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The Presentation and Classification of Anxiety in Autism Spectrum Disorder

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Research on the expression and prevalence of co-occurring anxiety disorders and autism spectrum disorders (ASDs) has produced variable results, in part due to the diversity in sample ascertainment and composition, methodology, and the operationalization of anxiety across studies. The present review organizes these findings to consider whether anxiety symptoms reported in ASD are better categorized as (a) a part of ASD or (b) a comorbid disorder. Although there is some support for the presence of co-occurring, potentially comorbid anxiety disorders in ASD, a shift toward measurement validation and dimensional approaches in future research is needed to determine the role of anxiety in ASD, particularly regarding its "typical" and "atypical" presentation in this population.

Key words: **anxiety, autism spectrum disorder, comorbidity, diagnostic classification, dimensional.** ***[Clin Psychol Sci Prac 19: 323–347, 2013]***

THE PRESENTATION AND CLASSIFICATION OF ANXIETY IN ASD

Anxiety has been an apparent, though ancillary symptom in autism since its conception, yet findings regarding the expression and prevalence of co-occurring anxiety and autism spectrum disorders (ASDs) are unclear. Empirical research on anxiety in ASD includes a diversity of samples, methodologies, and results, warranting a review to guide future research as well as inform issues in the diagnosis and treatment of co-occurring child psychopathologies (Kendall & Drabick, 2010). This review addresses the optimal conceptualization of the anxiety seen in ASD and asks if such symptoms are a part of ASD, a comorbid condition, or a novel presentation of anxiety altogether. Unlike comorbidity, co-occurrence is a descriptive term that does not imply distinct entities (Wood & Gadow, 2010); thus, for this review, concurrent anxiety and ASD will be described as co-occurring symptoms.

THE IMPACT OF COMORBIDITY

Difficulties defining comorbid psychopathology suggest that classifying the relationship of anxiety and ASD will be challenging (Lilienfeld, Waldman, & Israel, 1994; Regier, Narrow, Kuhl, & Kupfer, 2009); though, there is strong rationale for the effort. Twenty-two percent of adults who meet diagnostic criteria for one psychological disorder manifest a concurrent pathology within 12 months (Kessler, Chiu, Demler, & Walters, 2005), a rate that is doubled in individuals with ASD (Hofvander et al., 2009; Mattila et al., 2010; Simonoff et al., 2008). Further, comorbidly affected individuals exhibit more severe disorder symptoms, less social competence, a longer illness course, greater functional disability, and higher service utilization than those with monomorbid conditions (Angold, Costello, & Erkanli, 1999; Cerdá, Sagdeo, & Galea, 2008; Kessler, 1995; Kessler & Wang, 2008; Kessler, Berglund, et al., 2005; Tomlinson, Brown, & Abrantes, 2004).

Studies suggest comorbidity is typical among treatment seekers (Jacobi et al., 2004; Kendall et al., 2010; Wilk et al., 2006), particularly those with ASD (Mattila et al., 2010; Simonoff et al., 2008), a pervasiveness that may reflect a problem of dichotomous classification

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rather than a meaningful relationship between pathologies (Angold et al., 1999; Regier et al., 2009). Whereas medical disciplines may rely on organic differences in disorder onset, cause, and presentation to facilitate differential diagnosis, what constitutes comorbidity in psychopathology, where disorders are largely behaviorally defined, is less clear (Lilienfeld et al., 1994). Comorbidity may be an artifact of chance, sampling bias, symptom overlap, or heterogeneous symptom expression (Drabick & Kendall, 2010). Such methodological and artifactual explanations may be relevant to anxiety and ASD, which share symptoms, frequently co-occur, and have heterogeneous presentations (White, Oswald, Ollendick, & Scahill, 2009; Wood & Gadow, 2010).

Comorbid disorders may influence some empirically supported treatments (ESTs) (Brown & Barlow, 1992), and elevated ASD symptoms, specifically, may limit cognitive-behavioral treatment (CBT) of childhood anxiety disorders (e.g., Puleo & Kendall, 2010). There are ESTs for child anxiety (Kendall, Hudson, Gosch, Flannery-Schroeder, & Suveg, 2008; Silverman, Pina, & Viswesvaran, 2008; Walkup et al., 2008), and modified versions of these treatments for ASD youth are promising (MacNeil, Lopes, & Minnes, 2009; White et al., 2009). These preliminary findings suggest that comorbid anxiety may be more responsive to intervention than core ASD deficits (Rogers & Vismara, 2008), supporting the need for differentiation of these conditions.

POSSIBLE ROLES OF ANXIETY IN ASD

Wood and Gadow (2010) distinguished "true comorbidities" and "unique syndromes" when conceptualizing co-occurring anxiety in ASD. Per their definition, true comorbidity requires a comorbid condition to be etiologically and phenotypically identical to its monomorbid form. When these criteria are not met, they suggest that co-occurring symptoms may be unique, ASD-related variants of anxiety (Wood & Gadow, 2010). To clarify the role of anxiety in ASD, the present review summarizes the literature as it applies to three distinctions:

Distinction 1. Are they independent? Do anxiety symptoms in ASD represent an independent, co-occurring pathology or simply a manifestation of the ASD diathesis?

Distinction 2. If independent (as determined by Distinction 1), do anxiety symptoms represent a "true comorbidity" or a unique, ASD-related anxiety syndrome or variant?

Distinction 3. If comorbid or unique (as determined by Distinction 2), does anxiety represent a sequela of ASD, a covariant (i.e., a correlated, but causally unrelated characteristic resulting from shared risk), or a mixture of the two?

Given the prevalence of anxiety in ASD and the heterogeneity of ASD presentation, determining whether anxious behaviors are simply manifestations of ASD is a prerequisite to assessing comorbidity in this population. Pending support for the independence of these psychopathologies (as per Distinction 1), Distinctions 2 and 3 will attempt to determine whether anxiety in ASD presents as a true comorbid condition, resembling monomorbid anxiety in both presentation and etiology, or whether it is better understood as a syndrome or variant of anxiety altered in its expression by ASD deficits (Wood & Gadow, 2010).

DISTINCTION 1: INDEPENDENT PSYCHOPATHOLOGY OR ASD DIATHESIS

Accurate determination of comorbidity relies on the clear definition of each disorder. First, reliable behavioral differentiation of anxiety and ASDs should be achievable if two independent psychopathologies are present: the phenotype of anxiety disorders should not be entirely subsumed by that of ASD. Second, the prevalence of anxiety problems in ASD youth should provide clues as to whether anxiety is a core, omnipresent characteristic of ASD or a co-occurring symptom. Third, if a core feature of ASD, anxiety should be present, in some form, across diagnostic, intellectual, and developmental levels seen in persons with ASD (Mayes & Calhoun, 2011). For example, although the subject and expression of preoccupations in ASD may vary by age and intellectual ability, the tendency toward preoccupation would be constant. Fourth, if an independent pathology, anxiety should wax and wane over time at a different rate than that seen for core ASD symptoms (i.e., over days or months as opposed to the developmental changes evident in ASD traits over the life course; Davis et al.,

2010; Matson & Nebel-Schwalm, 2007). Finally, if independent from ASD, the presentation of anxiety symptoms in ASD individuals should be associated with distinct risk factors.

Diagnostic Overlap and Measurement Limitations

Although diagnostic overlap is often apparent in co-morbid disorders (Drabick & Kendall, 2010), this overlap should not be entire. Co-occurrence of two disorders is contingent on the reliable differentiation of both conditions despite some similarity. Such distinction is necessary to ensure that apparent co-occurrence is not artifactual, resulting from poor differential diagnosis. Studies comparing typically developing youth with anxiety disorders to those with high-functioning ASD suggest that communication and, to a lesser extent, social deficits may differentiate the disorders. Symptoms in the repetitive and restrictive interests domain appear less discriminating (Baron-Cohen & Belmonte, 2005; Cath, Ran, Smit, Van Balkom, & Comijs, 2008; Hartley & Sikora, 2009), with perseverative behavior in particular being associated with anxiety symptoms (Gadow, DeVincent, Pomeroy, & Azizian, 2005; Guttmann-Steinmetz, Gadow, DeVincent, & Crowell, 2010). In their study of youth (6–16 years) with high-functioning ASD (IQ ≥ 70; $n = 55$), anxiety disorders ($n = 23$) or attention-deficit hyperactivity disorders (ADHD; $n = 27$), Hartley and Sikora (2009) found that deficits in social and emotional reciprocity did not distinguish between youth with ASD versus anxiety disorders, perhaps due to reduced social reciprocity in severely anxious youth. By contrast, stereotyped language, impaired sharing, nonverbal social and imaginative abilities reliably predicted ASD status regardless of anxiety level. There are limitations to these studies, however. In the majority of published research on anxiety in ASD, anxiety disorders were determined by interviews and parent-reported measures not yet validated in youth with ASD. As such, whether these youth meet "gold standard" criteria for anxiety disorders remains unclear, a substantial limitation given the overlap of anxiety and ASD symptoms.

Wood and Gadow (2010) suggested that social avoidance, compulsive and ritualistic behavior, as well as some communication deficits are particularly problematic areas of overlap that must be distinguished by an assessment of symptom function typically lacking in studies on this topic. To date, only one study has employed an instrument designed and validated to differentiate anxiety and ASD symptomology: the Autism Comorbidities Interview (Leyfer et al., 2006). In developing this instrument, Leyfer et al. (2006) distinguished between social phobia and social avoidance as well as between generalized worry and the routine-related agitation evident in some community-referred youth with autism. Social phobia (8%) and generalized anxiety disorder (GAD) (2%) were infrequent in their sample, though highly prevalent in other, less discriminating studies (GAD: 35%, Green, Gilchrist, Burton, & Cox, 2000; social phobia: 29%, Simonoff et al., 2008).

Other strategies for differential diagnosis have been described (Muris, Steerneman, Merckelbach, Holdrinet, & Meesters, 1998; Simonoff et al., 2008), but these approaches have yielded variable results. Using semi-structured diagnostic assessments to characterize anxiety disorders in youth with autism ($n = 15$; M IQ = 70) and pervasive developmental disorder—not otherwise specified (PDD-NOS) ($n = 29$; M IQ = 79), Muris et al. (1998) reported that although 73% of their sample displayed ritualistic behavior, obsessive-compulsive disorder (OCD) was only diagnosed in those 11% of cases where parents identified ritual-related distress. Estimates of OCD have ranged from 6% to 37% across studies, with higher rates typically reflecting greater diagnostic reliance on parental speculation regarding the purpose of ritualistic behaviors (de Bruin, Ferdinand, Meester, de Nijs, & Verheij, 2007; Leyfer et al., 2006). Similarly, social phobia has been reported in 8–29% of ASD individuals depending on researchers' requirement of an articulated fear of social ridicule or rejection (Leyfer et al., 2006; Muris et al., 1998). Adding to these difficulties, no study has assessed whether physiological indicators of anxiety support these subjective anxiety measures, the validity of which may be tenuous given the communication and affect recognition deficits inherent to ASD.

Such difficulties are magnified when considering data from observer or child questionnaires, yet even fewer attempts have been made to modify or validate these measures. After removing potential ASD symptoms from several self-report measures of social anxiety, Kuusikko et al. (2008) found significantly higher levels

of social anxiety in youth with high-functioning ASD (IQ $\geq$80, 8–15 years) than in youth recruited from mainstream classrooms in the same community. Whether the remaining anxiety symptoms of this modified questionnaire provide a valid measure of social phobia in ASD was not assessed. Similarly, although Lecavalier (2006) found support for an anxiety cluster based on parent and teacher reports of behavioral issues in youth with ASD, they did not determine whether this cluster was associated with anxiety disorders.

Across studies, the prevalence of anxiety disorders has been influenced, but not negated, by these measurement inconsistencies. Similarly, there is evidence that elevated anxiety symptoms are apparent even after ambiguous behaviors, such as social avoidance, repetitive and restricted behavior, are excluded (Kuusikko et al., 2008; Lecavalier, 2006), a finding that is consistent with a co-occurring psychopathology. Confidence in these and much of the findings regarding anxiety in ASD is substantially limited, however, by a nearly unanimous reliance on subjective anxiety measures. Although it has been suggested that anxiety and ASD symptoms may be reliably differentiated via careful assessment of symptom function and motivation (Wood & Gadow, 2010), the majority of research studies have yet to follow these guidelines. This limitation influences the conclusions that can or cannot be drawn from the subsequent review of research findings.

Prevalence of Anxiety Disorders in ASD

In their review of the empirical literature, White et al. (2009) concluded that impairing anxiety presents in 11–84% of ASD youth. An updated review of 24 national and international studies (see Table 1) from both clinical and community-based samples supports this range despite the inclusion of 13 additional studies excluded from or published after White and colleagues' (2009) review. Prevalence appears largely influenced by sampling methods. In the two epidemiological studies reported to date, 42% of ASD youth recruited from a population-derived cohort in the United Kingdom (Simonoff et al., 2008) met criteria for an anxiety disorder based on a semi-structured interview, whereas a smaller number of youth (25%) in a Finnish epidemiological sample were identified via a parent questionnaire as displaying impairing anxiety problems (Hurtig et al., 2009). Community-based samples (i.e., samples that are neither population based, nor treatment seeking) yield similar ranges, with impairing anxiety symptoms reported in 11–42% and anxiety disorders reported in 39% (current) to 50% (lifetime) of individuals with ASD. Notably, although the majority of these studies employed assessment measures not yet validated in an ASD population, findings are generally consistent with the single study to employ a preferred measure (44%; Leyfer et al., 2006). In samples recruited from treatment settings, where cases may be more severe and comorbid (Mattila et al., 2010), estimates of problematic anxiety span somewhat higher, with anxiety symptom prevalence ranging from 14% to 59% of youth and anxiety disorder prevalence ranging from 35% to 55%. The highest prevalence estimates (e.g., 50–84%) appear linked to projects advertising their intent to study anxiety (Bellini, 2004; Muris et al., 1998).

Studies focusing on the prevalence of anxiety in ASD have been conducted in different countries, including the United States (Gadow, DeVincent, Pomeroy, & Azizian, 2004), the United Kingdom (Simonoff et al., 2008), Finland (Mattila et al., 2010), Norway (Bakken et al., 2010), and Singapore (Ooi, Tan, Lim, Goh, & Sung, 2011), across children and adults (Hofvander et al., 2009; Sukhodolsky et al., 2008), autism spectrum diagnoses (Gadow et al., 2004), and varying levels of intellectual impairment (Bradley, Summers, Wood, & Bryson, 2004; Hurtig et al., 2009; Sukhodolsky et al., 2008; see Table 1). The lack of ASD-specific anxiety assessment in most studies suggests that reported prevalence ranges may be overestimated (e.g., symptoms of ASD are misconstrued as anxiety) or underestimated (e.g., true anxiety symptoms are dismissed as symptoms of ASD). Yet, throughout this breadth of samples and anxiety measurements, no study has found evidence of anxiety problems in their complete sample of ASD individuals (Bellini, 2006; Helverschou & Martinsen, 2010; Leyfer et al., 2006; Wood & Gadow, 2010).

ASD Diagnosis

If anxiety is a core ASD feature, anxiety problems should present across ASD subtypes, including autism, Asperger's disorder, and PDD-NOS, and despite the severity of ASD pathology (Mayes & Calhoun, 2011).

Table 1. Studies focusing on prevalence

Author (year)	Sample size and type	Age range	IQ	Comparison group	Diagnostic instrument	Summary
Anxiety disorders (7 studies)						
de Bruin et al. (2007)	*N* = 94 PDD-NOS, clinic-referred sample	6–12 years, *M* = 8 years	*M* = 91, Range 55–120	None	Diagnostic Interview Schedule for Children (DISC-Dutch version)	55.3% diagnosed with an anxiety disorder (39% specific phobia, 12% social phobia, 6% OCD, 5% GAD); 40.5% had comorbid anxiety and disruptive behavior disorders
Green et al. (2000)	*N* = 40 (20 AS, 20 conduct disorder), clinic-referred sample	11–19 years, AS Youth *M* = 13.75 years	All in "normal range," AS *M* = 97	Adolescents with conduct disorder	Social and Emotional Functioning Interview (SEF); Isle of Wight Semi-Structured Interviews (IOW)	35% GAD, 25% OCD, 10% specific phobias
Hofvander et al. (2009)	*N* = 122 (5 autism, 67 AS, 50 PDD-NOS), clinic-referred sample	16–60 years, *M* = 29 years	Average IQ	None	Structured Clinical Interview for DSM-IV (SCID) or clinical interview	50% diagnosed with an anxiety disorder (24% OCD, 15% GAD, 13% social phobia, 6%specific phobia, 11% panic)
Leyfer et al. (2006)	*N* = 109 (autistic disorder), community sample	5–17 years, *M* = 9 years	*M* IQ = 83, Range 42–141	None	Autism Comorbidity Interview-Present and Lifetime (adapted KSADS)	44% specific phobias, 37% OCD, 12% SAD, 8% social phobia, 2% GAD, no panic disorder reported
Mattila et al. (2010)	*N* = 50 (autism and AS), combination of community and clinic referrals in Finland	9–16 years	IQ >80	Rates from national study in Finland used for comparisons	Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (KSADS)	39% with current and 50% with lifetime anxiety disorders in community sample only; 42% with anxiety disorders in combined community and treatment-seeking sample (28% current specific phobias, 33% lifetime, then 22% OCD) 14% with 2–3 anxiety disorders
Muris et al. (1998)	*N* = 44 (15 autism, 29 PDD-NOS), clinic-referred sample	5–14 years, *M* = 9 years	PDD-NOS IQ *M* = 79, Autism IQ *M* = 70	None	DISC—parent only	84% diagnosed with at least one anxiety disorder (63% specific phobia, 28% avoidant disorder, 27% SAD, 22% overanxious disorder, 11% OCD)
Simonoff et al. (2008)	*N* = 112 (62 autism, 50 ASD), epidemiological sample	10–14 years	*M* IQ = 73	None	Child and Adolescent Psychiatric Assessment—Parent Version (CAPA-P)	42% diagnosed with an anxiety disorder of some kind (29.2% social phobia, 13% GAD, 8% OCD, 8% specific phobia, 10% panic disorder, 0.5% SAD; 57% diagnosed with multiple comorbidities
Anxiety symptoms						
Bakken et al. (2010)	*N* = 194 (62 autism and intellectual disability, 132 intellectual disability only), epidemiological sample in Norway	14–57 years, *M* = 24 years	All had intellectual disabilities (32 mild to moderate, 30 severe)	Individuals with intellectual disability only	Psychopathology in Autism Checklist (PAC)	34% of ASD group met cutoff criteria for anxiety disorders versus 9% in intellectual disability only group

(Continued)

Table 1. *(Continued)*

Author (year)	Sample size and type	Age range	IQ	Comparison group	Diagnostic instrument	Summary
Bellini (2004)	*N* = 41 (16 AS, 19 HFA, 6 PDD-NOS), clinic-referred sample	12–16 years, *M* = 14.22 years	*M* = 99.94, SD = 18.81	None	Social Anxiety Scale for Adolescents (SAS-A), Multidimensional Anxiety Scale for Children (MASC), Behavior Assessment System for Children (BASC)	49% met cutoff scores for social phobia
Bradley et al. (2004)	*N* = 24 (12 autism and intellectual disability, 12 intellectual disability only), community sample	*M* = 16 years	IQ <75	Individuals with intellectual disability only	Diagnostic Assessment for the Severely Handicapped-II (DASH-II)	42% met cutoff for anxiety problems in ASD group; significantly more anxiety in youth with ASD/intellectual disability versus those with intellectual disability only
Gadow et al. (2004)	*N* = 824 (67 autism, 24 AS, 91 PDD-NOS, 135 non-PDD psychiatric disorders, 507 preschoolers in regular and special education classes)	3–5 years	*M* = 109	Preschoolers with non-PDD psychiatric disorders, preschoolers in special and regular education classes	Early Child Inventory-4 (ECI-4), Parent and Teacher	5% met cutoff scores for social phobia; significantly more teacher-reported social phobia, compulsions, and specific phobias found in ASD youth than youth with other psychiatric disorders
Gadow et al. (2005)	*N* = 919 (284 ASD, 189 non-PDD psychiatric disorders, 385 children in regular education classes, 61 in special education classes)	6–12 years	ASD *M* = 92, SD = 22.2	Children with non-PDD psychiatric disorders, preschoolers in special and regular education classes	Child Symptom Inventory-4, Parent and Teacher	12% met cutoff scores for social phobia; more teacher- and parent-reported compulsions, specific phobias and social phobia in ASD kids compared to all control groups
Hurtig et al. (2009)	*N* = 264 (24 AS, 23 autism, 217 youth from regular education classes), epidemiological study in Finland	11–17 years, ASD *M* = 13 years	IQ >70	217 youth from regular education classes in Finland	Child Behavior Checklist (CBCL), Teacher Report Form (TRF), Youth Self Report (YSR)	25% met cutoff score on anxiety subscale; YSR and CBCL internalizing subscale were greatest for ASD group even after exclusion of the autistic/bizarre symptom domain
Kim et al. (2000)	*N* = 1,810 (40 autism, 19 AS, 1,751 typically developing youth), community sample	Participants assessed at two ages: 4–6 years (*M* = 5 years) and 9–14 years (*M* = 12 years)	IQ >68	Typically developing community sample	Ontario Child Health Study (OCHS)—a revised version of the CBCL	13.6% met cutoff scores on clinical internalizing subscale, 13.6% on generalized anxiety subscale, 8.5% on separation anxiety subscale
Lecavalier (2006)	*N* = 487 (326 autism, 161 other developmental problems), community sample	*M* = 9.6 years	66% had intellectual disability (IQ <70)	Youth with other developmental problems	Nisonger Child Behavior Rating Form, Parent and Teacher	11% showed elevated scores in insecure/anxious subscale
Ooi et al. (2011)	*N* = 71 (all autism), clinic-referred sample in Singapore, 86% Chinese	6–18 years, *M* = 10.24 years	Described sample as "High Functioning Autism"	None	CBCL	26% met cutoff scores on CBCL anxious/depressed syndrome scale, 33.8% met cutoff scores on CBCL anxiety disorder subscale

(Continued)

Table 1. *(Continued)*

Author (year)	Sample size and type	Age range	IQ	Comparison group	Diagnostic instrument	Summary
Sukhodolsky et al. (2008)	*N* = 172 ASD (151 autism, 7 AS, 14 PDD-NOS), clinic-referred sample	5–17 years, *M* = 8 years	Mental age required to be at least 18 months; ranged from profound intellectual disability to average IQ	None	Child and Adolescent Symptom Inventory (CASI)	43% met screening criteria for at least one anxiety disorder (9% GAD, 31% specific phobia, 5% panic, 19% social phobia, 10% SAD); GAD, panic disorder, SAD, and overall anxiety severity were greater for those with an IQ >70; social phobia and specific phobia were equally prevalent in youth with IQs above and below 70

Note. ASD = autism spectrum disorder; AS = Asperger's syndrome; HFA = high-functioning autism; PDD-NOS = pervasive developmental disorder—not otherwise specified; GAD = generalized anxiety disorder.

Several studies have found no differences in the number of parent and self-reported anxiety problems, general internalizing or social anxiety symptoms of youth with Asperger's disorder versus high-functioning autism (Hurtig et al., 2009; Kim, Szatmari, Bryson, Streiner, & Wilson, 2000; Kuusikko et al., 2008). In a sample of preschoolers with autism, Gadow et al. (2004) reported no differences in anxiety symptoms by ASD diagnosis type. Further, in a sample of adolescents with ASD, Simonoff et al. (2008) found no relationship between the number of ASD symptoms and anxiety disorder severity.

This equivalency has not been universally demonstrated, potentially due to disagreements about ASD subtypes as well as a reliance on clinical diagnosis rather than evidence-based assessments of the subtypes. Some studies report significantly more GAD worries and avoidant personality traits (Thede & Coolidge, 2007), as well as more overall anxiety symptoms, after controlling for age and intellectual level (Tonge, Brereton, Gray, & Einfeld, 1999) in youth with Asperger's versus high-functioning autism. Gadow et al. (2005) found that youth with more pronounced ASD deficits had significantly fewer anxiety symptoms, potentially due to the poorer language abilities of children (aged 6–12 years) with PDD-NOS and autism as opposed to Asperger's in their sample. Higher rates of anxiety disorders (Muris et al., 1998) and symptoms (Weisbrot, Gadow, DeVincent, & Pomeroy, 2005), particularly those entailing higher-order cognition such as worry, foresight, imagery, or greater verbal articulation, have been noted in children with Asperger's and PDD-NOS compared to those with autism (these studies did not control for IQ). In a study of children with high-functioning autism and PDD-NOS (IQ ≥ 70), Kanai et al. (2004) reported both better social relatedness and more separation anxiety in PDD-NOS youth. Similarly, some studies suggest that obsessions, generalized worries, and GAD are more common in higher- as opposed to lower-functioning ASD youth and youth with autism (Gadow et al., 2005; Muris et al., 1998; Weisbrot et al., 2005). By contrast, some research suggests that behavioral indicators of anxiety in ASD (e.g., avoidance, restricted, ritualistic behavior) assume an opposite pattern, presenting more frequently in young children (17–36 months) with autism as opposed to PDD-NOS (Davis et al., 2010; Matson, Hess, & Boisjoli, 2010). Whether these symptoms truly reflect anxiety in youth as opposed to ASD is unclear given that the behavioral scales utilized in these studies were not designed or validated to differentiate anxiety and ASD symptoms.

Diagnostic differences in anxiety symptoms may be attributable to the cognitive functioning of youth with different ASDs. In a sample of ASD children (aged 2–14 years), Davis, Moree, et al. (2011) noted an interaction between ASD diagnosis and communication deficits, such that more communication difficulties were

associated with greater anxiety in youth with PDD-NOS, but less anxiety in those with autism. By contrast, in a sample of infants and toddlers (aged 15–37 months), Davis, Moree, et al. (2011) found that greater expressive and receptive language skills were associated with more anxiety symptoms in youth with PDD-NOS and autism, but not atypical development (i.e., developmental delays not amounting to ASD). Although these results should be considered preliminary given the aforementioned measurement issues, collectively they suggest that poorer language skills may minimize anxiety or the report of anxiety in children with ASDs. By comparison, mild to moderate, but not severe, communication deficits may result in greater anxiety for children and adolescents.

This pattern of findings is consistent with anxiety's classification as both a core element of ASD and a potential comorbidity, but should be considered preliminary given ongoing confusion regarding the differentiation of ASD syndromes as well as anxiety and ASD symptoms. Acknowledging these limitations, the presence of anxiety symptoms across ASD diagnoses and ASD severity levels suggests close ties to core ASD pathology. Alternatively, variability in the number and type of anxiety symptoms endorsed for lower- and higher-functioning ASD youth is consistent with the presence of a co-occurring disorder, potentially linked to the increased cognitive and verbal abilities of higher-functioning children.

Intellectual Functioning

Reports of impairing anxiety across levels of intellectual functioning may attest to the central role of anxiety in ASD. Impairing anxiety symptoms, measured via parent and teacher questionnaires of children's stressed or agitated behavior, have been reported in 11–42% of youth with ASD and mild-to-severe intellectual disabilities (Bakken et al., 2010; Bradley et al., 2004; Lecavalier, 2006; Sukhodolsky et al., 2008). Further, anxiety symptoms appear more common in intellectually impaired individuals with, rather than without, ASD (Bradley et al., 2004). Whether these observed behaviors reflect anxiety as opposed to other negative affects is unclear, particularly given the limited ability of intellectually impaired individuals to articulate their emotions/concerns.

Associations between IQ and co-occurring psychopathology in ASD have been inconsistent, with IQ predicting anxiety levels in some studies (Lecavalier, 2006; Sukhodolsky et al., 2008; Weisbrot et al., 2005), but not others (Brereton, Tonge, & Einfeld, 2006; Simonoff et al., 2008). In a sample of youth with PDD-NOS whose cognitive abilities ranged from profound intellectual disability to average, Sukhodolsky et al. (2008) found that individuals with IQs above 70 were significantly more likely to meet criteria for an anxiety disorder than those with impaired intelligence. Mayes, Calhoun, Murray, Ahuja, and Smith (2010) found that parents reported impairing anxiety in 79% versus 67% of high- (IQ $\geq$80) and low-functioning (117, IQ <80) ASD youth (6–16 years), respectively, with high-functioning youth demonstrating significantly greater scores on all symptoms of anxiety (e.g., worry, self-consciousness, "sick with worry"), except anxiety-related behavior problems (e.g., oppositional behavior, avoidance). Consistently, in a community sample of children with ASD, both Weisbrot et al. (2005) and Gadow et al. (2005) reported more anxiety symptoms, particularly GAD symptoms, as a function of increased intellectual ability in ASD youth. Among youth with varying levels of intellectual disability (i.e., mild, moderate, and severe), Lecavalier (2006) found that youth with severe to profound intellectual disability as opposed to low average abilities had fewer anxiety symptoms, suggesting an association between cognitive functioning and anxiety across a range of intellectual abilities in ASD.

The diagnosis of anxiety problems in youth with ASD and intellectual disability via solely subjective or observer report measures is inherently problematic, limiting confidence in published research. Nevertheless, reports of impairing anxiety in ASD individuals regardless of intellectual impairment are consistent with the notion that some features may be characteristic of ASD. Conversely, the alteration of these symptoms by intellectual ability, both in terms of symptom prevalence and expression, suggests co-occurring anxious pathology. In a sample of ASD youth of varying age (5–17 years) and IQ (profound mental disability to average intelligence), Sukhodolsky et al. (2008) found that parent reports of certain anxieties (e.g., specific and social phobias) were equally prevalent in ASD individ-

uals with and without intellectual disability, whereas generalized, separation, and panic-related anxiety/worries as well as total anxiety symptoms were greater in those with higher IQ. Intellectual abilities may be more predictive of the form of anxiety symptoms than their frequency. Conclusive evidence of co-occurring anxiety will depend on future validation of anxiety measures in this population.

Age and Development

How anxiety manifests across development may provide clues to its classification as co-occurring pathology or a symptom of a single (albeit multifaceted) pathology such as ASD. Whereas co-occurring pathologies may be particularly pronounced during specific developmental periods (e.g., increased social anxiety and the increased social demands of adolescence), core features may be more likely to be tied to the natural course of the disorder.

Research examining the influence of child age on anxiety symptoms in ASD has produced mixed results. Several studies have reported no relationship between age and anxiety severity (Sukhodolsky et al., 2008; White & Roberson-Nay, 2009), and some forms of anxiety, specifically specific and social fears and compulsions, appear elevated in ASD youth as early as 3–5 years of age, consistent with the early expression of ASD pathology (Gadow et al., 2004, 2005). Studies of ASD and anxiety in early development have relied on parent and teacher observations of child behaviors (e.g., avoidance) that may be closely tied to core ASD deficits. As such, the anxiety referenced in these very young age groups, and that found to be unrelated to age or intellectual ability (Sukhodolsky et al., 2008; White & Roberson-Nay, 2009), may be qualitatively different from that shown to fluctuate over time and elevate with increasing child awareness and age in other studies (Davis, Hess, et al., 2011).

This distinction informs studies that demonstrate a relationship between age and anxiety. Whereas teachers, but not parents, report anxiety problems in 3- to 5-year-olds with ASD, anxiety problems appear evident to both parents and teachers by 6–12 years of age (Weisbrot et al., 2005). Further, in two studies assessing anxiety symptoms in preschoolers and children with ASD, Gadow et al. (2004, 2005) noted that over twice as many children (12%) with ASD displayed impairing levels of social phobia than affected toddlers (5%), a discrepancy that may reflect an increase in social evaluation concerns or the ability to express them with age. Again, these studies are limited by their lack of differentiation of anxiety and ASD symptoms, which may be particularly difficult to discern in young children. In a study of 8- to 15-year-old youth (high-functioning ASD versus community controls), Kuusikko et al. (2008) observed that parent-reported social avoidance and fear of negative evaluation were not only elevated in ASD youth after removing potentially overlapping symptoms, but also increased with age, an inverse pattern from that observed in typically developing youth, whose fears reduced over time. More severe social anxiety symptoms, including increased generalized social avoidance, inhibition, and social discomfort, characterized ASD adolescents, but not children. Finally, in a cross-sectional study of toddlers (17–36 months), children (3–16 years), young adults (20–48 years), and older adults (49–65 years) with ASD, Davis, Hess, et al. (2011) suggested that the trajectory of anxiety symptoms in ASD largely resembles that seen in typically developing youth. Anxiety in ASD appeared to wax and wane with age, becoming increasingly severe in childhood and adolescence, reducing in adulthood, but rebounding again in later life (49–65 years).

Results of the reviewed studies, though tempered by measurement limitations, support multiple models of anxiety in ASD, potentially differentiated by the specific anxiety symptoms/behaviors being studied. Evidence of certain anxieties or anxiety-related behaviors in ASD across the life span, including at very young ages (3–5 years), supports the notion that such behaviors may be elements of the broader ASD phenotype or a variant of anxiety closely tied to ASD. This pattern is also consistent with the presence of a core diathesis for anxiety in ASD that may manifest as various anxiety disorders based on developmental (e.g., intellectual development) and environmental factors (social difficulties; Leonardo & Hen, 2008). By comparison, evidence of increased anxiety at key developmental periods, in addition to a disorder course resembling that of typical anxiety disorders, supports the existence of co-occurring psychopathology.

Compulsions and specific and social fears predominate in younger ASD children, remain constant over time, and may potentially underlie the lack of significant differences by age noted in some studies. Generalized worries and concern regarding social evaluation, by contrast, may be both more variable over time and more common in older ASD youth.

Risk Factors

The identification of distinct risk factors for anxiety problems in ASD, as opposed to ASD alone, would clarify whether or not these symptoms constitute a co-occurring psychopathology. Preliminary research suggests that ASD characterized by higher levels of anxiety may be different than that characterized by low-level anxiety (Wood & Gadow, 2010). Family studies suggest an association between anxiety disorders and ASD: anxiety disorders are more common in ASD individuals and their relatives than in relatives of children in the general population and children with other developmental problems (e.g., Down syndrome; Bolton, Pickles, Murphy, & Rutter, 1998; Piven & Palmer, 1999). In a study of youth with autism and controls with Down syndrome, elevated rates of OCD, social phobia, and depression in the parents of ASD youth were not accounted for by the burden of having a child with ASD or an increased genetic vulnerability to ASD, but rather directly associated with familial mood symptoms (Bolton et al., 1998). Mazefsky, Conner, and Oswald (2010) reported that mothers' anxiety levels were associated with increased anxiety in children with autism. Maternal mood symptoms correctly classified the internalizing status of 80% of their affected offspring. Associations between OCD and repetitive and restricted behaviors in ASD are also apparent. In a sample of youth with autism from multiplex families, Hollander et al. (2003) reported that ASD youth with high versus low levels of parent-reported restricted behaviors were significantly more likely to have parents with OCD traits (42% versus 22% in low group) and OCD (34% versus 4% in low group; Hollander et al., 2003). Gadow, DeVincent, and Schneider (2008) reported that a family history of mental health difficulties, but not ASD, predicted the presence of co-occurring mental health problems, such as anxiety, in ASD probands, suggesting that these features are more likely comorbidities than core features of ASD. Finally, several gene variants (e.g., DAT1, COMT, BDNF polymorphisms) associated with psychopathology (anxiety, executive, and tic disorders) in non-ASD samples are also associated with more social anxiety in ASD youth (Gadow, Roohi, DeVincent, Kirsch, & Hatchwell, 2009; Gadow et al., 2008), supporting the separation of anxiety and ASD as constructs in at least some cases (Wood & Gadow, 2010).

Conclusion 1: Is Anxiety a Core or Co-occurring Symptom of ASD?

There is a dearth of evidence-based standards and assessments for the differential diagnosis of anxiety and ASD, a limitation that applies in the majority of studies. Nevertheless, the review suggests great variability, not universality, in the prevalence of both anxiety disorders and impairing anxiety symptoms (range 11–84% across all studies), with anxiety disorders occurring in approximately 39–50% of epidemiological and community samples of ASD youth. Research on the behavioral and familial differentiation of ASD and anxiety symptoms further supports the independence of these difficulties, despite the notable diagnostic overlap. Cumulatively, the results suggest that anxiety is likely a co-occurring rather than characteristic feature of ASD; though, measurement limitations preclude a conclusive ruling.

This interpretation is tempered by differences in anxiety symptoms observed by ASD diagnostic categories, participant age, and severity of ASD pathology and intellectual impairment. Whereas some anxiety symptoms (e.g., generalized worry) vary by intellectual level and developmental age, other anxieties (e.g., specific fears, social discomfort, compulsions) appear minimally associated with these factors and potentially related to the ASD diathesis. The literature thus supports multiple characterizations of anxiety in ASD. First, there is evidence that some forms of anxiety are common and distinct from core ASD pathology, consistent with a co-occurring condition. Second, some anxieties (e.g., compulsions, social and specific fears) may be more easily mistaken for or associated with ASD pathology as well as more ubiquitous, suggestive of either core ASD psychopathology or an atypical variant of anxiety closely related to ASD. Valid multifaceted assessments of anxiety in ASD are needed to confirm these interpretations.

DISTINCTION 2: COMORBIDITY OR UNIQUE SYNDROME?

Given support for co-occurring anxiety problems in at least a portion of ASD cases, greater clarification regarding the quality of anxiety, its presentation as either a comorbidity or a unique syndrome of anxiety in ASD, is warranted. Although conclusions for Distinction 2 will again be qualified by ambiguities in anxiety measurement in ASD, consideration of the variable manifestations of anxiety in ASD may inform such diagnostic difficulties. To understand whether the anxiety symptoms commonly reported in ASD resembled a true comorbidity (phenotypically and etiologically proximal to a monomorbid anxiety disorder; Wood & Gadow, 2010), comparability will be assessed across five domains: (a) prevalence of specific anxiety disorders, (b) severity of anxiety, (c) presentation of anxiety, (d) disorder onset and trajectory, and (e) treatment response.

Anxiety Disorder Types and Symptom Severity

There is limited agreement regarding which anxiety disorders are most common in ASD. In the studies that examined types of anxiety disorders in ASD individuals, specific phobia, GAD, social phobia, separation anxiety disorder, and OCD are among the most common (see Table 1). This pattern is roughly equivalent to that seen in non-ASD populations, though compulsive behavior appears more common (6–37%; Bakken et al., 2010; Gillott, Furniss, & Walter, 2001) in ASD than in typically developing youth (1%; Rapee, Schniering, & Hudson, 2009).

There is minimal evidence to suggest more severe anxiety disorders in youth with compared to without ASD. In the majority of studies, overall anxiety symptoms were equally severe or milder than those of youth with psychiatric disorders other than ASD (Gadow et al., 2005) and youth with anxiety disorders (Cath et al., 2008; Farrugia & Hudson, 2006; Gillott et al., 2001; Russell & Sofronoff, 2005; Williamson, Craig, & Slinger, 2008). Deviating from other findings, Russell and Sofronoff (2005) reported increased severity of overall anxiety, obsessive–compulsive symptoms, and physical injury fears in adolescents with Asperger's syndrome according to parent, but not child report. Some differences in the expression of anxiety have been noted. Farrugia and Hudson (2006) suggested that adolescents with Asperger's syndrome have significantly more negative automatic thoughts than anxious controls, though the severity of their anxiety symptoms was comparable. Further, Helverschou and Martinsen (2010) observed significantly fewer physiological symptoms of anxiety in ASD youth, a phenomenological difference that may indicate milder (or the misperception of milder) anxiety symptoms in this population.

Quality and Presentation of Anxiety Symptoms

As in anxiety-disordered youth without ASD (Kendall et al., 2010), anxiety symptoms appear equally varied and prevalent in males and females with ASD (Worley, Matson, Sipes, & Koziowski, 2010). Comparing children (aged 6–12 years) with ASD and non-ASD disorders, Gadow et al. (2005) observed that, excepting compulsions and specific and social phobias, the distribution of co-occurring mental health problems was similar in both groups. Farrugia and Hudson (2006) found that both teenagers with anxiety disorders and those with Asperger's syndrome frequently reported symptoms of GAD, social phobia, and OCD; however, the Asperger's group reported more thoughts of physical injury and social threat. Russell and Sofronoff (2005) observed significantly more obsessive–compulsive symptoms and physical injury fears, but significantly less social evaluation concerns in adolescents with Asperger's syndrome compared to those with anxiety disorders alone. The increased prevalence of obsessive–compulsive symptoms, fears of physical injury, and social avoidance, despite reduced social evaluation concerns, supports the hypothesized distinctiveness of these symptoms from other, potentially co-occurring anxieties, which generally appear to occur at equal levels in youth with and without ASD (Gadow et al., 2005). This distinction is supported by variation in the symptom profiles of specific phobia, social phobia, and obsessive–compulsive disorder in ASD youth.

Specific phobias have been reported in as many as 44–63% of ASD youth (Leyfer et al., 2006; Muris et al., 1998), across variable levels of intellectual functioning (Sukhodolsky et al., 2008). Phobias in ASD, however, may have an unusual focus. In youth with autism and variable IQ, Leyfer et al. (2006) found that fears of shots/needles and crowds were most common, whereas phobias typical in normative samples (e.g.,

tunnels, flying, bridges) were rare. Further, 10% of ASD youth reported a fear of loud noises; though, this fear is relatively uncommon in the general population. Fears of the dark, storms, large crowds, and closed spaces also appear more common in youth with versus without ASD (Evans, Canavera, Kleinpeter, Maccubbin, & Taga, 2005). Evans et al. (2005) observed that ASD youth reported a different set of phobias, characterized by more medical, situational, and animal fears, when compared to children with Down syndrome and two groups of typically developing, chronological- and mental-age-matched control participants, suggesting that observed discrepancies were not attributable to the intellectual or developmental delays of youth with ASD. Whether these differences in specific phobia type reflects the alignment of these phobias with the ASD diathesis or the emergence of an ASD-related anxiety syndrome is unclear. Nevertheless, the evidence suggests that the focus of these phobias deviates from that of typically developing youth.

Some variability is also apparent in the expression of social phobia in ASD. One study found that fears of negative social evaluation (e.g., fears of appearing foolish or becoming embarrassed) were fewer in children with high-functioning autism (Gillott et al., 2001) compared to typically developing youth or youth with specific language impairment. Another study reported equal rates of both self-consciousness and avoidance according to parent reports in adolescents with anxiety disorders and those with Asperger's syndrome (Russell & Sofronoff, 2005). A portion of social phobias in ASD appear qualitatively distinct from monomorbid social phobia, lacking the fear of social evaluation often considered definitive to this disorder, yet there is also some suggestion of comorbid social anxiety in ASD. Although concerns have been raised that ASD-related social avoidance may be mistaken for social phobia, Kuusikko et al. (2008) observed elevated rates of other, distinct social anxiety symptoms in youth with high-functioning ASD after removing potentially ambiguous symptoms from a parent-report measure. Further, interfering social anxiety, sensitive to increased social pressures (Kuusikko et al., 2008) and social skills deficits (Bellini, 2004, 2006) as in typically developing youth, has been reported despite careful attempts at differential diagnosis in some studies. These results suggest that the social phobia in some, but not all, youth with ASD may be comparable to that of non-ASD youth (Bellini, 2004, 2006; Kuusikko et al., 2008).

Whether OCD symptoms in ASD are distinct from ASD-related rituals, perseverations, or other repetitive behaviors remains unresolved. Zandt, Prior, and Kyrios (2007) measured a range of repetitive behaviors in intellectually typical youth with ASD, OCD, and typically developing community controls. They observed that obsessions, routines, and rituals were most pronounced and complex in youth with OCD, followed by youth with ASD and then controls. The presentation of repetitive behaviors varied by age in the OCD group, but age was unrelated to the presentation of obsessions, compulsions, repetitive movements, or rigidity in ASD youth. Further, rates of OCD symptoms in ASD are lower in studies that require evidence of premonitory distress or a purposeful quality to compulsions (Muris et al., 1998; Simonoff et al., 2008). These results suggest that at least a portion of repetitive behaviors, potentially better classified as atypical anxiety or a part of the ASD phenotype, may be misattributed to OCD.

A different presentation of reported obsessions and compulsions in ASD has been suggested in some studies. Leyfer et al. (2006) observed that the most common compulsions in youth with autism and ranging intellectual abilities were a need to tell/ask and verbal or behavioral rituals involving another person. In a study comparing adults with ASD to typically developing adults with OCD, McDougle et al. (1995) reported that the ASD group demonstrated significantly more repeating, touching, tapping, and hoarding compulsions as well as significantly less cleaning, checking, counting, and aggressive obsessions than the OCD group. These findings should be interpreted with caution given a discrepancy in intellectual functioning between the ASD and OCD groups. Two studies comparing OCD in intellectually average adults with and without ASD suggest more similarities than differences in the presentation of OCD between groups (Cath et al., 2008; Russell & Sofronoff, 2005). Cath et al. (2008) reported that although obsessions appeared less severe for ASD/OCD youth, no group differences were evident for OCD symptoms or

egodystonia. Similarly, Russell and Sofronoff (2005) noted few differences between youth with ASD, OCD, and both disorders (25% of ASD sample). Adults with OCD displayed significantly more somatic obsessions, repeating and checking compulsions than ASD adults, and ASD/OCD adults reported significantly more sexual obsessions overall. Although the discrepancy in somatic obsessions between the OCD and ASD/OCD groups was pronounced, symptoms were otherwise largely equivalent across groups.

In sum, research suggests similarity in the distribution of disorders, severity, and symptoms of anxiety apparent in ASD versus anxiety-disordered youth. Some disorders and symptoms, potentially more aligned with or altered in presentation by ASD (e.g., compulsive behavior, social avoidance, unusual specific phobia), appear more common in ASD youth, whereas fears of social evaluation and obsessional content were found to be less frequent. These results are in keeping with the presence of both co-occurring anxious symptomology in ASD and atypical anxiety presentations that may represent either novel syndromes or manifestations of the core ASD diathesis.

Onset and Trajectory

Few studies have investigated the course of anxiety symptoms in ASD, but preliminary findings suggest similarities with monomorbid anxiety disorders. From a cross-sectional examination of anxiety symptoms in toddlers, children, and adults with ASD, Davis et al. (2010) reported that the trajectory of anxiety symptoms in ASD youth largely resembles that of typically developing youth; though, ASD may delay and mitigate the severity of this symptom course. As in typically developing youth, the development of higher cognitive abilities in ASD youth appears to predate and enable the experience of more abstract, anticipatory anxiety and worry. However, given that these abilities are typically delayed or deficient in ASD youth, abstract anxiety appears to occur later and to a lesser degree than that seen in typically developing youth.

Akin to monomorbid anxiety disorders, Davis, Hess, and colleagues' (2011) cross-sectional findings suggest that anxieties in ASD may wax and wane over the course of development, peaking in childhood, reducing in adulthood, and increasing again in later life. Further, the expression of anxiety vacillated with age. Whereas anxiety predicted greater behavioral problems in ASD toddlers, it was associated with greater inhibition in ASD children and adolescents, potentially reflecting the increased, if still impaired, social awareness and social withdrawal in older children. This pattern is consistent with the transition from oppositional "acting out" behavior (e.g., temper tantrums, somatic complaints, crying) to avoidant anxiety that corresponds with the development of emotion regulation abilities in typically developing youth (Albano, DiBartolo, Heimberg, & Barlow, 1995). Consistent with these results, Kuusikko et al. (2008) noted an increase in reported social anxiety, particularly fears of negative evaluation, with age in high-functioning ASD youth, but not typically developing controls, whose social and evaluative concerns lessened over time. These initial studies suggest that anxiety problems in ASD assume a similar, developmentally sensitive course to anxiety disorders in typically developing youth.

Treatment

Although comparing the treatment response of anxiety problems in ASD to that of typically developing youth cannot determine whether these symptoms reflect an equivalent psychopathology (e.g., aspirin may relieve headaches arising from a variety of unrelated causes, not an absence of aspirin in the system), such information provides an additional perspective. Treatment studies (Moree & Davis, 2010; Ooi et al., 2008; Reaven et al., 2009; White et al., 2009), including four randomized clinical trials (Chalfant, Rapee, & Carroll, 2007; Sofronoff, Attwood, & Hinton, 2005; Wood et al., 2009), suggest that anxiety in youth with ASD can be mitigated by CBT adapted to suit their cognitive and social needs. Although a case study by Davis, Kurtz, Gardner, and Carman (2007) found unmodified CBT successfully reduced specific phobias in a male with developmental disabilities, no larger studies have examined the effectiveness of unmodified CBT for ASD youth. Puleo and Kendall (2010) found that anxiety-disordered youth with elevated autism-related symptoms were more likely to respond to family CBT over individual child CBT, in part due to their reduced engagement and completion of at-home exposures in individual treatment. These findings

support the use of CBT and the adaptation of existing CBT programs (e.g., Kendall & Hedtke, 2006) to engage ASD youth (Davis et al., 2010; White et al., 2009; Wood et al., 2009). With flexibility for ASD, rates of positive treatment response at posttreatment and follow-up (50%) are close to the response rates to CBT in typically developing anxiety-disordered youth (e.g., Kendall et al., 2008; Silverman et al., 2008; Walkup et al., 2008).

The effectiveness of serotonin re-uptake inhibitors (SSRIs), a common medication for anxiety disorders in typically developing youth, for treating anxiety in ASD is unclear given the very small sample sizes of published studies ($N < 25$ in all studies; Buitelaar, Van der Gaag, & Van der Hoeven, 1998; Couturier & Nicolson, 2002; Namerow, Thomas, Bostic, Prince, & Monuteaux, 2003). The very preliminary results are consistent with published response rates for SSRIs in non-ASD youth (Walkup et al., 2008) treated with citalopram (Couturier & Nicolson, 2002; Namerow et al., 2003) and buspirone (Buitelaar et al., 1998).

Conclusion 2: Is There Evidence of Comorbid Anxiety Disorders in ASD?

Given the unclear relationship of anxiety and ASD symptoms (Distinction 1), interpretations regarding Distinction 2 should be considered preliminary. Nevertheless, comparisons of the distribution, severity, symptom presentation, developmental course, and treatment of anxiety problems and disorders in typically developing and ASD youth consistently support multiple models of anxiety in ASD. Resounding similarities across all points of comparison are consistent with the presence of comorbid anxiety disorders in ASD youth, particularly older youth with higher cognitive functioning. By contrast, the increased prevalence and unusual presentation of some forms of anxiety, particularly obsessive–compulsive behaviors that lack clear obsessional content or premonitory distress, specific phobias with unusual, uncommon foci, and social anxiety without a fear of social evaluation, support the presence of either atypical variants of anxiety disorders in ASD or anxiety-like symptoms of ASD. Determining the prevalence and role of such "typical" versus "atypical" manifestations of these symptoms will depend on the quality of measurement in future research.

DISTINCTION 3: IS ANXIETY A SEQUELA OF ASD, A COVARIANT, OR BOTH?

Empirical investigations regarding the development of anxiety in ASD are scant and considered preliminary given the still unclear classification of anxiety symptoms in ASD. It has been suggested that ASD may predispose to anxiety disorders, given that numerous risk factors for anxiety disorders are commonly associated with or entailed in an ASD diagnosis. However, the causal relationship between ASD and anxiety may be either more direct or artifactual. Social anxiety may be a consequence of repeated social rejection due to ASD social difficulties. Or, anxiety disorders and ASD may represent epiphenomenal comorbidities, associated with one another only via their mutual relationship to a third variable. Understanding the etiology of anxiety disorders in ASD may help elucidate their role as comorbidities, novel syndromes, or manifestations of the ASD diathesis.

Anxiety as a Sequela of ASD

Several research findings suggest that ASD may predispose, both directly and indirectly, to anxiety disorders. Anxiety disorders are significantly more common in ASD than in typically developing youth (White et al., 2009) as well as in children with specific language impairments (Gillott et al., 2001), conduct disorders (Green et al., 2000), learning disabilities (Burnette et al., 2005), and Down syndrome (Evans et al., 2005). The relationship between anxiety and ASD is less clear when examining ASD symptoms in youth with principal anxiety disorders. Elevated ASD symptoms have been reported by parents in approximately 13–62% of youth with principal anxiety or mood disorders, with variability attributable, in part, to the different measures of ASD symptomology employed (Pine, Guyer, Goldwin, Towbin, & Leibenluft, 2008; Towbin, Pradella, Gorrindo, Pine, & Leibenluft, 2005). Although these rates appear high and similar to the range of impairing anxiety symptoms reported by parents in ASD (White et al., 2009), comparable symptom levels have been reported in youth with a variety of non-ASD mental health diagnoses, ADHD, and mood disturbances (Pine et al., 2008; Reiersen, Constantino, Volk, & Todd, 2007; Towbin et al., 2005). Further, in a sample of youth (aged 8–18 years) with mood and anxiety

disorders, Towbin et al. (2005) suggested that elevated rates of ASD symptoms (62% of sample met cutoff criteria for a potential ASD according to several parent-report measures) across mood and anxiety diagnoses may reflect phenocopies, wherein the tail end of certain symptomologies resemble ASD symptoms due to their severity. The consequences of different severe psychopathologies may be similar and seemingly "autistic": intense psychological distress is often reflected by impoverished social relationships, pathological introversion, restricted interests and activities, and a flattening of affect. These findings are consistent with the notion that ASD may be a more specific and potent risk factor for anxiety problems than vice versa.

The fact that ASD pathology might contribute to anxiety disorder risk is partially supported by studies examining the relationship between ASD and anxiety severity. Successful treatment of anxiety disorders in high-functioning (IQ >70) ASD has improved participants' overall functioning and daily living skills, suggesting that the severity of ASDs may, in part, be aggravated by the presence of co-occurring anxiety (Drahota, Wood, Sze, & Van Dyke, 2011). Hyperactivity, social skill deficits, inappropriate speech, and perseverative behaviors appear heightened in ASD youth with greater anxiety (Bellini, 2004; Guttmann-Steinmetz et al., 2010; Sukhodolsky et al., 2008). The direction of this relationship is unclear, however, as such behaviors may be precursors, consequences, or manifestations of anxiety. In a longitudinal study of high-functioning (IQ >68) ASD youth, Kim et al. (2000) found no relationship between youths' severity of ASD symptoms at 4–6 years and parent-reported anxiety symptoms at 9–14 years. Although this finding may reflect the independence of anxiety and ASD, it may also attest to the complex relationship of these disorders. It is plausible that anxiety symptoms are predicted by ASD severity to a point, but become increasingly less common in youth who present with profound intellectual and verbal disabilities (Davis, Moree, et al., 2011).

Although preliminary, these findings support the notion that ASD may predispose to problematic anxiety. Anxiety symptoms appear more prevalent in ASD youth than other typically developing or developmentally delayed populations and may be more specifically related to ASD than vice versa. By contrast, elevated ASD symptoms appear equally apparent in various psychopathologies, including anxiety disorders. Although the relationship between ASD and anxiety severity is complex, there is some suggestion that heightened ASD symptoms may lead to greater anxiety when youth do not also present with profound intellectual or communication difficulties or both. These hypotheses warrant further clarification of the direct or indirect contributions ASD may pose to anxiety risk.

Theories of Direct Causation

Sensory over-responsivity (SOR) has been proposed as a potential cause of anxiety disorders in ASD youth (Ben-Sasson et al., 2008; Liss, Saulnier, Fein, & Kinsbourne, 2006; Pfeiffer, Kinnealey, Reed, & Herzberg, 2005). In this model, youth develop problematic fears due to an increased sensitivity to certain stimuli (e.g., sensitivity to sound linked to a specific phobia of loud noises). Examinations of this hypothesis have been muddied by poor methodological discrimination of anxiety and SOR. Both anxiety and SOR are commonly measured by increases in cortisol, overactivation of the amygdala, and behavioral observations of stress; thus, associations between these constructs may be methodological artifacts (Green & Ben-Sasson, 2010). In a study of typically developing adults, anxiety problems were associated with SOR as well as responsive to sensory-based treatments, suggesting that SOR may contribute to anxiety symptoms in some individuals (Pfeiffer & Kinnealey, 2003). Whether a similar pattern is evident in ASD, where SOR may be more pronounced (Ben-Sasson et al., 2008; Liss et al., 2006; Pfeiffer et al., 2005), has not been established.

It has been hypothesized that the social deficits evident in ASD may produce social anxiety (e.g., Bellini, 2004; White & Roberson-Nay, 2009). Repeated social failures can contribute to anxiety in social situations (Groden, Baron, & Groden, 2006; Portway & Johnson, 2005), and social deficits have been associated with increased anxiety in both typically developing and ASD youth (Bellini, 2004, 2006; Ginsburg et al., 1998; La Greca & Lopez, 1998). Youth with ASD may experience anxiety as a result of the spontaneous, socially complex nature of many interactions (Simpson & Myles, 1998; Volkmar & Klin, 2000), as well as their experience of repeated social failures (Attwood, 2006;

Groden et al., 2006; Morgan & Banerjee, 2006; Simpson & Myles, 1998; Volkmar & Klin, 2000). Notably, ASD youth with increased self-awareness, who recognize the social desirability of engagement and friendship, but lack the ability to establish these skills, may be particularly vulnerable to social fears and social anxiety (Bauminger, Shulman, & Agam, 2003).

Studies support the association of social impairment and anxiety in ASD. ASD youth demonstrate significantly more prevalent and more severe social worries than typically developing youth (Gillott et al., 2001; Kuusikko et al., 2008; Russell & Sofronoff, 2005), and adolescents with Asperger's syndrome report more automatic thoughts of social threat than youth with anxiety disorders, but not ASD (Farrugia & Hudson, 2006). Behavioral avoidance and fears of social evaluation have been shown to increase with age in ASD, potentially as children accrue more and more social failures and social issues become more developmentally salient (Kuusikko et al., 2008). Further, findings implicate self-awareness as a potential moderator of social anxiety in ASD. In a study of adolescents with ASD and average intellectual ability, Bellini (2004) noted that youth's perceptions of their social skills deficits predicted social anxiety, whereas parents' perceptions did not, suggesting that youth's understanding of their social deficits may be more influential and predictive of social anxiety than their actual social ability. Finally, although White and Roberson-Nay (2009) reported no association between social impairment and self-reported anxiety in ASD children and adolescents (aged 7–14 years; *M* IQ = 99), those with more social anxiety reported more loneliness, consistent with a higher level of social and self-awareness in these youth.

The relationship of social anxiety and ASD-related social deficits may be bidirectional. Social anxiety may be both a product of and contributor to social awkwardness and avoidance in ASD youth. Heightened social anxiety has been associated with reduced social initiation and more avoidance in lonely ASD youth (White & Roberson-Nay, 2009). Further, such social anxiety and withdrawal may aggravate youth's social deficits over time as they miss key opportunities to acquire and hone effective interpersonal skills and become increasingly swayed by the reinforcing properties of avoidance (Rubin & Burgess, 2001).

The existence of true social phobia in ASD, a disorder defined by a fear of social evaluation, has been questioned (Koning & Magill-Evans, 2001). Certain symptoms of ASD (e.g., theory-of-mind deficits, impaired perception of social skill, limited personal insight; Koning & Magill-Evans, 2001) appear antithetical to such prominent interpersonal concerns. ASD youth may not recognize or regret their social difficulties, and a reduced rate of social concerns is apparent in studies of social anxiety in ASD, particularly according to child reports (Gillott et al., 2001; Russell & Sofronoff, 2005). Whereas parents of ASD youth consistently attribute interpersonal concerns to their children, self-reports of anxiety symptoms are sporadic (Lopata et al., 2010). Despite these challenges, cumulative findings support the existence of social anxiety, emerging, in part, from a combination of social ineptitude and social awareness in a subset of ASD youth. Research is needed to confirm the presence of comorbid social phobia in ASD suggested, but not determined, by these findings.

Theories of Indirect Causation

It is plausible that characteristics and associated features of ASD indirectly heighten anxiety disorder risk. Several hypotheses have been proffered, but few directly tested. Kanner (1943) hypothesized that symptoms of restricted, rigid behavior in ASD may be anxiety driven, and several studies have reported associations between these constructs (Guttmann-Steinmetz et al., 2010; Sukhodolsky et al., 2008). Restricted cognitive abilities and behaviors may reflect inherent difficulties understanding and accurately predicting events in the surrounding environment that foster uncertainty and anxiety (Schopler & Mesibov, 1994). Similarly, it has been suggested that weak central coherence, a failure to integrate local details into global understanding (Frith & Happé, 1994), may lead ASD youth to experience everyday events as chaotic, stressful, and consequently anxiety provoking (Muris et al., 1998); however, a test of this hypothesis (Burnette et al., 2005) found no such relationship.

Increased stressors experienced more generally by ASD youth may heighten their anxiety risk. Gillott and Standen (2007) reported that stress and anxiety levels were highly correlated in ASD adults and that stress

resulted in three times the anxiety for ASD adults than an age-, gender-, and IQ-matched sample of intellectually disabled youth. Although this study requires replication, it suggests that ASD youth may be particularly vulnerable to the stressors associated with their disabilities. Given the numerous hardships experienced by ASD youth and their families, increased parental involvement is expected and may unintentionally contribute to the maintenance of anxiety in ASD youth, as has been suggested for typically developing youth with anxiety disorders (McLeod et al., 2007). Consistent with this hypothesis, Drahota et al. (2011) found that reductions in parental involvement were associated with both improved anxiety symptoms and daily living skills in high-functioning (IQ >70) ASD children with anxiety disorders who were treated with CBT. Additional research is needed to confirm these notions.

Autism spectrum disorders may increase vulnerability to anxiety problems due to overarching difficulties regulating emotion and arousal. It has been hypothesized that ASD individuals struggle to regulate and cope with anxiety due to inherent difficulties understanding and identifying emotion (Capps, Yirmiya, & Sigman, 1992). Limbic system dysfunction and behavioral inhibition have been implicated in both ASD and anxiety disorders (Bellini, 2006). Behavioral inhibition may be related to lower threshold arousal levels in the amygdala, leaving inhibited youth more prone to react and thus also be conditioned by negative experiences. A combination of physiological arousal and social skills deficits may predict more social anxiety in ASD youth, potentially because youth with higher base levels of arousal are both more likely to avoid and be conditioned by potentially risky or negative experiences (Bellini, 2006). The possibility that early dysregulation in emotional and arousal networks in ASD may predispose to anxiety disorders in ASD is supported by Kim and colleagues' (2000) longitudinal finding that childhood discrepancies in verbal and nonverbal IQ (a potential proxy for right hemispheric dysfunction) predicted more anxiety and mood problems in high-functioning (IQ >68) ASD youth entering adolescence. In sum, there are a variety of hypothesized pathways whereby ASD deficits may indirectly contribute to comorbid anxiety disorders, all of which require study.

Anxiety as a Covariant

It is possible that anxiety and ASD co-occur without causal relationship to one another, representing parallel, but independent reactions to a shared risk factor. There is limited empirical support for this hypothesis, but several theories have been proffered. If parallel as opposed to causally related syndromes, anxiety symptoms should present at relatively equal rates in ASD as ASD symptoms do in anxiety disorders. Studies of referred youth provide some support: the range of ASD symptoms in youth with anxiety and internalizing disorders is similar to that of anxiety symptoms in ASD youth, but not as specific (Pine et al., 2008; Puleo & Kendall, 2010; Towbin et al., 2005).

It is plausible that the co-occurrence of anxiety and ASD in individuals results from the familial comorbidity of both disorders (Angold et al., 1999). Higher rates of internalizing disorders noted in parents and relatives of ASD youth with co-occurring internalizing problems (Mazefsky, Folstein, & Lainhart, 2008; Mazefsky et al., 2010) may reflect a genetic loading or environmental predisposition (e.g., chaotic family life). Children with anxiety disorders have been found to have parents with predominantly anxiety disorders, whereas those with mixed anxious and depressed parents are also prone to a wider range of childhood disorders (Angold et al., 1999; Beidel & Turner, 1997). A similar process may apply to ASD youth. Structural and neurochemical brain disturbances, such as atypical amygdala volumes and 5HT neurotransmission, may predispose to both anxiety and ASD (Amaral, Bauman, & Mills Schumann, 2003; Apter & Allen, 1999; Chugani et al., 1999; Sukhodolsky et al., 2008). However, whether these neurological variations precede or result from these disorders is unclear. Alternatively, given that many ASD youth present with multiple co-occurring disorders (de Bruin et al., 2007; Simonoff et al., 2008), it is possible that anxiety disorders may be epiphenomenal comorbidities, arising from other comorbid disorders in ASD, such as depression, rather than ASD itself (Angold et al., 1999). Although anxiety disorders and problems are often associated with additional co-occurring mood and conduct disorders in ASD youth (de Bruin et al., 2007; Kim et al., 2000), this explanation of anxiety in ASD is unlikely to be sufficient, given that anxiety disorders also appear independently of

additional comorbidities in ASD (Mattila et al., 2010; Simonoff et al., 2008).

Conclusion 3: How Does Anxiety Arise in ASD?

Numerous explanations of the etiology of anxiety in ASD have been hypothesized, including theories of direct and indirect causation and covariation. At present, the etiology of anxiety in ASD is unknown and difficult to study given ongoing confusion about the differentiation and relationship of these disorders. There is initial support for the notion that ASD deficits contribute, at least partially, to the development of anxiety disorders. Some studies suggest that sensory and social abnormalities as well as stressful experiences may contribute to anxiety in ASD, but much research is needed. Given notable heterogeneity in the expression and prevalence of anxiety in ASDs, it is plausible that both causal and covariation models may also be applicable.

GENERAL CONCLUSION

A critical review of the literature provides some support for the presence of both (a) co-occurring anxiety disorders in individuals with ASD and (b) atypical anxiety symptoms whose role cannot presently be determined. A definitive answer regarding the co-occurrence of anxiety and ASD (Distinction 1) remains elusive due to limitations in both the methodologies of extant research and categorical diagnostic approaches, more generally. Similarly, this lack of consensus regarding the role of anxiety in ASD and the lack of validated diagnostic instruments have limited what conclusions can be drawn regarding the phenomenology (Distinction 2), etiology (Distinction 3), and, thus, also the "true comorbidity" of these disorders. Reviews of the findings and their limitations suggest both (a) that a single model (e.g., comorbidity or core feature) may not be sufficient to characterize the relationship of these disorders and (b) that a coordinated methodology is needed to understand the interplay of these disorders as well as the "plethora of comorbidity" that complicates current categorical diagnostic systems (Regier et al., 2009). The many complications inherent to differentiating and classifying anxiety and ASDs detailed in this review provide rationale for the identification of dimensions of behavior and neurobiological functioning (e.g., executive functioning, social processing systems) that may underlie disorders and may supplement traditional classification systems (Regier et al., 2009).

Distinction 1: Acknowledging these limitations, reviews of the prevalence, risk factors, and moderators of anxiety in ASD provide some support for the presence of co-occurring, potentially comorbid anxiety disorders in a portion of ASD youth. These co-occurring anxiety symptoms appear distinct from a variety of anxiety-like behaviors in ASD, such as compulsions, unusual specific phobias, and social avoidance, whose role remains undetermined. Such symptoms may either be closely related to the ASD diathesis or reflect anxiety altered in presentation by its co-occurrence with ASD.

Distinctions 2 and 3: Given the inability to conclusively rule on Distinction 1, conclusions regarding Distinctions 2 and 3 are preliminary and subject to the same methodological limitations. Regarding Distinction 2, phenomenological studies of anxiety in ASD youth offer evidence of both potentially comorbid anxiety disorder and distinct, "atypical anxiety" symptoms in youth with ASD. Whether these anomalies represent a variant of anxiety in ASD or core features of ASD that resemble anxiety requires further clarification. Regarding Distinction 3, little is known regarding the etiology of anxiety in ASD; though, some similarities (i.e., shared genetic and environmental risk factors, trajectories, developmental trends) to anxiety disorders in typically developing youth have been noted. Research is needed to determine whether anxiety results directly or indirectly from ASD symptomology, accompanies it, or arises via some combination of both causative and correlational models.

FUTURE DIRECTIONS AND CLINICAL IMPLICATIONS

Insufficient and inconsistent differential diagnosis of anxiety and ASD has contributed to discrepant reports regarding the prevalence and presentation of anxiety in ASD, prolonging confusion regarding the appropriate classification of these symptoms. The problem appears self-perpetuating: discrepant diagnostic standards and reliance on limited measures have restricted conclusions

that can be drawn. Diagnostic confusion is not unique to anxiety and ASD, but rather appears to be a chronic issue within current nosology, where "Not Otherwise Specified" diagnoses are utilized to classify the many individuals whose symptoms do not fit existing criteria (Regier et al., 2009). Further, an overreliance on subjective anxiety measures is a frequently cited limitation in anxiety disorder research (Davis, May, & Whiting, 2011; Davis & Ollendick, 2005).

It appears that different types of studies and a shift toward a diagnostic continuum approach are needed to address questions raised by this review. Although studies provide support for co-occurring anxiety symptoms in ASD (Distinction 1), they also suggest the presence of more "atypical anxiety" symptoms. Moreover, whether reported anxiety symptoms reflect true comorbidities phenomenologically (Distinction 2) and etiologically (Distinction 3) akin to monomorbid anxiety disorders remains unclear.

Consensus regarding how to diagnose anxiety disorders in ASD is needed. To this end, anxiety measures used with typically developing youth must be studied psychometrically in samples of ASD youth. Further, such a consensus could be informed by biologically based measurements (e.g., electrophysiological or neurobiological indicators) of anxiety. Alternative assessments are warranted given the inherent challenge of recognizing and reporting emotional states for individuals with ASD. Empirically based assessment of both "typical" anxiety symptoms and the "atypical," potentially ASD-specific anxiety symptoms discussed herein will help determine whether such atypical symptoms should be conceptualized as aspects of ASD, anxiety, or a unique behavioral dimension common to both disorders.

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