

# Medical and Behavioral Correlates of Depression History in Children and Adolescents With Autism Spectrum Disorder

Jessica L. Greenlee, BA,<sup>a</sup> Angela S. Mosley, BA,<sup>b</sup> Amy M. Shui, MA,<sup>c</sup> Jeremy Veenstra-VanderWeele, MD,<sup>d</sup> Katherine O. Gotham, PhD<sup>b</sup>

abstract

**BACKGROUND AND OBJECTIVES:** Depression is commonly associated with autism spectrum disorder (ASD) across the life span. We sought to identify medical and behavioral problems associated with a history of a parent-reported diagnosis of depression in a large sample of school-aged children and adolescents with ASD.

**METHODS:** A sample of 1272 participants (aged 6–17 years; mean [SD]: 9.56 [2.79] years) from the Autism Speaks Autism Treatment Network consortium were divided into “ever-depressed” ( $n = 89$ ) and “nondepressed” ( $n = 1183$ ) groups on the basis of caregiver endorsement of children’s current or previous diagnoses of depression.

**RESULTS:** In total, 7.0% of children with ASD (4.8% of those aged 6–12 years and 20.2% of those aged 13–17 years) were reported to have a history of a depression diagnosis. Positive depression history was associated with greater chronological age, higher IQ, and Asperger disorder diagnosis. After controlling for age, IQ, and within-spectrum categorical diagnosis, the ever-depressed group exhibited significantly greater rates of seizure disorders (odds ratio = 2.64) and gastrointestinal problems (odds ratio = 2.59) and trend-level differences in aggression, somatic complaints, and social impairments. The groups did not differ in autism severity, repetitive behaviors, sleep problems, eating problems, self-injurious behavior, or current intervention use.

**CONCLUSIONS:** Co-occurring depression is a particularly common problem in higher-functioning older children within the Autism Treatment Network. Our findings indicate that children with ASD and a history of a depression diagnosis are more likely to also have co-occurring medical problems, although the presence and direction of causality is unclear.

<sup>a</sup>Department of Psychology, Virginia Commonwealth University, Richmond, Virginia; <sup>b</sup>Department of Psychiatry, Vanderbilt University Medical Center, Nashville, Tennessee; <sup>c</sup>Massachusetts General Hospital Biostatistics Center, Boston, Massachusetts; and <sup>d</sup>Department of Psychiatry, Columbia University Medical Center, New York, New York

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Autism spectrum disorder (ASD) is associated with medical and psychiatric comorbidities at higher rates than are observed in typically developing (TD) children.<sup>1</sup> These problems can exacerbate the core symptoms of ASD and negatively impact a child's functionality and quality of life.<sup>2-4</sup>

Depression is an understudied comorbidity in ASD. Point prevalence estimates of depression range from 0.9% to 29% in child and adolescent ASD samples, depending on age range and distribution of the sample, sampling method, and assessment procedures.<sup>5-8</sup> In comparison, ~3% of children<sup>9</sup> and 11% of adolescents<sup>10</sup> in the general population are or have recently been depressed.

A number of demographic and other factors have been associated with risk of depression in TD children and adolescents. Rates of depression increase with chronological age from childhood throughout adolescence, with postpubertal females at higher risk than males.<sup>10-12</sup> Children and adolescents with depression are more likely to have a family history of psychiatric problems, including depression and anxiety.<sup>13</sup> Other correlates of youth depression in the general population include somatic symptoms, such as sleep problems<sup>14</sup> and gastrointestinal complaints,<sup>15</sup> and behavioral conditions, such as attention-deficit/hyperactivity disorder (ADHD)<sup>16</sup> and anxiety.<sup>17</sup> A variety of mediators and mechanisms between somatic and/or behavioral conditions and depression have been proposed, some of which seem plausible in the ASD population as well (eg, diminished social support and/or coping, emotion regulation difficulties, and self-esteem).<sup>18,19</sup>

A small body of research has examined similar correlates and potential risk factors for depression in children and adolescents with ASD. There is some evidence that children with ASD are at a greater risk of developing depression as they age<sup>20</sup>;

however, several studies have found minimal evidence of association between age and depressive symptoms or disorders, albeit in samples with relatively narrow age ranges.<sup>21-23</sup> Unlike TD children, girls with ASD appear to be no more likely to develop depression than boys with ASD, and in fact, depression may be less common in preadolescent girls with ASD than in boys.<sup>24</sup> Previous studies have reported that individuals with higher ASD symptom severity<sup>25</sup> tend to have both lower IQ and fewer depressive symptoms than those with milder ASD and a higher IQ.<sup>3,26-28</sup> This finding is complicated by the relative difficulty of assessing psychiatric symptoms in minimally verbal individuals who are less able to report their internal experiences.

Many of the physical and behavioral correlates associated with depression in TD children have been shown to be elevated in the ASD population. The co-occurrence of sleep problems in ASD is high,<sup>29,30</sup> with some evidence linking sleep problems to high rates of hyperactivity, anxiety, depression, mood swings, or aggression in ASD.<sup>31</sup> High rates of gastrointestinal problems also have been documented in children with ASD<sup>32</sup> and have been linked to psychiatric comorbidity,<sup>33</sup> anxiety, irritability, social withdrawal, and rigid-compulsive symptoms.<sup>34,35</sup> Self-injurious behavior (SIB) and aggressive behavior have also been linked to the co-occurrence of mood disorders in ASD.<sup>36,37</sup> Rates of ADHD in ASD have been found to be as high as 31%,<sup>5</sup> and Gadow et al<sup>38</sup> observed that children with comorbid ASD+ADHD were at greater risk of developing depression than those with ASD alone.

In summary, a small body of research has identified several medical or behavioral factors that could be linked to depression in both TD children and those with ASD. Such research must be replicated in large independent data sets to move the

field forward in understanding the mechanisms underlying depression in ASD, as well as the role these medical and behavioral correlates could play in diagnosis and treatment. In this study, we used data from the Autism Speaks Autism Treatment Network (ATN) to compare children with ASD who have a current or previous diagnosis of depression according to parent report to those with no history of depression on a number of variables related to physical and mental health. On the basis of previous studies, we hypothesized that school-aged and adolescent children with ASD who have current or past depression diagnoses will tend to be older and more likely to have milder ASD symptom severity and higher IQs; a family history of depression or other psychiatric disorders; greater difficulty with sleep, gastrointestinal and eating problems, somatic complaints, seizures, aggression, SIB, anxiety, repetitive and compulsive behaviors, and social and attention problems; and greater psychotropic medication use and use of behavioral, social, or educational interventions or therapies. In addition, we hypothesized that individuals who have current or past depression diagnoses will have higher scores on the Child Behavior Checklist (CBCL)<sup>39</sup> Withdrawn/Depressed and Anxiety subscales. Our objective was to identify or replicate potential medical or behavior correlates of depression in ASD that could shed light on the relationship between these complex disorders.

## METHODS

### Participants

The sample included 1272 children aged 6 to 17 years (mean [SD]: 9.56 [2.79] years; 15.4% female) participating in the ATN, a registry collection of data on children and youth with ASD across 17 sites in the United States and Canada. All

**TABLE 1** Demographic Characteristics of Registry Study Sample

	Nondepressed	Ever-Depressed	P
Age ( <i>n</i> = 1272), mean ± SD, y	9.4 ± 2.7	11.9 ± 2.7	<.001*
IQ measures, mean ± SD			
FSIQ ( <i>n</i> = 871)	83.1 ± 24.4	91.5 ± 16.7	.002*
VIQ ( <i>n</i> = 287)	74.3 ± 23.9	88.9 ± 20.1	.010*
NVIQ ( <i>n</i> = 291)	78.8 ± 23.2	93.5 ± 17.3	.007*
ASD diagnosis ( <i>n</i> =1272), <i>n</i> (%)			<.001*
Autistic disorder	706 (59.7)	35 (39.3)	
Asperger	202 (17.1)	31 (34.8)	
PDD-NOS	275 (23.2)	23 (25.8)	
Gender ( <i>n</i> = 1272), <i>n</i> (%)			.450
Female	180 (15.2)	16 (18.0)	
Male	1003 (84.8)	73 (82.0)	
Race ( <i>n</i> = 1223), <i>n</i> (%)			.999
Nonwhite	185 (16.3)	13 (15.4)	
White	954 (83.8)	71 (84.5)	
Ethnicity ( <i>n</i> = 1240), <i>n</i> (%)			.145
Hispanic/Latino	98 (8.5)	3 (3.6)	
Non-Hispanic/Latino	1059 (91.5)	80 (96.4)	
Caregiver education ( <i>n</i> = 1223), <i>n</i> (%)			.779
Eighth grade or some high school	41 (3.6)	4 (4.7)	
Finished high school, GED	169 (14.9)	15 (17.6)	
Some college	398 (35.0)	27 (31.8)	
Bachelor's degree	306 (26.9)	25 (29.4)	
Postgraduate degree	224 (19.7)	14 (16.5)	
Tanner stage ( <i>n</i> = 626), <i>n</i> (%)			<.001
Stage 1	444 (75.8)	12 (30.0)	
Stage 2	73 (12.5)	8 (20.0)	
Stage 3	32 (5.5)	5 (12.5)	
Stage 4	21 (3.6)	9 (22.5)	
Stage 5	16 (2.7)	6 (15.0)	

GED, General Educational Development; NVIQ, nonverbal IQ; PDD-NOS, pervasive developmental disorder—not otherwise specified; VIQ, verbal IQ.

participants met *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*<sup>40</sup> diagnostic criteria for autistic disorder (58.3%), Asperger syndrome (18.3%), or pervasive developmental disorder—not otherwise specified (23.4%) on the basis of a standard assessment including the Autism Diagnostic Observation Schedule (ADOS).<sup>41</sup> ATN exclusion criteria were deafness, blindness, foster care placement, or participation in another research study that could potentially interfere with ATN goals. Most families self-identified as Caucasian (83.8%) or non-Hispanic (91.9%). All data reported were from the initial (baseline) visit. (See Table 1 for sample details.) Data were gathered and analyzed under an institutional review board umbrella protocol used by the ATN/Autism Intervention Research Network on Physical

Health's Data Coordinating Center at Massachusetts General Hospital.

### Measures

Cognitive functioning was assessed by using the abbreviated Stanford Binet.<sup>42</sup> In terms of predictor variables, most of our potential correlates of interest were operationalized with a positive endorsement on any one of several indicators of the construct in question (eg, "history of anxiety" was defined as a parent-reported "yes" to present or past problems with anxiety on the Health and Mental Health History [HMHH] form and/or exceeding the clinical cutoff of 65 on the CBCL Anxiety subscale).

The ATN-created HMHH survey included a list of 29 health-related items to which caregivers could indicate "yes," "no," or "unsure" if their child had a current or past

problem related to that item ("please check yes for all items that have been a problem for your child now or in the past"). Participants were divided into 2 groups on the basis of caregivers' response to the HMHH item "Diagnosis of depression" (on which a "yes" indicated a current or past diagnosis): those with a history of a parent-reported diagnosis of depression ("ever-depressed"; *n* = 89) and those with no history of parent-reported diagnosis of depression ("nondepressed"; *n* = 1183). The HMHH survey also was used to assess gastrointestinal problems, eating problems, seizures, anxiety, repetitive/compulsive behaviors, and history of attention problems. Psychometric information was unavailable for the HMHH survey and the other specifically ATN-created instruments described below.

The Parental Concerns Questionnaire<sup>43</sup> is a 15-item

assessment that measures common behavioral symptoms of ASD with high internal consistency. Parents indicated “yes” to endorse sleep problems, gastrointestinal problems, anxiety, repetitive and compulsive behaviors, social impairments, hyperactivity, eating problems, seizures, aggression, and SIB. The Children’s Sleep Habits Questionnaire<sup>44</sup> is a parent-rated measure of behavioral and medically related sleep problems in school-aged children and has adequate internal consistency. Parents’ ratings of “sometimes” or “usually” on various Children’s Sleep Habits Questionnaire questions (about sleep anxiety, duration, onset delay, night waking, bedtime resistance, sleep-disordered breathing, parasomnias, and daytime fatigue) were also used as an endorsement of sleep problems. The DSM-IV<sup>41</sup> Checklist was completed by a trained ATN psychologist and was used to assess social impairments related to peer relationships and social interactions. On the ATN-specific assessment, the Diagnoses and Problems–Clinician form, clinicians assessed previous and current diagnoses, made observations of a number of physical and behavioral health issues (gastrointestinal problems, eating problems, sleep problems, seizure disorder, anxiety, aggression, attention problems, attention-deficit without hyperactivity, social impairment, and restrictive and repetitive behaviors) and listed current and past medications and behavioral and educational interventions.

We assessed the association between history of a parent-reported diagnosis of depression and current scores on 2 of the CBCL<sup>39</sup> syndrome scales, Withdrawn/Depressed and Anxiety. Research evaluating the psychometric properties of the CBCL in youth with ASD and emotional and behavioral disorders supports that the CBCL is a valid measure with

good to excellent scale reliability.<sup>45</sup> CBCL raw scores were converted to age- and gender-adjusted *z* scores for analysis. In addition, CBCL T scores of  $\geq 65$  on the Aggressive Behavior, Attention Problems, Anxiety, and Somatic Complaints subscales were used to define a history of each of those conditions, respectively.

### Design and Analysis

A cross-sectional analysis was conducted to examine group differences at the time of the initial ATN visit. Demographic and individual characteristics, including categorical ASD diagnostic subtype per DSM-IV, IQ, gender, age, pubertal status, race, ethnicity, and primary caregiver education, were tested for differences by depression history (ever-depressed versus nondepressed). These groups were compared by using *t* tests for continuous variables and Fisher’s exact tests for categorical variables. For any continuous variables that were tested by using *t* tests, the folded *F* test for equality of variances was run first. If a variable passed this test, then the pooled *t* test results, assuming equal variances, were reported. If a variable did not pass this test, then the Satterthwaite *t* test results, assuming unequal variances, were reported. Post hoc tests were conducted on variables with  $>2$  categories. Variables that differed significantly at a threshold of  $P < .05$  were included as covariates in the subsequent logistic regression models. On the basis of the depression literature in the general population, emotional, behavioral, and physical health symptoms were chosen as predictor variables for the current study. Logistic regression models at a significance threshold of  $P < .01$  were used to examine the emotional, behavioral, and physical health variables as predictors of depressive group status, with separate models including all

significant covariates and 1 predictor variable at a time.

## RESULTS

### Testing of Potential Covariates

On the basis of caregivers’ response to the depression item on the HMHH survey, 89 participants had a history of a reported diagnosis of depression and were included in the “ever-depressed” group. Prevalence of parent-reported depression was 7.0% for the entire sample (ages 6–17), 4.8% for those aged 6 to 12 years, and 20.2% in adolescents aged 13 to 17 years. Not surprisingly, current age (ie, at baseline ATN enrollment) differed significantly across groups ( $P < .001$ ), with an older ever-depressed group (mean [SD]: 11.9 [2.7] years) in comparison with the nondepressed group (mean [SD]: 9.4 [2.7] years). The ever-depressed group also had a higher average abbreviated full-scale IQ (FSIQ), verbal IQ, and nonverbal IQ (see Table 1); the abbreviated FSIQ ( $P = .002$ ) was therefore included as a covariate in subsequent analyses. Ever-depressed and nondepressed groups differed significantly on ASD diagnostic subtype ( $P < .001$ ), with the ever-depressed group more likely to be diagnosed with Asperger syndrome (34.8% vs 17.1% of the nondepressed group) and the nondepressed group more likely to be diagnosed with autistic disorder (59.7% vs 39.3% of the ever-depressed group) (see Table 1 for percentages by ASD subtype). The correlation between ASD diagnostic subtype and depression remained significant ( $P = .004$ ) after adjusting for IQ and age. Finally, those who had reached puberty (Tanner stages 3, 4, and 5) were at  $\sim 10.7$  times the odds of ever having a depression diagnosis compared with those in prepuberty (Tanner stage 1) (odds ratio [OR] = 10.73; 95% confidence interval [CI]: 5.02–22.92;  $P < .001$ ). However, the ever-depressed and nondepressed



**TABLE 2** Associations Between Medical and Behavioral Conditions and Depression History

	Endorsed in Ever-Depressed, <i>n</i> (%)	Endorsed in Nondepressed, <i>n</i> (%)	<i>R</i> <sup>2a</sup>	$\chi^2$	OR	(95% CI)	<i>P</i>
Seizures <sup>b</sup>	18 (37.5)	147 (18.0)	0.19	8.29	2.64	(1.36–5.11)	.004
History of gastrointestinal problems <sup>b</sup>	30 (62.5)	347 (42.4)	0.19	8.6	2.59	(1.37–4.90)	.003
Somatic complaints	22 (45.8)	201 (24.8)	0.18	5.66	2.12	(1.14–3.94)	.017
Eating problems	31 (64.6)	568 (69.0)	0.16	0.03	1.05	(0.55–2.01)	.873
Sleep problems	40 (83.3)	615 (74.7)	0.17	2.01	1.80	(0.80–4.04)	.156
SIB	18 (38.3)	220 (27.2)	0.18	2.58	1.69	(0.89–3.21)	.108
Aggression	32 (66.7)	454 (55.2)	0.18	5.79	2.24	(1.16–4.34)	.016
ADHD diagnosis/attention problems	47 (97.9)	764 (92.8)	N/A	N/A	N/A	N/A	N/A
History of anxiety	48 (100)	705 (85.7)	N/A	N/A	N/A	N/A	N/A
History of other psychiatric disorders	48 (100)	522 (63.4)	N/A	N/A	N/A	N/A	N/A
Family history of psychiatric disorders	20 (100)	561 (89.1)	N/A	N/A	N/A	N/A	N/A
Social impairment	45 (93.8)	806 (97.9)	0.17	5.12	0.20	(0.05–0.81)	.024
Repetitive/compulsive behavior	44 (91.7)	758 (92.1)	0.16	0.02	1.09	(0.36–3.25)	.883
Any psychotropic medication	28 (58.3)	332 (40.3)	0.17	1.66	1.51	(0.81–2.81)	.197
Any behavioral/educational intervention	35 (72.9)	607 (73.8)	0.16	0.39	1.25	(0.62–2.50)	.535
CBCL Withdrawn/Depressed subscale <sup>b</sup>	0.64 ± 0.95	−0.06 ± 0.97	0.19	12.11	1.69	(1.26–2.27)	.0005
CBCL Anxiety subscale <sup>b</sup>	0.35 ± 0.91	−0.18 ± 0.83	0.21	15.95	2.08	(1.45–2.98)	<.0001
Calibrated ADOS Severity	7.67 ± 1.94	7.34 ± 1.93	0.08	0.21	1.10	(0.74–1.63)	0.647

Data are presented as *n* (%) and means ± SDs unless otherwise indicated. N/A, not applicable.

<sup>a</sup> The *R*<sup>2</sup> value is max-rescaled *R*<sup>2</sup>.

<sup>b</sup> Significant outcome variables (*P* < .01) were based on logistic regression models controlling for age, diagnosis, and IQ.

groups did not differ significantly in Tanner staging after adjusting for participants' age ( $\chi^2$  [1, *n* = 545] = 3.22, *P* = .073). Furthermore, the sample size of those with Tanner stage data available was small, leading to a wide CI, whereas many more participants had age available. Thus, we controlled for age but not puberty status in subsequent analyses. Gender, race, ethnicity, and caregiver education did not differ significantly between groups (see Table 1). Analyses reported below are therefore adjusted for age, FSIQ, and ASD diagnostic subtype and include a smaller sample of 871 participants for whom FSIQ was available (ever-depressed: *n* = 48; nondepressed: *n* = 823). Unadjusted models yielded generally similar results.

### Medical/Somatic Problems

Seizures were reported significantly more often ( $\chi^2$  = 8.29, *P* = .004) in the ever-depressed group (37.5% positive) than in the nondepressed group (18%) (see Table 2 for all ORs and CIs). Gastrointestinal problems also were endorsed at a greater rate in the ever-depressed

group (62.5%) versus the nondepressed group (42.4%) ( $\chi^2$  = 8.60, *P* = .0003). Participants did not significantly differ ( $\chi^2$  = 1.7, *P* = .197) in reported use of psychotropic medications (ever-depressed: 58.3%; nondepressed: 40.3%) (see Table 2).

### Behavioral Problems

The ever-depressed group had greater reported levels of aggression (66.7% vs 55.2% in the nondepressed group) ( $\chi^2$  = 5.79, *P* = .016) and of somatic complaints (45.8% vs 24.8% in the nondepressed group) ( $\chi^2$  = 5.66, *P* = .017), although these comparisons failed to meet our stringent criterion for significance. A trend-level difference was also noted between ever-depressed (93.8%) and nondepressed (97.9%) groups on social impairments ( $\chi^2$  = 5.12, *P* = .024). Participants did not significantly differ ( $\chi^2$  = 0.03, *P* = .873) in their reported eating problems (ever-depressed: 64.6%; nondepressed: 69.0%).

We did not observe significant group differences on calibrated ADOS severity scores,<sup>27</sup> repetitive

and compulsive behaviors, sleep problems, SIB, or the use of behavior, social, or educational interventions or therapies within 1 month of the baseline visit (Table 2). We did not have sufficient variability within our sample to make statistical comparisons on family history of depression or other psychiatric disorders, parent-reported history of anxiety, history of psychiatric disorders, or ADHD and/or attentional problems, because 98% to 100% of the ever-depressed group endorsed these variables. We present the percentages of these variables endorsed within each group in Table 2.

For participants who received the CBCL 6-18, for each unit increase in the Withdrawn/Depressed subscale *z* score (mean [SD]: 0.64 [0.95] ever-depressed versus −0.06 [0.97] nondepressed), the odds of being in the ever-depressed group increased by ~69% ( $\chi^2$  = 12.11; OR = 1.69; 95% CI: 1.26–2.27; *P* = .0005), and for each unit increase in the Anxiety Problems subscale *z* score (mean [SD]: 0.35 [0.91] ever-depressed versus −0.18 [0.83] nondepressed), the odds of

being in the ever-depressed group more than doubled ( $\chi^2 = 15.95$ ; OR = 2.08; 95% CI: 1.45–2.98;  $P < .0001$ ).

## DISCUSSION

The aim of this study was to examine medical and behavioral factors that could be associated with depression in children and adolescents with ASD. Our findings suggest that parent-reported history of a depression diagnosis is associated with greater chronological age, higher IQ, DSM-IV–defined Asperger disorder, and a history of gastrointestinal complaints and seizures.

In our initial analysis, we attempted to identify participant characteristics that differed across those with and without a parent-reported history of a depression diagnosis. Despite gender being a robust predictor of depression in the general population (with postpubertal females at highest risk), we observed no significant effects of gender in our sample. Such a finding could result if females with ASD are at less risk of developing depression than those in the general population, although this was not suggested by our data, in which 20% of adolescents had a parent-reported depression history with no gender-by-age group interaction. Alternatively, the lack of gender differences might indicate that there is increased risk of depressive symptoms associated with being a male with ASD, at least during the school-age period. This interpretation has been supported in the recent literature.<sup>24</sup>

In line with our hypothesis, age was significantly associated with a current or past experience of depression, with the average age in the ever-depressed group being 2.5 years older than that in the nondepressed group. This finding could correspond to documented pubertal effects on depression risk, but it should be noted that older individuals also have had more years

of exposure to risk of a depressive episode. Our results corroborate previous findings that, within ASD, those with higher intellectual ability are at greater risk of depression.<sup>6,28</sup> Others have suggested that this relationship may be explained by low levels of social competence in combination with increased self-awareness,<sup>46</sup> particularly as the social context becomes more complex and demanding during adolescence. Of note, clinicians may also be less likely to diagnose depression in those who are less cognitively able due to diagnostic overshadowing, particularly in those who are minimally verbal. There were also significant effects of ASD diagnostic subtype, with the ever-depressed group more likely to have a DSM-IV diagnosis of Asperger syndrome and the nondepressed group more likely to have a diagnosis of autistic disorder. The association between Asperger and depression diagnoses could potentially reflect higher levels of insight or social interest (possibly related to depressive outcomes) or greater diagnostic ambiguity in individuals diagnosed with Asperger syndrome.<sup>47</sup>

After controlling for age and within-spectrum (DSM-IV) diagnostic subtype, the ever-depressed and nondepressed groups differed significantly on rates of gastrointestinal problems and seizure disorders and exhibited trend-level differences in social impairments, somatic complaints, and aggressive behavior. Previous data have linked aggression and SIB with mood disorders in ASD.<sup>36,37</sup> Within the ATN population, we do not know if subjects had aggressive behavior predating depression onset or if these behaviors developed after, and perhaps in response to, their depression. The latter might suggest that a worsening or new onset of maladaptive behaviors could serve as an indicator of possible depression in individuals who may not be able

to articulate cognitive or emotional symptoms.<sup>48</sup> It will be important to better understand the possible link between all of these somatic factors and depression, starting with their temporal relationship and moving to a study of shared mechanisms. For example, might the presence of long-term gastrointestinal discomfort lead to depression, or is a latent variable likely to cause both? Taken in combination with the association between functional somatic symptoms and depression in TD children,<sup>49</sup> our results indicate that the presence of these specific medical issues in individuals with ASD may indicate a need to screen for depressive symptoms, particularly in less cognitively able patients with ASD.

Contrary to our hypotheses, there were no group differences in ADOS severity scores, reports of repetitive and compulsive behaviors, sleep problems, SIB, psychotropic medication use, or use of behavior, social, or educational interventions or therapies within 1 month of the baseline visit. Rates of a family history of depression or other psychiatric disorders, parent-reported history of anxiety and history of other psychiatric disorders, and history of attention problems were high in both groups, and differences between the groups could not be assessed statistically due to a lack of variability in the sample. This finding is not surprising given that anxiety and attention problems are also reported as commonly co-occurring psychiatric disorders among children and adolescents with ASD.<sup>5,8,22</sup> However, as hypothesized, the ever-depressed group had significantly higher scores on both the Withdrawn/Depressed and Anxiety subscales of the CBCL.

Sample size and diagnostic rigor are often trade-offs in ASD research. Participants in this study were not formally assessed for depression upon enrollment into the ATN,

and no other information, such as duration of episode or response to treatment, was available. Elevated CBCL Withdrawn/Depressed subscale scores suggest that the ever-depressed group did have increased depressive symptoms at the time of enrollment, but information about formal depression criteria was not available. Parents of ever-depressed participants answered “yes” to a single question encompassing both current and past depression diagnosis. Combining these time periods increased our statistical power (which was still limited given the rate of depression in the overall sample), but it prevented us from differentiating between factors associated with current diagnosis and past diagnosis. It is possible that our results would have differed if groups were determined on the basis of a formal depression evaluation, diagnostic interview, or screening questionnaire, particularly because individuals whose parents were “unsure” of a previous diagnosis of depression were excluded from our study.

Although the prevalence of a history of a parent-reported diagnosis of depression in our total sample (7.0%) is similar to reports in the TD population<sup>9,10</sup> at similar ages, it stands in direct contrast to studies that used a more systematic approach to assessment, which found high rates of depressive symptoms in child and adolescent ASD samples.<sup>24,50</sup> The overall low prevalence in this ASD sample was likely driven by the substantially greater number of subjects aged 6 to 12 years (85.6% of the total sample; 4.8% with a parent-reported depression history), in which depression diagnoses are less common, and the much smaller number of adolescent participants (14.4% of the total sample), in which depression prevalence was 20.2%. By comparison, recent reports indicate lifetime depression prevalence of 8%

to 12% in TD adolescents.<sup>10</sup> Although replication is needed in large samples with the use of more formal diagnostic assessment, our findings suggest that adolescents with ASD could be at particular risk of developing depression. By relying on diagnosis rather than symptom level, the current data may underestimate the prevalence of this comorbidity, because it is relatively uncommon for children with ASD to receive a formal assessment or diagnosis of depression in standard clinical practice unless those related issues are marked and severe. Regardless of the accuracy of the prevalence rates, the relatively small number of participants with depression led to highly discrepant sample sizes between groups, which must also be taken into account when considering the generalizability of our findings.

Identification and diagnosis of depression have traditionally relied on subjective self-report information, which is difficult for many children with ASD to provide given social and communication deficits and difficulties in recognizing and communicating emotions.<sup>25</sup> Potential challenges to emotional self-reporting in ASD could lead to significant underreporting of depressive symptoms by caregivers and underdiagnosis by clinicians (conversely, the absence of self-report could lead to incorrect attribution of symptoms to depression). The possibility that a number of subjects were misclassified as not having a history of depression could bias the results by either over- or underestimating the relationship between depression and other behavioral or medical symptoms. To account for the impact of communication deficits, it will be important for future research to assess potentially different patterns in medical and behavior correlates of depression by verbal level of participants.

Further complicating the issue of valid assessment of depression in ASD, it is not clear if the presentation of depression is similar across TD children and adolescents and those with ASD. Many of the common symptoms of depression, such as irritability, anhedonia, and social withdrawal, can also be considered behavioral correlates of symptoms of ASD.<sup>50,51</sup> The ever-depressed group did show higher scores on the CBCL Withdrawn/Depressed subscale, but the Anxiety Problems subscale was actually a stronger predictor of depression diagnosis. This finding may indicate that trait anxiety is associated with depression in ASD as it is in the general population. Furthermore, the average CBCL Withdrawn/Depressed scores in the nondepressed subgroup were also above the CBCL norms, suggesting that this subscale may be less useful as a diagnostic tool for depression in the ASD population. Clearly, there is a need for standardized assessment measures of depression in children and adolescents with ASD. Future investigations should also consider the issue of measurement invariance across populations; widely used measures of depression in TD populations may not accurately reflect the experiences of a child or adolescent with ASD and depression. Similarly, we should take care to disentangle the impact of depression on symptom reporting in future research.

Our dichotomous approach to the analysis (eg, subjects were considered to have gastrointestinal problems if “yes” was indicated on any of a number of different items/instruments) also maximized our power but limited our specificity. For example, children and adolescents with ASD can present with a number of different eating complaints, such as selective eating or difficulty swallowing, but we combined these different problems together and were not able to consider gradations of

severity. Some of these categories, such as sleep problems, were so common in the ASD population that ceiling effects may have diminished our power to detect a statistically significant difference. Furthermore, this study design did not allow us to delve into possible mechanisms underlying the link between depression and these various behavioral and medical problems. Future research specifically focused on depression in ASD would benefit from both a broader array of potential correlates (eg, stressful life events and family dynamics) and more precise measurement to generate broader screening/diagnostic implications and to narrow in on mechanisms underlying depression in this special population.

## CONCLUSIONS

Although there is growing evidence that depression is a significant

clinical problem in the ASD population, perhaps especially for adolescents, the factors contributing to depression risk in ASD remain incompletely known. This study highlights medical and behavioral correlates that may help clinicians better understand the depressive phenotype in ASD. Our findings must be interpreted cautiously, insofar as they are based on a parent report of depression diagnosis, although this disorder may be uncommonly assessed in the ASD population. These findings warrant replication in large samples with more carefully phenotyped co-occurring diagnoses as well as characterization of subthreshold problems. Treatments that target specific problems associated with depression in ASD, such as gastrointestinal complaints, seizure disorder, or aggression, potentially could prevent or lessen the severity of a depressive episode. Because depression can be difficult

to notice and to assess in this population, these correlates also may represent indicators of the need for further assessment for depression in children and adolescents with ASD.

## ABBREVIATIONS

ADHD:	attention-deficit/hyperactivity disorder
ADOS:	Autism Diagnostic Observation Schedule
ASD:	autism spectrum disorder
ATN:	Autism Treatment Network
CBCL:	Child Behavior Checklist
CI:	confidence interval
DSM-IV:	<i>Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition</i>
FSIQ:	full-scale IQ
HMHH:	Health and Mental Health History
OR:	odds ratio
SIB:	self-injurious behavior
TD:	typically developing

Address correspondence to Katherine O. Gotham, PhD, Vanderbilt Bill Wilkerson Center, 1215 21st Ave South, Room 8310, Nashville, TN 37232. E-mail: katherine.gotham@vanderbilt.edu

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