Exploring the Nature and Function of Anxiety in Youth with Autism Spectrum Disorders

Jeffrey J. Wood, University of California, Los Angeles
Kenneth D. Gadow, Stony Brook University

This article considers the nosology and pathogenesis of anxiety disorders in youth with autism. The comparability of anxiety in the autism spectrum disorder (ASD) population in relation to the typically developing population has been suggested by some recent findings, but conceptual and empirical ambiguities remain. It is suggested that anxiety may play at least three roles: (a) a downstream consequence of ASD symptoms (e.g., via stress generation through social rejection); (b) a moderator of ASD symptom severity, such that certain core autism symptoms like social skill deficits and repetitive behaviors may be exacerbated by anxiety; and (c) as a proxy of core ASD symptoms. Suggestions for clarifying the nature and function of anxiety in autism are made.

Key words: **autism spectrum disorders, child anxiety disorders, comorbidity, differential diagnosis. [Clin Psychol Sci Prac 17: 281–292, 2010]**

Affecting as many as 1 of every 91 youth (1 in 58 boys) in the United States, autism spectrum disorders (ASD) are among the most common of the developmental disorders (Centers for Disease Control and Prevention, 2007; Fombonne, 2005; Kogan et al., 2009) and are characterized by social and communicative deficits as well as repetitive behaviors. High rates of anxiety have been reported among youth with ASD, but whether this anxiety represents ''true'' anxiety has yet to be determined. After synthesizing initial findings,

Address correspondence to Jeffrey J. Wood, UCLA, Psychological Studies in Education, 3132A Moore Hall, Los Angeles, CA 90095. E-mail: jeffwood@ucla.edu.

we pose key questions as well as a preliminary conceptual model to guide research.

The concept of comorbidity, as it applies to neurobehavioral syndromes (e.g., the pairs of concurrent *DSM-IV-TR* [American Psychiatric Association, 2000] disorders), is in some respects ambiguous because the pathogenesis of the syndromes is poorly understood. It is therefore difficult to determine whether co-occurring symptoms or disorders (i.e., anxiety and ASD), respectively, represent:

a. ''true'' comorbidity, wherein the comorbid condition (anxiety in ASD) is phenotypically and etiologically identical to the monomorbid condition (anxiety) in a typically developing individual (i.e., someone with no ASD diagnosis);
b. true anxiety phenotypically altered by ASD pathogenic processes, resulting in an ASD-specific variant that arguably could be considered a unique syndrome, but nevertheless is not a manifestation of the ASD diathesis;
c. an aspect of the ASD diathesis, possibly with partially differing etiology from individuals with ASD who do not evidence anxiety (i.e., phenotypic heterogeneity or unique subtypes of ASD rather than true comorbidity); or
d. false or artifactual comorbidity, stemming from inaccurate differential or dual diagnosis.

Owing to the lack of evidence about the pathogenesis of ASD, anxiety, and anxiety *within* the ASD phenotype, we have adopted the term *co-occurring* to refer to anxiety in individuals with ASD. Relatedly, a

distinction between scenarios *a*, *b*, and *c* (above), collectively, and scenario *d* is arguably the most realistic goal for reviewing the literature. Notably, the same basic nosological uncertainties that characterize the distinction between ASD and anxiety also apply to most other combinations of disorders. Additionally, no discussion of psychopathology would be complete without brief clarification of the distinction between symptoms and syndromes and dimensions and categories. We use the term *symptoms* to refer to dimensional assessment (typically with a behavior rating scale) and *syndrome* to refer to categorical assessment (typically determined with a structured interview). There are also different hybrids of the classification strategies. In this review, we highlight these distinctions when relevant.

PERVASIVENESS OF SYMPTOM CO-OCCURRENCE

Research indicates that anxiety is much more common in youth with ASD compared to typically developing peers (e.g., Bellini, 2004; Guttmann-Steinmetz, Gadow, DeVincent, & Crowell, 2010; Russell & Sofronoff, 2005) or youth with conduct disorder (Green, Gilchrist, Burton, & Cox, 2000) or attention-deficit/hyperactivity disorder (ADHD; Gadow, DeVincent, & Schneider, 2009). Gadow, DeVincent, Pomeroy, and Azizian (2005) found, based on a parent-completed *DSM-IV*-referenced rating scale, that 25% and 7% of 6- to 12-year-old referred boys with ASD *(N* = 242) exceeded the symptom cutoff for generalized anxiety disorder (GAD) and separation anxiety disorder (SAD), respectively. The anxiety symptom prevalence rates for the ASD group were comparable to non-ASD outpatient child psychiatric referrals: GAD (20%) and SAD (7%). For purposes of comparison, rates from a community-based sample of boys in regular elementary schools in the same geographic area were 3% each for GAD and SAD. In studies using standard diagnostic interview instruments, anxiety disorders have been reported in over 30% of youth with ASD (de Bruin, Ferdinand, Meesters, de Nijs, & Verheij, 2007; Leyfer et al., 2006; Sukhodolsky et al., 2008). Social anxiety, in particular, appears to occur at higher rates in youth with ASD than in the typically developing population, with about 20–57% of affected youth exhibiting clinically relevant symptoms of social anxiety (Bellini, 2004; Kuusikko et al., 2008; Simonoff et al., 2008; White & Roberson-Nay, 2009).

Although prevalence studies provide useful information about the relation between anxiety and ASD, they raise more questions about nosology than they answer. Not all youth with ASD are identified as having anxiety, and of those who are, there is no evident pattern of specific types of anxiety linked with ASD, suggesting that anxiety as traditionally measured is not a core feature of the ASD clinical phenotype. However, a critical question is, are evidence-based assessment instruments designed for typically developing youth and their manifestations of psychopathology reliable and valid in youth with ASD? It has been noted that the validity of psychiatric diagnostic interviews for youth with autism is not well established (White & Roberson-Nay, 2009). A second question, assuming that anxiety diagnoses generated by commonly used structured interviews are valid in ASD, is, why are anxiety disorders common in youth with ASD? An important related issue is the clinical significance of co-occurring anxiety. In addressing these questions, our approach involves integrating evidence from studies of both individuals with ASD as well as anxiety disorders to identify plausible hypotheses for further consideration. Based on our review, we preliminarily conclude that at least some children with ASD exhibit prototypical manifestations of clinical anxiety, this anxiety is linked to at least some of the same biopsychosocial variables evidenced in non-ASD samples, and this anxiety may contribute to functional impairment and reduced quality of life over and above ASD symptom severity. Space constraints preclude comprehensive referencing; cited studies are representative of the literature. Because of the modest empirical literature, we view most findings as tentative and we highlight possible directions for future research.

QUESTION 1: ARE REPORTS OF ANXIETY IN ASD ACCURATE?

Overlapping Symptoms

It is plausible that specific core symptoms of ASD may be misidentified as co-occurring anxiety. For example, social phobia (with or without ASD) is conceptualized as the avoidance of social interaction, resulting from anxious anticipation and the fear of embarrassment or

humiliation (American Psychiatric Association, 2000). Because ASD is defined in part by social communication deficits, without clarification as to whether social avoidance in ASD is anxiety-related or skill- and motivation-related, accurate dual diagnosis is impossible. It could be that the failure of structured interviews or anxiety rating scales to obtain this information limits their ability to facilitate a valid diagnosis of social anxiety disorder—a topic for future study. Several additional examples of potentially overlapping symptoms and diagnostic uncertainty, and possible solutions, are presented later.

Repetitive Behaviors. Researchers have commented on the similarity between the restricted interests and repetitive behaviors of ASD and the symptoms of obsessive-compulsive disorder (OCD; Zandt, Prior, & Kyrios, 2007). For example, a child who has all-consuming thoughts about a superhero or a more unusual topic such as fire hydrants might meet diagnostic criteria for ASD, OCD, or both. ASD and OCD are similar in producing repetitive thoughts and corresponding clinical impairment (e.g., by diverting attention away from the immediate environment; Attwood, 2003). However, whereas consuming thoughts about an *interest* such as a superhero may be a pleasant experience for a youth with ASD, the perseverative thoughts associated with OCD are usually threat-related and unpleasant (e.g., a mental image of the superhero harming others or being harmed). The child's emotional reaction to his or her perseverative thoughts may be a criterion for differential or dual diagnosis.

Adding to nosological complexity is the fact that repetition and perseveration evidenced in ASD may reflect an underlying cognitive disposition. For example, it is possible that cognitive deficits peculiar to ASD promote repetition and perseveration and serve as risk factors for becoming "stuck" on thoughts pertaining to threat, loss, or low self-worth, thus contributing to anxiety and mood dysfunction. Cross-sectional research indicates that a tendency toward experiencing repetitive thoughts is linked with more anxiety and depression in typically developing adults (Segerstrom, Tsao, Alden, & Craske, 2000), although little is known about these relations in children with ASD. Moreover, not all youth with ASD appear to have co-occurring anxiety

or related types of ruminative thoughts. If they did, anxiety and rumination would likely have been identified as diagnostic features of ASD.

Another complicating issue for differential and dual diagnosis pertains to the exemplars offered in *DSM*-keyed diagnostic interviews for the specific symptoms of anxiety disorders, which may overlap with repetitive behaviors that also characterize ASD—such as lining up sets of objects and making clothing on each side of the body "even." However, compulsions in non-ASD and OCD are often linked with specific obsessions (e.g., in response to contamination obsessions), which is often thought not to be the case with ASD, although there is little empirical evidence either way. Common OCD compulsions include repeated tapping, touching, and rubbing rituals, sometimes in response to superstitious obsessions such as "step on a crack and break your mother's back"; repeated door opening and closing, sometimes in response to obsessions about intruders; and repeated religious rituals, sometimes in reaction to obsessions about sin or evil. It is of course possible that the cognitive and communicative deficits linked with ASD, such as impaired thought recognition (Lainhart & Folstein, 1994), simply prevent youth with ASD from accurately reporting their own anxious mental states. It is therefore recommended that clinicians make extra efforts to attain collateral information about possible evidence of obsessions (e.g., concerns about germs or contaminants expressed to caregivers) when compulsive behaviors are present. Given the conceptual distinctiveness of obsessive symptoms from prototypical ASD repetitive behaviors, the presence of obsessions at a clinically impairing level could be a useful benchmark for considering a concurrent diagnosis of OCD in youth with ASD. Of course, this ASD–OCD taxon would require much additional study to determine its clinical implications, such as responsiveness to evidence-based OCD treatments.

Communication Deficits. Another overlap between ASD and anxiety is communication deficits, a defining feature of ASD. Disorders such as social anxiety disorder have a clear—probably causal—influence on speech and language functioning in situations that induce anxiety (Davis, Shisca, & Howell, 2007; Lewin, McNeil, & Lipson, 1996). For example, dysfluency, stuttering, and

word-finding problems are concomitants of social anxiety. Selective mutism (failure to speak in broad classes of situations, such as outside of the home), which has links to social anxiety disorder, may constitute a childhood-specific effect on functional speech (Manassis et al., 2007). In considering differential and dual diagnosis of ASD and social phobia, it may be important to note that the latter is characterized by situation-specific speech problems, primarily dysfluency, and reduced total speech output, whereas ASD is associated with disorder-specific, cross-situational communication impairments such as pronominal reversal, echolalia, and failure to develop receptive and expressive language at a normal rate, if at all.

Informant Issues

Use of child report can be problematic in ASD. Individuals with ASD are often characterized by diminished ability to think abstractly or communicate effectively through speech or facial expression, and often lack awareness of internal states or motivation to report symptoms (Lainhart & Folstein, 1994). Research has shown that children with ASD provide less coherent representations of emotional experiences than their typical peers (Losh & Capps, 2006). Such findings call into question the utility and accuracy of self-report with ASD. However, diagnosing anxiety in children has relied on symptom reports by parents *or* children (i.e., a disjunctive approach), and parent-reported symptoms are at least as strongly associated with child diagnostic status for both children and adolescents as are youth-reported symptoms in typically developing children (e.g., Wood, Piacentini, Bergman, McCracken, & Barrios, 2002). This may be because many anxiety symptoms are behavioral in nature (e.g., psychosomatic symptoms) and are not limited to private mental states. Hence, variability in emotional awareness alone would not be an irresolvable factor, although it likely adds some degree of error to the diagnostic process. This is, of course, an empirical question: do child-reported anxiety symptoms on diagnostic interviews have weaker validity coefficients for youth with ASD than for typically developing youth?

Extant assessment instruments for anxiety disorders may also have potential weaknesses, particularly the possible misattribution of ASD-related impairment to anxiety. For example, during the impairment section of a diagnostic interview, the clinician might ask whether the child's anxiety symptoms cause problems in peer relationships for the child. A typical parent may respond, ''Yes. He has no friends.'' However, this response is more ambiguous than, ''Yes. His social anxiety seems to be one of the reasons he has no friends.'' Parents making the first response may have overlooked the specific linkage between anxiety and social impairment implied in the diagnostician's question; in some cases, if clarified, the primary or sole reason for the child's social impairment (in the parent's opinion) might be ASD, not anxiety. Hence, we and others have suggested that proper diagnosis of anxiety in ASD should distinguish impairment in functioning owing to symptoms of anxiety from that owing to symptoms of ASD (e.g., a lack of participation in class because of fear of embarrassment or social rejection rather than communication deficits or distraction by preoccupations; Leyfer et al., 2006; Matson & Nebel-Schwalm, 2007; Wood, Drahota, Sze, Har, et al., 2009).

QUESTION 2: IS THERE EVIDENCE FOR THE CONSTRUCT VALIDITY OF ANXIETY SYNDROMES IN ASD?

A direct method for validating mental health syndromes is to simply compare individuals with and without the purported disorder using a well-established set of criteria such as those proposed by Robins and Guze (1970; Feighner et al., 1972). Although relatively straightforward, this process has been greatly hindered in ASD owing in part to serious, well-considered reservations about the existence of psychiatric syndromes in this clinical population (see Gadow et al., 2005). Not surprisingly, therefore, the formulation of *DSM-IV*-oriented assessment instruments for individuals with ASD is a recent development, and without such measures, a nosology of behavioral syndromes was in large part deadlocked. Nonetheless, a number of important non-*DSM*-referenced assessment instruments were developed based primarily on multivariate statistical procedures (see Aman et al., 2004; Lecavalier & Gadow, 2008). At present, relatively few studies have used Robins and Guze's (1970) conceptual strategy to validate *DSM-IV* anxiety syndromes in children with ASD.

A somewhat different approach to diagnostic validity is the use of statistical procedures to determine whether anxiety symptoms in children with ASD aggregate in ways similar to their non-ASD peers. In one such study, Lecavalier, Gadow, DeVincent, Houts, and Edwards (2009) used confirmatory factor analysis to examine the internal construct validity of the *DSM-IV* model of behavioral syndromes. Parents and teachers completed a *DSM-IV*-referenced rating scale for 498 referred children (ages 6–12 years) with ASD. Analyses supported a GAD factor that was distinct from a depression or mood disorder factor and disruptive behavior disorder factors.

In another study, individual symptom severity scores for GAD and SAD were correlated with scores for *DSM-IV*-defined communication deficits, social deficits, and perseverative behaviors in boys with diagnosed ASD (IQ ≥ 70) with and without co-occurring ADHD (Guttmann-Steinmetz et al., 2010). Analyses indicated much higher correlations of perseverative behaviors with anxiety symptoms than with either communication or social deficits. The association of anxiety severity with another repetitive behavior, tics, in youth with ASD (Gadow & DeVincent, 2005), as well as other neurobehavioral syndromes such as Tourette syndrome (Schneider, Gadow, Crowell, & Sprafkin, 2009), is consistent with these findings. Of note, the social and communicative deficits are generally considered to be the most representative of the ASD syndrome, with repetitive behaviors showing statistical separation from the other two core domains (Mandy & Skuse, 2008). A linkage between anxiety and the repetitive behaviors in ASD increases the complexity of the discriminant validity profile of anxiety in ASD, but it is consistent with the observation that emotional expression is often associated with seemingly purposeless muscle movements in both animals and humans, a phenomenon that is phylogenetically ancient (Belzung & Philippot, 2007; Bracha, 2006; Darwin, 1872; Sherrington, 1900). This unique linkage of anxiety and repetitive behaviors could signify a functional relationship wherein the latter are used—like compulsions in OCD—to cope with the former.

Biologically based strategies have been used to address the validity of anxiety syndromes within the ASD clinical phenotype, one of which is molecular

genetics. Here, research has focused primarily on common gene variants (polymorphisms) shown to be associated with anxiety, other syndromes commonly associated with anxiety, or personality characteristics such as neuroticism, in clinically referred and typically developing non-ASD samples. Several polymorphisms found to be associated with anxiety disorders or anxiety symptom severity in non-ASD samples are now being found in preliminary studies to be associated with anxiety in ASD samples (Cohen et al., 2003; Gadow, DeVincent, & Schneider, 2008; Gadow, Roohi, DeVincent, Kirsch, & Hatchwell, 2009; Gadow, Roohi, DeVincent, Kirsch, & Hatchwell, 2010, under review; Roohi, DeVincent, Hatchwell, & Gadow, 2009); however, these relations are tentative pending replication in larger independent samples. As effect sizes in both ASD and typically developing samples are in the low to moderate range, these genes are likely modulators of symptom severity, not major causes of anxiety disorder. Teachers' and parents' ratings of anxiety evidence different gene-behavior relations, and both the number and strength of associations appear to be greater for teachers' ratings, but this could well change with continued research. One plausible explanation for these findings is that stress experienced during school, such as restricted opportunities for repetitive behaviors and the demands of social interaction, may interact with child genotype to produce anxious responses that are less evident in the home environment. Collectively, results suggest children with ASD with more versus less severe co-occurring anxiety may be biologically different and that co-occurring anxiety may be part of more complex behavioral syndromes.

These preliminary research findings into gene-behavior associations for anxiety and other behaviors in children with ASD share many commonalities with the general literature about the molecular biology of behavioral traits. For example, it appears that many different genes contribute to anxiety (polygeny). The same gene may influence not only anxiety but other behavioral traits as well (pleiotropy), and this appears to be the case for repetitive behaviors. Associations with one gene variant may be influenced by another polymorphism at a different locus (epistasis). Different types of anxiety as defined by *DSM-IV* (e.g., generalized, separation, social phobia, OCD) in children with

ASD appear to be associated with a different but overlapping pattern of polymorphisms and mental health risk factors (Gadow, Roohi, DeVincent, & Hatchwell, 2008). These characteristics, when combined with contextual variations in behavior and gene × environment interactions, underscore the profound complexities of using molecular genetics to aid in validating anxiety syndromes in children with ASD, to say nothing of the nosological issue of whether they are "true" comorbidities versus unique clinical constructs.

Consistencies in the behavioral assessment of anxiety, such as informant agreement, to some extent reflect upon the meaningfulness of anxiety syndromes in ASD. However, it is well documented that parents and teachers often do not agree about the severity of child anxiety, and this is linked to some degree to the fact that most children behave somewhat differently in different environments (Achenbach, McConaughy, & Howell, 1987). The same applies to the symptoms of ASD (e.g., Lecavalier et al., 2009; Ronald, Happé, & Plomin, 2008). At present, evidence indicates that teachers rate some anxious behaviors more severely than mothers (Gadow et al., 2005; Weisbrot, Gadow, DeVincent, & Pomeroy, 2005), again suggesting that the school environment may be a particularly stressful place for the child with ASD. White and Roberson-Nay (2009) report nonsignificant correlations of trivial magnitude between parent and child reports of anxiety in an ASD sample of higher-functioning youth 7–14 years old. Furthermore, the authors suggested that some children may have been confused by the items or responded randomly. One possible direction for future research would be to develop self-reports of anxiety from youth with ASD that are easier to understand and, hence, have a greater capacity to accurately represent youth emotional experiences.

Response to treatment, some would argue, can be a criterion for diagnostic constructs. In this regard, several randomized clinical trials of cognitive behavioral therapy for anxiety in youth with ASD have been published in the past decade suggesting that, with ASD-relevant modifications, treatments similar to the evidence-based standard of care for youth anxiety disorders in the typically developing population (e.g., Kendall, 1994; Kendall, Hudson, Gosch, Flannery-Schroeder, & Suveg, 2008) may yield good treatment response for the majority of participants with ASD and co-occurring anxiety (e.g., Chalfant, Rapee, & Carroll, 2007; Reaven et al., 2009; Sofronoff, Attwood, & Hinton, 2005; Wood, Drahota, Sze, Har, et al., 2009; Wood, Drahota, Sze, Van Dyke, et al., 2009; see also Puleo & Kendall, 2010). Rates of positive treatment response and anxiety remission at posttreatment and follow-up have been over 50%, comparable to treatment response profiles in typically developing youth with anxiety disorders (e.g., Kendall, 1994; Walkup et al., 2008).

In sum, evidence generated from several strategies suggests children with ASD and co-occurring anxiety are different from children with ASD and low anxiety, lending weight to the preliminary conclusion that ASD and anxiety disorders are separable entities at least some of the time. Further work in validating diagnostic interviews for the ASD population and evaluating optimal means for discriminating among anxiety and autism symptoms would be useful. Furthermore, establishing convergent validity of putative measures of anxiety in ASD using a heteromethod assessment strategy is an important objective.

QUESTION 3: WHAT ARE THE DETERMINANTS AND CONSEQUENCES OF ANXIETY IN YOUTH WITH ASD?

At this time, less can be asserted about the etiology, clinical implications, or sequelae of anxiety in youth with ASD than about phenomenology. Nevertheless, we do know that anxiety symptoms and disorders are generally associated with significant functional impairment. For example, in youth with ASD, parent-rated anxiety is linked with greater impairments in social responsiveness (Sukhodolsky et al., 2008) and social skill deficits (Bellini, 2004). Several studies of children with ASD have found strong linkages between high anxiety and greater severity of ASD symptoms, including sensory symptoms (Ben-Sasson et al., 2008) and, as previously noted, repetitive behaviors (e.g., Sukhodolsky et al., 2008). In one study using causal modeling, higher anxiety was associated with greater total ASD symptoms even when controlling for intellectual impairment, social maladjustment, and degree of speech impairment (Kelly, Garnett, Attwood, & Peterson, 2008). In a recent study of cognitive-behavioral therapy for comorbid anxiety disorders in youth with

ASD, the more that anxiety symptoms remitted during treatment, the more parent-reported ASD symptoms declined as well (Wood, Drahota, Sze, Van Dyke, et al., 2009). In sum, high anxiety in youth with ASD covaries with more social maladjustment and core autism symptoms, suggesting the possibility of a causal relationship among the two families of syndromes.

Hypothetical Model

Although research indicates a positive association between anxiety and ASD severity and impairment, it does not clarify the direction of effects. Multiple underlying causal relations among variables likely account for this pattern of findings. There are at least three likely candidate explanations: anxiety may be (a) a downstream consequence of ASD symptoms (e.g., via stress generation through experiences like social rejection); (b) a mediator or moderator of ASD symptom severity; or (c) a proxy of core ASD symptoms (i.e., because of poor discriminant validity between measures of anxiety and ASD). Whereas the latter explanation could account for a portion of the covariance between anxiety and ASD symptoms, clinical observation and the psychometric and genetic research conducted to date also suggest that it is unlikely that phenotypically anxious behaviors are solely manifestations of ASD rather than related to underlying mood dysregulation. Figure 1 illustrates one model of the role of anxiety in ASD.

ASD symptoms could potentially generate stress for affected individuals when symptom expression is in conflict with social expectations or demands or when ASD symptoms cause punishing reactions from others (e.g., Bellini, 2004, 2006; Gillott & Standen, 2007; Goodwin, Groden, Velicer, & Diller, 2007). Many individuals with ASD encounter daily stressors (Gillott & Standen, 2007), and affected youth show cortisol patterns characteristic of chronic stress (Corbett, Mendoza, Wegelin, Carmean, & Levine, 2008). Putative sources of stress evaluated in these studies and observed in clinical practice include the following: (1) repeated demands of teachers and others to conform and engage in assigned activities rather than in preferred routines and circumscribed interests; (2) difficulty understanding the perspectives of others, making daily social interactions unpredictable and at times overwhelming; (3) sensitivity to sound, touch, or light, turning events like attending a fireworks show or even a simple congratulatory cheer into a stressful assault on the senses; and (4) teasing and rejection related to the social, communicative, and behavioral features of ASD (e.g., acting immaturely according to group standards).

ASD-related stresses could either contribute to increased global negative affectivity—a generalized, nonspecific risk factor for developing anxiety disorders—or, through automatic and reflective forms of learning, become specific foci of fear and anxiety (see,
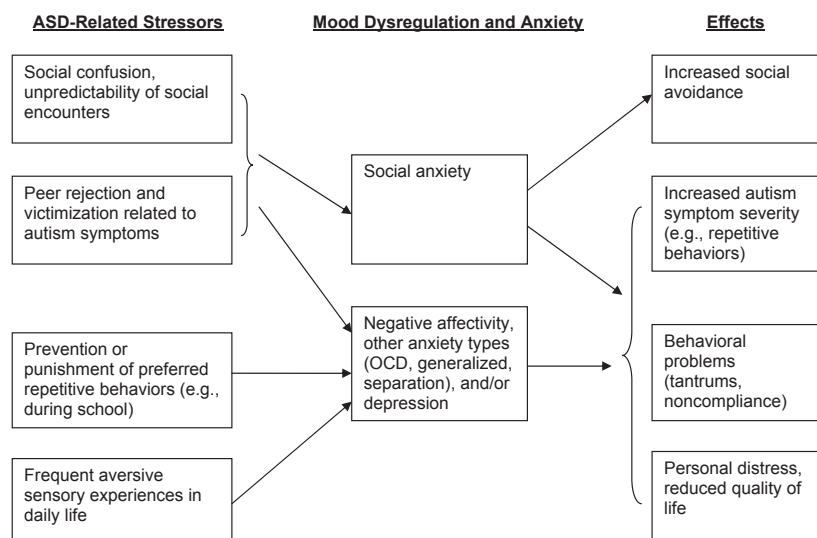

Figure 1. Hypothetical model of clinical anxiety in autism spectrum disorders.

e.g., Craske's [1999, p. 101] model of anxiety development; also see Stemberger, Turner, Beidel, & Calhoun, 1995). For example, a teen with high–negative affectivity and low–positive affectivity who experiences one or more humiliating incidents when meeting members of the opposite sex would be at risk for developing social anxiety disorder symptoms such as avoidance of parties and dances, belief in the high likelihood of further embarrassment and overvaluation of its consequences, impaired social performance when compelled to engage in such situations (e.g., dysfluency), and, possibly, panic-like symptoms when such situations are at hand. A similar scenario might apply to a youth with ASD and predisposing temperamental characteristics, where awkward social moments stemming from poor perspective taking (e.g., picking one's nose in public, disclosing an ''immature'' interest, confronting peers over minor school rule violations) could lead to humiliating, rejecting responses from peers and others (e.g., ''You like *that* cartoon?''), engendering a traumatic conditioning process that triggers social anxiety and avoidance. Empirical testing of this hypothesis would be informative.

The experience of heightened anxiety likely has an adverse impact on functioning, even in the context of clinically impairing ASD symptoms. Anxiety in typical populations has been linked with a variety of negative sequelae, such as reduced social networks and poorer self-esteem (e.g., Neal & Edelmann, 2003). Experimental studies with typically developing individuals have documented that fear and anxiety divert attention away from relevant stimuli toward threat-related stimuli and cognitions (e.g., Waters, Mogg, Bradley, & Pine, 2008), possibly accounting for the reduced performance in, for example, spontaneous speech or problem solving.

Hence, social anxiety—as opposed to low social motivation—could be a contributory or even primary determinant of socially avoidant behavior in peer settings for some children with ASD. Relatedly, some of the speech fluency and coherence deficits often seen in higher-functioning youth with ASD could be exacerbated (or, in theory, even primarily triggered) by social anxiety. Logic, as well as clinical observation, suggests that other types of interpersonal deficits often seen in ASD, such as hostility, tantrums, and insistence on doing things one's own way, also could be triggered in part by heightened anxiety. Certain manifestations of restricted interests and other repetitive behaviors could become more intense or take on more public and interfering forms in the presence of elevated anxiety, such that the pleasurable feelings associated with these repetitive behaviors are used as a shield or distraction from the concurrent dysphoric mood state (e.g., Attwood, 2003). Unfortunately, the cognitive features of ASD (e.g., rigidity) appear to place children with ASD at a disadvantage in forming effective emotion-coping skills (Groden, Baron, & Groden, 2006). In the absence of more adaptive coping strategies for controlling negative mood by altering thoughts or acting to change unpleasant circumstances, these manifestations of repetitive behaviors could be a default method of emotion regulation in ASD. Unfortunately, increased repetitive behaviors are unlikely to directly address causes of distress, thus representing a maladaptive coping response. Conceptually, anxiety could take the form of either a mediator or a moderator of such outcomes. In the role of a mediator, the greater the anxiety (as caused by one or more stressors), the greater the impact is hypothesized to be on peer relationships, communicative deficits, repetitive behaviors, and so forth (as depicted in Figure 1). In the role of a moderator, it would be expected that youth with both ASD and anxiety would fare worse on these outcomes than youth with just ASD.

In short, with regard to our third question, we propose that many of the core symptoms of ASD can lead to stressful experiences that promote anxiety. Heightened anxiety has the potential to increase the severity of certain ASD symptoms, such as speech and language deficits, rigidity, and repetitive behavior, as well as to contribute to or account for social avoidance, behavioral problems (e.g., tantrums), and poor perceived quality of life. These speculations are in need of empirical examination.

CONCLUSION

Although many youth with ASD evidence high rates of anxiety symptoms, relatively little can be said with confidence about the nature or origin of these behaviors or their differentiation into multiple anxiety syndromes. Research suggests that patterns of

behavioral variation within the ASD clinical phenotype show meaningful individual differences in anxiety symptomatology corresponding with the patterns seen in typical populations. There is very preliminary evidence associating the same genetic markers for anxiety in typically developing individuals with anxiety in youth with ASD. Initial psychometric evidence is also consistent with distinct anxiety construct(s) in ASD samples. The correlates of anxiety in youth with ASD also suggest that there could be both ASD-related stressors contributing to anxiety, as well as ASD-related consequences of anxiety in the form of more severe core autism symptoms, greater social impairment, and personal distress. Co-occurring anxiety ultimately could prove to be a target of treatment for some youth with ASD as part of an overall intervention strategy for reducing core symptom severity and impairment.

The validity of anxiety disorder diagnoses in ASD can be further explored using multitrait–multimethod matrix (MTMM) and cluster analytic or latent class analysis approaches. For example, the behavioral symptoms of social anxiety should aggregate in a syndrome and at the same time be relatively distinct from measures of ASD and social skills deficits. The use of objective measures of anxiety, such as physiological arousal and attentional bias paradigms, as benchmarks for further validating diagnostic interviews and anxiety rating scales in ASD could prove valuable. The MTMM framework is a powerful analytical tool for evaluating the validity of a trait in a population and has been used to explore the coherence and distinctiveness of anxiety and depression syndromes in groups of typically developing children (e.g., Cole, Truglio, & Peeke, 1997). Cluster analyses suggest that (a) high anxiety, (b) high depression, and (c) low symptoms each separate into distinct groups, supporting the discriminant validity of youth anxiety with a different analytic approach (Cannon & Weems, 2006). Employing similar methodology to distinguish between clinical anxiety and core autism symptoms would be a worthwhile direction for research in the ongoing effort to understand the role of anxiety in ASD.

REFERENCES

Achenbach, T. M., McConaughy, S. H., & Howell, C. T. (1987). Child/adolescent behavioral and emotional problems: Implications of cross–informant correlations for situational specificity. *Psychological Bulletin*, *101*(2), 213–232.

Aman, M. G., Novotny, S., Samango-Sprouse, C., Lecavalier, L., Leonard, E., Gadow, K. D., et al. (2004). Outcome measures for clinical drug trials in autism. *CNS Spectrums*, *9*, 36–47.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text revision). Washington, DC: Author.

Attwood, T. (2003). Framework for behavioral interventions. *Child and Adolescent Psychiatric Clinics of North America*, *12*, 65–86.

Bellini, S. (2004). Social skill deficits and anxiety in high-functioning adolescents with autism spectrum disorders. *Focus on Autism and Other Developmental Disabilities*, *19*, 78–86.

Bellini, S. (2006). The development of social anxiety in adolescents with autism spectrum disorders. *Focus on Autism and Other Developmental Disabilities*, *21*, 138–145.

Belzung, C., & Philippot, P. (2007). Anxiety from a phylogenetic perspective: Is there a qualitative difference between human and animal anxiety? *Neural Plasticity*, *59*, 676.

Ben-Sasson, A., Cermak, S. A., Orsmond, G. I., Tager-Flusberg, H., Kadlec, M. B., & Carter, A. S. (2008). Sensory clusters of toddlers with autism spectrum disorders: Differences in affective symptoms. *Journal of Child Psychology and Psychiatry*, *49*(8), 817–825.

Bracha, H. S. (2006). Human brain evolution and the ''Neuroevolutionary Time-Depth Principle.'' *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *30*, 827–853.

de Bruin, E. I., Ferdinand, R. F., Meesters, S., de Nijs, P. F., & Verheij, F. (2007). High rates of psychiatric co-morbidity in PDD-NOS. *Journal of Autism and Developmental Disorders*, *37*, 877–886.

Cannon, M. F., & Weems, C. F. (2006). Do anxiety and depression cluster into distinct groups? A test of tripartite model predictions in a community sample of youth. *Depression and Anxiety*, *23*(8), 453–460.

Centers for Disease Control and Prevention. (2007). Prevalence of autism spectrum disorders—autism and developmental disabilities monitoring network, 14 sites, United States, 2002. *Morbidity and Mortality Weekly Report. Surveillance Summaries*, *56*, 12–28.

Chalfant, A. M., Rapee, R., & Carroll, L. (2007). Treating anxiety disorders in children with high functioning autism spectrum disorders: A controlled trial. *Journal of Autism and Developmental Disorders*, *37*, 1842–1857.

Cohen, I. L., Liu, X., Schultz, C., White, B. N., Jenkins, E. C., Brown, W. T., et al. (2003). Association of autism

severity with A monoamine oxidase: A functional polymorphism. *Clinical Genetics*, *64*, 190–197.

Cole, D. A., Truglio, R., & Peeke, L. (1997). Relation between symptoms of anxiety and depression in children: A multitrait-multimethod-multigroup assessment. *Journal of Consulting and Clinical Psychology*, *65*(1), 110–119.

Corbett, B. A., Mendoza, S., Wegelin, J. A., Carmean, V., & Levine, S. (2008). Variable cortisol circadian rhythms in children with autism and anticipatory stress. *Journal of Psychiatry & Neuroscience*, *33*(3), 227–234.

Craske, M. G. (1999). *Anxiety disorders: Psychological approaches to theory and treatment*. Boulder, CO: Westview Press.

Darwin, C. (1872). *The expression of the emotions in man and animals*. London: John Murray.

Davis, S., Shisca, D., & Howell, P. (2007). Anxiety in speakers who persist and recover from stuttering. *Journal of Communication Disorders*, *40*(5), 398–417.

Feighner, J. P., Robins, E., Guze, S. B., Woodruff, R. A., Winokur, G., & Munoz, R. (1972). Diagnostic criteria for use in psychiatric research. *Archives of General Psychiatry*, *26*, 57–63.

Fombonne, E. (2005). Epidemiology of autistic disorder and other pervasive developmental disorders. *Journal of Clinical Psychiatry*, *66*, 3–8.

Gadow, K. D., & DeVincent, C. J. (2005). Clinical significance of tics and attention-deficit hyperactivity disorder (ADHD) in children with pervasive developmental disorder. *Journal of Child Neurology*, *20*, 481–488.

Gadow, K. D., DeVincent, C. J., Olvet, D. M., & Hatchwell, E. (under review). *Association of DRD4 polymorphism with severity of oppositional defiant, separation anxiety, and repetitive behaviors in children with autism spectrum disorder*. Manuscript submitted for publication.

Gadow, K. D., DeVincent, C. J., Pomeroy, J., & Azizian, A. (2005). Comparison of DSM-IV symptoms in elementary school-aged children with PDD versus clinic and community samples. *Autism*, *9*, 392–415.

Gadow, K. D., DeVincent, C., & Schneider, J. (2008). Predictors of psychiatric symptoms in children with an autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *38*, 1710–1720.

Gadow, K. D., DeVincent, C. J., & Schneider, J. (2009). Comparative study of children with ADHD only, autism spectrum disorder + ADHD, and chronic multiple tic disorder + ADHD. *Journal of Attention Disorders*, *12*, 474–485.

Gadow, K. D., Roohi, J., DeVincent, C. J., & Hatchwell, E. (2008). Association of ADHD, tics, and anxiety with dopamine transporter (*DAT1*) genotype in autism spectrum disorder. *Journal of Child Psychology and Psychiatry*, *49*, 1331–1338.

Gadow, K. D., Roohi, J., DeVincent, C. J., Kirsch, S., & Hatchwell, E. (2009). Association of COMT (Val158Met) and BDNF (Val66Met) gene polymorphisms with anxiety, ADHD and tics in children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *39*, 1542–1551.

Gadow, K. D., Roohi, J., DeVincent, C. J., Kirsch, S., & Hatchwell, E. (2010). Brief report: Glutamate transporter gene (SLC1A1) single nucleotide polymorphism (rs301430) and repetitive behaviors and anxiety in children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, doi: 10.1007/s10803-010-0961-7.

Gillott, A., & Standen, P. J. (2007). Levels of anxiety and sources of stress in adults with autism. *Journal of Intellectual Disabilities*, *11*(4), 359–370.

Goodwin, M. S., Groden, J., Velicer, W. F., & Diller, A. (2007). Brief report: Validating the stress survey schedule for persons with autism and other developmental disabilities. *Focus on Autism and Other Developmental Disabilities*, *22*(3), 183–189.

Green, J., Gilchrist, A., Burton, D., & Cox, A. (2000). Social and psychiatric functioning in adolescents with Asperger syndrome compared with conduct disorder. *Journal of Autism and Developmental Disorders*, *30*, 279–293.

Groden, J., Baron, M. G., & Groden, G. (2006). Assessment and coping strategies. In M. G. Baron, J. Groden, G. Groden, & L. Lipsitt (Eds.), *Stress and coping in autism* (pp. 15–41). New York: Oxford University Press.

Guttmann-Steinmetz, S., Gadow, K. D., DeVincent, C. J., & Crowell, J. (2010). Anxiety symptoms in boys with autism spectrum disorder, attention-deficit hyperactivity disorder, or chronic multiple tic disorder and community controls. *Journal of Autism and Developmental Disorders*, *40*(8), 1006–1016.

Kelly, A. B., Garnett, M. S., Attwood, T., & Peterson, C. (2008). Autism spectrum symptomatology in children: The impact of family and peer relationships. *Journal of Abnormal Child Psychology*, *36*(7), 1069–1081.

Kendall, P. C. (1994). Treating anxiety disorders in children: Results of a randomized clinical trial. *Journal of Consulting and Clinical Psychology*, *62*, 100–110.

Kendall, P. C., Hudson, J., Gosch, E., Flannery-Schroeder, E., & Suveg, C. (2008). Cognitive-behavioral therapy for anxiety disordered youth: A randomized clinical trial evaluating child and family modalities. *Journal of Consulting and Clinical Psychology*, *76*, 282–297.

Kogan, M. D., Blumberg, S. J., Schieve, L. A., Boyle, C. A., Perrin, J. M., Ghandour, R. M., et al. (2009). Prevalence of parent-reported diagnosis of autism spectrum disorder among children in the US, 2007. *Pediatrics*, *124*, 1–9.

Kuusikko, S., Pollock-Wurman, R., Jussila, K., Carter, A. S., Mattila, M., Ebeling, H., et al. (2008). Social anxiety in high-functioning children and adolescents with autism and Asperger syndrome. *Journal of Autism and Developmental Disorders*, *38*(9), 1697–1709.

Lainhart, J. E., & Folstein, S. E. (1994). Affective disorders in people with autism: A review of published cases. *Journal of Autism and Developmental Disorders*, *24*(5), 587–601.

Lecavalier, L., & Gadow, K. D. (2008). Pharmacology effects and side effects. In J. L. Matson (Ed.), *Clinical assessment and intervention for autism spectrum disorders* (pp. 221–263). New York: Elsevier Science.

Lecavalier, L., Gadow, K. D., DeVincent, C. J., Houts, C., & Edwards, M. C. (2009). Deconstructing the PDD clinical phenotype: Internal validity of the DSM-IV. *Journal of Child Psychology and Psychiatry*, *50*, 1246–1254.

Lewin, M. R., McNeil, D. R., & Lipson, J. M. (1996). Enduring without avoiding: Pauses and verbal dysfluencies in public speaking fear. *Journal of Psychopathology and Behavioral Assessment*, *18*(4), 387–402.

Leyfer, O. T., Folstein, S. E., Bacalman, S., Davis, N. O., Dinh, E., Morgan, J., et al. (2006). Comorbid psychiatric disorders in children with autism: Interview development and rates of disorders. *Journal of Autism and Developmental Disorders*, *36*, 849–861.

Losh, M., & Capps, L. (2006). Understanding of emotional experience in autism: Insights from the personal accounts of high-functioning children with autism. *Developmental Psychology*, *42*(5), 809–818.

Manassis, K., Tannock, R., Garland, E. J., Minde, K., McInnes, A., & Clark, S. (2007). The sounds of silence: Language, cognition and anxiety in selective mutism. *Journal of the American Academy of Child and Adolescent Psychiatry*, *46*(9), 1187–1195.

Mandy, W. P. L., & Skuse, D. H. (2008). Research review: What is the association between the social-communication element of autism and repetitive interests, behaviours and activities? *Journal of Child Psychology and Psychiatry*, *49*(8), 795–808.

Matson, J. L., & Nebel-Schwalm, M. S. (2007). Comorbid psychopathology with autism spectrum disorder in children: An overview. *Research in Developmental Disabilities*, *28*, 341–352.

Neal, J. A., & Edelmann, R. J. (2003). The etiology of social phobia: Toward a developmental profile. *Clinical Psychology Review*, *23*(6), 761–786.

Puleo, C., & Kendall, P. C. (in press). Anxiety disorders in typically developing youth: Autism spectrum symptoms as a predictor of cognitive-behavioral treatment. *Journal of Autism and Developmental Disorders*.

Reaven, J., Blakeley-Smith, A., Nichols, S., Dasari, M., Flanigan, E., & Hepburn, S. (2009). Cognitive-behavioral group treatment for anxiety symptoms in children with high-functioning autism spectrum disorders, a pilot study. *Focus on Autism and Other Developmental Disabilities*, *24*, 27–37.

Robins, E., & Guze, S. B. (1970). Establishment of diagnostic validity in psychiatric illness: Its application to schizophrenia. *American Journal of Psychiatry*, *126*, 983–987.

Ronald, A., Happé, F., & Plomin, R. (2008). A twin study investigating the genetic and environmental aetiologies of parent, teacher and child ratings of autistic-like traits and their overlap. *European Child & Adolescent Psychiatry*, *17*(8), 473–483.

Roohi, J., DeVincent, C. J., Hatchwell, E., & Gadow, K. D. (2009). Association of a monoamine oxidase-A gene promoter polymorphism with ADHD and anxiety in boys with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *39*, 67–74.

Russell, E., & Sofronoff, K. (2005). Anxiety and social worries in children with Asperger syndrome. *Australian and New Zealand Journal of Psychiatry*, *39*(7), 633–638.

Schneider, J., Gadow, K. D., Crowell, J. A., & Sprafkin, J. (2009). Anxiety in boys with ADHD with and without chronic multiple tic disorder. *Journal of Child and Adolescent Psychopharmacology*, *19*, 1–12.

Segerstrom, S. C., Tsao, J. C. I., Alden, L. E., & Craske, M. G. (2000). Worry and rumination: Repetitive thought as a concomitant and predictor of negative mood. *Cognitive Therapy and Research*, *24*(6), 671–688.

Sherrington, C. S. (1900). Experimentation in emotion. *Nature*, *62*, 328–331.

Simonoff, E., Pickles, A., Charman, T., Chandler, S., Loucas, T., & Baird, G. (2008). Psychiatric disorders in children with autism spectrum disorders: Prevalence, comorbidity, and associated factors in a population-derived sample. *Journal of the American Academy of Child and Adolescent Psychiatry*, *47*, 921–929.

Sofronoff, K., Attwood, T., & Hinton, S. (2005). A randomised controlled trial of a CBT intervention for anxiety in children with Asperger syndrome. *Journal of Child Psychology and Psychiatry*, *46*, 1152–1160.

Stemberger, R. T., Turner, S. M., Beidel, D. C., & Calhoun, K. S. (1995). Social phobia: An analysis of possible developmental factors. *Journal of Abnormal Psychology*, *104*(3), 526–531.

Sukhodolsky, D. G., Scahill, L., Gadow, K. D., Arnold, L. E., Aman, M. G., McDougle, C. J., et al. (2008). Parent-rated anxiety symptoms in children with pervasive developmental disorders: Frequency and association with core autism symptoms and cognitive functioning. *Journal of Abnormal Child Psychology*, *36*, 117–128.

Walkup, J. T., Albano, A. M., Piacentini, J., Birmaher, B., Compton, S. N., Sherill, J. T., et al. (2008). Cognitive behavioral therapy, sertraline, or a combination in childhood anxiety. *New England Journal of Medicine*, *359*, 2753–2766.

Waters, A. M., Mogg, K., Bradley, B. P., & Pine, D. S. (2008). Attentional bias for emotional faces in children with generalized anxiety disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, *47*(4), 435–442.

Weisbrot, D. M., Gadow, K. D., DeVincent, C. J., & Pomeroy, J. (2005). The presentation of anxiety in children with pervasive developmental disorders. *Journal of Child and Adolescent Psychopharmacology*, *15*, 477–496.

White, S. W., & Roberson-Nay, R. (2009). Anxiety, social deficits, and loneliness in youth with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *39*(7), 1006–1013.

Wood, J. J., Piacentini, J. C., Bergman, R. L., McCracken, J., & Barrios, V. (2002). Concurrent validity of the anxiety disorders section of the Anxiety Disorders Interview Schedule for DSM-IV: Child and parent versions. *Journal of Clinical Child and Adolescent Psychology*, *31*, 335–342.

Wood, J. J., Drahota, A., Sze, K. M., Har, K., Chiu, A., & Langer, D. (2009). Cognitive behavioral therapy for anxiety in children with autism spectrum disorders: A randomized, controlled trial. *Journal of Child Psychology and Psychiatry*, *50*, 224–234.

Wood, J. J., Drahota, A., Sze, K. M., Van Dyke, M., Decker, K., Fujii, C., et al. (2009). Brief report: Effects of cognitive behavioral therapy on parent-reported autism symptoms in school-age children with high-functioning autism. *Journal of Autism and Developmental Disabilties*, *39*, 1608–1612.

Zandt, F., Prior, M., & Kyrios, M. (2007). Repetitive behaviour in children with high functioning autism and obsessive compulsive disorder. *Journal of Autism and Developmental Disorders*, *37*(2), 251–259.