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Comorbid Psychiatric Disorders in Children with Autism: Interview Development and Rates of Disorders

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Abstract The Kiddie Schedule for Affective Disorders and Schizophrenia was modified for use in children and adolescents with autism by developing additional screening questions and coding options that reflect the presentation of psychiatric disorders in autism spectrum disorders. The modified instrument, the Autism Comorbidity Interview-Present and Lifetime Version (ACI-PL), was piloted and frequently diagnosed disorders, depression, ADHD, and OCD, were tested for reliability and validity. The ACI-PL provides reliable DSM diagnoses that are valid based on clinical psychiatric diagnosis and treatment history. The sample demonstrated a high prevalence of specific phobia, obsessive compulsive disorder, and ADHD. The rates of psychiatric disorder in autism are high and are associated with functional impairment.

Keywords Psychopathology · Autism · Psychiatric interview · Comorbidity

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Children with autism frequently have problematic emotional reactions and behaviors along with the features that define autism. Disturbances of emotion, attention, activity, and thought, and associated behavioral problems occur in children with autism of all ages (Lainhart, 1999). It is not yet known how often these additional difficulties are due to comorbid psychiatric disorders.

Accurate, reliable diagnosis of comorbid psychiatric disorders in children with autism is of major importance. Comorbid disorders may cause significant clinical impairment and additional burden of illness on children with autism and their families. When problematic behaviors are recognized as manifestations of a comorbid psychiatric disorder, rather than just isolated behaviors, more specific treatment is possible. Clinical experience suggests that specific treatment is more effective, i.e., associated with greater improvement in functioning, than nonspecific treatment. Diagnosis of a comorbid disorder may qualify the treatment of a child with autism for coverage by medical insurance. From a public health perspective, rates of comorbid psychiatric disorders in autism are an important consideration in planning for provision of services. Finally, from a research perspective, diagnosis may have several benefits. These include the refinement of

psychopharmacology research in autism and help in sorting out etiologic and neurobiological heterogeneity. The search for genes that increase the risk for autism may be aided by accurately sub-grouping children with autism according to comorbidity. Also, understanding comorbid disorders in autism may help elucidate brain mechanisms involved in the disorder. Post-mortem and neuroimaging studies of autism have yet to grapple with how comorbidity may affect findings.

There are good reasons why rates of psychiatric comorbidity in autism are not known, why comorbidity is often unrecognized clinically, and why knowledge about comorbidity is not yet helpful in autism neurobiological research. Comorbid psychiatric disorders in children and adults with autism can be difficult to diagnose. Communication with the patient is universally impaired to some degree in autism (Lord & Paul, 1997). Up to one-half of individuals with autism are functionally nonverbal. Individuals with autism who have adequate language have a variety of other types of communication impairment. In addition to communication problems, children and adults with autism have impairments in ''theory of mind'', complex information processing, central coherence, and executive functioning (Baron-Cohen, 1991a, 1991b; Baron-Cohen, Leslie, & Frith, 1985; Frith, 1996; McEvoy, Rogers, & Pennington, 1993; Minshew, Goldstein, & Siegel, 1997; Ozonoff, Strayer, McMahon, & Filloux, 1994; Pennington & Ozonoff, 1996; Tager-Flusberg, 1992; Tager-Flusberg & Sullivan, 1994). These cognitive problems make it difficult for individuals with autism to describe their mental states, mental experiences, and even daily life experiences. Thus, it can be challenging to determine if a child's difficulties are due to effects of the core features of autism, life experiences, or a comorbid psychiatric disorder superimposed on the autism and the life experiences of the child.

Instruments developed for the general population have been used to measure behavioral problems and aspects of comorbidity in individuals with developmental disorders including autism. These instruments include the Child Behavior Checklist (Achenbach, Howell, Quay, & Conners, 1991; Dekker, Koot, van der Ende, & Verhulst, 2002a; Dykens, 2000; Masi, Brovedani, Mucci, & Favilla, 2002; von Gontard et al., 2002); The Conners' Rating Scale (Conners, 1973; Fee, Matson, & Benavidez, 1994), the Diagnostic Interview Schedule for Children-IV (Dekker et al., 2002a; National Institutes of Mental Health, 1992; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000); the K-SADS (Masi, Favilla, & Mucci, 2000; Masi, Mucci, Favilla, & Poli, 1999), and the SADS-L (Meadows et al., 1991). To our knowledge, these instruments have not yet been tested for reliability and validity in autism and most other developmental disorders.

Other instruments have been specifically designed for use in individuals with developmental disorders and have contributed to the study of comorbidity in autism. They are the Aberrant Behavior Checklist (Aman, Singh, Stewart, & Field, 1985; McCracken et al., 2002; Rojahn, Aman, Matson, & Mayville, 2003), the Developmental Behavior Checklist (Clarke, Tonge, Einfeld, & Mackinnon, 2003; Dekker, Nunn, Einfeld, Tonge, & Koot, 2002b; Einfeld, Tonge, Turner, Parmenter, & Smith, 1999; Einfeld & Tonge, 1995, 1996a, b, 1999; Einfeld, Tonge, & Rees, 2001; Tonge & Einfeld, 2000), the Behavior Problems Inventory (Rojahn, Matson, Lott, Esbensen, & Smalls, 2001), the Anxiety, Depression, and Mood Scale (Esbensen, Rojahn, Aman, & Ruedrich, 2003) and others (Reiss, 1988; Tsiouris, 2001). Instruments for adults with intellectual disabilities include the Psychiatric Assessment Schedule for Adults with Developmental Disabilities (Moss, Prosser, & Goldberg, 1996; Murphy, Jones, & Owen, 1999), the Psychopathology Instrument for Mentally Retarded Adults (Senatore, Matson, & Kazdin, 1985), and the Diagnostic Assessment for the Severely Handicapped (Matson, Coe, Gardner, & Sovner, 1991a; Matson, Gardner, Coe, & Sovner, 1991b; Sevin et al., 1995). Several of these instruments were designed for the purpose of screening for psychopathology. The reliability and validity of these instruments have been tested in samples which have variably included some individuals with autism. However, validity of an instrument is established for a particular purpose in a particular population (Morgan, Gliner, & Harmon, 2001). To our knowledge, the validity and reliability of these instruments for diagnosing comorbid psychiatric disorders in individuals with autism have not been specifically tested. Possibly for this reason, some studies using these instruments have excluded individuals with autism (Deb, Thomas, & Bright, 2001).

Several studies have, nevertheless, examined psychiatric comorbidity in autism spectrum disorders. The studies have used a variety of criteria, reasons for referral, and age ranges. Some studies were only able to include subjects who had been referred for psychiatric treatment. Several of the studies used questionnaires that only inquire about current symptoms. None of the studies utilized an instrument that was modified or designed specifically for the population of individuals with autism. Thus is it not surprising that the rates of comorbid disorders in autism have varied significantly. Overall, high rates of several psychiatric disorders have been reported in individuals with autism.

Establishing the validity of instruments used to assess for comorbidity in developmentally disabled individuals, including those with autism, has been hampered by the lack of a ''gold standard'' diagnostic tool (McBrien, 2003). There is no valid, reliable instrument, i.e., no gold standard, for diagnosing present and lifetime psychopathology in

children with autism or other developmental disorders. The diagnoses of autism itself and establishing the validity of new instruments to screen for autism were problems until the development of the Autism Diagnostic Interview (ADI; Lord, Rutter, & Le Couteur, 1994).

The purpose of the collaborative work described in this paper is the development of an accurate, reliable instrument, i.e., a diagnostic gold standard tool, for diagnosing comorbid psychopathology in children with autism. We describe development and piloting of the interview and initial testing of its reliability and validity. We use the instrument to measure lifetime rates of comorbid psychiatric disorders in autism and examine patterns of comorbidity.

Methods

Sample

Our modification of the Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS; (Chambers et al., 1985; Kaufman et al., 1997; Ambrosini, 2000) for autism, which we call the Autism Comorbidity Interview-Present and Lifetime version (ACI-PL), was developed and piloted collaboratively in two samples by the investigators (SEF and HTF in Boston; JEL in Salt Lake City). The children in the Boston sample were participants in a longitudinal study of language and social functioning. All of the children in the Boston sample had some spoken language. They were recruited from community sources including schools and parent support groups. The children in the Salt Lake City sample were participants in a neuroimaging study of males with autism who had performance IQs greater than 65. Subjects in the Salt Lake City sample were recruited from community sources by advertisements in autism society newsletters and announcements at parent conferences. All children with autism, who met criteria for participation in the Boston and Salt Lake City studies, were consecutively recruited, unselected for comorbid psychiatric disorders, and assessed with the ACI-PL. Information was not available about children from families that did not volunteer to participate in the studies. The combined sample consisted of 109 children (65 from Boston, 45 from Salt Lake City), ranging in age from 5 to 17 years, all of whom met Autism Diagnostic Interview-Revised (ADI-R; Lord et al., 1994), Autism Diagnostic Observation Schedule (Lord et al., 2000), and DSM-IV-TR (American Psychiatric Association, 2000) criteria for autism. Known medical causes of autism were excluded by history, physical examination, karyotype, and Fragile X gene testing. The diagnosis of idiopathic autism was confirmed by an expert clinician.

Instrument Development

We made several modifications to the KSADS to make it more appropriate for use in autism.

Introductory Section

We added an initial section with questions to establish the nature of the child's emotions and behaviors at his/her best baseline. This information helps the interviewer understand if and how the child's emotions and behaviors, reported in the section on specific psychiatric disorders, are different qualitatively and quantitatively, from the child's best baseline.

Specific Psychiatric Disorders

The ACI-PL covers all psychiatric disorders inquired about in the adult and child versions of the SADS (Ambrosini, 2000; Chambers et al., 1985; Mannuzza, Fyer, Klien, & Endicott, 1986), and some additional disorders. Each disorder section begins with an introduction that describes how the disorder tends to be manifested in autism. The descriptions are based on reports in the literature and clinical experience. This is followed by the screening questions similar to those used in the K-SADS. Additional screening questions have been added in each disorder section. These screening questions inquire about other observable features that are common presenting concerns expressed by caregivers when individuals with autism have particular psychiatric disorders. For example, in DSM-IV, the most essential features of major depression are change of mood and loss of interest. However, in individuals with autism, the most common presenting symptoms of depression may be significantly increased agitation, self-injury, and temper outbursts (Sovner & Hurley, 1982a, 1982b; Lainhart & Folstein, 1994).

If screening questions are positive, more detailed questions are asked about specific signs and symptoms. Before asking about whether the child has/had a particular symptom, however, questions are provided for the interviewers to inquire about the applicability of the symptom to the child with autism. For example, before asking about the presence of feelings of guilt and worthlessness, which are DSM symptoms of depression, the interviewer asks if the child with autism has ever, in his/her life, indicated an understanding of guilt or expressed guilt. It is possible that a child with autism may not express feelings of guilt and worthlessness during a depressive episode because these are not in the child's repertoire. Coding choices incorporate this situation. The coding also defines and operationalizes signs and symptoms of disorders. For all signs and symptoms, mandatory probes are given along with additional questions that can be asked if further information is needed for coding.

Modifications of Symptom Criteria

For disorders that are episodic or tend to emerge during later childhood, the coding specifies that a particular behavior or emotional reaction, to be considered as a sign or symptom of a psychiatric disorder, must be different, qualitatively or quantitatively, from the behavior or emotion at the child's baseline. For example, the coding for separation anxiety disorder specifies that it must be clear that the child's anxiety is due to attachment-related aspects of separation from the parent, rather than due to change in routine or other reasons. For social phobia, the coding specifies that the child's fear and/or avoidance must be related to social, rather than non-social, aspects of the situation. Avoidance must not be due to lack of interest in the situation. Because individuals with autism may have unusual attention patterns, the coding for ADHD distinguishes between attention to special interests and attention in general.

Specification of Impairment due to Comorbid Psychiatric Disorder

The ACI-PL distinguishes impairment due to comorbid psychiatric disorders from impairment due to core features of autism. Episodic comorbid syndromes, such as major depression, are considered impairing if they are associated with significant impairment that is in addition to the child's baseline level of impairment. Non-episodic comorbid syndromes, such as attention deficit and hyperactivity, are considered impairing if they are associated with impairment that is above and beyond impairment associated with the core social, communication, and repetitive features of autism.

Modification of Diagnostic Criteria

The diagnostic criteria of DSM-IV-TR are used for all disorders in the ACI-PL with the exception that no diagnosis is excluded because the child has a pervasive developmental disorder. DSM-IV does not allow a diagnosis of separation anxiety disorder, generalized anxiety disorder, social phobia, or ADHD in individuals with autism-spectrum disorders (American Psychiatric Association, 2000). However, these disorders are not universally present in autism. The ACI-PL allows their diagnosis. This is important because specific treatment is available.

Subsyndromal Diagnostic Criteria

DSM diagnostic criteria may identify the "tip of the iceberg" of psychiatric disorders in developmentally disabled individuals. Some signs and symptoms that contribute to a DSM diagnosis cannot be evaluated in children with autism because of limitations in the child's language or other developmental and cognitive impairments. Because some DSM symptoms are not applicable to persons with autism, and DSM criteria "may not carve nature at its joints", we developed criteria for subsyndromal disorders (Kendler & Gardner, 1998; Sovner, 1986). Subsyndromal disorders are diagnosed when a child has a significantly impairing psychiatric syndrome (as defined above) that falls just short of meeting full DSM criteria. The subsyndromal category allows systematic study of why impairing comorbid disorders in individuals with autism do not meet DSM criteria. The subsyndromal category may also identify disorders in need of treatment that would not be identified with the use of DSM criteria alone.

Instrument Revision

The pilot version of the ACI-PL was administered to parents by clinicians with extensive experience with psychiatric disorders in children with autism and other developmental disabilities. Each case was discussed in detail between sites by conference calls, and changes were made in formatting, coding, and item wording in an iterative fashion. The current version performed well for most of the diagnoses in terms of the clarity of the questions for the parents, the questions' salience, and the mutual exclusiveness of coding choices. Three sections, including manic disorders, psychosis, and panic disorder, were rarely endorsed and could not be meaningfully piloted in this sample, which was not enriched for subjects with a previously diagnosed psychiatric disorder. Similar to the KSADS, psychiatric disorders were diagnosed in children taking psychotropic medications based on the child's symptoms before the medication was started or during periods when the medication was not taken. In addition, the ACI is designed to avoid the interviewer being biased by past diagnoses and treatments the child may have received. Symptoms, impairment, and other DSM criteria are inquired about and a disorder is coded by the interviewer as being present or absent *before* the interviewer inquires about past diagnoses of and treatment for a disorder.

Results

Subject Characteristics

The age, sex, and IQ of the children in the study are shown in Table 1.

Reliability

Inter-rater reliability was established for lifetime diagnoses of major depressive disorder, obsessive compulsive

Table 1 Characteristics of the children with autism

	Subjects with Autism (n = 109)
Age (years; months)	
Mean (SD); [range]	9.2 (2.7); [5.1–17]
Males (%)	94.29%
Females (%)	5.71%
Full scale IQ (n = 96)	
Mean (SD); [range]	82.55 (23.42); [42–141]
FSIQ > 70	67.71%
Verbal IQ (n = 94)	
Mean (SD); [range]	81.51 (24.45); [46–142]
VIQ > 70	57.45%
Nonverbal IQ (n = 93)	
Mean (SD); [range]	88.37 (22.22); [43–153]
NVIQ > 70	78.49%

disorder and ADHD by using audiotapes exchanged between the Boston and Salt Lake City sites. Inter-rater agreement for major depression was 90% and Cohen's kappa = .8 (P = .01). The inter-rater agreement for OCD was 90% and kappa = .7 (P = .037). For ADHD, the inter-rater agreement was 88% and kappa = .7 (P = .025). Long term test–retest reliability was calculated over an average duration of 5.2 years (range 2–6 years). Cohen's kappa = .61 for a lifetime diagnosis of major depression (P = .047) and .75 for a lifetime diagnosis of OCD (P = .028). All cases diagnosed with lifetime major depression and OCD at time 1 were diagnosed at time 2. In addition, several new cases of major depression and OCD were diagnosed at time 2. In all of these new cases, the onset of the disorder was after time 1. When disorders with onset after time 1 were excluded, kappa = 1.0 for lifetime major depression (P = .003) and lifetime OCD (P = .005). The concordance between time 1 and 2 for no ADHD was 100%. No test–retest data were available for cases diagnosed with ADHD

Validity

Two validity procedures were used. Criterion validity for the ACI diagnoses of depression and ADHD was established based on whether the child had received treatment for those disorders. ACI comorbid diagnoses were made blind to whether the child had ever received clinical treatment for comorbid symptoms or disorders. Major depression was validated in the Salt Lake City and Boston samples and ADHD was validated in the Boston sample. For major depression, the sensitivity was 100% and specificity was 93.7% in the Salt Lake City (SLC) sample and 100% and 83%, respectively, in the Boston sample. The ACI correctly diagnosed all cases of depression that had been diagnosed and treated by independent clinical evaluation by expert clinicians. It also picked up some cases

that had not been independently diagnosed. For ADHD, the sensitivity was 100% and specificity was 93%.

Concurrent evidence for the ACI diagnosis of OCD was examined by correlating the impairment scores for compulsion with similar items from the ADI-R (C. Lord et al., 1994). The ADI-R and ACI were carried out at different times by different interviewers who were blind to the results of each other's interview. The time between the ADI-R interview and the ACI interview varied between one month and one year. The combined score for impairment caused by compulsions and the time spent on compulsions were compared with a ''compulsion'' score from the ADI-R that was derived from a principal components analysis (Tadevosyan-Leyfer et al., 2003). The ADI-R compulsions cluster of variables included the following ADI items: stereotyped utterances, unusual preoccupations, compulsions and rituals, resistance to trivial changes in the environment, and unusual attachment to objects. The sum of the score for impairment caused by compulsions and the time spent on compulsions correlated well with the ''compulsion'' cluster score from the ADI-R (ρ = 0.57, P < .001).

Prevalence of Psychiatric Disorders in Children with Autism

The frequency of the DSM-IV diagnoses made using the ACI with the primary caregivers is presented in Table 2. In addition to the DSM-IV diagnoses, Table 2 also shows the rate of subsyndromal diagnoses, i.e., significantly impairing clusters of symptoms that fell just short of meeting DSM-IV criteria for the disorder. The numbers of subjects for each diagnostic category vary because some informants did not complete the later sections of the interview.

Specific Phobias

The most common DSM-IV lifetime diagnosis in the autism sample was specific phobia. Forty-four percent of the children with autism met diagnostic criteria. The majority of children with autism had phobias of more than one object or situation. Fear of needles and/or shots and crowds were the most common (32%). Specific types of phobias that are common in the general population of children, such as fears of flying, stores, standing in lines, bridges, and tunnels, occurred at very low rates in the autism children. Over 10% of the children with autism had a phobia of loud noises, which is not common in typically developing children.

Obsessive Compulsive Disorder

The second most frequent DSM-IV disorder was OCD, diagnosed in 37% of the children with autism. The most

Table 2 Lifetime prevalence of psychiatric disorders in children with autism

	Criteria Met			
	DSM-IV		Subsyndromal	
	N	(%)	N	(%)
Mood disorders				
Depressive disorder (n = 109)				
Major depressive episode (≥one episode)	11	(10.1)	15	(13.8)
Depression, NOS	3	(2.8)	NA[b]	
Hypomanic/manic disorders (n = 106)				
Manic episode	2	(1.9)		
Cyclothymia	1	(.94)		
Bipolar 1 disorder	2	(1.9)	1	(0.9)
Bipolar 2 disorder	1	(0.9)		
Hypomanic episode	1	(0.9)		
Mixed episode	2	(1.9)		
Schizophrenia, other	0	0		
Psychotic disorders				
Anxiety disorders				
Panic disorder	0	0		
Separation Anxiety (n = 101)[a]	12	(11.9)	7	(6.9)
Social Phobia (n = 94)[a]	7	(7.5)	3	(3.2)
Specific Phobia (n = 97)	43	(44.3)	NA[b]	
Generalized anxiety (n = 41)[a]	1	(2.4)	1	(2.4)
Obsessive compulsive disorder (n = 94)	35	(37.2)	5	(5.7)
Disruptive disorders				
ADHD (n = 85)[a]	26	(30.6)	21	(24.7)
ADHD subtypes				
Inattentive	17	(20.0)		
Hyperactive	3	(0.35)		
Combined	6 (0.70)			
Oppositional defiant disorder (n = 86)	6	(7.0)	4	(4.6)
Adjustment disorders				
Adjustment disorder, depressed mood	1	(0.9)	NA[b]	

[a] PDD exclusion suspended

[b] There was no subsyndromal diagnosis for this disorder

common type of compulsion was a ritual involving other individuals. Nearly half of the children diagnosed with OCD had compulsions that involved others having to do things a certain way. Examples included the parents *having* to perform certain daily routines and greeting and separation rituals, or having to act or respond in a certain way. Another frequent compulsive behavior was the ''need to tell/ask'', which mostly involved repeatedly *having* to ask the same question in extensive question-asking rituals or *having* to say the same statement over and over. Interestingly, the diagnosis of autism involves deficits in social reciprocity and the two most frequent compulsions in the autism group involve dysfunctional interaction with other people in a compulsive manner.

ADHD

The third most common diagnosis was ADHD, diagnosed in 31% of the children with autism. The rate is increased to nearly 55% when subsyndromal cases are included. Sixty-five percent of the children diagnosed with ADHD had the

inattentive sub-type. In children without developmental disorders, the hyperactive type is most common.

Major Depression

Ten percent of the children with autism had had at least one episode of major depression meeting DSM-IV criteria. When subsyndromal cases are included, the rate of major depression increased to nearly 24%.

Other Disorders

None of the children with autism met criteria for schizophrenia or related disorders or for panic disorder. Less than two percent of the children had had a manic episode and met criteria for bipolar I disorder.

Patterns of Comorbidity

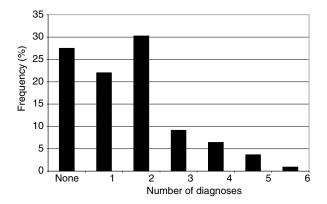Figure 1 shows the frequencies of multiple comorbid psychiatric diagnoses in the children with autism. The

Fig. 1 Frequency of the number of comorbid lifetime psychiatric diagnoses per child with autism. Only DSM-IV diagnoses are included

median number of diagnoses per child was 3, and the mode was 3 (30.28%). The frequency of multiple comorbid diagnosis we report is likely to be an underestimate. Parents were less likely to complete the later sections of the interview when multiple types of psychopathology were present in their child because it typically took longer to complete the interview.

We also examined concordance between a diagnosis of OCD and major depression in the children with autism because major depression commonly occurs in typically developing adults with OCD (Nestadt et al., 2001). Table 3 shows that 5.3% of the children with autism met DSM-IV criteria for both major depression and OCD.

Discussion

We present a new standardized interview, the Autism Comorbidity Interview (ACI), modeled after the K-SADS, designed to systematically diagnose comorbid psychiatric disorders in individuals with autism. The interview uses a semi-structured, investigator-based approach, a parent as the informant, and a clinically skilled interviewer. Given the complexity of comorbid psychiatric disorders in the context of autism and the current lack of biological markers of psychiatric disorders, we believe that the approach we have used is an essential starting point for accurate diagnosis. We used the instrument to measure rates of psychiatric comorbidity in a large pilot sample of children with

Table 3 Comorbidity of lifetime obsessive compulsive disorder (OCD) and major depressive disorder (MDD) in children with autism

	Autism (N = 94)	
Both OCD and MDD	5	5.3
OCD only	30	31.9
MDD only	6	6.4
Neither OCD or MDD	53	56.4

autism who were not selected for clinical referral. Our preliminary testing of the psychometric properties of the major depression, ADHD, and OCD sections of the instrument in individuals with autism showed good reliability and validity.

Psychiatric Comorbidity in Children with Autism

Our study confirms the frequent co-occurrence of autism with other psychiatric disorders. Seventy-two percent of the children in our study had at least one DSM-IV Axis I psychiatric disorder in addition to autism. Our finding in relatively high-functioning children with autism is consistent with the high rate of comorbidity estimated in a large epidemiologic study of 6–18-year-old intellectually disabled (IQ ≤ 80) children (Dekker & Koot, 2003). Using lay interviewers, this study found that 41% of intellectually disabled children who had a positive screen for pervasive developmental disorder met DISC-IV criteria for an impairing comorbid psychiatric disorder. Our study also shows that children with autism commonly meet criteria for not just one, but several comorbid psychiatric disorders. These findings emphasize the need for additional research in this area and additional clinical services for children with autism.

Why rates of comorbid disorders are so high in children with autism is not known. It is unlikely that the co-occurrence is solely due to chance. Accurate diagnosis of comorbid psychiatric disorders in children with autism, using the ACI, should allow the systematic study of the relationship between core features of autism, associated potential genetic, cognitive, and environmental risk variables, and psychiatric comorbidity in autism. Accurate diagnosis also allows neurobiological study of potential underlying developmental brain mechanisms involved in psychiatric comorbidity in autism.

Mood Disorders in Children with Autism

Major Depressive Disorder

Nearly a quarter of the children with autism in this study met lifetime diagnostic criteria for impairing major depression. Ten percent of children met full DSM-IV criteria for major depressive disorder and an additional 14% fell just short of meeting DSM-IV criteria. These rates are quite striking especially given the mean age of 9 years of the children in our study and the fact that none of the children had been pre-selected because of known psychiatric comorbidity. Other investigators have found increased rates of depression in individuals with autism-spectrum disorders (Abramson et al., 1992; Chung, Luk, & Lee,

1990; Ghaziuddin, Weidmer-Mikhail, & Ghaziuddin, 1998; Tantam, 1991). Despite methodological differences, the findings of our and other investigators' studies converge to show increased rates of major depression in children with autism.

Bipolar Disorder

Consistent with our clinical experience, we found low rates of DSM-IV manic episode and bipolar disorder. Reported rates of bipolar disorder in published studies of autism have varied (Ghaziuddin, Tsai, & Ghaziuddin, 1992; Tantam, 1991; Wozniak et al., 1997). Some investigators have found much higher rates than we did (Wozniak et al., 1997). However, the later study was carried out with children referred to a psychopharmacological clinic. Mania, hypomania, and bipolar disorder can be particularly difficult to diagnosis in the context of autism. At baseline, some children with autism frequently laugh in situations that are not funny to most people. In addition, the emotions of some children with autism tend to be quite reactive, poorly modulated, and fluctuate minute to minute with what is going on in their environment. These tendencies of emotion have not yet been systematically studied and their neurobiological basis in autism is unknown.

Anxiety Disorders in Children with Autism

Various types of anxiety are believed to be so common in autism that symptoms of anxiety disorders have been thought by some clinicians and investigators to be aspects of autism, rather than comorbid features. Impairing anxiety is, however, not a defining feature of autism or a universal phenomenon of autism. Reported rates of at least one anxiety disorders in individuals with autism have varied from 17% to 84% (Ando & Yoshimura, 1979; Muris, Steerneman, Merckelbach, Holdrinet, & Meesters, 1998; Rumsey, Rapoport, & Sceery, 1985). The variation is likely due to use of different instruments, the use of lay interviewers in some studies, and differences in characteristics of the samples tested.

Specific Phobic Disorder

We found Specific Phobia to be the most common DSM-IV disorder in children with autism. It was found in 44% of the children. Some studies have reported even higher rates (Muris et al., 1998). Over 10% of the children with autism in our study had a phobia of loud noises, which is not common in typically developing children. Further investigation is needed to determine whether abnormal sensitivity to sound found in some children with autism, and perhaps

abnormal cortical processing of loud sounds, contribute to the increased rate of phobia to loud noises in autism.

Separation Anxiety Disorder

Twelve percent of the children with autism in our sample met DSM-IV symptom criteria for separation anxiety (PDD exclusion suspended). This rate is similar to the rate found in some past studies of individuals with autism (Rumsey et al., 1985), but lower than findings of other studies (Muris et al., 1998), likely for the reasons mentioned above. Our findings show that DSM-IV separation anxiety disorder occurs in a small minority of unselected children with autism. Our findings do not support the need for DSM-IV criteria to exclude a diagnosis of separation anxiety disorder in children and adults with autism-spectrum disorders.

Social Phobia

Even though children with autism commonly are bothered by non-social aspects of social situations, such as noise, they have low rates of impairing anxiety to the social aspects of situations. The prevalence rate of social phobia in our sample of 7.4% is lower than that found in other samples (Muris et al., 1998), perhaps because the ACI specifically distinguishes between fear and avoidance of non-social versus social aspects of social situations.

Generalized Anxiety Disorder

We found that DSM-IV criteria for generalized anxiety disorder (GAD) usually did not capture the essential aspects of anxiety found in children with autism. Aspects not captured included the manifestations of anxiety, the contexts in which anxiety occurred, and the environmental precipitants of anxiety. Our observations must be considered tentative because the GAD section of the interview was completed on only 41 of the 109 children. One of the 41 children with autism (2%), whose parents completed the GAD section, met DSM-IV criteria for GAD. While some of the children with autism were anxious about many things, the anxiety did not usually vary over time, i.e., it appeared more trait- rather than state-related. Anxiety in the children with autism, over and above this chronic anxiety trait, was usually focused on one, rather than multiple things or it was related to transitions or changes in the environment. Our findings, albeit preliminary, do not support the DSM-IV exclusion of a diagnosis of generalized anxiety disorder in individuals with autism. Our findings do suggest that anxiety trait is common in autism. The findings also suggest that

impairing anxiety syndromes, other than GAD, may occur alone or be superimposed on anxiety trait in individuals with autism.

Obsessive Compulsive Disorder

In our sample, 37% of the children with autism met DSM-IV criteria for OCD. We adapted DSM-IV subjective criteria for developmentally disabled children by making the diagnosis of OCD based on signs and symptoms that could be observed by others. Only a small minority of the children would have met OCD criteria had we not allowed subjective mental experiences to be inferred from observations made by parents. The rate of OCD in individuals with autism reported by other investigators has varied from 1.5% to 81% (Ghaziuddin et al., 1992; Le Couteur et al., 1989; Muris et al., 1998; Rumsey et al., 1985). The wide variation is likely due to the different assessment methods and criteria used, including criteria for impairment. Our findings about the association between autism and OCD agree with the findings of an epidemiologic study of intellectually disabled children. Using the DISC-IV and lay interviewers, intellectually disabled children who had a positive screen for PDD were found to be 14 times more likely to meet DISC-IV criteria for OCD (Dekker & Koot, 2003).

Disruptive Disorders in Children with Autism

Attention Deficit Hyperactivity Disorder

Fifty-five percent of the children with autism in our sample had a significantly impairing ADHD syndrome. Thirty-one percent of the autism children met DSM-IV criteria for ADHD. An additional 24% fell just short of meeting DSM-IV criteria. Two-thirds of the children who met DSM-IV criteria for ADHD had the inattentive type, and 23% had the combined type.

Children with autism who fell just short of meeting DSM-IV criteria had long attention spans for their preferred activity but impaired attention in other situations. It is well known that some children with autism can attend almost indefinitely to a stimulus that they find interesting, be it functional or nonfunctional. Impaired attention is particularly obvious when children with autism are engaged in school and homework and other cognitively demanding activities. It has not been clear in the past how to diagnose ADHD in persons with autism because of these unusual and idiosyncratic attention-inattention patterns (Dawson & Lewy, 1989).

Our findings show that children with autism, even those who have relatively high IQ's as did the children in our study, frequently suffer from impairing inattention. The rate of ADHD in autism reported by other investigators has varied from 29% to 73%, the variability likely due to the factors mentioned previously (Ghaziuddin & Greden, 1998; Wozniak et al., 1997). The convergent findings of our study and the studies of other investigators suggest that impairing ADHD syndromes are common, but not universal phenomena, in autism.

Oppositional Defiant Disorder

Although children with autism frequently have difficulty with following directions, being cooperative, and doing things on other people's terms, the frequency of DSM-IV-defined oppositional defiant disorder (ODD) was not high in our sample. Only 7% of the children with autism met DSM-IV criteria for ODD. Cognitive and other factors associated with oppositionality in children with autism may be different than the factors reported in children without autism. We found that many children with autism do not even understand the concepts of spitefulness, vindictiveness, and intentionality, including deliberately annoying others and blaming others for one's behavior and mistakes. The relationship between oppositional behaviors in autism and cognitive impairments in autism, such as lack of appreciation of the mental states of others and problems with executive function such as rigid, inflexible thinking and behavior, need further study (Baron-Cohen, 1988, 1989, 1991a, b, 1993; Ozonoff, Pennington, & Rogers, 1991).

Other Disorders in Children with Autism

None of the children were diagnosed with schizophrenia or related psychotic disorder or panic disorder. The ACI may have failed to detect these disorders. More likely, our sample sizes were too small to detect these disorders and, similar to the general population, the prevalence of these disorders is low in children with autism (American Psychiatric Association, 2000; Volkmar & Cohen, 1991).

Limitations

The reliability and validity of the ACI were determined for only three DSM diagnoses and only in relatively high-functioning children with autism. An epidemiological sample was not used. The community sample we used was unbiased in terms of an increased probability of including children with psychiatric comorbidity. Further validity and reliability testing are needed for DSM disorders across the age, IQ, and verbal ability spectrums found in autism and for subsyndromal disorders. Use of the instrument in special populations that are enriched for psychiatric disorder will be needed to establish the psychometrics of the

instrument for disorders that rarely occur in individuals with autism. Validity and reliability testing of the ACI is also needed in children without autism so that rates and characteristics of psychiatric disorders can be compared in children with and without autism. Our preliminary use of the ACI in non-autistic language disordered children and typically developing children is promising.

Our study has several other limitations. The ACI-PL, as currently developed, only collects information about the child from a parent. It does not include information obtained directly from the child or from the child's teacher. Information from multiple sources, parent, child, and teachers, is important in diagnosing psychiatric disorders in non-autistic children. In this study, rates of comorbid psychiatric disorders were measured in a sample composed mostly of high-functioning, verbal males with autism. The parents of over half of the children in the sample did not complete the generalized anxiety disorder section of the interview. A large epidemiologic sample that completes the entire ACI is needed to determine the rates of comorbid psychiatric disorders in children with idiopathic autism in general.

We acknowledge the overlap between some behavioral symptoms of autism and comorbid disorders. We recognize that our decision to count what might be a symptom of autism as a symptom of a comorbid disorder may be controversial. To be considered a symptom of a comorbid disorder, the ACI requires that a symptom be conceptually the same, qualitatively and quantitatively, as described for the comorbid disorder in DSM-IV. The symptom must also be part of the cluster of mental state phenomena that define the comorbid disorder syndrome and the syndrome must be significantly impairing. A symptom in isolation is not considered a disorder.

We must emphasize, that our use of ''comorbid psychiatric disorders'' in this paper refers to empirically defined, clinically distinct syndromes, rather than neurobiologically defined disorders. The co-occurrence of autism with so many other *truly separate* psychiatric disorders, which is the definition of comorbidity, is most unlikely (Caron & Rutter, 1991). Advances in autism genetics, neuroimaging, pathology, and epidemiology will help determine why children with autism have features of so many other psychiatric syndromes. It is our hope that the instrument we have developed and our preliminary findings will encourage and facilitate further investigations into the nature of psychiatric comorbidity in autism.

Conclusion

We describe the development of a semi-structured psychiatric interview that is suitable for use in children with autism. In a group of children and adolescents who were unselected for psychiatric disorder, high rates of lifetime comorbid psychiatric disorders were found. Our findings underscore that children with autism may have impairing behaviors and emotions for a variety of reasons. One of the factors that should be included in the ''differential diagnosis'' of behavioral or emotional problems in a child with autism is the presence of another psychiatric disorder (or a medical disorder) superimposed on the autism. A qualitative or quantitative change from baseline in existing emotions and behaviors and new emotions and behaviors in a child with autism may herald the emergence of an additional disorder in the child. There is no specific treatment for autism, but there are treatments for many of the comorbid psychiatric disorders that occur in children with autism.

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