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Age-related differences in the prevalence and correlates of anxiety in youth with autism spectrum disorders

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ABSTRACT

Age-related differences in the prevalence and correlates of anxiety were cross-sectionally examined in 1316 children and adolescents with autism spectrum disorder (ASD) who presented for initial evaluation at 14 outpatient autism centers around the country and in Canada. The prevalence of clinical and subclinical anxiety as well as the correlates of anxiety were examined in three age groups of children: preschool, school age and adolescents. Findings showed that the prevalence of anxiety in each age group exceeded the prevalence of anxiety in the general population. Adolescents and school age children had the highest prevalence of clinical (40%) and subclinical anxiety (26%), respectively. Higher IQ and less ASD severity were each weakly correlated with more anxiety in preschool and school age children. Affective symptoms were strongly associated with anxiety in each age group. Age specific psychiatric comorbidities were also present. Anxiety was associated with attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD) symptoms in the preschool group, ODD and somatic symptoms in the school age children, and ADHD symptoms in adolescents. These data underscore the need for prevention and treatment of anxiety as well as research examining the characteristics of anxiety in children with ASD using a developmental framework.

1. Introduction

Anxiety symptoms and disorders frequently co-occur in children with autism spectrum disorder (ASD) (e.g., de Bruin, Ferdinand, Meester, de Nijs, & Verheij, 2007; Simonoff et al., 2008; Sukhodolsky et al., 2008). The presence of comorbid anxiety can aggravate core symptoms of ASD (Sukhodolsky et al., 2008), impair daily living skills (Drahota, Wood, Sze, & van

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Dyke, 2011), and negatively impact relationships with peers, teachers, and family (Kim, Szatmari, Bryson, Streiner, & Wilson, 2000). With autism prevalence estimates rising to epidemic proportions (United States Centers for Disease Control and Prevention, 2007), research on anxiety in ASD is of paramount importance.

A review of existing studies indicates that the prevalence of anxiety symptoms or disorders in children and adolescents with ASD varies widely and ranges from 11% to 84% (White, Oswald, Ollendick, & Scahill, 2009) with a meta-analysis of data showing that about 40% of children and adolescents have at least one anxiety disorder (van Steensel, Bogels, & Perrin, 2011). Most of these studies examine the prevalence of different types of anxiety disorders including generalized anxiety disorder, separation anxiety disorder, specific phobia, social phobia, and obsessive–compulsive disorder. Some studies report a higher prevalence of clinical anxiety in children with ASD compared to the prevalence of clinical anxiety in typically developing (TD) children (Russell & Sofronoff, 2005) and children with other clinical conditions such as conduct disorder (Green, Gilchrist, Burton, & Cox, 2000), language impairment (Gillott, Furniss, & Walter, 2001), Down syndrome (Evans, Canavera, Kleinpeter, Maccubbin, & Taga, 2005), and Williams syndrome (Rodgers, Riby, Janes, Connolly, & McConachie, 2012b). The wide-ranging prevalence of anxiety in children with ASD is likely due to method variance with respect to assessment instrument (interview versus self-report scale), informant (parent versus child), type of anxiety measured (e.g., social anxiety: Bellini, 2006; social, generalized and separation anxiety: Kim et al., 2000; obsessive–compulsive disorder: Reaven & Hepburn, 2003; all anxiety disorders: Leyfer et al., 2006; Simonoff et al., 2008), and anxiety classification (symptoms versus disorders). Furthermore, most of the studies were conducted in small samples (<100 subjects) and few studies report on anxiety in preschool (Gadow, deVincent, Pomeroy, & Azizian, 2004; Hayashida, Anderson, Paparella, Freeman, & Forness, 2010; Weisbrot, Gadow, deVincent, & Pomeroy, 2005) or lower functioning (Bradley, Ames, & Bolton, 2011; Bradley, Summers, Wood, & Bryson, 2004) children with ASD.

Few studies have examined rates of subclinical anxiety symptoms in children with ASD. Niditch, Varela, Kamps, and Hill (2012) reported that about 20% of toddler/preschool children (<6 years) and 9% of early elementary school children (6–9 years) with ASD had subclinical levels of anxiety. Strang et al. (2012) found that 21% of children with ASD exhibited subclinical anxiety, but this was across a broad age group of children (6–18 years). Subclinical or subthreshold symptoms reflect a potentially evolving anxiety disorder or a previous anxiety disorder that has partially remitted. Thus, data on both clinical and subclinical anxiety provide a more comprehensive picture of the course of anxiety in children with ASD. Identifying subclinical anxiety is also critical for prevention and treatment. For instance, Ginsburg (2009) found that high risk TD youth, as defined by those with a parental history of anxiety disorder, who received cognitive-behavioral therapy (CBT) had a significantly lower risk of developing anxiety disorders after one year compared to children assigned to a wait list control condition.

Most of the anxiety studies in the ASD population are cross-sectional, report on prevalence in a distinct age group (e.g., adolescents: Bellini, 2004; Bradley et al., 2004; Kim et al., 2000) or calculate a single prevalence across a wide age range of children (e.g., Leyfer et al., 2006: 5–17 years; Muris, Steerneman, Merckelbach, Holdrinet, & Meesters, 1998: 2–18 years). These data set the stage for future research on developmental differences in anxiety since interactions between children and their environment can result in distinct patterns of disease (i.e., with respect to prevalence, phenotype, and risk factors) across different age groups (Rutter, 1988). These patterns can be seen in TD children who exhibit developmental risk periods for anxiety disorders. For example, separation anxiety disorder and specific phobias frequently emerge before adolescence (Becker et al., 2007; Kessler et al., 2005; Wittchen, Kessler, Pfister, & Lieb, 2000) whereas social phobia typically occurs in late childhood and adolescence (Beesdo et al., 2007; Kessler et al., 2005; Wittchen & Fehm, 2003).

The degree to which age influences the level of anxiety in children with ASD remains unknown. Davis et al. (2011) showed that anxiety increased from toddlerhood to childhood, decreased through young adulthood, and then recurred from young adulthood to older age. Multiple hypotheses were posited to explain these trends including the lack of inhibitory control in toddlers and the use of both adaptive and maladaptive strategies to regulate anxiety in childhood. Strang et al. (2012) conducted a case-control study examining the effect of age (6–11 and 12–18 years) and IQ on emotional symptoms in youth with high functioning autism (HFA). Results showed that levels of anxiety were unaffected by age, IQ, ASD severity, or their interaction. Finally, Niditch et al. (2012) reported that levels of clinical anxiety remained the same from preschool to the early elementary school years among children with ASD. In light of these mixed findings, further research on the relationship between age and anxiety is warranted.

Beyond age, the two other correlates of anxiety in ASD that have been most frequently examined are IQ and ASD severity, neither of which shows any consistent findings. There has been considerable enthusiasm for the hypothesis that children with ASD and higher cognitive functioning may be at greater risk for anxiety because they are more aware of their differences. Empirical support for this hypothesis however has been mixed with some data supporting this relationship (e.g., Estes, Dawson, Sterling, & Munson, 2007; Mazurek & Kanne, 2010; Sukhodolsky et al., 2008) but other data showing no effect (Simonoff et al., 2008; Strang et al., 2012). One study found that the relationship between IQ and anxiety in preschool and early elementary school children with ASD is mediated by the level of aggression or social understanding (Niditch et al., 2012). In terms of ASD symptoms, some data report an inverse relationship between anxiety and a global measure of ASD severity (Mazurek & Kanne, 2010) whereas other data show that anxiety is positively correlated specifically with high levels of repetitive behavior (Rodgers, Glod, Connolly, & McConachie, 2012a; Spiker, Lin, van Dyke, & Wood, 2012; Sukhodolsky et al., 2008). One study found no correlation between the presence of early autistic symptoms and later emotional disorders (Kim et al., 2000).

Few studies have examined whether anxiety co-occurs with other psychiatric symptoms in children with ASD. For example, in TD children, extensive research shows that anxiety disorders are highly comorbid with depression and that depression sequentially follows anxiety in its onset (e.g., Brady & Kendall, 1992; Orvaschel, Lewinsohn, & Seeley, 1995; Seligman & Ollendick, 1998). Investigating comorbidity patterns in children with ASD has implications for delineating psychiatric subtypes that can inform research on pathophysiology and treatment (Gadow, Guttmann-Steinmetz, Rieffe, & deVincent, 2011). Preliminary evidence suggests that anxiety may be comorbid with externalizing disorders among children with ASD (de Bruin et al., 2007; Evans et al., 2005; Kim et al., 2000; Sukhodolsky et al., 2008); however, more research is needed on this topic.

In summary, the literature shows that anxiety research in the pediatric ASD population has increased during the past decade, and that the levels of anxiety may be higher in children with ASD compared to other clinical groups. However, few if any of these studies have incorporated a developmental framework to examine similarities and differences in anxiety characteristics across development. This approach is critical given the dynamic shifts in cognitive, socio-emotional, and neurobiological development that occur from birth to adulthood (Beesdo, Knappe, & Pine, 2009). Hence, the goal of this study is to use a cross-sectional design to explore the prevalence and correlates of anxiety in three age specific groups of children: preschool (under 6 years), school age (6–11 years), and adolescents (12–17 years). Three types of anxiety are examined: separation anxiety, generalized anxiety, and specific phobia, each of which has little overlap with core ASD symptoms. Findings from this study can inform initial hypotheses about age-related differences in anxiety that can be tested using a longitudinal study design. The study goals are exploratory and are as follows:

1. To compare the mean level of clinical anxiety in each age group with the prevalence of anxiety in the general population.
2. To compare anxiety (mean level, percentage of children with clinical anxiety, percentage of children with subclinical anxiety) across the three age groups.
3. To examine the relationship between anxiety and IQ as well as ASD severity within each age group.
4. To explore whether distinct psychiatric comorbidities are associated with anxiety in each age group.

2. Methods and measures

2.1. Participants and procedures

This is a cross sectional study of 1316 children and adolescents who were recruited through the Autism Treatment Network (ATN), a multi-site consortium funded by Autism Speaks. The ATN is a clinical and research program comprised of 14 outpatient autism centers in the United States and Canada (see Table 1 for recruitment data). Study data were collected from 2008 to 2010.The Institutional Review Board at each site approved the study.

Subjects included children, ages 2 years 0 months–17 years 6 months, with a confirmed diagnosis of ASD (i.e., Autistic Disorder, Asperger Disorder, or Pervasive Developmental Disorder Not Otherwise Specified) that was established by physician using DSM IV criteria (American Psychiatric Association, 2000). Physician assessment incorporated data from a multidisciplinary team evaluation that included review of developmental history, clinical interview with parents/caregivers, direct observation, and data from the psychological evaluation. Physician types included pediatricians, neurologists, and child psychiatrists. To enroll, the primary caregiver must have been able to communicate in English, the child could not be placed in foster care, and the child could not be blind or deaf. Parents completed forms regarding their child's medical, developmental, and behavioral history.

Data on 2716 children with an ASD diagnosis were available for the study, of which 2256 ($n = 460$ excluded) had available anxiety data. Of this group, 664 children were excluded due to missing medical and developmental data and 276 children

Table 1
Number of subjects from each site ($N = 1316$).

Site	*N* (%)
Oregon Health and Sciences University	77 (5.9%)
Massachusetts General Hospital	121 (9.2%)
Baylor College of Medicine	87 (6.6%)
Columbia University	95 (7.2%)
University of Missouri–Columbia	164 (12.5%)
Vanderbilt University	89 (6.8%)
Arkansas University	51 (3.9%)
University of Colorado	83 (6.3%)
University of Pittsburgh Medical Center	95 (7.2%)
Cincinnati University	106 (8.1%)
Kennedy Krieger Institute	74 (5.7%)
Kaiser Permanente	75 (5.7%)
University of Rochester	73 (5.6%)
Hospital for Sick Children (Toronto)	126 (9.6%)

were excluded due to genetic or neurological disorders. These two conditions are associated with a higher prevalence of anxiety than in the general population (genetic: Cordeiro, Ballinger, Hagerman, & Hessl, 2011; neurologic: Russ, Larson, & Halfon, 2012; Vasa et al., 2002). The final sample size therefore consisted of 1316 children who were divided into three age groups: preschool (<6 years, $n = 716$), school age (6–11 years, $n = 450$), and adolescents (12–17 years, $n = 150$). Sample sizes were smaller for select analyses due to missing data as indicated below.

2.2. Measures

2.2.1. Autism diagnostic observation schedule (ADOS)

Trained clinicians administered the ADOS, a standardized semi-structured interview with strong psychometric properties including inter-rater reliability (ADOS; Lord, Rutter, diLavore, & Risi). One of four modules, each with different types and numbers of activities, was administered to subjects based on their age and language level. The number of children who received each module was as follows: Module 1 ($n = 515$, Pre-Verbal/Single Words), Module 2 ($n = 317$; Phrase Speech-Non-fluent), Module 3 ($n = 399$, Fluent Speech-Child/Adolescent) and Module 4 ($n = 32$, Fluent Speech-Adolescent/Adult). A specific diagnostic algorithm was used to score each module and yielded cutoff values for classification of Autistic Disorder and ASD. At least 90% of the children enrolled at each site met ADOS criteria for an ASD. ADOS data were available on 93.5% of children (preschool: $n = 681$; school age: $n = 434$; adolescence: $n = 116$).

A standardized measure of ASD severity was calculated using an algorithm that adjusts for differences across ADOS modules 1–3 (Gotham, Risi, Pickles, & Lord, 2007). The algorithm yields three scores: social affect (i.e., sum of items from the social and communication domains, range 0–20), repetitive behaviors (range 0–8), and a total score that is the sum of the symptom scores (range 0–28). To note, the calibrated severity score, which was developed based on the revised algorithm, was not used since social/communication and repetitive behaviors cannot be assessed separately given that the algorithm only yields a total standardized score (Gotham, Pickles, & Lord, 2009).

2.2.2. Intelligence tests

For the majority of children, general intellectual functioning was measured using the Stanford–Binet Intelligence Scales of Intelligence Fifth Edition (SB5), Abbreviated Battery IQ (ABIQ; Roid, 2003, $n = 773$). The SB5 is a valid and reliable measurement of IQ in the general population (Roid, 2003), and the ABIQ largely reflects the full scale IQ score for children with ASD (Coolican, Bryson, & Zwaigenbaum, 2008). The remaining participants received the Mullen Scales of Early Learning: AGS Edition (MSEL: Mullen, 1997, $n = 245$) if the SB5 routing subtests were not expected to yield a valid score (e.g., inability to achieve a basal due to limited expressive/receptive language, significant behavioral interference, and cognitive level). For those children receiving the MSEL, the Early Learning Composite Standard Score was used as a measure of full scale IQ.

Some children did not undergo IQ testing due to insurance reimbursement challenges, having a recent cognitive evaluation, or behavioral challenges that interfered with testing. IQ data were therefore available for approximately 77% of the sample ($n = 557$ for preschool group, $n = 346$ for school age group, and $n = 115$ for adolescents).

2.2.3. Child behavior checklist (CBCL)

The CBCL is a widely used parent-report measure of child psychopathology with strong psychometric properties in TD children (e.g., Ebesutani et al., 2010; Ivanova et al., 2007; Kendall et al., 2007; Nakamura, Ebesutani, Bernstein, & Chorpita, 2009). The scale has two versions, one for children ages 1.5–5 years (Achenbach & Rescorla, 2000) and the other for 6–18 year olds (Achenbach & Rescorla, 2001). The CBCL has been increasingly used to assess psychopathology, including anxiety, in children with ASD (Kanne, Abbacchi, & Constantino, 2009; Pandolfi, Magyar, & Dill, 2009; Pandolfi, Magyar, & Dill, 2012; Strang et al., 2012). The CBCL yields five DSM-Oriented scales, seven narrow band subscales, and three broadband scales.

The CBCL DSM-Oriented Anxiety Problems scale was the primary anxiety metric. This scale assesses symptoms of generalized anxiety disorder, separation anxiety disorder, and specific phobia. The Anxiety Problems scale was chosen over the CBCL anxiety/depressed subscale because it only includes items that are specific to anxiety. The Anxiety Problems scale also has the advantage of not including symptoms of social phobia and obsessive–compulsive disorder, two disorders that include symptoms that overlap with core ASD symptoms. For prevalence calculations, raw scores were converted to standardized T scores ($M = 50$, SD = 10); T scores between 65 and 69 are indicative of subclinical ('at risk') anxiety, and T scores of 70 and above represent clinical anxiety. Group differences in the mean CBCL Anxiety Problems scale T scores as well as the percentage of children who met subclinical or clinical cutoffs for anxiety were examined.

The other CBCL DSM-Oriented scales were used to assess psychiatric comorbidities that may be associated with anxiety. For the under 6 years group, these scales included Affective Problems (includes depression and dysthymia only), Attention-Deficit/Hyperactive Problems (ADHD), Oppositional Defiant Problems (ODD), and Pervasive Developmental Problems (PDD). The PDD Problem scale data were not analyzed because ASD symptoms were assessed via clinician interview and the ADOS. For the older two groups, the DSM problem scales included Affective, Somatic, ADHD, ODD, and Conduct Problems. The clinical cutoffs for these DSM-Oriented scales are similar to the Anxiety Problems scale. For each age group, the CBCL yields three broadband scales: Internalizing, Externalizing, and Total Problem scale scores. The clinical cutoff for the broadband scales was a T score > 63.

2.3. Data analysis

The first step in the analysis was to perform ANOVA and chi-square analyses to compare overall differences between groups on the following variables of interest: demographic characteristics, IQ, ASD severity, mean CBCL *T* scores, the percentage of subjects with clinical and subclinical levels of anxiety, and the percentage of subjects with clinical psychopathology for all other CBCL scales. ADOS Module was not compared across age groups since module selection is based in part on age. If any differences existed among the age groups, between group contrasts were performed using linear and logistic regression analyses. Furthermore, effect sizes (Cohen's *d*: Cohen, 1998) were calculated based on the pooled standard deviation for continuous variables, while Odds Ratios (OR) served as effect sizes for dichotomous variables. One-sample *t*-tests were used to compare levels of anxiety in each age group to the general population. Pearson's correlations were performed to examine whether anxiety relates to ASD symptoms as well as IQ in each age group. For all of the above analyses, a Bonferroni correction was applied in order to reduce the likelihood of a Type I error. For these analyses, each independent variable was considered a separate hypothesis. With a total of 18 independent variables, significance was therefore present at $p < .003$ (.05/18 which was rounded up to four decimals from 0.00277) for both the bivariate and multivariate analyses (see below for details).

Lastly, given the exploratory nature of this study, multivariate linear regression analyses with backward elimination were performed for each age group to examine whether demographic variables (age, gender, race, level of parental education, public insurance), language level (ADOS module), and psychiatric comorbidities (CBCL DSM-Oriented scales) were associated with anxiety. As suggested by Achenbach and Rescorla (2001), raw CBCL scores were used in the regressions to account for the full range of variation in scores. To maximize sample size, IQ and ASD severity were entered into the models only if either significantly correlated with anxiety at $p < .003$ and only those variables significant at $p < .003$ remained in the final model. Regression diagnostics ensured that all assumptions were met and variance inflation factor (VIF) scores indicated minimal collinearity (VIF < 1.5). Analyses were performed using STATA (Version 12; College Station, TX).

3. Results

3.1. Comparing demographic and clinical characteristics among the age groups

Table 2 compares demographic and clinical characteristics (except for anxiety, see Section 3.2) across the age groups. Overall age group differences were found for ASD severity (social affect, repetitive behavior, and total score), IQ, and two psychopathology scales (all $p < .001$); no differences were present for demographic characteristics.

In terms of specific between group differences, school age children had a significantly higher mean IQ than preschool children ($\beta = 7.18$, 95% CI [4.03, 10.33], $d = .31$, $p < .001$). The school age group also had lower social affect ($\beta = -1.19$, 95% CI [−1.74, −.63], $d = .26$, $p < .001$), repetitive behavior ($\beta = -.52$, 95% CI [−.76, .28], $d = .26$, $p < .001$), and overall ASD severity ($\beta = -1.71$, 95% CI [−2.36, −1.05], $d = .31$, $p < .001$) scores compared to the preschool group. The school age group also had lower social affect scores ($\beta = -1.46$, 95% CI [−2.41, −.52], $d = .34$, $p < .01$) compared to the adolescent group.

In terms of psychopathology, both school age ($\beta = 6.14$, 95% CI [5.02, 7.26], $d = .63$, $p < .001$) and adolescent ($\beta = 3.70$, 95% CI [2.03, 5.37], $d = .41$, $p < .001$) groups exhibited higher mean *T* scores on the ADHD Problems scale compared to the preschool group. Additionally, a higher percentage of school age children met clinical criteria on the Conduct Problems scale compared to the adolescent group (OR = 3.51, 95% CI [1.57, 7.83], $p = .002$).

3.2. Comparing the mean level of anxiety in ASD for each age group with the mean level of anxiety in the general population

One sample *t*-tests were performed to compare the mean Anxiety Problems *T* score for each age group to the normative score of 50 (SD = 10). Results showed that the mean Anxiety Problems *T* score was significantly greater than the normative score in each group: preschool ($M = 58.8$, $SD = 10.1$; $t = 23.16$; $d = 0.87$), school age ($M = 62.5$, $SD = 8.3$; $t = 31.80$; $d = 1.36$), and adolescent ($M = 64.2$, $SD = 8.8$, $t = 19.87$; $d = 1.51$).

3.3. Comparing anxiety across the age groups

The mean CBCL Anxiety Problems scale *T* scores significantly differed across the three groups ($F = 33.81$, $p < .001$). The adolescent group had significantly higher mean *T* scores compared to the preschool group ($\beta = 5.47$, 95% CI [3.82, 7.13], $p < .001$, $d = 0.27$). The school age group also had significantly higher mean *T* scores than the preschool group ($\beta = 3.71$, 95% CI [2.60, 4.82], $p < .001$; $d = .20$). There were no significant differences in the mean anxiety *T* scores between the school age and adolescent groups ($p = .05$).

Significant age group differences in the percentage of children with clinical anxiety emerged ($\chi^2 = 34.77$; $p < .001$) as shown in Fig. 1. Adolescent youth were more likely to meet criteria for clinical anxiety compared to school age (41% versus 26%; OR = 1.90, 95% CI [1.29, 2.81], $p < .001$) and preschool (41% versus 19%; OR = 2.95; 95% CI [2.02, 4.29]; $p < .001$) children, and school age children were more likely to meet criteria for clinical anxiety compared to preschool children (26% versus 19%; OR = 1.55, 95% CI [1.17, 2.05], $p = 002$).

Significant age group differences in the percentage of children with subclinical anxiety emerged ($\chi^2 = 90.30$; $p < .001$) as presented in Fig. 1. There was a significantly higher percentage of school age children (26% versus 6%; OR = 5.37, 95% CI [3.69,

Table 2
Demographic and clinical characteristics ($N = 1316$).

	Preschool ($N = 716$)	School age ($N = 450$)	Adolescence ($N = 150$)	F or χ^2; p-value
Mean age (SD)	3.5 (1.2)	7.8 (1.7)	13.9 (1.6)	
# Male (%)	592 (83)	381 (85)	127 (85)	$\chi^2 = .94$; $p = .63$
# Caucasian (%)	550 (77)	357 (79)	125 (83)	$\chi^2 = 3.45$; $p = .18$
# Parents with education (%)				$\chi^2 = 10.0$; $p = .13$
Some high school or high school graduate	141 (20)	77 (17)	27 (18)	
Some college	192 (27)	152 (34)	48 (32)	
Bachelor's degree	205 (29)	110 (24)	47 (31)	
Postgraduate	140 (20)	93 (21)	23 (15)	
Not reported	38 (4)	18 (4)	5 (3)	
# Public insurance (%)	237 (33)	131 (29)	48 (32)	$\chi^2 = 2.04$; $p = .36$
Mean IQ (SD)	73.6 (23.4)	80.8 (23.4)[a]	76.8 (23.7)	$F = 10.04$; $p < .001$
ADOS module				
1	421 (62)	74 (17)	20 (13)	
2	203 (30)	93 (21)	21 (14)	
3 or 4	57 (8)	268 (62)	106 (72)	
ASD severity*				
Social affect	12.6 (4.6)	11.4 (4.7)[a,c]	12.9 (4.0)	$F = 10.12$; $p < .001$
Repetitive behaviors	3.8 (1.9)	3.3 (2.0)[a]	3.5 (2.2)	$F = 9.24$; $p < .001$
Total ASD severity score	16.4 (5.3)	14.7 (5.6)[a]	16.4 (5.4)	$F = 13.78$; $p < .001$
Affective problems				
Mean T score (SD)	62.2 (9.6)	63.2 (8.7)	63.4 (8.8)	$F = 2.24$; $p = .11$
% Clinical	30%	29%	27%	$\chi^2 = .48$; $p = .79$
ADHD problems				
Mean T score (SD)	63.3 (8.9)	69.4 (10.4)[a]	67.0 (9.1)[b]	$F = 59.44$; $p < .001$
% Clinical	35%	40%	26%	$\chi^2 = 10.8$; $p = .004$
ODD problems				
Mean T score (SD)	58.7 (9.2)	60.0 (8.3)	59.1 (8.0)	$F = 3.32$; $p = .04$
% Clinical	19%	19%	10%	$\chi^2 = 7.49$; $p = .02$
Conduct problems				
Mean T score (SD)		59.2 (8.0)	57.1 (6.8)	$F = 7.69$; $p = .006$
% Clinical		15%	5%[c]	$\chi^2 = 10.53$; $p = .001$
Somatic problems				
Mean T score (SD)		56.8 (8.3)	58.4 (9.3)	$F = 4.09$; $p = .04$
% Clinical		10%	14%	$\chi^2 = 2.30$; $p = .13$
Internalizing problems				
Mean T score (SD)	62.9 (9.8)	61.2 (9.7)	62.8 (9.2)	$F = 4.47$; $p = .01$
% Clinical	26%	22%	24%	$\chi^2 = 2.29$; $p = .23$
Externalizing problems				
Mean T score (SD)	59.5 (12.0)	59.0 (9.8)	56.6 (9.7)	$F = 4.32$; $p = .01$
% Clinical	19%	17%	8%	$\chi^2 = 10.15$; $p = .006$
Total problems				
Mean T score (SD)	63.1 (11.2)	64.9 (8.2)	64.7 (7.5)	$F = 5.18$; $p = .006$
% Clinical	29%	38%	31%	$\chi^2 = 10.84$; $p = .004$

A Bonferroni adjusted p value of $p < .003$ was considered significant for all comparisons.
[a] Significant difference between the 6–11 year old and 2–5 year old group.
[b] Significant difference between 12–17 year old group and 2–5 year old group.
[c] Significant difference between 12–17 year old group and 6–11 year old group.
* Higher scores for all domains indicate more ASD symptoms.

7.81], $p < .001$) and adolescents (13% versus 6%; OR = 2.41; 95% CI [1.37, 4.22], $p = .002$) with subclinical anxiety compared to preschool children (both $p < .001$). There was also a higher percentage of school age children with subclinical anxiety compared to adolescents (26% versus 13%; OR = 2.23; 95% CI [1.33, 3.73], $p = .002$).

3.4. Relationship between anxiety and ASD severity as well as IQ within each age group

Table 3 presents the correlational data between the CBCL Anxiety Problem scale score and ASD severity as well as IQ. In the preschool and school age groups, significant but weak negative correlations emerged between anxiety and the social

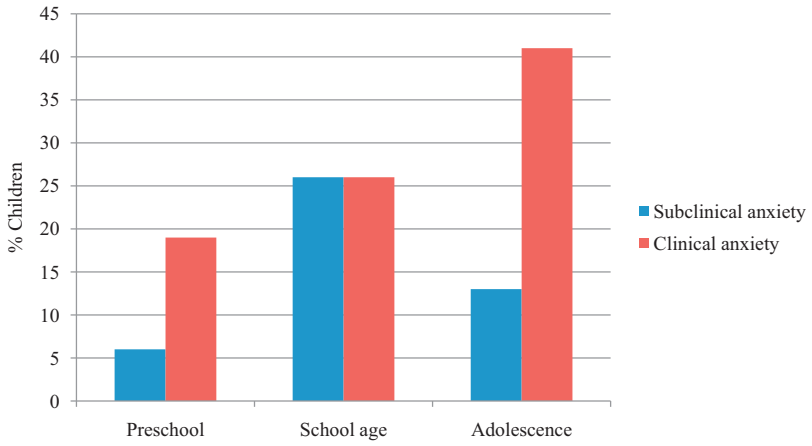

Fig. 1. Clinical anxiety was highest in the adolescent group. Subclinical anxiety was highest in the school age group (see text for results).

affect score as well as the total ASD severity score but these correlations were not present in the adolescent group. There were no significant correlations between anxiety and repetitive behaviors in any of the age groups.

With respect to IQ, significant but weak positive correlations were present between anxiety and IQ in both the preschool and school age groups. There was no correlation between anxiety and IQ in the adolescent group.

3.5. Examining psychiatric comorbidities associated with anxiety in each age group

Table 4 presents the final regression models for each age group. In the preschool group, Affective Problems had the strongest association with anxiety; other significant variables included ODD Problems and higher IQ. In the school age group, Affective Problems had the strongest relationship with anxiety followed by Somatic Problems. In the adolescent group, Affective Problems had the strongest association with anxiety followed by ADHD. The R^2 across the three models ranged from 0.32 to 0.36.

4. Discussion

This study examined the prevalence and correlates of anxiety in children with ASD using a developmental framework. Findings showed that the mean level of anxiety in preschool, school age, and adolescent youth was much higher than in the general population. Additionally, the percentage of children with clinical anxiety in each age group was markedly higher than the prevalence of anxiety in TD youth (preschool: 19% in our sample versus up to 9.5% in TD children; school age and adolescents: 26% and 41% in our sample versus up to 8.6% in TD children, see review by Costello, Egger, & Angold, 2005). A high prevalence of subclinical anxiety was also observed in this sample, particularly in school age children. Comparison of our data with other findings from the ASD-anxiety literature is limited due to the shortage of age group studies. One study of preschool children, however, found a 24% and 7% prevalence of clinical and subclinical anxiety, respectively, as measured by the CBCL Anxiety Problems scale, which is fairly similar to the results from the current study (Hayashida et al., 2010). It is important to highlight that our study measured only generalized anxiety, separation anxiety, and specific phobia symptoms. Therefore, the prevalence data are likely an underestimate of the true anxiety prevalence given that symptoms of social phobia and obsessive–compulsive disorder were not included.

Between group comparisons indicated that the percentage of children with clinical anxiety increased with age, with over 40% of adolescents experiencing clinical anxiety. This age-related increase was not present for any of the other CBCL psychopathology scales indicating that the adolescent group did not present with high levels of global psychopathology. Strang et al. (2012) also found high levels of clinical anxiety, as measured by the CBCL Anxiety Problems scale, in their sample of 6–18-year-old youth with ASD but found no association between age and anxiety symptoms. Our data are more similar to those of Davis et al. (2011) who found high levels of anxiety in 3–16 year old youth with ASD compared to other age cohorts (e.g., 20–48 year old group). However, their study did not compare levels of anxiety within this younger age group (e.g., preschool, school age, adolescence). Their study also differed with respect to sample size (131 versus 1316 in our study) and recruitment source (community and clinic sources in their study versus only clinic-based in our study). Neither the Davis et al. (2011) nor our study fully examined rates of anxiety during the critical transition from late adolescence to young adulthood (i.e., 18–24 years). Further research is therefore needed during this distinct developmental period.

Multiple interacting factors can be hypothesized to give rise to the high prevalence of clinical anxiety in children with ASD. In TD children, parental anxiety and depression can increase risk for offspring anxiety (Beidel & Turner, 1997; Lieb, Isensee, Höfler, Pfister, & Wittchen, 2002; Schreier, Wittchen, Höfler, & Lieb, 2008; Weissman et al., 2006). Preliminary evidence indicates that parental depression may similarly increase risk for anxiety in youth with ASD (Mazefsky, Folstein, &

Table 3
Pearsons correlations[a] between anxiety and both ASD severity and IQ.

	Preschool	School age	Adolescence
ASD severity			
Social affect	−0.13[a]	−0.16[a]	−0.04
Repetitive behaviors	−0.05	−0.03	−0.03
Total score	−0.13[a]	−0.14[a]	−0.04
IQ	0.15[a]	0.21[a]	−0.06

[a] A Bonferroni-adjusted p-value of $p < 0.003$ was considered significant for all correlations.

Table 4
Final linear regression models examining psychiatric comorbidities associated with anxiety in children with an ASD.

Independent variable	Preschool ($N = 300$)				School age ($N = 302$)				Adolescence ($N = 150$)			
	B	*SE*	*T*	*p*-value	*B*	*SE*	*T*	*p*-value	*B*	*SE*	*t*	*p*-value
Affective problems	.44	.05	9.11	<.001	.34	.03	9.65	<.001	.33	.06	5.84	<.001
ADHD problems									.07	.02	3.04	.003
ODD problems	.30	.05	7.36	<.001								
Somatic problems					.26	.06	4.39	<.001				
Public insurance												
IQ	.03	.006	4.46	<.001								
Adjusted R^2	.32				.36				.32			

Lainhart, 2008). Age specific environmental factors may also contribute to anxiety in children with ASD. For instance, in preschool children, factors such as fearful temperament, overprotective and overaccomodating parenting styles, communication impairments, and difficulty understanding one's environment may all contribute to anxiety (see reviews by Beesdo et al., 2009; Rapee, Schniering, & Hudson, 2009). Anxiety in the older age groups may be related to environmental and biological factors. School age children face a structured academic environment with greater focus on academic skills and less emphasis on social skills building, which may compromise development of friendships (Adreon & Stella, 2001) and increase risk for peer victimization (Shtayermman, 2007). By adolescence, cognitive and biological systems are changing and there is increased self-awareness and potential judgment by others (Bellini, 2004; Chamberlain, Kasari, & Rotheram-Fuller, 2007; Giedd, 2008; Mazurek & Kanne, 2010). Other stressors during adolescence include continued risk for social rejection, a more rigorous and abstract curriculum, and greater expectations of independence (Adreon & Stella, 2001). Sensory experiences and gastrointestinal problems may also contribute to anxiety at each stage of development (Green & Ben-Sasson, 2010; Mazurek et al., 2013). These hypotheses are speculative and not inclusive of all possible factors that may contribute to anxiety. Currently, there are few developmentally based models of anxiety in children and adolescents with ASD (Wood & Gadow, 2010). Future longitudinal studies are needed to examine the prevalence and factors that trigger and maintain anxiety at each developmental stage.

Weak negative and positive correlations were found between anxiety and ASD severity as well as IQ, respectively, but only in the preschool and school age groups. Absent correlations in the adolescent group may be due to its smaller sample size, lower IQ, exclusion of subjects who received ADOS Module 4 ($n = 32$) in the calculation of the ASD severity measure, and lack of assessment of social anxiety symptoms, which tend to be more common in adolescents. A number of studies have attempted to determine whether ASD symptom severity and cognitive functioning are risk factors for anxiety. Mazurek and Kanne (2010) reported nearly identical findings to ours in a large sample of children with ASD using fairly similar methods, i.e., parent-reported CBCL anxious/depressed scale scores, an ADOS derived ASD severity measure, but a more comprehensive IQ battery. Other data, however, do not support the positive correlation between anxiety and IQ (e.g., Simonoff et al., 2008; Strang et al., 2012). There is evidence supporting a positive relationship between anxiety and repetitive behaviors, however these studies vary with respect to sample composition (e.g., Rodgers et al., 2012a: high functioning children; Sukhodolsky et al., 2008: full range of IQ) and anxiety measures. More research on these relationships is needed.

Anxiety was also associated with a distinct profile of psychiatric comorbidities in each age group. Some researchers have hypothesized that the "load" of anxiety may predispose to other types of psychopathology (Beesdo et al., 2009; Woodward & Fergusson, 2001). Among the psychiatric comorbidities examined, affective problems had the strongest association with anxiety in each group, which is identical to the findings in TD youth (Brady & Kendall, 1992; Seligman & Ollendick, 1998). This relationship between anxiety and depression may result from shared involvement of serotonergic and noradrenergic systems (Boyer, 2000; Gorman, 1996), as well as heterotypic continuity with anxiety predicting future depression (Pine, Cohen, Gurley, Brook, & Ma, 1998). In terms of age specific findings, ADHD and ODD symptoms in the preschool group, ODD and somatic symptoms in the school age group, and ADHD symptoms in the adolescent group were each significantly associated with anxiety. These age-group findings may reflect developmental changes in the expression of distress. For example, young children frequently express anxiety as agitation, avoidance, and reactive aggression, which are symptoms that also reflect ADHD and ODD (Bubier & Drabick, 2009), whereas school-age children may report physiological

manifestations of anxiety since this would otherwise require more abstract and emotion-based language. In adolescents, ADHD symptoms may be exacerbated due to greater academic demands, which can lead to a vicious cycle of anxiety and attention problems exacerbating each other. Collectively, these data raise the hypothesis that anxiety may be part of a larger neurobehavioral syndrome at each stage of development (Lecavalier, Gadow, DeVincent, & Edwards, 2009; Wood & Gadow, 2010). Further research characterizing these syndromes and linking them to genetic vulnerabilities may provide insights into specific ASD phenotypes (Cohen et al., 2011; Cohen & Tsiouris, 2006; deLong, 2004).

4.1. Clinical implications

The high rate of clinical anxiety in each age group highlights the need for a thorough anxiety assessment when evaluating children of all ages with ASD. Moreover, given that anxiety appears to be a highly comorbid condition, children who present with other psychiatric comorbidities should be evaluated for anxiety. Assessment of young children is particularly crucial since this time period presents an opportunity to reduce long term impairment. The high rate of subclinical anxiety in school age years suggests that this may be a prime time to implement anxiety prevention strategies to prevent development of a full-blown disorder. Preliminary evidence suggests that CBT may be an effective treatment for clinical anxiety in children with HFA (Reaven, 2009; Wood et al., 2009). Similar prevention studies are needed in the ASD population. Novel treatment options such as computer-based CBT programs (Kendall, Khanna, Edson, Cummings, & Harris, 2011) that can be accessed across multiple settings as well as training of school professionals to detect and manage anxiety may prove useful in this population. Less research is available to guide treatment of anxiety in lower functioning children with ASD. The available data suggests that behavioral treatments including the use of graduated exposure and reinforcement are effective treatments for certain anxiety disorders in this population (Jennett & Hagopian, 2008).

4.2. Strengths and limitations

This is one of the first studies to examine age group differences in anxiety among children with ASD. The sample was a large, well-characterized cohort of children and adolescents with ASD who were demographically and clinically diverse. The diagnosis of ASD was established by a physician with the assistance of gold standard autism instruments. Another strength was the use of standardized measures that do not include social avoidance and obsessive compulsive symptoms, which overlap with ASD symptoms.

One limitation is that about half of the original sample had to be excluded from the analyses. About a third of these children were excluded because of either a documented genetic and neurologic disorder or the absence of documentation indicating the child had one of these two disorders (e.g., forms were missing). About 15% of children were excluded because their CBCL data were unavailable, i.e., parents did not bring the forms to the child's appointment. Some of the IQ and ADOS data were also missing. Excluding such a large volume of data could have resulted in sample bias. As a result, the data analyses employed a model selection procedure that maximized the sample size by minimizing the number of necessary covariates.

Some of the significant findings may have resulted from the high likelihood of finding significance in a large sample of children. For example, group differences were present in the social affect and repetitive behavior scores. The actual differences in group means, however, were small and therefore the clinical significance of these findings is questionable. Correlations between anxiety and IQ as well as ASD symptoms were present, but weak and inconsistent, thereby minimizing concerns about confounding due to these phenotypic variables, particularly among adolescents.

Parents were the only raters of child anxiety, which may have resulted in reporting biases (Frick, Silverthorn, & Evans, 1994). Although multi-informant approaches have been recommended in the assessment of child anxiety (e.g., MacNeil, Lopes, & Minnes, 2009; White et al., 2009), parent report is currently considered the most reliable report given the language and emotional impairments in this population (e.g., Lopata et al., 2010; Losh & Capps, 2006; Mazefsky, Kao, & Oswald, 2011; Shalom et al., 2006).

Another limitation pertains to the lack of validity data on the CBCL Anxiety Problems in children with ASD. Due to the severe shortage of psychopathology instruments designed specifically for the ASD population, researchers have been measuring anxiety in ASD using instruments designed for TD children. Considerable evidence supports the validity of the CBCL in measuring anxiety in TD children (Ebesutani et al., 2010; Ferdinand, 2008; Pauschardt, Remschmidt, & Mattejat, 2010). For example, in TD children, data show significant correspondence between subscale scores and clinical diagnosis, and better concurrent validity for the CBCL Anxiety Problems scale as compared to the CBCL Anxious/Depressed syndrome scale (Ebesutani et al., 2010). Several studies indicate that the CBCL possesses good psychometric properties in children with intellectual disabilities (e.g., de Ruiter, Dekker, Verhulst, & Koot, 2007; Perez-Garcia, Granero, Gallastegui, Pérez-Jurado, & Brun-Gasca, 2011), and is now becoming increasingly used to assess psychopathology in children with ASD (Kanne et al., 2009; Pandolfi et al., 2009, 2012) including anxiety (Strang et al., 2012). Some have cautioned that the CBCL is not a comprehensive measure of anxiety but rather a screener, given the relatively low number of items (Ferdinand, 2008; Pauschardt et al., 2010). Our prevalence data are therefore more likely to reflect the number of children meeting screening criteria for clinical anxiety.

Other limitations include the fact that subjects were recruited from medical or university settings across the country for concerns about development or autism; the sample is therefore geographically diverse but not truly representative of the

population. Some children may have been receiving treatment for anxiety, which may underestimate prevalence. Finally, potential method effects may influence the findings. Differences in informant (clinician based ADOS versus parent reported CBCL to assess anxiety) as well as method (semi-structured behavioral assessment to assess for ASD versus standardized rating scale to measure child anxiety) may minimize the strength of the observed correlations. Stronger correlations may have been observed if parents completed a standardized ASD rating form similar to the CBCL.

4.3. Future research

Currently, there are limited empirically based developmental psychopathology models of anxiety in children with ASD. Findings from this study can be used to generate hypotheses for longitudinal studies of anxiety. Given the high costs associated with conducting longitudinal studies, it may be more realistic to initially examine anxiety across specific transitional periods (e.g., preschool to school age, school age to adolescence) (Davis et al., 2011). Findings from the current study set the stage for generating hypotheses about the high rates of clinical anxiety in adolescents and subclinical anxiety in school age and children.

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