JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY
Volume 15, Number 3, 2005

Pp. 452–464

Autism Spectrum Traits in Children with Mood and Anxiety Disorders

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ABSTRACT

The autism spectrum disorders (ASDs) can present with symptoms commonly found in mood and anxiety disorders. The Social Communication Questionnaire (SCQ), Children's Communication Checklist (CCC-2), and the Social Reciprocity Scale (SRS) were used to screen children in a mood disorders research clinic setting for symptoms of ASD. Ninety-three patients (mean age, 12.7 ± 2.8 years; percent male, 63%) completed at least one scale, and 50 children completed all three. The prevalence of those screening positive for a possible ASD on one instrument was 62% and on all three measures was 8%. Fifty-seven percent (*n* = 21/37; odds ratio, 4.59 [95% confidence interval (CI) = 1.40–15.11]) of those scoring in the "ASD-likely" range on the SRS scored in that range on the CCC-2. Only 16% (*n* = 6/37; odds ratio, not significant (NS)) of those scoring in the ASD-likely range on the SRS, and 14% (*n* = 5/37; odds ratio, NS) of those scoring in the ASD-likely range on the CCC-2, scored similarly on the SCQ. These results demonstrate a need to develop valid and reliable instruments to screen for ASDs in children presenting outside of ASD clinics.

INTRODUCTION

The pervasive developmental disorders (PDDs) or autism spectrum disorders (ASDs) can present in diverse ways. For the purposes of this discussion, ASDs include autistic disorder, Asperger's Disorder, and pervasive developmental disorder—not otherwise specified (PDD- NOS). Definitional changes and better understanding of their presentation has produced a 10-fold increase in the reported prevalence rate of high-functioning ASD individuals (Fombonne 2003a). However, these changes in the field have also contributed to significant controversy concerning the appropriate boundaries of the ASDs (Fombonne 2003b). Studies suggest that many individuals with signs of mild-to-moderate ASDs present in clinical or research practice (Charman 2002; Harpaz-Rotem and Rosenheck 2004) but receive either no psychiatric diagnosis (Fombonne et al. 2004) or non-ASD diagnoses (Harpaz- Rotem and Rosenheck 2004).

We are particularly interested in children who present with signs of mild-to-moderate severity ASDs in a mood/anxiety disorder research clinic. Many symptoms are common to both mood/anxiety disorders and ASDs, but irritability and anxiety are particularly significant. Recurrent or protracted irritability often brings children to clinical attention, and irritability is a common symptom of anxiety dis-

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orders, mood disorders (mania, hypomania, and depression), and externalizing disorders (oppositional defiant disorder (ODD)), as well as ASDs.

In particular, many features of ASDs overlap with those of mania/hypomania (Wozniak and Biederman 1997). Aggressive and irritable behaviors are the leading symptoms that bring both ASD and bipolar children to mental health care (Arnold et al. 2003; Geller et al. 2000), and these symptoms are frequently the targets of pharmacological treatments. Reportedly, 25% of both higher and lower functioning ASD patients have a lifetime history of aggressive outbursts or irritability (Gillberg and Coleman 2000; Allen et al. 2001). Higher-functioning children with ASDs might be seen as exhibiting a number of the *Diagnostic and Statistical Manual of Mental Disorders,* 4th ed. (DSM-IV) symptoms of mania, including irritability, elevated mood, distractibility, psychomotor agitation, excessive involvement in pleasurable activity without regard for consequences, labile mood, and, perhaps, even grandiosity.

Given the frequency and severity of symptoms common to both mood/anxiety disorders and ASDs, it is not surprising that individuals with unrecognized signs of mild ASDs would surface in child psychiatry clinics. Individuals with higher-functioning ASDs often receive treatment for anxiety or mood conditions (Martin et al. 1999) and rates of mood and anxiety symptoms may be elevated among individuals with ASDs (Kim et al. 2000). Wozniak and Biederman (1997) noted that, in a general psychopharmacology clinic, 9% of children were diagnosed with a PDD. Gilmour et al. (2004) reported that 66% of patients with conduct disorder presenting to a general psychiatric clinic had impairment in pragmatic language and nonverbal communication behavior equivalent to a control group of children with ASDs. In addition, Piven and Palmer (1999) and Bolton et al. (1998) reported an elevated rate of affective disorders among family members of children with ASDs. The higher rates of anxiety and depression in family members of ASD probands compared to the general population has raised the possibility of some ASDs being related to depression, bipolar disorder, and anxiety disorders (DeLong 2004).

It is conventional to exclude individuals with severe comorbid ASDs from studies of patients with mood disorders. However, mood and anxiety disorder researchers must improve their ability to identify children with potential or milder ASDs, given their prevalence and clinical importance, as well as the recent controversy surrounding the boundaries of mild ASDs; indeed, the relationship between ASDs and mood disorders merits systematic study. Standard research diagnostic instruments, such as the K-SADS, DISC, and DICA, do not screen for ASDs (Skuse et al. 2004). Making a reliable ASD research diagnosis requires historical data on social and language development, often obtained using instruments such as the semi-structured Autism Diagnostic Interview—Revised (ADI-R) (Le Coutour et al. 1989; Lord et al. 1994), as well as reliable observational data, acquired with instruments such as the Autism Diagnostic Observation Scale (ADOS-G) (Lord et al. 1989; Lord et al. 2000). Depending solely on direct observations of restricted interests, stereotypy, or dedication to nonfunctional routines is a notoriously unreliable method of diagnosing ASDs. However, these standardized instruments demand 3–5 hours per patient and extensive interviewer training. Additionally, algorithms for diagnosing Asperger's Disorder or PDD-NOS with these instruments have yet to be developed (Walker et al. 2004). Using ordinary clinical procedures, experienced clinicians may obtain reasonably good agreement (κ = 0.67–0.95) about "ASD versus no ASD," but reliable assignment to ASD subgroups may be no better than chance (Volkmar et al. 1994; Mahoney et al. 1998). Indeed, the current controversy has occurred, in part, because, while pragmatic language and social reciprocity, the core features of ASDs, are continuously distributed in the population (Constantino and Todd 2003; Charman 2003), there are no agreed-upon cut-offs to discriminate between mild ASD and non-ASD conditions (Walker et al. 2004; Jensen et al. 1997; Skuse et al. 2004). As a result, diagnosis relies upon the poorly operationalized concept of impairment (Medical Research Council 2001), and clinicians do not have efficient, reliable tools to

assist them in determining whether children are socially impaired.

Recently, several screening instruments have emerged that are designed to identify children with a high likelihood of an ASD diagnosis—the Social Communication Questionnaire (SCQ©; Berument et al. 1999), the Children's Communication Checklist (CCC-2©; Bishop 1998), and the Social Reciprocity Scale (SRS©; Constantino et al. 2000). We compared the performance of these three screening instruments in a pediatric mood and anxiety disorder research clinic. We hypothesized that children with mood disorders entering research studies would have a high likelihood of displaying symptoms of ASDs. To test this hypothesis, we used each of these instruments to determine the prevalence of those screening positive for possible ASDs in our mood disorder research clinic. Secondly, we studied the extent to which the three scales identified the same individuals as being at-risk for ASDs.

METHODS

Subjects

Ninety-three pediatric subjects were evaluated for one of three ongoing studies at the National Institute of Mental Health (NIMH) Intramural Research Program (IRP). The three studies included children with bipolar disorder, those with severe mood dysregulation (see below), and those with major depression and/or anxiety disorders. The NIMH IRB approved all three studies. All children were between the ages of 8 and 18 years. Parents or guardians gave written, informed consent, and children gave their written assent prior to participation. Subjects were recruited through advertisements placed on websites of relevant support groups or distributed at professional conferences, and letters about the study were sent to child psychiatrists nationwide.

Children with bipolar disorder (BPD) were part of a longitudinal neurocognitive and neuroimaging study. These children met criteria for the narrow phenotype of pediatric BPD (Leibenluft et al. 2003), meeting DSM-IV criteria for BPD, including a history of at least one hypomanic or manic episode lasting more than 4 days, during which the child exhibited abnormally elevated or expansive mood plus at least three other criterion "B" mania symptoms. Children with a history of "irritability only" without elevated or expansive mood were excluded.

Children with severe emotional dysregulation (ED) were enrolled in a double-blind, placebo-controlled investigation of lithium in this "broad phenotype" of bipolar disorder. These children have a chronic course of functionally impairing irritability, excessive reactivity to negative emotional stimuli, and hyperarousal (Leibenluft et al. 2003). They do not have hypomanic or manic episodes, expansive or elated mood, or other cardinal symptoms of mania. The relationship of this clinical phenotype to the narrow phenotype of BPD is controversial and was one focus of our study.

Children with major depression or anxiety were part of a neurocognitive and neuroimaging study, including treatment with fluoxetine, placebo, and/or cognitive behavioral therapy. All children met DSM-IV criteria for major depression or one anxiety disorder (generalized anxiety, separation anxiety, social phobia, panic).

Exclusion criteria for all three studies were: An IQ of less than 70; psychosis that interferes with the child's capacity to understand and comply with study procedures; unstable medical illness (i.e., severe asthma); medical illness that could cause the symptoms of a mood disorder (i.e., multiple sclerosis, thyroid disease); pregnancy; substance abuse within 2 months of the initial evaluation; or autistic disorder or severe pervasive developmental disorder. The latter was determined based on a medical record review, telephone conversations with treating clinicians and parents, and initial review of these clinical data by a team of experts in developmental psychopathology. Individuals with ASD diagnoses or histories highly suggestive of ASDs were excluded. In addition, children were excluded from the ED study if they had severe psychosis, and from the depression and anxiety studies if they had had antidepressant treatment for this episode of depression, had attention-deficit/hyperactivity disorder (ADHD) requiring stimulant treatment, or had conduct, Tourette's, obsessive-compulsive, or posttraumatic stress disorders.

Measures

The measures used in this study are the Social Communication Questionnaire (SCQ©), previously termed the Autism Screening Questionnaire (Berument et al. 1999), the Children's Communication Checklist (CCC-2©; Bishop 1998), and the Social Reciprocity Scale (SRS©) (Constantino et al. 2000) (Table 1). The SCQ and SRS are available from Western Psychological Services (Los Angeles, CA) and the CCC-2 is available from the Psychological Corporation (London, UK); all were used with permission.

The SCQ, previously termed the Autism Screening Questionnaire (Berument et al. 1999), was designed to use current (DSM-IV and ICD-10) criteria to screen for ASDs. It covers a broad age range, captures past and present functioning, and includes a broad scope of behaviors. It asks a primary caretaker to report on the presence of normative communication and social behaviors, such as directing another person's attention, nodding one's head, or initiating a social gesture and deviant communication or social behaviors, such as using odd phrases over and over or asking embarrassing questions to strangers. Nineteen items rate present functioning (within the last 3 months), and 20 others rate functioning during the period when the child was 4–5 years of age. Each of the scale's 39 items are scored present or absent (1 or 0), yielding a summary between 0 and 39. The items correspond to the ADI-R domains of "reciprocal social interaction," "language and communication," and "repetitive behaviors or stereotyped interests."

The CCC-2 is a qualitative measure of pragmatic language, a function that is not assessed adequately by standardized clinical assessments of communication and language. In order to measure pragmatic language, Bishop (1998) created a caregiver-rated instrument assessing the presence of normative communication skills in children 4–16 years of age, such as the ability to tell a story, refraining from telling people information they know already, or to the ability to read others' facial expressions. The 70-item scale has seven subscales and produces two composite measures—the General Communication Composite (i.e., GCC, which assesses grammar, articulation, and syntax) and the Social Interaction Deviance Composite (SIDC), which assesses social communication. Each item on the CCC is rated 0–2 ("doesn't apply," "applies somewhat," and "definitely applies"). Specific subscales capture speech, syntax, inappropriate intiation of conversation, coherence, stereotyped conversation, use of context, rapport, social ability, and interests. By definition, all children with ASDs display severe impairments in social communication and/or pragmatic language (Bishop and Baird 2001). Thus, by screening for children with severe pragmatic language impairments, the CCC-2 can identify those who are likely to have an ASD diagnosis. However, although the CCC-2 allows one to compare a child's score to those of children with ASDs, it does not assess the full array of ASD features (see Table 1). Thus, the CCC-2 is not specifically a screening instrument for ASDs, but it does allow one to identify persons with severely

TABLE 1. COMPARISON OF THREE SCALES ASSESSING DOMAINS OF ASD

			ASD domains, n (% of total no. of questions)			
Scale	*No. of items*	*Range of scores/item*	*Social reciprocity*	*Communication*	*Stereotypy and restricted interests*	*Other*
SCQ[a]	39	0–1	20 (51)	10 (26)	9 (23)	
CCC-2[b]	70	0–2	10 (14)	38 (54)	7 (10)	15 (21)
SRS	65	0–3	35 (53)	6 (9)	20 (31)	4 (6)

ASD = Autism Spectrum Disorders; SCQ = Social Communication Questionnaire; CCC = Children's Communication Checklist; SRS = Social Reciprocity Scale.

[a]Domain designation based on factor analysis.

[b]CCC-2 items were never related to ASD subdomains.

impaired pragmatic language, which is an important feature of ASDs.

Of the three instruments, the SRS is the only one created for epidemiological purposes (Constantino et al. 2000). Like the other scales, the SRS probes for explicit, observable behaviors and is intended to be completed by parents or care providers who see the child regularly. Each item is rated from 0 to 3 ("not true" to "always true"). It was developed to study how "social reciprocity behaviors" among children and adolescents were distributed in the general population and how these behaviors aggregate in extended families of children with ASDs. Thus, the measure was intended to ascertain social behaviors across the entire continuum of social function, including within the autism spectrum. Studies (Constantino and Todd 2003) indicate that the scale has a normal distribution in the population, and that reciprocal social behaviors ascertained by the SRS are explained best by "a single, continuously distributed factor" (Constantino et al. 2004). The SRS places the heaviest emphasis on social reciprocity and the least on language and language use (Table 1). Four questions probe for behaviors, such as clinging and poor personal hygiene, that are not specific to autism but are frequently associated with it.

Data collection

All patients were assessed with the Kiddie-Schedule for Affective Disorders Present and Lifetime Version (K-SADS-PL), a semistructured diagnostic clinical interview instrument, completed with parent and child individually (Kaufman et al. 1997). Trained clinicians with graduate and postgraduate level training and established inter-rater reliability completed the K-SADS-PL on every participant. Clinical assessments were made concurrent with the K-SADS interview. For children with BPD or ED, K-SADS diagnoses were made in a consensus conference of research staff led by at least one child and adolescent psychiatrist and using best-estimate procedures. In children with BPD, comorbid diagnoses were assessed by inquiring about the presence of symptoms during a time of relative euthymia (i.e., not during a depressed or manic episode). For children with depression or anxiety, trained clinicians completed K-SADS and made diagnoses using best estimate procedures.

The SCQ, CCC-2, and SRS were completed at the first visit by the parent or guardian who knows the child best. Each checklist was presented with its standard printed directions. Parents were asked to complete them and offered assistance if they had any questions.

Data analysis

The SCQ scoring paradigm calls for individuals with scores above 15 to be considered likely to have an ASD.

The CCC-2 subscales generate two independent scores—a General Communication Composite (GCC) and Social Interaction Deviance Composite (SIDC). A child can be placed in the "ASD-likely range" if he/she has:

(1) a very low SIDC score (less than −15), regardless of the GCC score, or
(2) a low SIDC score (less than 0) and a low GCC score (less than 55).

For the SRS, the suggested cut-off for likely ASD is a raw score greater than 70 for boys and 65 for girls (Constantino, personal communication).

Odds ratios were used to examine the extent to which the three instruments identified the same children as being in the ASD range. Spearman rho correlation coefficients were calculated to study the association between total scores on the SRS, SCQ, GCC, and SIDC. All calculations were preformed using SPSS 11.5 and significance level was set at $p < 0.05$.

RESULTS

The mean age of the subjects was 12.7 ± 2.8 and 63% were male. Tables 2 and 3 display the diagnoses in this cohort.

Of the 93 subjects examined, 25% (n = 23) completed only two screening instruments and 54% (n = 50) completed all three. Sixty-two percent (n = 58) of the entire cohort scored in the ASD-likely range on any one measure.

TABLE 2. DIAGNOSES IN STUDY SAMPLE

Diagnosis (total n = 93)	*n (%)*
Bipolar Disorder	43 (46)
Type I	34 (37)
Type II	9 (10)
Anxiety Disorder	53 (57)
Separation anxiety disorder	26 (28)
Generalized anxiety disorder/ overanxious disorder	48 (52)
Obsessive compulsive disorder	5(5)
Posttraumatic stress disorder	5 (5)
Social phobia	24 (26)
Agoraphobia	4 (4)
Simple phobia	16 (17)
Panic disorder	3 (3)
Major depressive disorder	27 (29)
Attention-deficit/hyperactivity disorder	57 (61)
Oppositional defiant disorder	49 (53)
Severe mood and behavioral dysregulation	29 (31)
Psychosis	10 (11)
Conduct disorder	1 (1)
Tourette's disorder	1 (1)

Note. Sum of $n > 93$, percent > 100 because individuals may have multiple diagnoses.

Specifically, 63% (27/43) of "narrow phenotype" BPD, 72% (21/29) of "broad phenotype" ED, and 48% (10/21) of depression/anxiety children scored in the ASD-likely range on at least one instrument.

Sixty-one percent (n = 37) of the 61 subjects who completed the SRS and 56% (n = 37) of the 66 subjects who completed the CCC-2 were found to be in the ASD range, compared to only 13% (n = 12) of the 90 subjects who completed the SCQ (Table 4). Of the 50 subjects who completed all three instruments, 24% (n = 12) did not score in the ASD range on any instrument, 34% (n = 17) were in the ASD-likely range on one instrument, 34% (n = 17) on two instruments, and 8% (n = 4) on all three instruments (Fig. 1).

Pairwise comparisons showed that 57% (n = 21/37) of those scoring in the "ASD-likely" range on the SRS also scored in that range on the CCC-2. However, only 16% (n = 6/37) of those scoring in the ASD-likely range on the SRS also scored in that range on the SCQ, and 14% (n = 5/37) of those in the ASD-likely range on the CCC-2 scored similarly on the SCQ. Odds ratios were calculated to estimate the likelihood that a subject who scored in the

TABLE 3. COMORBID DIAGNOSES BY PRIMARY DIAGNOSIS

Primary diagnosis	*Comorbid diagnoses*	*n (%)*
BP-I		34 (100)
	Depression	11 (50)
	Anxiety	17 (79)
	Psychosis	10 (29)
	ADHD	22 (65)
	ODD	12 (35)
	ASD Range[a]	21 (62)
BP-II		9 (100)
	Depression	3 (33)
	Anxiety	7 (78)
	Psychosis	0 (0)
	ADHD	6 (66)
	ODD	6 (66)
	CD	0 (0)
	ASD Range[a]	6 (67)
Emotionally Dysregulated		29 (100)
	Depression	20 (69)
	Anxiety	12 (41)
	Psychosis	0 (0)
	ADHD	26 (90)
	ODD	26 (90)
	CD	1 (3)
	ASD Range[a]	21 (72)
Depressed/Anxious		21 (100)
	Depression	8 (38)
	Anxiety	17 (81)
	Psychosis	0 (0)
	ADHD	3 (14)
	ODD	5 (24)
	ASD Range[a]	10 (48)
Total		**93**

ADHD = attention-deficit/hyperactivity/disorder; ODD = oppositional defiant disorder; ASD = Autism Spectrum Disorders; CD = conduct disorder.

[a]Defined as scoring in the ASD range on one or more measures.

TABLE 4. MEAN TOTAL SCALE SCORE AND PERCENTAGE OF SUBJECTS IN THE ASD RANGE

	n	*Mean (SD)*	*n (%) in ASD range*
SCQ	90	8.3 (5.2)	12 (13.3)
SRS	61	69.2 (26.1)	37 (60.7)
CCC	66	—	37 (56.1)[a]
GCC		56.7 (20.8)	22 (33.3)[b]
SIDC		−10.2 (9.7)	21 (31.8)[c]

SCQ = Social Communication Questionnaire; SRS = Social Reciprocity Scale.

[a]Identified by either CCC-2 method.

[b]Identified by GCC (General Communication Composite) <55 and SIDC <0.

[c]Identified by SIDC (Social Interaction Deviance) ≤ −15 alone.

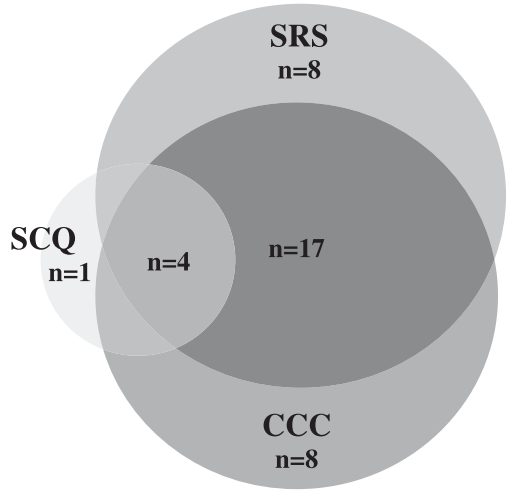

FIG. 1. Of subjects who completed the SRS, CCC-2, and SCQ (n = 50), number of subjects scoring in the ASD-likely range on any one instrument (total n scoring in ASD range = 38). SRS = Social Reciprocity Scale; CCC = Children's Communication Checklist; SCQ = Social Communication Questionnaire; ASD = Autism Spectrum Disorders.

ASD range on one instrument would also score in that range on another instrument (Table 5). Children in the ASD range on the SRS were significantly more likely to be in the ASD range on the CCC-2, compared to those who were not in the ASD range on the SRS (odds ratio, 4.59; [95% CI = 1.40–15.11]). There were no significant associations between the SCQ and the other instruments.

Spearman rho correlation coefficients were used to examine the relationship between the total raw scale scores on the SRS, SCQ, GCC, and SIDC (Table 6). Total scores from the SRS, GCC, and SCQ scales were moderately but significantly correlated with each other (r = 0.376–0.469; $p < 0.01$). The SIDC was correlated with the GCC ($r = -0.417$; $p < 0.01$), but not with the SCQ (r = 0.115; p = NS) or SRS ($r = -0.203$; p = NS).

DISCUSSION

Several major findings emerged from this study. Firstly, in this population of children presenting for participation in studies of mood and anxiety disorders, we found a relatively high prevalence of individuals scoring in the range typically found in children with ASD diagnoses. Secondly, in this sample of children, the SRS and CCC-2 performed similarly. That is, scores on these two measures were correlated weakly but significantly and each measure identified a similar number of children as being in the ASD range. In addition, a child scoring in the affected range on one of these two scales was likely to score as affected on the other (odds ratio = 4.59). The SCQ, on the other hand, identified a much smaller percentage of children as being in the ASD range.

It is remarkable that, overall, 62% of our cohort scored in the "ASD-likely range" on at least one measure. Given our interest in relatively severe and persistent mood or anxiety disorders, it is possible that the National Institutes of Health (NIH) population is not representative of patients who are seen in general and specialty child psychiatry clinics elsewhere. Yet, prospective participants were screened to exclude individuals with ASD diagnoses or clear-cut ASD symptoms. Nearly all children included in this sample had been seen previously by a mental health professional (many by child and adolescent psychiatrists); none had been diagnosed with ASDs. Therefore, it is possible that mild-to-moderate ASDs are often unrecognized in clinical

TABLE 5. ODDS RATIOS OF BEING IDENTIFIED IN THE ASD RANGE BETWEEN MEASURES

	n	*OR*	*95% CI—lower*	*95% CI—upper*
Given SRS + PDD, odds of CCC + PDD	51	4.59	1.40	15.11
Given SRS + PDD, odds of SCQ + PDD	60	4.26	0.48	37.90
Given SCQ + PDD, odds of CCC + PDD	63	2.02	0.36	11.29

ASD = Autism Spectrum Disorders; OR = odds ratio; CI = confidence interval; PDD = pervasive development disorder; SRS = Social Reciprocity Scale; CCC = Children's Communication Checklist; SCQ = Social Communication Questionnaire.

Table 6. Spearman Rho Correlation Coefficients of Total Score Per Measure

	SRS	*GCC*	*SIDC*
SCQ	0.376[a]	−0.469[a]	0.115
n	60	63	63
SRS		−0.423[a]	−0.203
n		51	51
GCC			−0.417[a]
n			66

SRS = Social Reciprocity Scale; GCC = General Communication Composite; SIDC = Social Interaction Deviance Composite.

[a]$p < 0.01$.

practices. Alternatively, the screening instruments used in this study may rely on low thresholds to determine risk for ASDs, yielding high sensitivity at the expense of low specificity. Indeed, 64%–90% of children with PDD-NOS and 35%–86% of children with ADHD were noted to have SIDC scores greater than two standard deviations from normal control children (Bishop and Baird 2001; Geurts et al. 2004), and 65% of children with conduct or oppositional defiant disorders seen in a general clinic setting score in the "ASD-likely" range on the CCC-R (Skuse et al. 2004). On the other hand, studies of the SRS report that patients with psychiatric illnesses other than ASDs do not score higher than healthy controls (Constantino et al. 2004; Constantino et al. 2000).

Taken together, our data and those in ADHD, conduct disorder, and ODD (Gilmour et al. 2004; Geurts et al. 2004; Bishop and Baird 2001) suggest that many psychiatrically impaired children seen in clinical settings may have deficits in social communication and pragmatic language. These data raise essential questions about the relationships among ASDs, more common forms of childhood-onset psychopathology (e.g., ADHD, mood/anxiety disorders, ODD), and deficits in social-linguistic functioning. On the one hand, ASDs may represent a far more prevalent form of psychopathology than previously recognized, frequently co-occurring with common forms of mood, anxiety, and disruptive behavior disorders. On the other hand, conditions resembling mild ASDs that occur in children with such common psychopathologies may represent "phenocopies" that bear little pathophysiologic resemblance to classic PDD. That is, such "comorbidities" may simply represent the "tail end" of traits that are normally distributed throughout the population but are not caused by the same factors that produce ASD. If children with common psychopathologies are indeed at the "tail end" of the normal distribution of social and language ability, an important area for future research is whether being impaired in these domains increases the risk for ADHD, mood/anxiety disorder, and so forth (Yule and Rutter 1987; Cohen et al. 1993; Cohen et al. 1998a, Cohen et al. 1998b), or, conversely, whether these deficits are, to some degree, a result of the children's other psychopathology (Yule and Rutter 1987).

Data from clinical studies, such as in our study, are unlikely to address these issues adequately. Rather, clinical and phenomenological data must be supplemented by studies of neuropsychology, longitudinal outcome, family genetics, and therapeutics. The current data in mood and anxiety disorders, much like published data in disruptive behavior disorders (Skuse et al. 2004; Gilmour et al. 2004; Geurts et al. 2004; Bishop and Baird 2001), should stimulate studies on the relationships among common developmental psychopathologies, social information-processing deficits, and aspects of neuroscience, therapeutics, and genetic epidemiology.

The correlation coefficients comparing these three instruments show, with the exception of the SCQ and the SIDC, weak but statistically significant associations. In addition, the GCC and SIDC subscales of the CCC-2 are highly correlated with one another, though they were designed to measure different language impairments. While the correlations among the SCQ, CCC-2, and SRS were significant, they were not high enough to ensure that they identified the same children as being at-risk for ASDs. Indeed, although a similar number of individuals scored in the ASD-likely range on the SRS and CCC-2, only 47% of them scored in that range on both instruments. Of those individuals who completed all three instruments, only 8% of those scoring in the ASD-likely range on any one measure scored in the same range on the other two.

As noted above, the SRS and the CCC-2 show more overlap in performance than does either scale with the SCQ. The SRS, which was designed for use in epidemiological studies, quantifies impairment in reciprocal social interaction, which is the most prominent feature in individuals at the milder end of the ASD spectrum (Constantino et al. 2000; Paul et al. 2004; Walker et al. 2004; Carter et al. 1998). In contrast, the SCQ draws from the three autistic spectrum domains (social, communication/ abnormal language, stereotyped behavior) and asks about more deviant behaviors than are typically seen in mild ASDs. As a result, the SCQ may be less sensitive to ascertaining individuals with nonautistic ASDs (Charman 2003). In addition to these differences in emphasis, the SCQ may function as a more restrictive screening measure than the SRS or CCC-2 because of the methodology that was used to construct and validate it. Firstly, the SCQ was validated in parents who had completed the ADI-R, a lengthy interview designed to identify ASD traits (Berument et al. 1999), raising questions about the generalizability of the results to ASD naïve caregivers (Bishop and Norbury 2002). Secondly, compared to the CCC-2 and SRS, the SCQ offers the fewest probes while covering all three domains, perhaps limiting its sensitivity. Thirdly, the SCQ, like the ADI-R, asks parents to recall their child's language and social function at 4–5 years of age, thus introducing possible recall bias. In addition, symptoms at 4–5 years of age may not be robust predictors of current impairment, particularly in high-functioning ASD individuals (Starr et al. 2003). Lastly, the SCQ has only one scoring metric for all individuals older than 6 years, whereas CCC-2 and SRS scores are standardized by age and gender.

CONCLUSION

Our findings are consistent with other recent studies demonstrating the high prevalence of unrecognized ASDs in children presenting with common developmental psychopathologies (Bishop and Baird 2001; Geurts et al. 2004; Gilmour et al. 2004). These data suggest that high rates of mild-to-moderate ASDs may be "flying under the radar" of traditional research diagnostic methods. Alternatively, children lying on the tail end of normally distributed traits, such as social communication ability, may be over-represented in clinical samples. Finally, the current findings may reflect referral biases; the children entering our studies differ in a variety of ways from those seen in typical child psychiatry clinics in the community. It is highly likely that they are more severely and chronically impaired than children seen in typical office practices or in general psychiatry clinics. However, previous studies in children with disruptive disorders seen in general child psychiatry clinics have controlled for this potential limitation (Geurts et al. 2004; Gilmour et al. 2004; Bishop and Baird 2001) and reported rates comparable to ours. Further study could clarify whether the comorbidity found in our study represents the ascertainment bias of a specialized research setting or is consistent with ASD traits seen in most clinics and practices or in other clinics where children with severe psychopathology are evaluated. Further investigation would shed light on whether there is any characteristic pattern of social or language deficits in children with broad or narrow phenotype bipolar disorder, and whether there is any specific pattern of mood or behavioral symptoms among children with ASDs.

In addition, data comparing these instruments to clinical diagnoses is needed from specialty clinics that provide comprehensive multidisciplinary evaluations of ASDs, and general child psychiatry clinics seeing children with severe psychopathology. There has been a surprising paucity of data on these instruments from PDD specialty clinics. Small studies, one with the SRS (Constantino et al. 2003) and another with the CCC-R (Bishop and Baird 2001), suggest good agreement with information from the ADI-R.

In any case, our results demonstrate that there is a pressing need to validate user-friendly, reliable instruments that screen for ASD disorders in children presenting outside of ASD clinics. Based on our experience, we are unable to offer recommendations about which of the three instruments that we used might be most appropriate for this purpose. At this point, the use of multiple instruments may be necessary in order

to feel confident that screening has been adequate. In any case, screening devices cannot substitute for well-trained, experienced clinicians in sorting out differential diagnoses.

Our experience with these three scales indicates that many parents rate their children as having ASD symptoms that have not been recognized by the treating clinicians. As noted above, the disparity between clinician impression and scores on these instruments may suggest that the screening tools overestimate the likelihood of having an ASD (Medical Research Council 2001; South et al. 2002). More investigation with larger, more diverse samples may indicate more appropriate cut-offs for the scales (Gilmour et al. 2004). Of course, there is also the possibility that, compared to parents who participated in the original reliability studies with the SRS, SCQ, and CCC-2, the parents who brought children to our studies were less reliable in their ratings or assessments, although this seems unlikely when they are reliable on other measures (such as those for anxiety or depression) that they are asked to complete. Furthermore, in the study of Geurts et al. (2004), parent ratings from a general clinic correlated closely with clinical diagnoses.

Alternatively, clinicians may not recognize social impairment, or they may not see it as a symptom of an ASD. This suggests that training and continuing education programs might raise awareness in the clinical community about the assessment of ASDs. But it also points up the pressing need for pediatricians, child neurologists, and general child psychiatrists to have available practical-screening instruments (South et al. 2002; Geurts et al. 2004; Skuse et al. 2004). Our experience points to the necessity for collaborations between pediatric psychiatric disorder investigators and ASD researchers to develop reliable, practical screening tools.

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Appendix

Vignette 1: "Steve"

"Steve" is a 15-year-old boy who resides at home with his mother and stepfather, a stepsister and a half brother. When he was 13 years of age, Steve entered a research study of bipolar disorder after a K-SADS revealed lifetime diagnoses of BP I, avoidant disorder of childhood, simple phobia, social phobia, overanxious disorder, generalized anxiety disorder, enuresis, and ADHD. History of his mood problems revealed that he had a period of depression that lasted several months at 9 years of age. This was characterized by depressed mood, anhedonia, suicidal ideation, and social withdrawal. He was hospitalized and all medication was withdrawn. During this period he became manic with euphoria, grandiosity, pressured speech, racing thoughts, distract-ibility, impulsivity, and hypersexuality part of the day on most days. He was noted to be psychotic, endorsing statements about hearing voices telling him to hurt himself, and expressing concerns about an alien invasion. There were 2–3 other periods of depressed mood between 8 and 12 years of age that met symptom criteria for depression, but were no more than 8–9 days in duration.

Steve was hospitalized on a research inpatient unit 2 years after first being in our studies. He was noted to be oddly related and had unusual ways of communicating. A detailed developmental history showed that Steve had very significant language delays and social impairment long before the onset of his first manic or depressive episode. He responded so awkwardly to others' social overtures that he was an outcast. He never had a friend, had never been invited to a birthday party, and was unable to understand others' emotions or reactions. On the unit, he displayed no mood symptoms, but told "tall tales" of adventures and exploits that were transparent fantasies, although held tenaciously to their truthfulness to save face. In other moments, he acknowledged making these up. He had fantastical, eccentric ideas (e.g., that his parents were giving him gills for Christmas). His ideation was highly immature, and he showed a poor understanding of the difference between reality and fantasy (e.g., cartoons versus real events). Discussions with Steve's mother revealed that Steve displayed these kinds of misunderstandings since early childhood.

Steve also had a history of significant language deficits, with a monotone voice, odd word expressions, and eccentric definitions for words. These misunderstandings often created trouble for Steve. For example, on one occasion he was quite insistent that his father was a colonel in the army. After being challenged on this several times by another patient, he asked, "Is a colonel the same as a sergeant?" He also defined rape as "asking a girl over and over to go out with you."

During the course of Steve's participation in the study, his half brother was diagnosed with an autistic disorder.

Based on his mother's ratings, Steve's scores on the Social Communication Questionnaire (SCQ) were 5 (low), Social Reciprocity Scale (SRS) were 55 (low), and Children's Communication Checklist (CCC-2) suggested language disorder, with a General Communication Competence of 30 and Social Interaction Deviance Composite of 10. Subscales of the CCC-2 further identified deficits as being in the areas of speech, coherence, inappropriate initiation, use of context, and social subscales, all of which were more than 2 standard deviations from average. At discharge, Steve was diagnosed with bipolar disorder and PDD-NOS. Prominent features of inattention and distractibility were also noted.

Vignette 2: "Mike"

"Mike" is a 10-year-old boy who lives at home with this mother and stepfather. Mike entered a study of emotional dysregulation after many years of aggressive behaviors, oppositional behavior, restlessness, impulsivity, and over-reaction to the slightest difficulties.

Mike's symptoms were first evaluated at around 3–4 years of age. Besides the symptoms of emotional dysregulation, he also exhibited a significantly elevated tolerance to pain, intolerance of loud noises, and aversion to specific textures. In face-to-face, separate interviews with Mike and his mother, neither discrete episodes of mood symptoms nor cardinal symptoms of mania were elicited. The pattern of symptoms that emerged was chronic irritability, hyperarousal, and extreme responses to adverse events.

In our research hospital setting, Mike displayed an extreme inability to understand others' needs, wishes, desires, or beliefs, despite excellent cognitive abilities. He was masterful in his acquisition of facts, discrete pieces of information (e.g., Egyptology), and rote skills. However, his higher-order reasoning and ability to understand others' feelings were significantly impaired. With regard to language, he had good vocabulary and syntax, but was unable to engage in even simple narrative exchanges. Mike never asked spontaneously about thoughts or experiences of peers or staff. Off medications, Mike typically engaged others by barking like a dog or making sounds like a wild monkey (which were carried off with remarkable skill). Indeed, his ability to imitate all kinds of sounds (for example, an ambulance siren) were extraordinary. Mike also displayed some excessive interests. For example, he started an extensive "cheap" pen collection in the hospital that was so compelling to him that he often focused on the pen rather than the person holding it, and he could talk at length about his collection. He also demonstrated a rigid adherence to routines and would become upset to the point of tantrums if these routines were not sustained.

When completing rating forms, Mike's mother gave him an SCQ of 6, an SRS of 74, and a CCC-2 that suggested significant pragmatic language impairment with a General Language Composite (GCC) of 74 and Social Interaction Deviance Composite (SIDC) of −18. At discharge, Mike was diagnosed with ADHD, PDD-NOS, and the research diagnosis of severe mood and behavioral dysregulation (Leibenluft et al. 2003).