Parent-Rated Anxiety Symptoms in Children with Pervasive Developmental Disorders: Frequency and Association with Core Autism Symptoms and Cognitive Functioning

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Abstract

Background In addition to the core symptoms, children with Pervasive Developmental Disorders (PDD) often exhibit other problem behaviors such as aggression, hyperactivity, and anxiety, which can contribute to overall impairment and, therefore, become the focus of clinical attention. Limited data are available on the prevalence of anxiety in these children. We examined frequency and correlates of parent-rated anxiety symptoms in a large sample of children with PDD.

Methods The goals of this study were to examine the frequency and correlates of parent-rated anxiety symptoms in a sample of 171 medication-free children with PDD who participated in two NIH-funded medication trials. Twenty items of the Child and Adolescent Symptom Inventory (CASI) were used to measure anxiety.

Results Forty three percent of the total sample met screening cut-off criteria for at least one anxiety disorder. Higher levels of anxiety on the 20-item CASI scale were associated with higher IQ, the presence of functional language use, and with higher levels of stereotyped behaviors. In children with higher IQ, anxiety was also associated with greater impairment in social reciprocity.

Conclusion Anxiety is common in PDD and warrants consideration in clinical evaluation and treatment planning. This study suggests that parent ratings could be a useful source of information about anxiety symptoms in this population. Some

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anxiety symptoms such as phobic and social anxiety may be closer to core symptoms of PDD. Further efforts to validate tools to ascertain anxiety are needed, as are studies to empirically test approaches to treat anxiety in PDD.

Keywords Pervasive developmental disorders · Autism · Anxiety · Comorbid psychiatric psychopathology

Abbreviations
ABC   Aberrant Behavior Checklist
ADI-R   Autism Diagnostic Interview-Revised
CASI   Child and Adolescent Symptom Inventory
PDD   Pervasive Developmental Disorders
RUPP   Research Units on Pediatric Psychopharmacology

Introduction

Children with Pervasive Developmental Disorders (PDD), including autistic disorder, Asperger's disorder and PDD-NOS share common symptoms in the core domains of social reciprocity, communication, and repetitive behaviors. In addition to the core symptoms, children with PDD often exhibit symptoms across multiple diagnostic domains including explosive behavior and aggression (Research Units on Pediatric Psychopharmacology (RUPP) Autism Network 2002), hyperactivity (Research Units on Pediatric Psychopharmacology (RUPP) Autism Network 2005), and anxiety (Weisbrot et al. 2005). From a diagnostic standpoint, it may be argued that these co-occurring symptom clusters can be attributed to PDD (American Psychiatric Association 2000). Alternatively, insofar as symptoms such as aggression, hyperactivity or anxiety are common, but not core features of PDD, a separate diagnostic label may be more appropriate.

Numerous case reports and small clinical series indicate that children with PDD are at high risk for meeting criteria for other psychiatric disorders, such as Attention Deficit/Hyperactivity Disorder (ADHD), disruptive behavior disorders, mood, and anxiety disorders (Ghaziuddin et al. 1998; Sverd 2003; Tsai 1996). Larger samples of children with PDD have also shown that externalizing and internalizing psychopathology are common when examined dimensionally (Lecavalier 2006) or categorically (Gadow et al. 2004, 2005; Leyfer et al. 2006; Weisbrot et al. 2005). Furthermore, Gadow et al. (2004) showed that the levels of psychiatric symptoms in children with PDD were similar to those in psychiatrically referred children without PDD. Although the etiological relationship between PDD and these associated symptom clusters remains uncertain, the presence of these co-occurring problems may add to the overall impairment in children with PDD and may require additional treatment.

Anxiety was described in the initial account of autism (Kanner 1943). Abnormal reactions such as "excessive fearfulness in response to harmless objects" are included as associated features of autistic disorder in DSM-IV (American Psychiatric Association 2000). Anxiety in PDD is of particular interest because it has been hypothesized to be closely tied to the core symptoms. For example, "insistence on sameness" could be argued to be a reflection of anxiety. It has been observed that changes in routines and interruption of stereotyped behaviors may increase anxiety, tension, and emotional upset in children with PDD (Volkmar et al. 1999). On the one hand, it is possible that children with PDD may engage in repetitive behavior to reduce anxiety (Bodfish et al. 2000). On the other hand, repetitive behavior may be unrelated to anxiety as some children with PDD may derive pleasure from their restricted interests and repetitive behavior (McDougle et al. 2000). Awareness of social deficits and the legacy of failure in the social domain may amplify social anxiety in youth with higher functioning forms of PDD (Bachevalier and Loveland 2006; Bellini 2004; Chamberlin et al. 2007).

The causal mechanisms of anxiety in children with PDD have not been well studied but several possible explanations have been proposed. Weak integration capacity, i.e., failure to integrate local details into a global entity (Frith and Frith 1999) has been noted as one possible explanation, whereas the difficulties in relating to diverse sources of information would lead children with PDD to experience everyday situations as chaotic and, therefore, frightening (Happe 1994; Muris et al. 1998). However, a recent study failed to find an association between weak central coherence and anxiety in 20 children with high-functioning autism (Burnette et al. 2005). Pathological features of the amygdala, which is involved in both social and emotional processes (LeDoux 2000), have been documented in PDD (Baron-Cohen et al. 2000; Nacewicz et al. 2006; Schultz 2005; Schumann et al. 2004) and implicated in co-occurring PDD and anxiety (Amaral et al. 2003). To this end, one study revealed a significant association between anxiety and increased total and right amygdala volumes in 49 children with PDD (Juranek et al. 2006). On another level, abnormalities of serotonin (5HT) neurotransmission could represent a shared causal factor in PDD (Chugani et al. 1999) and anxiety, and suggest paths for intervention.

Most of what is known about the occurrence of anxiety disorders in children with PDD is derived from clinical samples. Using the anxiety disorders section of the Diagnostic Interview Schedule for Children, Muris and colleagues (Muris et al. 1998) reported that 84% of 44 children with autism and PDD-NOS (age range from 2 to 18 years) met criteria for at least one anxiety disorder. Using a case control study, Kim and colleagues (Kim et al. 2000) compared 59 nine to 14-year-old children with high functioning autism or

Asperger's disorder to a sample of community controls. The rate of parent-rated anxiety problems was significantly higher in children with PDD and the presence of anxiety added to the levels of overall disability. Two studies used child self-report of anxiety in children with high functioning autism. In one study, 8–12 year old children ($n=15$) scored significantly higher than matched samples of language impaired and normally developing children (Gillott et al. 2001). Similar results were observed in a sample of 23 children with high functioning autism (Sutton et al. 2005). Parent and child reports of anxiety in a clinical series of 65 children aged 10–13 with Asperger's disorder were compared with those of children diagnosed with social phobia and healthy controls (Russell and Sofronoff, 2005). As predicted, the levels of anxiety in children with Asperger's disorder were greater than in healthy controls and similar to those in children diagnosed with social phobia. Taken together, these reports suggest that anxiety is a frequent and impairing problem in children with PDD. However, small samples in studies to date did not allow the investigators to adequately evaluate psychometric characteristics of anxiety measures in children with PDD and to examine the association of anxiety with core symptoms and associated clinical characteristics of PDD.

Most studies of anxiety in children with PDD have been conducted with high functioning autism or Asperer's Disorder (Bellini 2004; Gillott et al. 2001; Kim et al. 2000; Russell and Sofronoff 2005). Given the prevalence of cognitive impairment in PDD, it is important to examine the effects of cognitive functioning on anxiety. One study reported that higher IQ was associated with more severe anxiety in children with PDD (Gadow et al. 2005). However, there is also evidence that children with autism and severe mental retardation have higher levels of anxiety than children of similar cognitive functioning without autism (Bradley et al. 2004). Taken together with the evidence of elevated anxiety in children with mental retardation (Gullone et al. 1996; Muris et al. 2002; Sarphare and Aman 1996), it is likely that anxiety may be present in children with PDD with or without cognitive impartment. Therefore, the effects of cognitive impairment (IQ below 70) on anxiety were examined in the present study. We also tested whether the association of anxiety with the core autism symptoms varies in children with lower and higher cognitive functioning.

Anxiety in children with PDD has been the focus of clinical attention in several studies (Buitelaar et al. 1998; Martin et al. 1999; Sofronoff et al. 2005). Moreover, anxiety may compound deficits in adaptive behavior (Kim et al. 2000) as well as excesses in disruptive behavior (Canitano 2006) in this population. The primary goals of this study were twofold: 1) to examine the frequency and distribution of anxiety symptoms in a large, well-characterized sample of children with PDD; and 2) to examine the association between anxiety symptoms with the core autism symptoms and cognitive functioning. We also explored the association between anxiety and the measures of adaptive functioning and behavioral problems. In order to accomplish these goals we examined psychometric characteristics of a 20-item anxiety scale derived from the Child and Adolescent Symptom Inventory (CASI) (Gadow and Sprafkin 1994, 1997).

Methods

Subjects

The sample consisted of 172 medication-free children who participated in one of two randomized clinical trials conducted by the RUPP Autism Network. The first study was a double-blind, placebo-controlled trial of risperidone in children with autism accompanied by aggression, tantrums and self-injury (RUPP Autism Network 2002). All children in this clinical trial met the DSM-IV criteria for autistic disorder and had high levels of tantrums, aggression, self-injurious behaviors as evidenced by a score of ≥18 on the Irritability scale of the Aberrant Behavior Checklist (Aman et al. 1985). Other enrollment criteria included an age of 5 to 17 years, a weight of at least 15 kg, and a mental age of at least 18 months as determined by intelligence testing. The children had to be free of serious medical disorders and of other psychiatric disorders requiring medication. Each child's past and current treatments for autism were reviewed and, in consultation with parents, children receiving a psychotropic drug that was deemed effective for the treatment of aggression, tantrums, or self-injurious behavior were excluded. Ineffective medications were gradually withdrawn, and a drug-free interval of 7 to 28 days, depending on the drug, was required before enrollment.

The second study was a double-blind, placebo-controlled crossover trial of methylphenidate in children with PDD accompanied by hyperactivity (RUPP Autism Network 2005). Participants in this clinical trial were aged 5 to 14 years and met the DSM-IV criteria for the diagnoses of autistic disorder, Asperger's disorder or PDD-NOS. All of the participants had to have interfering symptoms of hyperactivity and/or impulsiveness as evidenced by a total score ≥27 on both the parent-rated and teacher-rated Swanson, Nolan, and Pelham-version IV ADHD scale (Swanson 1992). Other eligibility criteria for the methylphenidate trial included: no concurrent psychotropic medications for at least 1 to 3 weeks, mental age of at least 18 months as determined by intelligence testing, no other neuropsychiatric disorders that might require alternative medical management, and good physical health. Written informed consent was provided by a parent or guardian. Complete CASI data were available in

171 cases; the sample comprised 144 males and 27 females with a mean age of 8.2 ± 2.6 years (range 5 to 17). Demographic and clinical characteristics of children whose data were used in this study are reported in Table 1.

Procedures

All data reported in this study were collected at pretreatment assessments during the two medication trials (RUPP Autism Network 2002, 2005). Pretreatment assessments included complete medical and psychiatric history, mental status examination, physical examination, intelligence testing, structured and semi-structured clinical interviews by clinicians experienced in the assessment of PDD, and comple-

tion of parent-rated questionnaires. The Autism Diagnostic Interview-Revised was administered to corroborate the DSM-IV diagnosis of autistic disorder based on clinical interview and examination. Because the Autism Diagnostic Interview-Revised does not have a diagnostic algorithm for Asperger's disorder or PDD NOS, these diagnoses followed the DSM-IV, taking all available information into account.

Measures

Child and Adolescent Symptom Inventory (CASI) The CASI is a 132-item, DSM-IV-referenced rating scale that combines the non-overlapping symptom modules of both the Child Symptom Inventory-4 (Gadow and Sprafkin 1994,

Table 1 Demographic and clinical characteristics of the participants

Variable	Frequency	Percent	Mean (SD)
Study source			
Risperidone study	101	59	
Methylphenidate study	70	41	
Gender (% male)	144	84	
PDD diagnosis			
Autistic disorder	151	88	
Asperger's disorder	6	4	
PDD-NOS	14	8	
Cognitive ability (IQ)			
No score	17	10	
Average (≥86)	22	13	
Borderline (71–85)	26	15	
Mild mental retardation [MR] (50–70)	40	23	
Moderate MR (36–49)	24	14	
Severe MR (21–35)	25	15	
Profound MR (≤20)	17	10	
Ethnicity/race			
White/Caucasian	120	70	
Black/African American	20	12	
Asian/Pacific Islander	13	8	
Hispanic/Latino	10	6	
Other	8	4	
Age			8.2 (2.6)
Vineland Adaptive Behavior Scales			
Communication			50.83 (20.38)
Daily living skills			43.67 (20.78)
Socialization			53.52 (15.98)
Composite			45.18 (17.87)
Aberrant Behavior Checklist			
Irritability			22.20 (9.86)
Social withdrawal			14.61 (8.99)
Stereotypy			8.95 (5.36)
Hyperactivity			32.46 (9.02)
Inappropriate speech			5.82 (3.94)
Autism Diagnostic Interview-Revised			
Social interaction			23.89 (5.07)
Communication—nonverbal			10.83 (3.34)
Communication—verbal			17.30 (4.56)
Stereotyped behavior			7.63 (2.67)

2002) and the Adolescent Symptom Inventory-4 (Gadow and Sprafkin 1997, 1998). Items are scored as 0 = never, 1 = sometimes, 2 = often, and 3 = very often; scores of 2 and 3 are considered clinically significant. Individual items are scored in two different ways: Symptom Count (categorical) and Symptom Severity (dimensional) scores. The Symptom Count is the total number of symptoms rated as 2 or 3 (i.e., *often* or *very often*) in a specific disorder category. If the Symptom Count is equal to or greater than the criterion number of symptoms necessary for a DSM-IV diagnosis Symptom Criterion score, the child exceeds threshold for that disorder. This scoring method resulted in sensitivity ranging from 0.64 to 0.80 and specificity ranging from 0.65 to 0.96 when compared with diagnoses taken from medical records or structured psychiatric interviews for a multitude of disorders (disruptive behavior disorders, PDD, anxiety disorders and depression) (Gadow and Sprafkin 2002). The item scores within each category can also be summed to generate a Symptom Severity score for each disorder. Symptom Severity scores for specific symptom categories of the CASI demonstrate satisfactory internal consistency, reliability, and validity in community-based, clinic-referred, and PDD samples (Sprafkin et al. 2002).

The CASI contains 26 items across 8 anxiety disorders: generalized anxiety disorder and separation anxiety disorder are covered by eight items each; PTSD, somatization, social phobia and obsessive–compulsive disorder are each indexed by two items; and specific phobia and panic disorder each have a single item. To reduce the risk of measurement confounding (Angold et al. 1999) in assessing co-occurrence

of anxiety in children with PDD, four of these 26 items were excluded. Item #2 "Has difficulty paying attention to tasks or play activities" was excluded due to the overlap with ADHD, and item #50 "Is irritable for most of the day" was excluded due to the overlap with Oppositional Defiant Disorder. Both irritability and hyperactivity were measured by the Aberrant Behavior Checklist, which provided additional rationale for not using these items to measure anxiety. Item #56 "Feels compelled to perform unusual habits" was excluded due to overlap with repetitive behaviors, a core symptom of PDD. The repetitive behaviors in this study were measured by the ADI-R. Item #88 "Has low energy level or is tired for no apparent reason" was excluded due to overlap with dysthymia. We also excluded two PTSD items (#57 "Has experienced an extremely upsetting event and continues to be bothered by it" and #58 "Has distressing memories or dreams about an extremely upsetting event") because they were rarely endorsed, and because assessment of PTSD requires evaluation of traumatic exposure and differs from assessment of other anxiety disorders (Connolly et al. 2007). Indeed, no parent endorsed the "2 = often" or "3 = very often" response categories suggesting that these two items were not relevant in this sample. The abbreviated contents of 20 items included in the analysis are reported in Table 2.

Aberrant Behavior Checklist (ABC) The ABC is a 58-item informant-based scale comprising 5 subscales: I. Irritability (tantrums, aggression and self-injury, 15 items); II. Lethargy/ Social Withdrawal (response to others, initiation of interac-

Table 2 Descriptive statistics and item-total correlations for the 20 anxiety items in children with PDD

Item number and abbreviated content	Mean	SD	N (%) above cutoff	Item-total correlation
47 is over concerned about abilities	0.43	0.78	25 (14%)	0.45
48 has difficulty controlling worries	0.62	0.92	40 (17%)	0.54
49 acts restless or edgy	1.64	1.04	94 (55%)	0.41
51 is extremely tense or unable to relax	1.20	1.01	61 (36%)	0.41
52 has difficulty falling asleep	1.36	1.10	69 (40%)	0.31
53 is overly fearful of specific objects	1.09	1.06	53 (31%)	0.50
54 complains about heart pounding	0.19	0.53	9 (5%)	0.49
55 cannot get distressing thoughts out of mind	0.45	0.84	23 (13%)	0.63
61 complains about physical problems	0.37	0.66	11 (6%)	0.55
62 worries about physical health	0.16	0.53	6 (3%)	0.54
63 is more anxious in social situations that most children	1.56	1.05	87 (51%)	0.47
64 is excessively shy with peers	0.91	1.00	45 (26%)	0.34
65 gets very upset when expects to be separated from parents	1.05	0.96	41 (24%)	0.41
66 worries that parents will be hurt or leave and not be back	0.40	0.80	18 (10%)	0.52
67 worries that some disaster will separate from parents	0.24	0.62	11 (6%)	0.55
68 tries to avoid going to school to stay with parents	0.48	0.80	19 (11%)	0.35
69 worries about being left home alone or with a sitter	0.26	0.55	5 (3%)	0.32
70 afraid to go to sleep unless near parents	0.82	1.09	40 (23%)	0.41
71 has nightmares about being separated from parents	0.09	0.36	2 (1%)	0.34
72 complains about feeling sick when expects separation from parents	0.13	0.41	3 (2%)	0.51

tion, 16 items); III. Stereotypic Behavior (mannerisms and repetitive movements, 7 items); IV. Hyperactivity (16 items); and V. Inappropriate Speech (excessive talking, repeating phrases, 4 items). Items are rated on a four-point scale; higher scores indicate more severe problem behavior. These factors and normative data in developmentally disabled populations have been confirmed in several studies (Aman et al. 1985; Brown et al. 2002; Marshburn and Aman 1992). This scale was used to examine the association of anxiety with other behavioral problems that may be present in children with PDD.

Autism Diagnostic Interview-Revised (ADI-R) The Autism Diagnostic Interview-Revised is a structured parent interview used to support the diagnosis of autism or related condition in children and adults. It has demonstrated excellent reliability and validity for the diagnosis of autism (Lord et al. 1997; Rutter et al. 2003). Training to reliability on the ADI-R is rigorous. It begins with several didactic sessions, supervised administration of a live interview by the new rater followed by reliable co-rating of a taped interview and demonstrated competence in at least three taped interviews which are then reviewed by an experienced new rater. The interview consists of 93 items, 34 of which are used in the diagnostic algorithm. Algorithm items are scored 0, 1, or 2. Sum of the scores of the algorithm items for each of the domains (social interaction, communication, and stereotyped patterns of behavior) can be calculated and used as severity scores (Lord et al. 1994). Higher scores indicate greater levels of symptom severity.

Vineland Adaptive Behavior Scales The Vineland is a semi-structured, parent interview designed to measure the child's competence in communication, daily living skills, and socialization. The scale is a standard assessment in children with developmental disabilities and has excellent reliability and validity for each domain (Sparrow et al. 1984). The raw scores are converted to standard scores (Mean=100, SD= 15), and higher scores indicate more mature adaptive functioning. This scale was used to examine the association of anxiety with the levels of adaptive functioning in children with PDD.

Intellectual Functioning Children were assessed on one of several intelligence tests: WISC-III (Wechsler 1991) if they were able and qualified by age (29% of the sample) or Wechsler Preschool and Primary Scale of Intelligence-Revised (Wechsler 1989) (2% of the sample); if not able to perform on the Wechsler, they were tested by the Leiter International Performance Scale-Revised (Roid and Miller 1997) (28% of the sample); and if the above measures were not suitable, the Mullen Scales of Early Learning (Mullen 1995) (23% of the sample); or Slosson Intelligence Test

(Jensen and Armstrong 1985) (14% of the sample) were administered. Seventeen subjects (10%) could not be tested. Because several different tests were employed, children were classified categorically in order to characterize the sample (e.g., average ability, borderline, mild, moderate or severe mental retardation). In order to examine the effects on cognitive impairment on anxiety in children with PDD, a dichotomous IQ variable with a cutoff point at 70 was created. This cut-off was selected based on its common use for evaluation (Borkowski et al. 2007) and diagnosis of individuals with intellectual disabilities (American Psychiatric Association 2000). This cutoff has been frequently used in studies of the effects of cognitive functioning in children and adults with autism (Volkmar and Pauls 2003).

Statistical Analyses

The internal consistency reliability of the 20-item anxiety severity scale was examined using Cronbach's alpha statistic. We examined the distributions of scores on CASI anxiety items and the frequency of subjects who met or exceeded established cut-off scores on the existing CASI subscales. Unpaired *t*-tests were used to compare subgroups based on age (using median split; median age=7.75), ethnicity (white versus all other), and PDD diagnosis (autism versus Asperger's disorder and PDD-NOS). Chi-square analyses were used to test the difference between categorical variables. Pearson's correlation was used to examine the association of the anxiety scores with other continuous variables. Because these analyses were exploratory, the alpha level was set at 0.05 and we did not correct for multiple comparisons. To evaluate the difference between two correlations, Fisher's *r*-to-*z* transformation was used. Hierarchical regression analyses were used to explore unique contributions of the dichotomous variables, cognitive functioning (IQ below 70=0; IQ above 70=1) and functional language use (Yes=1; No=0), and scores on three continuous variables derived from the Autism Diagnostic Interview-Revised: social impairment, communication abnormalities, and stereotyped behaviors. IQ data were available for 154 of 171 subjects. Thus, analyses involving IQ included 154 subjects. SPSS version 14.0 (SPSS, Inc., Chicago) was used for all data analyses.

Results

Frequency and Distribution of Anxiety Symptoms in PDD

The internal consistency of the 20-item anxiety scale was moderately high (Cronbach's alpha=0.85). The item-total correlations, i.e., the correlations of each item with the sum

Table 3 Number and percent of subjects who met the CASI screening cut-off score criteria for the DSM-IV anxiety disorders

Anxiety disorder	Total sample (n=171)		IQ>70 (n=48)[a]		IQ≤70 (n=106)		Analysis		
	n	%	n	%	n	%	Chi square[b]	p-value	OR (95% CI)[c]
Generalized anxiety	16	9.4	12	25.0	4	3.8	15.9	<0.001	8.5 (2.3–33.6)
Simple phobia	53	31.0	18	37.5	33	31.1	0.6	0.44	1.3 (0.6–2.9)
Panic disorder	9	5.3	5	10.4	4	3.8	2.6	0.10	2.9 (0.6–13.9)
Somatization disorder	12	7.0	7	14.6	5	4.7	4.5	0.03	3.4 (0.9–13.4)
Social phobia	34	19.9	11	22.9	23	21.7	0.3	0.87	1.1 (0.4–2.6)
Separation anxiety	18	10.5	9	18.8	8	7.5	4.2	0.04	2.8 (0.9–8.8)
Any anxiety disorder	73	42.7	28	58.3	42	39.6	4.6	0.03	2.1 (1.0–4.5)

[a] IQ scores were unavailable for 17 subjects
[b] Fisher exact test used when cell sizes less than 5
[c] Odds ratio with 95% confidence interval

of remaining items, ranged from 0.31 to 0.55 (see Table 2). Table 2 also presents per-item means and standard deviations, number and percent of subjects who endorsed "often" and "very often" response categories (cut-off scores), and item-total correlations. Anxiety scores, computed as a sum of responses to 20 items, ranged from 0 to 42 (Mean=13.5, SD=8.5) and were normally distributed (Skewness=0.97, Kurtosis=1.15). The same analyses were run for the subsamples of children with IQ above 70 (n=48) and below 70 (n=106) and yielded nearly identical results with alpha coefficients of 0.87 and 0.83 in the two IQ groups, respectively.

Table 3 reports the frequency of subjects who met or exceeded the screening cut-off scores for the six CASI anxiety categories: generalized anxiety, simple phobia, panic disorder, somatization disorder, social phobia, and separation anxiety. Forty three percent of the total sample met screening cut-off criteria for at least one of these anxiety disorders. Because three of the excluded items (#2, #50, and #88) are part of the screening cutoff calculation for generalized anxiety disorder, we calculated this cutoff score first with and then without these items; the number of subjects who met or exceeded the screening cutoff scores was not affected. As shown in Table 3, children with IQ below 70 were less likely to meet the cut-off criteria for generalized anxiety, somatization disorder, separation anxiety disorder or any anxiety disorder as compared to children with IQ above 70.

Table 4 Correlations between anxiety and the Aberrant Behavior checklist, the Vineland adaptive behavior scales, and the Autism diagnostic interview-revised in children with PDD by two levels of cognitive functioning

Variable/measure	Total sample (n=171)	IQ>70 (n=48)[a]	IQ≤70 (n=106)[a]	z-score[b]
	r	r	r	
Aberrant Behavior Checklist				
Irritability	0.35**	0.42**	0.41**	0.06
Social withdrawal	0.36**	0.42**	0.37**	0.33
Stereotypy	0.17*	0.30*	0.26**	0.24
Hyperactivity	0.29**	0.08	0.43**	2.16*
Inappropriate speech	0.42**	0.22	0.52**	1.97*
Vineland Adaptive Behavior Scales				
Communication	0.25**	0.05	0.19*	0.79
Daily living skills	0.16*	−0.13	0.20*	1.87
Socialization	0.18*	−0.05	0.20*	1.41
Autism Diagnostic Interview-Revised				
Social interaction	0.04	0.33*	0.12	1.24
Communication—nonverbal	−0.15*	0.01	−0.10	0.62
Communication—verbal	0.07	0.07	−0.14	1.18
Stereotyped behavior	0.22**	0.17	0.30**	0.77

*p<.05
**p<.01
[a] IQ scores were unavailable for 17 subjects
[b] Fisher's r-to-z transformation was used to compare correlations in the lower and higher IQ groups

Table 5 Hierarchical regression analysis of anxiety as a function of severity of autism symptoms controlling for IQ and functional language

Variables	Total R^2	R^2 Change	B	SE B	β	t
Step 1	.08***	.08**				
IQ (above or below 70)			3.38	1.57	0.18	2.16*
Functional language (yes/no)			3.37	1.55	0.17	2.18*
Step 2	.16***	.08**				
ADI−R social interaction			0.09	0.21	0.05	0.45
ADI−R communication			−0.59	0.34	−0.23	−1.77
ADI-R stereotyped behaviors			0.73	0.30	0.23	2.41*
Step 3[a]	.20	.04				
IQ × ADI-R social interaction			3.75	1.62	0.31	2.32*
IQ × ADI-R communication			−0.41	1.63	−0.04	−0.25
IQ × ADI-R stereotyped behaviors			−0.80	1.32	−0.06	−0.6

ADI-R Autism diagnostic interview-revised

*p<.05

**p<.01

***p<.001

[a] One of the interaction terms was significant, but the change in R^2 was not significant

Association of Anxiety with Demographic and Clinical Characteristics

There were no differences in anxiety severity between younger (below median) and older children (above median) (t_{169}=1.28, p=.201), boys and girls (t_{169}=1.34, p=.181), Caucasian and all other ethnic groups (t_{169}=.04, p=.965), and between children with the diagnosis of autism versus children with the diagnoses of Asperger's or PDD-NOS (t_{169}=.86, p=.389). Pearson's correlations were used to examine the associations of the scores of the 20-item anxiety scale with the subscales of the Aberrant Behavior Checklist, the Vineland Adaptive Behavior Scales, and the Autism Diagnostic Interview-Revised (see Table 4). These analyses, conducted first for the total sample and then separately for the two IQ groups, revealed small to moderate correlations between anxiety and measures of behavioral problems, adaptive functioning, and autism symptoms with the values of significant correlation coefficients (r) ranging from −.15 to .52. In children with IQ below 70, the correlations of anxiety with Hyperactivity (z-score=2.16, p<0.05) and Inappropriate Speech (z-score= 1.97, p<0.05) were significantly stronger than in children with IQ above 70.

A hierarchical regression analysis was performed to explore associations of anxiety with the severity of the core symptoms of autism as measured by the ADI-R: social interaction, communication, and stereotyped patterns of behavior (see Table 5). Diagnosis, age, and ethnicity were not associated with the levels of anxiety and therefore were not included in the hierarchical regression. However, the levels of anxiety were significantly different between children with IQ above 70 versus those with IQ below 70,

and between children with or without functional language use. Consequently, we entered dichotomously coded IQ and functional language status in the first step of the model. ADI-R scores on social interaction, communication, and stereotyped patterns of behavior were entered in the second step. To evaluate whether the core autism symptoms have different association with anxiety for children with higher versus lower levels of cognitive functioning, the interaction terms of IQ and the three centered variables for the core autism symptoms were included in the third step. The autism symptom variables were centered, i.e., converted to deviation scores so that each variable has a mean of zero, in order to avoid multicollinearity (Aiken and West 1991). Within each block, the variables were entered simultaneously. The R^2-change values are reported for each step and regression coefficients are reported for the final step. Higher levels of anxiety were associated with higher IQ (β=.18, p<.05), the presence of functional language use (β=.17, p<.05), and stereotyped behaviors (β=.23, p<.05). There was also a significant interaction between IQ and social impairment (β=.31, p<.05). A plot of these data suggests that the combination of higher IQ and higher social impairment resulted in greater severity of anxiety than either of these variables alone.

Discussion

We examined the distribution of anxiety symptoms as measured by a 20-item scale derived from the CASI in a well-characterized, medication-free sample of 171 children with PDD. Scoring this parent-rated scale in the standard

fashion showed that 43 percent of the subjects met the CASI screening cut-off criteria for one or more of the six DSM-IV anxiety disorders. This number of children with PDD who met the screening symptom criteria of anxiety disorders is twice as high as the 20 percent estimates of the lifetime prevalence rates of pediatric anxiety disorders in the general population (Costello et al. 2005; Shaffer et al. 1996) and similar to the estimates of frequency of anxiety problems in other studies of children with PDD (Gadow et al. 2004, 2005; Muris et al. 1998; Sverd 2003; Weisbrot et al. 2005).

The 20-item anxiety measure derived of the CASI items, demonstrated good internal consistency in children with or without cognitive impairment. This 20-item scale also revealed small-to-moderate correlations with other parent and clinician measures of behavioral symptoms, adaptive function, and core symptoms of autism. Higher levels of anxiety were associated with higher IQ, the presence of functional language use, and with higher levels of stereotyped behaviors. Greater impairment in nonverbal communication as measured by the ADI-R was significantly and inversely associated with the level of anxiety. It is possible that children with lower communication skills are less expressive about their worries, which was reflected in the lower parent ratings of anxiety. In children with higher IQ, anxiety was also associated with the levels of impairment in social reciprocity as measured by the ADI-R. Clarifying the nature of anxiety experiences in children with PDD is complicated by both the abnormalities of emotional awareness in this population and by the difficulties that parents or other observers may have in interpreting possibly extreme or incongruent reactions of these children (Capps et al. 1992). This study strongly supports the suggestion that anxiety symptoms are common in PDD, and provides initial support to the reliability and validity of parent-rated anxiety symptom assessment in children with PDD. Furthermore, the association of anxiety symptoms with stereotypy also bolsters the contention that anti-anxiety treatments may be beneficial in managing impairing stereotypic behaviors.

The present study revealed that higher levels of IQ were associated with some, but not all, forms of greater anxiety in children with PDD. This result is similar to earlier studies which reported that higher IQ was positively correlated with more severe anxiety (Lecavalier 2006; Weisbrot et al. 2005). However, there is also evidence that children with autism and severe mental retardation have higher levels of anxiety than children of similar cognitive functioning without autism (Bradley et al. 2004). The observation that both symptoms of simple phobia and social phobia were equally common in higher and lower IQ subjects is intriguing, and might be hypothesized to show that these specific forms of anxiety fall closer to the core phenotype of the PDDs as opposed to representing comorbidities, as also suggested by family studies (Smalley et al. 1995). Our data also showed

that in children with IQ below 70, the correlations of anxiety with hyperactivity and inappropriate speech were significantly stronger than in children with IQ above 70.

Our finding of the significant association between anxiety and impairment in social reciprocity parallels the finding of the significant association between anxiety and social impairment in normally developing children (Spence et al. 2000). We speculate that it is possible that even when children with PDD have a good understanding of appropriate peer behavior, anxiety can undermine their actual use of social skills in natural peer contexts. Clinical studies are needed to understand whether higher levels of anxiety may be a factor that contributes, in addition to other features such as deficits in affective sharing, to the poor generalization of social skills training approaches in patients with autism as well as with related developmental disabilities (Sukhodolsky and Butter 2006; Weiss and Harris 2001).

Limitations The high rate of anxiety problems observed in these samples may be due to ascertainment bias as the PDD subjects were identified from clinical treatment studies. The sample size was insufficient to examine differences among children with autism, Asperger's disorder, and PDD-NOS. For example, Sutton et al. (2005) reported that, compared to normally developing controls, children with high functioning autism had greater levels of self-reported social anxiety but similar levels of generalized anxiety. This limitation can be addressed in future studies with larger community samples. The limited age range of our sample also might lead to underestimation of some forms of anxiety which characteristically emerge in older individuals, although our observed rate is comparable to other reports. It is also important to note that our methods did not yield actual DSM-IV diagnoses but screening threshold scores. Another limitation is that several IQ tests were used, which dictated the use of categorical classification of IQ and restricted our ability to evaluate the relationship of IQ and anxiety. Our analysis of the association of anxiety with other behavioral problems and adaptive functioning were exploratory and not corrected for multiple comparisons. Further studies with larger samples and a priori hypotheses are needed to confirm these effects. Finally, parental reports on their children's anxiety symptoms may be influenced by parent characteristics such as parental anxiety (Bernstein et al. 2005). It was also noted that anxiety may reflect parental attributions regarding child behavior problems (March et al. 2000). However, despite these potential limitations of parent rating of anxiety, this study suggests that parent ratings could be a useful source of information about anxiety symptoms in this population. Behavioral observation may also be a valuable source of information about anxiety in persons who are unable to share their subjective experiences because of cognitive and communication impairments (Glennon and

Weisz 1978). Evaluation of psychometric characteristics of such observational measures of anxiety in children with PDD would be a worthwhile focus of future research.

Clinical implications Anxiety is a common feature in PDD and should be considered in clinical evaluation and treatment planning. Parents of children with PDD might benefit from greater awareness about the association of anxiety with the core symptoms of autism, and education on approaches for treatments to reduce anxiety, be they medical or psychosocial. Our study revealed that anxiety symptoms may be manifested differently in children with PDD functioning within normal level of intelligence compared to those with below average intelligence. The high frequency of anxiety symptoms in our study calls out for concerted research efforts testing approaches of anxiety management in similar populations.

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