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Youth at clinical high-risk for psychosis with an autism spectrum diagnosis: Symptomatology, premorbid adjustment, and current functioning

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Abstract

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By Derek M. Novacek

Psychotic and autism spectrum disorders (ASD) are neurodevelopmental disorders characterized by social, communicative, and cognitive impairments. Previously conceptualized as unrelated, more recent evidence suggests the two share genetic, prenatal, and environmental risk factors. Psychosis research has focused on identifying predictors and mechanisms that contribute to the disorder's onset. Despite this, few studies have examined how ASD might influence the development of psychosis during the clinical high-risk (CHR) period. A prodromal period of functional decline and attenuated psychotic symptoms often precedes the onset of psychosis. Given the multitude of factors that influence risk for psychosis, it is assumed that there are multiple developmental pathways to psychosis. With retrospective studies findings that 7-50% of individuals with ASD also had a comorbid psychotic disorder, it is possible that ASD is associated with one or more of these pathways, manifesting in the trajectory of functional decline and prodromal symptomatology. The present study examined whether CHR youth with (n = 25) and without (n = 739) an ASD diagnosis exhibited differences in prodromal symptoms, premorbid adjustment, and current functioning. The Structured Interview for Prodromal Syndromes assessed prodromal symptoms and determined CHR status. The Premorbid Adjustment Scale and the Global Functioning Social and Role Scales assessed premorbid adjustment and current functioning respectively. Results revealed that ASD group endorsed greater severity of social anhedonia and decreased ideational richness. The ASD group also endorsed more impairment in sociability, peer relationships, and adaptation to school in both childhood and early adolescence. In current functioning, the ASD group endorsed more deficits in social functioning, but no differences were found in role functioning. These findings provide evidence of differing developmental trajectory to the psychosis prodrome for youth with ASD.

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Table of Contents

Youth at clinical high-risk for psychosis with an autism spectrum diagnosis: Differences in symptomatology and functional trajectory

Schizophrenia and autism spectrum disorder share a history that has challenged the diagnostic boundaries used to classify psychopathology in both research and in clinical settings. This shared history began with Eugene Bleuler (1911) when he coined the term “autism”, derived from the Greek word “autos” meaning self, to describe the tendency of individuals suffering from schizophrenia to live in a world of their own and remain isolated from others. Leo Kanner and others noticed “disturbances in affective contact”, or what he referred to as autistic symptoms in children, leading many to use the term autism to refer to a childhood onset of schizophrenia (Cappon, 1953; Kanner, 1943). Researchers continued to conceptualize the disorders as related, using autism and childhood schizophrenia interchangeably, until the early 1970s. Work by Kolvin and colleagues helped distinguish the two disorders based on discrepancies in the age of onset and differing developmental trajectories (Kolvin, 1971; Kolvin, Ounsted, Humphrey, & McNay, 1971; Kolvin, Ounsted, Richardson, & Garside, 1971; Rutter, 1972). The onset of schizophrenia and other psychotic disorders typically occur in late adolescence and young adulthood. Autism, however, is typically diagnosed in early childhood, although signs may be visible in early infancy (Jones & Klin, 2013).

In 1980, the Diagnostic and Statistical Manual of Mental Disorders Third Edition (DSM-III) formally introduced the term autism (American Psychiatric Association, 1980). Since then, most have viewed the two as distinct disorders. However, recent evidence examining the disorders at multiple levels suggests that the boundaries between the two are much more ambiguous than previously thought. With overlapping

symptomatology, common neurobiological correlates, shared etiological factors, and evidence for developmental links, research examining the two disorders suggests that we need to reconceptualize our understanding of the relations between schizophrenia and autism. However, we still lack prospective studies that examine possible differences between the two disorders in developmental trajectories. An investigation of autism spectrum disorder in youth experiencing attenuated psychotic symptoms may help elucidate symptom and functional trajectories that distinguish the two spectra.

Overlapping Symptomatology and Clinical Features

Psychotic and autism spectrum disorders are both complex, heterogeneous neurodevelopmental disorders characterized by severe deficits in social functioning, communication, and various domains of cognition (Bagner, Melinder, & Barch, 2003; Bellack, Morrison, Wixted, & Meuser, 1990; Happé, Ronald, & Plomin, 2006; Volkmar et al., 2004; Wing & Gould, 1979). Hallmark symptoms of schizophrenia are often divided into positive, negative, disorganized, and cognitive symptom categories. Positive symptoms incorporate hallucinations (auditory, visual, or olfactory), delusions, ideas of reference, and suspiciousness or persecutory ideas. Negative symptoms generally include anhedonia, flat affect, alogia, and avolition. Disorganized symptoms generally include odd appearance or behavior, thought disorder, and communication disturbances (American Psychiatric Association, 2013). Cognitive impairments include deficits in attention and working memory among others. Schizophrenia is only one of the disorders that fall on the psychosis spectrum, which also includes schizoaffective disorder, brief psychotic disorder, schizophreniform disorder, and affective psychoses (e.g., bipolar disorder or depression with psychotic features). In the updated DSM-5, Autistic Disorder,

Asperger's Syndrome, and Pervasive Developmental Disorder-Not-Otherwise Specified (PDD-NOS) were combined to form one disorder, Autism Spectrum Disorder (ASD). The hallmark features of ASD include persistent deficits in social interaction (e.g., social-emotional reciprocity), impairment in both verbal and nonverbal communication, as well as restricted or repetitive patterns of behavior, interests, and activities (e.g., stereotyped motor movements, preoccupation with unusual objects, etc.; APA, 2013).

Similarities in the clinical presentation of ASD and schizophrenia partly initiated the resurgence in the literature investigating the overlap between the schizophrenia and autism spectra. In a classic study examining symptom similarities, Konstantareas and Hewitt (2001) examined 14 males diagnosed with ASD and 14 diagnosed with paranoid schizophrenia. Based on semi-structured clinical interviews, 7 of the 14 males with ASD also met criteria for disorganized schizophrenia. In contrast, none of the males with paranoid schizophrenia met criteria for ASD. When assessing positive and negative symptoms, 5 of the 14 males with ASD endorsed one or more positive symptoms whereas 6 of the 14 endorsed one or more negative symptoms. The schizophrenia group endorsed statistically more positive symptoms than the ASD group, whereas there was no statistical difference between the two groups in the amount of negative symptoms endorsed. In another study, 14.8% met criteria for schizophrenia or another psychotic disorder in a sample of adults with ASD, highlighting symptom overlap and possible comorbidity (Stahlberg, Soderstrom, Rastam, & Gillberg, 2004). Moreover, Unenge Hallerbäck, Lugnegård, Gillberg (2012), obtained results that indicated around half of the sample of individuals with schizophrenia met criteria for an algorithm diagnosis of ASD using retrospective parental report.

Adding to the accumulating evidence, Spek and Wouters (2011) examined the presence of autistic and schizotypal traits in a sample of adults with schizophrenia and another sample with ASD. When measuring autistic traits with the Autism Spectrum Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001), the authors found that the two groups did not differ in their impairment levels in attention to detail and imagination. When assessing schizotypal symptoms with the Schizotypal Personality Questionnaire (SPQ; Raine, 1991), the two groups endorsed similar levels of negative and disorganized symptoms. The schizophrenia group, however, reported significantly more positive symptoms.

While positive symptoms are thought by some to distinguish ASD from SSD, individuals with ASD have been shown to endorse elevated levels of paranoid and persecutory ideas compared to healthy individuals (Abell & Hare, 2005; Blackshaw, Kinderman, Hare, Hatton, 2001; Craig, Hatton, Craig, & Bentall, 2004). After initially finding similar levels of paranoia in individuals with ASD compared to those with schizophrenia (Pinkam, Hopfinger, Pelphrey, Piven, and Penn, 2008), Pinkham and colleagues (2012) sought to replicate these findings in a different sample of individuals with ASD and those with schizophrenia who were experiencing active paranoia. Using the Paranoia Scale (Fenigstein & Vanable, 1992), no significant differences in paranoia were found between the ASD and the paranoid schizophrenia groups, consistent with previous findings. However, further analyses revealed that two groups were characterized by different underlying factors. Paranoia for individuals with schizophrenia reflected victimization, suspicion, and threat of harm, whereas paranoia for the ASD group was distinctly reflective of social cynicism. Although individuals with ASD and those with

schizophrenia endorse similar levels of paranoia, distinct factors suggest possible differences in the determinants of paranoid ideations between the two disorders. In a study conducted by Dykens, Volkmar, & Glick (1991), researchers found evidence of thought disorder (e.g., poverty of speech) and cognitive slippage in high-functioning adults with ASD. These findings have been supported by subsequent studies (Solomon, Ozonoff, Carter, & Caplan, 2008).

In addition to studies that have examined the overlap of symptoms in clinical populations, there is also evidence for an overlap in nonclinical populations. Hurst, Nelsen-Gray, Mitchell, and Kwapil (2007) examined relations between autistic traits assessed with the AQ and the schizotypal traits using the SPQ in a sample of college students. Their results revealed that composite scores of autistic and schizotypal traits were positively correlated. Further analysis indicated that the interpersonal factor of the SPQ was positively correlated with the social skills domain of the AQ, whereas the SPQ disorganized communication factor was positively correlated with the AQ communication domain. These similarities in symptoms cause many problems for clinicians attempting to make a differential diagnosis between the two disorders (Nylander, Lugnegård, & Unenge Hallerbäck, 2011). Some argue that the overlap in symptomatology simply represents flaws in the categorical diagnostic system, whereas others view it as evidence for a shared etiology.

Disorders of Social Dysfunction

Many of the symptoms of both disorders are social in nature, which has led to numerous studies examining deficits in social cognition, the cognitive domain that enables individuals to perceive, understand, and interact with their social world. These

deficits in social cognition and functioning constitute core features of both disorders (Sasson, Pinkham, Carpenter, & Belger, 2011). Impairments in theory of mind (Chung, Kang, Shin, Yoo, & Kwon, 2008; Penn, Sana, & Roberts, 2005; Pflum, Irani et al, 2006; Gooding, & White, 2013), emotion perception (Addington, Penn, Woods, Addington, & Perkins, 2008; Kohler, Walker, Martin, Healey, & Moberg, 2010), and social perception (Corrigan & Green, 1993; Sergi et al., 2009) have been found in individuals across the schizophrenia spectrum and in clinical-high risk populations. Similar to SSD, individuals with ASD show various impairments in domains of social cognition such as theory of mind (Baron-Cohen et al., 1985; Colle, Baron-Cohen, & Hill, 2007; Williams & Happé, 2010), emotion perception (Balconi & Carrera, 2007; Celani et al., 1999; Kennedy & Adolphs, 2012) and social perception (Klin, Jones, Schultz, Volkmar, & Cohen, 2002). Comparative studies have demonstrated comparable levels of deficits in theory of mind (Craig et al., 2004; Lugengård, Unenge Hallerbäck, Hjärthag, & Gillberg, 2013; Pilowsky, Yirmiya, Arbelle, & Mozes, 2000) and emotion perception (Eack et al., 2013) among individuals with schizophrenia and ASD. These similarities at the phenotypic level have furthered the need to investigate commonalities in the pathogenesis of these overlapping clinical syndromes.

Shared Neurobiology

Similar behavioral phenotypes do not always indicate a shared etiology. However, multiple levels of analysis suggest that this is the case with regard to autism and psychosis. de Lacy & King (2013) reviewed evidence that suggests autism and schizophrenia are both disorders of cerebral specialization beginning in the embryonic period. Moreover, developmental differences in brain structure are evident in both

disorders, including abnormalities in white and gray matter volume. Numerous studies have indicated that total brain volume is larger in autism than controls, which is believed to be largely driven by increased white matter volume (Herbert et al., 2013). Analyses of white matter volume in schizophrenia are less conclusive, but suggest that abnormalities are implicated in the pathogenesis of schizophrenia (Kubicki et al, 2007). Regarding gray matter volume, results from a meta-analysis of voxel-based morphometry studies indicate there is a significant reduction of gray matter volume in the bilateral amygdala-hippocampus complex, particularly on the right side, as well as reduction in the bilateral medial parietal cortex among individuals with ASD compared to controls (Via, Radua, Cordoner, Happé, & Mataix-Coles, 201). In schizophrenia, gray matter volume reduction has been found in the cerebrum and prefrontal cortex (Pol et al., 2002) as well as in the amygdala and superior temporal gyrus (Honea, Crow, Passingham, & Mackay, 2005). This decline is also present before the onset of psychosis and differentiates those who go on to develop psychosis with those whose symptoms remit (Cannon et al., 2014). Results regarding gray matter volume have been mixed in autism, but there are fewer investigations compared to schizophrenia.

More recent evidence suggests that the neural underpinnings of social cognitive impairments in both disorders originate in the same brain regions. In one of the few studies that has directly compared individuals with schizophrenia and individuals with ASD, both groups showed hypoactivation in the right amygdala, fusiform face area, and left ventrolateral prefrontal cortex compared to controls when completing social cognitive tasks (Pinkham et al., 2008). Despite the many uncertainties that remain in our understanding of the neurobiological abnormalities and mechanisms implicated in ASD

and psychosis, our current understanding indicates that the two spectra do share a similar pathophysiology, particularly in regions associated with social cognitive deficits.

Etiological Commonalities

Findings from large national longitudinal studies conducted in multiple countries show that psychotic disorders and ASD tend to co-occur in families. In a case-control study of a large Swedish national cohort, the presence of schizophrenia in parents increased the risk for ASD in the probands (odds ratio = 2.9). Similarly, schizophrenia in siblings was associated with a 2.6 increase in odds of ASD in the Swedish sample as well as a separate Israeli cohort (Sullivan et al., 2012). This is consistent with previous findings from another study in Sweden (Daniels et al., 2008) and one in Denmark (Larsson et al., 2005), both of which indicated that parental psychosis increased the odds of offspring having ASD. The co-occurrence of psychotic disorders and ASD in families raises the question of whether these two spectrum disorders share a common genetic pathogenesis.

Research findings regarding shared genetic vulnerabilities between schizophrenia and ASD have accumulated in recent years, especially when the story of *de novo* (non-inherited) mutations began to unfold. Rare copy number variants (CNVs), for instance, are believed to be risk factors for various neurodevelopmental disturbances (Cook & Scherer, 2008). CNVs are segments of DNA in which copy number changes have occurred through duplications, insertions, deletions, or other allelic rearrangements (Redon et al., 2006). Studies have shown that several CNVs may be risk factors for both ASD and psychotic disorders such as schizophrenia (Awadalla, et al., 2010; Burbach & van der Zwaag, 2009; King & Lord, 2010). Examples include the 15q13.3 deletion

(Pagnamenta et al., 2009; Stefansson et al., 2008), 16p11.2 deletions and duplications (McCarthy et al., 2009; Weiss et al., 2008), disruptions in Neurexin 1 (NRXN1; Kim et al., 2008; Kirov et al., 2009) and 22q11.2 deletions. For a more detailed review, please see Carroll & Owen (2009). The 22q11.2 deletion is one of the most studied chromosomal abnormalities in relation to psychosis and ASD. 22q11DS occurs in approximately 1 out of every 4,000 births (Wilson et al., 1994) and presents variable physical phenotypes, including heart defects, cleft palate, immune deficiencies, skeletal abnormalities, and minor facial anomalies (Esterberg, Ousley, Cubells, & Walker, 2013). Individuals with 22q11.2 deletion syndrome (22q11DS) have shown to be at a heightened-risk of developing psychosis and ASD as well as experiencing subclinical symptoms of both disorders. In a sample of adolescents with 22q11DS, 45% experienced attenuated psychotic symptoms, 85% endorsed moderate negative symptoms, 55% experienced disorganized symptoms, and 25% had a diagnosis of ASD (Stoddard, Niendam, Hendren, Carter, & Simon, 2010. When examined for prodromal symptoms, 60% of the 22q11DS individuals met criteria for being at clinical high-risk of developing psychosis (Shapiro, Cubells, Ousley, & Walker, 2011). Given the high percentage of individuals with 22q11DS endorsing psychotic symptoms or meeting criteria for the prodrome, it is of no surprise that several studies have shown that around 30% of individuals with 22q11DS developed psychosis (Antshel et al., 2010; Gothelf et al., 2007; Kates et al., 2011, Murphy & Owens, 2001). Vorstman and colleagues (2006) reported that more than 11% of their sample were diagnosed with a psychotic disorder, whereas more than half had ASD. In some cases, individuals with 22q11DS have comorbid diagnoses of both psychosis and ASD. Ousley and colleagues (2013) indicated that 40%

of their 22q11DS sample that met criteria for ASD also met criteria for a schizophrenia spectrum disorder. However, using more stringent diagnostic criteria for ASD revealed only a 20% comorbidity rate. In addition, Esterberg and colleagues (2013) found that individuals with 22q11DS were more likely endorse communication impairments typical of individuals with ASD than controls. Overlapping psychotic and autistic symptomology in 22q11DS emphasizes the need to understand the etiological commonalities between psychosis and ASD using a prospective developmental psychopathology framework.

Karayigorgou and colleagues (2010) hypothesize that autistic behaviors in children with 22q11DS are actually prodromal-like symptoms that precede the later onset of psychosis. It is also possible that these shared genetic underpinnings, yet differing developmental trajectories, in ASD and psychosis are a result of neuropsychiatric pleiotropy, which occurs when a single genetic variant results in two or more divergent phenotypic manifestations. Vortsman and colleagues (2013) found that 22q11DS patients with ASD were not more likely to develop psychosis in adulthood compared to 22q patients without ASD. These results suggest that ASD and psychosis in 221q11DS represent two distinct phenotypic expressions consistent with the idea of neuropsychiatric pleiotropy. However, this study was retrospective regarding autistic symptoms in childhood, and therefore, a longitudinal design is needed in order to fully answer the question of pleiotropy regarding psychosis and ASD.

Consistent with the neurodevelopmental hypothesis, both psychosis and ASD are associated with various prenatal, perinatal, and environmental risk factors. Some of these risk factors known to be linked with both spectra include fetal hypoxia (Clarke, Harley, & Cannon, 2006; Glasson et al., 2004), prenatal maternal exposure to stressful life events

(e.g., natural disasters), obstetric complications, low birth weight (Rapoport, Gied, & Gotgay, 2012), increases in maternal levels of cytokine tumor necrosis factor-alpha (Abadallah et al., 2013; Buka et al., 2001), increased IgG antibody to *Toxoplasma gondii* (Brown et al., 2005; Grether, Croen, Anderson, Nelson, Yolken, 2010; Mortensen et al., 2007), and prenatal exposure to rubella (Kinney, Munir, Crowley, & Miller, 2008; Verdoux, 2004).

In addition to these prenatal risk factors, risk can begin even in the pre-zygotic period. Numerous studies have revealed that risk for both schizophrenia and ASD increases significantly with the father's age at conception (Brown et al., 2002; Croen, Najjar, Fireman, & Grether, 2007; Kong et al. 2012; Lampi et al., 2013; Malaspina et al., 2001). It appears that as men age, the number of *de novo* mutations in sperm increase in a linear fashion, which in turn increases the likelihood of offspring carrying a mutation that could lead to schizophrenia or ASD (Kong et al., 2012).

In sum, these findings regarding shared genetic, perinatal, and environmental risk factors in autism and psychosis highlight the need for advancing our understanding of how, in terms of the etiology, shared risk factors progress to heterogeneous clinical syndromes.

Developmental Links

Given the risk factors discussed above, it is of no surprise that psychosis and ASD co-occur in some individuals. Volkmar and Cohen (1991) initially reported that the prevalence of schizophrenia was no higher in an ASD sample than in the general population, although more recent studies have shown evidence to the contrary. Although few studies have followed individuals with ASD longitudinally, a recent review

conducted by de Lacy and King (2013) reported that 7-50% went on to develop schizophrenia or another psychotic disorder. In a case control study using a psychiatric register to examine children diagnosed with ASD, 5.8% received a later diagnosis of schizophrenia or another psychotic disorder with an average observation period of 32.5 years (Mouridsen, Rich, Isager, & Nedergaard, 2008). This lower prevalence rate compared to the findings of de Lacy and King (2013) may be due to the limitations of using a psychiatric register or to changes in diagnostic criteria. It is possible that some individuals without updated records may have received a psychotic disorder diagnosis. In a sample of adults with ASD, 14.8% met criteria for schizophrenia or another psychotic disorder, again highlighting symptom overlap and co-occurrence (Stahlberg, Soderstrom, Rastam, & Gillberg, 2004). Moreover, the presence of childhood autistic features has been associated with increased psychotic experiences later on in early adolescence (Bevan Jones, Thapar, Lewis, & Zammit, 2012; Sullivan, Rai, Goulding, Zammit, & Steer, 2013). Using the Avon Longitudinal Study of Parents and Children (ALSPC), researchers examined a population-based birth cohort of 6,439 children born between 1991-1992 in Avon, United Kingdom. Bevan and colleagues (2012) found that children endorsing early autistic traits, specifically deficits in communication and odd rituals or unusual behaviors by the age of 7, were at a greater risk of developing psychotic experiences at the age of 12. Seeking to replicate these findings, Sullivan and colleagues (2013) took an additional step by examining children with an ASD diagnosis in addition to those who endorsed autistic traits. An ASD diagnosis increased the likelihood of psychotic experiences nearly three-fold (odds ratio = 2.81, 95% confidence interval = 1.70, 7.34) at 12 years of age. Childhood autistic traits (e.g., social and communication

impairments, restricted interests, and stereotyped behavior), which were assessed through maternal report up to when the child was nine years old, also increased the likelihood of psychotic experiences at 12 years of age (odds ratio = 1.15, 95% confidence interval = 1.05, 1.26). In sum, these results indicate that ASD is associated with increased risk of subsequent psychotic symptoms.

Childhood onset schizophrenia (COS), defined as an onset before the age of 13 and extremely rare in prevalence, is often comorbid with ASD (Rapoport et al., 2009). Prior to the onset of psychosis in COS, it has been observed that many of these children display developmental disturbances characteristic of ASD in communication, motor development, and social relatedness (Algahband-Rad et al., 1995; Hollis & Rapoport, 2008). In a study conducted at UCLA, 39% of their COS sample endorsed autistic symptoms prior to the onset of schizophrenia. Using DSM-III-TR criteria (Spitzer, Williams, Gibbon, & First, 1990) 55% met criteria for autistic disorder or PDD-NOS (Watkins, Asarnow, & Tanguay, 1988). Additionally, Cannon and colleagues (2002) found that substantial impairments in neuromotor, receptive language, and cognitive development were present only among ASD children who went on to develop a schizophrenia spectrum disorder. Furthermore, these developmental impairments predicted psychotic symptoms at 11 years old. Early findings from a National Institute of Mental Health study examining COS indicate that 28% of the children met criteria for PDD-NOS and exhibited an inability to develop reciprocal social behaviors distinct from their later psychotic symptoms (Rapoport et al., 2009). These findings illustrate the difficulties in drawing clear-cut lines between ASD and SSD, especially in younger populations.

A unique model has been proposed that may explain a developmental continuum between COS and ASD. Multiple Complex Developmental Disorder (MCDD), believed to be a subtype of PDD-NOS, is characterized by affect dysregulation, anxiety, social impairment, and thought disorder early on in childhood (Sprong et al., 2008; Towbin, Dykens, Pearsons, & Cohen, 1993). Individuals with MCDD appear to be at a greater risk of developing psychosis. Van Engeland and Van der Gaag (1994) found that 22% of children with MCDD who were followed until adolescence, and 64% who were followed until adulthood, developed psychosis. Results from a more recent study indicate that 78% of adolescents with MCDD met criteria for a psychosis-risk syndrome (clinical high-risk (CHR); Sprong et al., 2008). No differences were found between the MCDD group and a separate help-seeking CHR sample in terms of thought perception, motor functioning, schizotypal traits, disorganized, and general prodromal symptoms. The help-seeking CHR group, did however, endorse significantly more positive and negative symptoms while the MCDD group showed more autistic traits. These preliminary findings suggest there to be a phenotypic developmental pathway from the autism spectrum to later psychosis in some individuals. This warrants further examination in order to determine the relation of ASD with the development of psychosis.

Examining ASD in the Prodrome

Findings in the current literature stress the need for additional investigations into the development of psychosis among individuals with a history of ASD. Specifically, prospective studies that follow youth with an autism diagnosis in adolescence and young adulthood might shed light on how clinical symptomatology changes throughout development with the onset of psychotic symptoms. Exploring the role of ASD within the

prodrome of psychosis serves as one possible avenue to help further elucidate etiological and developmental links between the ASD and psychotic disorders. The prodrome, a phase of functional decline and attenuated psychotic symptoms that arises prior to the onset of psychosis (Cannon et al., 2008), could potentially be a crucial period for examining the relation of ASD with the development of psychosis. The prodromal period typically has its onset in adolescence or early adulthood.

Currently, the Structured Interview for Prodromal Syndromes (SIPS; McGlashan, Miller, Woods, Hoffman, & Davidson, 2001) is the most widely used assessment tool for determining whether individuals meet CHR criteria for the prodrome. The SIPS is used to determine CHR criteria through a clinical assessment of positive, negative, disorganized, and general symptomatology. Of those who meet CHR criteria using the SIPS, 25-35% go on to develop a psychotic disorder within two years (Cannon et al., 2008). However, little is known how an early developmental history of autistic features might influence the prodromal clinical presentation. Given the complex etiology of psychosis, it is assumed that there are multiple etiologic subtypes or developmental pathways. Given that retrospective have found 7-50% of individuals with ASD developed a psychotic disorder (de Lacy & King, 2013), it is possible that an early history of ASD is associated with one or more of these developmental pathways, manifesting in clinical and functional presentation. Examining the prevalence of ASD within a sample of CHR youth and whether this early developmental history is related with CHR symptomatology and functioning could aid in our understanding of the developmental trajectory for those with comorbid presentations. Moreover, studies of individuals in the prodrome with and without ASD help eliminate age differences and retrospective research strategies that

have plagued previous studies directly comparing the two disorders (Sasson et al., 2011). The prodrome also represents a favorable period for targeted interventions.

The present study investigates whether a childhood diagnosis of ASD has implications for prodromal symptomatology (i.e., attenuated positive and negative symptoms), premorbid adjustment, and current functioning in a large sample of CHR youth. Given early developmental deficits and symptoms that previous research has shown to overlap with negative symptoms of schizophrenia, it is hypothesized that CHR youth with a history of ASD will endorse significantly more negative symptoms: social anhedonia, reduced expression and experience of emotion, decreased ideational richness, and occupational functioning. There is no empirical support that suggests youth with ASD experience decreased motivation, thus no differences are expected between the two CHR groups. No differences in positive prodromal symptoms are predicted, given that CHR status is defined on the basis of attenuated positive symptoms, thus restricting the range. Because features of autism and their associated impairments manifest at an earlier age, it is also hypothesized that CHR youth with an ASD diagnosis will exhibit greater impairments in premorbid functioning, both in childhood and in early adolescence, compared to CHR youth without an ASD diagnosis. Earlier developmental disturbances and maladjustment will also manifest in poorer current social and role functioning for the ASD group.

Method

Participants

The present study consists of participants enrolled in the North American Prodrome Longitudinal Study (NAPLS) II, a multisite longitudinal study of youth at

clinical high-risk (CHR) for psychosis (Addington et al., 2012). Eight research sites (Emory University, Harvard University, Zucker Hillside Hospital, Yale University, the University of California at San Diego, the University of California at Los Angeles, the University of Calgary, and the University of North Carolina at Chapel Hill) constitute the NAPLS consortium, which aims to identify biological and clinical predictors of the development of psychosis. Participants were recruited through referrals from clinical practitioners as well as media announcements. Exclusion criteria were, 1) being outside the age of 12-35 years old, 2) meeting diagnostic criteria for an Axis I psychotic disorder, 3) having an IQ below 70, a current or lifetime history of a central nervous system disorder that accounts for the symptomatology (e g., epilepsy, documented brain trauma), or a substance abuse disorder six months prior to baseline assessment. More details on participant recruitment are reported elsewhere (Addington et al., 2012).

The total CHR sample consisted of 764 participants (436 males, 328 females) ranging from 12 to 35 years of ages (M=18.5, SD=4.23). These participants were 57% Caucasian, 15.4% Black, 8% Asian, 1.7% Native American, and 12.7% Interracial. Additionally, 18.6% identified as Hispanic. (For a detailed description of the recruitment procedures and sample characteristics, see Addington et al., 2012.)

Information on previous psychiatric diagnoses was obtained through medical history information provided by informants, both the participant and, in the case of minors, their parents as well as administration of the Structured Clinical Interview for DSM-IV (SCID-IV; First, Spitzer, Gibbons, & Williams, 2002). Because ASD is typically diagnosed in early childhood, the criteria for inclusion in the ASD+ group was either a reported medical history of an ASD diagnosis and/or evidence from the SCID

that the individual likely met criteria for an ASD. Twenty-five of the CHR participants (3 males, 22 females) reported receiving a previous autism spectrum diagnosis. Twenty-five participants without a previous ASD diagnosis were selected to match the ASD+ group on age, sex (88% male), years of education, and racial/ethnic background (74% Caucasian).

Measures

Prodromal Symptomatology. The Structured Interview for Prodromal Syndromes (SIPS; McGlashan, Miller, Woods, Hoffman, & Davidson, 2001) is a semi-structured diagnostic interview used to assess prodromal symptomatology (e.g., positive, negative, disorganized, and general symptoms). Positive symptoms are used to determine whether or not an individuals meets clinical high-risk criteria (CHR) for psychosis. Each symptom is rated from 0 to 6. Zero to two is characterized as normal/subsyndromal, three to five indicates a prodromal level/CHR status, and six suggests conversion to psychosis. The SIPS has shown to have good inter-rater reliability (ICC=0.75-0.95) and predictive validity in identifying those at risk for psychosis (Miller et al., 2003). Trained interviewers who met reliability standards for NAPLS conducted the interviews (Addington et al., 2012). A prodromal syndrome was diagnosed if an individual met one of the following criteria: 1) manifested a rating of 6 on a positive symptom in the past 3 months, but did not meet criteria for a psychotic disorder (i.e., Brief Intermittent Psychotic Syndrome; BIPS); 2) received at least one rating of 3, 4, or 5 on a positive symptom (i.e., Attenuated Positive Symptom Syndrome; APSS), 3) had a first degree relative with a nonaffective psychotic disorder and has shown a functional decline over the past year (i.e., Genetic Risk and Deterioration Syndrome; GRDS), or 4) were >18

years of age at baseline and met criteria for Schizotypal Personality Disorder (SPD). CHR individuals can meet criteria for more than one prodromal syndrome.

Premorbid Functioning. The Premorbid Adjustment Scale (PAS; Cannon-Spoor, Potkin, & Wyatt, 1982) is a clinician-rated 28-item scale used to evaluate the degree of achievement of developmental goals at several periods of an individual's life. It assesses functioning in five domains (i.e., social accessibility-isolation, development of appropriate peer relationships, adaptation to school, academic performance, and the capacity to form intimate socio-sexual ties) across four life periods: childhood (up to 11 years of age), early adolescence (ages 12-15), late adolescence (ages 16-18), and adulthood (19 years and above). The scores range from 0 (healthiest adjustment) to 6 (unhealthiest adjustment). The PAS has shown good internal consistency with Cronbach's alpha at 0.80+ and good validity in a sample of schizophrenia spectrum patients (Krauss, Marwinski, Held, Rietschel, Freyberger, 1998).

Current Functioning. The Global Functioning: Social and Role Scales (GF:S and GF:R; Cornblatt et al., 2007) are clinician-rated scales used to assess functioning with age and phase of illness taken into account. The GF:S assess quantity and quality of peer relationships, level of peer conflict, age-appropriate intimate relationships, and involvement with family members. The GF:R assesses the level of functioning based on the primary role of the participant (student, employee, or homemaker). For both scales, total scores range from 1 (extreme dysfunction) to 10 (superior functioning). Both measures showed good reliability, construct validity, and convergent validity as they correlated with established measures of functioning (Cornblatt et al., 2007).

Procedure

The same measures and procedures were utilized at all eight NAPLS research sites. An initial screening interview was conducted using the SIPS. Once study inclusion diagnosis and other criteria were established over a consensus clinical conference call, participants were enrolled for the baseline assessment. The present study focuses on data collected during the screening and baseline assessments. A detailed description of the study protocols and procedures is presented elsewhere (Addington et al., 2012).

Analytic Strategy

Data analyses were conducted using IBM SPSS 21.0. Analyses of variance (ANOVA) and covariance (ANCOVA), as well as between-subjects independent samples t-tests tested group differences in demographic characteristics, prodromal symptomatology, and premorbid functioning. Two different analytic approaches were used to test the hypotheses. The first was a matched-group comparison approach, with CHR youth with a previous ASD diagnosis (ASD+) and CHR youth without a previous ASD diagnosis (ASD-), matched on number of participants in each group, sex, age, and years of education. In the unmatched group analyses, ASD+ participants were compared with the entire sample of ASD- CHR participants, and age and years of education were used as covariates. For hypothesis testing, a *p*-value of less than 0.05 was considered significant.

Results

Demographic Characteristics

Chi-square analysis revealed a significant difference in sex between the ASD+ and ASD- CHR subjects; those in the ASD+ group were significantly more likely to be male than the ASD- group, $c^2(1, N=764) = 10.09$, $p=0.001$. This is consistent with an

extensive body of literature indicating a higher rate of ASD in males than females. Similarly, as would be expected, there were significant differences between the ASD+ and ASD- CHR groups in years of education, $t(756)=-2.62$, $p=0.009$, and age, $t(762)=-2.15$, $p=0.032$. The ASD- CHR group was older and completed more years of education. There were no significant differences in racial/ethnic backgrounds.

Group Differences in Prodromal Symptomatology

Given the differences in demographic characteristics, the analyses were conducted using two analytic approaches as described above (see analytic strategy subsection). In the unmatched groups, age and participant years of education were covariates. Multivariate analysis of covariance (MANCOVA) using Pillai's trace revealed no significant overall effect of ASD group status (i.e., ASD or no ASD diagnosis) on positive prodromal symptoms, $V = 0.006$, $F(5,749) = 0.945$, $p = 0.451$. However, MANCOVA using Pillai's trace revealed a significant overall effect of ASD group status on negative prodromal symptoms, $V = 0.036$, $F(6,727) = 4.563$, $p < 0.001$. Follow-up univariate analyses revealed significant differences between the ASD+ and ASD- CHR groups in social anhedonia, $F(1,732) = 13.42$, $p < 0.001$, and ideational richness, $F(1,732)$, $p = 0.040$. The ASD+ CHR group endorsed greater severity of social anhedonia and greater decreased ideational richness. No significant differences were observed in avolition, $F(1,732)$, $p = 0.819$, expression of emotion, $F(1,732)$, $p = 0.784$, experience of emotion and self, $F(1,732)$, $p = 0.073$, or occupational functioning, $F(1,732)$, $p = 0.322$, between the ASD+ and ASD- CHR groups. Please refer to Figure 2 in the Appendix for a graphical display.

In the matched group analyses, MANOVA using Pillai's trace revealed no significant overall effect of ASD group status on positive prodromal symptoms, V = 0.076, $F(5,44) = 0.945$, p =0.606. Consistent with the first analytic approach, the overall MANOVA testing differences in positive prodromal symptoms was significant, V = 0.362, $F(6,43) = 4.07$, p =0.003. Separate univariate ANOVAs demonstrated significant group differences, as the ASD+ CHR group endorsed higher levels of social anhedonia, $F(1,48) = 12.15$, $p = 0.001$, and decreased ideational richness, $F(1,48) = 5.64$, $p = 0.022$. No significant differences were observed in avolition, $F(1,48)$, $p = 0.850$, expression of emotion, $F(1,48)$, $p = 0.803$, experience of emotion and self, $F(1,732)$, $p = 0.282$, or occupational functioning, $F(1,732)$, $p = 0.443$, between the ASD+ and ASD- CHR groups.

In sum, the ASD+ CHR group endorsed significantly greater severity of social anhedonia and decreased ideational richness than the ASD- CHR group. There were no significant differences in positive symptoms.

Group Differences in Premorbid Functioning

Multivariate analyses of covariance (MANCOVA) were conducted to examine possible differences in premorbid functioning between CHR youth with and without an ASD diagnosis in childhood and early adolescence in the unmatched groups. MANCOVA using Pillai's trace revealed a significant overall effect of ASD group status on premorbid adjustment in childhood, $V = 0.030$, $F(6,727) = 5.430$, $p < 0.001$. Follow up univariate analyses reveled that CHR participants with an ASD diagnosis endorsed greater impairment in sociability, $F(1,703) = 11.73$, $p = 0.001$, development of appropriate peer relationships, $F(1,703) = 14.71$, $p < 0.001$, scholastic performance,

$F(1,703) = 3.90$, $p = 0.049$, and adaptation to school, $F(1,703) = 12.12$, $p = 0.001$, compared to CHR youth without an ASD diagnosis in childhood.

For the matched group analyses, independent samples t-tests were conducted. The ASD group reported worse adjustment in sociability, $t(48) = -2.290$, $p = 0.026$, development of appropriate peer relationships, $t(48) = -2.024$, $p = 0.049$, and adjustment to school, $t(48) = 0.044$, $p = 0.044$. In contrast to the unmatched groups, no differences were evident in scholastic performance, $t(48) = -1.152$, $p = 0.255$.

For early adolescence, MANCOVA using Pillai's trace revealed a significant overall effect of ASD group status on premorbid adjustment in early adolescence, $V = 0.074$, $F(5,693) = 11.000$, $p = 0.000$. Follow up univariate analyses revealed significant differences in sociability, peer relationships, adaptation to school, and in social-sexual life, but not scholastic performance in the unmatched groups. CHR youth with an ASD diagnosis endorsed greater impairment in sociability, $F(1,697) = 18.19$, $p < 0.0001$, development of appropriate peer relationships, $F(1,697) = 41.03$, $p = 0.000$, adaptation to school, $F(1,697) = 9.03$, $p = 0.003$, and social-sexual life, $F(1,697) = 21.05$, $p < 0.00001$. There was no observed difference between the groups in scholastic performance, $F(1,700) = 0.148$, $p = 0.700$.

In the matched groups, the ASD group endorsed greater impairment in sociability, $t(47) = -2.588$, $p = 0.013$, development of appropriate peer relationships, $t(47) = -4.044$, $p < 0.001$, and social-sexual life, $t(47) = -2.410$, $p = 0.020$. No differences were evident in adaptation to school, $t(47) = -1.307$, $p = 0.198$, or scholastic performance, $t(47) = 1.486$, $p = 0.144$.

In sum, the ASD+ CHR group endorsed significantly more impairment in sociability, development of appropriate peer relationships, and adaptation to school in childhood across both analytic approaches. However, in the unmatched analyses, the ASD+ CHR group also endorsed more impairment scholastic performance. For early adolescence, the ASD+ CHR group endorsed greater impairment in sociability, development of appropriate peer relationships, and social-sexual life using both analytic approaches. The two approaches differed, however, as the ASD+ CHR group endorsed more impairment in adaptation to school in the unmatched, but not matched-group approach.

Group Differences in Current Functioning

ANCOVAs were conducted to test whether there were differences in current social and role functioning between the ASD+ and ASD- CHR groups. In the unmatched groups, the ASD+ group exhibited greater impairment in social functioning, $F(1,553) = 16.98$, $p < 0.0001$, with age and participant years of education as the covariates. However, no differences were evident between the two groups in role functioning, $F(1,552) = 1.116$, $p = 0.291$.

For the matched groups, independent samples t-tests were used to determine whether there were significant group differences. Consistent with the unmatched group results, the ASD+ group exhibited greater impairment in social functioning, $t(47) = 3.995$, $p < 0.001$. There were no differences between the two groups in role functioning, $t(47) = -0.095$, $p = 0.925$.

Discussion

The present study examined functional and prodromal symptom presentations in CHR youth with and without a previous ASD diagnosis. As hypothesized, CHR youth with an ASD diagnosis endorsed greater severity of social anhedonia and decreased ideational richness. No differences were evident in attenuated positive symptoms. ASD+ youth also exhibited worse premorbid adjustment in the domains of sociability, development of appropriate peer relationships, scholastic performance, and adaptation to school in childhood. In early adolescence, CHR youth with an ASD diagnosis endorsed greater impairment in sociability, development of appropriate peer relationships, adaptation to school, and social-sexual life, but not scholastic performance. Additionally, worse current social functioning was observed in the ASD group, but no differences were evident in current role functioning. These results were consistent using two different analytic approaches (i.e., matched groups and unmatched groups using the entire NAPLS CHR sample) for symptoms and current functioning, but there were slight differences in the results yielded by the two analytic approaches for premorbid functioning. This might be due to the fact that the matched groups analyses eliminated important variance.

Developmental Pathways to Psychosis: Evidence of Equifinality?

These findings indicate that although CHR youth with an ASD diagnosis do not present different positive symptoms profiles, they exhibit elevated levels of negative symptoms and greater functional impairments, particularly in the social domain, evident from childhood (i.e., before the age of 11). Earlier functional impairments and younger age at ascertainment for prodromal symptoms indicate a different developmental course for CHR youth with a history of autistic features. These results are consistent with the notion of equifinality, which assumes that multiple pathways can result in the same

behavioral outcome in terms of attenuated positive symptoms (Cicchetti & Rogosch, 1996). Thus, CHR youth with an ASD diagnosis may represent a different developmental pathway to psychosis, which manifests in worse premorbid adjustment and impaired functioning in early childhood, yet results in a similar presentation of attenuated positive symptoms in adolescence.

Nonspecific risk factors of this differing developmental pathway that increase risk for autism might later interact with disruptions in adolescent hormonal and neuromaturational processes giving rise to psychosis. Some of these nonspecific factors that influence this pathway are likely genetic variants. Some findings from recently published genetic research offer new perspectives on potential nonspecific determinants of risk for psychosis and ASD. Recent evidence suggests that segments of DNA that have undergone accelerated change in the human genome subsequent to divergence from non-human primates, may be implicated in the pathogenesis of schizophrenia (Xu, Schadt, Pollard, Roussos, & Dudley, 2015) and autism. Specifically, both disorder spectra appear to involve common genetic variants and rare, or *de novo*, mutations in regions of the genome that determine higher-level cognitive processes in humans (Clarke et al., 2015). These findings highlight the need for further investigation at multiple levels of analysis in order to identify specific and nonspecific risk factors, and to determine whether childhood ASD represents a distinct developmental pathway to psychosis.

Anhedonia and the Autism Spectrum

The present findings also shed light on our understanding of anhedonia among individuals with ASD, an area of that has received little attention in autism research. With the ASD+ CHR endorsing significantly greater levels of social anhedonia than the ASD-

group, the results corroborate the few previously published studies demonstrating elevated levels of anhedonia, particularly social anhedonia, in individuals with ASD. In a study investigating self-reported experiences of pleasure in samples of adolescents with and without ASD, no significant differences were evident in the experience of physical pleasure between the groups. However, adolescents with ASD reported experiencing significantly less pleasure from social situations, suggesting heightened levels of social anhedonia (Chevallier, Grèzes, Molesworth, Berthoz, & Happé, 2011). In contrast, Berthoz, Lalanne, Crane, and Hill (2013) found that adults with ASD endorsed both greater physical and social anhedonia. The results from the current study as well as the two previous studies investigating anhedonia in autism support the social motivation theory of autism, which posits that disruption of social motivation mechanisms constitutes the primary social deficits in autism, and has a downstream effects leading to impaired social cognitive abilities (Chevallier, Kohls, Troiani, Brodkin, & Schulz, 2012). Evidence of impaired social orienting (Klin, Jones, Schultz, Volkmar, & Cohen, 2002), decreased seeking and liking social interactions (Chevallier et al., 2011; Demurie, Roeyers, Baeyens, & Sonuga-Barke, 2011; Lekam & Ramsden, 2006) and less use of social maintaining behaviors (Barbaro & Dissanayke, 2007; Hobson & Lee, 1998) corroborates the claim of disrupted social motivation in individuals with ASD. The present study's findings regarding differences between the ASD+ and ASD- groups in social, but not role functioning, suggest that motivational deficits in autism might be particular to social domains. This is further corroborated by there being no evident differences between the two groups in avolition, which primarily assesses decreased motivation in completing daily activities (e.g., schoolwork, chores, etc.).

Future research may want to integrate behavioral and neurobiological components of the social motivation theory of autism with models of negative symptoms in schizophrenia, particularly the pleasure and motivation dimension. Kring and Barch (2014) recently provided a comprehensive review of the pleasure and motivation dimension of negative symptoms and their possible neural substrates. Translating their model of the temporal experience of emotion and reward processing to individuals with autism may elucidate common neural mechanisms implicated in social deficits that are disrupted in both populations. It would beneficial for future research to investigate the mechanisms that underlie negative symptoms and functional deficits in CHR youth with ASD given their comorbid clinical presentation.

Negative Symptoms and their Implications for Treatment

The present study findings point to the need for further examination of factors that influence the presentation of negative symptoms during the CHR period. A prior NAPLS investigation revealed that negative symptoms are predictive of conversion to psychosis, in that they are more severe and persistent among CHR youth who convert (Piskulic et al., 2012). The present results regarding the ASD+ CHR group endorsing both elevated social anhedonia and worse premorbid adjustment are also consistent with the literature on schizophrenia, in which poorer premorbid adjustment, particularly in sociability and withdrawal, was associated with more severe negative symptoms (Strous, et al., 2004). Moreover, greater severity of negative symptoms, particularly social anhedonia, carries significant treatment implications, as socially anhedonic individuals report more family conflict and poorer social support (Blanchard et al., 2011). Notably, Strous and colleagues also found that poorer premorbid adjustment was associated with increased

time to treatment response. In CHR samples, it is often the negative symptoms and decline in functioning, rather than attenuated positive symptoms, that lead individuals to seek mental health treatment (Lencz, Smith, & Auther, Correll, & Cornblatt, 2004; Yung & McGorry, 1996).

With this knowledge, treatment providers should identify youth with autism spectrum conditions who are exhibiting attenuated psychotic symptoms for early interventions that particularly focus on improving daily and social cognitive functioning. It is possible that social interventions typically used with youth with ASD could also be beneficial for those that are exhibiting attenuated psychotic symptoms given the social deficits that often precede symptoms. Relatedly, the present study's findings regarding decreased ideational richness in the ASD group suggests greater cognitive impairments. It will be important for future research to investigate possible differences in neuropsychological functioning between the two CHR groups. Social cognition may be an important therapeutic target as previous studies have demonstrated that social cognition has a greater influence on functional outcomes than neurocognition (Fett et al., 2011). Moreover, there is even evidence to suggest that social cognition mediates the relationship between neurocognition and functioning in both chronic (Addington, Saeedi, & Addington, 2006a; Sergi, & Rassovsky, Nuechterlein, & Green, 2006) and first-episodes psychosis (Addington, Saeedi, & Addington, 2006b). This has yet to be examined, however, in CHR or ASD samples.

Strengths & Limitations

There are several notable strengths of the present study. To date, this is the largest sample of youth at CHR for psychosis. As a result, there was sufficient statistical power

to detect small effects. Additionally, to our knowledge this was the first prospective longitudinal study to compare the symptoms and developmental history of CHR individuals with previous ASD. Previous studies that have examined the presence of psychotic symptoms in the autism spectrum have been limited by their retrospective designs.

In addition to the strengths, there are also several factors that should be considered when interpreting the results of the study. Because the larger NAPLS II study was not initially designed to answer questions regarding childhood onset disorders, neither past medical records formally documenting ASD or thorough retrospective diagnostic assessments were conducted. It also possible, of course, that other participants without previous or current ASD syndromes could have met diagnostic criteria for ASD. At the same time, however, not all individuals who manifest ASD spectrum symptoms have received comprehensive and rigorous assessments in childhood, thus our sample may be more representative of the ASD spectrum in the general community, rather than those who underwent formal diagnostic assessments.

Conclusions

Investigating the co-occurrence of ASD within the prodromal phase of psychosis will provide a unique opportunity to examine mechanisms and other factors implicated in the transition to psychosis. The present study revealed that CHR youth with an ASD diagnosis exhibited greater functional impairments beginning in early childhood and presented with more severe negative symptoms, suggesting a differing developmental pathway to psychosis. These findings highlight the value of further research aimed at examining the neurodevelopmental correlates of ASD+ CHR subjects. The NAPLS

project offers the opportunity to do so. In particular, it is possible that the symptomatic and developmental differences in functioning demonstrated here are linked with differences in brain developmental trajectories, as measured by magnetic resonance imaging (MRI).

Also, to extend the present findings, it is of interest for future research to determine whether social cognitive deficits are associated elevated levels of social anhedonia. Social cognitive impairments may mediate the relation of ASD with elevated social anhedonia in CHR youth. Moreover, an examination into the neural correlates of social deficits could also help elucidate mechanisms involved in the differing functional trajectory and negative symptom presentation. Areas such as the amygdala, hippocampus, fusiform face area, and superior temporal sulcus would be of particular interest given their associations with social cognitive deficits. Finally, further research is needed to determine whether conversion to psychosis is higher in CHR youth with ASD. This would also aid in pursuing one of the chief goals of NAPLS; improving the specificity of prediction algorithms.

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Appendix

Table 1

Demographic Characteristics

Variable		ASD (n = 25)	Non-ASD (n = 739)
Age (Mean ± SD)*		16.72 ± 3.94	18.56 ± 4.23
Years of Education (Mean ± SD)*		9.84 ± 2.84	11.33 ± 2.80
Sex (n, %)*	Male	22 (88%)	414 (56%)
	Female	3 (12%)	325 (44%)
Race (n, %)	Asian	1 (4.0%)	53 (7.17%)
	Black	2 (8.0%)	116 (15.7%)
	Caucasian	18 (72.0%)	419 (56.7%)
	Central/South American	1 (4.0%)	33 (4.47%)
	Middle Eastern	0 (0.0%)	7 (0.95%)
	Native American	1 (4.0%)	12 (1.62%)
	Native Hawaiian or Pacific Islander	0 (0.0%)	3 (0.41%)
	Interracial	2 (8.0%)	95 (12.9%)
	Not Reported	0 (0.0%)	1 (0.14%)

Table 2

Mean Scores and Standard Errors for SIPS Positive Symptoms

Symptom	ASD+ CHR		ASD- CHR	
	M	*SE*	*M*	*SE*
Unusual Thought Content & Ideas	3.34	0.267	3.34	0.049
Suspiciousness and Persecutory Ideas	2.24	0.300	2.78	0.055
Grandiosity	1.20	0.260	0.99	0.048
Perceptual Abnormalities and Hallucinations	3.07	0.299	3.19	0.055
Disorganized Communication	1.90	0.293	1.74	0.054

Note. Scores range from 0 (absent) to 6 (psychotic) on the SIPS. Scores from 3-5 signify a clinical high-risk level symptom. The mean scores and standard errors were adjusted for age and years of education as covariates.

Table 3

Mean Scores and Standard Errors for SIPS Negative Symptoms

Symptom	ASD+ CHR		ASD- CHR	
	M	*SE*	*M*	*SE*
Social Anhedonia	3.60	0.345	2.32	0.064
Avolition	2.53	0.327	2.45	0.061
Expression of Emotion	1.45	0.305	1.36	0.057
Experience of Emotion and Self	1.16	0.337	1.77	0.063
Decreased Ideational Richness	1.68	0.258	1.14	0.048
Occupational Functioning	2.44	0.402	2.85	0.075

Note. Scores range from 0 (absent) to 6 (severe) on the SIPS. 3-5 signifies a clinical high-risk level symptom. The mean scores and standard errors were adjusted for age and years of education as covariates.

Table 4

Mean Scores and Standard Errors Scores Premorbid Adjustment in Childhood

Adjustment Domain	ASD+ CHR		ASD- CHR	
	M	*SE*	*M*	*SE*
Sociability & Withdrawal	2.65	0.320	1.53	0.061
Development of Appropriate Peer Relationships	2.55	0.278	1.46	0.053
Scholastic Performance	2.32	0.296	1.72	0.056
Adaptation to School	1.92	0.246	1.05	0.047

Note. Scores range from 0 (healthiest adjustment) to 6 (unhealthiest adjustment) on the Premorbid Adjustment Scale. Mean scores and standard errors were adjusted for age and years of education as covariates.

Table 5

Mean Scores and Standard Errors for Premorbid Adjustment in Early Adolescence

Adjustment Domain	ASD+ CHR		ASD- CHR	
	M	*SE*	*M*	*SE*
Sociability & Withdrawal	3.41	0.331	1.97	0.063
Development of Appropriate Peer Relationships	3.22	0.272	1.44	0.052
Scholastic Performance	2.36	0.315	2.48	0.060
Adaptation to School	2.67	0.298	1.76	0.057
Social-Sexual Life	3.16	0.324	1.65	0.062

Note. Scores range from 0 (healthiest adjustment) to 6 (unhealthiest adjustment) on the Premorbid Adjustment Scale. Mean scores and standard errors were adjusted for age and years of education as covariates.

Table 6

Mean Scores and Standard Errors for Current Social and Role Functioning

Functioning Domain	ASD+ CHR		ASD- CHR	
	M	*SE*	*M*	*SE*
Social Functioning	4.91	0.328	6.31	0.092
Role Functioning	5.62	0.442	6.10	0.125

Note. Scores range from 0 (extremely poor functioning) to 10 (optimal level of functioning) on the Global Functioning Social and Role Scales. These scores were determined at baseline. Mean scores and standard errors were adjusted for age and years of education as covariates.

Figure 1

Group mean differences in attenuated positive symptoms between CHR youth with (ASD+) and without (ASD-) an ASD diagnosis.

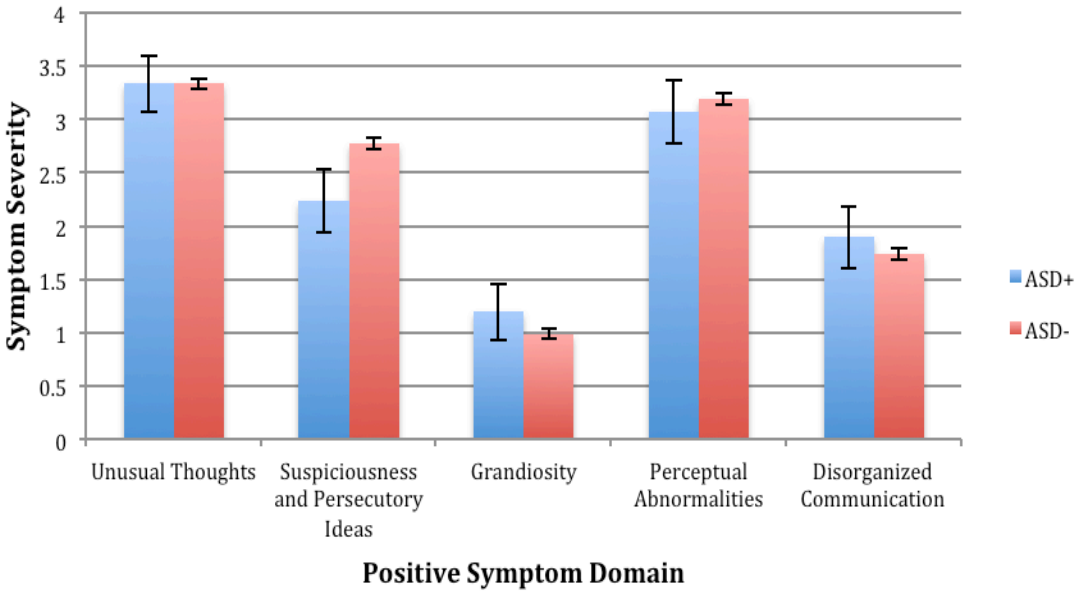

Figure 1. The means reflected in this group were adjusted for age and years of education as covariates.

Figure 2

Group mean differences in negative symptoms between CHR youth with (ASD+) and without (ASD-) an ASD diagnosis.

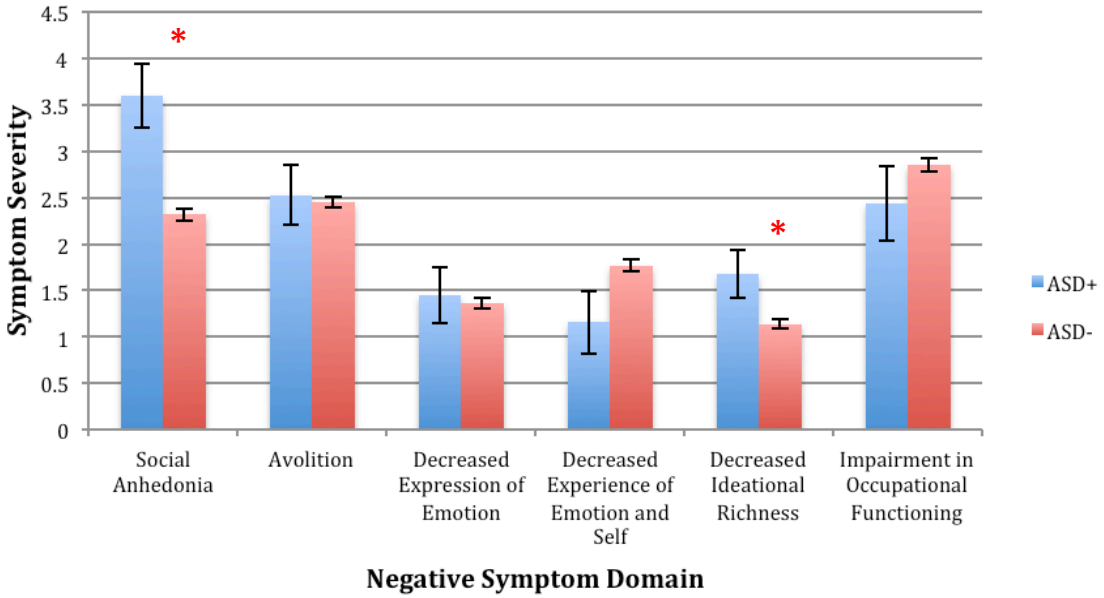

Figure 2. The means reflected in this group were adjusted for age and years of education as covariates.

Figure 3

Group Mean Differences in Childhood Premorbid Functioning between CHR Youth with an ASD (ASD+) and without (ASD-) an ASD Diagnosis.

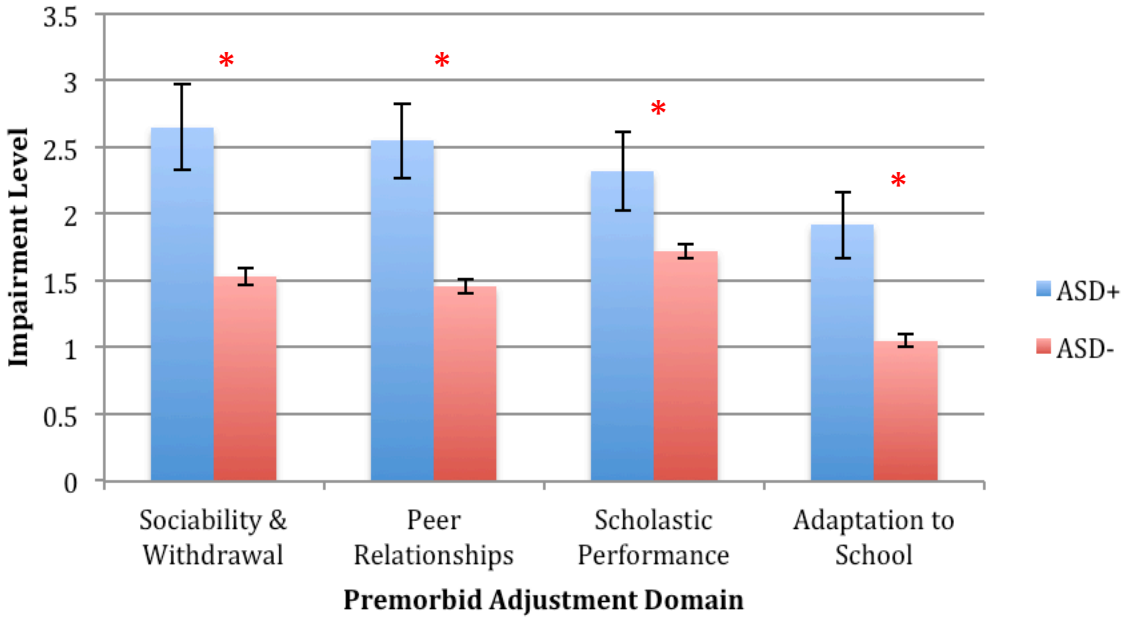

Figure 3. The means reflected in this group were adjusted for age and years of education as covariates.

Figure 4.

Group Mean Differences in Early Adolescent Premorbid Functioning between CHR Youth with an ASD (ASD+) and without (ASD-) an ASD Diagnosis.

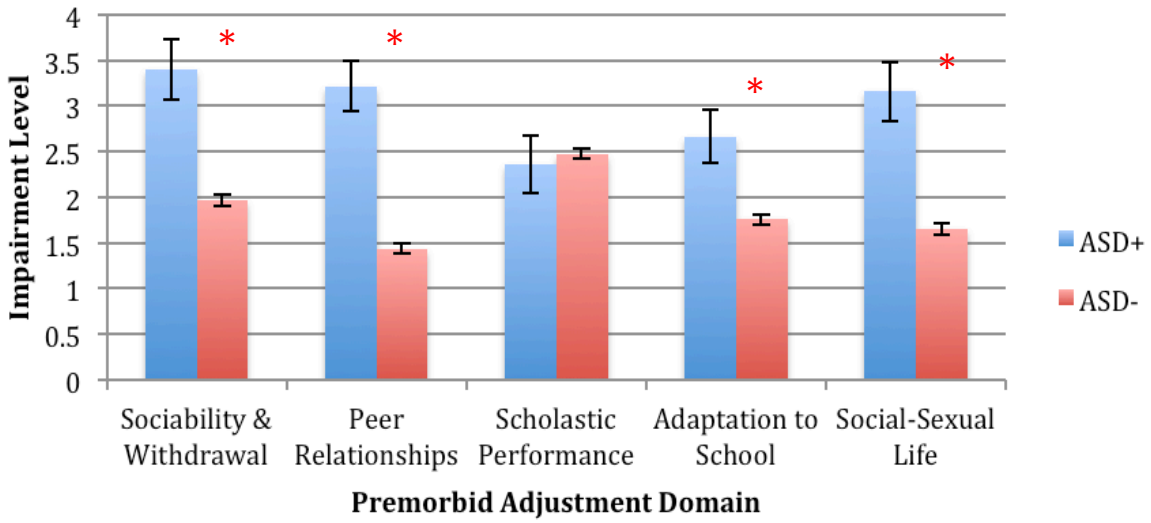

Figure 4. The means reflected in this group were adjusted for age and years of education as covariates.

Figure 5

Group Mean Differences in Current Social and Role Functioning between CHR youth with (ASD+) and without (ASD-) an ASD Diagnosis.

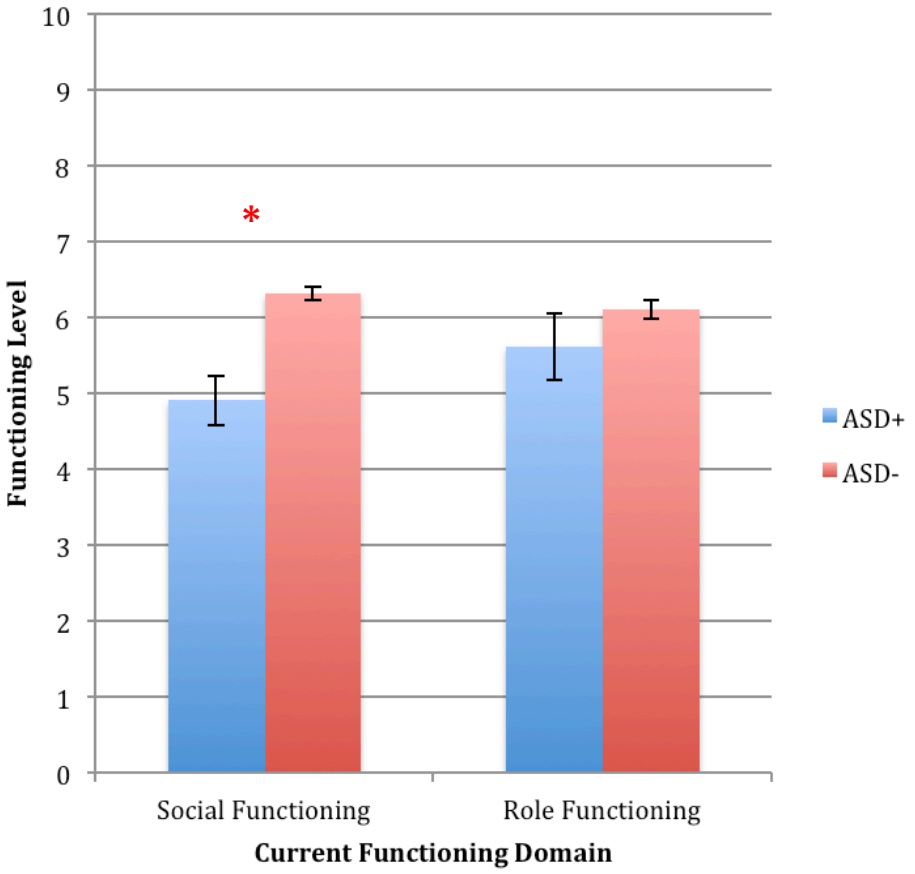

Figure 5. The means reflected in this group were adjusted for age and years of education as covariates.