

**TYPICAL AND ATYPICAL ANXIETY IN CHILDREN WITH AUTISM  
SPECTRUM DISORDER**

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## ABSTRACT

**Objective.** There is confusion regarding the presentation and correct classification of anxiety symptoms in autism spectrum disorders (ASD) as comorbid anxiety disorders, core ASD symptoms or a separate syndrome. The present study examined the degree to which Diagnostic Statistical Manual-Fourth Edition (DSM-IV) anxiety disorders (“typical anxiety”) can be reliably distinguished from atypical presentations in ASD (“atypical anxiety”). To inform their classification, the study also assessed how these typical and atypical presentations were differentially related to child characteristics (i.e. IQ, language ability) and features of anxiety disorders (i.e., anxious self-talk) and ASDs (i.e., ASD symptomology, sensory abnormalities).

**Method.** Youth (N = 59; 7 – 17 years; IQ > 60) diagnosed with ASD and their parents completed a semi-structured diagnostic interview (ADIS-C/P) adapted to measure both typical and atypical presentations of anxiety as well as self- and parent-report measures.

**Results.** Seventeen percent of the sample met criteria for a typical anxiety disorder, 15% for an atypical anxiety disorder and 31% for both typical and atypical disorder variants. Whereas IQ, language ability, anxious self-talk and sensory sensitivity significantly predicted typical anxiety, atypical anxiety was significantly associated with anxious self-talk and ASD symptomology.

**Conclusions.** Results suggest that ASD youth display two, phenomenological distinct classes of anxiety. These typical and atypical presentations likely reflect comorbid anxiety and a novel variant of anxiety, which may be missed by current, unmodified anxiety measures. How these presentations differentially respond to interventions and contribute to the range of results regarding the prevalence and presentation of anxiety in ASD warrants investigation.

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This study is dedicated to my husband.

TABLE OF CONTENTS

|  | PAGE |
|--|------|
| ABSTRACT.....                              | iii  |
| ACKNOWLEDGEMENTS.....                      | iv   |
| DEDICATION.....                            | v    |
| LIST OF TABLES.....                        | vii  |
| LIST OF FIGURES.....                       | viii |
| CHAPTERS                                   |      |
| 1. MANUSCRIPT IN JOURNAL ARTICLE FORM..... | 1    |
| CHAPTER 1 ENDNOTES.....                    | 26   |
| 2. LITERATURE REVIEW.....                  | 46   |
| 3. EXPANDED RESULTS.....                   | 89   |
| REFERENCES.....                            | 115  |
| APPENDIX: COMMONLY USED ABBREVIATIONS..... | 138  |

## LIST OF TABLES

| Tables  | Page |
|---|------|
| 1. Sample Characteristics.....  | 90   |
| 2. Pharmacological Interventions.....   | 91   |
| 3. Correlation Matrix of All Potential Independent and Dependent Variables.....                         | 92   |
| 4. Relationship of the Sensory Avoidance and Sensory Sensitivity Subdomains of the Sensory Profile..... | 93   |
| 5. Independent and Dependent Variable Summary.....  | 94   |
| 6. Inter-rater and Test-Rest Reliability on ADIS-C/P.....   | 95   |
| 7. Child and Parent Agreement on ADIS-C/P.....  | 96   |
| 8. Comparability of Full and 1-2 Week Follow-up Sample.....   | 97   |
| 9. Frequency of DSM-IV and Atypical Anxiety Disorders.....  | 98   |
| 10. DSM-IV and Atypical Anxiety Disorder Rates.....   | 99   |
| 11. Multiple Regression Models: Predictors of Typical and Atypical Anxiety.....                         | 100  |
| 12. Multiple Regression Models: Sensitivity Analyses.....   | 101  |
| 13. Full and Partial Correlations of Typical Anxiety, Atypical Anxiety and the SRS...                   | 102  |
| 14. One-way ANOVA of Typical Anxiety Severity by IQ Level.....  | 103  |
| 15. Summary of Studies Focusing on Prevalence of Anxiety in ASD.....                                    | 104  |

## LIST OF FIGURES

|   |     |
|---|-----|
| 1. Figure 1. Breakdown of DSM-IV and Other Disorders.....             | 111 |
| 2. Figure 2. Frequency of Typical and Atypical Anxiety Disorders..... | 112 |
| 3. Figure 3. Predictors of Typical and Atypical Anxiety.....          | 113 |
| 4. Figure 4. IQ, Typical and Atypical Anxiety.....                    | 114 |

CHAPTER 1  
MANUSCRIPT IN JOURNAL ARTICLE FORM

## **Typical and Atypical Anxiety in Children with Autism Spectrum Disorders**

Research suggests that co-occurring anxiety disorders may both commonly arise and exacerbate autism spectrum disorders ASDs (de Bruin et al., 2007; Drahota, Wood, Sze & Van Dyke, 2011; Kim et al., 2000; Simonoff, et al., 2008; White, Oswald, Ollendick, & Scahill, 2009), yet studies have yielded variable results. Youth with ASD experience significantly more anxiety than typically developing youth (Gadow, Devincent, Pomeroy, & Azizian, 2005; Hurtig et al., 2009; Kim et al., 2000) as well as youth with specific language impairments (Gillott, Furniss & Walter, 2001), William's Syndrome (Rogers, Riby, Janes, Connolly & McConchie, 2012), conduct disorders (Green, Gilchrist, Di Burton & Cox 2001), learning disabilities (Burnette, Mundy, Meyer, Sutton, Vaughan, & Charak, 2005), and Down syndrome (Evans et al., 2005). Still, the prevalence of impairing anxiety problems in ASD may range anywhere from 11 to 84% (Kerns & Kendall, in press; White et al., 2009) and efforts to identify predictors and characteristics of anxiety in ASD have resulted in inconsistencies.

Anxiety symptoms have been associated with higher intellectual ability, ASD severity, language ability, and child age in some studies (Davis, Hess et al., 2011; Davis, Moree et al., 2011; Kuusikko et al., 2008; LeCavalier et al., 2006; Sukhodolskey et al., 2008; Weisbrot et al., 2005), but not others (Brereton et al. 2006; Mayes et al., 2010; Pearson et al., 2006; Simonoff et al., 2008; Zandt, Prior, & Kyrios, 2007). With regard to presentation, studies suggest that the anxiety of children with ASD is less, equally, or more severe than that of typically developing youth with anxiety disorders (Cath et al., 2008; Farrugia & Hudson, 2006; Gadow et al., 2005; Helverschou & Martinsen, 2010; Russell & Sofronoff, 2005; Williamson, Craig, & Slinger, 2008), and there is little

agreement about which of the several anxiety disorders is most common in ASD (White et al., 2009). Whereas some studies find few differences in the quality and variety of anxiety symptoms in ASD compared to non-ASD youth (Kerns & Kendall, in press), others suggest that youth with ASD experience more fears of physical injury, unusual specific phobias, and compulsive and ritualistic behaviors (Cath et al., 2008; Evans et al., 2005; Farrugia & Hudson, 2006; Russell & Sofronoff, 2005). Associations between anxiety, sensory processing differences and repetitive and restricted behaviors, such as rituals, in ASD further support this distinct pattern (Bellini, 2004; Boyd et al., 2010; Gabriels et al., 2008; Kern et al., 2006). Some studies also suggest fewer fears of negative social evaluation, less self-consciousness, fewer obsessions, and fewer repeating and checking compulsions in anxious youth with ASD (Farrugia & Hudson, 2006; Gillott et al., 2001; Russell & Sofronoff, 2005), a potentially meaningful discrepancy given that negative thoughts (e.g., obsessions, self-doubt) are considered to play an important role in the etiology, mediation, and maintenance of childhood anxiety disorders (Treadwell & Kendall, 1996; Kendall & Treadwell, 2007; Leung & Wong, 1998; Ronan, Kendall & Rowe, 1994).

Discrepant results regarding the prevalence and presentation of anxiety in ASD may be attributable, in part, to differences in sampling and assessment methods. For example, a more restricted prevalence range (25-55%) has been reported in epidemiological and community samples (Hurtig et al., 2009; Simonoff et al., 2008; Leyfer et al., 2006; de Bruin, et al., 2005), than in clinical samples (i.e. samples recruited from treatment settings; 14-59%), where participants are often more severe and more likely to present with comorbidities (Mattila et al., 2010). Similarly, studies using

diagnostic interviews (39-84%) suggest a higher prevalence range than those relying on parent questionnaires (11-59%; Kerns & Kendall, in press), potentially due to the more comprehensive nature of diagnostic assessments.

Variable estimates regarding the prevalence and presentation of anxiety in ASD may also reflect ongoing confusion regarding the ambiguity of many anxiety and autism spectrum symptoms (Skokauskas, & Gallagher, 2010; Wood & Gadow, 2011). Social avoidance and awkwardness, reduced emotional reciprocity, compulsive and ritualistic behavior, and communication difficulties are areas of potential overlap between anxiety and ASD (Wood & Gadow, 2011). Moreover, youth with ASD often present with unusual fears, worries and rituals, whose proper classification as anxiety or autism is unclear. In his seminal paper, *Autistic Disturbances of Affective Contact* (1943), Kanner describes anxiety symptoms in ASD that appear qualitatively different from those reported in children without ASD. Kanner describes in one case:

“...a good deal of ‘worrying.’ He frets when the bread is put in the oven to be made into toast, and is afraid it will get burned and be hurt...He is upset that the moon does not always appear in the sky at night.”

Kanner also reports unusual obsessiveness, a compulsive need for sameness, and phobias of atypical focus, including fears of running water, spinning tops, gas burners, wind, and mechanical noise, symptoms also described in Hans Asperger’s *Autistic Psychopathology of Early Childhood* (Frith, 1991) and still captured in current diagnostic interviews for ASD (e.g. “difficulties with minor changes in routine,” Lord et al., 1994). Whether these atypical symptoms reflect an aspect of ASD or long-documented, but potentially overlooked symptoms of a co-occurring anxiety disorder remains unclear and in many studies unaddressed.

Some qualitative guidelines for differential diagnosis have been offered, but not yet tested by previous investigators (Wood & Gadow, 2011; Leyfer et al., 2006). Wood and Gadow (2011) suggest that anxiety and ASD symptoms may be distinguished by their quality and function. Whereas repetitive, seemingly compulsive behavior may have a perseverative, enjoyable quality in ASD, compulsions in obsessive-compulsive disorder (OCD) are typically undesired, anxiety-related behaviors, designed to mitigate a distressing obsession. Though social avoidance may reflect ambivalence in ASD, it serves a palliative function in social phobia by postponing or eliminating the feared consequence of social rejection (Pontonski, Heimberg, Turk, & Coles, 2008). Additionally, distinctions have been made between the rigid, agitated temperament of some ASD youth and generalized anxiety disorder (GAD; Leyfer et al., 2006), as well as between unusual specific fears evident in ASD (i.e. fear of loud sounds) and the specific phobias of typically developing youth in some studies (Evans et al., 2005; Leyfer et al., 2006).

Though promising, suggestions for differential diagnosis have only recently been offered (Wood & Gadow, 2011), lack supporting empirical data or investigation and appear infrequently and inconsistently across studies. Much of the literature has relied on the results of brief parent, teacher or child questionnaires of anxiety, developed in youth without ASD and thus potentially poorly equipped to make subtle diagnostic distinctions (Bakken et al., 2010; Brereton et al., 2006; Gadow et al., 2004, 2005; Hurtig et al., 2009; Kim et al., 2000; Sukhodolsky et al. 2008; Weisbrot et al., 2005). Moreover, studies employing diagnostic interviews have differed in their treatment of these ambiguous symptoms, a variation that may contribute to the range of reported anxiety disorder

characteristics and prevalence in ASD. In their assessment of 44 ASD youth, Muris and colleagues (1998) reported that though 73% of their sample displayed ritualistic behaviors, OCD was only diagnosed in 11% of cases where parents identified ritual-related distress. Leyfer and colleagues (2006) noted that the rate of OCD in their sample (37%) would have been substantially reduced if they had not allowed parents to infer their child's mental state. Similarly, social phobia has been reported in approximately 8 – 29% of ASD individuals depending on researchers' requirement of a clear, articulated fear of social ridicule and rejection (Leyfer et al., 2006; Muris et al., 1998; Siminoff et al., 2008). After distinguishing between social phobia and mere social avoidance as well as between generalized worry and routine-related distress in youth with autism, Leyfer and colleagues (2006) found much lower rates of social phobia (8%) and GAD (2%) in their sample than have been reported in other, less discriminating studies (GAD – 35%, Green et al., 2000; social phobia – 29%, Siminoff et al., 2008). Variable estimates of specific phobias (Range: 6 – 63%) and separation anxiety disorder (SAD; Range: 0.5% - 27%) from study to study are likely related to similar conceptual issues (Kerns & Kendall, in press).

Finally, accurate measurement of comorbid anxiety symptoms in ASD has been complicated by a confusion regarding the potential role of anxiety in ASD. Possible explanations for anxiety symptoms in ASD include that they represent (a) an independent, comorbid psychopathology, qualitatively and etiologically similar to monomorbid anxiety disorders, (b) a manifestation of the ASD diathesis misinterpreted as anxiety, and (c) a separate syndrome or variant of anxiety, altered in expression by its co-occurrence with ASD (Wood & Gadow, 2011). In a recent review, Kerns and Kendall (in

press) suggested that variability in anxiety prevalence and presentation may be attributable to the presence of *both* comorbid anxiety disorders and a variety of more ambiguous behaviors in individuals with ASD whose role is less clear. Specifically, Kerns and Kendall (in press) proposed that anxiety symptoms that closely resemble anxiety disorders in typically developing youth, appear to occur in a subgroup of ASD youth and vary according to intellectual and communicative ability in a manner suggestive of comorbid psychopathology. By contrast, they propose that more ambiguous symptoms in ASD (e.g. compulsiveness, rigidity, unusual specific phobias) appear more similar to and associated with core ASD characteristics and present differently from typical anxieties (Evans et al., 2005; Russell & Sofronoff, 2005; Leyfer et al., 2006; Zandt et al., 2007). They suggest that these ambiguous symptoms may or may not reflect anxiety and thus may account for the lack of significant differences in anxiety symptoms by age, intellectual ability and ASD severity reported in some studies.

In contrast to previous studies that have offered but not directly tested guidelines for differential diagnosis, the present study assessed Kerns and Kendall's (in press) hypotheses. Specifically, the study examined if "typical" anxiety symptoms (i.e. anxiety symptoms that present similarly in youth with and without ASD) can be distinguished from more "atypical" symptoms of anxiety in ASD (i.e. anxiety symptoms that appear more ambiguous and qualitatively distinct from DSM-IV anxiety disorders). It then investigated whether these typical and atypical anxiety symptoms in ASD reflect (a) comorbid anxiety disorders, (b) a separate variant of anxiety in ASD or (c) symptoms of ASD that resemble anxiety.

It was hypothesized that typical anxiety symptoms would present like comorbid anxiety disorders: they would (a) vary according to IQ and verbal skill, and (b) be positively associated with self-reported anxious cognitions, features that differentiate youth with and without anxiety disorders (Sood & Kendall, 2007; Treadwell & Kendall, 1996). By contrast, it was hypothesized that atypical anxiety symptoms would more closely resemble symptoms of ASD: they would be (a) apparent in ASD youth, regardless of age, intellectual or verbal abilities; (b) associated with known abnormalities in ASD (e.g., sensory processing differences) and (c) associated with a continuous measure of ASD symptomology. The degree to which atypical anxiety symptoms were also associated with indicators of typical anxiety disorders, such as anxious cognitions and typical anxiety symptoms, would inform their classification as either a separate syndrome of anxiety in ASD or symptoms of ASD that resemble anxiety.

## **Method**

### **Participants**

Participants were 59 youth (7 – 17 years) diagnosed with ASD and their parents. All were recruited from an ongoing, community-based study on brain imaging and genetics at the Center for Autism Research (CAR) at Children’s Hospital of Philadelphia (CHOP). Only 12 contacted families declined to participate, all for scheduling reasons. As part of this ongoing study, all youth met criteria for ASD according to the Autism Diagnostic Interview-Revised (ADI-R), Autism Diagnostic Observations Scale (ADOS) and clinical judgment within the past year. Children were required to have a full scale IQ of 60 or greater as determined by the Differential Abilities Scale (DAS) or, in one case,

the Weschler Intelligence Scale for Children (WISC-IV)<sup>1</sup>. Exclusionary criteria were (a) a lack proficiency in English in youth and at least one parent; (b) chronological age below 7 years, active psychosis or sensory-motor difficulties that would preclude valid use of diagnostic instruments; (c) a history of traumatic brain injury or other significant medical or neurological abnormality affecting motor or higher cortical functioning; (d) conditions that would prohibit magnetic resonance imaging, such as body metal, claustrophobia, pregnancy, or uncorrected auditory impairment, given the brain imaging requirements of the original study. Youth taking psychotropic medications were included.

### **Measures**

**Differential Abilities Scales, Second Edition (DAS-II; Elliot, 2007).** The DAS, for youth age 2 – 18 years, yields an overall cognitive ability score, the General Conceptual Ability (GCA) composite, considered an estimate of full IQ given its correlation ( $r = .77$ ) with other IQ tests (Dumont, Cruse, Price, & Whelley, 1996).

**Clinical Evaluation of Language Fundamentals, Fourth Edition (CELF-4; Semel & Wiig, 2003).** The CELF-4 is an assessment of expressive and receptive language in youth ages 3 – 21 years. The CELF-4 generates a Core Language Index, a measure of language functioning with retest reliability ( $r = .88 - .92$ ), internal consistency (Cronbach's alpha = .87 - .95), split-half reliability ( $r = .87 - .95$ ) and inter-rater reliability ( $r = .88 - .99$ ) as well as strong sensitivity and specificity for the detection of language disorders (Semel & Wiig, 2003).

**Negative Affectivity Self-Statement Questionnaire (NASSQ; Ronan, Kendall, & Rowe 1994).** The NASSQ is a 70-item self-report measure assessing negative and anxious

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<sup>1</sup> Previous research suggests that agreement between the DAS and WISC-IV is high ( $r = .77$ ; Dumont, Cruse, Price, & Whelley, 1996)

self-statements associated with affective and anxiety disorders. A 33-item anxiety subscale, the NASSQ-A, has been found to differentiate anxious from non-anxious youth without ASD (Sood & Kendall, 2007). It has acceptable alpha reliability ( $r = .89-.96$ ), sensitivity (.81) and specificity (.80), 2-week retest stability ( $r = .73-.96$ ) and is sensitive to treatment (Kendall & Treadwell, 2007; Treadwell & Kendall, 1996).

**Sensory Profile (SP; Dunn, 1999).** The SP is a parent-report of behaviors associated with abnormal sensory responses (Rogers et al., 2003). Internal consistency of SP factors range from .70 - .90. The SP has a reliability of .90, internal consistency (.70-.90) and discriminative validity in identifying children with and without sensory modulation dysfunction (McIntosh et al., 1999). It has been associated with electrodermal ratings of physiological responses to sensation (Dunn, 1999) as well as restricted, repetitive, stereotyped behaviors and interests in youth with ASD (Gabriels et al., 2008). In the present study, children's categorization as "Much Less than Most," "Less than Most," "Same as Most," "More than Most" and "Much More than Most" on the four SP subdomains, Low Registration, Sensory Seeking, Sensory Sensitivity, and Sensory Avoidance, were represented by 1 to 5 scale, with 1 reflecting "Much Less" and 5 "Much More".

**Social Responsiveness Scale-Parent Version (SRS-P; Constantino & Gruber, 2005).** The SRS is a 65-item, parent report measuring a continuum of social deficits characteristic of ASD that are relatively independent of other psychopathology (Constantino, Hudziak, & Todd, 2003) and IQ (Constantino et al., 2003). The SRS evidenced retest reliability ( $r = .83$ ; Constantino et al. 2003), inter-rater reliability (between parents,  $r = .91$ ; Constantino et al., 2003) and internal consistency (Cronbach's alpha = .97;

Constantino & Gruber, 2005). The SRS has shown convergent validity with the Autism Diagnostic Interview-Revised (ADI-R), a standard diagnostic instrument ( $r = .7$ ; Lord, Rutter & LeCouteur, 1994; Constantino et al., 2003) and measures ASD severity (Hilton et al., 2010; Wang, Lee, Sigman, & Dapretto, 2007). For the present study, a second raw total score (Cronbach's alpha = .79) was calculated after removing items from the SRS Mannerisms domain that may have overlapped with the atypical anxiety construct (e.g. "Does your child dislike changes in his/her routine?")

### **Diagnostic Assessments**

**Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter & LeCouteur, 1994).** The ADI-R is a parent-report interview for diagnosing ASD. It has demonstrated internal consistency, inter-rater reliability, and retest reliability and yields an algorithm score that differentiates autism from other developmental disorders at high levels of sensitivity and specificity ( $> .90$  for both) for subjects with mental ages of 18 months and older (Lord et al., 1994).

**Autism Diagnostic Observational Schedule-Generic (ADOS-G; Lord et al., 2000).** The ADOS-G is semi-structured, standardized diagnostic observation to aid in ASD diagnosis. The ADOS-G shows inter-rater reliability, internal consistency and retest reliability on item, domain and classification levels for ASD (Lord et al. 2000). Diagnostic validity for autistic versus non-spectrum disorders was found to be excellent (Lord et al. 2000; Gotham et al., 2008).

**Anxiety Disorders Interview Schedule- Child and Parent Versions (ADIS-C/P; Silverman & Albano, 1996).** The ADIS-C/P is a semi-structured interview for diagnosing DSM-IV anxiety and other disorders (e.g. depression, dysthymia, externalizing disorders,

enuresis, schizophrenia, eating disorders) in youth with favorable psychometric properties in typically developing youth (March & Albano, 1998), including high inter-rater reliability (Chavira, Stein, Bailey, & Stein, 2004), retest reliability (Silverman, Saaverdra, & Pina, 2001) and convergent validity (Wood, Piacentini, Bergman, McCracken, & Barrios, 2002). Parents and youth provide global interference ratings (GIR) to quantify the impairment associated with each disorder and inform clinical severity ratings (CSRs), which range from 0 (not a problem) to 8 (a debilitating problem), with 4 required for a diagnosis. Anxiety symptoms that lack sufficient severity or duration to meet criteria for a disorder, receive a subclinical rating ( $CSR \leq 3$ ). Composite CSR scores (i.e. the highest CSR awarded for a particular anxiety based on either parent or child report on the ADIS-C/P) for the most severe anxiety problem for each child were the focus of this study.

**Modifications to the ADIS-C/P.** The ADIS-C/P was adapted to assess both anxiety symptoms consistent with DSM-IV criteria (“typical anxiety”) and anxiety symptoms that do not meet DSM-IV criteria due to their atypical presentation (“atypical anxiety”), but which nonetheless were endorsed by youth or their parents as highly distressing, problematic and/or interfering. Like typical anxiety symptoms, atypical anxiety symptoms that were reported, but which did not appear to cause substantial impairment or interference also receive subclinical ratings ( $CSR \leq 3$ ).

Differential diagnosis of typical and atypical anxiety presentations was guided by DSM-IV diagnostic criteria, clinical judgment and prior research (Leyfer et al., 2006; Muris et al., 1998; Wood & Gadow, 2011). Atypical and typical anxiety CSRs could occur in the same child. For example a child could receive CSR scores for both a typical specific phobia of dogs and an atypical specific phobia of running water.

**GAD versus Atypical GAD.** Kanner (1943) described one feature of ASD to be “an anxiously obsessive desire for the maintenance of sameness,” a trait that, though it appears anxiety-related, is qualitatively distinct from GAD and typically described as a symptom of ASD. Consistent with this original distinction and prior comorbidity research in ASD (Leyfer et al., 2006), youth who endorsed interfering, daily worries regarding changes to their schedule or other unusual, likely ASD-related concerns, such as worry related to intense preoccupations or rigidity, received a CSR for “atypical GAD” rather than GAD.

**Social Phobia versus Atypical Social Phobia.** Consistent with distinctions described in the Autism Comorbidities Interview (Leyfer et al., 2006), youth who lacked a fear of negative social evaluation (a definitive feature of social phobia), but displayed consistent social avoidance and social discomfort, despite some desire for socialization, received a CSR for “atypical social phobia.” CSRs for social phobia were only assigned to youth who expressed a desire for social interaction, an undue fear of social ridicule or rejection, and impaired functioning attributable to social anxiety as opposed to ASD alone.

**OCD versus Atypical OCD.** Consistent with Muris and colleagues (1998), a CSR for OCD was only given when reported obsessive thoughts and compulsive behaviors were clearly distressing to the child, such that the child aimed to escape or eliminate obsessional content (as opposed to perseverating on a preferred thought) or used compulsive behavior to mitigate anxiety (rather than experiencing anxiety solely as a result of the compulsion being interrupted). A CSR for “atypical OCD” was assigned for compulsive behaviors and intrusive thoughts that did not meet these criteria.

**Specific Phobia versus Atypical Specific Phobia.** As unusual, highly specific fears have also traditionally been considered features of ASD (Kanner, 1943; Le Couteur,

Haden, Hammal, & McConachie, 2008) and are rarely seen in typically developing youth or youth with intellectual disability (Evans et al., 2005; Leyfer et al., 2006), specific phobias of an unusual focus (e.g. fear of graffiti, fear of running water) were given a CSR for “atypical specific phobia” rather than a DSM-IV specific phobia.

**Modifications to Administration.** Given the social, cognitive and communication difficulties experienced by many children with ASD, the ADIS-C/P was administered with the following modifications: (a) parents and youth were asked to report on the incremental interference of anxiety symptoms, whether typical or atypical, above and beyond ASD symptoms to inform CSRs; (b) youth were directed to focus on the interference of one or two concrete symptoms when providing GIRs rather than more abstract, overarching anxiety concepts such as GAD or social anxiety; (c) the ADIS-C/P was administered concurrently to parents and youth to encourage participant engagement and understanding for all but 6 participants.

### **Study Procedures**

As part of a prior brain imaging study, and within 1 year of the current study, youth completed comprehensive diagnostic evaluations for ASD (ADI-R, ADOS-G), cognitive (DAS) and language (CELF) assessments, as well as parent questionnaires of ASD symptomology (SRS) and sensory response (SP). Informed consent and assent to utilize these data and collect new data was obtained from parents and youth prior to the study. Over the course of 1 day all participants completed a semi-structured interview of anxiety and other clinical disorders (ADIS-C/P) as well as a self-report questionnaire, the NASSQ. Parents also provided information on their child’s behavior, emotional states, medical history and current medications.

All interviews and assessments were completed by a team of psychologists and a doctoral candidate at CAR who were trained and reliable on the ADI-R/ADOS-G. ADIS-C/P reliability was established for both typical and atypical anxiety disorders and CSRs (intraclass correlation (ICC) > .7) prior to and throughout the study (based on a random selection of 35% of the sample). One to 2-week retest reliability ( $M = 10$  days) for the ADIS-C/P was assessed in 25% ( $n = 15$ ) of the sample. The same clinician conducted both initial and retest interviews to minimize variance due to factors other than time, reflect common clinical practice and maintain consistency with clinical trial and retest reliability procedures for the original ADIS-C/P (Silverman, Saavedra, & Pina, 2001). Families were compensated for their time (\$10 per hour of assessment) and travel expenses in addition to receiving a summary of diagnostic results, recommendations for their child's care and appropriate referrals.

### **Statistical Analyses**

Examination of the sample distribution (histogram, skewness, kurtosis) and variance (boxplots, residual scatterplots, review of DfBETAs, and leverage) determined that all normality, linearity and homogeneity assumptions were met and that results were not unduly influence by outliers. Frequencies, means and standard deviations were calculated for all demographic, independent and dependent variables. Severity of typical and atypical anxiety was represented by the most severe composite CSR scores (range 0 – 8) given for typical and/or atypical anxiety disorders. Preliminary Pearson correlations identified the most powerful predictors of typical anxiety (NASSQ-A, IQ, CELF Core Language Index) and atypical anxiety (SP-Sensory Seeking, SRS-P) for inclusion in the final analyses. The SP sensitivity and avoidance domains, also strong predictors of

typical anxiety, were averaged to create a single sensory sensitivity/avoidance (SP-SA) scale given their consistency (Cronbach's  $\alpha = .83$ ). Data were missing for a small number of some scales, including 4 CELFs, 3 NASSQs, and 2 SPs. As such, hierarchical regressions were conducted with a slightly smaller sample ( $n = 54$ ).

Two hierarchical multiple regressions assessed the associations of 5 identified predictors with (a) typical anxiety severity, and (b) atypical anxiety severity respectively (Model 1). Two additional hierarchical multiple regressions assessed the differential contributions of SP\_SA to typical and atypical anxiety respectively (Model 2). Finally partial correlations assessed the relationship between ASD symptoms (SRS-P) with and without the SRS-P mannerisms domain (items measuring stereotyped and restricted behaviors characteristic of ASD), with typical and atypical anxiety.

## **Results**

### *Preliminary Analyses*

Table 1 displays sample characteristics. Participants were a mean age of 10.48 years ( $SD = 2.63$ ). The sample was predominantly Caucasian (93%) and male (78%) with moderate to high family income (75% of families reported annual family income  $\geq$  \$60,000). There were no significant differences in the mean severity or distribution of principal typical and atypical anxiety CSRs. Youth displayed a wide range of intellectual (IQ range: 67 to 158;  $M = 104.69$ ,  $SD = 19.05$ ) and language abilities (CELF Core Language Index Range: 48 to 138;  $M = 96.84$ ,  $SD = 19.61$ ). Overall mean ratings for the SRS and NASSQ-A were in the “at risk” ranges for ASD ( $M = 77.76$ ,  $SD = 10.67$ ) and anxiety disorders ( $M = 58.47$ ,  $SD = 21.59$ , 57% “at-risk”), respectively. Overall mean ratings for SP sensory seeking and SP-SA scales were in the “Same as Most” to “More

than Most” ranges, suggesting that ASD youth displayed equal to slightly greater amounts of sensory seeking and avoidance behavior on average than a normative sample of typically developing youth. Forty-nine percent of the sample took medication (31% SSRIs, 19% stimulants, 7% sympatholytics, 7% antipsychotics, 5% Buspar); however, there were no significant differences in the rates or severity of typical anxiety ( $t = -.13$ , *n.s.*) or atypical anxiety ( $t = -1.06$ , *n.s.*) for youth on or off medication.

#### *Reliability of the ADIS-C/P*

No significant differences in child age, ASD severity (SRS-P), typical or atypical anxiety were found for youth who did or did not complete retest assessments; however, youth who completed the retest had significantly higher IQ ( $t(58) = -2.16$ ,  $p = .04$ ). Interrater reliability of ADIS-C/P CSR scores conducted in 35% ( $n = 21$ ) of the sample for both typical anxiety (*ICC* range: .89 to .98) and atypical anxiety (*ICC* range: .96 to .99) was excellent. Percent exact agreement regarding typical and atypical anxiety disorders, calculated instead of Cohen’s Kappa due to the lower base rates of disorders in the subsample, was also highly consistent (percent exact agreement: 95% to 100%). Retest reliability ( $n = 15$ ) for typical anxiety (*ICC* range: .77 to .95) and atypical anxiety CSRs (*ICC* range: .88 to 1.00) suggested consistency over time. Percent exact agreement regarding all anxiety diagnoses from Time 1 to Time 2 was 100%.

#### *Prevalence of Disorders*

Table 2 summarizes the prevalence of atypical and DSM-IV anxiety disorders. Twenty five percent of youth with ASD had no co-occurring mental disorders. DSM-IV anxiety disorders (48%) and atypical anxiety disorders (46%) were the most prevalent co-occurring disorders, followed by ADHD (39%) and Major Depressive Disorder (20%).

Twenty four percent of youth presented with multiple co-occurring DSM-IV disorders in addition to ASD, and 24% presented with multiple DSM-IV anxiety disorders. Fifty percent of youth with one DSM-IV anxiety disorder also had another, whereas only 15% of youth with one atypical anxiety disorder also had another atypical anxiety disorder.

#### *Breakdown of Typical and Atypical Anxiety Disorder Prevalence*

Thirty-one percent of youth presented with both typical and atypical anxiety disorders (see Table 2). Seventeen percent of youth presented with only typical anxiety disorders and 15% presented with only atypical anxiety disorders. Thirty-seven percent of youth presented with neither typical nor atypical anxiety disorders. Amongst the anxiety disorders, specific phobias (30%) and GAD (22%) were most common, followed by social phobia (17%), separation anxiety disorder (10%), and OCD (2%) respectively. Panic disorder was not reported. Regarding atypical anxiety disorders, 22% presented with atypical GAD, 12% with atypical specific phobias, 8.5 % with atypical social phobia and 8.5% with atypical OCD.

#### *Predictors of Typical Anxiety Disorders*

Hierarchical, multiple regression analyses (Table 3) found that lower IQ ( $\beta = -.41$ ,  $t = -2.01$ ,  $p = .04$ ), more anxious self-talk (NASSQ-A  $\beta = .31$ ,  $t = 2.32$ ,  $p = .03$ ) and greater language ability ( $\beta = .46$ ,  $t = 2.39$ ,  $p = .02$ ) were independently associated with increased severity of typical anxiety (see Figure 1). The contribution of these variables to the model ( $\Delta R^2 = .22$ ,  $p = .006$ ) was substantially greater than that of SP –Sensory Seeking ( $\beta = .092$ ,  $t = .73$ ,  $n.s.$ ) and the SRS total ( $\beta = .09$ ,  $t = .68$ ,  $\Delta R^2 = .02$ ,  $n.s.$ ), which were not significantly associated with typical anxiety severity.

A one-way ANOVA revealed significant differences in typical anxiety severity by youths' category of IQ ( $F(2, 56) = 3.85, p = .03$ ): children with above average IQ ( $> 115; M = 1.67$ ) had significant less typical anxiety than children with below average ( $M = 3.63$ ) and average IQ ( $M = 3.46$ ), according to a Scheffé contrast,  $F(1, 56) = 7.02, p < .05, \omega^2 = .09$ .

In a second hierarchical multiple regression, SP-SA also significantly predicted typical anxiety severity and increased the amount of variance explained ( $\Delta R^2 = .1, p = .01$ ) after controlling for all Model 1 predictors. When IQ, anxious self-talk, language ability and sensory sensitivity were included in one model, 34% of the variance in typical anxiety levels was explained.

#### *Predictors of Atypical Anxiety*

When the same variables were examined as predictors of atypical anxiety, a different pattern emerged (Table 3; Figure 1). Whereas IQ ( $\beta = .001, t = .004, n.s.$ ) and language ability ( $\beta = .06, t = .33, n.s.$ ) were not significantly associated with atypical anxiety, anxious self-talk was (NASSQ-A  $\beta = .29, t = 2.09, p = .04$ ). In contrast to predicting typical anxiety models, this first block of variables did not significantly improve the model ( $\Delta R^2 = .07, n.s.$ ). ASD symptomology, a factor unrelated to typical anxiety, was the strongest predictor of atypical anxiety (SRS  $\beta = .30, t = 2.32, p = .03$ ). Further, the SRS when combined with sensory seeking tendencies, which were associated with atypical anxiety, but not independently significant (SP – Sensory Seeking  $\beta = .18, t = 1.37, p = .18$ ), significantly improved the amount of variance in atypical anxiety explained ( $\Delta R^2 = .15, p = .01$ ), an opposite pattern than that seen for typical anxiety. Also in contrast to typical anxiety, sensory sensitivity was not significantly associated with

atypical anxiety (SP-S/A  $\beta = .11$ ,  $t = .66$ ;  $\Delta R^2 = .007$ , *n.s.*). Collectively these variables explained 22% of the variance in atypical anxiety, in large part due to the contributions of autism symptomology and anxious self-talk to the model.

#### *Autism Symptoms, Typical and Atypical Anxiety*

Partial correlations examined the relationship of the SRS, typical and atypical anxiety scores (see Table 4). Whereas there was not a significant relationship between typical anxiety and SRS scores ( $R = .07$ , *n.s.*), both typical anxiety ( $R = .44$ ,  $p < .01$ ) and SRS scores ( $R = .33$ ,  $p < .01$ ) were significantly associated with atypical anxiety. Notably atypical anxiety was significantly associated with the SRS, even after potentially overlapping items from the SRS Mannerisms domain were removed ( $R = .34$ ,  $p = .01$ ). Further, the relationship between typical and atypical anxiety ( $R = .44$ ,  $p < .01$ ) was not diminished after controlling for the association of SRS and atypical anxiety.

### **Discussion**

The present study is the first to demonstrate (a) that anxiety, though prevalent in ASD, is not uniform; and (b) that some symptoms, previously considered aspects of ASD, may instead reflect an underlying, phenotypically distinct anxiety disorder. Specifically, findings suggests that “typical” and “atypical” presentations of anxiety disorders can be reliably distinguished in ASD across raters and over time (1-2 weeks) and are associated with divergent patterns of child characteristics. Typical anxiety symptoms were associated with IQ, language ability, and sensory sensitivity, whereas atypical anxiety symptoms were not. Both typical and atypical anxieties were predicted by anxious self-talk and significantly associated with one another, consistent with the notion that both reflect symptoms of anxiety disorders in ASD. However, only atypical

anxiety symptoms were also predicted by ASD severity and sensory seeking behavior, suggesting that they are both symptoms of anxiety and closely related to abnormalities inherent to ASD. Thus, consistent with Kerns and Kendall's (in press) proposal, results support the presence of both (a) typical, DSM-IV-consistent anxiety disorders in youth with ASD and (b) a separate variant of anxiety ("atypical anxiety") potentially altered by and/or related to ASD. These findings offer a novel perspective, which may elucidate inconsistencies regarding the prevalence and presentation of anxiety in ASD and inform future psychosocial and pharmacological treatments.

Findings suggest a prevalence of "typical," likely comorbid anxiety disorders in children with ASD. Excluding atypical anxiety symptoms, youth met full diagnostic criteria for a range of co-occurring DSM-IV anxiety disorders, including specific phobias (30%), generalized anxiety disorder (22%), social phobia (17%), separation anxiety disorder (10%) and OCD (2%). With the exception of OCD, these prevalence rates are substantially higher than those reported in the population (Merikangas et al., 2010), but within the range reported for children with ASD (White et al., 2009). Consistent with the high co-occurrence of childhood anxiety disorders generally (Silverman et al., 2001), 50% of ASD youth with at least one anxiety disorder met criteria for another anxiety disorder. Typical anxiety disorders were not related to the severity of ASD symptoms, rather, they were most likely to arise in a subset of youth with low to average IQ, whose verbal abilities were generally more proximal to those of typically developing children and who displayed cognitive and sensory vulnerabilities to anxiety (e.g. negative thinking, sensory sensitivity and avoidance; Kendall & Treadwell, 2007; Leung & Wong, 1998; Bellini, 2006). These findings are consistent with hypotheses that heightened

physiological arousal predisposes some youth to anxiety problems (Bellini, 2006), and that anxiety disorders may be harder to recognize in youth with more severe communication difficulties (Davis, Moree et al., 2001).

Atypical presentations of anxiety were as prevalent as typical anxiety disorders (46% and 48%, respectively). The co-occurrence of atypical and typical anxiety disorders was common, but not universal. Results suggest atypical anxiety as a distinct variant of anxiety in ASD rather than as a construct solely attributable to the ASD diathesis. Atypical anxiety was significantly associated with not only ASD symptomology and related sensory seeking behavior, but also greater typical anxiety and anxious self-talk, indicators of a separate, anxiety-based dimension. These results are consistent with Farrugia and Hudson's (2006) finding that youth with anxiety and Asperger's syndrome had significantly more negative automatic thoughts than youth with anxiety disorders alone, despite similar levels of typical anxiety. In the present study, the proportion of children (57%) meeting cut-off scores for anxiety disorder risk by the NASSQ-A was closer to that of children displaying typical or atypical anxiety disorders (63%) than those displaying typical anxiety disorders alone (48%). This discrepancy in negative automatic thoughts and typical anxiety symptoms across studies supports the idea that some anxious psychopathology in ASD youth (e.g. atypical anxiety) may be missed by unmodified, DSM-IV-based anxiety measures. Similarly, though the ADIS-C/P relies largely on a child's ability to articulate their fears to others, an inherently challenging task for many ASD youth, results do *not* indicate that atypical anxiety is simply a manifestation of typical anxiety in more impaired children. Whereas typical anxiety was associated with stronger language skills, atypical anxiety was apparent in children with a range of

intellectual and verbal abilities. Language difficulties may thus limit the diagnosis of typical, DSM-IV anxiety disorders, but likely do not account for the expression of atypical anxiety.

The Research Domain Criteria Project (RDoC; Sanislow, et al., 2010) offers a promising template for understanding and further researching the relationship of autism spectrum deficits with typical and atypical anxiety symptoms. According to this approach, anxiety, including the typical and atypical variants identified here, may best be understood as variable expressions of vulnerability within particular RDoC domains, such as the negative valence systems (i.e. active threat “fear”, potential threat “anxiety”, sustained threat “stress”). Whereas a child’s ASD symptoms may be largely related to abnormalities in RDoC systems for social processes (e.g. social imitation, theory of mind) or cognitive systems (e.g. attention), their anxiety may result from the confluence of these deficits within a vulnerable negative valence system (e.g., anxious cognitive style). Consistent with this reasoning, anxious self-talk, a construct related to anxiety disorder risk (Kendall & Treadwell, 2007), predicted both typical and atypical anxiety severity in the present study. Whether the atypical presentation of anxiety in some youth with ASD, in particular, reflects the interaction of such difficulties with ASD deficits (i.e., whether intense fears of novelty and change in ASD result from the combination of an anxious cognitive style and attention shifting difficulties inherent to ASD) should be explored in future research.

Future research must also address limitations in the present study. Given the ambiguity of atypical anxiety symptoms and the historical classification of at least some of these symptoms (e.g. insistence on sameness, unusual fears) as part of ASD, it is

possible that symptom overlap drove the association of SRS and atypical anxiety severity. This explanation is unlikely given that visual examination of the SRS items found few similar items and removal of these items did not significantly alter results. IQ was not associated with typical anxiety severity in the expected direction; rather, the typical anxiety of youth with very high IQ (greater than 115) in the present study was less severe than those with average to low IQ. This finding may be due to the novel distinction of typical and atypical anxiety as well as the unusually high intellectual abilities of some participants in the current study relative to previous samples (Leyfer et al., 2006; Simonoff et al., 2008; Sukhodolsky et al., 2008), but requires further study.

Other limitations include the emphasis of the ADIS-C/P on anxiety, which may have resulted in an underestimation of other childhood psychological disorders, and the higher intellectual abilities of youth who participated in the 1-2 week retest. Examination of whether anxiety in ASD youth with lower intellectual abilities can be reliably measured overtime is needed. Further, though there were advantages to conducting retest reliability analyses with the same rater, a manner consistent with prior psychometric studies of the ADIS-C/P and representative of how the interview has been used in clinical practice and controlled trials (Silverman et al., 2001), this method as well as the expertise of the present diagnosticians, may have inflated reliability findings. The reliable measurement of the typical and atypical anxiety disorders in less favorable conditions should be explored. Finally, the lack of demographic diversity in the current sample suggests that these results may not be generalizable to ASD youth of lower socioeconomic status and non-white race, an important area of future expansion.

The present findings require replication. How the distinction of typical and atypical anxiety disorders may influence findings regarding the prevalence and presentation of anxiety in ASD, moderate intervention outcomes, and influence estimations of ASD severity should be tested. The exclusion and inconsistent operationalization of atypical anxiety symptoms in prior studies highlights the limitations of existing anxiety measures, which may not distinguish the full range of co-occurring anxiety disorders in youth with ASD. Furthermore, whether anxiety measures and interventions developed for typically developing youth are equally appropriate and effective for the typical and atypical anxiety of youth with ASD is unclear. Though cognitive behavioral therapy (CBT) interventions for anxiety in ASD are promising, approximately 40 to 50% of youth continue to meet criteria for an anxiety disorder following treatment (Reaven, Blakely-Smith, Culhane-Shelburne, & Hepburn, 2012; Wood et al., 2009a). Poor distinction of typical and atypical anxiety variants may also explain, in part, why CBT interventions have been found to improve both anxiety and ASD symptoms (Wood et al., 2009b). More standardized, comprehensive characterization of the atypical anxiety construct, its behavioral and neurobiological commonalities as well as its distinctiveness from traditional anxiety symptoms, is needed to inform these questions, elucidate the relationship of anxiety and ASD, and determine the full implications of the present findings.

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## TABLES

*Table 1. Characteristics of Sample (n = 59)*

| <i>Descriptive Variables</i> | <b>N (%)</b> |   | <b>M (SD)</b>  | <b>Range</b> |
|------------------------------|--------------|---|----------------|--------------|
| Male                         | 46 (78%)     | Child Age in Months                       | 10.48 (2.63)   | 7 to 17      |
| Race                         |              | IQ  | 104.69 (19.05) | 67 to 158    |
| Caucasian                    | 54 (93%)     | CELF (n = 55)                             | 96.84 (19.61)  | 48 to 138    |
| Black                        | 2 (3.5%)     | SRS Total Raw Score                       | 77.76 (10.67)  | 52 to 90     |
| Biracial                     | 2 (3.5%)     | NASSQ Anxiety Scale (n = 56)              | 58.47 (21.59)  | 33 to 123    |
| Family Income (n = 53)       |              | Sensory Profile (n = 58)                  |                |              |
| Less than 60k                | 8 (15%)      | Sensory Seeking                           | 3.61 (1.07)    | 1 to 5       |
| 60k to < 100k                | 15 (25%)     | Sensory S/A                               | 3.93 (.83)     | 1 to 5       |
| 100k or more                 | 30 (50%)     |   |                |              |
| Not Reported                 | 6 (10%)      | <i>ADIS-C/P Clinical Severity Ratings</i> |                |              |
| Autism Spectrum Diagnosis    |              | DSM-IV Anxiety Severity                   | 3.12 (2.13)    | 0 to 8       |
| Autistic Disorder            | 43 (73%)     | ASD Anxiety Severity                      | 2.61 (2.26)    | 0 to 7       |
| Asperger's Disorder          | 5 (8.5%)     |   |                |              |
| PDD-NOS                      | 11 (18.5%)   |   |                |              |
| Taking Psychotropic          |              |   |                |              |
| Medication                   | 29 (49%)     |   |                |              |

*\*IQ calculated from the General Conceptual Abilities index of the Differential Abilities Scale or the Full Scale IQ of the Weschler Intelligence Scale for Children (n=1); CELF = Clinical Evaluation of Language Fundamentals, SRS = Social Responsiveness Scale, NASSQ = Negative Affective Self-Statement Questionnaire, PDD-NOS= Pervasive Developmental Disorder-Not Otherwise Specified; ADIS-C/P = Anxiety Disorders Interview- Child/Parent version; Sensory S/A = Sensory Sensitivity/ Avoidance.*

Table 2. DSM-IV Anxiety, Atypical Anxiety and Other Disorder Rates (N = 59)

| <i>Typical and Atypical Anxiety Disorder</i>                      | <b>N (%)</b> |
|---|--------------|
| No Anxiety Disorders  | 22 (37%)     |
| DSM-IV Anxiety Disorder   | 10 (17%)     |
| Atypical Anxiety Disorder   | 9 (15%)      |
| DSM-IV and Atypical Anxiety Disorders                             | 18 (31%)     |
| <i>Breakdown of DSM-IV Disorders</i>                              |              |
| No Comorbid Disorders   | 15 (25%)     |
| Generalized Anxiety Disorder                                      | 13 (22%)     |
| Separation Anxiety Disorder                                       | 6 (10%)      |
| Social Phobia   | 10 (17%)     |
| Specific Phobias  | 18 (30%)     |
| Obsessive Compulsive Disorder                                     | 1 (2%)       |
| Panic Disorder  | 0 (0%)       |
| ADHD  | 23 (39%)     |
| Major Depressive Disorder (Lifetime)                              | 12 (20%)     |
| Oppositional Defiant Disorder                                     | 4 (7%)       |
| Atypical Anxiety Disorder   | 27 (46%)     |
| <i>Breakdown of Multiple Comorbidities</i>                        |              |
| 2 or More DSM-IV Anxiety Disorders                                | 14 (24%)     |
| 2 or More Atypical Anxiety Disorders                              | 4 (7%)       |
| Multiple DSM-IV Comorbidities (DSM-IV anxiety and other disorder) | 12 (24%)     |

*Note. ASD = Autism Spectrum Disorder; ADHD = Attention Deficit-Hyperactivity Disorder*

Table 3. Multiple Regression Models: Predictors of Typical and Atypical Anxiety (n = 54)

| <i>Typical Anxiety</i>             | Model 1 |          |         | Model 2 |          |        |
|------------------------------------|---------|----------|---------|---------|----------|--------|
|                                    | $\beta$ | <i>t</i> | $R^2$   | $\beta$ | <i>T</i> | $R^2$  |
| Typical Predictors $\Delta R^2$    |         |          | 0.22 ** |         |          | —      |
| IQ                                 | -0.41   | -2.01 *  |         | -0.39   | -2.04 *  |        |
| NASSQ-A                            | 0.31    | 2.32 *   |         | 0.31    | 2.46 *   |        |
| CELF                               | 0.46    | 2.39 *   |         | 0.43    | 2.34 *   |        |
| Atypical Predictors $\Delta R^2$   |         |          | 0.02    |         |          | —      |
| SP seeking                         | 0.092   | 0.73     |         | -0.12   | -0.79    |        |
| SRS                                | 0.09    | 0.68     |         | 0.01    | 0.09     |        |
| Additional Predictors $\Delta R^2$ |         |          |         |         |          | 0.1 ** |
| SP - scale                         |         |          |         | 0.4     | 2.72 **  |        |
| $R^2$                              |         |          | 0.24    |         |          | 0.34   |

| <i>Atypical Anxiety</i>            | Model 1 |          |        | Model 2 |          |       |
|------------------------------------|---------|----------|--------|---------|----------|-------|
|                                    | $\beta$ | <i>t</i> | $R^2$  | $\beta$ | <i>T</i> | $R^2$ |
| Typical Predictors $\Delta R^2$    |         |          | 0.07   |         |          | —     |
| IQ                                 | 0.001   | 0.004    |        | 0.01    | 0.03     |       |
| NASSQ-A                            | 0.29    | 2.09 *   |        | 0.29    | 2.08 *   |       |
| CELF                               | 0.06    | 0.33     |        | 0.06    | 0.28     |       |
| Atypical Predictors $\Delta R^2$   |         |          | 0.15 * |         |          | —     |
| SP seeking                         | 0.18    | 1.37     |        | 0.13    | 0.8      |       |
| SRS                                | 0.3     | 2.32 *   |        | 0.29    | 2.1 *    |       |
| Additional Predictors $\Delta R^2$ |         |          |        |         |          | 0.007 |
| SP - scale                         |         |          |        | 0.11    | 0.66     |       |
| $R^2$                              |         |          | 0.22   |         |          | 0.22  |

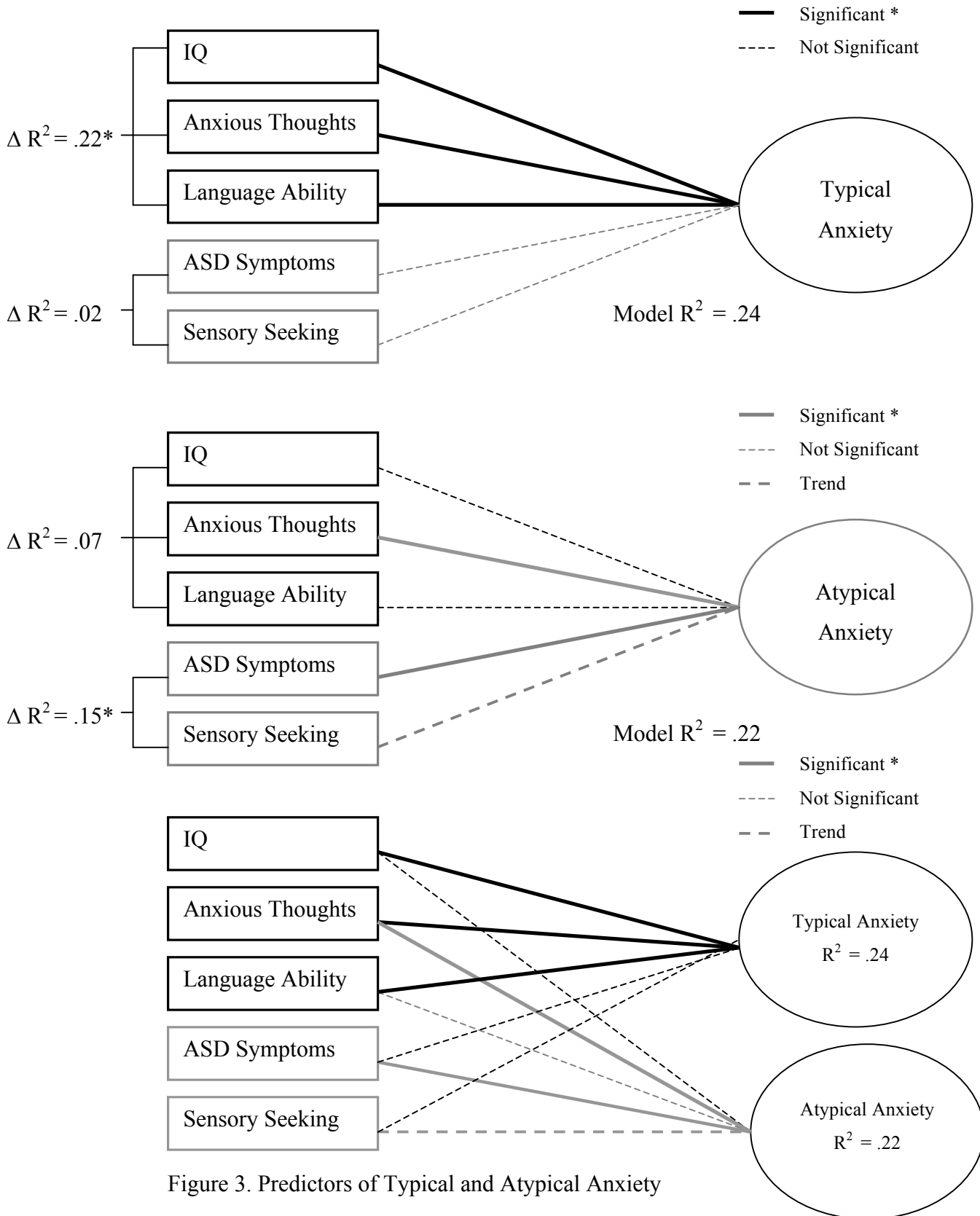
\* $p < .05$ , \*\* $p < .01$ ; NASSQ-A = Negative Affectivity Self-Statement Questionnaire – Anxiety Scale; CELF = Clinical Evaluation of Language Fundamentals; SP = Sensory Profile; SRS = Social Responsiveness Scale.

Table 4. Correlations and Partial Correlation of Anxiety, Atypical Anxiety and the SRS (N = 59)

|  | Typical Anxiety | Atypical Anxiety |
|--|-----------------|------------------|
| No Control Variables                         |                 |                  |
| Typical Anxiety                              | -               | -                |
| Atypical Anxiety                             | 0.44**          | -                |
| SRS – Total                                  | 0.07            | 0.33**           |
| SRS – Total (Mannerisms<br>Subscale Removed) | 0.08            | 0.29 *           |
| Controlling for SRS Total Score              |                 |                  |
| Typical Anxiety                              | -               | 0.44**           |

\*  $p < .05$ ; \*\*  $p < .01$ ; SRS = *Social Responsiveness Scale Total Raw Score*

FIGURES



CHAPTER 2  
LITERATURE REVIEW

## **The Presentation and Classification of Anxiety in ASD**

Anxiety has been an apparent, if 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 on these disorders as well as inform issues in the diagnosis and treatment of co-occurring child psychopathologies (Kendall & Drabick, 2010). This review addresses whether the anxiety symptoms seen in ASD are part of the ASD phenotype, true comorbidity [two disorders with distinct etiologies, pathologies and treatment implications present in the same individual in a manner consistent with their monomorbid form (Wood & Gadow, 2010)] and/or a novel syndrome of anxiety in ASD. 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, while evidence supporting the use of the term “comorbidity” is evaluated.

## **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 will manifest a concurrent pathology within 12 months (Kessler, Chiu, Demler, & Walters, 2005), a rate doubled in individuals with ASD (Hofvander, Delorme, Chaste, Nyden, Wentz, et al., 2009; Mattila, Hurtig, Haapsamo, Jussila, Kuusikko-Gauffin, et al.,

2010; Simonoff, Pickles, Charman, Chandler, Loucas, & Baird, 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, Berglund, Demier, Jin, Merikangas, & Walters, 2005; Kessler & Wang, 2008; Tomlinson, Brown, & Abrantes, 2004; Cerda et al., 2008).

Studies suggest comorbidity is typical in treatment seekers (Jacobi, Wittchen, Höltling, Höfler, Pfister, et al., 2004; Kendall, Compton, Walkup, Birmaher, Albano, et al., 2010; Wilk, West, Narrow, Marcus, Rubio-Stipec, 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 rather than a meaningful relationship between pathologies (Angold et al., 1999; Regier, Narrow, Kuhl, & Kupfer, 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 behaviorally defined, is less clear (Lilienfeld, Waldman, & Israel, 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 limit some empirically-supported treatments (ESTs) (Brown & Barlow, 1992), and elevated ASD symptoms may detract from child CBT for

anxiety disorders (Puleo & Kendall, 2010). There are ESTs for child anxiety (Silverman, Pina & Viswesvaran, 2008; Kendall, Hudson, Gosch, Flannery-Schroeder, & Suveg, 2008; Walkup, Albano, Piacentini, Birmaher, Compton, et al., 2008) and modified version of these treatments for ASD youth have produced promising gains (MacNeil, Lopes, & Minnes, 2009; White et al., 2009). These preliminary findings suggest that comorbid anxiety may be substantially 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. 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 sequelae 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 anxiety in ASD (as per Distinction 1), Distinction 2 and 3 will attempt to determine if anxiety in ASD presents as a true comorbid condition, resembling monomorbid anxiety in both presentation and etiology, or if it is better understood as a syndrome or variant of anxiety altered in its expression by ASD deficits (Wood & Gadow, 2010).

### **Distinction 1: Independent Pathology 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, 2010). For example, though 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 overtime 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, Fodstad, Jenkins, Hess, Moree, 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**

Though diagnostic overlap is often apparent in comorbid 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 phenotypic 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 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; Guttman-Steinmetz, Gadow, DeVincent, & Crowell, 2010). In their study of youth (6-16 years) with high-functioning ASD (IQ  $\geq$  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 clinical interviews and parent report 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, Folstein, Bacalman, Davis, Dinh, 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 (n = 109). Consequently, social phobia (8%) and 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 et al., 1998; Simonoff et al., 2008), but these approaches lack validation and have yielded variable results. Using semi-structured diagnostic assessments to characterize anxiety disorders in youth with autism (n = 15; M IQ = 70) and PDD-NOS (n = 29; M IQ = 79), Muris et al. (1998) reported that though 73% of their sample displayed ritualistic behavior, 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 (Leyfer et al., 2006; de Bruin, Ferdinand, Meester, Nijs, & Verheijs, 2007). Similarly, social phobia has been reported in approximately 8 to 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 is 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 ( $n = 54$ ;  $IQ \geq 80$ , 8-15 years) than in youth recruited from mainstream classrooms in the same community ( $n = 305$ ). Whether the remaining anxiety symptoms of this modified questionnaire provide a valid measure of social phobia in ASD was not assessed. Similarly, though Lecavalier (2006) found support for an anxiety cluster based on parent and teacher reports of behavioral issues in 487 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 some 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), consistent with a co-occurring psychopathology. Confidence in these and much of the findings regarding anxiety in ASD is substantially limited, however, by a lack of consensus regarding the differentiation of anxiety and ASD as well as by a nearly unanimous reliance on subjective anxiety measures. Though 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 not used 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) reported 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 the White et al. (2009) review. Prevalence appears largely influenced by sampling methods. In the two epidemiological studies reported to date, 42% of 112 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, Kuusikko, Mattila, Haapsamo, Ebeling, 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 to 42% and anxiety disorders reported in 39% (current) to 50% (lifetime) of individuals with ASD. Notably, though 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 an acceptable measure (44%; Leyfer et al., 2006). In samples recruited from treatment settings, where cases are likely to be more severe and comorbid (Mattila et al., 2010), estimates of problematic anxiety are somewhat higher, with anxiety symptom prevalence ranging from 14 – 59% of youth and anxiety disorder prevalence ranging from 35-55%. The highest prevalence estimates (e.g., 50-84%) appear accounted for by 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), United Kingdom (Simonoff et al., 2008), Finland (Mattila et al., 2010), Norway (Bakken, Helverschou, Eilertsen, Heggelund, Myrrbakk, & Martinsen, 2010) and Singapore (Ooi, Tan, Lim, Goh, & Sung, 2011), across children and adults (Hofvander et al., 2009; Sukhodolsky, Scahill, Gadow, Arnold, Aman, 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 entire sample of ASD

individuals (Gadow & Wood, 2010; Helverschou & Martinsen, 2010; Leyfer et al., 2006; Bellini, 2006).

### **ASD Diagnosis**

If anxiety is a core ASD feature, anxiety problems should present across ASD subtypes, including autism, Asperger's Disorder, and pervasive developmental disorder – not otherwise specified (PDD-NOS), and despite the severity of ASD pathology (Mayes & Calhoun, 2010). 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 112 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, however, potentially due to disagreements about ASD subtypes as well as a reliance on clinical diagnosis rather than evidence-based assessment 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 (ages 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 ( $IQ \geq 70$ ), Kanai, Koyama, Kato, Miyamoto, Osada, and Kurita (2004) observed both better social relatedness and more separation anxiety in PDD-NOS youth. Similarly, obsessions, generalized worries and generalized anxiety disorder (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, 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 66 ASD children (ages 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 ( $n = 33$ ), but less anxiety in those with autism ( $n = 33$ ). By contrast, in a larger sample of 735 infants and toddlers (ages 15-37 months), Davis et al. (2012) 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). Though 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 infants with ASDs. By comparison, mild to moderate, but not severe communication deficits, may result in greater anxiety for children and adolescents.

The pattern of these 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 reliable 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 in some cases, potentially engendered or elucidated by 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). Notably, whether these observed behaviors reflect

anxiety as opposed to other negative affects (e.g., anger, frustration) is unclear, particularly given the limited ability of intellectually impaired individuals to articulate their 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 172 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, Murray, Ahuja, & Smith (2010) observed that parents reported impairing anxiety in 79% versus 67% of high ( $n = 233$ ,  $IQ \geq 80$ ) and low functioning ( $n = 117$ ,  $IQ < 80$ ) 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. Further, amongst 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. Still, reports of impairing anxiety in ASD individuals regardless of intellectual impairment are consistent with the notion that some of these behaviors may be characteristic of ASD. Conversely, the alteration of these symptoms by intellectual ability, both in terms of symptom prevalence and expression, suggests potential, 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, such as specific and social phobias, were equally prevalent in ASD individuals with and without intellectual disability, whereas generalized, separation, and panic related worries as well as total anxiety symptoms were greater in those with higher IQ. Intellectual abilities may thus be more predictive of the form of anxiety symptoms, than the frequency of this pathology per se. 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 often corresponds with the increased social demands of adolescence), core features are 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 (Sukhodoksy et al., 2008; White & Robertson-Nay, 2009), and some forms of anxiety, such as 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). Notably, studies of ASD and anxiety in early development 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 & Roberston-Nay, 2009), may be qualitatively different from that shown to fluctuate overtime and elevate with increasing child awareness and age in other studies (Davis, Hess, Moree, Fodstad, Dempsey, et al., 2011).

This distinction informs studies that demonstrate a relationship between age and anxiety. Whereas teachers, but not parents, report anxiety problems in 3-5 year olds with ASD, anxiety problems appear more pronounced, evident to both parents and teachers, by age 6-12 years (Weisbrot et al., 2005). Further, in two studies assessing anxiety symptoms in preschoolers and children with ASD youth, 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 359, 8 to 15 year-old youth (54 high-functioning ASD versus 305 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 increased with age, an inverse pattern from that observed in typically developing youth, whose fears reduced overtime. Further, 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, again support multiple models of anxiety in ASD, potentially differentiated by the specific anxiety symptoms or behaviors being studied. Evidence of certain anxieties or anxiety-related behaviors in ASD across the lifespan, 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, specific and social fears predominate in younger ASD

children, remain constant overtime 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, may clarify whether or not these symptoms constitute a co-occurring psychopathology. Preliminary research suggests that ASD characterized by higher levels of anxiety may be biologically 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 99 youth with autism and 36 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, & Oswald (2010) reported that mothers' anxiety levels were associated with increased anxiety in 17 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 176 youth with autism from 57 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) observed that a family history of psychiatric difficulties, but not ASD, predicted the presence of co-occurring psychiatric problems, such as anxiety, in 238 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, DeVincent, & Schneider, 2008; Gadow et al., 2009), 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 weakness apparent in the majority of studies. Acknowledging this limitation, a review of studies suggests great variability, not universality in the prevalence of both anxiety disorders and impairing anxiety symptoms (range 11-84% across all studies), with anxiety problems occurring in approximately 40-55% 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 notable diagnostic overlap and association. Cumulatively, these 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 also 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, such as 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. Validated, multi-faceted assessments (e.g., bio-physiological as well as behavioral measures) 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. Like Distinction 1, though conclusions for Distinction 2 will be qualified by ambiguities currently inherent to anxiety measurement in ASD, consideration of the variable manifestations of anxiety in ASD may also inform such diagnostic difficulties. To determine if the anxiety symptoms commonly reported in ASD resembled a true comorbidity, phenotypically and etiological proximal to a monomorbidity anxiety disorder (Wood & Gadow, 2010), comparability will be assessed across five domains: (1) prevalence of specific anxiety disorders, (2) severity

of anxiety, (3) presentation of anxiety, (4) disorder onset and trajectory, and (5) treatment response.

### **Anxiety Disorder Types and Symptom Severity**

There is limited agreement regarding which anxiety disorders are most common in ASD. In the studies to examine types of anxiety disorders in ASD individuals, specific phobia, generalized anxiety disorder (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 behaviors appear more common (6-37%; Bakken et al., 2010; Gillott, Furnice, & Walter, 2001) in ASD youth than in typically developing populations (1%; Rapee, Schneiring, & Hudson, 2009).

There is minimal evidence to suggest more severe anxiety disorders in youth with ASD compared to youth without ASD. In the majority of studies, overall anxiety symptoms were equally severe or milder than those of youth with non-ASD psychiatric disorders (Gadow et al., 2005) and anxiety-disordered youth (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 65 adolescents with Asperger's syndrome according to parent, but not child reports. Further, some differences in the expression of anxiety have been noted. Farrugia and Hudson (2006) found that adolescents with Asperger's syndrome have significantly more negative automatic thoughts than anxious controls, though the severity of their anxiety symptoms was equivalent. 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 (ages 6-12 years) with ASD (n=284) and non-ASD disorders (n = 189), Gadow et al. (2005) observed that, excepting compulsions, 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 also 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 this population may have an unusual focus. In 109 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. The focus of specific phobias also often deviates between ASD and typically developing youth, with fears of the dark, storms, large crowds and closed spaces being more common only in ASD samples (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 this deviation 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 at least a portion of these phobias deviate from the phobias of typically developing youth in their focus.

Some diagnostic ambiguity and variability is 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 characteristic of this disorder, yet there is also some suggestion of comorbid social anxiety in this population. Though 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 demonstrated despite 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; Bellini, 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, & Kyrios (2007; N = 54) measured a range of repetitive behaviors in intellectually typical youth with ASD, OCD and typically developing controls recruited from the community. They observed that obsessions, routines and rituals were most pronounced and complex in youth with OCD, followed by youth with ASD and then controls. Whereas as the presentation of repetitive behaviors varied by age in the OCD group, age was unrelated to the presentation of obsessions, compulsions, repetitive movements or rigidity in ASD youth. Further, rates of OCD symptoms in ASD are substantially 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, but not all 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 50 adults with ASD to 50 typically developing adults with OCD, McDougle, Kresch, Goodman, Naylor, Volkmar, 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, however, given a notable 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 though 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. Though 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 preliminary results are in keeping with the proposed 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) observed 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 anxieties appears to occur later and to a lesser degree than that seen in typically developing youth.

Akin to monomorbid anxiety disorders, Davis, Hess et al.'s (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 (n = 359), but not typically developing controls (n = 305), whose social and evaluative concerns lessened overtime. These initial studies suggest that anxiety problems in ASD assume a similar, developmentally sensitive course to anxiety disorders in typically developing youth.

### **Treatment**

Though 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), such information provides an additional perspective. Treatment studies (Moree & Davis, 2010; Ooi, Lam, Sung, Tan, Goh, et al., 2008; Reaven, Blakeley-Smith, Nichols, Dasari, Flanigan, & Hepburn, 2009; White et al., 2009), including four randomized clinical trials (Chalfant et al. 2006; Sofronoff, Attwood, & Hinton, 2005; Wood, Drahota, Sze, Van Dyke, Decker et al., 2009), suggest that anxiety in youth with

ASD can be mitigated by cognitive behavioral treatment (CBT) adapted to suit their cognitive and social needs. Though a case study by Davis, Kurtz, Garder, 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 a family, rather than individual modality of CBT, in part due to their reduced engagement and completion of at-home exposures in individual treatment. These findings support the modification of existing manualized CBT programs to better engage ASD youth (Davis, et al., 2010; White et al., 2009; Wood et al., 2009). With adjustments for ASD, rates of positive treatment response at posttreatment and follow-up have exceeded 50%, consistent with response rates to CBT in typically developing anxiety disordered youth (e.g., Kendall et al., 2008; Silverman, Pina & Viswesvaran, 2008; Walkup et al., 2008).

The effectiveness of serotonin re-uptake inhibitors (SSRIs), a common pharmacological treatment for anxiety disorders in typically developing youth, in treating anxiety in ASD is unclear given the very small samples sizes of published studies ( $N < 25$  in all studies; Buitelaar, Van der Gaag, & Van der Hoeven, 1998; Couturier & Nicholson, 2002; Namerow, Thomas, Bostic, Prince, & Monuteaux, 2003). Preliminary results are consistent with published rates for SSRIs in non-ASD youth (Walkup et al., 2008), with 59 to 80% of ASD individuals displaying significant anxiety reductions following treatment with citalopram (Couturier & Nicholson, 2002; Namerow et al., 2003) and buspirone (Buitelaar et al., 1998). One very small study ( $N = 8$ ) observed that

higher-functioning ASD children (under age 7 year) appeared more responsive to SSRIs than those who are more severely affected (Awad, 1996).

**Conclusion 2: Is there evidence of comorbid anxiety disorders in ASD?**

Given the unclear relationship of anxiety and ASD symptoms per Distinction 1, interpretations regarding Distinction 2 should be considered preliminary. 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 Sequelae of ASD, a Covariant or Both?**

Relative to studies of anxiety prevalence and phenomenology, empirical investigations regarding the development of anxiety in ASD are scant and should be 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, such as another disorder, brain abnormality or shared genetic variant. 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 Sequelae 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, Mundy, Meyer, Sutton, Vaughan, & Charak, 2005), and Down syndrome (Evans et al., 2005). Further, 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 to 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). Though 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 psychiatric diagnoses, ADHD and mood disturbances

(Pine et al., 2008; Reiersen, Constantino, Volk, & Todd, 2007; Towbin et al., 2005). Further, in a sample of 93 youth (ages 8- 18 years) with mood and anxiety disorders, Towbin et al. (2005) suggested that elevated rates of ASD symptoms (62% of sample met cut-off 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. <I don't follow this conclusion

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; Guttman-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 59 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. Though 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).

Though 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. Though 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 and/or communication difficulties. 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, Cermak, Orsmond, Tager-Flusberg, Kadlec, & Carter, 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 may result in 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), requires investigation.

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 contribute to anxiety in social situations (Grodén, Baron, & Groden, 2006; Portway & Johnson, 2005) and social deficits have been associated with increased anxiety in both typically developing and ASD youth (Bellini, 2004; Bellini, 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 (Bauminger, Shulman, & Agam, 2003).

A growing number of 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 have been found to 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 41 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 children's understanding of their social deficits may be more influential and predictive of social anxiety than their actual social ability. Finally, though White & Roberson-Nay (2009) reported no association between social impairment and self-reported anxiety in 20 ASD children and adolescents (ages 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 & Robertson-Nay, 2009). Further, such social anxiety and withdrawal may aggravate youth's social deficits overtime 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, a disorder defined by a fear of social evaluation, in ASD 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 are 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, Thomeer, Volker, Toomey, Nida, 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. Further research is needed to confirm the presence of comorbid social phobia in ASD suggested, but not determined by these findings.

### **Theories of Indirect Causation**

Whereas social impairment and sensory hyper-reactivity have been suggested by some to predispose to anxiety disorders in ASD, it is also 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 direct 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 ( $n = 34$ ) than an age, gender and IQ matched sample of intellectually disabled youth. Though 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, Wood, & Weisz, 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 40 high functioning ( $IQ > 70$ ) ASD children with anxiety disorders who were treated with CBT. Still, much additional research is needed to confirm these hypotheses.

ASD may also be vulnerable to anxiety problems due to overarching difficulties regulating emotion and arousal. It has been hypothesized that ASD youth struggle to regulate and cope with anxiety due to inherent difficulties understanding and identifying

emotions (Capps, Yirmiya, and 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 has been shown to 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 et al.'s (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 further empirical investigation.

### **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. As discussed previously, studies of referred youth provide some support for this prediction: 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 pure 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, & Schumann, 2003; Apter & Allen, 1999; Chugani, Niimura, Chaturvedi, Muzik, Fakhouri, 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). Though 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 can 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 some 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 additional 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 subsequent lack of “gold standard,” 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 suggests both that (a) 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 autism spectrum disorders detailed in this review provide rationale for the identification of dimensions of behavior and neurobiological functioning (e.g., executive functioning, social processing systems) that likely underlie many 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 this 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 if anxiety results directly or indirectly from ASD symptomology, accompanies it, or arises via some combination of both causative and correlational models. At present, both causal and epiphenomenal models of anxiety in ASD have been proposed and require confirmation.

### **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 this populations, prolonging confusion regarding the appropriate classification of these symptoms. The problem appears self-perpetuating: discrepant diagnostic standards, a lack of valid, discriminating diagnostic instruments and reliance on limited measures have restricted what conclusions can be drawn from extant research. Diagnostic confusion is not unique to anxiety and ASD, but rather appears to be a chronic issue within current psychiatric nosology, where “Not Otherwise Specified” diagnoses are commonly 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/or a shift toward a diagnostic continuum approach are needed to more accurately address the questions raised by this review. Though studies provide support for co-occurring anxiety symptoms in ASD

(Distinction 1), they also suggest the presence of more atypical anxiety symptoms whose independence from the ASD diathesis is unclear. Moreover, whether reported anxiety symptoms reflect true comorbidities, phenomenologically (Distinction 2) and etiologically (Distinction 3) akin to monomorbid anxiety disorders is still unclear and may be difficult to determine without substantial changes in research methodologies.

Consensus regarding the differential diagnosis of anxiety disorders in ASD is needed. To create this consensus, anxiety measures developed in typically developing populations must be studied psychometrically in samples of ASD youth. Further, such a consensus would ideally be informed by biologically-based measurements (e.g., electrophysiological or neurobiological indicators) of anxiety. Such alternative assessments are warranted given the inherent challenge of recognizing and reporting emotional states for individuals with ASD. Biological contributions to anxiety may also help clarify the etiology of anxiety in ASD, a question integral to determining the presence of comorbidity. Empirically-based assessment of both traditional anxiety symptoms and the atypical, potentially ASD-specific anxiety symptoms discussed herein will help determine if such atypical symptoms should be conceptualized as aspects of ASD, anxiety or a unique behavioral dimension common to both disorders. Finally, a more comprehensive understanding of anxiety and ASD may call for a willingness to defer the notion of comorbidity and consider instead behavioral and neurobiological dimensions of functioning (e.g., emotion dysregulation, executive dysfunction) that may underlie and link both disorders.

In an effort to evaluate various models of anxiety in ASD and ultimately distinguish one, this review has instead implicated many. Indicated roles for anxiety in

ASD include that of a comorbid disorder, a core feature of ASD, and possibly a novel syndrome. Further, the relationship of ASD to co-occurring anxiety may be causal, correlational or a combination of the two. Confirmation and clarification of these roles, their origins, and their reliable differentiation in youth with ASD will be instrumental to progressing the future research, understanding and successful treatment of these disorders as well as provide a novel, potentially generalizable model of psychological comorbidity.

CHAPTER 3  
EXPANDED RESULTS

## EXPANDED RESULTS

Sample characteristics are summarized in Table 1. Participants for the present study were a mean age of 10.48 years ( $SD = 2.62$ ). The sample was predominantly Caucasian (93%) and male (78%) with moderate to high family income (75% of families reported that their yearly family income was \$60,000 or more). By their own report, 12% of fathers had completed high school, 10% a 2-year degree, 31% a bachelor's degrees and 24% a graduate degree. Eight percent of mothers had completed high school, 15% a 2-year degree, 44% a bachelor's degree, and 22% had received a graduate degree. Twenty three percent of fathers and 11% of mothers did not report on their educational level.

Table 1. Sample Characteristics (n = 59)

| <i>Descriptive Variables</i> | <b>N (%)</b>  |
|------------------------------|---------------|
| Male                         | 46 (78%)      |
| Race                         |               |
| Caucasian                    | 55 (93%)      |
| Black                        | 2 (3.5%)      |
| Biracial                     | 2 (3.5%)      |
| Family Income (n = 53)       |               |
| Less than 60k                | 8 (14%)       |
| 60k to < 100k                | 15 (25%)      |
| 100k or more                 | 30 (51%)      |
| Not Reported                 | 6 (10%)       |
| Autism Diagnosis             |               |
| Autistic Disorder            | 43 (73%)      |
| Asperger's Disorder          | 5 (8.5%)      |
| PDD-NOS                      | 11 (18.5%)    |
|                              | <b>M (SD)</b> |
| Child Age in Years           | 10.48 (2.62)  |

*Note. PDD-NOS= Pervasive Developmental Disorder-Not Otherwise Specified*

Table 2. Pharmacological Interventions (N = 59)

|                    | N (%)    | N                |                      |                         |                        |
|--------------------|----------|------------------|----------------------|-------------------------|------------------------|
|                    |          | No Anxiety<br>DX | DSM-IV<br>Anxiety DX | DSM-IV &<br>Atypical DX | Atypical<br>Anxiety DX |
| No Medications     | 30 (51%) | 13               | 6                    | 7                       | 4                      |
| Taking Medications | 29 (49%) | 9                | 4                    | 11                      | 5                      |
| SSRIs              | 15 (31%) | 5                | 2                    | 5                       | 3                      |
| Sympatholytic      | 4 (7%)   | 1                | 0                    | 2                       | 1                      |
| Buspar             | 3 (5%)   | 1                | 0                    | 2                       | 0                      |
| Stimulants         | 11 (19%) | 3                | 2                    | 2                       | 4                      |
| Antipsychotics     | 4 (7%)   | 2                | 0                    | 1                       | 1                      |

*Note.* Sympatholytic (*Guanfacine, Clonidine*); SSRIs = *Sympathetic Reuptake Inhibitors (Fluoxetine, Sertraline)*, Stimulants (*Adderall, Ritalin, Focalin, Concerta*); Antipsychotics (*Abilify, Risperdal*); CSR = *Clinician Severity Rating*

Chi square analyses revealed were no significant differences in the frequency of typical, atypical or both atypical and typical anxiety disorders in youth who were or were not taking medication overall or by each medication type.

Table 3. Correlation Matrix of All Potential Independent and Dependent Variables

|                         | Pearson's <i>R</i> |         |         |        |        |       |        |       |        |        |        |        |        |        |        |
|-------------------------|--------------------|---------|---------|--------|--------|-------|--------|-------|--------|--------|--------|--------|--------|--------|--------|
|                         | 1                  | 2       | 3       | 4      | 5      | 6     | 7      | 8     | 9      | 10     | 11     | 12     | 13     | 14     | 15     |
| 1 Child Age             | 1                  | -       | -       | -      | -      | -     | -      | -     | -      | -      | -      | -      | -      | -      | -      |
| 2 IQ                    | 0.02               | 1       | -       | -      | -      | -     | -      | -     | -      | -      | -      | -      | -      | -      | -      |
| 3 Verbal IQ             | 0.12               | 0.84**  | 1       | -      | -      | -     | -      | -     | -      | -      | -      | -      | -      | -      | -      |
| 4 Nonverbal IQ          | -0.12              | 0.89**  | 0.59**  | 1      | -      | -     | -      | -     | -      | -      | -      | -      | -      | -      | -      |
| 5 Spatial IQ            | 0.04               | 0.80**  | 0.46**  | 0.65** | 1      | -     | -      | -     | -      | -      | -      | -      | -      | -      | -      |
| 6 CELF Index            | -0.07              | 0.76**  | 0.82**  | 0.57** | 0.51** | 1     | -      | -     | -      | -      | -      | -      | -      | -      | -      |
| 7 SRS Total             | 0.04               | 0.10    | -0.03   | 0.12   | 0.21   | 0.10  | 1      | -     | -      | -      | -      | -      | -      | -      | -      |
| 8 SRS (no mannerisms)   | -0.06              | 0.13    | -0.08   | 0.18   | 0.26   | 0.08  | 0.91** | 1     | -      | -      | -      | -      | -      | -      | -      |
| 9 SP Low Registration   | -0.24              | -0.13   | -0.15   | -0.06  | -0.11  | -0.07 | 0.20   | 0.19  | 1      | -      | -      | -      | -      | -      | -      |
| 10 SP Seeking           | -0.50**            | -0.19   | -0.28*  | -0.08  | -0.12  | -0.21 | 0.23   | 0.23  | 0.42** | 1      | -      | -      | -      | -      | -      |
| 11 SP Sensitivity       | -0.29*             | -0.01   | -0.02   | -0.01  | 0.02   | 0.06  | 0.22   | 0.24  | 0.55** | 0.49** | 1      | -      | -      | -      | -      |
| 12 SP Avoidance         | -0.14              | -0.14   | -0.17   | -0.09  | -0.07  | -0.15 | 0.40** | 0.34* | 0.66** | 0.50** | 0.71** | 1      | -      | -      | -      |
| 13 SP-S/A               | -0.23              | -0.08   | -0.1    | -0.06  | -0.03  | -0.05 | -0.11  | 0.31* | 0.65** | 0.54** | 0.93** | 0.92** | 1      | -      | -      |
| 14 NASSQ-A              | -0.02              | -0.37** | -0.35** | -0.30* | -0.33* | -0.24 | 0.33*  | -0.10 | -0.06  | 0.07   | 0.00   | -0.01  | -0.01  | 1      | -      |
| 15 Typical Anxiety CSR  | -0.02              | -0.19   | -0.11   | -0.16  | -0.20  | 0.05  | 0.09   | 0.08  | 0.10   | 0.14   | 0.35** | 0.31*  | 0.36** | 0.36** | 1      |
| 16 Atypical Anxiety CSR | -0.05              | -0.05   | -0.07   | 0.01   | -0.10  | -0.02 | 0.33** | 0.29* | 0.09   | 0.27*  | 0.24   | 0.31*  | 0.30*  | 0.24   | 0.44** |

\*  $p < .05$ , \*\*  $p < .01$ ; CELF = Clinical Evaluation of Language Fundamentals, SRS = Social Responsiveness Scale, SP = Sensory Profile, SP-S/A = Sensory Profile - Sensitivity/Avoidance, NASSQ-A = Negative Affective Self-Statement Questionnaire - Anxiety Subscale; CSR = Clinical Severity Rating

A correlation matrix guided the selection of variables for the final analyses. Whereas child age was not included as a predictor due to its low correlations with either dependent variable, IQ and language ability (CELF core language index) were retained due to great theoretical support for including these variables. Specifically, language deficits may interfere with report and characterization of anxiety symptoms and both IQ and language abilities have been repeatedly studied, with mixed results, as predictors of anxiety in ASD youth (Davis et al., 2012; Gadow et al., 2005; Sukhodolskey et al., 2008). Correlation strength guided the selection of SP-Seeking as a predictor of atypical anxiety, the averaging of SP-Sensitivity and SP-Avoidance into one SP\_SA variable, and the inclusion of that SP-SA variable as an additional predictor in the multiple regression models.

Table 4. Relationship of the Sensory Avoidance and Sensory Sensitivity Subdomains of the Sensory Profile

|                        |      |
|------------------------|------|
| Cronbach's Alpha       | 0.83 |
| Intraclass Correlation | 0.83 |
| Pearson Correlation    | 0.71 |

Table 4 provides additional support for the averaging of the SP-Sensitivity and SP-Avoidance variables given the high association and consistency of these constructs.

Table 5. Independent and Dependent Variable Summary (N = 59)

|   | <b>M (SD)</b>  | <b>Range</b> |
|---|----------------|--------------|
| <i>Independent Variables</i>              |                |              |
| IQ  | 104.69 (19.05) | 67 to 158    |
| CELF (n = 55)                             | 96.84 (19.61)  | 48 to 138    |
| SRS Total Raw Score                       | 77.76 (10.67)  | 52 to 90     |
| NASSQ Anxiety Scale (n = 56)              | 58.47 (21.59)  | 33 to 123    |
| <i>Sensory Profile (n = 58)</i>           |                |              |
| Sensory Seeking                           | 3.61 (1.07)    | 1 to 5       |
| Sensory Sensitivity/ Avoidance            | 3.93 (.83)     | 1 to 5       |
| <i>ADIS-C/P Clinical Severity Ratings</i> |                |              |
| DSM-IV Anxiety Severity                   | 3.12 (2.13)    | 0 to 8       |
| ASD Anxiety Severity                      | 2.61 (2.26)    | 0 to 7       |

*Note.* IQ calculated from the General Conceptual Abilities index of the Differential Abilities Scale or the Full Scale IQ of the Weschler Intelligence Scale for Children (n=1); CELF = Clinical Evaluation of Language Fundamentals, SRS = Social Responsiveness Scale, NASSQ = Negative Affective Self-Statement Questionnaire; ADIS-C/P = Anxiety Disorders Interview- Child/Parent version.

Means and standard deviations for all independent and dependent variables are presented in Table 5. Youth displayed a wide, but normally distributed range of intellectual and language abilities. IQ ranged from 67 to 158, with a mean of 104.69 (SD =19.05).

Language ability, measured by the Core Language Index of the CELF, ranged from 48 to 138, with a mean of 96.84 (19.61). Data was missing for a small number of some scales, including 4 CELFs, 3 NASSQs, and 2 sensory profiles. Overall mean ratings for the SRS and NASSQ-A were in the “at risk” ranges for ASD and anxiety disorders, respectively.

Overall mean ratings for the SP sensory seeking and SP sensitivity/avoidance scales were

in the “Same as Most” to “More than Most” ranges, suggesting that ASD youth displayed equal to slightly more amounts of sensory seeking and avoidance behavior on average than a normative sample of typically developing youth.

Table 6. Interrater and Test-Retest Reliability on ADIS-C/P

|                     | Interrater Reliability (n = 21; 35%) |             | Test-Retest Reliability (n = 15; 25%) |             |
|---------------------|--------------------------------------|-------------|---------------------------------------|-------------|
|                     | Reliability                          |             | Reliability                           |             |
|                     | of CSRs                              | % Agreement | of CSRs                               | % Agreement |
| Typical Anxiety     |                                      |             |                                       |             |
| SAD                 | 0.96                                 | 100%        | 0.85                                  | 100%        |
| Social Phobia       | 0.98                                 | 95%         | 0.77                                  | 100%        |
| Specific            |                                      |             |                                       |             |
| Phobia              | 0.97                                 | 100%        | 0.85                                  | 100%        |
| GAD                 | 0.98                                 | 100%        | 0.95                                  | 100%        |
| OCD                 | 0.89                                 | 100%        | -                                     | -           |
| Atypical Anxiety    |                                      |             |                                       |             |
| Atypical Social     |                                      |             |                                       |             |
| Phobia              | 0.98                                 | 100%        | 1                                     | 100%        |
| Atypical            |                                      |             |                                       |             |
| Specific Phobia     | 0.99                                 | 100%        | 0.98                                  | 100%        |
| Atypical GAD        | 0.98                                 | 100%        | 0.88                                  | 100%        |
| Atypical OCD        | 0.96                                 | 100%        | 0.89                                  | 100%        |
| Principal Diagnosis | 0.97                                 | 91%         | 0.91                                  | 100%        |

*Note. Percent agreement for diagnoses was calculated instead of Cohen’s Kappa due to the low base rate of individual diagnoses in these sub-samples. Additionally, test-retest reliability could not be calculated for OCD as these symptoms were not present in the selected sub-sample.*

*ADIS-C/P = Anxiety Disorders Interview Schedule-Child/Parent, CSR = Clinical Severity Rating, SAD = Separation Anxiety Disorder, GAD - Generalized Anxiety Disorder, Obsessive Compulsive Disorder, ASD = Autism Spectrum Disorder*

Inter-rater and 1-2 week re-test reliability for both typical and atypical CSR ratings and diagnoses was excellent (Table 6). There was also good agreement regarding which disorders were the most severe in each child (i.e. principal diagnosis). Table 7 displays the reliability of parent and child ratings of typical and atypical anxiety disorders on the ADIS-C/P. Results suggest moderate consistency between children and parents with the exception of OCD.

Table 7. Child and Parent Agreement on ADIS-C/P

|                         | Reliability of GIRs<br>(Pearson's R) | Reliability of<br>GIRs (ICCs) | % Agreement on<br>Diagnosis |
|-------------------------|--------------------------------------|-------------------------------|-----------------------------|
| <b>Typical Anxiety</b>  |                                      |                               |                             |
| SAD                     | 0.66                                 | 0.65                          | 90%                         |
| Social Phobia           | 0.66                                 | 0.76                          | 88%                         |
| GAD                     | 0.79                                 | 0.77                          | 85%                         |
| OCD                     | 0.29                                 | 0.29                          | 97%                         |
| <b>Atypical Anxiety</b> |                                      |                               |                             |
| ASD Social Phobia       | 0.66                                 | 0.60                          | 92%                         |
| ASD Specific Phobia     | 0.45                                 | 0.45                          | 85%                         |
| ASD GAD                 | 0.52                                 | 0.48                          | 78%                         |
| ASD OCD                 | 0.59                                 | 0.56                          | 95%                         |

*Note. ADIS-C/P = Anxiety Disorders Interview Schedule-Child/Parent, GIR = Global Interference Rating, SAD = Separation Anxiety Disorder, GAD - Generalized Anxiety Disorder, Obsessive Compulsive Disorder, ASD = Autism Spectrum Disorder*

Table 8. Comparability of Full and 1-2 Week Follow-up Sample

|                      | Mean (SD)      |                | Critical Value (df) |
|----------------------|----------------|----------------|---------------------|
|                      | No Follow-Up   | Follow Up      |                     |
| IQ Level             | 101.77 (2.32)  | 113.27 (21.63) | $t(57) = -2.07^*$   |
| Child Age            | 127.09 (34.19) | 122.00 (22.41) | $t(57) = 0.54$      |
| SRS Total            | 78.72 (12.27)  | 77.00 (10.67)  | $t(57) = 0.49$      |
| Typical Anxiety CSR  | 3.00 (2.13)    | 3.47 (2.17)    | $t(57) = 0.47$      |
| Atypical Anxiety CSR | 2.57 (2.32)    | 2.73 (2.12)    | $t(57) = 0.81$      |

\*  $p < .05$ ; CSR = clinician severity rating

Table 8 compares youth who did and did not complete the follow-up assessments.

Though youth who completed the follow-up assessment had significant higher IQ, they were no different from youth who did complete follow-up assessments in terms of age, ASD, typical or atypical anxiety severity.

Table 9. Frequency of DSM-IV and Atypical Anxiety Disorders (N = 59)

| <i>Breakdown of Multiple Comorbidities</i> |          |
|--|----------|
| No Comorbid Disorders                      | 15 (25%) |
| 2 or More Anxiety Disorders                | 14 (24%) |
| 2 or More ASD Anxiety Disorders            | 4 (7%)   |
| Multiple Comorbidities (anxiety and other) | 12 (24%) |
| <i>Breakdown of DSM-IV Disorders</i>       |          |
| Generalized Anxiety Disorder               | 13 (22%) |
| Separation Anxiety Disorder                | 6 (10%)  |
| Social Phobia                              | 10 (17%) |
| Specific Phobias                           | 18 (30%) |
| Obsessive Compulsive Disorder              | 1 (2%)   |
| Panic Disorder                             | 0 (0%)   |
| ADHD                                       | 23 (39%) |
| Major Depressive Disorder (Lifetime)       | 12 (20%) |
| Oppositional Defiant Disorder              | 4 (7%)   |
| ASD Anxiety Disorder                       | 28 (47%) |

*Note.* ASD = Autism Spectrum Disorder; ADHD = Attention Deficit-Hyperactivity Disorder

Twenty five percent of youth with ASD had no co-occurring mental disorders. DSM-IV anxiety disorders (48%) and atypical anxiety disorders (46%) were the most prevalent co-occurring disorders, followed by ADHD (39%) and Major Depressive Disorder (20%). Twenty four percent of youth presented with multiple co-occurring disorders in addition to ASD, and 24% presented with multiple anxiety disorders. Multiple atypical anxiety disorders were less common (7%). Amongst these complex profiles of multiple co-occurring disorders, anxiety disorders were the most severe co-occurring disorder (34%), followed by atypical anxiety (19%) and ADHD (19%). Amongst the anxiety disorders,

specific phobias (30%) and GAD (22%) were most common, followed by social phobia (17%), separation anxiety disorder (10%), and OCD (2%) respectively. Panic disorder was not reported. See Figure 1.

Table 10. DSM-IV and ASD Anxiety Disorder Rates (N = 59)

|                                       | <b>N (%)</b> |
|---------------------------------------|--------------|
| No Anxiety Disorders                  | 22 (37%)     |
| DSM-IV Anxiety Disorder               | 10 (17%)     |
| Atypical Anxiety Disorder             | 9 (15%)      |
| DSM-IV and Atypical Anxiety Disorders | 18 (31%)     |

*Note. ASD = Autism Spectrum Disorder*

Thirty-one percent of youth presented with both typical and atypical anxiety disorders. By contrast, 17% of youth presented with only typical anxiety disorders and 15% presented with only atypical anxiety disorders. Thirty-seven percent of youth presented with neither typical nor atypical anxiety disorders. See Figure 2.

Table 11. Multiple Regression Models: Predictors of Typical and Atypical Anxiety (n = 54)

| <i>Typical Anxiety</i>            | Model 1 |          |         | Model 2 |          |        |
|-----------------------------------|---------|----------|---------|---------|----------|--------|
|                                   | $\beta$ | <i>T</i> | $R^2$   | $\beta$ | <i>t</i> | $R^2$  |
| Typical Predictors $\Delta R^2$   |         |          | 0.22 ** |         |          | —      |
| IQ                                | -0.41   | -2.01 *  |         | -0.39   | -2.04    |        |
| NASSQ-A                           | 0.31    | 2.32 *   |         | 0.31    | 2.46 *   |        |
| CELF                              | 0.46    | 2.39 *   |         | 0.43    | 2.34 *   |        |
| Atypical Predictors $\Delta R^2$  |         |          | 0.02    |         |          | —      |
| SP seeking                        | 0.092   | 0.73     |         | -0.12   | -0.79    |        |
| SRS                               | 0.09    | 0.68     |         | 0.01    | 0.09     |        |
| Ambiguous Predictors $\Delta R^2$ |         |          |         |         |          | 0.1 ** |
| SP - scale                        |         |          |         | 0.4     | 2.72 **  |        |
| $R^2$                             |         |          | 0.24    |         |          | 0.34   |

| <i>Atypical Anxiety</i>           | Model 1 |          |        | Model 2 |          |       |
|-----------------------------------|---------|----------|--------|---------|----------|-------|
|                                   | $\beta$ | <i>T</i> | $R^2$  | $\beta$ | <i>t</i> | $R^2$ |
| Typical Predictors $\Delta R^2$   |         |          | 0.07   |         |          | —     |
| IQ                                | 0.001   | 0.004    |        | 0.01    | 0.03     |       |
| NASSQ-A                           | 0.29    | 2.09 *   |        | 0.29    | 2.08 *   |       |
| CELF                              | 0.06    | 0.33     |        | 0.06    | 0.28     |       |
| Atypical Predictors $\Delta R^2$  |         |          | 0.15 * |         |          | —     |
| SP seeking                        | 0.18    | 1.37     |        | 0.13    | 0.8      |       |
| SRS                               | 0.3     | 2.32 *   |        | 0.29    | 2.1 *    |       |
| Ambiguous Predictors $\Delta R^2$ |         |          |        |         |          | 0.007 |
| SP - scale                        |         |          |        | 0.11    | 0.66     |       |
| $R^2$                             |         |          | 0.22   |         |          | 0.22  |

\* $p < .05$ , \*\* $p < .01$ ; NASSQ-A = Negative Affectivity Self-Statement Questionnaire – Anxiety Scale; CELF = Clinical Evaluation of Language Fundamentals; SP = Sensory Profile; SRS = Social Responsiveness Scale.

Hierarchical, multiple regression analyses found that lower IQ ( $\beta = -.41, t = -2.01, p = .04$ ), greater anxious thoughts (NASSQ-A  $\beta = .31, t = 2.32, p = .03$ ) and language ability ( $\beta = .46, t = 2.39, p = .02$ ) were independently associated with increased typical anxiety severity (see Figure 2). The contribution of these variables to the model ( $\Delta R^2 = .22, p = .006$ ) was significantly greater than that of SP seeking ( $\beta = .092, t = .73, n.s.$ ) and SRS scores ( $\beta = .09, t = .68, \Delta R^2 = .02, n.s.$ ), which were not associated with typical

anxiety severity. In a second hierarchical multiple regression model, sensory sensitivity/avoidance (SP-SA) also significantly predicted typical anxiety severity and increased the amount of variance explained ( $\Delta R^2 = .1, p = .01$ ) after controlling for all Model 1 predictors. When IQ, anxious thoughts, language ability and sensory sensitivity were included in one model, 34% of the variance in typical anxiety levels was explained.

When the same variables were examined as predictors of atypical anxiety, a distinct pattern emerged. Whereas IQ ( $\beta = .001, t = .004, n.s.$ ) and language ability ( $\beta = .06, t = .33, n.s.$ ) were not significantly associated with atypical anxiety, anxious thoughts were (NASSQ-A  $\beta = .29, t = 2.09, p = .04$ ). In contrast to typical anxiety models, this first block of predictors did not significantly improve the model ( $\Delta R^2 = .07, n.s.$ ). Autism symptomology, a factor unrelated to typical anxiety, was the strongest predictor of atypical anxiety ( $\beta = .30, t = 2.32, p = .03$ ). Further, the SRS when combined with sensory seeking tendencies, which were associated with atypical anxiety, but not significant ( $\beta = .18, t = 1.37, p = .18$ ), significantly improved the amount of variance atypical anxiety explained ( $\Delta R^2 = .15, p = .01$ ), an opposite pattern than that seen for typical anxiety. Also, in contrast to typical anxiety, sensory sensitivity was not significantly associated with atypical anxiety ( $\beta = .11, t = .66; \Delta R^2 = .007, n.s.$ ). Collectively these variables explained 22% of the variance in atypical anxiety, in large part due to the contributions of autism symptomology and anxious self-talk to the model. See Figure 3.

Table 12. Multiple Regression Models: Sensitivity Analysis (n = 50)

| <i>Typical Anxiety</i>            | Model 1 |          |                       | Model 2 |          |                       |
|-----------------------------------|---------|----------|-----------------------|---------|----------|-----------------------|
|                                   | Slope   | <i>T</i> | <i>R</i> <sup>2</sup> | Slope   | <i>t</i> | <i>R</i> <sup>2</sup> |
| Typical Predictors $\Delta R^2$   |         |          | 0.21 *                |         |          | —                     |
| IQ                                | -0.4    | -1.91    |                       | -0.28   | -1.46    |                       |
| NASSQ-A                           | 0.3     | 2.13 *   |                       | 0.33    | 2.52 *   |                       |
| CELF                              | 0.45    | 2.27 *   |                       | 0.35    | 1.92 *   |                       |
| Atypical Predictors $\Delta R^2$  |         |          | 0.03                  |         |          | —                     |
| SP seeking                        | 0.16    | 1.13     |                       | -0.17   | -1.05    |                       |
| SRS                               | 0.04    | 0.31     |                       | -0.04   | -0.32    |                       |
| Ambiguous Predictors $\Delta R^2$ |         |          |                       |         |          | 0.14 *                |
| SP - scale                        |         |          |                       | 0.52    | 3.16 **  |                       |
| <i>R</i> <sup>2</sup>             |         |          | 0.24                  |         |          | 0.38                  |
| <i>ASD Anxiety</i>                | Model 1 |          |                       | Model 2 |          |                       |
|                                   | Slope   | <i>T</i> | <i>R</i> <sup>2</sup> | Slope   | <i>t</i> | <i>R</i> <sup>2</sup> |
| Typical Predictors $\Delta R^2$   |         |          | 0.06                  |         |          | —                     |
| IQ                                | -0.07   | -0.35    |                       | -0.04   | -0.2     |                       |
| NASSQ-A                           | 0.27    | 1.86     |                       | 0.27    | 1.89     |                       |
| CELF                              | 0.04    | 0.2      |                       | 0.02    | 0.07     |                       |
| Atypical Predictors $\Delta R^2$  |         |          | 0.18 *                |         |          | —                     |
| SP seeking                        | 0.18    | 1.27     |                       | 0.09    | 0.49     |                       |
| SRS                               | 0.34    | 2.46 *   |                       | 0.32    | 2.24 *   |                       |
| Ambiguous Predictors $\Delta R^2$ |         |          |                       |         |          | 0.01                  |
| SP - scale                        |         |          |                       | 0.14    | 0.76     |                       |
| <i>R</i> <sup>2</sup>             |         |          | 0.24                  |         |          | 0.25                  |

\**p* < .05, \*\**p* < .01; NASSQ-A = Negative Affectivity Self-Statement Questionnaire – Anxiety Scale; CELF = Clinical Evaluation of Language Fundamentals; SP = Sensory Profile; SRS = Social Responsiveness Scale.

Given the high DFBETA values for SP Seeking for some participants (n = 4), a sensitivity analysis, in which these potentially influential participants were removed, was conducted. Results suggest a similar pattern of findings despite the restriction of sample size and thus also power. Though some associations were slightly weaker and thus no longer significant (e.g. IQ for typical anxiety and NASSQ-A for atypical anxiety), the distinct pattern of predictors for typical and atypical anxiety remained clear and consistent with the original analyses.

Table 13. Full and Partial Correlations of Typical Anxiety, Atypical Anxiety and the SRS (N = 59)

|                                  | Typical Anxiety | Atypical Anxiety |
|----------------------------------|-----------------|------------------|
| No Control Variables             |                 |                  |
| Typical Anxiety                  | -               | -                |
| Atypical Anxiety                 | 0.44**          | -                |
| SRS – Total                      | 0.07            | 0.33**           |
| SRS – Total (Mannerisms Removed) | 0.08            | 0.29 *           |
| Controlling for SRS Total Score  |                 |                  |
| Typical Anxiety                  | -               | 0.44**           |

\*  $p < .05$ ; \*\*  $p < .01$ ; SRS = Social Responsiveness Scale Total Raw Score

Partial correlations were conducted to clarify the relationship of the SRS, typical and atypical anxiety scores. Whereas there was not a significant relationship between typical anxiety and SRS scores, both typical anxiety ( $R = .439, p < .01$ ) and SRS scores ( $R = .33, p < .01$ ) were significantly associated with atypical anxiety. Notably atypical anxiety was significantly associated with the SRS, even after potentially overlapping items from the SRS Mannerisms domain were removed ( $R = .34, p = .01$ ). Further, the relationship between typical and atypical anxiety was not explained by the association of SRS and atypical anxiety ( $R = .44, p < .01$ ).

Table 14. One-way ANOVA of Typical Anxiety Severity by IQ Level

|                | Mean (SE)   | <i>F</i> ( <i>df</i> ) | <i>P</i> |
|----------------|-------------|------------------------|----------|
| IQ Level       |             | 3.85                   | 0.03     |
| Less than 85   | 3.89 (2.57) |                        |          |
| 85 to 114      | 3.46 (1.99) |                        |          |
| 115 or Greater | 1.67 (1.72) |                        |          |

A one-way ANOVA revealed significant differences by youth's category of IQ ( $F(2, 56) = 3.85, p = .03$ ; Table 9). Specifically, children with above average IQ (greater than 115;  $M = 1.67$ ) had significant less anxiety than other children ( $M = 3.63$  for youth with IQ < 85 and  $M = 3.46$  for youth with IQ between 86 and 114), according to a Scheffé contrast,  $F(1, 56) = 7.02, p < .05, \omega^2 = .09$ . See Figure 4.

Table 15. Studies Focusing on Prevalence of Anxiety in ASD

| Author (Year)            | Sample Size and Type  | Age range                             | IQ                               | Comparison Group                  | Diagnostic Instrument  | Summary  |
|--------------------------|---|---------------------------------------|----------------------------------|-----------------------------------|--|--|
| <i>Anxiety Disorders</i> |   |                                       |                                  |                                   |  |  |
| de Bruin et al. (2005)   | N = 94 PDDNOS, 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 disorders (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 | age M = 29 years, age R = 16-60 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)   |

Table 15, continued

|                      |  |                           |                                     |   |  |  |
|----------------------|--|---------------------------|-------------------------------------|---|--|--|
| 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 1 anxiety disorder (63% specific phobia, 28% avoidant disorder, 27% SAD, 22% overanxious disorder, 11% OCD)  |
| 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   |

Table 15, continued

|                         |   |                                |  |   |  |   |
|-------------------------|---|--------------------------------|--|---|--|---|
| Simonoff et al. (2008)  | N = 112 (81 autism, 77 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) |
| <i>Anxiety Symptoms</i> |   |                                |  |   |  |   |
| 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 cut-off criteria for anxiety disorders versus 9% in intellectual disability only group   |
| Bellini (2004)          | N = 41 (19 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 cut-off scores for social phobia  |

Table 15, continued

|                       |   |            |                     |  |   |  |
|-----------------------|---|------------|---------------------|--|---|--|
| Bradley et al. (2004) | N = 24 (12 autism and intellectual disability, 12 intellectual disability only) community sample  | M = 16 yrs | IQ < 75             | Individuals with Intellectual disability only  | Diagnostic Assessment for the Severely Handicapped-II (DASH-II) | 42% met cut-off 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 cut-off 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 (103 autism, 80 AS, 118 PDD-NOS, 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 cut-off scores for social phobia; more teacher and parent report compulsions, specific phobias and social phobia in ASD kids compared to all control groups                          |

Table 15, continued

|                     |   |  |   |   |   |   |
|---------------------|---|--|---|---|---|---|
| Hurtig et al (2009) | N = 264 (24 AS, 23 autism, 217 youth from regular education classes) epidemiological study in Finland | 11-17 years, ASD<br>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 = 1810 (40 autism, 19 AS, 1751 typically developing youth) community sample                         | Participants assessed at 2 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 cut-off scores on clinical internalizing subscale, 13.6% on OAD subscale, 8.5% on SAD 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. (2010)   | 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  | 33.8% met cut-off scores on CBCL anxiety disorder subscale  |

Table 15, continued

|                           |  |                           |  |      |   |  |
|---------------------------|--|---------------------------|--|------|---|--|
| 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 1 anxiety disorder (9% GAD, 31% specific phobia, 5% panic, 19% social phobia, 10% SAD); GAD, panic disorder, SAD and overall anxiety severity was greater for those with an IQ > 70; social phobia and specific phobia were equally prevalent in youth with IQs above and below 70 |
|---------------------------|--|---------------------------|--|------|---|--|

*ASD = autism spectrum disorder, AS = Asperger's Syndrome, PDD-NOS = pervasive developmental disorder - not otherwise specified*

FIGURES

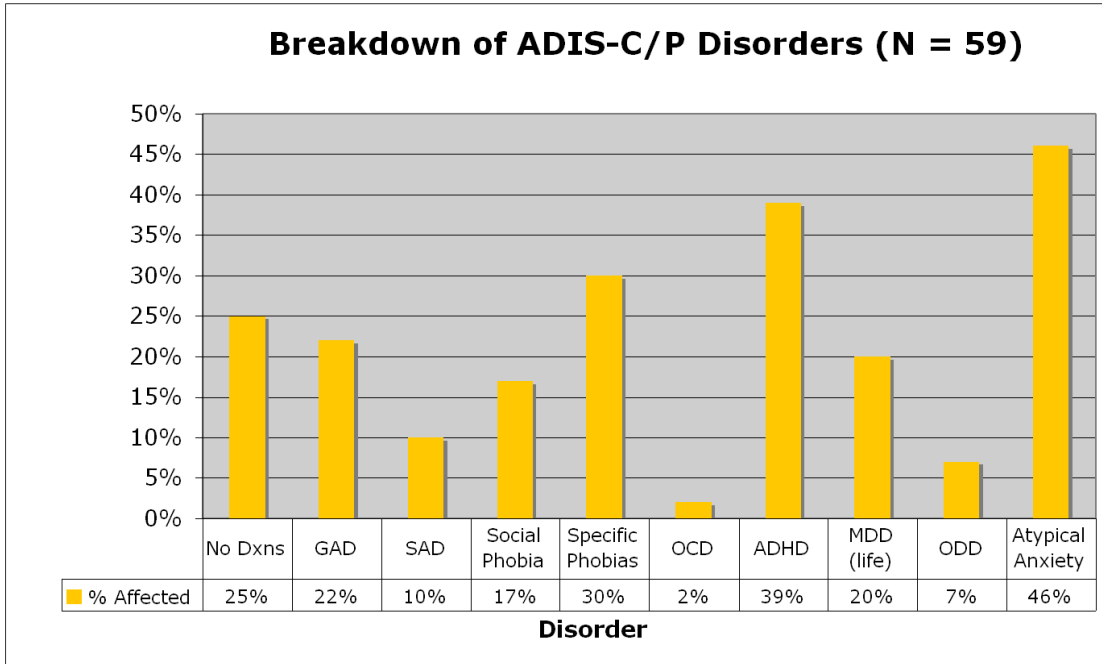


Figure 1. Breakdown of Anxiety and Other Disorders per ADIS-C/P

## Typical & Atypical Anxiety

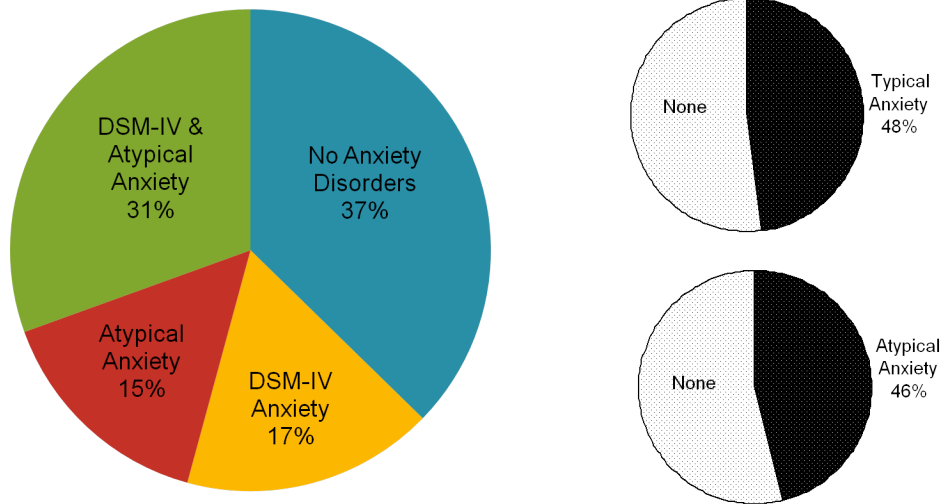


Figure 2. Frequency of Typical and Atypical Anxiety Disorders

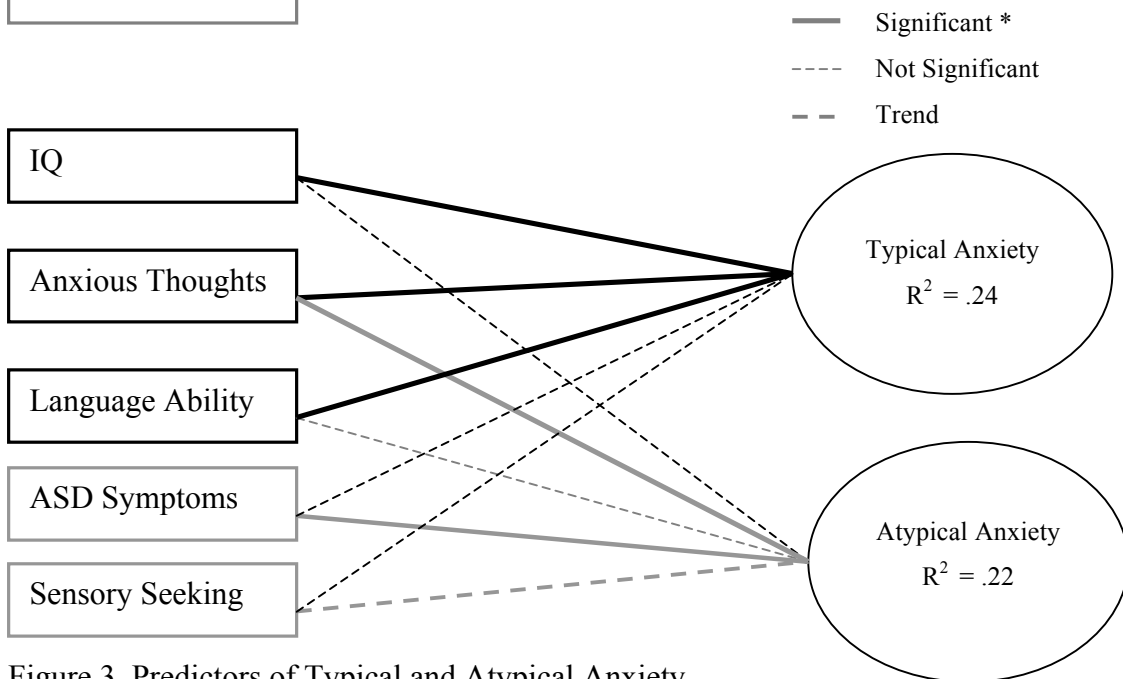
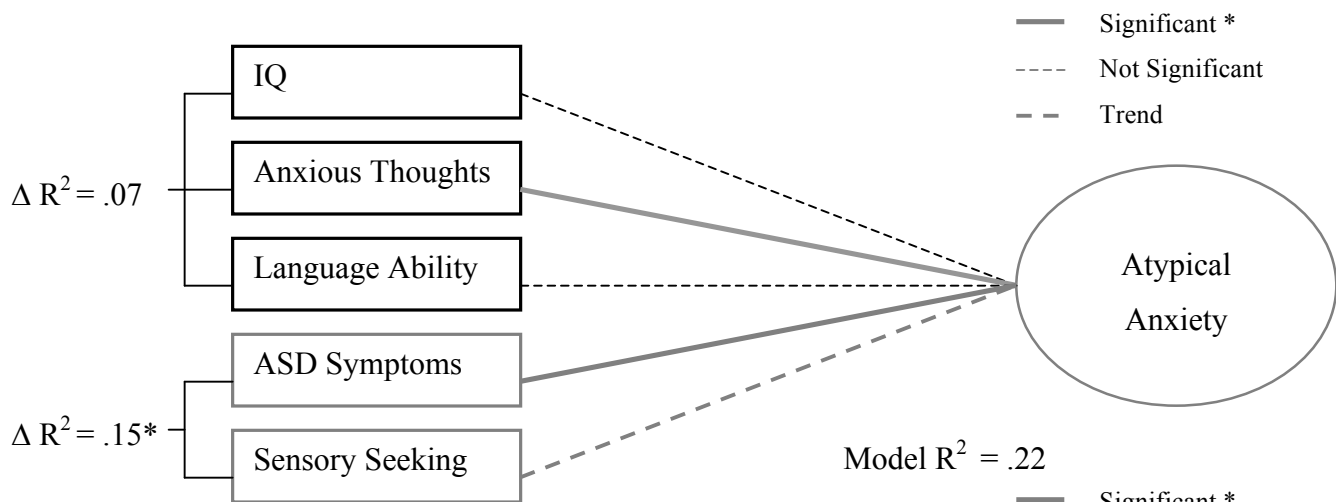
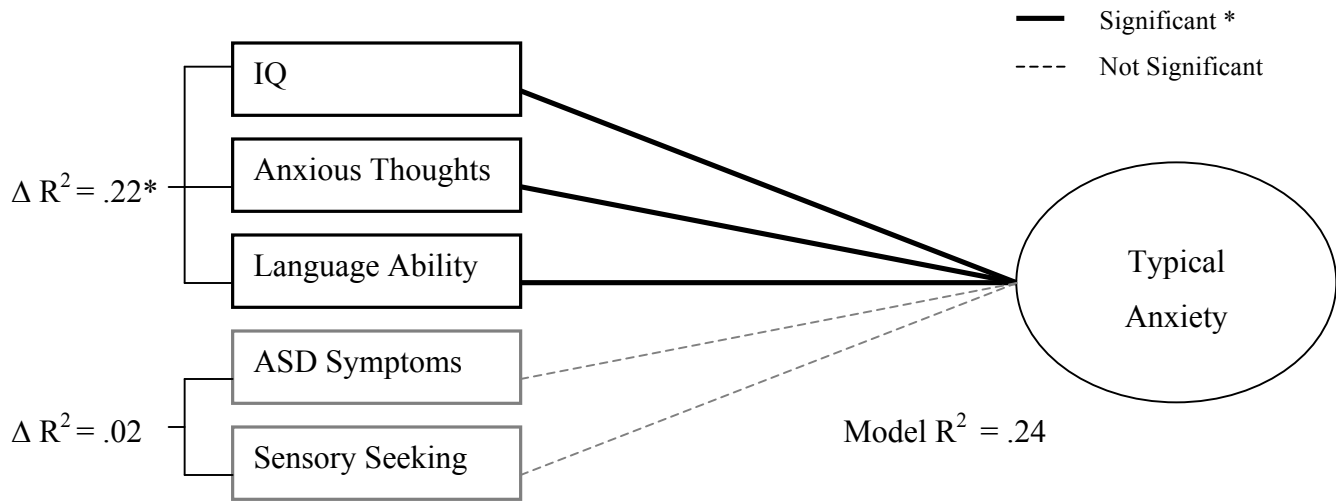


Figure 3. Predictors of Typical and Atypical Anxiety

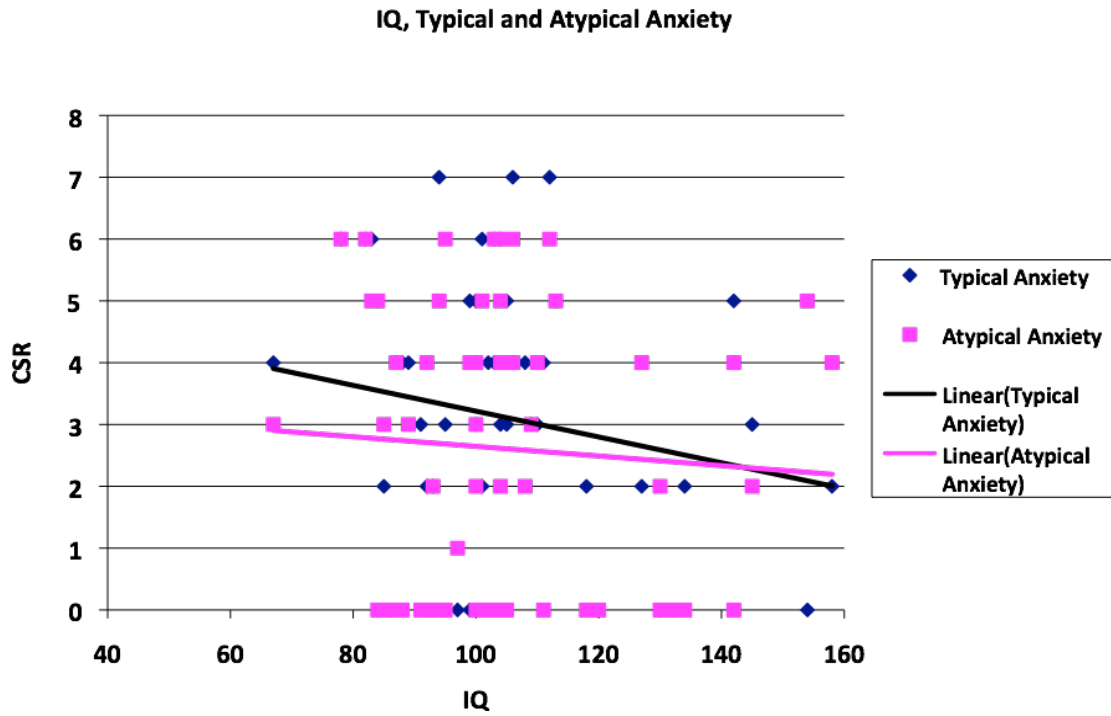


Figure 4. IQ, Typical and Atypical Anxiety

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APPENDIX: COMMONLY USED ABBREVIATIONS

## **Commonly Used Abbreviations**

Anxiety Disorders Interview Scale, Child & Parent Version (ADIS-C/P)

Autism Spectrum Disorder (ASD)

Clinician Severity Rating (CSR)

Clinical Evaluation of Language Fundamentals (CELF)

Cognitive Behavioral Therapy (CBT)

Diagnostic Statistical Manual, Fourth Edition (DSM-IV)

Generalized Anxiety Disorder (GAD)

General Cognitive Abilities Index (GCA)

Intelligence Quotient (IQ)

Negative Affective Self-Statement Questionnaire – Anxiety Scale (NASSQ-A)

Obsessive Compulsive Disorder (OCD)

Sensory Profile (SP)

Sensory Profile – Sensitivity/Avoidance Subdomain (SP\_SA)

Separation Anxiety Disorder (SAD)

Social Responsiveness Scale (SRS)