Psychiatric Disorders in Children With Autism Spectrum Disorders: Prevalence, Comorbidity, and Associated Factors in a Population-Derived Sample

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ABSTRACT

Objective: Autism spectrum disorders are now recognized to occur in up to 1% of the population and to be a major public health concern because of their early onset, lifelong persistence, and high levels of associated impairment. Little is known about the associated psychiatric disorders that may contribute to impairment. We identify the rates and type of psychiatric comorbidity associated with ASDs and explore the associations with variables identified as risk factors for child psychiatric disorders. **Method:** A subgroup of 112 ten- to 14-year old children from a population-derived cohort was assessed for other child psychiatric disorders (3 months' prevalence) through parent interview using the Child and Adolescent Psychiatric Assessment. *DSM-IV* diagnoses for childhood anxiety disorders, depressive disorders, oppositional defiant and conduct disorders, attention-deficit/hyperactivity disorder, tic disorders, trichotillomania, enuresis, and encopresis were identified. **Results:** Seventy percent of participants had at least one comorbid disorder and 41% had two or more. The most common diagnoses were social anxiety disorder (29.2%, 95% confidence interval [CI)] 13.2–45.1), attention-deficit/hyperactivity disorder (28.2%, 95% CI 13.3–43.0), and oppositional defiant disorder (28.1%, 95% CI 13.9–42.2). Of those with attention-deficit/hyperactivity disorder, 84% received a second comorbid diagnosis. There were few associations between putative risk factors and psychiatric disorder. **Conclusions:** Psychiatric disorders are common and frequently multiple in children with autism spectrum disorders. They may provide targets for intervention and should be routinely evaluated in the clinical assessment of this group. *J. Am. Acad. Child Adolesc. Psychiatry*, 2008;47(8):921–929. **Key Words:** autism, child psychiatric disorders, prevalence, Special Needs and Autism Project.

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Recent epidemiological studies have converged in finding that child autism and pervasive developmental disorders, collectively referred to as autism spectrum disorders (ASDs), are more common than previously thought and have a prevalence of ~0.6% to 1% in child and adolescent populations.[1,2] From a public health perspective, ASDs are an important cause of morbidity and high service utilization[3] because of their early onset, lifelong persistence, high level of associated impairment, and absence of effective treatment for the core problems. Impairment due to the social and cognitive deficits that constitute the core features of autism is well demonstrated in autism. A further, less well-investigated cause of impairment may be psychiatric comorbidities. For other child psychiatric disorders, comorbidity is common,[4–6] although the causes are often not well

understood.[7,8] Delineating psychiatric comorbidity may identify targets for specific intervention that could reduce overall impairment and improve quality of life.

The infrequent identification of comorbid psychiatric disorders in ASD may be due to the same diagnostic overshadowing identified for intellectual disability in which psychiatric symptoms are attributed to the intellectual disability.[9] Specific challenges to comorbid psychiatric assessment in ASD are the wide IQ range and communication problems, which make personal interviewing difficult and may produce uncertainty among caregivers about their ability to make inferences regarding mental state. Comorbid psychiatric problems were first reported in a number of studies using unstandardized assessments[10–12] and subsequently confirmed by questionnaires studies in both children[13–15] and adults.[16,17] These studies suggest that as many as three fourths may reach threshold for caseness,[18] a finding supported by studies using structured interviews that show high rates of anxiety[19,20] and affective disorders.[19,21,22] To date, the common, standardized psychiatric interview tools available have not been used to identify other psychiatric disorders among children with ASDs. More recently Leyfer et al.[23] reported high rates of lifetime psychiatric disorders in children with autism, using a new interview, the Autism Comorbidity Interview-Parent and Lifetime Version, modified from the Schedule of Affective Disorders and Schizophrenia for School-Age Children.[24] With the most comprehensive coverage of psychiatric disorders, just less than three fourths met criteria for one or more *DSM-IV* disorders, with the median number of diagnoses being three.

However, none of the studies using standardized assessments of psychiatric disorder have involved population-representative samples. In our epidemiological sample, two thirds of those receiving an ASD diagnosis had not been diagnosed as such by local services (although almost all of them had other diagnoses), indicating that clinical ascertainment is incomplete and possibly biased.[1] We make use of this epidemiological sample of children with well-characterized ASD to determine whether the prevalence of common *DSM-IV* child psychiatric disorders is as high as previous reports suggest. We explore whether reported child, family, and contextual risk factors for psychiatric disorders reported in children without ASDs are also associated in this population. To our knowledge, this is the first report of structured assessments using a population-derived sample.

METHOD

Sample

The Special Needs and Autism Project sample was drawn from a total population cohort of 56,946 children. All of those with a current clinical diagnosis of pervasive developmental disorder (N = 255) or considered to be at risk for being an undetected case by virtue of having a Statement of Special Educational Needs (N = 1,515) were surveyed using the Social Communication Questionnaire (SCQ[25]). A Statement of Special Educational Needs is a legal document issued by U.K. education authorities when children require significant additional support in school due to any learning

TABLE 1
Prevalence of *DSM-IV* Disorders

Disorder	3-Mo Point Prevalence/100	95% CI
Any disorder	70.8	58.2–83.4
Any main disorder[a]	62.8	49.8–75.9
Any emotional disorder[b]	44.4	30.2–58.7
Any anxiety or phobic disorders[c]	41.9	26.8–57.0
Generalized anxiety disorder	13.4	0–27.4
Separation anxiety disorder	0.5	0–1.6
Panic disorder	10.1	0–24.8
Agoraphobia	7.9	3.0–12.9
Social anxiety disorder	29.2	13.2–45.1
Simple phobia	8.5	2.8–14.1
Obsessive-compulsive disorder	8.2	3.2–13.1
Any depressive disorder	1.4	0–3.0
Major depressive disorder	0.9	0–2.3
Dysthymic disorder	0.5	0–1.4
Oppositional or conduct disorder	30.0	14.9–45.0
Oppositional defiant disorder	28.1	13.9–42.2
Conduct disorder	3.2	0–7.1
Attention-deficit/hyperactivity disorder	28.2	13.3–43.0
Other disorders[d]	24.7	14.1–35.3
Enuresis	11.0	4.1–17.7
Encopresis	6.6	1.8–11.4
Tourette syndrome	4.8	0.1–9.5
Chronic tic disorder	9.0	3.3–14.6
Trichotillomania	3.9	0–10.3

Note: CIs = confidence intervals.

[a] Includes attention-deficit/hyperactivity disorder, oppositional and conduct disorders, and any emotional disorder.

[b] Includes all anxiety disorders, phobias, and mood disorders.

[c] Includes anxiety disorders, panic disorder, phobias, and obsessive-compulsive disorder.

[d] Includes Tourette syndrome, chronic tics, trichotillomania, enuresis, and encopresis.

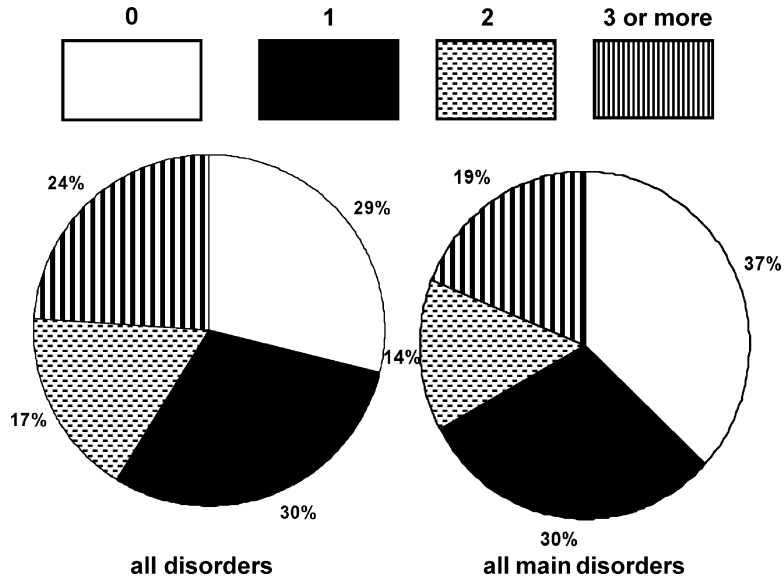

Fig. 1 Weighted rates of comorbidity are shown for all of the disorders and for all of the main disorders, in which the latter includes ADHD, oppositional defiant or conduct disorder, and any emotional disorder (separation anxiety disorder, generalized anxiety disorder, simple phobia, social phobia, agoraphobia, panic disorder, major depressive disorder, and dysthymic disorder).

and/or behavioral problems. The study was approved by the South East Multicentre Research Ethics Committee (REC) (00/01/50). Written consent was obtained from all of the parents.

Measures

A stratified subsample (n = 363) was randomly drawn using a two-way stratification (four levels of SCQ score and presence of local ASD diagnosis) and 255 children (70%) were assessed. The comprehensive diagnostic assessment included the Autism Diagnostic Observation Schedule-Generic[26] and the parent-informed Autism Diagnostic Interview-Revised,[27] language and IQ, and a medical examination. *International Classification of Disease-10 (ICD-10)* research criteria were used to derive a clinical consensus diagnosis of childhood autism (n = 81: 77 male, 4 female) and other ASDs (n = 77: 65 male, 12 female).[1]

The Child and Adolescent Psychiatric Assessment-parent version (CAPA) was used to identify *DSM-IV* diagnoses in the first 142 of the 255 children studied in depth; funding arrangements did not permit CAPA assessments of the full cohort. Of these, 112 had an ASD and an SCQ score ≥15 and are the subject of this report. Eleven children with an ASD diagnosis and an SCQ score <15 were not included in the present analyses because they were disproportionately drawn from the sampling cells of low SCQ score and positive local diagnosis and were thought to be nonrepresentative of the ASD sample.

CAPA has been used in both general population[4,6] and clinical samples, including patient groups with intellectual disability,[28] and

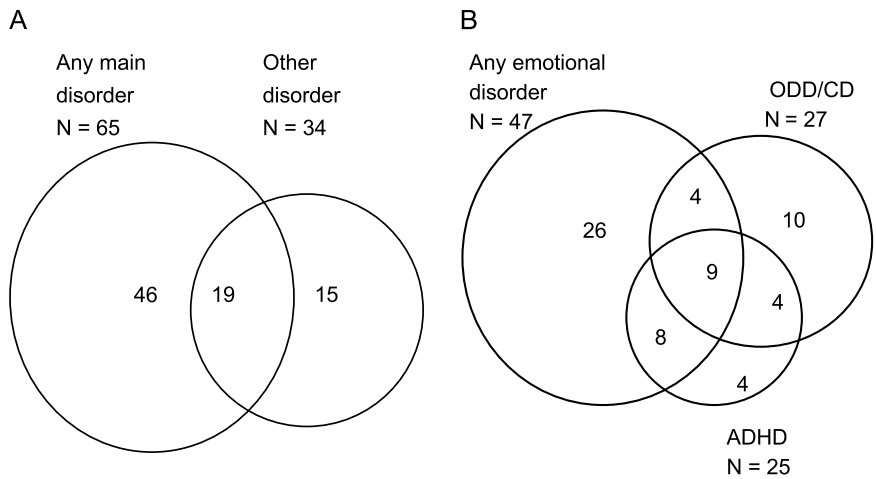

Fig. 2 Overlap among main areas of comorbidity. Numbers given are weighted sample sizes.

TABLE 2
Association of Potential Risk Factors to Psychiatric Disorders

	Unadjusted Odds Ratios (95% CIs)			
	Any Main Disorder[a]		ADHD	
	All	Males Only	All	Males Only
Child characteristics				
Autism severity	1.03 (0.84–1.26)	1.05 (0.84–1.32)	1.01 (0.82–1.25)	1.18 (0.95–1.47)
Presence of epilepsy	17.54* (1.89–162.31)	6.58 (0.66–65.73)	1.61 (0.27–9.75)	2.86 (0.39–21.08)
Lower IQ	1.00 (0.98–1.02)	1.01 (0.99–1.04)	1.00 (0.97–1.02)	1.01 (0.98–1.04)
Lower Vineland composite score	0.99 (0.95–1.02)	0.99 (0.96–1.03)	0.99 (0.94–1.04)	0.96 (0.93–0.99)
Parental characteristics				
Lower parental education	0.70 (0.47–1.05)	0.74 (0.49–1.11)	0.60 (0.36–1.00)	0.63 (0.41–0.96)
Lower parental SES	0.84 (0.64–1.10)	0.93 (0.68–1.27)	0.82 (0.60–1.12)	0.93 (0.68–1.28)
High maternal GHQ score	0.99 (0.90–1.08)	1.03 (0.93–1.15)	0.97 (0.84–1.11)	1.06 (0.97–1.16)
Parental distress	1.03 (0.97–1.11)	1.03 (0.97–1.11)	1.03 (0.97–1.03)	1.04 (0.97–1.11)
Contextual factors				
Higher family deprivation	3.62 (0.99–13.3)	7.77** (1.85–32.70)	2.22 (0.45–10.79)	4.86 (0.98–24.07)
Higher area deprivation	1.21 (0.92–1.59)	1.09 (0.81–1.47)	1.50** (1.12–1.99)	1.36* (1.05–1.76)
Attending mainstream school	3.10 (0.96–10.06)	1.99 (0.61–6.49)	2.27 (0.53–9.76)	1.40 (0.36–5.37)

Note: ADHD = attention-deficit/hyperactivity; SES = socioeconomic status; GHQ = General Health Questionnaire.
[a]Any emotional disorder, oppositional defiant disorder, conduct disorder, or attention-deficit/hyperactivity disorder.
[b]Oppositional defiant or conduct disorder.
[c]Any anxiety or phobic disorder or depression.
[d]Separation anxiety, generalized anxiety disorder, agoraphobia, or simple or social phobia.
*$p < .05$; **$p < .01$.

has good test-retest reliability with κ values ranging from 0.5 to 0.9.[29] We used CAPA because it requires behavioral descriptions of symptoms, which may decrease the chance that symptoms of ASD would be incorrectly double-coded as other behavioral problem (e.g., repetitive language in autism being incorrectly coded as the anxiety symptoms of excessive need for reassurance). CAPA has a detailed glossary providing operationalized symptom definitions and application rules. The time frame is the past 3 months, but duration of symptoms is elicited in a manner that is compatible with diagnostic frameworks. CAPA is modular, and the following disorders were assessed in the present study: separation anxiety disorder, generalized anxiety disorder, panic disorder, social anxiety, simple phobia, obsessive-compulsive disorder, major depressive disorder, dysthymic disorder, attention-deficit/hyperactivity disorder (ADHD), oppositional defiant disorder, conduct disorder, Tourette syndrome, chronic tic disorder, trichotillomania, enuresis, and encopresis. We used only the parent version here because the majority of children had not attained the mental age necessary to give reliable and valid information. *DSM-IV* requires the presence of both symptoms and psychosocial impairment; the latter was assessed in 15 domains of personal life (self-care, chores, homework, leaving the house), family relationships (parent and sibling), school (school life, suspension/exclusion, teacher–student relationships, peer relationships), and leisure activities (spare-time activities/employment, relationships with peers/adults during these activities). Symptom-dependent impairment is endorsed when the informant reports that impairment is causally or temporally associated with the impairment domain (e.g., separation anxiety symptoms leading to school refusal). Psychosocial impairment criteria were not applied to chronic tics, Tourette syndrome, trichotillomania, enuresis, and encopresis. Diagnostic endorsements did not use the exclusionary rules in *DSM-IV* with regard to autism; meeting the symptom and impairment criteria was the sole basis for diagnosis. The rationale for this was to allow empirical examination of the occurrence of additional disorders that may warrant treatment in their own right. All of the CAPA interviews were undertaken by four postdoctoral researchers or pediatricians with extensive previous experience in ASDs and developmental disorders. All of them were trained in the use of CAPA, including specific distinctions between autism symptoms and those of other disorders, such as obsessive-compulsive disorder.

The analyses presented use systematically collected variables reported as risk factors for psychiatric disorders in non-ASD populations. The following child characteristics relevant to the presence of psychiatric disorders were measured. Severity of autism was indexed by a count of *ICD-10* symptoms (0–12) completed as part of the diagnostic review; the (weighted) mean was 7.4 (SE 0.4, SD 2.6) and the range was 3 to 12. IQ was measured using the WISC-III UK version,[30] Raven's Standard matrix (SPM) or Coloured Progressive matrices (CPM).[31] For the 18 cases in which the SPM or CPM but not WISC was available, an imputed Full Scale IQ was calculated using the regression relation of WISC Full Scale IQ to SPM/CPM IQ within each diagnostic group. For the one case in which no cognitive testing was possible, the Adaptive Behavior Composite on the Vineland Adaptive Behavior Scale[32] gave a score <20 and an IQ score of 19 was assigned. Among the subsample included here, the mean (SE, SD) IQ was 72.7 (2.0, 21.6) with a range of 19–124. The Vineland Adaptive Behavior Scale, additionally used as a predictor, revealed a mean (SE, SD) of 46.4 (2.0, 14.8) and a range of 19 to 93. Epilepsy was systematically elicited and coded if children had ever had one or more nonfebrile convulsion ($N = 16$).

Unadjusted Odds Ratios (95% CIs)					
Any Behavioral Disorder[b]		Any Emotional Disorder[c]		Any Anxiety Disorder[d]	
All	Males Only	All	Males Only	All	Males Only
1.01 (0.82–1.23)	1.06 (0.88–1.29)	0.95 (0.78–1.17)	0.99 (0.78–1.24)	0.91 (0.73–1.12)	0.94 (0.74–1.20)
11.09** (2.34–52.66)	5.40 (0.85–34.40)	0.63 (0.14–2.96	5.31 (0.82–34.5)	0.71 (0.15–3.35)	6.16 (0.94–46.43)
0.98 (0.95–1.02)	1.01 (0.97–1.05)	1.00 (0.98–1.03	1.01 (0.98–1.03)	1.01 (0.98–1.03)	1.01 (0.99–1.04)
0.99 (0.94–1.03)	0.99 (0.96–1.02)	1.02 (0.98–.1.05)	1.00 (0.96–1.04)	1.03 (0.99–1.07)	1.01 (0.97–1.06)
0.83 (0.53–1.31)	0.97 (0.70–1.35)	0.74 (0.49–1.12)	.86 (0.59–1.26)	0.74 (0.48–1.13)	0.87 (0.59–1.29)
0.58 (0.39–0.84)	0.65 (0.44–0.96)	0.94 (0.74–1.25)	1.01 (0.74–1.36)	0.93 (0.68–1.26)	0.99 (0.72–1.36)
0.97 (0.88–1.07)	1.01 (0.93–1.11)	0.98 (0.91–1.07)	1.05 (0.95–1.17)	0.97 (0.90–1.06)	1.04 (0.95–1.14)
1.01 (0.96–1.07)	1.01 (0.95–1.08	1.02 (0.95–1.10)	1.03 (0.95–1.11)	1.02 (0.95–1.10)	1.03 (0.94–1.11)
2.00 (0.42–9.32)	5.31* (1.11–25.46)	1.66 (0.40–6.91)	2.22 (0.46–10.64)	1.72 (0.41–7.26)	2.38 (0.49–11.43)
1.25 (0.91–1.79)	1.06 (0.78–1.42)	1.14 (0.89–1.47)	0.97 (0.76–1.23)	1.11 (0.85–1.46)	0.91 (0.71–1.16)
3.22 (0.76–13.76)	1.41 (0.35–5.74)	3.25 (0.86–12.27)	3.08 (0.84–11.22)	2.76 (0.70–10.81)	2.37 (0.63–8.92)

Family characteristics included parental socioeconomic status (highest parental occupational level) using the 8-point scale of the U.K. Office for National Statistics[33]; 53 (weighted 41%) families were in managerial/professional occupations; 38 (35%) in technical, lower supervisory, or small employers' occupations; 15 (19%) in routine/semiroutine occupations; and 5 (4%) were long-term unemployed, and no information for one family. Highest household parental education was coded on a 6-point scale ranging from no high school diploma to postgraduate qualifications; 61% of households had at least one parent with education beyond a high school diploma. Maternal General Health Questionnaire,[30,34] available in 91 cases, provided continuous scores with a sample mean (SE, SD) of 4.6 (1.0, 6.7) and a range of 0 to 25 out of a possible total of 30; 35% scored above the threshold indicating psychiatric distress. The Parenting Stress Index Short Form[35] measures difficulties in the parent–child relationship on three subscales: disturbed child, parental distress, and parent-child dysfunctional interaction. Parental distress was used here to index the parental component of stress as it attempts to measure parental characteristics rather than aspects of the parent–child relationship, which may be affected by the presence of an ASD in the child. Scores were available in 95 cases with a mean (SE, SD) of 31.0 (1.5, 9.4) and a range of 12 to 53 out of a maximum possible score of 60.

In relation to contextual characteristics, neighborhood characteristics were measured from full post codes using the Carstairs Index, which combines overcrowding, male unemployment, proportion of the population in Registrar General social class 4 and 5, and households without a car, with total population U.K. scores ranging from −5.71 (least deprived) to 16.50 (median [SD] −0.88 [3.41]).[36] The present sample had a mean (SE, SD) Carstairs score of −0.14 (0.4, 2.5) and a range of −4.3 to 6.7. Parental report of car ownership and housing tenure were used to construct a crude income index (from income differences reported in Macintyre et al.[37]) as a family-based measure of deprivation. In a binary classification 18% of families were in the more deprived group. Children's school placements were dichotomized according to whether they attended a mainstream school or attached unit with or without personal support (41%) or a special school for intellectual disabilities, emotional/behavioral problems, or autism. Contextual variables were available in all of the cases.

Data Analysis

Stratification of the sample, previously described in detail,[1] was based on whether a child had a locally recorded ASD diagnosis (yes/no) and four levels of SCQ score (low score [<8], moderately low score [8–14], moderately high score [15–21], or high score [≥22]). Inverse probability weights were generated for the sample included in the present report, taking account of sampling probability from the two-way stratification table, differential response to the initial screening questionnaire based on local ASD diagnosis, health district, and child's sex. These allow all of the statistics to be presented as target population estimates. Wald test statistics (adjusted t and F tests) and p values were calculated using the linearization version of the robust

parameter covariance matrix as implemented by the svy procedures of Stata 9.2.[38]

RESULTS

Of the 112 children included, 98 were male (7:1 male:female ratio), with a mean age of 11.5 years (range 10–13.9). Fifty children (39 male) had an *ICD-10* diagnosis of other pervasive developmental disorders and 62 children (59 male) of childhood autism; 106 (95%) were white British.

Rates of Disorder

The weighted 3-month prevalence rates (Table 1) for the *DSM-IV* diagnoses elicited show that 70.8% of children had at least one current psychiatric disorder (any disorder); 62.8% had a main disorder of ADHD, an emotional or behavioral (oppositional defiant or conduct) disorder (referred to as any main disorder), and 24.7% another disorder of Tourette syndrome, chronic tics, trichotillomania, enuresis, or encopresis (any neuropsychiatric disorder). Whether an ASD had been diagnosed by clinical services did not affect the rate of any disorder (73% in diagnosed cases versus 69% in unrecognized cases, $p = .97$), any main disorder (54% versus 66%, $p = .27$), or any neuropsychiatric disorder (37% versus 21%, $p = .15$). Type of ASD diagnosis did not predict rates for any disorder (77% autism versus 67% other ASD, $p = .34$), any main disorder (66% versus 61%, $p = .71$), or any neuropsychiatric disorder (35% versus 22%, $p = .23$). There were no significant sex differences in rates of any disorder (69% males versus 76% females, $p = .62$), any main disorder (59% versus 77, $p = .28$), or any neuropsychiatric disorder (29% versus 17%, $p = .37$), although the power to detect any effect was low.

The most common disorders were social anxiety disorder (29.2%), ADHD (28.1%), and oppositional defiant disorder (28.1%). Other disorders occurring in ≥10% of children with an ASD were generalized anxiety disorder (13.4%), panic disorder (10.1%), and enuresis (11%); however, rates of major depressive disorder (0.9%), dysthymic disorder (0.5%), and conduct disorder (3.2%) appeared low. A further 10.9% of children had a significant period of depression or irritability not meeting *DSM-IV* depression/dysthymic disorder criteria.

Comorbidity

For any psychiatric disorder, the majority of children who had at least one disorder have multiple diagnoses (41% of the 71%, or 57%) and one third of these (24% of 71%) have three or more disorders in addition to the ASD (Fig. 1). The same pattern applies when only main psychiatric disorders are considered; 52% had multiple diagnoses and 38% had three or more disorders.

Roughly one fourth of those with a main psychiatric disorder also had a neuropsychiatric disorder (Fig. 2). Within the main psychiatric disorders, 80% of those with ADHD had an emotional or behavioral disorder or both; the same applied to roughly 60% of those with a behavioral disorder and 40% of those with an emotional disorder.

Associations Between Disorder and Putative Risk Factors

Associations between putative risk factors and psychiatric disorders were tested, for both sexes together and boys only, in a series of bivariate logistic regressions using disorder categories with sufficient affected numbers to identify associations (Table 2). For none of the disorder categories was autism severity a significant predictor of other disorders. The presence of epilepsy, past or present, was associated with any main disorder (odds ratio [OR] 17.84, 95% confidence interval [CI] 1.89–162.31) and also for any behavioral disorder (OR 11.09, 95% CI 2.34–52.66), but only when the analyses included the entire sample; when restricted to males only, the ORs were somewhat attenuated. Neither IQ nor the Vineland Adaptive Behavior Scale score was associated with any other psychiatric disorder category. To confirm the surprising absence of relationship to IQ and check whether a nonlinear relationship was obscured by the use of a continuous variable, the Stata command *fracpoly* that fits multiple fractional polynomial terms. For none of the disorder categories did this produce a significant association with IQ.

No significant associations were found for any family characteristics. A limited set of associations were identified with respect to contextual characteristics, including a positive relationship between family deprivation and any main disorder for males (OR 7.77, 95% CI 1.85–32.7) and just short of significance for the entire sample (OR 3.62, 95% CI 0.99–13.3), between family deprivation and any behavioral disorder for males only (OR 5.31, 95% CI 1.11–25.46), and between area deprivation and attention-deficit/hyperactivity disorder for both the entire sample (OR 1.50, 95% CI 1.12–1.90) and males only (OR 1.36, 95% CI

1.05–1.76). Type of school (mainstream or special unit/school) attended was not associated with any disorder category.

DISCUSSION

To our knowledge, this is the first study of comorbid psychopathology in ASDs using an epidemiological, population-derived sample, and a standardized interview measure to determine the rates of *DSM-IV* disorders. The present research confirms the high rates of many psychiatric disorders in children with ASDs previously reported in less systematic studies. Although it is difficult to make direct comparisons with other samples, findings from an overlapping age group in the general population studied in the Great Smoky Mountains Study provide contrast.[4] Although the "any disorder" category was more comprehensive in the Great Smoky Mountains Study (including substance use disorders eating disorders and bipolar disorder), the reported rates range from 8.2% to 19.7% across the same age, in contrast to our 70.8%.

Our high rates of ADHD are consistent with other reports[10–12,18,23] on children with ASDs and also with studies examining the rate of autistic symptoms among those with ADHD.[39–41] Although Green et al.[19] report only 5% with hyperkinetic disorder, the sample was small; 15% had pervasive overactivity or inattention symptoms and a further 40% situation-specific ADHD symptoms. Current criteria exclude the diagnosis of ADHD when an ASD is present, although research indicates that stimulant treatment is effective for this group.[42] The exclusion should be reconsidered. Our failure to find sex differences in the rate of ADHD clearly differs from findings in the general population but is consistent with other reports in ASD.[18]

We found high rates of oppositional defiant disorder but not conduct disorder, consistent with previous questionnaire studies.[10,11,15,18] Leyfer et al.[23] reported lower rates of oppositional defiant disorder (7%), and it is unclear whether the difference lies primarily with definitions or population. Only Green et al.[19] report high rates of conduct disorder as well as oppositional defiant disorder (25% for each); this could reflect referral bias to their study comparing adolescents with conduct disorder and Asperger's syndrome.

All of the studies systematically assessing anxiety disorders report high rates,[10,11,15,18–20,23,43] and our overall rate of 41.9% is no exception. Our findings are most directly comparable with those of Leyfer et al.[23] and Muris et al.[20] because these studies probed for the range of anxiety disorders, although Muris et al.[20] report on *DSM-III-R* diagnoses. Whereas Muris et al.[20] and the present investigators found high rates of social anxiety disorder (20.5% and 29.2%, respectively) Leyfer et al.,[23] who specifically modified their definition to exclude social avoidance, reported a rate of 7%, suggesting that definition may be important in ASDs. At face value, it may be difficult to reconcile the underlying social deficits inherent in ASDs with social phobia. However, many individuals with ASD are not aloof and have an interest in other people. The definition of social phobia in CAPA requires the presence of anxiety intrusive into at least two activities that is at least sometimes uncontrollable and not merely avoidance of social situations. Future research should explore whether interest in other people and insight into social deficits are among the factors predisposing to the development of social phobia. Our rate of obsessive-compulsive disorder (8.2%) is lower than those of Leyfer et al.[23] (37.2%) and Green et al.[19] (25%), and this may also reflect definitional differences because our interviewers were instructed to use the CAPA definitions, which require a purposeful quality to obsessional thoughts and compulsions.

Rates of major depression and dysthymic disorder (1.4%) were not increased over those reported in the Great Smoky Mountains Study (0.9%–4.6%[4]), although other studies suggest higher rates.[19,21,23] Brereton et al.[18] found that depressive symptoms increased with age, and our population may not have entered the major risk period for affective disorders.

There are two alternative approaches to psychiatric diagnosis. The hierarchical approach, in which symptoms that would otherwise meet criteria for an additional disorder are conceptualized as part of the primary disorder, has the advantage of parsimony. The alternative, used in the present analyses, identifies all of the symptom constellations meeting diagnostic criteria. This approach allows examination of the causes of comorbidity and the identification of symptom constellations that may improve with targeted intervention. Until exclusionary rules are based on evidence demonstrating that additional symptom constellations are best conceptualized as a clinical variant of the underlying disorder, we advocate for research purposes the identification of multiple disorders.

The absence of associations with putative risk factor is striking. One explanation is that the presence of an ASD "trumps" other risk factors. This would be supported by the intellectual disability literature in which, for example, the male preponderance for ADHD is attenuated in children with lower ability.[44] The finding that autism severity was not itself a predictor does not refute this hypothesis because all of the subjects included had sufficient autism symptoms to warrant an ASD diagnosis. Although it is possible that some risk factors operate more specifically and are obscured by diagnostic "lumping," this seems improbable given that previous studies using broad diagnostic categories have been able to detect robust risk factors. Although IQ is one of the most consistent risk factors for psychiatric disorder in the non-ASD child population, our failure to find a relationship is consistent with the report of Brereton et al.,[18] who failed to find an association using the Developmental Behavior Checklist.[45] Replications, longitudinal data, and more focused specification of risk factors are required to explore this more fully.

Strengths of the present study include the use of a carefully assessed, population-derived sample of children with ASD, increasing the confidence that the rates of disorder reported here are derived from the broader ASD population. The inclusion of other variables allowed us to look for putative risk factors for psychiatric disorder. The use of weights allowed us to estimate prevalence rates for the population of children with ASD and SCQ scores >15 of this age. Although one of the largest studies to date, it is nevertheless limited by the moderate overall sample size. In particular, the small number of girls provides little power to examine sex differences in prevalence, comorbidity, and risk factors. The male preponderance for ASDs in the present study is consistent with the literature but highlights that future studies may need to oversample girls. Only parent informants were used, and this is likely to have reduced the symptoms that would be identified among higher functioning children if self-report had been included. Furthermore, diagnoses were not validated by direct observation or teacher data in this report. Although the current approach allows direct comparison with other populations using CAPA, it leaves unanswered the question of how well parent information agrees with that of other informants and clinical observation in this patient group. A number of potentially important comorbid psychiatric disorders, including bipolar, psychotic, and sleep disorders, were not assessed. The narrow age range may limit generalizability of the findings and prevent the exploration of developmental changes, although this would also require larger samples.

There is a lack of consensus as to whether and how symptom definitions should be varied to take account of specific characteristics of people with ASDs. A wider debate has received most attention from those researching severe intellectual disability in which the lack of verbal skills may inhibit direct mental state examination and some symptoms may require intact intellectual function to be experienced.[46] In this study, we applied no additional rules to the detailed definitions provided in the CAPA glossary, whereas the development of the Autism Comorbidity Interview-Parent and Lifetime Version has varied the Schedule of Affective Disorders and Schizophrenia for School-Age Children definitions to account for characteristics of people with ASDs. Previous experience with altering diagnostic criteria for specific groups, such as depression in children or altered diagnostic criteria for people with significant intellectual disability, has usually led to uncertainty about the classification validity.[47,48] A head-to-head comparison of instruments would be a useful next step in developing clinical and research assessment tools for comorbid psychiatric disorders.

These systematic studies challenge the frequently held clinical view that structured clinical assessments are inappropriate or impossible[23] and demonstrate that their completion identifies much higher rates of psychiatric comorbidity than are otherwise identified.[49] Our findings suggest that diagnosis of an ASD should be routinely followed by systematic assessment for other psychiatric disorders.

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