



HHS Public Access

Author manuscript

Clin Child Psychol Psychiatry. Author manuscript; available in PMC 2015 May 10.

Published in final edited form as:

Clin Child Psychol Psychiatry. 2008 January ; 13(1): 81–94.

Use of the ADOS and ADI-R in Children with Psychosis: Importance of Clinical Judgment

JUDITH A. REAVEN, SUSAN L. HEPBURN, and RANDAL G. ROSS

University of Colorado at Denver and Health Sciences Center, USA

Abstract

The Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview – Revised (ADI-R) are considered to be the ‘gold standard’ in diagnostic evaluations for autism. Developed as research tools and now gaining wide clinical use, the ADOS/ADI-R assessment package has been demonstrated to differentiate children with autism from those with other developmental disabilities; however, little work concerning the reliability and validity of the tools in children with a known history of psychosis has been undertaken. We report on the administration of the ADOS, ADI-R and clinical judgment in three cases of Childhood-Onset Schizophrenia. All 3 children met both ADOS and ADI-R criteria for an autism spectrum diagnosis, even though none of them received a clinical diagnosis of autism from either a research child psychiatrist or an experienced clinically trained, research psychologist with expertise in autism. Issues concerning overlap of symptom presentation and implications for research and clinical use of these assessment tools are discussed.

Keywords

assessment; autism; children; psychosis

The autism diagnostic observation schedule (ADOS; Lord et al., 1999) and the Autism Diagnostic Interview – Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994) are considered to be the ‘gold standard’ in diagnostic evaluations for autism, particularly when combined with clinical judgment (de Bildt et al., 2004). Developed as research tools and now gaining wide clinical use, the ADOS/ADI-R assessment package has been demonstrated to differentiate children with autism from those with other developmental disabilities (LeCouteur et al., 1989; Lord et al., 1994). Sensitivities of the tool have been reported to range from 86 to 100 per cent and specificity with other developmental disabilities is 73 to

Copyright © 2008 SAGE Publications

contact: Judith A. Reaven, JFK Partners, Department of Psychiatry, University of Colorado at Denver and Health Sciences Center, Education 2 South (L28) - C-234, 13121 E. 17th Ave., 5th Floor, Aurora, CO 80045, USA. [judy.reaven@uchsc.edu].

JUDITH A. REAVEN PHD is an Assistant Professor in the Departments of Psychiatry and Pediatrics, University of Colorado at Denver and Health Sciences Center whose research focuses on psychiatric comorbidities with autism spectrum disorders.

SUSAN L. HEPBURN PHD is an Assistant Professor in the Department of Psychiatry, University of Colorado at Denver and Health Sciences Center whose research focuses on the development of autism symptoms across childhood.

RANDAL G. ROSS MD is a Professor in the Departments of Psychiatry and Pediatrics, University of Colorado at Denver and Health Sciences Center whose research focuses on the developmental pathways to major mental illnesses.

100 per cent. Psychometric properties of the tool are even stronger when comparing children with autism to those with a history of typical development (Lord et al., 1999).

Although agreement between the two tools is usually very strong, there are a number of child-specific variables that can influence the reliability of the instruments. The algorithm of the ADI-R is not recommended for use with children who have nonverbal mental ages of 18 months or below or for children who are not yet walking (Lord, Storoschuk, Rutter, & Pickles, 1993). Additionally, the sensitivity and specificity of the combined use of the tools is a little less robust in children under 3 years (Cox et al., 1999; LeCouteur et al., 1989). De Bildt et al. (2004) found better agreement between the ADI-R and the ADOS for children between 5 and 8 years than for older children and adults. In addition, some studies suggest that persons with severe mental retardation are overly identified as having autism within the ADOS/ADI-R system (Fombonne, 1992).

Given the various child characteristics that influence the reliability and validity of the two tools, it is not surprising that researchers continue to advocate for use of clinical judgment in addition to these measures (Bishop & Norbury, 2002; Lord et al., 1999). Expert clinical opinion has also been shown to be more predictive of a stable diagnosis of an autism spectrum diagnosis, when compared to the strict interpretation of the DSM-IV (McConachie, Le Couteur, & Honey, 2005). These issues become particularly relevant when attempting to differentiate complex psychiatric conditions from autism spectrum disorders.

The usefulness of the ADOS and ADI-R has been well demonstrated in distinguishing between autism and delays of development. However, little psychometric evaluation of the sensitivity and specificity of the tools for children with other neurodevelopmental disorders or serious psychiatric disorders, such as Childhood-Onset Schizophrenia (COS), Bipolar Disorder or Major Depression, have been undertaken. Many clinical settings are seeing an increase in referrals for autism-related assessments, perhaps related to increased media attention and planned nationwide campaigns to increase awareness. Increasingly, referrals to clinics serving school-aged children and adolescents are less about distinguishing autism from other developmental disabilities, but rather distinguishing autism from serious psychiatric conditions.

The relationship between Autistic Disorder and COS is complex and has evolved over the past half-decade. Originally thought to be an early manifestation of childhood schizophrenia, autism and childhood schizophrenia were first identified as separate and distinct conditions more than 30 years ago (Green, Padron-Gayol, Hardesty, & Bassiri, 1992; Kolvin, 1971; Petty, Ornitz, Michelman, & Zimmerman, 1984). Age of onset and specific pattern of symptoms were identified as two of the most notable differences between the two disorders (Ghaziuddin, 2005). Onset of symptoms consistent with autism is generally present prior to 30 months, and rarely occurs after 3 years of age.

The classic symptoms of schizophrenia and autism are noticeably different. Children with COS typically present with grossly disorganized behaviors, hallucinations and delusions, and disordered thinking (American Psychiatric Association [APA], 1994, 2000; Ghaziuddin, 2005; Russell, 1994). Children with autism on the other hand, have marked deficits in

reciprocal social interaction and communication, that are typically characterized by an absence of appropriate development in social and communication areas including joint attention behaviors, social/emotional reciprocity, imaginative play, gaze monitoring, affect sharing, and pragmatic communication (APA, 1994, 2000; Filipek et al., 1999). In addition, the presence of restricted and repetitive play behaviors in children with autism has been well documented (South, Ozonoff, & McMahon, 2005). Historically, in fact, it was the presence of hallucinations and delusions that made a diagnosis of autism contraindicated (Kolvin, 1971).

Ghaziuddin (2005) and others have identified additional differences between autism and COS, including higher co-occurrences of mental retardation and seizure disorders in individuals with autism spectrum disorders compared with schizophrenia. The presence of specific psychiatric and developmental disorders in first-degree relatives also differentiates these groups. Individuals with ASDs (Autistic Spectrum Disorders) are more likely to have first-degree relatives with ASDs while individuals with schizophrenia are more likely to have relatives with schizophrenia and other psychotic disorders (Ghaziuddin, 2005).

Most researchers and clinicians accept that autism spectrum disorders and schizophrenia are separate and distinct conditions; however, while there are significant differences between the conditions, there are also similarities. Recent reviews suggest that many children with diagnoses of COS have noteworthy premorbid histories that are characterized by a number of neurodevelopmental concerns and delays, including language, motor and social disturbances (Alagband-Rad et al., 1995; Ross, Schaeffer et al., 2003; Schaeffer & Ross, 2002; Sporn et al., 2004). It is these histories that may be confused with the early histories of individuals who present with autism spectrum disorders. A review of these studies further highlights the social impairment in children with COS as the most common feature noted. Further complicating the diagnostic process has been the documented presence of early symptoms of pervasive developmental disorder in several studies of COS; a recent study found that 25 per cent of a COS sample had a lifetime diagnosis of pervasive developmental disorder (Sporn et al., 2004), indicating that the two conditions can co-occur (Ghaziuddin, 2005; Petty et al., 1984). The extent to which pervasive developmental disorders and COS co-occur is unclear, although previous research has indicated that schizophrenia was no more likely to occur in adolescents and adults with autistic disorder than would be expected by chance (Volkmar & Cohen, 1991).

Thus, overall, the research to date supports the position that ASDs and COS are primarily separate and distinct conditions, particularly for children who present with a classic symptom picture reflective of either autism or COS. However, research review also suggests a significant overlap in symptom presentation, particularly when comparing the premorbid histories of children with COS with children who have ASDs, including the presence of marked social impairments, making the diagnostic process complex and challenging.

This report focused on the administration of the ADOS/ADI-R to three children with Childhood-Onset Schizophrenia and compared those scores to clinical judgments made by a research child psychiatrist and an experienced clinically trained research child psychologist with expertise in autism. The purpose of the study is to examine the extent to which the

autism specific instruments – the ADOS/ADI-R package – are sensitive to the symptom differences between autism spectrum disorders and schizophrenia.

Method

Participants

The Colorado Childhood-Onset Schizophrenia Research Program is focused on genetic etiology (Buervenich et al., 2000; Leonard et al., 2002), physiologic correlates (Ross, 2003; Ross et al., 1999), and treatment (Ross, Novins, Farley, & Adler, 2003) of children who develop schizophrenia or schizoaffective disorder prior to their 13th birthday. All children referred to the program were diagnosed using DSM-IV (APA, 1994) criteria, using a structured diagnostic interview (Kaufman et al., 1997). Both parent and child versions of the Kiddie-SADS-PL were administered, although for children, the child interview was limited to affective and psychotic symptomology. Structured interviews were completed by experienced research clinicians with advanced degrees (MSW, DO, or MD), and medical records were reviewed. Final diagnosis was a best-estimate diagnosis. Participants were 3 sequentially diagnosed children from this research program with a diagnosis of COS. All 3 children were assessed using high-resolution cytogenetic screening and FISH for 22q11 deletion; no genetic abnormalities were identified.

Child A

Early history—A is a 9-year and 4-month-old Hispanic Caucasian male who lived with his mother and younger brother. At 31-weeks gestation, the placenta separated leading to bradycardia and an emergency C-section. He was born at 3 lbs. 8 ounces and spent his first month in the neonatal ICU for bradycardia and sleep apnea. He experienced an additional medical hospitalization for bradycardia. He was on oxygen supplementation until 7 months of age. He is currently diagnosed with asthma and multiple environmental allergies. Developmental milestones were delayed, as he walked at 20 months of age, had one word at 24 months and 3 words by the time he was 3½ years old. Socially, from the age of 3, he was described as having little interest in interacting with peers, would only interact with his family and a limited number of teachers. A has a long history of limited interests as well as limited thematic play prior to age 6. In addition to developmental delays, A was noted to have ‘bad tantrums’ at school that included screaming, rocking, attempting to take his clothes off at school, biting and a dislike for many sensory stimuli including sand and water. He has a Full Scale IQ of 70.

Onset of psychotic symptoms—By age 3, A was noted to stare and babble at blank walls; by age 4 he was pointing to blank walls and reported that he saw ‘a lady’ and that the lady had given him an apple. By age 7, he had ongoing complaints of auditory hallucinations and at present, the ‘voices’ began to be ‘bad voices’, telling him to ‘kill his mother’. He complained of ‘seeing a guy in my mother's eyes telling me to kill her’ and began to ask for surgery to ‘open up my head and get the thoughts [voices] out of my head’. He would often point at nothing in particular and begin screaming. At the age of 5-6 years, A would often begin screaming for his mother and she would find him complaining of ‘things crawling on me’ slapping at himself to ‘get rid of the bugs’. There was no history of olfactory or

gustatory hallucinations. A often reported that the voices in his head have taken over his body and controlled his actions. He intermittently complained that the people on television stare at him and tell him to do things. In public places, if anyone laughs, he believes the person is laughing at him.

Summary of pharmacological intervention—Various medications were tried with Child A over the years. He was initially placed on olanzapine (antipsychotic). At first he became more engageable, with significantly improved thought processes. However, this medication was subsequently discontinued due to an associated weight gain. Psychotic symptoms escalated including experiencing hallucinations throughout the day. Quetiapine (atypical antipsychotic) was prescribed but again this medication was discontinued due to significant side effects. Molindone (antipsychotic) was effective in treating his psychotic symptoms and he tolerated this medication well for several years. Eventually Child A was gradually changed from the molindone to ziprasidone (atypical antipsychotic) because of his weight gain. Although his weight did not decrease he did experience good symptom relief with the ziprasidone (Beresford, Hepburn, & Ross, 2005).

Child 6

Early history—B is a 10-year and 11-month-old Caucasian male who lived with mother, father, older brother and grandparents. B was born via scheduled C-section at term. Medical problems included recurrent otitis media that required ear tube placement five times, and gastroesophageal reflux surgically treated with a fundal placcation at age 7 years. He has a diagnosis of Waardenberg Syndrome CD40 deficiency (inunune deficiency disease) and recent onset of obesity of unknown etiology. Developmental milestones were typical for motor development, but delayed for speech language skills. Social interaction skills were delayed as well, with little preschool interaction with peers and little to no thematic play observed. B was first evaluated at age 2 and therapies, including speech, occupational and physical therapies have continued to date. When B was 5 years old, he was administered an intelligence test, yielding a Full Scale score in the mid-70s.

Onset of psychotic symptoms—Beginning at age 8, B became reclusive, refusing to talk or interact with unfamiliar peers or adults, complaining he was hearing the devil talk to him, seeing the devil and slowly increasing aggressiveness towards others. At around 8 years old, B began complaining of hearing 'Lucifer's voice'. The voice frequently swears at him, tells him to hurt others, and generally describes him as an evil person. B occasionally hears 'God' but this is rare and he cannot specifically identify what God tells him. B often hears 'things in my ear', but denies other auditory hallucinations. B often sees Lucifer around his room and in other locations. B describes feeling, several times per day, as though Lucifer is touching his private parts. There are no reported olfactory or somatic hallucinations. B does describe that Lucifer will take over his body and make him do evil things, such as hit his brother. B becomes agitated (about once a month) because he believes that 'we're all going to die', from a hurricane, war, earthquake, and so on. B often complains to his mother that others are looking at him and that they are going to do something bad to him. No information regarding pharmacological intervention was available for Child B.

Child C

Early history—C is an 11-year and 10-month-old Caucasian male who was adopted at 7 months after placement in a foster home. Reports indicated that he had violent tantrums from the age of 2 years or earlier and could be violent in a bizarre, unprovoked manner. For instance, he once walked over to his half-sister and pressed on her eyeballs with his thumbs. When he was first seen at a child development center at 2½ years of age, he was diagnosed defiant disorder. In addition there was concern about pervasive developmental disorder, as having possible depression, possible bipolar disorder, and oppositional NOS and attachment disorder. He was also found to have severe dyspraxia. A medical work-up including an MRI, BEG, DNA for Fragile X, karyotype, and metabolic studies was negative. Family history was significant for severe mental illness in the biological mother – either schizophrenia or bipolar disorder. His IQ was measured by the same neuropsychologist at ages 7 and 10. At age 7 he had a verbal score of 74, a performance score of 63, and a full scale score of 66. At age 10, he had a verbal score of 60, a performance score of 54 and a full scale score of 53. The neuropsychologist who completed both assessments indicated that the decline in scores over time was more representative of a failure to progress, rather than a frank pattern of deterioration.

Onset of psychotic symptoms—At approximately 3 years 9 months C first told his mother that he had noises in his head like a ‘radio in his head’. He also spoke often to his mother of an elaborate, friendly group of imaginary friends; it is noteworthy that he had many imaginary friends, not just one or two. When C was close to 6 years of age, he was experiencing constant auditory hallucinations, such as crunching sounds, radio sounds, and voices he called ‘Yahoos’. He also spoke of being able to see things, for example, non-existent trails in the snow. He could so readily visualize things that the contents of a benign story could cause him to scream in terror and hide. At times he ‘smelled’ bugs in the tap water and refused to drink it. He believed that his younger half-sister was always out to hurt him. C tried to control her every move, even telling her when to take a bite of food. He believed that the ‘Yahoos’ lived inside him and ate all of his medicine. He feared being poisoned and would not eat if he saw that something had been altered on his plate when he was away. He believed he could cast spells. At times of frustration, he would fall to the ground, hold his head and say ‘they’ were too loud. When entirely off medication, he was grossly disorganized and unable to hold a conversation. During that time, C was in and out of the hospital and required one-to-one assistance in all settings.

Summary of pharmacological intervention—Numerous medications were tried with Child C including trials of clonidine (alpha-2 adrenergic agonist), valproic acid and carbamazepine (both anticonvulsants used as mood stabilizers) without marked success. Stimulant and antidepressant medication caused severe agitation. Various psychotic medications such as thioridazine, risperidone, olanzapine and molindone had been tried and were partially helpful. Eventually Lithium carbonate (mood stabilizer), combined with clozapine (atypical antipsychotic), Abilify (atypical antipsychotic), and propranolol (beta blocker for anxiety) have been the most helpful in addressing psychotic symptoms as well to manage behavior (Beresford et al., 2005).

Measures

The *Autism Diagnostic Observation Schedule* (ADOS; Lord et al., 1999) is a semi-structured, play-based observational interview of children or adults suspected of presenting with an autism spectrum disorder. The ADOS yields a diagnostic algorithm using scores from social and communication domains, and provides two diagnostic categories: Autism and ASDs (including autism, as well as PDD-NOS and other forms of ASDs). The ADOS is presented in four modules that are organized around tasks and materials appropriate for children and adults of different expressive language levels and age, from nonverbal preschool children to verbally fluent, high-functioning adults and takes about 45 minutes to administer. It requires substantial training, skill and experience on the part of the examiner to administer correctly and only allows for scoring of behaviors that occur during its administration, so it does not include history or information about daily life. Because all three children were verbally fluent (at least a 4-year-old level in functional expressive language; Lord et al., 1999) they were administered Module 3 of the ADOS-G.

The *Autism Diagnostic Interview – Revised* (ADI-R; Lord et al., 1994) is a semi-structured caregiver interview that yields scores in three areas: Social reciprocity, communication and repetitive behaviors, as well as onset, based on history for children over age 5. The ADI-R has an algorithm for autism based on scores in these three areas and on onset. There is no cut-off for the broader spectrum of autistic disorders, such as Pervasive Developmental Disorder Not Otherwise Specified or Asperger's Syndrome. It is a caregiver interview, so it can be done without the presence of the child, but it is quite lengthy and requires substantial training.

Procedures

Each of the parents was interviewed using the ADI-R and each child was administered the ADOS-G, Module 3. The ADOS/ADI-R was administered by a research assistant trained to research reliability on the instruments,¹ All of the ADOS/ADI-R administrations were videotaped and also scored by one of the authors (SLH), a research psychologist and certified ADOS/ADI-R trainer. Interobserver agreement for the ADOS scores was computed across the full complement of items and exceeded 88 per cent on all three administrations. Interobserver agreement for the ADI-R was not obtained; instead, the protocol was scored by an ADI-R certified trainer alone (SLH). All ADOS, ADI-R, and historical data (standard research questionnaires including reason for referral, history of the presenting problem, school history, and information regarding therapeutic interventions) were reviewed by two of the authors (SLH and RGR). Diagnostic criteria for pervasive developmental disorders as described in DSM-IV-TR (APA, 2004) were subsequently applied to all of the data described herein. Each child received three diagnostic codes (1) diagnosis as determined by the ADOS cutoff scores; (2) diagnosis as determined by ADI-R cutoff scores; and (3) diagnosis as determined by clinical judgment.

¹Research reliability is established through a rigorous training program that includes observing, practice administrations, and scoring videotapes of individuals participating in the ADOS or ADI-R. Reliability on these videotaped administrations must be established (80%) with a certified trainer across all scoring items, as well as the algorithms established by the authors. Lord et al. (1999), before researchers are able to administer the ADOS or ADI-R.

Results

All three children met research criteria for autism in the three core deficit areas measured by the ADI-R-R: Qualitative impairments in reciprocal social interaction, communication, and repetitive behaviors and stereotyped patterns. In addition, the parents of all three children had significant concerns (social, communicative or behavioral concerns) about their children's development prior to 3 years of age (Table 1). Similarly, the ADOS-G, Module 3 was administered to all 3 children. The results of the ADOS Algorithm indicated that all 3 children met research criteria for an autism spectrum disorder by meeting or exceeding the cut-off scores in the communication and social interaction domains (see Table 2). Furthermore, the sum of the subtest scores of communication and social interaction for all 3 children exceeded the ASDS cut-off and in one case, the sum total exceeded the autism cut-off score of 10. Although not necessary for purposes of diagnosis, the ADOS Algorithm also includes subtest scores on imagination/creativity and stereotyped behaviors and restricted interests. All of the participants displayed either mild or moderate limitations in imagination and creativity, and 2 out of the 3 children demonstrated stereotyped behaviors and restricted interests.

A clinical psychologist (the second author) conducted record reviews, watched video tapes of participants during the ADOS, reviewed all data and determined that none of the three children presented with an autism spectrum disorder. A second author (RGR) concurred that none of the 3 children presented with ASDS. Despite obtaining scores above the cut-off on both the ADOS and ADI-R, the 3 children demonstrated a qualitatively different profile of social and communicative behaviors than observed in autism. More specifically, social initiations and responses were limited and unusual; however, all 3 children monitored the nonverbal behaviors of others, integrated gestures appropriately with vocalization, and demonstrated markedly better social quality with familiar, versus nonfamiliar persons. Two boys seemed actively distracted by internal events throughout the assessment, were easily agitated, and resisted participating in some of the activities, suggesting that their poor scores may have been influenced by poor motivation, as opposed to core deficits in social reciprocity. The examiners commented that building a relationship with two of the boys was quite difficult within the ADOS session, and the children responded with agitation to the questions concerning social difficulties and relationships and provided terse responses reflecting little insight.

Discussion

The present study provides preliminary data supporting the assertion that use of the ADI-R/ADOS assessment package alone for the diagnosis of autism spectrum disorders may have limited clinical and research utility when working with children who present with early onset psychosis. All 3 children in this report presented with known histories and clinical presentations consistent with childhood psychosis. When the ADI-R/ADOS package was administered to the children and their parents, the scores on these measures exceeded cut-offs for ASDs in all core deficit areas across both instruments. However, when a research child psychiatrist and research clinical psychologist with expertise in autism reviewed the

early developmental histories of the children, as well as the clinical presentation of these children, none of the children received a clinical diagnosis on the autism spectrum.

There are at least three possible explanations for each of these children meeting the structured diagnostic criteria for an autism spectrum disorder: (a) Many of the diagnostic symptoms of autism are nonspecific and also occur in COS; or (b) the children actually have autism and not COS, or (c) the ADOS and ADI-R questions may not be sensitive to the differences in symptom presentation between children with ASDs and early onset psychosis.

Symptoms of autism and Childhood-Onset Schizophrenia

Children with COS have notable early developmental histories that include delays in language, motor and social arenas (Alaghband-Rad et al., 1995; Sporn et al., 2004); histories once thought to be unique to children with ASDs and/or other developmental disorders but not COS. Furthermore, the research reviewing the premorbid histories of children with COS also highlights social impairment as a common feature and the early symptoms of pervasive developmental disorder have been described in children with COS (Sporn et al., 2004). Thus, both groups of children share similarities in their early developmental histories, and include interpersonal challenges as part of their shared clinical picture.

However, the classic symptoms of autism and COS are noticeably distinct. Children with COS generally present with grossly disorganized behaviors, hallucinations, delusions and disordered thinking (APA, 1994, 2000), while children with autism present with deficits in three primary areas: Reciprocal social interaction, communication, and repetitive and restricted interests and behaviors (APA, 1994, 2000; Filipek et al., 1999).

Thus, a careful review of the developmental histories and clinical presentations of these two disorders suggests that while there are clear areas of overlap between autism and COS, there are also areas of distinct differences between the disorders, particularly for 'classic' presentations of each disorder. Unfortunately, many children do not neatly present in a 'classic' or straight forward manner when referred to community clinicians for diagnostic clarification. Clinical experience would suggest that there are a number of children who present with features of each of the disorders without meeting full criteria for either disorder, highlighting the difficulties many front-line clinicians face in making accurate diagnoses.

Considerations for a diagnosis of autism

Because all three children received clinically significant scores on the ADOS/ADI-R, both clinically experienced researchers reviewing the data had to carefully consider the extent to which these children could actually have an autism spectrum diagnosis. Variables such as the nature of the psychotic symptoms, the relative stability of a psychotic diagnosis in young children particularly in light of documented intellectual deficits, and the children's response to medications were all variables that needed to be examined.

All 3 children in this study were described as having symptoms of psychosis that were present for nearly 3 years. In order to more fully understand the diagnostic implications of these symptoms it was important to differentiate the nature of these psychotic symptoms, that is, to what extent were these symptoms reflective of eccentric thinking and unusual

preoccupations (more common in ASDs) compared to the bizarre and delusional thinking more typically described for individuals with psychosis (APA, 1994, 2000). While it is true that illogical and tangential thinking may be present in individuals with ASDs (perhaps because of common speech/language deficits), the presence of these difficulties may not necessarily reflect true psychotic thinking (Ghaziuddin, 2005). In the present case studies, the bizarre content of the hallucinatory experiences described (i.e. complaints of 'things crawling on me', hearing 'Lucifer's voice', or voices directing one of the children to 'kill his mother') are not typically reported in children with autism, and tend to be more characteristic of COS.

Moreover, there has been some concern generated that a schizophrenia diagnosis can be difficult in more severely ill, tertiary-care hospitalized primarily adolescent patients (McClellan, Werry, & Ham, 1993; Werry, McClellan, & Chard, 1991) or in a nationally recruited sample (McKenna et al., 1994); however, samples drawn from local populations of chronically psychotic children show diagnostic stability into adulthood (Asarnow, Tompson, & Goldstein, 1994; Eggers & Bunk, 1997; Maziade et al., 1996). All 3 participants described here had chronic psychosis.

Results from intellectual assessments obtained on all 3 children, indicated that they had IQ scores that fell in the mentally retarded range and/or borderline range of functioning. In light of these scores, it is important to consider the stability of psychosis in the presence of cognitive limitations. Previous research suggests that diagnoses of COS can be made reliably in individuals with mental retardation, provided that the assessments are carefully structured and comprehensive (Lee, Moss, Friedlander, Donnelly, & Honer, 2003). In a study evaluating 20 children with mental retardation 10 children were identified with an initial diagnosis of schizophrenia. Two years later the children were reassessed and 8 of the 10 children received confirmation of their initial diagnosis of schizophrenia (Lee et al., 2003). This study suggests that psychotic symptoms can be stable over time, even in an intellectually disabled population.

Information regarding pharmacological intervention for 2 of the 3 children reflects the use of multiple medications, many of which were antipsychotic medications. Both Child A and C responded well to antipsychotic medications. Although response to medications is not a defining diagnostic feature, it is important to highlight that these children presented with clear psychotic symptoms that generally abated with the use of anti psychotic medications. Thus, the chronicity of symptom presentation, stability of symptoms even in the presence of cognitive deficits, and a generally positive response to antipsychotic medications present a compelling case for COS in these participants.

Clinical sensitivity of the ADOS/ADI-R for challenging clinical populations

Diagnostic distinctions between autism and Childhood-Onset Schizophrenia may be simultaneously clearly defined and only vaguely distinct. The authors who reviewed all data carefully examined the clinical profiles of all 3 children and noted that these children had qualitatively different profiles of social and communicative behaviors that are not commonly observed in autism, even in light of the clinically significant findings on the ADOS/ADI-R.

An informal inspection of specific items on both instruments reveals how positive findings for autism could be obtained in the face of clinical judgment suggesting otherwise.

On the ADOS, the participants tended to display poor eye contact and flat affect, limited insight into the nature of social relationships, and decreased amounts of reciprocal social communication, including conversation between the participants and the examiner. While the authors of the ADOS consider these symptoms to be highly characteristic of children with ASDs, the symptoms may also occur in children with COS or perhaps even other psychiatric disorders. The presence of these symptoms may have been less reflective of the core deficits of poor affective and social reciprocity, and more reflective of disorganized thinking, internal distraction and delusional thinking for these children. Symptoms that are more unique to a diagnosis of ASDs (i.e. stereotyped or rote phrases, echoed speech, or repetitive behaviors or stereotyped mannerisms) were generally not present in this small sample of participants. Additionally, during the ADOS, the participants typically monitored the nonverbal behaviors of others and gestures were integrated appropriately with vocalizations. Further, limited social responsiveness and overtures may have been related to the unfamiliarity and perhaps even distrust of the examiner, rather than reflecting a true deficit in reciprocal social interaction.

A review of the ADI-R-R indicated that symptoms endorsed by the parents generally included deficits in range of facial expression, interest in other children, including group play with peers and development of appropriate friendships. By history these children displayed a lack of social-emotional reciprocity, including appropriateness and quality of social responses and overtures. As with the ADOS, the authors of the ADI-R-R have described these symptoms as characteristic of children with ASDs, but it is also possible that these symptoms are present in other psychiatric disorders, including COS, especially in light of research suggesting similarities in early developmental history including interpersonal challenges (Sporn et al., 2004). Again, symptoms most unique to children with ASDs (i.e. lack of shared enjoyment, presence of rote and stereotyped phrases/behaviors and use of nonverbal behaviors with the exception of range of facial expression) were only minimally endorsed. Clinical impressions as offered by the authors, supported the diagnosis of COS, suggesting that the questions and activities of the ADOS and ADI-R, designed to differentiate autism from other developmental disorders, may not be sensitive to differences between autism and schizophrenia. The difficulties in diagnostic differentiation are no doubt in part related to the symptom overlap between the two disorders.

However, a review of the early histories of the 3 children presented in this article indicated that there were elements of their early histories that are characteristic of children with COS (e.g. hallucinatory experiences, ideas of reference, and unprovoked serious aggressive behaviors). Documenting these histories will likely be helpful in assisting interviewers in making these important diagnostic distinctions. In order to capture these early experiences during the administration of standardized assessments, clinicians or researchers administering the ADI-R may want to ask parents an additional set of questions. For example, it may be helpful for the interviewer to specifically inquire about the presence of unusual behaviors. Parents could be asked to speak directly to the presence of hallucinations (auditory, visual, tactile or olfactory), ideas of reference (TV or radio speaking directly to

them), or delusions in their children. Additionally, because command hallucinations can also be present in children (voices telling them to do bad things), it would be important to ask the parent whether their child experiences voices telling him/her to do things he/she does not want to do. Inquiring whether the child frequently misinterprets the behaviors of others could also be included in this set of questions. Information regarding language and communication functioning, as well as the social development and play of children are explored during the ADI-R. Similarly, inquiries regarding neologisms/idiosyncratic language (symptoms that may be characteristic of children with COS) are already included in the interview; however, additional questions such as asking about variability in the child's conversational speech (e.g. highly disorganized speech with evidence of an inability to converse at times, compared with periods when conversation is much easier to sustain) could provide further clarifying information for some children. Questions about the presence of imaginary friends may also shed additional light into the nature of the child's social development. Additional instruments designed to specifically assess the presence of psychotic symptoms through parent report, such as the Schedule for Affective Disorders and Schizophrenia for School-age Children (K-SADS-PL; Kaufman et al., 1997) may be warranted should diagnostic confusion persist.

While the ADI-R explores a child's early developmental history through parent interview, the ADOS provides information regarding the child's current functioning in social, communication and play areas through a structured play session. Earlier, it was suggested that some of the symptoms that were positively endorsed on the ADOS and thus scored as consistent with autism, could also reflect COS. In particular, lack of motivation and interest in engaging with the examiner, even distrust of the examiner was mentioned as influencing the interview. In order to capture this behavioral presentation, examiners could make note of additional abnormal behaviors. Overactivity/agitation, tantrums, aggression, or other disruptive behaviors, and anxiety are already scored on the ADOS. Examiners who suspect a complicated diagnostic picture or even COS in particular, could make note of the presence of hallucinatory behaviors, delusions, and/or disorganized speech. Examiners could also be encouraged to document his/her clinical impression of the quality of the information that was obtained throughout the ADOS. This prompt may remind researchers and clinicians administering the instrument to carefully consider the extent to which the child was fully engaged in the interview, when interpreting the results of the ADOS.

Utility of the ADI-R/ADOS in psychiatric populations The results from the current study suggest that children with psychosis may be over identified as having an autism spectrum disorder within the ADI-R/ADOS system. The symptom overlap between the two groups as well as a lack of sensitivity and specificity of the ADI-R/ADOS to differentiate autism from psychosis, most likely contributes to the over identification.

Implications for research and clinical practice

The developers of the ADI-R/ADOS have indicated all along that clinical judgment, combined with the psychometric findings of the instruments, is in effect the 'gold standard' for autism assessment (Lord et al., 1999). The results of the study support this assertion and highlight the diagnostic confusion that can occur in some children. However, it is important

to note that this study was based on only 3 children with COS. Future studies involving more children with COS are recommended, not only to further characterize COS but to obtain additional information that would contribute to the diagnostic challenges outlined in this article.

As the public's awareness of autism spectrum disorders increases, so do the number of individuals referred to clinical settings for purposes of diagnostic clarification. Teasing ASDs apart from serious psychiatric illness including Childhood-Onset Schizophrenia, Bipolar Disorder, and Obsessive compulsive Disorder may be extremely complex and challenging, yet a common presenting problem for settings serving older children and adolescents. Thus it is increasingly important for clinicians at the forefront of these diagnostic decisions to not only achieve clinical reliability on the ADI-R/ADOS assessments, but to develop clinical expertise in the diagnosis and evaluation of autism spectrum disorders as well as other psychiatric disorders. This may also entail a careful review of symptom presentation and an in-depth understanding of the qualitative differences between developmental and psychiatric disorders. Because of the limitations of these instruments, clinical judgment, perhaps paired with consultation, are essential components in the assessment process.

Similarly, research studies with individuals who have autism spectrum disorders have prominently featured the ADI-R/ADOS system as the instruments of choice to determine the inclusion/exclusion of participants. Because these instruments may over identify autism in individuals with COS or other psychotic disorders, it is essential that clinical judgment be included as part of the diagnostic decision making process, rather than relying on the results of the ADI-R/ADOS alone.

References

- Alaghband-Rad J, McKenna K, Gordon CT, Albus KE, Hamburger SD, Rumsey JM, et al. Childhood-onset schizophrenia: The severity of pre-morbid course. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1995; 34:1273–1283. [PubMed: 7592264]
- American Psychiatric Association. (APA). *Diagnostic and statistical manual of mental disorders*. 4th Ed.. Author; Washington, DC: 1994.
- American Psychiatric Association. (APA). *Diagnostic and statistical manual of mental disorders*. 4th Ed.. Text Revision (DSM-IV-TR). Author; Washington, DC: 2000.
- Asarnow J, Tompson M, Goldstein M. Childhood-onset schizophrenia: A follow-up study. *Schizophrenia Bulletin*. 1994; 20:599–617. [PubMed: 7701271]
- Beresford C, Hepburn S, Ross R. Schizophrenia in preschool children: Two case reports with longitudinal follow-up for 6 and 8 years. *Clinical Child Psychology and Psychiatry*. 2005; 10:429–439.
- Bishop D, Norbury C. Exploring the borderlands of autistic disorder and specific language impairment: A study using standardized diagnostic instruments. *Journal of Child Psychology and Psychiatry*. 2002; 43:917–929. [PubMed: 12405479]
- Buervenich S, Carmine A, Arvidsson M, Xiang R, Zhiping Z, Sydow O, Jonsson E, et al. NURRI mutations in schizophrenia and manic depressive disorder. *American Journal of Medical Genetics*. 2000; 96:813.
- Cox A, Klein K, Charman T, Baird O, Baron-Cohen S, Swettenham J, et al. Autism spectrum disorders at 20 and 42 months of age: Stability of clinical and ADI-R diagnosis. *Journal of Child Psychology and Psychiatry*. 1999; 40:719–732. [PubMed: 10433406]

- de Bildt A, Sytema S, Ketelaars C, Kraijer D, Mulder E, Volkmar R, Minderaa R. Interrelationship between Autism Diagnostic Observation Schedule-Generic (ADOS-G), Autism Diagnostic Interview-Revised (ADI-R), and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) Classification in Children and Adolescents with Mental Retardation. *Journal of Autism and Developmental Disorders*. 2004; 34:129–137. [PubMed: 15162932]
- Eggers C, Bunk D. The long-term course of childhood-onset schizophrenia: A 42-year follow-up. *Schizophrenia Bulletin*. 1997; 23:105–111. [PubMed: 9050117]
- Filipek PA, Accardo PJ, Baranek GT, Cook EH, Dawson G, Gordon B, Gravel JS, et al. The screening and diagnosis of autistic spectrum disorders. *Journal of Autism and Developmental Disorders*. 1999; 29:439–484. [PubMed: 10638459]
- Fombonne E. Diagnostic assessment in a sample of autistic and developmentally impaired adolescents. *Journal of Autism and Developmental Disorders*. 1992; 22:563–581. [PubMed: 1483977]
- Ghaziuddin, M. *Mental health aspects of autism and Asperger syndrome*. Jessica Kingsley Publishers; Philadelphia, PA: 2005.
- Green WH, Padron-Gayol M, Hardesty AS, Bassiri M. Schizophrenia with childhood onset: A phenomenological study of 38 cases. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1992; 31:968–976. [PubMed: 1400132]
- Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, Williamson D. Schedule for affective disorders and schizophrenia for school-age children - Present and lifetime version (K-SADS-PL): Initial reliability and validity. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1997; 36:980–988. [PubMed: 9204677]
- Kolvin I. Studies in childhood psychoses I: Diagnostic criteria and classification. *British Journal of Psychiatry*. 1971; 118:381–384. [PubMed: 5576635]
- Le Couteur A, Rutter M, Lord C, Rios P, Robertson S, Holdgrafer M, McLennan JD. Autism Diagnostic Interview: A semi-structured interview for parents and caregivers of autistic persons. *Journal of Autism and Developmental Disorders*. 1989; 19:363–387. [PubMed: 2793783]
- Lee P, Moss S, Friedlander R, Donnelly T, Honer W. Early-onset schizophrenia in children with mental retardation: Diagnostic reliability and stability of clinical features. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2003; 42:162–169. [PubMed: 12544175]
- Leonard S, Gault J, Hopkins J, Logel J, Vianzon R, Short M, Drebing C, et al. Promotor variants in the nicotinic acetylcholine receptor subunit gene are associated with an inhibitory deficit found in schizophrenia. *Archives of General Psychiatry*. 2002; 59:1085–1090. [PubMed: 12470124]
- Lord C, Risi S, Lambrecht LK, Cook EH, Leventhal BL, DiLavore PC, Pickles A, Rutter M. The Autism Diagnostic Observation Schedule - Generic: A standard measure of social and communication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorders*. 1999; 30:205–223. [PubMed: 11055457]
- Lord C, Rutter M, Le Couteur A. Autism Diagnostic Interview - Revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders*. 1994; 24:659–685. [PubMed: 7814313]
- Lord C, Storoschuk S, Rutter M, Pickles A. Using the ADI-R-R to diagnose autism in preschool children. *Infant Mental Health Journal*. 1993; 14:234–252.
- McClellan J, Werry J, Ham M. A follow-up study of early onset psychosis: Comparison between outcome diagnoses of schizophrenia, mood disorders, and personality disorders. *Journal of Autism and Developmental Disorders*. 1993; 23:243–262. [PubMed: 8331046]
- McConachie H, Le Couteur A, Honey E. Can a diagnosis of Asperger syndrome be made in very young children with suspected autism spectrum disorder? *Journal of Autism and Developmental Disorders*. 2005; 35:167–176. [PubMed: 15909403]
- McKenna K, Gordon C, Lenane M, Kaysen D, Fahey K, Rapoport J. Looking for childhood-onset schizophrenia: The first 71 cases screened. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1994; 33:636–644. [PubMed: 8056726]
- Maziade M, Bouchard S, Gingras N, Charron L, Cardinal A, Roy M, et al. Long-term stability of diagnosis and symptom dimensions in a systematic sample of patients with onset of schizophrenia in childhood and early adolescence II: Positive/negative distinction and childhood predictors of outcome. *British Journal of Psychiatry*. 1996; 169:311–378.

- Petty LK, Omitz EM, Michelman JD, Zimmerman EG. Autistic children who become schizophrenic. *Archives of General Psychiatry*. 1984; 41:129–135. [PubMed: 6696593]
- Ross R. Early expression of a pathophysiological feature of schizophrenia: Saccadic intrusions into smooth pursuit eye movements in school-age children vulnerable to schizophrenia. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2003; 42:468–476. [PubMed: 12649634]
- Ross R, Novins D, Farley G, Adler L. A one-year open-label trial of olanzapine in school-age children with schizophrenia. *Journal of Child and Adolescent Psychopharmacology*. 2003; 13:301–309. [PubMed: 14642018]
- Ross R, Olincy A, Harris J, Radant A, Hawkins M, Adler L, Freedman R. Evidence for bilinear inheritance of physiological indicators of risk in childhood-onset schizophrenia. *American Journal of Medical Genetics*. 1999; 88:188–199. [PubMed: 10206241]
- Ross R, Schaeffer J, Compagnon N, Heinlein S, Beresford C, Farley G. Creating school-age versions of semistructured interviews for the prodrome to schizophrenia: Lessons from case reviews. *Schizophrenia Bulletin*. 2003; 29:729–736. [PubMed: 14989410]
- Russell AT. The clinical presentation of childhood-onset schizophrenia. *Schizophrenia Bulletin*. 1994; 20:633–646.
- Schaeffer J, Ross R. Childhood-onset schizophrenia: Premorbid and prodromal diagnostic and treatment histories. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2002; 41:538–545. [PubMed: 12014786]
- South M, Ozonoff S, McMahon W. Repetitive behavior profiles in Asperger Syndrome and high-functioning autism. *Journal of Autism and Developmental Disorders*. 2005; 35:145–158. [PubMed: 15909401]
- Sporn AL, Addington AM, Gogtay N, Ordonez AE, Gomic M, Clasen L, et al. Pervasive developmental disorder and childhood-onset schizophrenia: Comorbid disorder or a phenotypic variant of a very early onset illness? *Biological Psychiatry*. 2004; 55:989–994. [PubMed: 15121482]
- Volkmar FR, Cohen DJ. Comorbid association of autism and schizophrenia. *American Journal of Psychiatry*. 1991; 148:1705–1707. [PubMed: 1957933]
- Werry J, McClellan J, Chard L. Childhood and adolescent schizophrenic, bipolar, and schizoaffective disorders: A clinical and outcome study. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1991; 30:457–465. [PubMed: 2055884]

Table 1

ADI-R algorithm scores (short form of ADI)

Participants	Qualitative impairments in reciprocal social interaction cut-off = 10	Communication cut-off- 8	Repetitive behaviors and stereotyped patterns cut-off= 3	Abnormality of development evident before 36 months
Child A	14	13	8	Yes
Child B	10	13	4	Yes
Child C	16	22	4	Yes

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2

ADOS algorithm scores

Participants	Communication (autism cut-off = 3; ASD cut-off = 2)	Reciprocal social interaction (autism cut-off = 6; ASD cut-off = 4)	Communication + social interaction (autism cut- off = 10; ASD cut-off = 7)	Imagination! creativity	Stereotyped behaviors and restricted interests
Child A	2	7	9	1	2
Child B	2	6	8	1	0
Child C	4	9	13	2	2

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript