

Anxiety disorders

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Because of their high prevalence and their negative long-term consequences, child anxiety disorders have become an important focus of interest. Whether pathological anxiety and normal fear are similar processes continues to be controversial. Comparative studies of child anxiety disorders are scarce, but there is some support for the current classification of anxiety disorders in children and adolescents, except for generalized anxiety disorder. The greatly differing rates of anxiety disorders in child population studies, and of specific disorders in clinical samples, inconsistent findings regarding course, and disparate placebo response rates all suggest a need for more precise, validated, criteria for symptoms, distress, and impairment. Several treatments have documented efficacy, and promising prevention efforts are encouraging. **Keywords:** Anxiety disorders, normal vs. pathological anxiety, validity of child anxiety disorders, need for precision for impairment, ADHD, hormones, personality, mediation.

In population studies of adults, anxiety disorders are common, have earlier onset than all other major disorders (Kessler et al., 2005), and incur considerable economic and medical costs related to medical treatments, and compromised work productivity (Greenberg et al., 1999). These observations have spurred interest in child anxiety disorders ('child' throughout refers to 'child and adolescent'). This discussion of some of the clinical and research issues concerning child anxiety disorders excludes obsessive-compulsive and stress-related disorders since empirical evidence separates them from other 'anxiety disorders'. Owing to space restrictions, this not a comprehensive review of child anxiety disorders. Most substantive points are summarized and referenced elsewhere (Pine & Klein, 2008).

Prior to the DSM-III (APA, 1980), anxiety disorders often were aggregated as 'emotional disorders', and given little importance. For example, 'Overanxious reaction of childhood (or adolescence)' was the single diagnosis for pediatric anxiety (APA, 1968). The DSM-III introduced multiple childhood anxiety disorders that had little empirical basis, and were not universally welcomed. As an example, the classification was criticized for making unwarranted clinical distinctions (Rutter & Shaffer, 1980) and pathologizing normal childhood anxiety [e.g. (Garmezy, 1978)]. These concerns are relevant to this day.

Normal versus pathological anxiety

Objections to diagnosing childhood anxiety remain vocal (Lane, 2007), based on the fallacious argument that because anxiety symptoms reflect variations from common behaviors, they are not pathological. Examples abound of undisputed illnesses whose symptoms vary in degree, viz. temperature, blood

pressure, and many more (Meehl, 1992). Addressing this point requires consensus of what we mean by a 'disorder'. Much attention has been given to this important topic which is beyond our scope (e.g., Klein, 1999; Wakefield, 1999). However, regardless of definitional standards for what constitutes a disorder, it behooves us to provide evidence of validity for diagnoses whose symptoms resemble children's normal behavioral repertoire.

A central issue is whether so-called normal fear and pathological anxiety reflect similar underlying processes. Are we dealing with differences in kind or degree? There is current strong sentiment that pathological mental states are best understood as states representing variations of dimensional constructs, rather than discrete conditions, and efforts are underway to adapt this model of psychopathology to the DSM-V (e.g., Helzer et al., 2008). The 'dimensional view' has direct bearing on what research we should implement to advance our understanding of child anxiety disorders. If the same etiological and regulatory mechanisms are implicated in developmentally normal and pathological anxiety, knowledge of the neurobiology and other features related to normal fear will greatly contribute to our grasp of abnormal anxiety states. If, on the other hand, pathological anxiety is not the extreme of normal fear, there is little to be gained from the study of non-pathological anxiety for clinical purposes.

Normal fear, a response to danger, is represented in a distributed neural circuit on the amygdala. The functional and structural aspects of this 'neural fear circuit' are highly preserved across mammalian development (e.g., Panksepp, 1998). However, beyond the amygdala and within specific amygdala nuclei, there is diversity in structures engaged in various fear-related experiences. In some instances, functional and structural aspects of the fear circuit appear similar for unlearned and learned fear, even when learned fear extends over time, and specific

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circuits have been delineated for fear extinction (e.g., Isiegas, Park, Kandel, Abel, & Lattal, 2006). Moreover, specific environmental conditions early in development cause perturbations in animals' neural circuits and behavior (Pine, 2007). These effects, which may occur with acute stressors, are relatively more marked and sustained when they occur in developing than in mature organisms. Therefore, they appear particularly relevant to human development. However, neurobiological changes, and factors that mediate them, are highly complex, and not amenable to straightforward application to humans (Pine & Klein, 2008). As an example, maternal behavior in mice affects hundreds of genes (Weaver, Meaney, and Szyf, 2006), precluding a direct interpretation of the impact of stressful upbringing on brain function.

Defining characteristics of child anxiety disorders

Diagnosis ideally provides clear defining characteristics that foster communication, and informs on pathophysiology, treatment, and etiology (and ultimately, prevention).

Since anxiety disorders are grouped together (except for separation anxiety disorder, listed in the 'child' section of the DSM-IV-TR (APA, 2000)), they are often lumped together, with the implication that diagnostic distinctions are unwarranted (Buckley, Michels, & Mackinnon, 2006). The common practice of disregarding individual diagnoses may be misguided since the overarching class of anxiety disorders was created arbitrarily, without demonstration of external validation.

Generalized anxiety disorder (GAD) reflects a pattern of worry that has no defined content. Worry is a clinical feature common to many disorders, and links between GAD and multiple other conditions indicate poor diagnostic distinction. In children, GAD replaced the DSM-III diagnosis of overanxious disorder, which was removed because its symptoms, which overlapped with other anxiety disorders, were not based on clinical, much less empirical, evidence (see R.G. Klein, 1994; Werry, 1991). It has been suggested that this change was mistaken, and that overanxious disorder should be reinstated (Bittner et al., 2007).

Social phobia encapsulates two overlapping, but distinct aspects of social anxiety – performance and interpersonal anxiety. Social phobia can be specified as 'generalized' if anxiety occurs in most social situations. This qualifier is insufficiently precise, as evidenced by the marked inconsistencies with which it is applied to describe both performance and interpersonal anxiety. Several validating features differentiate the two forms of social phobia. The interpersonal (generalized) form has been reported to have relatively earlier onset, more chronicity,

comorbidity, and to be more familial than performance anxiety (Wittchen, Stein, & Kessler, 1999), and also to have different treatment indications (Blanco, Raza, Scheier, & Lebowitz, 2005).

Impaired social skills have been invoked as causal antecedents of social phobia in children. Indeed, such impairments have been found during interactions with unfamiliar people (e.g., Erath, Flanagan, and Bierman, 2007). However, it is possible that poor social behavior in unfamiliar situations reflects performance inhibition, rather than deficient social knowledge. Establishing poor social skills as important contributors requires observations of social interactions with familiar persons. These are lacking. It is likely that the disorder has contrasting origins, and encompasses a mix of children, only some with social skill deficits, leading to heterogeneity.

Panic disorder emerges in adolescence and is rarely identified in children. Panic attacks occur with multiple anxiety states, but spontaneous, 'out of the blue', uncued panic attacks are specific to panic disorder. Failure to attend to this important feature may contribute to inconsistent diagnostic practices.

Agoraphobia may be diagnosed if a child avoids situations for fear of having panic symptoms, without ever having had panic disorder. The great variability in prevalence across investigators suggests poor diagnostic clarity. For example, the diagnosis has been applied to reflect avoidance of elevators (Biederman et al., 2007), which may be considered a specific phobia.

Separation anxiety disorder is common in childhood, but uncommon in adolescence. It may be diagnosed at any age, but must have an onset prior to age 18. It is the only DSM-IV anxiety disorder which requires a childhood onset. This criterion has been questioned based on retrospective reports by adults with separation anxiety disorder, who did not recall having experienced it in childhood (Shear et al., 2006). Problematically, we do not know whether anxiety symptoms are recalled with accuracy over extended periods of time.

Specific phobia is one of the least reliable anxiety diagnoses in children, perhaps due, in part, to imprecision in standards for distress and impairment since the threshold between a fear and a phobia is not always straightforward.

Impairment or marked distress is required for all psychiatric disorders; problematically, standards for judging anxiety as dysfunctional vary across environmental contexts, cultural values, and family attitudes. The degree to which anxiety-related behaviors are perceived as abnormal is also influenced by the child's age. For example, parents of very young children did not judge avoidance of being alone, a symptom of separation anxiety, to be impairing behavior (Egger & Angold, 2006). Furthermore, distress is difficult to assess in young children. The field would be served by more precise

definitions of impairment and distress for specific anxiety symptoms at various stages of development; their import could then be tested through longitudinal studies and other validating strategies. As things stand, there is little empirical support for distinguishing various forms of phobias in childhood.

Assessment

Varied means exist to assess anxiety and anxiety disorders in children – multiple rating scales, clinical and structured interviews. Among the many interviews, there is no indication of relative merits (Klein & Pine, 2002; Pine & Klein, 2008). Questions about the validity of child anxiety diagnoses generated by lay structured interviews arise from inconsistent findings regarding the disorders' prevalence and predictive significance. In adults, the high frequency of agoraphobia without panic disorder in epidemiological samples raised questions about the validity of the diagnosis since the condition is uncommon in clinical samples. Clinical reevaluation documented that the epidemiologically based diagnoses had been erroneous – they mostly were specific phobias, and panic disorder (Horwath, Lish, Johnson, Hornig, & Weissman, 1993). Another epidemiological study found that agoraphobia without panic attacks had been accurately diagnosed (Faravelli, Cosci, Rotella, Faravelli, & Dell'Osso, 2008). Thus, of 39 individuals in the population diagnosed with agoraphobia, 10 (26%) did not report panic attacks. Rather, the cause indicated was fear of sudden incapacitation. This symptom may be considered akin to fear of developing panic-like symptoms, a DSM-IV criterion for agoraphobia. Similar work is needed in children diagnosed as having agoraphobia by non-clinicians.

Assessment dilemmas are endemic, but children pose special problems since diagnosis relies on parent, child, and/or teacher reports. These are notorious for lack of agreement, even between parents. There is scant information regarding circumstances under which reports should be aggregated (as often done). In addition, considerable method variance is due to inconsistencies across assessments. Despite uniform diagnostic criteria, standards differ for confirming their presence. Diagnostic criteria are translated in questionnaires and interviews that vary in content, form, and the clinical constructs they tap. These sources of variance most likely contribute to inconsistent findings at all levels – prevalence, correlates, course and antecedents. Highly inconsistent prevalence rates of anxiety disorders across population and clinical studies signal a lack of diagnostic clarity. For example, similar studies of children at high risk for anxiety vary greatly in rates of agoraphobia (e.g., none in Pine and colleagues (Pine et al., 2005b), versus up to 27% (Biederman et al., 2006)). We may be speaking the same words,

but not the same language. In the case of child anxiety disorders, we seem to fail the minimal nosological requirement for common referents.

To complicate matters further, anxiety scale results are often treated as equivalent to diagnostic findings, despite contradictory evidence. We do not know whether findings of correlates, genetics, etc. based on elevated anxiety ratings in normal children inform pathological anxiety. In sum, the lack of common means for the study of child anxiety disorders is bound to cause imprecision. It is difficult to argue for uniform diagnostic standards in research; at the least, the validity of differing strategies should be addressed.

Comorbidity

Comorbidity among childhood anxiety disorders raises questions regarding their distinctiveness. Comorbidity is especially marked in GAD. Since it is hardly ever 'pure', comorbidity may index severity, or complications of other disorders. If so, even if one controls for other psychopathology, residual relationships between GAD and various outcomes may reflect a severity factor, rather than specific contributions of GAD. For example, some studies seemingly report on GAD, but clear interpretation of findings is precluded since overlap with other anxiety disorders is almost complete (i.e., 90% or more; McClure et al., 2007b).

There has been no systematic examination of possible symptomatic overlap in comorbid individuals. Also complicating straightforward interpretation of comorbidity is that primary features of a disorder may be associated features of another, or common final clinical pathways. For example, children with separation anxiety frequently experience fear of the dark. We do not know whether adding a diagnosis of a specific fear of the dark reflects a meaningful comorbidity. Clinical complications of anxiety disorders might also contribute to comorbidity. Children with anxiety disorders are often resistant to conform to demands that risk exposure to feared situations, and may display marked oppositional behavior and irritability. Could this be a reason for the high comorbidity between oppositional defiant disorder and anxiety disorders (e.g., Bittner et al., 2007)? Such considerations are not trivial since oppositional defiant disorder may be a precursor of conduct disorder; by extension, it is conjectured that anxiety disorders may incur serious risk, and consequently deserve concerted prevention efforts (Bittner et al., 2007).

Natural history

Knowledge of the course of anxiety disorders is important on several grounds. For research purposes, valid diagnostic distinctions are essential,

and longitudinal data are quintessential contributors to such validity. From a public health viewpoint, vigorous treatment and prevention efforts should target disorders that portend costly dysfunction.

Follow-up studies in community and clinical samples document longitudinal associations in anxiety disorders, but with little relationship between specific child and adult anxiety disorders. Although there is consensus that child anxiety disorders predict major depression, and a few studies have found evidence of long-term specificity for social phobia and specific phobia, follow-up studies on separation anxiety and GAD have not provided clear longitudinal associations. While some clinical follow-up studies find that separation anxiety predicts panic disorder (Klein, 1995; Aschenbrand, Kendall, Webb, Safford & Flannery-Schroeder, 2003 (only for primary separation anxiety disorder)), these findings are not consistent with population studies; in fact, one population study is unusual in finding that panic disorder was the only adult anxiety disorder not associated with a child anxiety disorder (Gregory et al., 2007). GAD has been linked to a multitude of subsequent psychiatric disorders, and does not appear to have a specific course. Problematically, child and adult GAD may represent different conditions since adult GAD is not predicted by GAD in childhood and, in contrast to findings in adults, GAD and major depression in children may not have similar risk factors (Moffitt et al., 2007).

In terms of homotypic continuity, the best evidence is for social phobia; for heterotypic prediction, it is of an association between child anxiety disorders, especially social phobia, and later depression, as well as the association between either OAD or GAD and a diversity of adult disorders (reviewed in Pine & Klein, 2008). A major challenge is to identify mechanisms that account for variability in this trajectory.

In a recent population follow-up, the DSM-III diagnosis of overanxious disorder (removed by the DSM-IV (APA, 1994)) was stable over time, and predicted a wide array of disorders. This led to the recommendation that it be restored in the forthcoming DSM-V (Bittner et al., 2007). The disorder had been criticized (R.G. Klein, 1994; Werry, 1991), notably for lack of syndromal specificity, a *sine qua non* for a disorder. Moreover, the failure to identify a specific longitudinal course argues against the validity of the diagnosis. Empirically validated descriptors would seem necessary to reintroduce the disorder.

Much of the outcome data for pediatric anxiety disorders derives from epidemiological studies. These have the major advantage of eliminating referral biases, allowing application of findings to the population level. However, they incur other serious problems. First, they rely on highly structured inquiry (verbal questionnaires) in which anxiety diagnoses rarely have clinical validation. Second, in

spite of large samples, frequencies of specific disorders may be very small, e.g., in one population of over 1,000 adolescents, only 17 had social phobia (Essau, Conradt, & Petermann, 1999); in another epidemiological study of over 1,000 children that aimed, in part, to test the relationship between early separation anxiety disorder and later panic disorder, no individual had panic disorder in adolescence, and only 1.5% had spontaneous panic attacks (Bittner et al., 2007). In such situations, detection of meaningful relationships may not be possible. Third, perhaps anxiety bears negative long-term consequences only when it is severe. Moderate or mild anxiety disorders may not incur significant liability. If one assumes that number of anxiety disorders is a proxy for severity, admittedly a weak one, this seems likely (Woodward & Fergusson, 2001). If severity matters, it is not surprising that clinical and epidemiological findings fail to agree. No estimate of severity is provided in population studies. Fourth, a prospective population study reported that persistence rather than cross-sectional occurrence of childhood shyness predicted anxiety disorders (Prior, Smart, Sanson, & Oberklaid, 2000). This feature is not considered in prospective studies that typically report on relationships of dysfunction between time points. These issues complicate a clear understanding of the fate of children with anxiety disorders. The overwhelming evidence is that most remit, but it is unclear whether this is so regardless of severity and duration. Identifying predictive factors has important implications since a history of childhood anxiety is frequent in adults with anxiety and depressive disorders.

Problematically, the failure to find longitudinal predictive validity for anxiety disorders in many population studies is not interpreted by investigators as possibly invalidating the childhood diagnoses; something that the lack of diagnostic specificity reasonably suggests.

Genetics

The scarce genetic studies of child anxiety disorders support familial concordance. In some twin studies, heritability is estimated from scale ratings that may not tap pathological anxiety. They indicate modest heritability, i.e., accounting for about 40% of the variance. Based on studies of adults, non-shared environmental factors appear to be most contributory (Hettema, Neale, & Kendler, 2001; Hettema, Prescott, Myers, Neale, & Kendler, 2005), but caution is necessary in interpreting findings since all sources of error, including unreliability, contribute to estimates of non-shared environment, and may overemphasize its role. Conversely, variance attributed to gene-environment interactions is captured in heritability estimates, which underplay environmental influences.

In general, there is little specificity of concordance between parental and offspring anxiety disorders. Some evidence supports an association between parental panic disorder and separation anxiety in offspring (Biederman et al., 2007; Capps, Sigman, Sena, Henker, & Whalen, 1996; Pine & Klein, 2008). Parental panic disorder coupled with major depression appears to confer relatively higher risk to offspring (Biederman et al., 2001; Biel et al., 2008; Pine et al., 2005b).

The import of this comorbidity remains to be elucidated. Pine and his group have found that parental panic disorder mediates hypersensitivity to CO₂ in offspring with separation anxiety (Roberson-Nay et al., submitted). A shared diathesis for the child and adult disorders has been posited based on genetic findings, and similar respiratory vulnerability to CO₂ (Battaglia et al., 2009).

To enhance study of genetic influence, efforts have been made to identify endophenotypes of anxiety disorders. The expectation is that endophenotypes are closer reflections of causal, underlying pathophysiology than phenotypes (manifest disorders). In this vein, a recent longitudinal twin study of adults found significant genetic overlap between CO₂ hypersensitivity and spontaneous panic attacks (Battaglia, Pesenti-Gritti, Spatola, Ogliari, & Tambs, 2008), suggesting that CO₂ hypersensitivity may be an endophenotype for panic disorder. These findings are relevant to children since CO₂ hypersensitivity also occurs in children with separation anxiety, especially in the presence of parental panic disorder.

Work linking polymorphism of the serotonin transporter gene and stress in the development of depression exemplifies the potential for addressing challenging clinical questions (Caspi et al., 2003). Similar findings have been reported for anxiety disorders (Battaglia et al., 2008). Interactions between serotonin transporter gene polymorphism and stress, on depression, may be mediated by genetic variations on the expression of childhood anxiety, which, in turn, enhances risk of depression.

Attentional bias to threat has been viewed as an underlying feature of anxiety at all ages, and some evidence supports the differential effect of exposure to threat in children with anxiety disorders (Pine & Klein, 2008). However, not all anxiety-provoking stimuli and anxiety disorders are equal. In contrast to exposure to CO₂, 'threatening' faces have been found to be a provocation for children with social anxiety, but not separation anxiety (Pine et al., 2005a).

Anxiety sensitivity, a related function, refers to the extent that one fears a negative or harmful outcome from unpleasant feelings. Put otherwise, it is the anticipation of harm from relatively minor threats. Anxiety sensitivity has been considered a trait that may augur future panic disorder, and may be relevant as an endophenotype to the development of panic disorder (Eley, Gregory, Clark, & Ehlers,

2007). However, anxiety sensitivity is associated with all types of child anxiety. Future research may inform more fully on this relationship.

Multiple, but not all, studies of brain structure (MRI), and blood flow changes (fMRI) during conditions designed to elicit responses to emotional processing, implicate amygdala activation in childhood anxiety disorder amygdala (Pine & Klein, 2008). However, whether brain differences reflect causal mechanisms or consequences of anxiety disorders remains an open question. If preliminary findings that greater left amygdala activity predicts response to psychopharmacotherapy (McClure et al., 2007a) are confirmed in placebo-controlled studies, they will, for the first time, give clinical relevance to functional imaging. So far, imaging studies have included mixed child anxiety disorders, and none have examined specific anxiety disorders, much less contrasted them with regard to brain activation in response to emotional stimuli that evoke different types of anxious responses.

Twin studies document unshared environmental factors in child anxiety, but their nature is unknown. Parent-child interactions have been proposed as influential (independent of parents' anxiety disorders) since they are related to child anxiety; however, which came first is obscure.

Risk factors

None of the above correlates of anxiety disorders have been established as risk factors. The most consistent and heuristic finding in developmental psychopathology is the role of behavioral inhibition as a risk for social phobia (Fox, Henderson, Marshall, Nichols, & Ghera, 2005a). The significance of this relationship has been bolstered by findings of amygdala over-reactivity to novelty in adolescents with early behavioral inhibition, and of evidence of gene-environment interaction in predicting shyness at age 7 (Fox et al., 2005a, 2005b). As is typical of predictive studies, only a minority develop pathological anxiety. Here, possible moderators of developmental course have been noted. It may be that some inhibited children suffer from unidentified anxiety disorders; if so, their portending later anxiety disorders would be expected. The prevalence of behavioral inhibition is widely quoted as 15%. However, this proportion was selected arbitrarily for research purposes. Undoubtedly, future work will inform on those inhibited children at especially high risk.

As noted, parental anxiety disorders (especially coupled with depression) also represent documented risks for child anxiety disorders.

Treatment and prevention

Treatment efficacy has been supported for cognitive behavior therapy (CBT), behavior therapy and

antidepressants (selective serotonin reuptake inhibitors (SSRIs) and venlafaxine) (reviewed in Pine & Klein, 2008). SSRIs, whose use in children followed their documented efficacy in adult anxiety disorders, do not appear to have specific diagnostic indications in children. The use of another compound, D-cycloserine, derives from a neurophysiological model of extinction. Animal studies have shown that D-cycloserine affects receptor sites implicated in extinction of conditioned fear. Studies in adults with various anxiety disorders, who were receiving behavior therapies, find that the drug moderately enhances the effect of behavioral treatments (Norberg, Krystal, & Tolin, 2008; Wilhelm et al., 2008). So far, no trial has been reported in children.

In contrast, CBT derives from a model of anxiety that posits that ordinary experiences are perceived as threatening. An important goal is to rectify the child's cognitive distortions. Behavior, or exposure, therapy differs in that it aims at reducing anxiety through exposure to the feared situations which, over time is expected to extinguish the fear reaction, followed by the elimination of anticipatory anxiety. Overall, CBT has been found superior to wait-list controls, but not to credible controls in children with various anxiety disorders (Spielman, Pasek, & McFall, 2007). Few treatment trials for specific anxiety disorders have been conducted. The exception is social phobia, for which group behavior therapy (minus cognitive components) has been found effective in children (Beidel, Turner, & Morris, 2000). In a recent trial, social phobic adolescents treated with group exposure therapy, or an SSRI (fluoxetine), were markedly better than those who received a placebo (79%, 36%, 6% improvement, respectively); exposure therapy was superior to medication and was the only treatment that significantly enhanced social skills (Beidel et al., 2007). Findings suggest that cognitive restructuring is not a necessary component of behavioral interventions, at least in social phobia, and that behavioral treatment that emphasizes exposure is the best established treatment option for this disorder.

Placebo response rates vary widely across studies for the same disorder (i.e., from 6% (Beidel et al., 2007; Masia Warner, Fisher, ShROUT, Rathor, & Klein, 2007) to 37% in social phobia (March, Entusah, Rynn, Albano, & Tourian, 2007)). These disparate placebo response rates also indicate diagnostic heterogeneity across studies, and highlight the need for placebo controls in treatment studies of child anxiety disorders.

Treatment offers opportunities for clarifying some of the diagnostic conundrums. For example, in cases of comorbid GAD and social phobia, does the successful treatment of the latter coincide with remission of GAD? Such an outcome would support the notion that true comorbidity is unlikely.

The same approach can be applied to multiple comorbidities (i.e., separation anxiety accompanied by specific fear of the dark). The identification of syndromal remissions might elucidate diagnostic confusions. Another provocative example comes from findings that D-cycloserine has greater impact on extinction of anxiety in patients than on conditioned fear in normals. This differential effect might be indicative of different mechanisms in pathological anxiety and learned fear. Along the same lines, citalopram (an SSRI), an anti-anxiety agent, enhanced responses to conditioned fear in non-anxious individuals (Grillon, Levenson, & Pine, 2006). Finally, SSRIs are effective in multiple disorders but effective dosage varies (on average, it is relatively higher for OCD and depression than for panic disorder, for example). Variation in effective dose levels as a function of diagnosis may also suggest possible distinct pathophysiology. We do not have such information in children. These reports do not yield strong evidence of distinctions between 'learned' fear and symptomatic anxiety, or across various disorders, but are illustrative of the potential for treatment research to contribute to knowledge of anxiety disorders, including whether they are on a severity continuum with normal fearful reactions.

Prevention efforts have been encouraging for children with high anxiety in select settings (e.g., Rapee, Kennedy, Ingram, Edwards, & Sweeney, 2005). However, designs of cost-effective prevention studies are limited by the sparse knowledge of factors that influence long-term liability for children with anxiety disorders.

The majority of children with anxiety disorders are not referred for treatment. To enable identification and treatment of children with anxiety, interventions will need to be implemented in non-psychiatric centers, such as schools and primary care settings.

Comment

The literature abounds with irreconcilable results, beginning with simple prevalence, but it is difficult to identify contributory reasons. The most basic requirement of taxonomy is that it provides a common language for disorders with clear distinguishing features. This minimal goal is only partially met for child anxiety disorders. A useful step might be for investigators to provide clinical descriptions of diagnosed children. This should be doable with web techniques. Unfortunately, there has been no attempt to discuss, much less reconcile, reasons for disparate findings. The literature is unfortunately reminiscent of a 'dialogue of the deaf'.

It bears reminding that diagnostic criteria first introduced in the DSM-III were not intended as 'operational'. Rather, they were aimed to be guides

for shared understanding of clinical constructs or of central thematic unity, with specific examples that did not exhaust variations in symptomatic presentation. This point is still explicit in the DSM-IV (see p. xxiii (APA, 1994)). Diagnoses and criteria have been reified as natural categories. This practice has had the unfortunate consequence of limiting clinical focus, and perhaps precluding the creative discovery of novel relevant clinical features, and possibly disorders. The nomenclature, all agree, does not carve nature at its joints, but it seems unlikely that perpetuating its uncritical application will improve it. Research has relied exclusively on verbal reports. We do not know whether we can improve accuracy through systematic observations. It is possible that these would contribute valuable clinical information that would enhance diagnostic validity.

It is typical for anxious individuals to dread forthcoming feared situations. The severity of anticipatory anxiety, which varies greatly, affects function, above and beyond the actual anxiety. Whether the mechanisms underlying anticipatory and actual anxiety are identical is not known. The study of anxiety disorders has ignored possible distinctions, and the role of anticipatory anxiety for predictive purposes, such as treatment response, or long-term outcome.

In spite of limitations, some evidence supports distinctions across child anxiety disorders, especially specific phobia, separation and social anxiety disorders. GAD fails to meet a basic tenet of the DSM-IV-TR (APA, 2000): a diagnosis should

reflect the same condition through development; albeit with different behavioral manifestations at different ages. The place of GAD in children is unclear.

It is indisputable that current diagnostic conventions are not wholly satisfactory. As a remedy, there is keen interest in replacing the categorical approach with dimensional constructs that would enable multifactorial individual profiles (anxiety disorders and depression would be 'internalizing' conditions). Unfortunately, there is no evidence that dimensional systems provide better thresholds for caseness, for treatment guidelines, or for opportunity to identify markers and causes. Science cannot exist without classification, whether it is botany, zoology, biology, or behavior. In medicine, the overwhelming pattern is of increasing differentiation. Before we aggregate disorders, we might consider whether they would benefit from greater differentiation. The challenge is to disprove this possibility before dismissing it.

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Key points

- Controversy continues as to whether 'normal' fear and pathological anxiety are on a continuum of severity or represent different processes, and fundamental questions remain concerning how best to separate them.
- Anxiety disorders in the DSM-IV-TR that are common in children and adolescents (separation anxiety, social phobia, specific phobia, generalized anxiety disorder), were introduced originally based on clinical rather than empirical evidence. Yet, except for generalized anxiety disorder, on the whole, research has supported their distinction.
- The strikingly different rates of child anxiety disorders reported by different clinical centers and epidemiological surveys point to key needs for precise and commonly agreed-upon definitions of the disorders, and of impairment and distress for specific anxiety symptoms at various stages of development.
- The potential contribution of epidemiological studies is great, but the lack of clinical diagnostic validation of lay interviews limits clear interpretation of findings, especially since these are inconsistent.
- We know very little about the antecedents of childhood anxiety disorders. There is a need for work to identify vulnerability genes and their interactions, as yet unknown, with environmental risk factors.
- The little work done so far on the biology of child anxiety disorders has yielded promising leads that distinguish separation anxiety from social phobia; but the scope has been limited. For example, no neuroimaging studies of children have focused on a discrete anxiety disorder.
- Substantial progress has been made with regard to treatment, and initial prevention efforts have been encouraging. However, since most children with anxiety disorders are not identified, interventions need to be transported to non-clinical settings.

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