1998; Walker, Garber, & Greene, 1994). There is some evidence to suggest that parental anxiety may even be predictive of the later development of childhood GI symptoms, which suggests a possible causal role (Ramchandani, Stein, Hotopf, Wiles, & The Alspac Study Team, 2006). Family members of adults with a history of childhood RAP are more likely to suffer from generalized anxiety disorder (GAD) than those of controls, but are no more likely to suffer from FGIDs (Campo et al., 2001). In addition to increased anxiety in parents of young people with GI symptoms, recent evidence suggests that siblings of children with GI symptoms may report significantly greater levels of emotional and behavioral symptoms than siblings of healthy comparison children (Guite, Lobato, Shalon, Plante, & Kao, 2007).

There are a number of potential explanations for the high levels of comorbidity between anxiety symptoms/disorders and GI symptoms/disorders in young people. These include unidirectional causal models (e.g., anxiety causes GI symptoms or vice versa) and shared vulnerability models (e.g., anxiety and GI symptoms share risk factors) (Hyams & Hyman, 1998; Merikangas & Stevens, 1997). Clearly, with high levels of anxiety also evident in parents, genetic risk factors are important to consider (e.g., Hettema, Neale, & Kendler, 2001). Recent research has also found that children who display anxious behaviors elicit certain behaviors from parents/adult caregivers (Hudson, Doyle, & Gar, 2009). Clearly further prospective research is required in order to better understand risk and vulnerability factors, and the inter-relationships between them.

Treatment Implications for GI Symptoms and Anxiety in Children

The number of psychological treatment outcome studies for childhood FGIDs has grown considerably over the 15 years (e.g., Ball, Shapiro, Monheim, & Weydert, 2003; Bury, 1987; Edwards, Finney, & Bonner, 1991). The majority of these studies evaluate treatment efficacy by looking at pain outcomes (e.g., frequency, intensity, and remission of pain), as well as number of missed activities (e.g., school absences), and medical utilization. Psychological interventions have evaluated a variety of strategies, including psychoeducation, behavioral/contingency management, relaxation, biofeedback, and individual or family-based CBT (see Brent, Lobato, & LeLeiko, 2008 for a review). The methodology of these studies vary considerably, ranging from case reports to randomized controlled trials incorporating multiple methods and standardized outcome measures. Although one study by Edwards et al. (1991) did not demonstrate improved pain outcomes with psychological intervention, all other studies have demonstrated a positive effect, and none have demonstrated negative effects. Given the accumulating evidence, the American Academy of Pediatrics Subcommittee on Chronic Abdominal Pain in Children have recently rated CBT as an "efficacious" treatment (American Academy of Pediatrics, 2005). Unfortunately, none of these studies included measures of anxiety symptoms/disorders.

While it is unlikely that the studies described above resulted in improvements in GI symptoms and daily functioning but not anxiety, to the authors' knowledge, only one study to-date has sought to look at treatment outcomes for anxiety symptoms/disorders comorbid with GI symptoms in young people (Campo, Perel, et al., 2004). This study evaluated the efficacy of citalopram (an SSRI) in the treatment of abdominal pain. Twenty-five clinically referred youth (7–18 years) with abdominal pain participated in a 12-week,

flexible-dose, open-label trial. Eighteen participants (72%) were diagnosed with a comorbid anxiety disorder at baseline. The primary outcome measure was the Clinical Global Impression Scale-Improvement (GCI-I), and secondary measures included self- and parent-reports of pain, anxiety, and depression. Results revealed that 21 participants (84%) could be classified as treatment responders, with ratings on all outcome measures improving significantly over the course of treatment compared with baseline. Only six of the 21 young people who completed treatment (29%) and nine of the original 25 (36%) continued to meet criteria for an anxiety disorder at post-treatment.

This study is the first to intentionally examine effects of treatment on anxiety disorders in young people with GI symptoms. It highlights the importance of including comorbid psychiatric symptoms and disorders in the design of clinical trials of intervention for GI disorders of childhood (Lydiard & Falsetti, 1999). The cross-sectional design of the study precludes the conclusion that improvements in GI symptoms can be attributed to successfully treating the psychiatric disorder, although it does pave the way for randomized controlled trials of psychological interventions (e.g., CBT) focused on the treatment of both GI symptoms and anxiety symptoms/disorders. Psychological interventions also offer an alternative to some of the challenges in using SSRIs in the treatment of FGIDs such as the lack of information concerning the optimal duration of treatment and the rate of return of symptoms when medication treatment is discontinued. The common side effects of weight gain and decreased sexual functioning in adults at least may be a barrier to the use of these treatments in some children and adolescents (Graff, Walker, & Bernstein, 2009).

GI conditions in childhood are highly prevalent, associated with high rates of medical utilization, school absence, functional impairment, and personal and familial distress. There is a high level of comorbidity between GI conditions and anxiety symptoms and disorders in young people, and in first degree relatives. It is encouraging that researchers are beginning to include measures of anxiety (and depression) in studies of childhood GI conditions. However there is substantial scope for improvement in this area, particularly with regard to better understanding the nature of the association, and in the identification and treatment of comorbid psychiatric disorders. It is highly likely that psychological treatments already demonstrated to be efficacious for childhood GI conditions (i.e., CBT) might be helpful in achieving symptom relief and/or remission in childhood anxiety, and vice versa. There is a strong case for psychological treatments to be offered to children with FGIDs as part of routine care, as they offer the potential to decrease or eliminate psychological and/or physical symptoms, provide young people with sustainable pain management and coping skills, and perhaps ultimately, be a cost-effective solution (Campo, Perel, et al., 2004). Clinical research trials in this area would be welcome.

Anxiety and Diabetes in Children

The implications of a child being diagnosed with diabetes, has changed dramatically over the decades. Prior to the discovery of insulin in 1922, a childhood diagnosis of diabetes amounted to a death sentence. Today, it is rare for child to die from diabetes. However, the life of a child with diabetes remains far from easy for a number of reasons. In order to fully understand the psychological implications of juvenile diabetes, it is important to have some awareness of the medical underpinnings and potential medical consequences of the disease.

Diabetes in Children

There are many subtypes of diabetes sharing the common underlying problem of too much glucose in the blood either due to inadequate production of insulin or insulin resistance (Rubin & Peyrot, 2001). Type 1 Diabetes Mellitus (T1DM), is a subtype of diabetes whereby insulin is not produced by the pancreas usually due to pancreatic cell destruction (Craig, Hattersley, &

Donaghue, 2006). Because the pancreas is unable to produce insulin naturally, children with T1DM are completely dependent upon exogenous insulin that is either injected multiple times per day, or is released via an insulin pump (Boland, Grey, Oesterle, Fredrickson, & Tamborlane, 1999). Although it accounts for approximately 90% of childhood and adolescent diabetes, T1DM is relatively rare and occurs in approximately 0.02% of young people under 14 years (Craig et al., 2006; Daneman, 2009).

Type 2 Diabetes Mellitus (T2DM) occurs due to insulin resistance, and in the USA and Europe, occurs almost exclusively in overweight or obese youth (Rosenbloom, Silverstein, Amemiya, Zeitler, & Klingensmith, 2008). Although previously rare in children and adolescents, the incidence of T2DM is increasing along with the increase in overweight and obese young people. T2DM can sometimes be managed by changes to diet and exercise regimes in conjunction with insulin injections. T2DM in young people most frequently occurs after age 10 years, with the mean age of onset being 13.5 years (Rosenbloom et al., 2008). Much of the research investigating pediatric diabetes has been concerned with T1DM due to the higher incidence level within the child and adolescent population. Thus, the discussion below relates to young people with T1DM unless otherwise specified.

Diabetes can lead to a myriad of serious medical complications if the diabetic regime is not rigorously adhered to: visual impairment and blindness, renal failure and hypertension, pain, parethesiae, muscle weakness, autonomic dysfunction, cardiac disease, peripheral vascular disease and stroke (Donaghue, Chiarelli, Trotta, Allgrove, & Dahl-Jorgensen, 2007). Less commonly, diabetes is associated with hypothyroidism, hyperthyroidism, Coeliac Disease, vitiligo, Addison's Disease, and limited joint mobility (Kordonouri et al., 2007). Furthermore, a number of the abovementioned complications may come together to increase the risk of gangrene and consequent amputation of lower limbs (Rubin & Peyrot, 1999). Although the medical complications listed here are relatively rare in childhood and adolescence, early markers of these problems may present themselves only a few years after diabetes onset (Donaghue et al., 2007). Thus, in order to prevent future serious medical complications, adherence to the medical regime for diabetes is essential during childhood.

Medical Treatment

The main goal of medical treatment for diabetes is the maintenance of blood glucose at levels that are as normal as possible. Too much glucose in the blood (hyperglycemia) not only increases the risk of diabetic-related complications, but in those with T1DM, can increase until ketoacidosis (a build up of ketones in the blood) occurs, a condition that is potentially fatal (Rubin & Peyrot, 2001). Hyperglycemia can result from underdosing, forgetting insulin injections or oral medications, overeating or infections (Drotar, Witherspoon, Zebracki, & Peterson, 2006). In contrast, too little glucose in the blood (hypoglycemia) can occur when too much insulin is delivered, if the child overeats, or when substantial physical activity is engaged in (Drotar et al., 2006). In its mild form, hypoglycemia results in shakiness, sweating and rapid heartbeat (Rubin & Peyrot, 2001). In its more severe form, hypoglycemia can affect brain function and lead to headache, confusion and unconsciousness (Rubin & Peyrot, 2001).

The burden of treatment for young people with diabetes is large. Children with diabetes spend a significant portion of their day engaged in treatment tasks, with one study demonstrating that 56.9 ± 27.8 min/day are spent on the diabetic medical regime (Ziaian et al., 2006). Young persons with diabetes must monitor their blood glucose levels by using a glucometer multiple times per day. This process involves their pricking their finger to draw blood, and placing the blood on a strip that is then inserted inside the glucometer to secure a reading.They must then calculate the dose of insulin required according to the reading they receive, and inject the required dose usually into either the stomach or thigh. Additionally, children with diabetes must be acutely aware of what they eat, and must engage in sufficient exercise activity to assist in the maintenance of

normal-level blood glucose. The medical management of childhood diabetes is therefore complex and burdensome to the diabetic children and their families.

Psychological Impact of Diabetes

Given the above description of the medical treatment regime required for diabetic children ,and the potential medical consequences of the disorder, the question really should not be "why do young people with diabetes experience psychological problems?" but rather "why wouldn't they?" Not surprisingly, many children diagnosed with T1DM develop adjustment problems and other psychological disorders. Kovacs, Ho, and Pollock (1995) found that of 92 children newly diagnosed with T1DM, 33 developed an adjustment disorder, and five developed other clinical-level psychiatric disorders in response to diagnosis. The adjustment disorder was found to continue for an average of 3 months, and all children were found to eventually recover from it. However, those who initially developed an adjustment disorder were much more likely to go on to develop a psychiatric diagnosis (mainly depressive and anxiety disorders) during the following 5-year period. Similarly, a longitudinal study by Kovacs et al. (1997) of 8–13 year-old children newly diagnosed with T1DM, found that 47.6% developed a psychiatric diagnosis of some kind over the following 10-year period, with the time of highest risk being in the first year following diagnosis. Of those who developed a psychiatric diagnosis, 26.1% developed a depressive disorder, 19.6% developed an anxiety disorder (most frequently GAD), and 16.3% developed a behavioral disorder. More recently, Northam, Matthews, Anderson, Cameron, and Werther (2005) found that 37% of Australian adolescents met criteria for a psychiatric disorder 10 years following their initial diagnosis of T1DM, a rate approximately double that in the larger Australian community. Depression, anxiety, and eating disorders were each present in 17% of the participants, and almost 20% exhibited a behavioral disorder. Furthermore, approximately two thirds of the adolescents had two or more psychiatric diagnoses, with females and older participants being at higher risk for developing a psychiatric disorder of some kind.

Adolescence appears to be a particularly turbulent time for young peoplewith diabetes, with adjustment and psychiatric problems peaking during this period. A recent study has found that although prepubescent children with diabetes report minimal differences with respect to quality of life, internalizing and externalizing problems compared to their nondiabetic peers, adolescents report significantly more psychological problems, and a lower quality of life (Nardi et al., 2008). Furthermore, adolescence is also a peak time for deterioration in glycemic control, or the degree to which blood sugar levels are stabilized (Court, Cameron, Berg-Kelly, & Swift, 2008). Glycemic control difficulties during adolescence may be partially attributable to the biological changes that occur during puberty, such as endocrine changes and weight gain (Amiel, Sherwin, Simonson, Lauritano, & Tamborlane, 1986). Indeed, many diabetic males, and to an even greater extent females, become overweight during adolescence (Bryden et al., 2001).

Although biological changes are likely to be at least partially responsible for adolescent problems with glycemic control, poor treatment adherence during this period is also likely to contribute (Court et al., 2008). For instance, the weight gain experienced by many young people during puberty may lead to the development of disorderly eating practices (and/or eating disorders) that interfere substantially with glycemic control. Similarly, "normal" adolescent concerns, such as not wishing to appear different from peers, striving for increased autonomy, and the introduction of alcohol into the social context, serve to decrease adherence to the diabetic regime and reduce glycemic control. Furthermore, there is some evidence that adolescents who think negatively about their friends' and peers' reactions to their medical regime are more likely to anticipate difficulties with their diabetic regime adherence, which in turn leads to increased stress, and subsequently poorer glycemic control (Hains, Berlin, Davies, Parton, & Alemzadeh, 2006; Hains et al., 2007).

Thus, the poor glycemic control evident in adolescence may be due to a complex interplay of biological, psychological and social factors.

Anxiety in Children with Diabetes

As noted above, many children with diabetes develop psychological problems, with anxiety disorders being highly prevalent (Northam et al., 2005), and GAD being the most common anxiety disorder experienced. Indeed, approximately 12% of diabetic youngsters have been found to suffer with GAD (Kovacs et al., 1997). With respect to risk factors associated with the development of anxiety disorders in diabetic youth, both diabetes-related hospitalizations, and pre-existing psychological problems have been found to increase the likelihood of developing an anxiety disorder (Kovacs et al., 1997). Indeed, Kovacs et al. (1997) found that children with a psychiatric disorder prior to the onset of diabetes were 3.51 times more likely to develop a new anxiety disorder after onset. Furthermore, young people who perceive their diabetes to have affected their lives, tend to subsequently experience more anxiety (Skinner & Hampson, 2001).

It is important for people working with young diabetic people to be aware of areas that they may see as particularly worrisome, so that efforts may be madeto assess, and consequently reduce either clinical or sub-clinical levels of anxiety. . Rubin and Peyrot (2001) have identified a number of areas that young people with diabetes tend to find stressful. First, the restrictions to a youngster's diet are difficult for both the young person and their family. Birthday parties and other school and social activities can be stressful for the diabetic child, as he or she is unable to eat sweets and other foods high in sugar that can lead to hyperglycemia .. By not partaking of these foods, the child may not only feel deprived, but may also become anxious that he or she is behaving in a way that is different to their peers.

Second, Rubin and Peyrot (2001) suggest that there can be considerable stress concerning the monitoring of blood glucose levels. The unpredictable nature of blood glucose levels is a constant source of frustration and stress to diabetic people of all ages. There are times when, despite doing everything "right," glucose levels are too high or too low, and glycemic control is difficult to attain and sustain. The glucose monitoring (finger prick) itself, can also be painful and stressful to diabetic children, leading to considerable anxiety and behavioral problems surrounding it.

Third, Rubin and Peyrot (2001) report that young people can become very stressed about the taking of insulin itself. There is the more obvious concern, and in some cases phobia, of inserting the needle into the skin. For some children, this is a painful process that requires a certain level of skill to achieve. Furthermore, many children fear giving themselves too much insulin, and subsequently inducing hypoglycemia. Indeed, Amillategui, Mora, Calle, and Giralt (2009) found that one of the main concerns advocated by children about their diabetes, was their ability to recognize hypoglycemia and to self-administer their insulin.

Finally, Rubin and Peyrot (2001) suggest that the process of diabetes management can lead to conflict with both health professionals and caregivers that can be stressful and anxiety-provoking for young persons. The developing independence of adolescence, the fear associated with injection, the deprivation of childhood-related foods, and the concern regarding being "different" to their peers, are but a few reasons that young diabeticpersons may resist the diabetic regime, or at least become distressed about it, and subsequently engage in conflict with those who are trying to help them.

It is clear from the above discussion that children with diabetes experience significant stress and anxiety concerning their disorder, and that anxiety disorders (particularly GAD) are highly prevalent. Those working with diabetic youngsters should assess for anxiety related to restriction of diet, the monitoring of blood glucose levels, insulin injections, hyperglycemia, and conflict regarding the diabetic medical regime. A thorough assessment of anxiety in these areas will better inform the treatment plan and subsequently increase the likelihood of treatment success.

Metabolic Control and Anxiety

A meta-analytic review conducted by Anderson et al. (2002) concluded that anxiety disorders were significantly associated with hyperglycemia in adults with diabetes. Furthermore, there is evidence that in adults, anxiety is a significant risk factor for T2DM that is not mediated by traditional risk factors such as single-status, physical inactivity, smoking, low educational level, high triglycerides level, low HDL cholesterol level or central obesity (Engum, 2007). The mechanism by which anxiety may have its effect on reduced glycemic control however, remains a topic of debate and continuing research. Some suggest that anxiety may interfere with self-care and adherence to the diabetic regime, which in turn may affect glycemic control (Rubin & Peyrot, 2001). Others suggest that biological processes associated with anxiety, such as heightened sympathetic nervous system reactivity and cortisol levels may lead to glycemic control problems (Hoehn-Saric & McLeod, 1988; Schlotz, Schulz, Hellhammer, Stone, & Hellhammer, 2006). Whether it is through treatment adherence, biological processes, or a combination of the two, it would seem that in adults, there is a relationship between anxiety and poorer glycemic control.

In young people, evidence for a negative association between anxiety and glycemic control is less clear. There has been relatively little research conducted with young people in this area, and the few studies that have investigated the relationship (e.g., Grey, Cameron, & Thurber, 1991; Maronian, Vila, Robert, & Mouren-Simeoni, 1999) have failed to find a significant association. Methodological problems associated with the studies in question may partially explain the null results (Dantzer, Swendsen, Maurice-Tison, & Salamon, 2003). However, there may also be other explanations for the lack of association that are specific to children. For instance, if adherence to the diabetic regime influences the relationship between anxiety and glycemic control, the fact that parents remain in relative control of their children with respect to diet, exercise, and the monitoring of blood glucose levels, may lessen the association. Furthermore, the effect of cortisol on glycemic control has its effect through insulin resistance (Reinehr & Andler, 2004), which is problematic for the much less prevalent (in children) T2DM rather than T1DM. Clearly, more research is required in this area before firm conclusions can be drawn.

In discussing the relationship between anxiety and glycemic control, Dantzer et al. (2003) suggest that anxiety may be seen as both a consequence of diabetes and as an indication that the child is not adapting well to the disease in terms of factors such as coping strategies. Indeed, the stress and coping literature may be of relevance and assistance to the understanding and reduction of anxiety in children with diabetes. A study by Peyrot, McMurray, and Kruger (1999) found that, in adults, an anxious, emotional style of coping was associated with an increase in stress, lower adherence to the diabetic regime, and reduced glycemic control. Similarly, it has been found that adolescents using avoidant or withdrawal coping strategies, have less glycemic control at 2- and 3-year follow-up (Seiffge-Krenke & Stemmler, 2003), and that adolescents using active coping strategies have better glycemic control (Graue, Wentzel-Larsen, Bru, Hanestad, & Sovir, 2004).

Treatment

There is a paucity of research investigating the treatment of anxiety disorders in diabetic children specifically, and to the authors' knowledge, there have been no randomized controlled trials conducted with this population. Rose, Firestone, Heick, and Faught (1983) investigated the usefulness of anxiety management training on the diabetic regulation of five adolescents with poor glycemic control. The results suggested that although the adolescents did not report significant decreases in anxiety, diabetic control improved significantly. Similarly, Moore, Geffken, and Royal (1995) reported a behavioral intervention aimed at reducing the distress of two diabetic children aged 11 and 13 years during self-injection. The authors found a substantial reduction in the amount of time needed for injections and in the levels of anticipatory distress.

Most research conducted on the psychological treatment of young people with diabetes, involves

multi-component treatment strategies aimed at a variety of treatment outcomes. Diabetic regime adherence and glycemic control are frequently targeted in these interventions, although the components of the individual treatment strategies vary considerably. There are a number of excellent recent reviews on psychological interventions for chronic illnesses generally (e.g., Beale, 2006; Kahana, Drotar, & Frazier, 2008) and diabetes specifically (e.g., Drotar et al., 2006; Hampson et al., 2000; Plante & Lobato, 2008). In their review of behavioral interventions for adolescents with T1DM, Hampson et al. (2000) found that, contrary to their hypotheses, the mean effect size for psychosocial and self-management outcomes was smaller than for metabolic outcomes. However, when they removed two studies finding very strong results for metabolic outcome that they deemed "outliers," there were no significant differences. Furthermore, when they assessed the four studies that examined both psychosocial and metabolic outcomes, the effects for psychosocial variables were stronger.

It is advocated here, that when treating a diabetic young person with clinical anxiety disorders, that the clinician adhere to empirically validated CBT strategies for the particular anxiety disorder under consideration. However, it is also advocated here, that he take into consideration diabetes-specific anxieties such as those discussed above, in the assessment, conceptualization and treatment of anxiety in diabetic young people. For instance, psychoeducation should not only include information pertaining to anxiety, but also to information regarding the ways in which anxiety might lead to difficulties in treatment adherence and glycemic control. Below are some specific points that a clinician might like to pay particular attention to ,with respect to the assessment and treatment of anxiety in diabetic youngsters. Specifically, it is important that the clinician assess thoroughly for, and subsequently include if necessary, in the conceptualization and treatment of:

- GAD, aiming to elucidate both diabetic and nondiabetic related worries that the child may be having.
- Weight-related anxiety and eating disorders, particularly with adolescents.
- Anxiety related to diet. In particular, anxiety related to appearing "different" from peers with respect to eating practices.
- Anxiety related to pain associated with the glucose monitoring (finger-prick) procedure.
- Anxiety related to the possible medical complications that may result from diabetes.
- Injection phobia.
- Anxiety related to appearing different to peers with respect to self-injection.
- Fear of hypoglycemia and hyperglycemia.
- Anxiety related to conflict with caregivers and health professionals.

Diabetes is a serious medical condition that requires specialist and burdensome medical attention. In addition to the deleterious consequences of anxiety that indiscriminately affect children with and without diabetes, there is the additional concern that anxiety might affect glycemic control in the diabetic child. Thus, the detection, assessment and treatment of anxiety in children with diabetes is extremely important.

Considerations in Assessing and Treating Anxiety in the Context of Chronic Health Conditions

Psychosocial treatments (such as various approaches to CBT, Chorpita, 2007; Rapee, Wignall, Hudson, & Schniering, 2000), and in more recent years pharmacotherapy (The Research Unit on Pediatric Psychopharmacology Anxiety Study Group, 2007; Walkup et al., 2008), have been well established as treatments for anxiety disorders in childhood and adolescence. It is unlikely that these treatments will be found to be ineffective in cases in which there are comorbid health problems. Cognitive behavioral approaches in particular have been applied to a wide range of health problems in addition to anxiety (Andrasik & Schwartz, 2006; White, 2001).

While many mental health specialists are comfortable treating anxiety problems in children ,some may be less comfortable dealing with anxiety with other chronic health conditions. Similarly, health professionals who provide services for chronic health problems in children,

may be less comfortable in dealing with comorbid anxiety problems. In both cases, clinicians may not develop a comprehensive approach to treatment – hoping that the problem will be handled by someone more familiar with the presence of comorbid disorders. Often there is not a service provider available, who is more familiar with dealing with anxiety in the context of the health problems, so we encourage mental health specialists to familiarize themselves with approaches to these problems. The materials in the previous sections covered many specific concerns in children with asthma, diabetes, and functional gastro-intestinal disorders. In this final section, suggestions for the mental health specialist treating the various health problems that may present with comorbid anxiety problems are considered.

Assessment

Many of the readers will be familiar with cognitive behavioral assessment of anxiety problems. In our experience, there are a number of additional questions to consider in assessing anxiety problems (not limited to anxiety disorders) in the context of comorbid medical conditions. Below are questions useful as part of a comprehensive assessment:

- What is the parents' and child's understanding of the medical condition?
- What is the history of the medical condition, treatment, and attempts to cope with the situation on the part of the child and the parents?
- What is the history of the anxiety problem and attempts to cope on the part of the child and the parents? How does this relate to the medical condition?
- How is the child functioning in terms of school performance, relationships with family members, and relationships with other children?
- Are there other problems or life stresses for the child or the family that should be considered?
- Are there actions the child and or parents need to take to manage the health problem? Are these carried out effectively? Is the child developing age appropriate independence in managing the problem?
- What is the relationship between the symptoms (the medical condition), and important environmental factors? Assessment may involve using diaries or a similar approach to assess the symptoms and their relationship to other important factors, such as school attendance, interpersonal stress, parent responses, and cognitive variables.
- Are there areas of excessive avoidance related to the health or anxiety problem?
- Has the child withdrawn unnecessarily from some normal activities due to anxiety or the health problem? In some cases there may be a neglect of the development of the very important peer relationships and friendships that are an important developmental task of childhood.
- Are there excessive safety behaviors on the part of the child or the parent? One example is excessive checking of health status.
- Does the child engage in excessive reassurance seeking? What is the parents' response to this situation?
- Are there indications of excessive health care utilization? Do the parents have a good understanding of when it is appropriate to seek health services?
- What are the areas of strength that should be considered in planning?
- What are the child's goals for the situation?
- What are the parents' goals?

Treatment

A first step is to become familiar with the nature of the health problem. It is much easier to establish a case formulation and intervention plan (Nezu, Nezu, & Lombardo, 2004) when there is a good understanding of the health problem. One reliable source of information about health problems is discussion with colleagues with expertise in the area. There are also excellent resources for clinicians who may not have had extensive experience with a specific health problem previously (e.g., Beers, 2003; Beers & Berkow, 2006). In considering approaches to the treatment of health-related anxiety in children and adolescents, Furer, Walker, and Stein (2007) suggested additional principles that are particularly important.

Family Involvement

Parents are especially important in helping a child to deal with the challenges of a health problem. Assessment and treatment planning should involve a consideration of the overall family situation, and how this may influence the child's experiences. In the case of younger children, the main focus may be to work with the parents,so that they can support effective coping in the child with the health problem and with anxiety. There are excellent resources available for parents to help their children cope with anxiety and these may be used to assist with treatment (Manassis, 2008; Rapee, Spence, Cobham, & Wignall, 2008). The developers of the Positive Parenting Program (Triple P, Sanders, 2008) have been adapting their parent support materials to deal with particular health problems such as obesity (risk of diabetes) and developmental disabilities (Roberts, Mazzucchelli, Studman, & Sanders, 2006).

Collaboration Among Health Professionals

Parents and children are assisted in their coping with health problems when there is good collaboration among professionals. The mental health professional can develop a more effective intervention if there is communication with other health care providers involved in a child's treatment. This communication may help in problem solving (below), and in clearing up any sources of misunderstanding (which are common in dealing with health problems).

A Problem-Solving Approach

The systematic approach to problem solving that has been developed as part of many CBT approaches is very helpful in dealing with health problems and related anxiety (Nezu et al., 2004). What are appropriate approaches to deal with symptoms? When is avoidance appropriate and when is it excessive? How can a child explain a health problem to adults and peers if necessary? Working with parents and children on problem solving ,and in rehearsing the solutions that are developed can be very effective. For example, it may take repeated behavioral rehearsal ,with occasional booster sessions ,for a child to develop confidence in using an inhaler for asthma, an epipen for severe allergic reactions, and in explaining health problems and procedures to peers and significant adults.

School Involvement

In many cases, it is important to include school or childcare staff in assessment and treatment planning. If there is a health problem seen at the school (e.g., allergies, migraine headaches, GI problems, problems with dietary control), it is important that the school is fully informed ,and a plan developed for how the staff can manage problems that are likely to arise. Related to this, is the importance of assisting the child or adolescent to be involved in a normal school program. Problems with somatization are often a factor in school refusal (Egger, Costello, & Angold, 2003). Research on school refusal (e.g., Kearney, 2001) suggests that the longer a child is away from a normal school program, the more difficult it is to return. It is, therefore, a high priority to help the child and family to maintain as normal as possible a school routine while coping with health problems. The approaches developed in treating school refusal (Heyne & Rollings, 2002; Kearney, 2001) may be helpful for children who have difficulty with school attendance related to health problems.

How Sick is Sick Enough to Stay Home or to Leave School?

One dilemma that parents may face is when to allow a child to stay home from school. It is difficult to know just how ill a child is feeling. While many parents develop guidelines regarding this issue, some children will test the rules. Staying home may be more interesting and fun than going to school. Rather than engaging in debates about "Are you sick enough to stay home from school?" a helpful approach is to establish a routine in the home for sick days. So, if a child is ill, it is appropriate for them to rest quietly in their bedroom. We discourage the use of TV during school hours, and the practice of watching more television on out-of-school days than on school days. (Some children sleep late on these days and then watch extra television in the evenings.) In order for a child to pass the time on a sick day, we encourage

reading or doing homework. Evening activities or visits from friends may be canceled on days when a child is not in school, and reinstated when the child is back in school. (These rules can be adjusted for the child who is away from school for an extended time due to health problems. In these cases it may be desirable to encourage social activities.) The kind of *sick day* routine described above is not meant as a punishment for staying home, but, rather, it describes a reasonable routine that could be followed if a child were away from school with a bad cold. When these family rules and routines are established, it is important to communicate them to others who will be providing childcare, and to the school if required to be part of the program.

Waiting for Specialist Visits or Medical Tests

Occasionally a family may be waiting for specific consultations or tests in order to have a better understanding of a health problem. The family may take the approach of suspending normal behavioral expectations while waiting for more information. This may cause difficulty over time with getting back to normal routines. It is best to encourage the child and family to have as normal a routine and school attendance as possible during these periods. Even children with very serious health problems tend to do better if they continue to be involved in normal activities as much as possible, including school activities.

Modeling Healthy Behavior in the Family

Children learn to deal with common health problems through experiences in the family. Parents teach children how to handle common health problems (headaches, stomach aches, colds, flu) through their examples. They can assist their child to develop age-appropriate self-reliance and confidence (teaching a child self-care skills and how to deal with common problems in a relaxed way). It is important for children to learn that experiencing a variety of aches, pains, and illnesses is normal. They should have the opportunity to ask questions, and express their concerns about these symptoms. At the same time, children benefit from continuing to stay as involved as possible in normal activities while they are dealing with health problems. Much of the disability caused by health problems relates to excessive avoidance and disengagement from the positive activities of life.

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Immune and Endocrine Function in Child and Adolescent Obsessive Compulsive Disorder

33

Tanya K. Murphy and Kelley Yokum

Theory for Autoimmune and Infection Triggered Causes of Anxiety

Dr. Laurence Selling made one of the earliest reported cases of this potential correlation between the onset of tics and infectious disease in 1929 when he described three cases of tics associated with sinusitis (Selling, 1929). Subsequently, psychoanalytic theories prevailed in etiologic theories of Tourette Syndrome (TS) (Kushner & Kiessling, 1996). Just before the "medicalization" of (TS) in 1965, Langlois and Force described a 6-year-old child with TS and Sydenham chorea (SC) symptoms following several infectious illnesses that were successfully treated with antibiotics and neuroleptics (Langlois & Force, 1965). They argued that Tourette was wrong to say TS was incurable and separate from SC, but that TS should be viewed as sequel to acute chorea. After a lag of approximately 20 years, the argument reappeared that, in at least some cases, tics and obsessive compulsive disorder (OCD) are related to infectious processes. In the late 1980s, researchers noted that patients with SC often developed OCD symptoms, and further inquiry found that patients with SC often had tics as well. Additional investigation found that some patients with Group A Streptococcus (GAS) infections, but without the neurological findings of SC, also presented with OCD symptoms (Allen, Leonard, & Swedo, 1995; Swedo & Leonard, 1994). Similarly, around this same time, Louise Kiessling and colleagues reported on the association of tics during GAS outbreaks as seen in a developmental pediatric practice (Kiessling, Marcotte, & Culpepper, 1993). The first case report (Allen et al., 1995) detailed four children who presented with sudden onset or worsening of OCD and/or tics following an infection (2 viral, 2 GAS). Subsequently in 1998, based on these observations and reports, a group from the National Institute of Mental Health further characterized (in a 50 patient case series) an entity they called "pediatric autoimmune neuropsychiatric disorders associated with streptococcus" (PANDAS). Careful reading of these case series suggests that GAS is the inciting trigger, but future exacerbations are activated not only by GAS infection but GAS exposure and viral illness as well.

After assimilating the presentation of these non-SC GAS triggered neuropsychiatric disorders, criteria were established to definitively establish the phenotype to minimize the overlap with more typical OCD/tic presentations and the common childhood occurrence of GAS unrelated to neuropsychiatric presentation. These criteria for the diagnosis of PANDAS include: (1) the existence

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7_33,

of OCD or tic symptoms, (2) prepubertal onset, (3) symptoms occurring intermittently or following a "sawtooth" course, (4) temporal relationship of OCD/tic symptoms to GAS infection,and (5) presence of other neurological findings such as hyperactivity or choreiform movements. Since the initial description of this infection triggered subtype, many studies have attempted to further elucidate the immune relationship and the potential pathophysiology that may be involved in PANDAS. While some challenges remain in solidifying this association, sufficient indication exists that GAS infection is related to onset of some cases of OCD/tics to support continued exploration.

What Does the Phenotype for PANDAS Look Like?

Traditionally, OCD has been seen as a chronic condition with symptoms that are relatively stable over time. While this description accurately describes many patients with OCD, a subgroup of children and adolescents that has a dramatically different presentation has piqued the interest of many pediatric clinicians and researchers. Classically, the presentation is foudroyant; where previously high functioning and well-adjusted children change before their parents' eyes in a matter of 24–72 h. In these cases, the OCD/tic symptoms may then diminish significantly, or resolve completely over the course of 6–8 weeks. Sometimes, symptoms never reappear, while in others subsequent episodic exacerbations may occur with either complete resolution between episodes, or a progressively worsening course over time. In this "sawtooth-progressive" presentation, each subsequent episode may cause more significant impairment, and the intervals between episodes, while still representing a relative improvement in symptoms, may worsen over time as well.

In addition to this atypical presentation in time course and symptom exacerbation, other associated findings may differentiate PANDAS from typical OCD, and often account for the alarm that parents express about the change in their child. Symptoms such as separation anxiety, nightmares, personality changes, rage episodes, psychotic symptoms, and/or oppositional behaviors also cause significant disruption to family, peer and school functioning. A decline in handwriting and math skills may be observed, as well as the appearance of ADHD-like symptoms. These patients may begin bedwetting for the first time in their lives, and they may develop choreiform movements or other neurological "soft signs" (Swedo et al., 1998), though the choreiform movements in PANDAS patients are often milder, and resemble piano-playing on a stressed neurological examination as compared to those seen in SC (Pichichero, 2009). Alternative presentations of neuropsychiatric symptoms have also been reported to begin following GAS infection such as Anorexia Nervosa (Puxley, Midtsund, Iosif, & Lask, 2008; Sokol, 2000), stuttering (Murphy unpublished), spasmodic torticollis (Murphy unpublished) or dysphonia, and ADHD (Peterson et al., 2000; Swedo et al., 1998). Often these symptoms will be readily correlated with a strep infection that may follow or precede the onset of OCD/tic symptoms by a few days. Longer lag times of over 2 weeks are not often seen and if present, may suggest that a subclinical strep infection occurred making the correlation between the onset of infection and the initiation of OCD/tic symptoms difficult to confirm. Longer lag times have been well documented in rheumatic fever (RF), a disease that is clearly correlated with GAS infection, and even longer in SC. However, the GAS correlation, even in RF, is not always easy to delineate. For example, in one study, nearly two-thirds of cases occurred with minimal or no prior symptoms of pharyngitis (Ayoub, 1992).

The Role of Group A Strep in Causing Infections

GAS is a bacterium that has the capability of causing a wide range of infectious illnesses. These range from suppurative infections including pharyngitis, impetigo, necrotizing fasciitis, scarlet fever and septicemia, to nonsuppuriative illnesses including RF, glomerulonephritis and reactive arthritis. "Strep throat" is most commonly seen in children, ages 5–15 years old.

In many cases of strep infections, symptoms are minimal and patients recover without ever making a visit to their physician. Typical symptoms in streptococcal pharyngitis include sore throat, fever and swollen tonsils and lymph nodes. In younger children, strep may present with abdominal pain, nausea and vomiting, or perineal/vaginal erythema. The role of streptococcal skin infections such as impetigo or folliculitis in triggering neuropsychiatric symptoms has not been fully considered or explored, although an etiologic role has been theorized for RF (McDonald et al., 2006).

Strains of group A strep have been changing over time. More recent strains have shown an increasing variety of mechanisms that allow the bacteria to avoid host defenses including antiphagocytic factors and capsule formation that were lacking in earlier strains (Bisno, Brito, & Collins, 2003). This increase in diversity among different strains of GAS, as well as the incorporation of more effective virulence factors is responsible for the increasing incidence and severity of strep infections such as necrotizing fasciitis (Efstratiou, 2000). On the other hand, other virulence factors may be responsible for an increase in incidence of strep infections that present with minimal symptoms of pharyngitis (Krause, 2002). For example, an increase in incidence of RF in the 1980s was frequently associated with no prior history of symptoms of pharyngitis (Ayoub, 1992).

Linking GAS to OCD/Tics

One of the most contentious and challenging tasks is how best to definitively correlate the GAS infection with the onset of OCD/tic symptoms. A child presenting with a documented GAS infection coincident with onset of neuropsychiatric symptoms is not considered strong enough evidence, as some children are streptococcal carriers. The gold standard for making the case for GAS relatedness would require either documentation of infection with a strep subtype that previously had not been present or, ideally, documentation of serial strep titers showing a temporal relationship between the onset of symptoms and the titer rise. An increase of 0.2 log or greater in strep titers following the onset of OCD/tic symptoms when compared to baseline levels would be considered strong evidence for a correlation. Simply demonstrating the presence of elevated strep titers after the onset of OCD/tic symptoms is insufficient, as the presence of elevated titers is common in the 7–12 age group, even among children without symptoms of strep infections (Kaplan, Rothermel, & Johnson, 1998; Shet & Kaplan, 2002). As many children that present with PANDAS are very young (ages 3–6 years old), age adjusted titer thresholds may need to be used, since many laboratories use threshold values, e.g., an ASO of 200 IU/mL or DNAse of 400 IU/mL or higher is needed to be considered elevated (Renneberg, Soderstrom, Prellner, Forsgren, & Christensen, 1989).

In clinical settings, these lines of evidence are rarely obtained. It would be uncommon for a clinician to have baseline strep titers for a patient prior to or at the onset or exacerbation of OCD/tic symptoms. In addition, clinicians may be unlikely to subject patients to blood tests to determine strep titers within 6 weeks of onset of symptoms. Further, in clinical practice, strep cultures are generally not used to determine the presence of specific strains of GAS; rather they are used to determine the presence or absence of a strep infection, which then guides treatment with an antibiotic. In one study of pediatricians, 79% reported that they would treat a presumed strep infection with antibiotics without a positive culture (Paluck et al., 2001). Many children presenting with a PANDAS-like presentation do not have this level of documentation to support GAS infection. Rigorous application of full diagnostic criteria for PANDAS is not always being employed in the community setting, and the practice of unwarranted use of antibiotics in children without objective laboratory evidence of infection could increase antibiotic resistance in the pediatric population (Gabbay et al., 2009). It is this lack of a definitive diagnosis of GAS infection that lends to ambiguity and skepticism in establishing the GAS relatedness to OCD/tic onset.

As in the clinical setting, establishing a correlation between GAS infection and OCD/tics in the research setting is also difficult. One retrospective study examined patients, age 5–17 years old who developed tics. In this group, 53% were found to have an abrupt onset of symptoms and of this subset, 21% were shown to have the onset within 6 weeks of infection (Singer, Giuliano, Zimmerman, & Walkup, 2000). Another study examined strep titers in a group of 150 children at their initial evaluation for tics, and showed that 38% with tics had elevated ASO titers compared to 2% in the control group (Cardona & Orefici, 2001). While those with a tic disorder did differentiate from the control group suggesting a recent streptococcal infection, another possibility is that patients with persistently elevated titers may reflect a chronic immune response that then leaves patients more susceptible to exacerbations from other infections and stress (Benatar, Beatty, & Human, 1988; Read et al., 1986). A recent study by Schrag et al. (2009) did not support the relationship between streptococcal infection and postinfectious recurrences of OCD and TS. Limitations of the database, however, did not allow for determining a close temporal association of the streptococcal infection with the onset of OCD or tics. By making this association at 2 and 5 years mitigates the detection of a temporal signal above the background GAS incidence in a typical pediatric population. Also, the average age of onset for OCD was 16 years old, well beyond the usual age of PANDAS presentation. Another study found that patients with an episodic presentation in OCD/tic symptoms were more likely to have chronically elevated strep titers when compared to patients with a steadier course of symptoms (Murphy et al., 2004). Conversely, those with persistently elevated titers may only reflect the occurrence of frequent GAS infections. For some patients with a PANDAS presentation, symptoms emerge only after repeated GAS infections over a relatively short time. The risk of developing tics appears increased in children who have had frequent GAS infections (Mell, Davis, & Owens, 2005). Potential sequelae of frequent GAS infections are not limited to OCD/tic symptoms. In one study that followed 693 school age children with monthly strep cultures and behavioral observations, an increase in behavioral and motoric symptoms was seen especially in children who had repeated strep infections (Murphy et al., 2006). These findings suggest that a cumulative threshold of antibody is needed to trigger symptoms in some patients. While studies have linked antecedent GAS infections to symptom exacerbations, the majority occur without evidence of antecedent infection, suggesting that GAS infection may not be the only agent responsible for exacerbations(Kurlan, Johnson, & Kaplan, 2008), which has also been reported for SC (Berrios, Quesney, Morales, Blazquez, & Bisno, 1985).

Support for Infection Triggered Pediatric Neuropsychiatric Disorders

Currently, the predominating theory to explain the pathophysiology behind PANDAS is molecular mimicry, whereby antibodies intended to target group A strep target brain proteins instead. Potential mechanisms by which these autoantibodies cause clinical manifestations in CNS diseases include direct stimulation or blockade of receptors in the basal ganglia, or immune complexes promoting inflammation of these brain regions (Giedd, Rapoport, Garvey, Perlmutter, & Swedo, 2000; Giedd, Rapoport, Leonard, Richter, & Swedo, 1996). Antineuronal antibody binding to basal ganglia tissue was found in both patients with PANDAS (Pavone et al., 2004) and patients with ADHD (Sanchez-Carpintero, Albesa, Crespo, Villoslada, & Narbona, 2009), while in SC patients increased antineuronal antibody binding to basal ganglia tissue correlates with symptom severity (Church et al., 2002; Husby, van de Rijn, Zabriskie, Abdin, & Williams, 1976; Kotby, el Badawy, el Sokkary, Moawad, & el Shawarby, 1998). Research by Kirvan and colleagues suggests a neuropsychiatric significance of *N*-acetyl-beta-D-glucosamine, the dominant epitope of GAS carbohydrate (Kirvan, Swedo, Heuser, & Cunningham, 2003; Kirvan, Swedo, Snider, & Cunningham, 2006). The anti-carbohydrate A antibody (ACHO) measures the immune response to this GAS epitope (Bloem, Jurgens, Eichmann, & Emmrich, 1988). This antibody has shown interesting clinical relevance

in studies of rheumatic heart disease, and has been shown to fluctuate with OCD symptom changes (Murphy et al., 2004). Monoclonal antibodies in SC patients that were targeted to *N*-acetyl-beta-D-glucosamine were noted to also show specificity to mammalian lysoganglioside, a CNS ganglioside that influences neuronal signal transduction (Kirvan et al., 2003; Kirvan, Swedo, Snider, et al., 2006). However, brain cross reactivity of ACHO from a nonclinical sample was not found (Sabharwal et al., 2006). Sera from these SC and PANDAS patients contained antibodies that targeted human neuronal cells and specifically induced calcium/calmodulin-dependent protein (CaM) kinase II activity, while sera from patients convalescing or from patients with other streptococcal-related diseases lacked activation of this enzyme. The binding of autoantibodies to these neuronal cell surface antigens may promote signal transduction, leading to the release of excitatory neurotransmitters, and may explain mechanistically the symptoms of SC and PANDAS. Patients with PANDAS were found to have an intermediate level of CAMKII activation relative to SC and healthy controls. CAMKII activity may demonstrate threshold effects on clinical presentation as those PANDAS patients with isolated tics showed the highest level of CAMKII activity, approaching that of SC. Activation of CaM kinase II has been shown to cause increased dopamine release in brain tissue, a potential mechanism by which clinical symptoms ensue (Kantor, Hewlett, & Gnegy, 1999; Roberts-Lewis, Welsh, & Gnegy, 1986). In contrast, not all studies conducted have shown that antibrain antibodies correlate with clinical exacerbations in PANDAS and are a topic of continued debate (Morer et al., 2006; Singer, Gause, Morris, & Lopez, 2008).

A large proportion of current research into the pathophysiology of PANDAS has focused on exploring the role of alterations in the adaptive and innate immune function of affected youth. Support for an exaggerated immune response to GAS was found in youth with tics when compared to youth presenting with pharyngitis (Bombaci et al., 2009). In another study, a defect of regulatory T cells, which help prevent autoimmunity when properly functioning, was shown to occur in children with TS (Kawikova et al., 2007). Genetic vulnerability to this type of immune response is likely as there has been some documentation of PANDAS in multiple siblings (Dranitzki & Steiner, 2007), however this PANDAS presentation can be notably discordant in identical siblings (Murphy et al., in press). This described clinical presentation is likely the result of a gamut of gene-environment interactions involving patient specific attributes such as immune vulnerability/resistance genes, the innate immune system, cellular immunity, familial risks, environmental risks, as well as pathogen specific attributes.

Controversies in Establishing an Infectious Trigger

In 2004, a study by Perrin et al. showed that both viral and GAS infections can lead to the acute behavioral changes (Perrin et al., 2004). This study's primary aim was to assess for a delayed response to GAS after removing the acute behavioral group (those with concurrent behavior changes and GAS infection at baseline) from the analysis. Our experience suggests that the relationship of GAS inducing behavioral changes more often occurs concurrently with evidence of the infection. Hoekstra, Manson, Steenhuis, Kallenberg, and Minderaa (2005) found tic exacerbations to occur after a cold but did not find a GAS association. (Hoekstra et al., 2005) A more recent study found that a large percentage (87.5%) of symptom exacerbations among PANDAS patients cannot be definitively attributed to GAS infections, though GAS related exacerbations did occur (Kurlan et al., 2008). Moreover, reports of non-GAS triggered neuropsychiatric symptoms call into question the specificity of GAS in PANDAS-like presentations. Our experience suggests that tic disorders involving eyes, throat clearing, and facial movements are more frequently associated with viral infections. Simple tics involving the extremities, complex tics, and OCD symptoms more frequently show an association with GAS. Clearly not all symptom exacerbations are due solely to GAS and case reports support this possibility (see Table 33.1).

Table 33.1 Contributions towards establishing an immune and infection association with OCD and tics*

	Pros	Cons	Inconclusive
GAS association	Cardona and Orefici (2001), Church and Dale (2002), Guerrero et al. (2003), Kirvan, Swedo, Kurahara, and Cunningham (2006), Kirvan, Swedo, Snider, et al. (2006), Mell et al. (2005), Muller et al. (2001), Murphy and Pichichero (2002), Murphy et al. (2006), Swedo et al. (1998)	Luo et al. (2004), Schrag et al. (2009), Singer et al. (2008)	Perrin et al. (2004), Peterson et al. (2000)
ABGA	Church, Dale, Lees, Giovannoni, and Robertson (2003), Dale, Heyman, Giovannoni, and Church (2005), Hoekstra et al. (2003), Kiessling, Marcotte, and Culpepper (1994), Martino, Church, Dale, and Giovannoni (2005), Pavone et al. (2004), Rizzo, Gulisano, Pavone, Fogliani, and Robertson (2006), Singer et al. (1998)	Loiselle, Lee, Moran, and Singer (2004), Singer, Hong, Yoon, and Williams (2005), Singer, Mink, et al. (2005)	Morer et al. (2006), Murphy et al. (1997)
Immune treatment	Elia et al. (2005), Heubi and Shott (2003), Orvidas and Slattery (2001), Perlmutter et al. (1999), Selling (1929), Snider, Lougee, Slattery, Grant, and Swedo (2005)	Hoekstra, Minderaa, and Kallenberg (2004), Nicolson et al. (2000)	Garvey et al. (1999)
Immune markers	Black, Lamke, and Walikonis (1998), Carpenter et al. (2002), Denys, Fluitman, Kavelaars, Heijnen, and Westenberg (2004), Kansy et al. (2006), Kawikova et al. (2006), Leckman et al. (2005), Mercadante et al. (2000), Monteleone, Catapano, Fabrazzo, Tortorella, and Maj (1998), Morshed et al. (2001), Ravindran, Griffiths, Merali, and Anisman (1999), Roy et al. (1994)	Carpenter et al. (2002), Morer et al. (2005)	Luo et al. (2004)
D8/17	Murphy et al. (1997), Swedo et al. (1997), Chapman, Visvanathan, Carreno-Manjarrez, and Zabriskie (1998), Hoekstra et al. (2001)	Inoff-Germain et al. ((2003), Hamilton, Garvey, and Swedo (2003), Eisen et al. (2001)	Weisz et al. (2004), Murphy et al. (2001)
Animal studies	Hallett, Harling-Berg, Knopf, Stopa, and Kiessling (2000), Hoffman, Hornig, Yaddanapudi, Jabado, and Lipkin (2004), Taylor et al. (2002)	Loiselle et al. (2004), Singer, Mink, et al. (2005)	
Genetics	Lougee, Perlmutter, Nicolson, Garvey, and Swedo (2000), Zai et al. (2004)	Huang et al. (2004)	
Non-GAS pathogens	Allen et al. (1995), Budman, Kerjakovic, and Bruun (1997), Giulino et al. (2002), Khanna, Ravi, Shenoy, Chandramuki, and Channabasavanna (1997), Muller et al. (2004), Muller, Riedel, Forderreuther, Blendinger, and Abele-Horn (2000), Singer et al. (2000)		

*Due to limitations of space, not a comprehensive summary

What are the Best Evaluation and Treatment Options in the Meantime?

During the history gathering process, careful attention should be given to reports of repeated, frequent infections, evidence of GAS in a young child (e.g., unexplained abdominal pain accompanied by fever), scarlet fever, brief episodes of tics, OCD or compulsive urination that is remitted, and especially sudden onset of OCD or tics accompanying an infectious illness. In patients with abnormal neurological examination evidenced by muscle weakness, abnormal reflexes (slow return of patellar reflex, i.e., hung-up) or chorea, further follow up is indicated. In patients with new onset OCD or tics, or recent symptom exacerbation, a throat culture is a relatively benign procedure that will help rule out the possibility of symptoms being triggered by a subclinical GAS infection. Streptococcal titers obtained at symptom onset should be repeated to examine for a rise in titers 4–6 weeks later. In patients with onset exceeding 4 weeks prior, streptococcal titers add support, but do not provide definitive proof of a streptococcal trigger. However, elevated titers may not be seen in very young patients.

Antibiotics: A Complicated Option

Proof that antimicrobial prophylaxis significantly reduces recurrence, and/or exacerbation of OC/tic symptoms, suggest a supportive role for infectious agents in the onset or worsening of these conditions. By examining the scant literature of using antibiotics to prevent SC recurrences, the complications in determining efficacy become apparent. Although prophylactic antibiotic therapy in patients with SC appears successful in the prevention of neuropsychiatric exacerbations (Gebremariam, 1999), other investigators report that about a third will continue to have a recurrence (Terreri et al., 2002). Studies where SC patients received monthly prophylactic injections of benzathine penicillin G, showed that not all SC recurrences appear to be GAS triggered (Korn-Lubetzki, Brand, & Steiner, 2004), and that recurrences may occur after infections too mild or too brief to be easily detected (Berrios et al., 1985). While these studies suggest that some improvement occurs after prophylactic antibiotics, sample sizes were small, none were blinded, and since most patients with SC are recommended to take prophylactic antibiotics until their late teens, no comparison data exists on the overall neuropsychiatric severity of those receiving treatment to those that do not (Gebremariam, 1999).

While the PANDAS hypothesis remains unsettled, the current treatment for patients meeting the PANDAS criteria continues to be the standard care practices for patients with OCD and/or TS. Since a definitive association between GAS and OCD/tics has yet to be established, protocols for diagnosis and treatment of PANDAS are provisional Studies have been faced with criticisms of study design and small sample size (Kurlan & Kaplan, 2004). No conclusive evidence that the antibiotic reduced clinical exacerbations was revealed in a clinical trial involving the use of prophylactic oral penicillin in treating apparent episodes of PANDAS (Garvey et al., 1999). An active trial comparing penicillin and azithromycin (Snider et al., 2005) was also considered inconclusive by critics (Budman et al., 2005; Gilbert & Gerber, 2005). In this study, 11 subjects were maintained on penicillin and 12 were maintained on azithromycin during the 12-month study. Subjects randomized to both drugs had a reduced number of streptococcal infections, as well as a reduced number of neuropsychiatric exacerbations during the study year with no side effects or reports of any adverse effects from the medications. The authors suggest that both antibiotics may be safe and effective in preventing GAS infection, and in decreasing the number of neuropsychiatric exacerbations in these children without any significant differences between groups. This study was limited by the comparison of retrospective data for the baseline year to prospective data of the treatment year and by using an active comparator. Anecdotal reports by patients receiving antibiotics (in clinical settings) suggest that some beta lactam antibiotics are

more effective than penicillin. Studies are needed first to establish antibiotic efficacy and second, to determine which antibiotic is most effective in improving neuropsychiatric symptoms.

Another issue to be addressed is that antibiotics may serve an additional, nonantimicrobial role in the treatment of some disorders, although it has not yet been supported by clinical studies. Anecdotal reports of symptom improvement in PANDAS after 2–6 weeks of antibiotic treatment are intriguing, and suggest other possible mechanisms besides prevention of GAS reinfection. One possible mechanism is that penicillin decreases antigenic load from undetected and asymptomatic intracellular GAS (Sela, Neeman, Keller, & Barzilai, 2000). Another possibility is via cytokine modulation. GAS is a potent inducer of interferon gamma (IFNγ) and most proinflammatory cytokines (Miettinen et al., 1998). Penicillin perhaps serves a synergistic role in symptom improvement by specifically conjugating to IFNγ and reducing IFNγ's activity (Brooks, Hart, & Coleman, 2005; Brooks, Thomas, & Coleman, 2003). Interesting but not fully explored parallels are that SSRIs, which are currently the pharmacologic treatment of choice for OCD, have been found to exert antiinflammatory effects through suppression of IFNγ (Kubera et al., 2001). GAS infections have been reported to also lead to tryptophan degradation, which may influence serotonin function (Murr, Gerlach, Widner, Dierich, & Fuchs, 2001). Antibiotic therapy, theoretically, could allow for normalization of tryptophan levels. Moreover, penicillin may serve an additional, nonantimicrobial role in the treatment of some disorders (Rothstein et al., 2005), although it has not yet been supported by clinical studies. A recent screening of FDA approved medications discovered that beta-lactam antibiotics such as ceftriaxone and penicillin promoted the expression of glutamate transporter GLT1 and demonstrated a neuroprotective role *in vivo* and *in vitro* when used in models of ischemic injury and motor neuron degeneration, both based in part on glutamate toxicity. These findings indicate that positive promoters of GT expression may have a unique role in neuroprotection in neurological disorders such as amyotrophic lateral sclerosis (Rothstein et al., 2005), and potential role of glutamatergic therapies in OCD (Pittenger, Krystal, & Coric, 2006). PANDAS symptom improvement during antibiotic therapy is primarily expected to be secondary to antimicrobial effects, but the potential for multiple roles of penicillin (or other beta lactam antibiotics) would open the door for other mechanisms in PANDAS pathophysiology and treatment.

The results of a plasmapheresis or intravenous immunoglobulin (IVIG) trial in the treatment of children with PANDAS add additional support for an immune mediated pathology of OCD and tics (Perlmutter et al., 1999). These treatment gains, however, appear to be specific to children who *clearly* meet the criteria for PANDAS, as plasma exchange in four children with severe *chronic* OCD did not result in significant improvements (Nicolson et al., 2000), and IVIG did not show efficacy for patients with tic disorders (Hoekstra et al., 2004). For these patients, it is possible that a previous immune-mediated process resulted in a chronic neurological state that is less responsive to immune therapies or that this group represented patients with nonimmune mediated etiologies of their illness.

Neurological and Cardiac Concerns

In PANDAS, studies have presented evidence that an overall worsening of neurological performance occurred with or followed OCD/tic symptoms (Murphy et al., 2004; Swedo et al., 1998). Choreiform movements that represented an overall worsening of neurological performance were noted to occur about 3 months following a tic exacerbation (Murphy et al., 2004). This type of lag is consistent with the finding that OCD symptoms precede the appearance of any motoric manifestation by days or weeks in patients with RF (Mercadante et al., 2000). The presence of neurological soft signs (NSS), such as choreiform movements and pronator sign/drift are a frequently observed comorbidity among childhood onset OCD, tics, and ADHD; the significance of NSS in relationship to GAS infections has never been prospectively examined until recently

(Murphy et al., 2006). In addition to choreiform movements, other subtle signs of neurological impairment have been reported to be associated with PANDAS (Swedo et al., 1998). However neuropsychological dysfunction is commonly reported with OCD/tics (Bloch et al., 2006; Kuelz, Hohagen, & Voderholzer, 2004), and those with PANDAS may not have differentiating neuropsychological profile when compare to youth with typical (non-PANDAS) OCD and TS (Hirschtritt et al., 2009).

In addition to these ,reports suggest that other non-SC neurological sequelae may be secondary to GAS. More recently, neurological sequelae including myoclonus (DiFazio, Morales, & Davis, 1998), poststreptococcal basal ganglia encephalopathy (Dale et al., 2001), and restless legs syndrome (Matsuo, Tsuchiya, Hamasaki, & Singer, 2004), have been reported to be associated with GAS suggesting that GAS may elicit a wide array of phenotypes that render varying degrees of overlap with RF. It is the absence of frank chorea and absence of carditis that differentiates PANDAS from SC. It is estimated that rheumatic carditis is found in 30–64% of all SC patients, while data do not support a risk of developing rheumatic carditis for a child originally presenting with GAS, triggered OCD, or tics (Snider, Sachdev, MaCkaronis, St Peter, & Swedo, 2004). A milder spectrum of presentation maybe possible as these children may be at higher risk for clinically insignificant echocardiographic findings (Cardona et al., 2004; Segarra & Murphy, 2008).

Endocrine Dysregulation in Anxiety

Many studies have shown abnormal functioning of the endocrine system in various forms of anxiety including OCD. The HPA axis, consisting of hypothalamic release of corticotrophin releasing hormone (CRH) to induce anterior pituitary secretion of adreno-corticotrophin hormone (ACTH), thus stimulating the adrenal gland to release cortisol, is regulated by various negative feedback loops when cortisol levels are too high. Elevated cortisol is a finding in OCD along with nonsuppression of cortisol during suppression tests, but these results remain controversial due to inconsistent findings in the literature due to variations in methodology and small study sizes (Catapano, Monteleone, Maj, & Kemali, 1990; Coryell, Black, Kelly, & Noyes, 1989; Cottraux, Bouvard, Claustrat, & Juenet, 1984; Jenike et al., 1987; Lieberman et al., 1985). In one study, nocturnal ACTH and cortisol levels were measured in adults with OCD every 20 minutes between 11 PM and 7 AM and found to have a similar pattern with higher elevation in both hormones as compared to controls (Kluge et al., 2007). A higher early-morning cortisol level, and lower cortisol levels in response to stress, were observed in school age children with OCD as compared to controls, but limitations of this study (Gustafsson, Gustafsson, Ivarsson, & Nelson, 2008) are many. Dysregulation of the hypothalamic-pituitary-thyroid (HPT) axis in anxiety has also been considered, and a recent study in adolescent patients showed an elevation in TSH, T3, and T4 when matched with controls; 40% of these patients were pharmacotherapy naïve thus decreasing the impact medication may have had on the findings (McCracken & Hanna, 2005). Adolescents with OCD have been shown to have a particular body habitus that is shorter and lighter (Hamburger, Swedo, Whitaker, Davies, & Rapoport, 1989). Although this finding was not replicated in males with anxiety (Pine, Cohen, & Brook, 1996),young females with anxiety did appear to be smaller when compared to peers. Somatostatin,which inhibits the release of both growth and thyroid hormone, and plays a role in serotonin release, may have a specific influence on height in youth with OCD. CSF somatostatin levels have been reported to be higher in subjects with OCD, when compared to controls (Kruesi, Swedo, Leonard, Rubinow, & Rapoport, 1990). If true group differences exist, the etiology is likely to be multifactorial with additional and varying contributions from HPA dysfunction and stress, as well as from influences of nutrition, medication and illness. A recent study in males used MRI to assess pituitary volume, and found a smaller volume for medication naïve patients with OCD as compared to both medicated patients with OCD and controls; the fact that pharmacotherapy was associated

with an increased volume reflects the role medication may play on the pituitary (Jung et al., 2009). Another study measuring pituitary volume in adults of both genders found a smaller volume associated with OCD, a finding that was previously noted to occur in pediatric patients with OCD (Atmaca et al., 2009).

The implications of neuroendocrine malfunction in anxiety are wide-ranging, affecting especially the future of pharmacologic treatments. For example, if persistent corticotrophin releasing factor (CRF) ultimately leads to cortisol elevation, it is possible that blocking the CRF1 receptor, and even the CRF2 receptor, may adequately treat or prevent anxiety (Hauger, Risbrough, Brauns, & Dautzenberg, 2006; Stahl, 2008). CRF has been shown to affect multiple neurotransmitter systems that are implicated in anxiety disorders, but the role of CRF in each specific type of anxiety disorder is controversial (Risbrough & Stein, 2006). Vasopressin regulates ACTH release in the HPA axis,in both resting and stressful situations (Tanoue et al., 2004) and antagonism of the Vasopressin 1b receptor (V1b) is being studied in both mood and anxiety (Griebel et al., 2002; Pacher & Kecskemeti, 2004). In many cases, OCD onset is preceded by stressful or traumatic events (Thomsen & Mikkelsen, 1995) that have the potential to disrupt the psychoneuroimmune balance (Tait, Butts, & Sternberg, 2008). The specific contribution of each component in the interplay of stress, genetics, CNS insults, and infectious triggers in those presenting with anxiety is truly difficult to unravel. Treatment in the future may involve direct regulation of neuroendocrine function as well.

Discussion

An infectious association to the onset of pediatric neuropsychiatric symptoms would certainly help explain the enigmatic changes that can quickly occur in an otherwise healthy child. Because many infections can seemingly be insignificantly present, their pathology is often underestimated. One analogy to the current dilemma we face in determining GAS association to OCD/tics is the *Helicobacter pylori* story (Ahmed, 2005). Over 100 years ago, microbes were implicated in gastrointestinal disease (Konturek, 2003). Subsequently, this notion was dismissed (Kuelz et al., 2004) after the 1940s when psychosomatic causes were believed to be at the root of gastric/peptic ulcers. Only in the 1970s did the potential of bacteria causing GI illness rekindle. In 2005, Warren and Marshall received the Nobel Prize for the 1982 discovery of *H.pylori* in a gastric ulcer. Since this definitive association, *H. pylori* have been implicated in an array of GI illnesses from gastritis to gastric lymphoma (Suerbaum & Michetti, 2002). Host and pathogen traits, likewise have the potential to alter neuroendocrine and neuroimmune responses that collectively contribute to neuropsychiatric disease formation.

For now we have to offer only our standard therapies in treating OCD/tics, but one day we may have evidence that also allows us to add antibiotics or other immune specific treatments to our armamentarium.

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D. McKay and E.A. Storch (eds.), *Handbook of Child and Adolescent Anxiety Disorders*,
DOI 10.1007/978-1-4419-7784-7, © Springer Science+Business Media, LLC 2011