

Autism Spectrum Disorder Scale Scores in Pediatric Mood and Anxiety Disorders

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ABSTRACT

Objective: To compare scores on autism spectrum disorder (ASD) symptom scales in healthy youths and youths with mood or anxiety disorders. **Method:** A total of 352 youths were recruited (107 healthy participants, 88 with an anxiety disorder, 32 with major depressive disorder, 62 with bipolar disorder, and 63 with a mood disorder characterized by severe nonepisodic irritability). Participants received structured psychiatric interviews and parent ratings on at least one of three ASD symptom scales: Children's Communication Checklist, Social Communication Questionnaire, and Social Responsiveness Scale. **Results:** Relative to healthy youths, youths with mood or anxiety disorders exhibited higher scores on each ASD symptom scale. ASD symptom scale scores also showed an association with impairment severity and attention-deficit/hyperactivity disorder. Among patients with mood disorders but not those with anxiety disorders, consistent, statistically significant associations between diagnosis and ASD symptom scale scores remained even after controlling for potential confounders. **Conclusions:** Patients with mood disorders exhibit higher scores on ASD symptom scales than healthy youths or youths with anxiety disorders. These data should alert clinicians to the importance of assessing ASD symptoms to identify social reciprocity and communication deficits as possible treatment targets in pediatric mood and anxiety disorders. *J. Am. Acad. Child Adolesc. Psychiatry*, 2008;47(6):652-661. **Key Words:** mood disorder, anxiety disorder, autism spectrum, impairment.

Perturbed social reciprocity, communication, and stereotyped behaviors represent core features of autism spectrum disorders (ASDs). Prevalence estimates of ASDs have increased recently,^{1,2} and contemporary studies indicate that children with ASDs appear less impaired than those diagnosed previously.² Thus, increased ASD prevalence at least partially reflects

greater ascertainment of mild ASDs, suggesting that ASDs may be viewed along a continuum.³⁻⁶ Consistent with this view, studies find high ratings on ASD symptom scales in youths with disruptive behavior disorders or attention-deficit/hyperactivity disorder (ADHD).^{7,8} Much of this work relies on three standardized scales. The Social Communication Questionnaire (SCQ)⁹ was developed as an ASD screener, the Social Responsiveness Scale (SRS)¹⁰ was created to measure autistic traits, and the Children's Communication Checklist (CCC)¹¹ was designed to assess pragmatic language. As such, each scale was designed for somewhat different purposes and emphasizes somewhat different symptoms of ASDs. Community-based studies find that scores on the SCQ and SRS exhibit continuous distributions throughout the population.^{1,12}

Although developers of the SCQ and SRS consider them ASD screens, in various populations, questions remain as to the degree to which these and the CCC measure distinct constructs and central features of ASDs.¹³⁻¹⁵ These measures contain probes that tap the three ASD symptom domains. However, consistent with

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2. Lord C, Risi S, Lambrecht L, et al. The Autism Diagnostic Observation Schedule–Generic: a standard measure of social and communication deficits associated with the spectrum of autism. *J Autism Dev Disord.* 2000;30:205–223.
3. Joseph RM, Tager-Flusberg H, Lord C. Cognitive profiles and social-communicative functioning in children with autism spectrum disorders. *J Child Psychol Psychiatry.* 2002;43:807–821.
4. de Bildt A, Sytema S, Ketelaars C, et al. Interrelationship between Autism Diagnostic Observation Schedule–Generic (ADOS-G), Autism Diagnostic Interview–Revised (ADI-R), and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) classification in children and adolescents with mental retardation. *J Autism Dev Disord.* 2004;34:129–137.
5. Lord C, Rutter M, DiLavore P, Risi S. *Autism Diagnostic Observation Schedule Manual.* Los Angeles: Western Psychological Services; 1999.
6. Constantino JN, Gruber CP, Davis C, Hayes S, Passanante N, Przybeck T. The factor structure of autistic traits. *J Child Psychol Psychiatry.* 2004;45:719–726.
7. Lecavalier L, Aman MG, Scahill L, McDougle CJ, McCracken JT, Vitiello B. Validity of the autism Diagnostic Interview–Revised. *Am J Ment Retard.* 2006;111:199–215.
8. Lord C, Risi S, DiLavore R, Shulman C, Thurm A, Pickles A. Autism from two to nine. *Arch Gen Psychiatry.* 2006;63:694–701.
9. Walker DR, Thompson A, Zwaigenbaum L, Goldberg J, Bryson SE, Mahoney WJ. Specifying PDD-NOS: a comparison of PDD-NOS, Asperger syndrome, and autism. *J Am Acad Child Adolesc Psychiatry.* 2004;43:172–180.
10. Rutter M, LeCouteur A, Lord C. *Autism Diagnostic Interview–Revised–WPS.* WPS ed. Los Angeles: Western Psychological Services; 2003.
11. DiLavore P, Lord C, Rutter M. Pre-Linguistic Autism Diagnostic Observation Schedule (PL-ADOS). *J Autism Dev Disord.* 1995;25:355–379.
12. Mullen E. *Mullen Scales of Early Learning.* AGIS ed. Circle Pines, MN: American Guidance Service; 1995.
13. Wechsler D. *Wechsler Intelligence Scale for Children,* 4th ed. San Antonio, TX: Psychological Corporation; 2003.
14. Siegel B, Vukicevic J, Elliott G, Kraemer H. The use of signal detection theory to assess DSM-III-R criteria for autistic disorder. *J Am Acad Child Adolesc Psychiatry.* 1989;28:542–548.
15. Muthen LK, Muthen BO. *M-plus User's Guide.* Los Angeles: Muthen & Muthen; 1998.
16. Browne MW, Cudeck R. Alternative ways of assessing model fit. In: Bollen KA, Long JS, eds. *Testing Structural Equation Models.* Newbury Park, CA: Sage Publications; 1993:136–162.
17. MacCallum R, Widaman K, Preacher K, Hong S. Sample size in factor analysis: the role of model error. *Multivariate Behav Res.* 2001;36:611–637.
18. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 4th ed (DSM-IV).* Washington, DC: American Psychiatric Association; 1994.

Prevalence of Correlates, Disability, and Comorbidity of DSM-IV Drug Abuse and Dependence in the United States Compton WM, Thomas YF, Stinson FS, Grant BF

Background: Current and comprehensive information on the epidemiology of DSM-IV 12-month and lifetime drug use disorders in the United States has not been available. **Objectives:** To present detailed information on drug abuse and dependence prevalence, correlates, and co-morbidity with other Axis I and II disorders. **Design, Setting, and Participants:** Face-to-face interviews using the Alcohol Use Disorder and Associated Disabilities Interview Schedule of the National Institute on Alcohol Abuse and Alcoholism in a large representation sample of US adults (N = 43 093). **Main Outcome Measures:** Twelve-month and lifetime prevalence of drug abuse and dependence and the associated correlates, treatment rates, disability, and comorbidity with other Axis I and II disorders. **Results:** Prevalences of 12-month and lifetime drug abuse (1.4% and 7.7%, respectively) exceeded rates of drug dependence (0.6% and 2.6%, respectively). Rates of abuse and dependence were generally greater among men, Native Americans, respondents aged 18 to 44 years, those of lower socioeconomic status, those in the West, and those who were never married or widowed, separated, or divorced (all $P < .05$). Associations of drug use disorders with other substance use disorders and anti-social personality disorder were diminished but remained strong when we controlled for psychiatric disorders. Dependence associations with most mood disorders and generalized anxiety disorder also remained significant. Lifetime treatment- or help-seeking behavior was uncommon (8.1% abuse; 37.9% dependence) and was not associated with sociodemographic characteristics but was associated with psychiatric comorbidity. **Conclusions:** Most individuals with drug use disorders have never been treated, and treatment disparities exist among those at high risk, despite substantial disability and comorbidity. Comorbidity of drug use disorders with other substance use disorders and antisocial personality disorder, as well as dependence with mood disorders and generalized anxiety disorder, appears to be due in part to unique factors underlying each pair of these disorders studied. The persistence of low treatment rates despite the availability of effective treatments indicates the need for vigorous educational efforts for the public and professionals. Reprinted with permission from *Arch Gen Psychiatry* 2007;64:566–576. Copyright © 2007, American Medical Association. All rights reserved.

the somewhat distinct purposes for which these three scales were designed, neuropsychological and genetic studies also dissociate ASD symptom domains.^{4,5,16} As a result, these scales may tap only partially overlapping constructs.

We approached this study recognizing that high scores on ASD symptom scales are not equivalent to an ASD diagnosis.¹³⁻¹⁵ Rather, our study was designed to determine whether high scores on scales typically used to assess ASD symptoms occur in children without frank ASD who present for clinical evaluation of non-ASD conditions. Such research is needed to characterize profiles on ASD symptom scales across a wide range of mental syndromes.

Although the number of studies using ASD symptom scales has increased, work is needed in pediatric mood and anxiety disorders. Such work can determine the degree to which clinicians need to integrate relevant assessments into treatment planning. The present study adds to this literature by using the SRS, SCQ, and CCC to examine questions raised by the only previous study in pediatric mood or anxiety disorders.¹⁷ The 93 participants in that initial study are included in the present study of 352 participants that tested three specific hypotheses.

First, the initial study found that 62% of patients with mood or anxiety disorders scored above standard cutoffs on the SRS, SCQ, and CCC. However, patients were recruited from a research setting, and their scores were not compared with those of concurrently assessed healthy youths. Because ASD symptom scales scores lie along a continuum, it is important to clarify the degree to which elevated scores occur specifically in patients with mental disorders, relative to other youths volunteering for psychiatric research. Specifically, the previous study examined four patient groups (i.e., major depressive disorder [MDD], anxiety disorders, bipolar disorder [BD], severe mood dysregulation [SMD]), but not healthy youths. The present study is the first to test the hypothesis that each of these four patient groups exhibit higher ASD symptom scale scores than healthy youths.

Second, in the previous study, ASD symptom scale scores were not compared among patient groups. Previous findings suggest that pediatric patients with BD exhibit deficits in social cognition similar to those found in ASDs¹⁸ as well as particularly high ASD symptom scale scores.¹⁷ Thus, we hypothesized that patients with BD or SMD would score higher than

other patient groups. Patients with MDD and anxiety disorders were chosen as comparisons because, like patients with BD or SMD, they experience prominent emotional problems. Demonstrating differences among BD, SMD, and other emotional disorders would clarify the degree to which high ASD symptom scale scores occur in either a broad or narrow range of emotional disorders.

Finally, we had questions about the degree to which anxiety disorders exhibit associations with ASD symptom scale scores. Considerable work documents similarities in the course, familial aggregation, and neuropsychology of three pediatric anxiety disorders: social phobia (SoPh), separation anxiety disorder (SAD), and generalized anxiety disorder (GAD).¹⁹ Nevertheless, data from a family study suggest that ASD symptoms exhibit particularly strong associations with SoPh.⁶ Therefore, we hypothesized that ASD symptom scale scores would be higher in pediatric SoPh than SAD or GAD. Although previous studies note a familial association between SoPh and ASD symptoms, no previous study examines, within individual children, the degree to which specific anxiety disorders are associated with high ASD symptom scale scores. Clinicians developing treatment approaches for specific patients need to understand the extent to which ASD symptom scale scores exhibit associations with specific anxiety disorders.

METHOD

Participants

Children and adolescents entering research studies between 2002 and 2006 at the NIMH Mood and Anxiety Program were invited to participate, resulting in 352 participants. Participants were recruited by advertisements and postings as described previously.^{18,20,21} Five groups were included: healthy youths and youths with anxiety disorders, MDD, BD, or SMD. All of the participants and their parents provided written assent/consent to participate in institutional review board-approved protocols. Data for the current study were collected as part of intake assessments in participants who had to be 7 to 17 years old with an IQ >70.

All of the participants were required to have no more than mild signs of ASD, based on questionnaires, medical records, discussions with treating clinicians in the community, clinical assessment at the NIMH, and expert review of all available material. All of the

participants with moderate to severe autism were excluded. Exclusion of a patient with signs of mild ASD was based on expert consensus. Specifically, participants were excluded if they presented with severe impairment from long-standing dysfunction in communicative or social reciprocity domains. Thus, children with severe ASD symptoms were excluded, although high-functioning children meeting *DSM-IV* criteria for ASD could be included as long as they exhibited no more than mild social and language impairment due to ASD. Such children were identified for further in-depth screening based on their scores on the ASD symptom scales that serve as the focus of the present article, supplemented by observations from the clinician completing the structured psychiatric interview. Because these methods relied on clinician decisions, the clinical staff was unblinded with regard to patient's diagnostic status. However, because parents completed ASD symptom rating scales before group assignment had been determined, group assignment and ASD symptom scale scores were determined independently.

Our approach to diagnostic classification used a hierarchical scheme that was included in previous research and, in some instances, outlined in *DSM-IV*. Thus, youths with a history of mania as well as MDD and/or an anxiety disorder are considered to have BD. SMD is a category designed to capture those youths who frequently receive the diagnosis of BD despite not meeting *DSM-IV* BD criteria. Thus, with regard to comorbid MDD or anxiety disorders, the same hierarchical rules are used as for BD. The criteria for SMD are written so that the diagnoses of BD and SMD are mutually exclusive, and all of the children meeting criteria for SMD are included in the SMD category, as opposed to the anxiety or MDD groups. Previous research on anxiety and MDD typically categorizes youths with MDD and anxiety disorders as having MDD with co-occurring anxiety rather than anxiety with co-occurring MDD. This convention emerged because MDD typically presents with co-occurring anxiety, although anxiety frequently presents without MDD. The use of these conventions resulted in four diagnostic categories: anxiety disorders, MDD, BD, and SMD.

Anxiety. This group ($n = 88$) met criteria for current SAD, GAD, or SoPh. Other inclusion criteria comprised clinically significant anxiety on the Pediatric Anxiety Rating Scale (score ≥ 9)²² and persistent anxiety during 3 weeks of psychoeducation and monitoring.

Exclusion criteria comprised current Tourette syndrome, MDD, obsessive-compulsive disorder, or conduct disorder, trauma exposure, suicidal ideation, and lifetime history of mania or psychosis.

MDD. Patients with MDD ($n = 32$) were required to meet criteria for MDD, with or without an anxiety disorder, as well as clinically significant depressive symptoms (score >39) on the Children's Depression Rating Scale.²³ All of the other criteria were the same for MDD as for patients with anxiety.

BD. Patients with BD ($n = 62$) were required to meet criteria for narrow phenotype BD,²⁴ with at least one *DSM-IV* (hypo)manic episode (i.e., 4 days for hypomania, 7 days for mania, elevated/expansive mood, and 3 other "B" symptoms).

SMD. SMD characterizes youths with symptoms sometimes conceptualized as broad phenotype BD.²⁴ Patients with SMD ($n = 63$) were required to have no history of *DSM-IV* (hypo)mania. Inclusion criteria were abnormal mood (anger or sadness) present at least half of the day most days, hyperarousal (≥ 3 of insomnia, agitation, distractibility, racing thoughts/flight of ideas, pressured speech, intrusiveness), markedly increased reactivity to negative emotional stimuli manifest verbally or behaviorally at least three times weekly, symptoms that cause severe impairment in at least one setting (home, school, or peers) and at least mild impairment in a second setting, and SMD symptom onset must have occurred before age 12 and be present for at least 12 months without symptom-free periods for more than 2 months.²⁴ Of note, by design, children with SMD were not eligible to be included in any other diagnostic category.

Healthy. Healthy participants ($n = 107$) were required to have no psychiatric history, ongoing medical illness, regular medication use, or exposure to extreme trauma. Of note, healthy volunteers were recruited primarily to participate in biologically oriented research, whereas patients were recruited for both these same biological studies and treatment or longitudinal studies. In general, biologically oriented studies recruited older subjects than treatment or longitudinal studies because the latter included some children younger than the lower limit for some biological studies.

Measures

Diagnosis and Impairment. Diagnosis was determined using the Schedule for Schizophrenia and Affective Disorders for School-Age Children-Present and Lifetime

Version,²⁵ including an addendum to ascertain SMD. All of the assessments were completed by experienced clinicians trained to achieve reliability for all of the diagnoses ($\kappa > .75$). Training and reliability testing involved the observation of random interviews by an expert and ratings by clinicians of videotaped diagnostic interviews. Reliability was maintained by regular training and expert review sessions.

Patients' detailed assessments ended with overall impairment ratings on the Children's Global Assessment Scale (CGAS), a scale shown previously to be rated with high reliability.²⁶ Reliability was not assessed in the present study, however. The CGAS was used for the patients, but not the psychiatrically healthy participants, who were free of clinically meaningful impairment.

Intelligence. IQ was obtained using the Wechsler Abbreviated Scale of Intelligence.²⁷

ASD Symptoms. The SRS is a parent-reported checklist of 65 items rated from 0 to 3 ("not true" to "always true").¹⁰ SRS scores >70 for males and >65 for females (approximately 1.5 SDs from the population mean for each sex) are above the clinical cutoff for ASD signs. The SCQ is a 40 "yes-no" item, parent-reported checklist of salient questions from the Autism Diagnostic Interview-Revised (ADI-R).^{9,28} Like the ADI-R, the SCQ asks about functioning in multiple domains in the past 3 months and when the child was 4 to 5 years old. SCQ scores >15 fall within the clinical cutoff for ASD signs. High SRS and SCQ scores indicate high impairment. The CCC-2 is a 70-item parent-reported checklist designed to identify specific and pragmatic language impairments in children.¹¹ The CCC generates two composite scores: the General Communication Composite (GCC) of core language skills (e.g., grammar, articulation, syntax), and the Social Interaction Deviance Composite (SIDC) measure of pragmatic abnormalities of social communication. Low scores on the GCC and SIDC indicate high symptoms and greater impairment. The clinical cutoff for ASD signs on the CCC is based on SIDC scores ≤ 15 with any GCC score or SIDC scores < 0 and GCC scores < 55 . The SCQ and SRS are available from Western Psychological Services and the CCC-2 is available from the Psychological Corporation; all of the scales were used with permission. Of note, although both the CCC and SRS emphasize social and communicative domains, all of these scales include items about repetitive behaviors and restrictive interests. All three scales were intended to ascertain

ASD-related symptoms as opposed to mood and anxiety disorders. Therefore, questions are worded to avoid overlap with questions in mood or anxiety disorder scales. Nevertheless, target behaviors associated with ASD symptoms show some overlap with behaviors manifest in pediatric mood and anxiety disorders. In the absence of empirical data firmly establishing the degree to which ratings on specific items on ASD symptom scales correlate with ratings on specific items on mood and anxiety scales, definitive conclusions cannot be made concerning the specificity of relationships among ASD symptom scale scores, one or another ASD domain, and behaviors specific to pediatric mood and anxiety disorders.

Data Analysis

Because not all of the participants' parents completed all of the ASD symptom scales, data from each scale were analyzed in a separate model to maximize available sample sizes. Groups were compared first on age, IQ, sex, and ethnicity using χ^2 or analysis of variance statistics. Because age and IQ differed significantly between groups (Table 1), subsequent analyses included these variables as covariates. Although ethnicity also differed among groups, it showed no association with any ASD measure and therefore was not included as a covariate, although identical results were obtained in analyses including ethnicity as a covariate.

The first analysis tested the hypothesis that each patient group would exhibit elevated ASD symptom scale scores relative to the healthy group. Groups were compared using analysis of covariance (ANCOVA), covarying for age and IQ, with Bonferroni-corrected post hoc tests.

The second analysis tested the hypothesis that BD/SMD patients would show higher ASD symptom scale scores than other groups. ANCOVA tested differences between the four patient groups, with CGAS score, age, and IQ as covariates. Thus, this analysis differs from other analyses both by including the CGAS and by not including healthy subjects, reducing the sample size. Because this limits statistical power, negative results should be interpreted cautiously. One also can debate the appropriateness of covarying CGAS, given that CGAS ratings may capture important attributes of mood and anxiety disorders; thus, controlling CGAS may remove relevant variance. This concern does not

TABLE 1
Sample Demographics and Comorbidities

	Healthy (<i>n</i> = 107)	Anxious* (<i>n</i> = 88)	Depressed (<i>n</i> = 32)	Bipolar (<i>n</i> = 62)	SMD (<i>n</i> = 63)	Statistics
Demographics						
Age, <i>y</i> (<i>X</i> ± <i>SD</i>)	12.61 ± 2.71 ^{ab}	10.96 ± 2.24 ^{acd}	13.13 ± 2.46 ^{cc}	12.13 ± 2.65 ^d	11.25 ± 2.32 ^{bc}	$F_{4,351} = 8.38, p < .001$
IQ (<i>X</i> ± <i>SD</i>)	111.09 ± 12.99 ^a	111.50 ± 14.91 ^b	104.06 ± 13.90	108.10 ± 15.02	103.9 ± 13.89 ^{ab}	$F_{4,351} = 4.37, p < .005$
CGAS (<i>X</i> ± <i>SD</i>)	NA	49.50 ± 7.41 ^a	46.13 ± 6.58	44.27 ± 11.50 ^a	47.22 ± 6.64	$F_{3,174} = 3.46, p < .02$
Sex, % (<i>n</i>) male	48.6 (52)	56.8 (50)	43.8 (14)	54.8 (34)	69.8 (44)	$\chi^2_4 (N = 352) = 9.14, ns$
Ethnicity, % (<i>n</i>) white	62.6 (67)	72.7 (64)	59.4 (19)	91.9 (57)	85.7 (54)	$\chi^2_8 (N = 352) = 29.82, p < .001^{\dagger}$
Present diagnoses						
SoPh, % (<i>n</i>)	NA	58.0 (51)	43.8 (14)	11.3 (7)	9.5 (6)	—
GAD, % (<i>n</i>)	NA	44.3 (39)	50.0 (16)	30.6 (19)	30.2 (19)	—
SAD, % (<i>n</i>)	NA	37.5 (33)	25.0 (8)	22.6 (14)	28.6 (18)	—
MDD, % (<i>n</i>)	NA	—	100.0 (32)	54.8 (34)	14.3 (9)	—
ADHD, % (<i>n</i>)	NA	18.2 (16)	21.9 (7)	43.5 (27)	81.0 (51)	—
ODD, % (<i>n</i>)	NA	19.3 (17)	21.9 (7)	37.1 (23)	81.0 (51)	—

Note: Diagnostic groupings based on having completed one of the three autism spectrum disorder measures. ^{a-c} Means with the same letter are significantly different. SMD = severe mood dysregulation; CGAS = Children's Global Assessment Scale; NA = not applicable; SoPh = social phobia; GAD = generalized anxiety disorder; SAD = social anxiety disorder; MDD = major depressive disorder; ADHD = attention-deficit/hyperactivity disorder; ODD = oppositional defiant disorder.

* Anxious group includes youths with an SAD, GAD, or SoPh diagnosis and no MDD diagnosis.

[†] Likelihood ratio is reported because four cells have an observed count of less than five.

apply, of course, to findings that emerge independent of CGAS.

The final set of analyses focused on associations with specific anxiety disorders using multiple regression with dummy codes for the three anxiety disorders (i.e., GAD, SAD, SoPh) while also including ADHD as a covariate. Oppositional defiant disorder, although common among diagnostic groups, was not included because it showed no association with ASD symptom scale scores, independent of ADHD. Thus, each of the four ASD symptom scale scores was regressed on age, IQ, CGAS, ADHD, BD, SMD, and the three dummy variables (one for each anxiety disorder). All of the tests used an a priori $\alpha = .05$ and Cohen *d* for effect size.²⁹

RESULTS

Sample Characteristics

Groups differed on age, IQ, and ethnicity (Table 1). Patients with anxiety or SMD were younger than healthy participants; anxiety patients also were younger than patients with MDD and BD; patients with SMD were younger than patients with MDD. IQ differences reflected lower scores in the SMD group relative to the

healthy and anxious groups. BD and SMD groups were primarily white. Patients differed in levels of impairment on the CGAS, with patients with BD showing lower functioning than anxiety patients. Comorbidity also was considerable, with high rates of ADHD and oppositional defiant disorder in each group. Rates appeared particularly high in SMD.

ASD Symptom Scale Scores

Controlling for age and IQ, significant differences on ASD symptom scale scores were found between the healthy group and each patient group (Table 2, all *p* values < .001). Post hoc tests showed that all four patient groups differed from the healthy group on three scales (all *p* values < .05). However, contrary to the hypothesized difference between the patients with BD or SMD and those with MDD, no differences emerged among these groups. For example, mean SRS score in the healthy group (23.2 ± 2.1) was significantly lower than in the anxiety group (55.0 ± 2.5), which was significantly lower than in the MDD (64.9 ± 4.4), BD (68.7 ± 2.7), and SMD (75.5 ± 2.7) groups, with no differences among the latter three groups. Similar or identical patterns emerged for the SCQ, GCC, and SIDC.

TABLE 2
Clinical Cutoffs and Means on All Autism Spectrum Disorder (ASD) Measures by Group

	Healthy	Anxious*	Depressed	Bipolar	SMD	Statistics
% (<i>n</i>) > ASD scale score cutoff ^f						
SRS (<i>n</i> = 308) [†]	1.0 (1)	24.6 (17)	38.1 (8)	56.9 (33)	75.0 (45)	—
SCQ (<i>n</i> = 298)	0 (0)	4.0 (3)	7.4 (2)	8.3 (4)	8.3 (4)	—
CCC (<i>n</i> = 197)	0 (0)	16.7 (6)	60.0 (9)	53.5 (23)	51.0 (25)	—
Mean ASD scale scores [‡]						
SRS ($X \pm SE$) [§]	23.19 ± 2.06 ^{abcd}	54.95 ± 2.47 ^{acdf} (<i>d</i> = -1.42)	64.88 ± 4.43 ^b (<i>d</i> = -2.05)	68.74 ± 2.65 ^{ce} (<i>d</i> = -2.35)	75.53 ± 2.68 ^{df} (<i>d</i> = -3.25)	$F_{4,301} = 78.36$, $p < .001$
Adjusted for CGAS	NA	54.76 ± 3.27 ^{ab}	66.20 ± 6.22	68.13 ± 3.32 ^a	75.69 ± 3.25 ^b	$F_{3,146} = 6.91$, $p < .001$
SCQ ($X \pm SE$) [§]	2.32 ± 0.40 ^{abcd}	4.99 ± 0.47 ^{acdf} (<i>d</i> = -0.77)	6.41 ± 0.77 ^b (<i>d</i> = -1.03)	8.50 ± 0.57 ^{ce} (<i>d</i> = -1.79)	7.59 ± 0.58 ^{df} (<i>d</i> = -1.36)	$F_{4,291} = 25.87$, $p < .001$
Adjusted for CGAS	NA	4.92 ± 0.68 ^a	7.10 ± 1.12	8.65 ± 0.77 ^a	7.31 ± 0.74	$F_{3,137} = 4.43$, $p < .01$
GCC ($X \pm SE$) [§]	82.60 ± 2.69 ^{abc}	70.87 ± 3.31 ^{def} (<i>d</i> = 0.60)	39.46 ± 5.06 ^{ad} (<i>d</i> = 2.00)	55.15 ± 2.96 ^{bc} (<i>d</i> = 1.41)	49.82 ± 2.84 ^{cf} (<i>d</i> = 1.81)	$F_{4,190} = 26.06$, $p < .001$
Adjusted for CGAS	NA	69.59 ± 4.16 ^{ab}	40.58 ± 5.81 ^a	53.09 ± 3.54 ^b	48.87 ± 3.16 ^c	$F_{3,102} = 6.81$, $p < .001$
SIDC ($X \pm SE$) [§]	1.64 ± 1.15 ^{abcd}	-3.87 ± 1.41 ^{acdf} (<i>d</i> = 0.68)	-7.55 ± 2.16 ^b (<i>d</i> = 1.21)	-10.66 ± 1.26 ^{ce} (<i>d</i> = 1.46)	-11.78 ± 1.21 ^{df} (<i>d</i> = 1.93)	$F_{4,190} = 20.11$, $p < .001$
Adjusted for CGAS	NA	-7.18 ± 1.79	-7.97 ± 2.50	-8.11 ± 1.52	-12.13 ± 1.36	$F_{3,102} = 2.25$, $p = ns$

Note: Diagnostic groupings based on having completed one of the three ASD measures. SRS/SCQ/CCC data available for 100/100/54 controls, 69/75/36 with anxiety, 21/27/15 with depression, 60/48/49 with bipolar, and 58/48/43 with SMD. ^{a-f} Means with the same letter are significantly different. SMD = severe mood dysregulation; SRS = Social Responsiveness Scale; SCQ = Social Communication Questionnaire; CCC = Child Communication Checklist; CGAS = Children's Global Assessment Scale; NA = not applicable; GCC = General Communication Composite; SIDC = Social Interaction Deviance Composite.

* Anxious group includes youths with separation anxiety disorder, generalized anxiety disorder, or social phobia diagnosis and no major depressive disorder diagnosis.

[†] SRS cutoff score reflects different clinical cutoffs for each sex.

[‡] For SRS and SCQ, higher scores indicate greater impairment; for CGAS, GCC, and SIDC, higher scores indicate less impairment. The CCC comprises the GCC and SIDC subscales. Only cases passing a consistency check on both SIDC and GCC are included in analyses involving the CCC, SIDC, or GCC.

[§] For each ASD measure, means are adjusted for the covariates of age and IQ on the first row and for age, IQ, and CGAS two rows below as noted. All of the post hoc tests used a Bonferroni correction.

Correlations

All but one correlation (Table 3) among ASD symptom scale scores was significant; namely, given that the SIDC and GCC subscales of the CCC were designed explicitly to tap orthogonal constructs, these two CCC subscales did not correlate. Despite significant CGAS-ASD symptom scale correlations, the overall magnitude of these associations was not large: the CGAS accounted for less than 12% of the variance in any ASD symptom scale. This contrasts with the substantially larger correlations among the ASD symptom scales, although the SIDC showed relatively weak correlations with the other three scales. The magnitude of the correlation among the SRS, SCQ, and GCC suggests

that behaviors tapped by each of these three scales accounts for approximately 50% of the variance on any one scale.

Impact of Impairment

The three mood disorder groups exhibited greater impairment than the anxiety disorder group, although these differences did not always reach conventional significance levels (Table 1). We conducted analyses to test the hypothesis that ASD symptom scale scores would be higher in BD and SMD than in other groups, independent of impairment. Specifically, ANCOVA was repeated on each ASD measure for the patient groups while covarying CGAS scores in addition to IQ and age.

TABLE 3

Pearson Correlations Among the CGAS and Autism Spectrum Disorder Measures^a

	CGAS	SRS	SCQ	GCC	SIDC
CGAS	—				
SRS	-0.29**	—			
SCQ	-0.23**	0.65**	—		
GCC	0.29**	-0.72**	-0.61**	—	
SIDC	0.26**	-0.49**	-0.24**	0.09	—

Note: N varies from 109 to 263 depending on measures included in the correlation analysis. For SRS and SCQ, higher scores indicate greater impairment; for CGAS, GCC, and SIDC, higher scores indicate less impairment; CGAS = Children's Global Assessment Scale; SRS = Social Responsiveness Scale; SCQ = Social Communication Questionnaire; GCC = General Communication Composite; SIDC = Social Interaction Deviance Composite.

^a Only cases passing a consistency check on both SIDC and GCC are included in correlations between the two CCC subscales and other measures.

* $p < .05$; ** $p < .01$; *** $p < .001$.

When CGAS was included as a covariate, group effects remained significant on the SRS, SCQ, and GCC, but not the SIDC. For the SRS, the BD and SMD groups differed significantly from the anxiety group, but the MDD group did not differ from any group (Table 2). Of note, between-group differences that did emerge occurred despite the loss of power associated with the exclusion of healthy subjects,

although the equivocal findings in MDD may reflect this loss of power. BD and anxiety groups differed significantly on the SCQ. On the GCC, all three mood disorder groups differed significantly from the anxiety group, with no significant differences among mood disorder groups. CGAS ratings had a significant effect on SRS ($p < .005$) and SIDC scores ($p < .01$), but not on SCQ or GCC scores. Finally, only CGAS and age predicted SIDC scores, with no differences among groups. Moreover, age did not moderate associations with psychopathology, as no interactions emerged between age and diagnosis in models predicting ASD symptom scale scores.

Thus, CGAS scores predicted scores on two of the four ASD symptom scales. Once CGAS scores were covaried, there were no between-group differences on the SIDC. However, differences remained between the anxiety and SMD groups on the SRS and GCC, between the anxiety and BD groups on the SRS and SCQ, and between the anxiety and MDD groups on the GCC.

ASD Symptom Scale Scores in Anxiety

The final analyses tested the hypothesis that ASD symptom scale scores (Table 4) would be higher for SoPh than for SAD or GAD. These analyses also considered the effect of ADHD comorbidity. Regression models for each ASD symptom scale included the

TABLE 4

Final Models From Hierarchical Linear Regressions of Demographic and Diagnostic Characteristics on Social Communication Measures

	SRS (n = 153)		SCQ (n = 144)		GCC (n = 109)		SIDC (n = 109)	
	$\beta \pm SE$	t	$\beta \pm SE$	t	$\beta \pm SE$	t	$\beta \pm SE$	t
Age	-.19 ± .08	-2.56*	-.11 ± .09	-1.25	.001 ± .09	0.01	.12 ± .10	1.26
IQ	-.16 ± .08	-2.07*	-.08 ± .09	-0.91	.18 ± .10	1.81	-.26 ± .10	-2.54*
CGAS	-.18 ± .08	-2.37*	-.12 ± .09	-1.44	.16 ± .10	1.66	.26 ± .10	2.54*
MDD	.13 ± .08	1.58	.18 ± .09	2.01*	-.27 ± .10	-2.78**	-.16 ± .10	-1.51
SAD	-.03 ± .08	-0.34	-.02 ± .09	-0.19	.03 ± .10	0.36	-.12 ± .10	-1.08
SoPh	.17 ± .09	1.92	.08 ± .09	0.85	-.06 ± .10	-0.62	-.05 ± .11	-0.50
GAD	-.01 ± .08	-0.12	-.07 ± .08	-0.79	-.04 ± .10	-0.44	-.05 ± .10	-0.49
BD	.20 ± .10	2.08*	.24 ± .10	2.46*	-.12 ± .12	-1.04	-.09 ± .13	-0.73
SMD	.34 ± .10	3.36***	.14 ± .10	1.40	-.27 ± .13	-2.11*	-.37 ± .14	-2.75**
ADHD	.16 ± .08	1.98*	.14 ± .09	1.60	-.14 ± .10	-1.41	.04 ± .19	0.34

Note: For SRS and SCQ, higher scores indicate greater impairment; for GCC and SIDC, higher scores indicate less impairment. The GCC and SIDC subscales comprise the Child Communication Checklist. Only cases passing a consistency check on both SIDC and GCC are included. SRS = Social Responsiveness Scale; SCQ = Social Communication Scale; GCC = General Communication Scale; SIDC = Social Interaction Deviance Composite; CGAS = Children's Global Assessment Scale; MDD = major depressive disorder; SAD = separation anxiety disorder; SoPh = social phobia; GAD = generalized anxiety scale; BD = bipolar disorder; SMD = severe mood dysregulation; ADHD = attention-deficit/hyperactivity disorder.

* $p < .05$; ** $p < .01$; *** $p < .001$.

following predictors: age, IQ, CGAS, MDD, each anxiety disorder, BD, SMD, and ADHD. CGAS predicted scores on two scales (SRS and SIDC), with no additional variance explained by any anxiety diagnoses. Moreover, although ADHD related to symptom scores in one model, MDD, BD, and SMD predicted scores among the four scales, with ADHD and CGAS controlled.

DISCUSSION

Three findings emerged from this report. First, all four patient groups scored higher on ASD symptom scales than healthy youths, with effect sizes in mood disorders appearing particularly large (Cohen *d* across diagnoses ranged from 0.6 to 3.3 [Table 2]). These findings extend our previous findings, generated in a subset of subjects from the present sample. Because previous findings did not include data in concurrently assessed healthy subjects, the previous study relied on external norms to draw conclusions about the degree to which patients with mood and anxiety disorders present with high ASD symptom scale scores. The present findings suggest that this previous observation reflects specific associations with mood and anxiety disorders, as opposed to other factors associated with attending our unique research setting.

The second hypothesis, concerning scores in BD or SMD, received only limited support, due largely to the fact that the MDD group scored more similarly to the SMD and BD groups than to the healthy or anxious groups. In fact, independent of impairment, the MDD group did not differ from either the SMD or BD groups on any scale, whereas patients with MDD differed significantly from those with anxiety disorders on the GCC even when controlling for impairment. As expected, however, patients with SMD or BD did show higher scores on some scales than patients with anxiety. Surprisingly, no group differences emerged for the SIDC, controlling for impairment. Third, contrary to our hypothesis, ASD symptom scale scores showed no association with anxiety disorder subtype; that is, with impairment covaried, SoPh, SAD, and GAD did not predict scores on any ASD symptom scale.

These findings suggest that pediatric patients with mood disorder exhibit impaired social reciprocity, language deficits, and behavioral rigidity/stereotypy. Indeed, the present data document associations compar-

able in magnitude to those observed previously in learning or behavior disorders.^{7,8,30} Overall CGAS impairment showed moderate associations with ASD symptom scale scores. Nevertheless, for each mood disorder group, relative to anxiety disorders, at least one association with an ASD symptom scale score persisted while controlling for CGAS.

These findings suggest that pediatric mood disorders are associated with high ASD symptom scale scores, indicative of symptoms appearing similar to, but less intense than, those of children presenting to ASD specialty clinics. As such, these findings underscore the need for clinicians to assess symptoms tapped by ASD symptom scales in patients presenting for treatment of various psychopathologies not typically considered ASDs. This includes youths presenting with primary complaints related to mood disorders. By using standardized ASD symptom rating scales, clinicians may identify targets for treatment in patients with mood disorders that they may otherwise overlook. Previous research, in particular, finds that social reciprocity traits reside along a continuum.^{12,16} The present findings suggest that patients with mood disorders fall at the tail of this continuum: 40% to 80% exhibited profiles above clinical cutoffs.

Of note, the approach used here applies a rating scale developed to assess symptoms of impairment in disorders of social communication/reciprocity among patients diagnosed in another domain, mood and anxiety disorders. Previous research using scales, originally developed for use in one context, such as for screening in the community, and then applied in an alternative context, such as among children presenting for clinical research, raises questions about the degree to which identical meanings of the scales emerges in the two contexts. Thus, in the present study, high ASD symptom scale scores could be conceptualized as manifestations of relatively mild ASDs, overlap between mood and ASD symptoms, or nonspecific correlates of psychopathology. Because the present study represents one of the few to use ASD symptom scales in pediatric patients with mood and anxiety disorders, such questions cannot be answered here and should be a focus of future research. Regardless, our findings suggest that patients with mood disorders may frequently exhibit high ASD symptom scale scores. Clinicians may consider in these patients the utility of treatments, typically used in ASDs, to target social reciprocity and communicative deficits.

These findings may also inform research on ASDs. Recent epidemiological studies find higher rates of ASDs than in samples ascertained previously,¹ due at least in part to the identification of many ASD cases with average or superior intelligence and mild impairment.² These studies generally have not conducted the types of assessments used in the present study to assess mood and anxiety disorders, nor do they typically examine relations among ASD symptoms and psychopathologies other than ASDs. Our data raise questions about the degree to which youths with high ASD symptom scale scores would be classified in other settings as having an ASD.

One question raised by these and other published data is whether ASD symptoms should be viewed as correlates of illness severity or of other nonspecific features of developmental psychopathologies. The answer to this question seems to vary by diagnosis and ASD symptom scale. Whereas overall impairment exhibited associations with scores on all scales, associations between psychopathology and ASD symptom scale scores remained even after accounting for impairment, with the exception of the SIDC.

With regard to diagnosis, among pediatric anxiety disorders, level of impairment but not specific symptom profiles predicted ASD symptom scale scores. Because the negative findings in SoPh were unexpected, the finding requires replication. In contrast, high scores occurred in mood disorders, relative to anxiety disorders, independent of impairment. This particularly strong relationship between ASD symptom scale scores and mood disorders may suggest that social and communicative deficits represent more central aspects of pediatric mood than anxiety disorders. Consistent with this possibility, considerable previous research demonstrates a strong association between pediatric mood disorders, or risk factors for such disorders, and perturbations in social function.^{31,32} Such observations have led to the development of therapies that target social problems in these patients.³³ Moreover, mood disorder diagnosis also was a stronger predictor than demographic variables: neither age nor intelligence showed as consistent a relationship with ASD symptom scale scores, although one may expect associations with age in larger samples.

The present findings should be considered in light of significant limitations in sampling and assessment. First, our sample consisted of youths receiving treatment.

Moreover, only children eligible for participation in other studies focusing on biology were included. Such samples are not representative of children in the community.³⁴ As a result, our findings require replication in patients with pediatric mood and anxiety disorders identified in various other settings, including both nonresearch clinics and epidemiological samples.

Second, it was not feasible to complete comprehensive assessments of ASDs with measures such as the Autism Diagnostic Observation Scale (ADOS) and the ADI-R because these youths and their families underwent lengthy assessments to confirm diagnoses of mood and anxiety disorders. Moreover, even for the current gold standard measures, the ADOS and ADI-R, questions remain about the suitability of these instruments for assessing pediatric patients who present with mild ASD.^{15,35} Future work in this group should consider the best means for deriving independent assessments of all of the relevant conditions. Regardless of the precise method that is ultimately chosen for such future work, here, the absence of data for the ADOS and ADI-R clearly represents a limitation. In the absence of such data, it is impossible to state confidently the degree to which some subgroup of subjects in the current study may be conceptualized as having a categorically defined ASD, as typically assessed with the ADOS and ADI-R.

Third, our assessment on ASD symptom scales only occurred at one point in time. Previous research generally views scores on these scales as trait factors, based on observations of stability in various populations. Nevertheless, in studies of patients with mood and anxiety disorders, research on other factors typically viewed as traits, such as scores on personality scales, does find state-related effects. Therefore, future research should examine the degree to which ASD symptom scale scores change following successful treatment. This research may clarify the degree to which elevated ASD symptom scale scores represent signs of an ASD versus correlates of mood disorders.

Fourth, although the present study recruited patients meeting categorical definitions of mood and anxiety disorders, data in epidemiological settings show that mood and anxiety disorder symptoms, like ASD symptoms, may be conceptualized as lying along a continuum. The categorical approach of the present study was used to facilitate our biological studies, designed to test hypotheses about patients with unequivocal signs of relatively severe and impairing mood and