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Social Deficits and the Schizophrenia-Spectrum Prodrome

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B.S., Psychology, Georgia State University, 2005

M.P.H., Behavioral Sciences, Emory University, 2007

Advisor: Elaine F. Walker, Ph.D.

An abstract of

A thesis submitted to the Faculty of the

James T. Laney School of Graduate Studies of Emory University

in partial fulfillment of the requirements for the degree of

Master of Arts in Psychology

2011

Abstract

Measurement, classification and remediation of social deficits have been a top research priority in the field of schizophrenia and other psychotic disorders. Such deficits have been found to be related to impairments in social cognition, likely stemming from dysfunction in neural systems underlying these processes. Research on schizophrenia-spectrum disorders has focused on social dysfunction as an illness precursor, characterizing both the premorbid and prodromal (pre-psychotic) periods. Despite differences in symptom presentation, age of onset, and developmental course, autism-spectrum disorders are also characterized by impaired social functioning. Further, recent genome-wide association studies reveal overlap in the genetic abnormalities associated with the two disorder spectra, and this has raised questions about the phenomenological boundaries between them, especially in the domain of social behavior. Of particular interest is the elucidation of similarities and differences in the childhood social deficits associated with autism- and schizophrenia-spectrum disorders. The present study addresses this issue using a well-established measure (the Social Responsiveness Scale - SRS) designed to assess a broad range of socioemotional deficits associated with autism-spectrum disorders. The focus is on adolescents who meet standard clinical criteria for the prodrome to psychosis. Study results indicate that the SRS is a useful measure of social deficits in individuals meeting criteria for the prodrome to psychosis and provide evidence for the ability of the SRS to discriminate adolescents at clinical high risk for conversion to psychosis from healthy and psychiatric control groups.

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People with schizophrenia and other psychotic disorders frequently have marked deficits in social skills, which contribute to impairments in social competencies essential for initiating and maintaining meaningful relationships and obtaining employment, (Bellack, Morrison, Wixted, & Muser, 1990). Many studies show that deficits in social functioning are already present by the first episode of psychosis (Drake et al., 2007; Gòrna, Jaracz, Rybakowski, & Rybakowski, 2008; Grant, Addington, Addington, & Konnert, 2001), and research on premorbid development indicate that there are measurable impairments in socioemotional behavior throughout childhood, which tend to become more severe in the years/months prior to illness onset (Cannon, Tarrant, Huttunen, & Jones, 2003; Done, Crow, Johnstone, & Sacker,1994; Fish, 1987, Hans, Auerbach, Asarnow, Styr, & Marcus, 2000; Niemi, Suvissari, Tuulio-Henriksson, & Lonnqvist, 2003). However, there are sex differences, and females with schizophrenia-spectrum disorders tend to have milder interpersonal deficits and better social functioning than males in both the premorbid and post-onset periods (Hass & Garratt, 1998).

Autism, another debilitating psychiatric disorder characterized by major social deficits, was at one time considered to have a common etiology with schizophrenia, and it was once viewed as an early onset of schizophrenia, with greater symptom severity (Bender, 1947). Some suggested that autism involved a more "penetrant" form of the same genetic liability underlying schizophrenia (Gottesman & Gould, 2003). From the publication of the second edition of the Diagnostic and Statistical Manual (DSM-II; American Psychiatric Association, 1968) to that of the DSM-III (American Psychiatric Association, 1980), schizophrenia and autism were differentiated into two separate diagnostic classifications, with subsequent DSM-IV, and DSM-IV-TR (American Psychiatric Association, 1980, 1987, 2000) editions further differentiating

them. Thus, current diagnostic classifications present autism- and schizophrenia-spectrum disorders as diagnostically distinct, based on both symptomatology and age at onset.

However, more recent advances in molecular genetics (Awadalla et al., 2010; Chao et al., 2010; Crepel, 2010; Duan, Sanders, & Gejman, 2010; Gauthier et al., 2010; Hoffman & State, 2010; Kao et al., 2010; Moreno-De-Luca et al., 2010) and research findings on prenatal risk factors (Weiser et al., 2008) are raising questions about the etiological distinctions between autism- and schizophrenia-spectrum disorders. Moreover, at the level of phenomenology, recent studies are revealing similarities in the social deficits associated with these two disorder spectra (Cederlund, Hagberg, & Gillberg, 2010; Couture et al., 2010; Esterberg et al., 2008). The present study is intended to extend this line of research, and examine the presence of autistic-like abnormalities in social behavior among youth at clinical risk for psychosis, based on the presence of prodromal or schizotypal syndromes.

Schizophrenia, conceptualized as a neurodevelopmental disorder, typically has onset during late adolescence or early adulthood, and affects approximately 1% of the population over the course of a lifetime (Jablensky, 1997). Individuals who meet DSM criteria for schizophrenia manifest a constellation of symptomatology that includes positive psychotic symptoms (e.g., delusions, hallucinations), negative symptoms, (e.g., flat affect, alogia), and impaired cognition. Accumulating data from molecular and behavioral genetic studies raise questions about the diagnostic distinction between schizophrenia and other forms of psychosis, such as mood disorders with psychotic features, as based on the DSM, in that some of the same genetic risk factors are observed in both (Horan, Blanchard, Clark, & Green, 2008; Maier, 2008). Similarly, schizotypal personality disorder (SPD), a syndrome that involves ‘subclinical’ manifestations of psychotic symptoms, is considered to be at the mild end of the schizophrenia-spectrum because it

is both genetically (Nicolson et al., 2003; Tienari et al., 2003) and developmentally linked with schizophrenia (Miller et al., 2002; Yung et al., 2003). With respect to the latter, it has been shown that youth who meet criteria for SPD have an elevated risk for developing a psychotic disorder in early adulthood (Asarnow, 2005; Mittal, Saczawa, Walder, Willhite, & Walker, 2008; Thompson, Nelson, & Yung, 2010; Woods et al., 2009). These and other findings have led researchers to conceptualize a "schizophrenia-spectrum" or "psychosis-spectrum" of disorders that vary along a continuum of severity and have overlapping etiologies.

Comparatively, autism is classified in the DSM-IV (American Psychological Association, 2000) as a pervasive developmental disorder (PDD), and it affects 10 in 1,000 children, with males four times more likely than females. Defined by early-onset and gross impairments in communication and social relatedness, and the presence of stereotyped behaviors, autism is typically diagnosed within the first three years of life. Although role functioning (e.g., school, work, and interpersonal relationships) varies from person to person, approximately 75% of those diagnosed with an autistic disorder have poor social outcomes (Tsatsanis, 2003). As is the case with schizophrenia, research findings, including genetic data, have led to the conceptualization of a spectrum of autistic disorders, with classical early-onset autism at one end, and Asperger's, a less severe disorder, at the other (Spiker, Lotspeich, Dimiceli, Myers, & Risch, 2002; Volkmar, Klin & Pauls, 1998).

Overlapping Risk Factors in the Schizophrenia and Autism Spectra

Recent findings from studies of prenatal complications, as well as genetic research, indicate that autism- and schizophrenia-spectrum syndromes have overlapping risk factors. For example, fetal exposure to prenatal maternal infections, fetal nutritional deficiency, and indicators of fetal dysmaturation, such as elevated rates of minor physical anomalies, have been

found in both schizophrenia and autism (Adrien et al., 1991; Caliguri, Lohr, & Jeste, 1993; Campbell, Geller, Small, Petti, & Ferris, 1978; Gupta et al., 1995; Marsden, 1982; Heinrichs & Zakzanis, 1998; Ohta, Nagai, Hara, & Saski, 1987; Ornitz, Guthrie, & Farley, 1977; Rapin, 1997; Rinehart, Bradshaw, Brereton, & Tonge, 2001; Walker, 1994). More recently, a review of the literature also suggests commonality of specific risk genes and rare chromosomal microdeletions or duplications that influence both neuronal development and neuronal regulation (Rapoport, Chavez, Greenstein, Addington, & Gogtay, 2009). Furthermore, Guilmatre and colleagues (2009) found recurrent or overlapping copy number variations among individuals with schizophrenia, autism, and mental retardation. Finally, 22q deletion syndrome, a chromosomal abnormality, is associated with dramatically elevated risk for both autism- and schizophrenia-spectrum disorders (Fine et al., 2005; Goodman, 1994; Murphy, 2002; Vorstman et al., 2006; Williams & Owen, 2004).

Crespi and colleagues (2010) recently examined four alternative hypotheses for the genomic and developmental relationship between autism and schizophrenia. Findings from that investigation suggest that shared genes result in developmental processes both in the same direction and in different directions when comparisons are made between both disorders. Based on these findings, and those presented previously, there seems to considerable evidence for partially shared pathways involved in the diathesis for these disorders. Thus it is not surprising that there is some overlap in the phenotypic expression in the domain of socioemotional behavior between syndromes of the autism and schizophrenia spectra.

Socioemotional Behavior in the Autism and Schizophrenia Spectra

Despite the differentiation of autism- and schizophrenia-spectrum disorders through diagnostic classification (American Psychiatric Association, 2000), it is important to note the

phenomenological overlap between these spectra, especially in the syndromes that are considered to be at the mild end. Asperger's disorder involves milder forms of the symptoms of autism, and SPD is a milder syndrome within the schizophrenia-spectrum. Both Asperger's and SPD are characterized by socioemotional deficits, as well as odd behaviors.

In addition to shared prenatal and genetic risk factors, research has provided evidence of overlap in childhood behavior deficits. The diagnostic criteria for autism include childhood social functioning that is grossly impaired. Diagnostic criteria include abnormalities in nonverbal behaviors (e.g., establishing eye contact, and use of facial expressions, posturing, and gesturing) and in the ability to develop social relationships with peers and family members (e.g., deficits in social and emotional reciprocity, and not enjoying interactions with others). Several reviews of emotional functioning in children with autistic disorder have highlighted their difficulties with social relationships, emotional awareness, and the social use of language (Loveland, 2005; Volkmar, Carter, Grossman, & Klin, 1997). At the milder end of the autistic-spectrum, children with Asperger's disorder show similar, but less debilitating and severe social impairments.

Children who later develop psychotic disorders sometimes manifest deficits in social behavior that are similar to those observed in autistic-spectrum disorders, albeit less severe and debilitating (Bellack, Morrison, Wixted, & Mueser, 1990; Bellack, Mueser, Gingerich, & Agresta, 1997, 2004; Loveland 2005, Volkmar et al., 1997). For individuals with schizophrenia-spectrum disorders, research has shown deficits in the ability to accurately perceive social cues, detect attributes of social settings, provide appropriate and timely verbal responses in social interactions, and make eye contact with others (Bellack et al., 1990, 1997, 2004; Corrigan, 1997; Davison, Frith, Harrison-Read, & Johnstone, 1996; Edwards, Jackson, & Pattison, 2002; Mueser,

Bellack, Douglas, & Morrison, 1991). As noted, deficits in social functioning are present in the first episode of psychosis, are detectable in individuals in the prodromal phase of a primary psychotic disorder, and increase as a function of chronicity within such disorders (Addington, Penn, Woods, Addington, & Perkins, 2008; Drake et al., 2007; Gòrna et al., 2008; Grant et al., 2001; MacDonald, Jackson, Hayes, Baglioni, & Madden, 1998; Voges & Addington, 2005). Further, impairments in performance on measures of social cognition are related to functional deficits (Couture, Penn, & Roberts, 2006). It is, therefore, not surprising that social skills training is a key area of focus for intervention efforts, as social skills are an integral part of a variety of life roles (Bellack et al. 1997, 2004).

Measurement of Social Functioning in Schizophrenia-Spectrum Disorders

Numerous scales have been developed to measure social functioning in individuals with schizophrenia-spectrum disorders, including: the Assessment of Interpersonal Problem-Solving Skills (AIPSS; Donahoe, et al., 1990); the Multnomah Community Ability Scale (MCAS; Barker, Barron, McFarland, & Bigelow, 1994), the World Health Organization Disability Assessment Schedule (WHODAS-II; Annicchiarico, Gibert, Cortés, Campana, & Caltagirone, 2004; Chisolm, Abrams, McArdle, Wilson, & Doyle, 2005; Chopra, Couper, & Herrman, 2004); the Community Adjustment Form (CAF; Test et al. 1991); the Social Functioning Scale (SFS; Birchwood, Smith, Cochrane, Wetton, & Copestake, 1990); and the Premorbid Adjustment Scale (PAS; Cannon-Spoor, Potkin, & Wyatt, 1982). However, these measures tend to focus on current or very recent levels of social functioning in community settings, and they assess molar aspects of functioning, such as frequency and duration of social activity and relationships, and preference for social activity.

For example, studies utilizing the SFS tend to characterize their samples with regard to current social functioning across several domains (e.g., social engagement, employment, prosocial activities, and personal independence) in which associations between those domains and clinically relevant sociodemographics, as well as current level of symptomatology, are examined (Addington et al., 2008; Górna, et al., 2008; Goulding, Franz, Bergner, & Compton, 2010; Voges & Addington, 2005). The PAS, however, measures across social and academic functioning from childhood through adulthood, until the onset of subthreshold psychotic symptoms indicating the onset of the prodromal period (Cannon-Spoor et al., 1982). Research with the PAS focuses on the characterization of study samples through illuminating patterns of functioning (or deterioration) and associations between these domains and sociodemographic characteristics (e.g., years of education; marital status), age of onset of the prodrome and/or psychosis, and current level of symptomatology (Allen, Frantom, Strauss, & van Kammen, 2005; Cannon et al., 1997; Monte, Goulding, & Compton, 2008). Both the SFS and the PAS have been utilized in a large number of studies involving first-episode psychosis patients.

As evident from the above research, measures used to study social competence in schizophrenia-spectrum disorders have a more global focus and generally lack a developmental approach in characterizing the nature and course of premorbid and prodromal (pre-psychotic) social impairment. A recent National Institute of Mental Health (NIMH) workshop delineated social cognition as a high priority topic within schizophrenia-spectrum disorders, specifying a need for research in five overlapping areas: theory of mind, social perception, social knowledge, attributional bias, and emotion processes (Green et al., 2008). Stressed by the authors is the need for reliable and valid instruments that measure and classify specific social deficits in individuals with schizophrenia-spectrum disorders.

However, as a main diagnostic criterion, negative symptoms have importance for research on social cognition in individuals with schizophrenia-spectrum disorders (Newnan, 2004). Although social cognition is related to, yet distinct from negative symptoms (Sergi et al., 2007), affect has many systematic and pervasive relations with social cognitive processes and is suggested to serve as a "tuning function" for social cognition (Higgins & Sorrentino, 1990; Sorrentino & Higgins, 1986, 1996). Therefore, consideration of negative symptoms in investigations assessing social deficits is of importance in this heterogeneous spectrum of disorders.

Measures of Social Functioning in Autism-Spectrum Disorders

Because social deficits are a defining feature of the autism-spectrum, several reliable and valid measures have been developed to examine micro-level aspects of interpersonal behavior and social skill development. Such measures have been shown to detect subthreshold autistic traits along a continuum of social impairment both within family members of individuals with autism (Constantino et al., 2004; Piven, Palmer, Jacohbi, Childress, & Arndt, 1997; Spiker, Lotspeich, Dimiceli, Myers, & Risch, 2002) and within individuals diagnosed with Asperger's disorder or PDD not otherwise specified (Constantino, Hudziak, & Todd, 2003). These include qualitative structured interviews and quantitative instruments used for diagnostic assessment through algorithmic scoring procedures (Lord, Rutter, & Le Couteur, 1994) or as screening instruments in batteries of tests designed to lead to clinical diagnosis of autism-spectrum disorders (Constantino 1998, 2002).

The Autism Diagnostic Interview-Revised (ADI-R; Lord et al., 1994), a qualitative semi-structured interview consisting of 93-items, is a widely recognized gold standard parent-report purposed to provide diagnostic assessment of autistic signs in adults and children. The ADI-R

assesses symptoms in each of three domains: impairments in reciprocal social behavior; delays in language development; and restricted, repetitive behaviors. Following the administration of the interview to the primary caregiver, using an algorithm based on ICD-10 (Isaac, Janca, & Sartorius, 1994) and DSM-IV (American Psychiatric Association, 2000) criteria, responses are then scored by the assessor based on descriptions of the child's behavior that were provided during that interview. Prior research on the ADI-R has demonstrated acceptable reliability and validity within a variety of samples and its usefulness in discriminating between individuals with autism and those with mental retardation and language impairments (Hill et al., 2001; Lord & Paul, 1997; Lord, Rutter, & LeCouteur, 1994; Lord, Rutter, Storochuck, & Pickles, 1993).

The Social Reciprocity Scale (SRS; Constantino, 1998), currently known as the Social Responsiveness Scale (Constantino & Gruber, 2005), is a 65-item quantitative measure designed for the purposes of screening individuals who may be at risk for autism-spectrum disorder and as one of many diagnostic tools. Prior investigation has shown that the SRS has good agreement with information from the ADI-R (Constantino et al., 2003). This reliable and valid informant questionnaire taps into both molar and micro-level aspects of social behavior, and provides an overall score as an index of severity in social deficits. In fact, it was originally created for epidemiological purposes – to study how social reciprocity behaviors among children and adolescents are distributed in the general population (Constantino et al., 2000).

The SRS has been determined to be explained best by a "single continuously distributed factor", but it also yields five highly correlated subscales (Constantino et al., 2000; Constantino et al., 2004) that assess impairments within the specific domains (Constantino & Gruber, 2005). The Social Motivation subscale measures the extent to which an individual is motivated to engage in social-interpersonal behavior, the Autistic Mannerisms subscale includes stereotypical

behaviors/highly restricted interests that are characteristic of autism-spectrum disorders, and the three remaining scales measure specific aspects of reciprocal social behavior. More specifically, the Social Awareness subscale measures ability to pick up on social cues (sensory aspects), while the Social Cognition subscale measures ability to interpret social cues once they are picked up (cognitive-interpretive aspects), and the Social Communication subscale taps expression (motoric aspects). Though useful for screening and evaluation of intervention within clinical settings, utility of these subscales in differentiating among subtypes of autistic-spectrum disorder has not yet been systematically explored (Constantino & Gruber, 2005).

Research conducted with the SRS total scale score has revealed its usefulness in the identification of social deficits ranging from subtle to severe within the autism-spectrum of disorders (Constantino, Przybeck, Friesen, & Todd, 2003), with some indicating a strong genetic component for social impairment, independent of factors known to influence general psychopathological symptomatology (Constantino et al., 2003; Constantino & Todd, 2000). In particular, the SRS detects subthreshold autistic traits along a continuum of social impairment both within family members of individuals with autism (Constantino et al., 2004; Piven et al., 1997; Spiker et al., 2002) and within individuals diagnosed with Asperger's disorder or PDD not otherwise specified (Constantino et al., 2003). Additionally, the SRS has been shown to be helpful in the identification of subthreshold autistic symptoms in children with a wide variety of psychological problems (Constantino & Gruber, 2005). In fact, even if the degree of social impairment measured falls below the threshold of an autism-spectrum diagnosis, evidence suggests that social impairment measured by the SRS is positively associated with the severity of other psychiatric conditions in children and adolescents (Constantino et al., 2000).

For example, one recent investigation (Pine, Guyer, Goldwin, Towbin, & Lieibenluft, 2009) involved 352 participants categorized into five diagnostic groups: healthy controls, anxiety disorders, major depressive disorder (MDD), bipolar disorder (BD), or severe mood dysregulation (SMD). Each of the four patient groups had significantly higher rate of social impairment, as measured by the SRS scores, than healthy controls. These associations are comparable in magnitude to those documented in one prior study of mood and anxiety disorders (Towbin, Pradella, Gorrindo, Pine, & Leibenluft, 2005), as well as other studies concerning children with learning or behavioral disorders such as attention deficit hyperactivity disorder and conduct disorder (Bishop & Baird, 2001; Geurts et al., 2004; Gilmour, Hill, Place, & Skuse, 2004). In that study, the authors point out that there also seemed to be a linear trend, evidenced by increasing mean scores in the order of anxiety disorders, major depressive disorder, bipolar disorder, and individuals classified as meeting criteria for severe mood dysregulation (Towbin et al., 2005). However, when considering covariates (age, IQ, and a measure of impairment) in comparisons among clinical groups, only those participants with anxiety disorders scored significantly lower than the other clinical groups.

Social Deficits and their Neural Basis in Autism- and Schizophrenia-Spectrum Disorders

Neurobiological models of social cognition posit that a network of neural structures is critically involved in processing social stimuli (Adolphs, 2001; Brothers, 1990a, 1990b; Phillips, Drevets, Rauch, & Lane, 2003), and provide a foundation for understanding neural mechanisms underlying social deficits in disorders such as schizophrenia and autism. Despite evidence of abnormal activation in neural systems for both (Pelphrey, Adolphs, & Morris, 2004; Pinkham, Penn, Perkins, & Lieberman, 2003), only recently have studies begun to directly compare the neural substrates underlying social cognitive deficits in schizophrenia- and autism-spectrum

disorders. In doing so, it is possible that the general and specific mechanisms for these deficits and their etiology may be illuminated. Subsequent measurement of the phenotypic expression of endophentypic markers may differentiate the two disorders or reveal genes shared by both.

Cheung and colleagues (2010) recently conducted a meta-analysis using Anatomical Likelihood Estimation (ALE), a technological advance able to synthesize multiple imaging datasets within a common framework, in order to examine 25 voxel-based studies of autism and schizophrenia-spectrum disorders. Comparisons of 313 foci from non-clinical controls and two clinical groups (autism-spectrum disorders and first-episode schizophrenia patients) revealed significantly lower grey matter volume within the limbic-striato-thalmic circuitry for both clinical groups. Specifically, lower grey matter volume was found within the limbic basal ganglia loop system (considered to be important in sensorimotor gating) for both clinical groups; which may partly explain their shared socioemotional symptomatology (Cheung et al., 2010). Even though results indicated areas of lower grey matter volume specific to each disorder, results from these analyses also suggest that there are considerable brain structural similarities between the two spectra of disorder.

Pinkham and colleagues (2008) have utilized event-related functional magnetic resonance imaging (fMRI) in order to compare neural activation in discrete brain regions between four groups (high functioning autism, paranoid schizophrenia, non-paranoid schizophrenia, and controls) engaged in the task of measuring the complex social judgment of trustworthiness in faces. As expected, all four groups showed significant activation of the social cognitive network, including the amygdala, fusiform face area (FFA), superior temporal sulcus (STS), and ventrolateral prefrontal cortex (VLPFC). However, individuals in the autism and paranoid schizophrenia groups showed significantly reduced neural activation in the right amygdala, FFA,

and left VLPFC when compared with controls, and in the left VLPFS when compared to those with non-paranoid schizophrenia (Pinkham et al., 2008). These findings support the notion that specific neural mechanisms may underlie social cognitive impairments in both disorders.

In an attempt to refine the behavioral phenotypes of autism- and schizophrenia-spectrum disorders, Couture and colleagues (2010) utilized a battery of social cognitive measures previously linked to specific brain regions in a study designed to compare deficits between two clinical samples (schizophrenia and high functioning autism) and non-clinical controls. Individuals with high functioning autism and those with schizophrenia performed similarly to each other on social cognitive tasks, with both groups differing significantly from controls. Furthermore, exploratory examination of the patterns of social cognitive deficits using schizophrenia negative symptoms and paranoid subgroups indicated preliminary evidence suggesting more similarity between individuals with high functioning autism and those in the negative symptom subgroup (Couture et al., 2010).

A recent investigation (Esterberg et al., 2008) provided empirical support for the phenomenological overlap between autism- and schizophrenia-spectrum disorders. Using the ADI-R, childhood and current signs of autism-spectrum disorders were examined in a sample of adolescents, comparing healthy adolescent controls to individuals with SPD and those with other personality disorders. Although not determined to be linked with conversion to psychosis, findings indicated that past and current autistic signs were more common in adolescents with SPD. Furthermore, analyses revealed that the ADI-R also taps the social deficits (e.g., constricted affect, social anxiety, odd/peculiar behavior) characteristic of SPD (Esterberg, et al., 2008). More specifically, and most relevant to this current study, social impairment was also

found to be predictive of greater severity in negative, positive, disorganized, and general prodromal symptoms of the schizophrenia-spectrum of disorders.

Bell, Fiszdon, Greig, and Wexler (2010) attempted to demonstrate the utility of the Social Attribution Test – Multiple Choice (SAT-MC), a measure originally developed for autism research, for assessing social cognitive impairments in individuals diagnosed with schizophrenia. Findings indicated that individuals affected by schizophrenia had significantly poorer scores than a community sample. Furthermore, the instrument showed strong discriminant validity, shared variance with other social cognitive measures (e.g., affect recognition, theory of mind, self-reported egocentricity, and the Social Cognition Index from the MATRICS battery), and was modestly correlated with measures of neurocognition (Bell et al., 2010). However, while this instrument may be useful in investigations of social cognitive deficits in individuals with schizophrenia, intervention studies would require that additional forms be developed in order to allow for pre- and post-testing alternatives.

Summary and Conclusions

Further clarification of the specificity of social cognitive deficits in autism- and schizophrenia-spectrum disorders has the potential to result in the refinement of behavioral phenotypes, speculated to provide a simpler link to genes than those provided by more complex behaviors, including broad diagnostic categories (Gottesman & Gould, 2003). In particular, there is a need for studies of the micro-level aspects of social behavior deficits in the schizophrenia-spectrum using instruments developed for the study of such impairments in the autistic-spectrum. Given the aforementioned research, the SRS is an instrument that has been established as a reliable and sensitive measure of a range of social behaviors, yet has not yet been used in the study of schizophrenia-spectrum disorders.

The current study uses the SRS to examine multiple facets of social deficits in a sample of individuals who meet standard criteria for the prodrome of schizophrenia and other psychotic disorders. Assessing social deficits during the prodrome has greater potential to avoid confounds associated with the effects of schizophrenia-spectrum illness and treatment. Examination of the SRS in a clinical sample of individuals deemed at-risk for conversion to a schizophrenia-spectrum disorder has the potential to further elucidate the phenotypic overlap between the autism and schizophrenia spectra.

The present study will test the following hypotheses. First, greater severity of social deficits, as measured by the SRS, is predicted in adolescents at-risk for psychosis than in psychiatric and healthy controls. Further, given evidence of sex differences in SRS ratings and in social functioning in schizophrenia spectrum disorders, more severe social deficits are predicted in at-risk males than in at-risk females. Based on findings from use of the ADI-R in a similar population (Esterberg et al., 2008), SRS scores were expected to be positively associated with severity of negative symptoms, severity of positive symptoms, severity of disorganized symptoms, and severity of general symptoms. In addition to testing these hypotheses, the present study will examine the specific associations of the prodromal symptom scales with the SRS subscales, Social Awareness, Social Cognition, Social Communication, Social Motivation, and Autistic Mannerisms.

Method

Participants

This current study includes adolescents (*n*=122) from the Atlanta area who were recruited for a prospective longitudinal study conducted at Emory University. The present sample is comprised of those from a larger sample (n=131), including only those whose behavior was

assessed with the Social Reciprocity Scale (SRS; Constantino, 1998), currently known as the Social Responsiveness Scale (Constantino & Gruber, 2005). Descriptive statistics for the sample, by diagnostic group, are provided in Table 1. Participants were 67 males and 55 females between the ages of 11 and 18 (14.2 ± 1.8) years who self-identified as belonging to one of four racial categories: White/Caucasian (*n* = 72, 59.0%), African American (*n* = 43; 35.2%), Asian American (*n* = 4, 3.3%), and "Other" (*n* = 3, 2.5%). Based on the results of the baseline diagnostic assessments described below, adolescents were classified into three diagnostic categories; healthy controls (HC; *n* = 45, 36.9%), other disorder controls (OD; *n* = 28, 23.0%), and individuals at-risk for psychosis (n = 49, 40.2%), hereafter referred to as the clinical high risk (CHR) group. Included in the OD group was: obsessive-compulsive PD, schizoid PD, paranoid PD, narcissistic PD, borderline PD, avoidant PD, and antisocial PD.

Procedures

Participants in this current study took part in the baseline cross-sectional portion of a National Institute of Mental Health (NIMH)-funded prospective, longitudinal research study of youth at risk for psychosis. Recruitment of CHR participants was largely through announcements targeting parents and clinicians. The HC group was primarily recruited through the Emory University Research Participant Registry, which includes children and adolescents in the greater Atlanta area. Telephone interviews were conducted as an initial screening of participants based on the following exclusionary criteria: presence of a neurological disorder, mental retardation, diagnosis of an Axis I disorder, or current substance addiction (based on DSM-IV criteria).

Immediately prior to conducting baseline assessment interviews, informed consent and assent were obtained from adolescents and their primary caregivers through procedures approved

by the Emory University Institutional Review Board Human Subjects Review Committee. Baseline structured diagnostic assessment interviews, using the battery described below, were then conducted by graduate-level clinical interviewers under the direct supervision of the principal investigator, a licensed clinical psychologist. Participants were included in the CHR group if they met DSM-IV diagnostic criteria for SPD (n=4), the Scale of Prodromal Symptoms (SOPS; Miller et al., 2002) criteria for Attenuated Positive Symptom Syndrome (APSS; n=17), or both risk criteria (n=28). As with the telephone screening, exclusion criteria at baseline were diagnosis of mental retardation, neurological disorder, Axis I disorder, or current substance addiction (based on DSM-IV criteria).

Training of interviewers was conducted over a 2-month period of time. All assessments were videotaped to allow for monitoring of interrater reliability throughout the duration of the entire study. Furthermore, videotapes allowed for confirmation of diagnostic status by the principal investigator. Interrater reliabilities for symptom ratings exceeded the minimum criterion of 0.80 (Pearson product-moment correlation coefficient), and the mean Kappa was 0.85 for diagnostic status.

Measures

Diagnostic Classification

The *Structured Interview for Prodromal Syndromes* (SIPS; Miller et al., 1999) is a reliable and valid (Miller et al., 2002), semi-structured diagnostic interview used to classify individuals as meeting criteria for potentially prodromal states considered to be indicative of an at-risk status for conversion to psychosis. Symptoms are rated on a seven-point scale reflecting severity, frequency, duration, and intensity/degree of conviction. Scores range from zero to six, with scores of zero to two (absent, questionable, or mild) reflecting what is considered to be

normal/subprodromal symptomatology, three to five (moderate, moderately severe, or severe) evidencing symptomatology indicative of a prodromal level of symptomatology/clinically high risk status, and scores of six suggestive of a potential psychotic state. Items allow for the assessment of five positive symptoms, six negative symptoms, four disorganized symptoms, and four general symptoms, in addition to recording data on criteria for Schizotypal Personality Disorder, family history of mental illnesses, and current- and past-year global functioning (GAF). Ratings are averaged to derive a score for each of the four symptom dimensions.

The SIPs ratings were used to identify individuals meeting criteria for the Attenuated Positive Symptom Syndrome (APS) (COPS; Miller et al., 2002). APS is characterized by onset or worsening of symptomatology considered to be sub-psychotic (rating >=3 and ≤5) over the past 12-month period, with frequency of occurrence of at least once per week. Following SIPS procedures, participants were classified in the CHR group if they received at least one rating of three, four or five on a positive symptom and therefore met SOPS symptom severity criteria for APS (Miller et al., 2002).

The *Structured Interview for DSM-IV Personality Disorders* (SIDP-IV; Pfohl, Blu, & Zimmerman, 1997) is a semi-structured interview designed to rate personality disorder criteria based on DSM-IV Axis II criteria. Items are rated on a scale from zero (not present) to three (strongly present), with average ratings of symptom criteria resulting in a total symptom score. Because SPD is genetically and developmentally linked with psychosis (Siever, Koenigsberg, & Reynolds, 2003), it is included as a prodromal syndrome. Adolescents with SPD therefore were included in the CHR group, while those with other personality disorder diagnoses were included in the OD group.

The *Structured Clinical Interview for DSM-IV Axis I Disorders* (SCID-IV; First, Spitzer, Gibbon, & Williams, 2002) is a semi-structured interview designed to verify and categorize the presence of Axis I disorders according to DSM-IV criteria. Shown to have a good interrater reliability when used with adolescents (Martin, Pollock, Bukstein, & Lynch, 2000), the SCID was used to diagnose Axis I disorders for the exclusionary purposes.

Assessment of Social Deficits

As mentioned previously, the *Social Reciprocity Scale* (SRS; Constantino, 1998), currently known as the *Social Responsiveness Scale* (SRS; Constantino & Gruber, 2005), was created for epidemiological purposes as a rapid and reliable screening measure that provides an overall score as an index of severity in social deficits characteristic of autism-spectrum disorders. Capable of differentiating along a continuum of severity in social impairment in children from four to 18 years of age (Constantino, et al., 2004; Constantino, Hudziak, & Todd, 2003; Constantino & Todd, 2003), the SRS was designed to be administered as a screening measure and takes 10-20 minutes to complete. The measure is administered to a parent, teacher or other primary caregiver who knows the child well and can rate their behaviors over the prior 6-month period of time.

The SRS total scale score is derived from summation of 65 items rated on a scale of severity from zero (never true) to three (almost always true), with higher scores indicating greater severity of social impairment (for a list of the 65 items, see Appendix A). Internal consistency coefficients for the SRS have been shown to range from 0.93–0.97 (Constantino & Gruber, 2005). Evidence for validation has been garnered through several studies wherein the SRS was compared with clinical interviews and significantly discriminated autism-spectrum disorders from other psychiatric disorders, and concurrent validity has been established in comparison of the SRS with the ADI-R (Constantino, Davis, Todd, et al., 2003), the gold standard for

measuring autistic traits. The five subscales (social awareness, social cognition, social communication, social motivation, and autistic mannerisms) are highly intercorrelated and have been shown to have internal consistency coefficients ranging from 0.77 – 0.92 (Constantino & Gruber, 2005).

Data Analysis

All analyses were performed using SPSS version 17.0. Basic descriptive statistics on sociodemographics and clinical characteristics were calculated to determine central tendency and variability across and within diagnostic categories. Appropriate statistical techniques, including Spearman correlation coefficients, independent samples *t*-tests, chi-square, and analysis of variance (ANOVA) were utilized for examination of descriptive statistics, analysis of specific hypotheses, and additional exploratory analyses.

Results

Demographic and clinical characteristics for the sample are reported in Table 1. There were no significant differences in any of the demographic characteristics (age, sex, or race) between the three groups. However, as expected, the three groups differed significantly with regard to mean positive, negative, disorganized and general symptom scores, as measured by the SIPS. Adolescents in the CHR group scored significantly higher on positive symptoms [$F(2, 117) = 122.53$, $p < 0.001$], negative symptoms [$F(2, 117) = 20.59$, $p < 0.001$], disorganized symptoms [$F(2, 118) = 38.59$, $p < 0.001$], and general symptoms [$F(2, 118) = 21.33$, $p < 0.001$]. There were no significant differences in mean positive, negative, disorganized, and general symptom scores between HC and OD groups.

Internal consistency coefficients for SRS total score and subscale scores for the overall sample and by diagnostic group are presented in Table 2 and descriptive statistics for SRS total

and subscale scores for the overall sample and for all three diagnostic groups are reported in Table 3. As shown in Table 3, comparisons of mean SRS total scores revealed significant diagnostic group differences [F (2, 119) = 10.49, p < 0.001]. Specifically, the CHR group had significantly higher mean SRS total score than both the OD (t = 2.36, p = 0.021) and the HC (t = 4.375, p < 0.001) groups. Furthermore, the OD group had a significantly higher mean SRS total score than the HC group (t = 2.37, p = 0.021).

Mean SRS subscale scores, by diagnostic group, are presented in Figure 1. As shown in Table 3, comparisons of mean SRS subscale scores revealed significant diagnostic group differences for the Social Cognition [F (2, 106) = 7.88, p < 0.001], Social Communication [F(2, 105) = 11.79, p < 0.001], Social Motivation [F (2, 101) = 10.96, p < 0.001], and Autistic Mannerism [F (2, 119) = 10.49, p < 0.001] subscales. More specifically, the CHR group had a significantly higher mean Social Cognition subscale score, indicating more deficits, when compared to the HC group (t = 3.72, p < 0.001). With regard to the Social Communication subscale, the CHR group had significantly higher mean scores than both the OD and the HD groups (t = 2.07, p = 0.04 r and t = 4.69, p < 0.001, respectively), and the OD group had a significantly higher mean score than the HC group (t=2.03, p=0.05). Additionally, the CHR and the OD groups each had a significantly higher mean Social Motivation subscale score than the HC group (t = 4.62, p < 0.001 and t = 2.89, p = 0.01, respectively). Finally, the CHR group had significantly higher mean Autistic Mannerism subscale scores than both the OD (t=3.36, p=0.001) and the HC (t = 4.15, p < 0.001) groups.

Sex differences in SRS scores within the CHR group are reported in Table 4. Descriptive statistics and independent samples t-test results were provided for the SRS total score and, for exploratory purposes, the SRS subscale scores. Contrary to expectation, although males (83.3 ±

31.4) had higher mean scores than females (77.5 ± 30.7), indicating more deficits, there was no significant difference in SRS total scale score by sex ($t = 0.62$, $p = 0.536$) in the CHRgroup. Exploratory analyses of SRS subscale scores by sex also revealed no statistically significant differences. Furthermore, additional exploratory analyses of symptom domain scores by sex also revealed no statistically significant differences for the CHR group.

Correlations between SRS total score and symptom domains (as measured by the SIPS) within the CHR group are shown in Table 5. As expected, the SRS total score was significantly associated with the mean positive ($r = 0.30$, $p < 0.05$), negative ($r = 0.64$, $p < 0.01$), disorganized ($r = 0.37$, $p < 0.01$) and general ($r = 0.62$, $p < 0.01$) symptom scores. Standardized comparisons of differences in associations between SRS total score and SIPS symptom domains are shown in Figure 2. Fisher's *z*-tests revealed that the magnitude of the correlation coefficient for negative and general symptoms was significantly greater than the magnitude of the correlation coefficient for positive symptoms ($z = 2.12$, $p = 0.02$ and $z = 1.98$, $p = 0.02$, respectively). Furthermore, the magnitude of the correlation coefficient for negative symptoms was significantly greater than the magnitude of the correlation coefficient for disorganized symptoms ($z = 1.76$, $p = 0.04$). All other comparisons of the magnitudes of correlation coefficients relating symptom domains to the SRS total scale score resulted in nonsignificant differences.

Exploratory analyses of the relation between SRS subscales and SIPS symptom domains also revealed significant correlations, as shown in Table 4. The mean positive symptoms score was significantly associated with two subscale scores, Social Communication and Social Motivation ($r = 0.33$ and $r = 0.34$, both $p < 0.05$). The mean negative symptoms score was significantly associated with the Social Awareness subscale score ($r = 0.37$, $p < 0.05$), as well as

the Social Cognition, Social Communication, Social Motivation, and Autistic Mannerisms subscale scores (r = 0.42–0.64, all $p < 0.01$). The mean disorganized symptoms score was significantly associated with three subscales, Social Awareness and Social Cognition (r = 0.33 and r = 0.34, both $p < 0.05$), and Social Communication (r = 0.39, $p < 0.01$). The mean general symptoms score was significantly associated with all SRS subscale scores (r = 0.39–0.62, all $p <$ 0.01).

Standardized comparisons of differences in associations between SRS subscale scores and SIPS symptom domains are shown in Figure 3. Fisher's *z*-tests revealed that the magnitude of the correlation coefficient pertaining to the Social Motivation subscale was significantly greater for general symptoms when compared to positive symptoms (z = 1.96, p = 0.02) and for negative symptoms when compared to disorganized symptoms (z = 1.94, p = 0.03). Furthermore, the magnitude of the correlation for negative symptoms was significantly greater than the correlation for positive symptoms with regard to relatedness to the Autistic Mannerisms subscale score (z = 2.03, p = 0.02), as well as the Social Communication subscale score (z = 1.88, p = 0.03). All other comparisons of the magnitudes of correlation coefficients relating symptom domains to the SRS total scale score resulted in nonsignificant differences, although the magnitude of the correlation coefficient pertaining to the Social Communication subscale score came close to being significantly greater in relatedness to negative symptoms than positive symptoms (z = 1.57, p = 0.06).

Discussion

As described above, there is increasing evidence from genetic research that conventional diagnostic boundaries between autism- and schizophrenia-spectrum disorders may be obscuring shared etiologic factors. The present study examined socioemotional deficits

associated with autism-spectrum disorders, as measured by the SRS, in a sample of adolescents who meet standard criteria for the prodrome to psychosis. The findings from this investigation lend support to all but one of the three main study hypotheses, and provide evidence of phenomenological overlap.

Diagnostic Group Differences

As predicted, based on the SRS total score, the CHR group was rated as having significantly greater overall social deficits than the OD and HC groups, and the OD group was rated as having significantly greater overall social deficits than the HC group. Furthermore, these findings suggest a linear trend of increasing social deficits in order of HC, OD and CHR groups. Taken together with prior research on learning and behavioral disorders (e g., ADHD and CD) (Bishop & Baird, 2001; Geurts et al., 2004; Gilmour et al., 2004), and mood and anxiety disorders (Pine et al., 2008; Towbin et al., 2005), these findings extend the body of literature demonstrating the ability of the SRS to discriminate among diagnostic groups across a wide variety of psychiatric disorders. Furthermore, they provide evidence of the usefulness of the SRS to discriminate among diagnostic groups based on putative clinical risk for schizophrenia-spectrum disorders.

Analyses of mean subscale scores indicated that the CHR group had significantly greater deficits on the Social Cognition, Social Communication, and Social Motivation subscales than the HC group. Additionally, the OD group had a higher mean Social Communication and Social Motivation subscale scores than the HC group. Finally, the CHR group had significantly higher mean Autistic Mannerism subscale scores than both OD and the HC group. Although no significant differences were found in mean Social Awareness subscale scores by diagnostic group, the internal consistency for that subscale was low relative to all of the other SRS

subscales both in this current investigation and previous studies of autism-spectrum disorders (Constantino & Gruber, 2005). Further research on the latent factor structure of the SRS may be beneficial when considering the SRS subscale domains in future studies.

For reference purposes, the mean SRS total scale scores obtained from a validation study of the SRS in both normal and autism-spectrum subjects (Constantino et al., 2003) are presented in Figure 4. Although the mean SRS total score for the HC group is a bit higher than those in prior investigations, it is noteworthy that the HC groups in those studies largely utilized community samples without diagnostic assessment, while in this study the HC group was selected based on study-specific criteria through a diagnostic screening process. Furthermore, it is also notable that although significantly higher than both the OD and HC groups, the mean SRS total score for the CHR group is still well below the mean score for the Asperger/PDD-NOS and Autism groups involved in that validation study.

Sex Differences in SRS Scores within the CHR Group

Contrary to expectation, although present in the overall sample, there were no significant sex differences in ratings of overall social deficits, as measured by the SRS total score, within the CHR group. Additional exploratory analyses of SRS subscales revealed similar results. The significant effect of sex on SRS total score in the overall sample is consistent with the current body of literature accumulating on the use of the SRS total score as a continuous measure of social deficits (Constantino & Gruber et al., 2005). However, the absence of significant sex differences in SRS total score in the CHR group is contrary to previous research regarding sex differences in social functioning impairment in schizophrenia-spectrum disorders, as well as the general population (Hass & Garratt, 1998). This may indicate that the SRS is sensitive to social deficits that are independent of sex in clinically high risk populations. However, while this lack

of significant finding may be informative, it could also be that issues stemming from a relatively small sample size in each diagnostic group and restriction of range with regard to the age span are also playing a role in inability to detect sex differences.

Relation of SRS Scores with SIPS Symptom Ratings within the CHR Group

As predicted, greater severity of overall social deficits was found to be positively correlated with severity of positive, negative, disorganized, and general symptoms within the CHR group. Therefore, as severity in any one of those four symptom domains increases, so does the display of social deficits. These results are consistent with prior research demonstrating that ADI-R ratings of social impairment were positively associated with positive, negative, and general symptomatology (Esterberg et al., 2008). Furthermore, they are consistent with findings from the literature linking social cognition to severity of symptoms such as paranoid delusions (Bentall et al., 2009; Lysaker et al., 2009; Martin & Penn, 2002; Peer et al., 2004), and negative/disorganized symptoms (Corcoran et al., 1995; Garety & Freeman, 1999; Greig et al., 2004). Thus, the SRS total score may tap a dimension that distinguishes individuals in the schizophrenia-spectrum of disorder from the HC and OD control groups. Furthermore, the SRS total score is at least partially related to severity of diagnostic symptomatology, as measured by the SIPS.

Examination of the relationship between severity of specific domains of social deficits and severity of positive, negative, disorganized, and general symptomatology revealed several interesting findings. Severity of positive symptomatology was significantly positively associated with severity of deficits in the Social Communication and Social Motivation subscale domains. Disorganized symptom severity was also significantly positively associated with severity of deficits in the Social Communication and Social Motivation subscale domains, as well as the

Social Awareness subscale domain. Finally, severity of both negative and general symptomatology was significantly positively associated with severity of deficits in all subscale domains.

Furthermore, it is interesting to note that the magnitude of the coefficients relating negative and general symptoms with the SRS total score and subscale scores were greater than those relating positive symptoms with SRS total score, while those for disorganized symptoms were relatively similar to the magnitude of the correlation coefficients for positive symptoms. In order to explore these differences further, the magnitudes of the coefficients were compared using *z*-score transformations. Comparisons revealed that the magnitude of the coefficients relating negative symptom severity were significantly stronger than those relating positive, and disorganized severity for the SRS total scale score. Additionally, those relating general symptom severity were significantly stronger than those relating positive symptom severity for the SRS total scale score. With regard to the subscale scores, correlation coefficients relating negative symptom severity were significantly stronger than those relating positive symptom severity to the Social Communication and the Autistic Mannerisms subscale scores, as well as for those relating the disorganized symptom severity to the Social Motivation subscale score. Further, the magnitude of the coefficients relating general symptom severity was significantly stronger than those relating positive symptom severity to the Social Motivation subscale. All other comparisons of the magnitudes of correlation coefficients relating symptom domains to the SRS total and subscale scores resulted in nonsignificant differences.

It is not surprising that the coefficients relating negative symptoms to severity of overall social deficits are stronger than for the positive and disorganized symptom domains. Prior research findings have suggested that presence of autistic symptoms co-vary with negative

symptoms (Sheitman, Kraus, Bodfish, & Carmel, 2004). Furthermore, although related, yet distinct (Sergi et al., 2007), negative symptoms may develop from a similar affective processing dysfunction as social cognitive impairments (Adolph, 2003; Pinkhan et al., 2003). As mentioned previously, affect has been shown to have numerous systematic and widespread associations with social cognitive processes and has been suggested to serve as a "tuning function" for social cognition (Higgins & Sorrentino, 1990; Sorrentino & Higgins, 1986, 1996).

The fact that negative symptom severity was also more strongly related to the Social Communication subscale (purposed to evaluate expressive deficits) than positive symptom severity is also not surprising given that the SIPS negative symptom domain measures items such as social anhedonia, avolition, expression of emotion, experiences of emotion and the self, and ideational richness, all components that lend to the interactive expressive aspect of social competency. Further, the significantly stronger relation of negative symptom severity to the Autistic Mannerisms subscale than positive symptom severity also isn't surprising given items included in that subscale. For example, "thinks or talks about the same things over and over again", "can't get his or her mind off something once he or she starts thinking about it," and "has an unusually narrow range of interests" can also be viewed through the lens of negative symptomatology, particularly anhedonia and avolition.

The fact that general symptom severity was more strongly correlated with the SRS total scale score than the positive symptom domain, and in particular, the Social Motivation subscale score, is also understandable given the nature of the items assessed by that subscale In particular, items such as "more fidgety in social situations" and "is too tense in social situations" may present as being indicative of one's impaired tolerance to normal stress, forms of motoric disturbances or the irritability associated with dysphoric mood, which are all a part of the general

symptoms domain. In addition, items such as "would rather be alone," "doesn't join in unless told to do so," and "avoids social interactions," may explain the stronger relatedness of negative symptom severity to the Social Motivation subscale than disorganized symptom severity. In particular, this subscale tends to measure perceived oddities rather than outright obvious and/or bizarre behaviors that the disorganized symptom domain is purposed to tap (e.g., odd behavior or appearance, trouble with focus and attention, hygiene, bizarre thinking).

Taken together, the results of the bivariate correlational analyses and assessment of significant differences between the magnitudes of those coefficients reveal interesting findings regarding social deficits in individuals considered to be at clinical high risk for conversion to a primary psychotic disorder. Currently there is a paucity of research examining the subscales outside of interventions targeting the improvement of them within clinical setting for individuals affected by autism-spectrum disorders. Future research should continue to assess not only the usefulness of the SRS total scale score for discriminating between diagnostic groups, but also the utility of these specific subscales. In particular, it would be useful to continue to examine how the SRS total scale score and the subscale scores relate to the diagnostic criteria for psychological disorders, such as the schizophrenia-spectrum of disorders.

Conclusions

In summary, the current study illustrates the utility of the SRS in detecting social deficits in youth at clinical high risk for schizophrenia-spectrum disorders. Prior research and the present study also illuminate important relationships between symptomatology and SRS scores, and give evidence for the ability of the SRS to discriminate between HC, OD, and CHR adolescents. Further research on the genetic overlap between or influence of parental age on the development of autism- and schizophrenia-spectrum disorders may benefit from also including

the SRS as a measure of autism-spectrum social deficits. Such a combination may have the potential to inform the accumulating body of evidence suggesting partially overlapping etiological pathways for the development of these two disorder spectra.

For example, a recent report reviewed extant genomic and genetic data to test the predictions that differentiate among various models of the relationship between autism and schizophrenia (Crespi, Stead, & Elliot, 2010). The authors conclude that "the presence of genetically-based risk factors common to autism and schizophrenia, including deletions, duplications, or specific alleles shared between the conditions" lend support to the notion of partially-overlapping etiology in that some genetic variants appear to increase liability to both spectra. At the same time, they note that there is also evidence that the two spectra represent "diametric conditions" in that they tend not to co-occur in families, involve different patterns of brain abnormality, and are associated with a differential pattern of dysfunction in genes that regulate growth signaling pathways in brain development.

It is possible that the 'autistic-like' social deficits observed in the present sample of youth at risk for psychosis reflect the shared genetic risk factors that have been reported in studies of autism and schizophrenia. Nonetheless, the diagnostic distinctions between the two spectra include differences in the developmental onset and course of the disorders. Most notable, autism-spectrum disorders are, by definition, syndromes that are apparent within the first 3 years of life. In contrast, psychotic disorders have a modal age of onset in young adulthood, and the childhood developmental course is typically well within normal limits, although there are exceptions. There are several promising lines of investigation that could shed light on both the shared and diametric aspects of autism- and schizophrenia-spectrum disorders. First, research aimed at relating social deficits with the genetic risk factors that have been shown to be shared

by both disorder spectra may prove fruitful in elucidating the origins of the phenomenological overlap. Second, genetic studies comparing prototypical early-onset autism patients with schizophrenia patients who manifest high levels of childhood functioning have the potential to reveal marked distinction between them in genes that regulate growth signaling pathways.

Several limitations of the present study should be considered in interpreting the findings. First, as the SRS was only utilized at baseline, this current investigation was limited to the cross-sectional baseline portion of a longitudinal study. Longitudinal assessment of the progression of social deficits and symptom domains is warranted, given prior research indicating the ability to detect social functioning in the prodrome, their presence at the first-episode, and their increase as a function of chronicity in schizophrenia-spectrum disorders (Addington, Penn, Woods, Addington, & Perkins, 2008; Drake et al., 2007; Gòrna et al., 2008; Grant et al., 2001; MacDonald et al., 1998; Voges & Addington, 2005). Second, although of a relatively short duration (past six months), SRS ratings are subject to limitations inherent in retrospective informant-report. Third, although of adequate size for the current investigation, the sample size does limit the types of data analyses possible with the SRS scale. With a larger sample, an examination of the latent structure of the overall SRS would be permissible and perhaps of benefit to future investigations seeking to provide support for the design and implementation of socioemotional interventions in studies attempting to address and monitor outcome variables of interest.

Despite these limitations, taken together with prior research, the present findings suggest the SRS as a useful measure of social deficits in individuals deemed to be at clinical high risk for developing psychotic disorder. Additionally, future studies of social deficits (as measured by the SRS) that compare individuals with autism-spectrum disorders to those diagnosed with

schizophrenia-spectrum disorders would be of great benefit. Furthermore, given the aforementioned research indicating social functioning deficits detectable in the prodrome and present in the early course of primary psychotic disorders (Addington et al., 2008; Drake et al., 2007, Gòrna et al., 2008), research utilizing the SRS should also consider assessing social deficits in studies comparing individuals at-risk for conversion to psychosis to those early on in the course of a schizophrenia-spectrum disorder. Given that severity of child psychiatric conditions is intensified by comorbid social impairment, even when considered subthreshold (Constantino et al., 2000), measurement of social deficits with the SRS may prove useful for not only a greater understanding of shared and distinct etiological influences on autism- and schizophrenia-spectrum disorders, but also in the ability to predict clinical course in general for primary psychotic disorders.

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Appendix A

The SRS Scale items

1. Seems much more fidgety in social situations than when alone
2. Expressions on his or her face don't match what he or she is saying
3. Seems self-confident when interacting with others
4. When under stress, he or she shows rigid or inflexible patterns of behavior that seem odd
5. Doesn't recognize when others are trying to take advantage of him or her
6. Would rather be alone than with others
7. Is aware of what others are thinking or feeling
8. Behaves in ways that seem strange or bizarre
9. Clings to adults, seems too dependent on them
10. Takes things too literally and doesn't get the real meaning of a conversation
11. Has good self-confidence
12. Is able to communicate his or her feelings to others
13. Is awkward in turn-taking interactions with peers (e.g., doesn't seem to understand the give-and-take of conversations)
14. Is not well coordinated
15. Is able to understand the meaning of other people's tone of voice and facial expressions
16. Avoids eye contact or has unusual eye contact
17. Recognizes when something is unfair
18. Has difficulty making friends, even when trying his or her best
19. Gets frustrated trying to get ideas across in conversations

20. Shows unusual sensory interests (e.g., mouthing or spinning objects) or strange ways of playing with toys
21. Is able to imitate others' actions
22. Plays appropriately with children his or her age
23. Does not join group activities unless told to do so
24. Has more difficulty than other children with changes in his or her routine
25. Doesn't seem to mind being out of step with or "not on the same wavelength" as others
26. Offers comfort to others when they are sad
27. Avoids starting social interactions with peers or adults
28. Thinks or talks about the same thing over and over
29. Is regarded by other children as odd or weird
30. Becomes upset in a situation with lots of things going on
31. Can't get his or her mind off something once he or she starts thinking about it
32. Has good personal hygiene
33. Is social awkward, even when he or she is trying to be polite
34. Avoids people who want to be emotionally close to him or her
35. Has trouble keeping up with the flow of a normal conversation
36. Has difficulty relating to adults
37. Has difficulty relating to peers
38. Responds appropriately to mood changes in others (e.g., when a friend's or playmate's mood changes from happy to sad)
39. Has an unusually narrow range of interests
40. Is imaginative, good at pretending (without losing touch with reality)

41. Wanders aimlessly from one activity to another
42. Seems overly sensitive to sounds, textures, or smells
43. Separates easily from caregivers
44. Doesn't understand how events relate to one another (cause and effect) the way other children his or her age do
45. Focuses his or her attention to where others are looking or listening
46. Has overly serious facial expression
47. Is too silly or laughs inappropriately
48. Has a sense of humor, understands jokes
49. Does extremely well at a few tasks, but does not do as well at most other tasks
50. Has repetitive, odd behaviors such as hand flapping or rocking
51. Has difficulty answering questions directly and ends up talking around the subject
52. Knows when he or she is talking too loud or making too much noise
53. Talks to people with an unusual tone of voice (e.g., talks like a robot or like he or she is giving a lecture)
54. Seems to react to people as if they were objects
55. Knows when he or she is too close to someone or is invading someone's space
56. Walks in between two people who are talking
57. Gets teased a lot
58. Concentrates too much on parts of things rather than seeing the whole picture. For example, if asked to describe what happened in a story, he or she may talk only about the kind of clothes the characters are wearing
59. Is overly suspicious

60. Is emotionally distant, doesn't show his or her feelings
61. Is inflexible, has a hard time changing his or her mind
62. Gives unusual or illogical reasons for doing things
63. Touches others in an unusual way (e.g., to make contact and walk away without saying anything)
64. Is too tense in social settings
65. Stares or gazes off into space

Scoring Instructions*:*

For each of the 65 items above, behavior over the past six months is rated as 0 (not true), 1 (sometimes true), 2 (often true), or 3 (almost always true). Items 3, 7, 11, 12, 15, 17, 21, 22, 26, 32, 38, 40, 43, 45, 48, 52, and 55 are reverse-scored prior to summation of total and subscale scores. Individual items for the separate subscale domains are listed below.

Social Awareness Subscale (8 items):

2, 7, 25, 32, 45, 52, 54, 56

Social Cognition Subscale (12 items):

5, 10, 15, 17, 30, 40, 42, 44, 48, 58, 59, 62

Social Communication Subscale (22 items):

12, 13, 16, 18, 19, 21, 22, 26, 33, 35, 36, 37, 38, 41, 46, 47, 51, 53, 55, 57, 60, 61

Social Motivation Subscale (11 items):

1, 3, 6, 9, 11, 23, 27, 34, 43, 64, 65

Autistic Mannerisms Subscale (12 items):

4, 8, 14, 20, 24, 28, 29, 31, 39, 49, 50, 63

Table 1

Demographic and Clinical Characteristics for Overall Sample and by Diagnostic Group

Variable	Overall Sample (*n*=122)	Healthy Controls (*n* = 45)	Other Disorders (*n* = 28)	Clinical High Risk (*n* = 49)	Test Statistic [a]
Age, years (mean ± SD)	14.2 ± 1.8 (range:11.0 – 18.0)	14.2 ± 1.9 (range: 11.0–18.0)	14.5 ± 1.8 (range: 12.0– 7.0)	14.1 ± 1.7 (range: 11.0–18.0)	$F_{2,119}$=0.37, p=0.690
Sex, *n* (%)					
Males	67 (54.9%)	23 (51.1%)	12 (42.9%)	32 (65.3%)	χ^2_2=(N=122)=4.04
Females	55 (45.1%)	22 (48.9%)	16 (57.1%)	17 (34.7%)	p=0.132
Race, *n* (%)					
White/Caucasian	72 (59.0%)	23 (59.0%)	16 (57.1%)	33 (67.3%)	
African American	43 (35.2%)	21 (46.7%)	9 (32.1%)	13 (26.5%)	χ^2_6=(N=122)=7.97
Asian American	4 (3.3%)	0 (0.0%)	2 (7.1%)	2 (4.1%)	p=0.240 [b]
Other	3 (2.5%)	1 (2.2%)	1 (3.6%)	1 (2.0%)	
SIPS Symptoms Subscales (mean ± SD)					
Positive	1.1 ± 0.9 (range: 0.0 – 3.6)	0.5 ± 0.6 (range: 0.0 – 1.6)	0.5 ± 0.4 (range: 0.0 – 1.4)	2.0 ± 0.4; (range: 0.0 – 3.6)	$F_{2,117}$= 122.53, p < 0.001*
Negative	0.9 ± 0.9 (range: 0.0 – 3.7)	0.4 ± 0.4 (range: 0.0 – 1.8)	0.8 ± 0.8 (range: 0.0 – 2.3)	1.5 ± 0.8 (range: 0.0 – 3.7)	$F_{2,117}$=20.59, p < 0.001*
Disorganized	0.7 ± 0.9 (range 0.0 – 1.25)	0.2 ± 0.3 (range: 0.0 – 1.25)	0.4 ± 0.3 (range: 0.0 – 1.25)	1.4 ± 1.0 (range: 0.0 – 3.8)	$F_{2,118}$=38.59, p < 0.001*
General	0.9 ± 0.9 (range: 0.0 – 4.25)	0.4 ± 0.5 (range: 0.0 – 1.5)	0.7 ± 0.5 (range: 0.0 – 2.0)	1.4 ± 0.5 (range: 0.0 – 4.3)	$F_{2,118}$= 21.33, p < 0.001*

[a] One-way analysis of variance comparisons between diagnostic groups.
[b] Likelihood ratio is reported because six cells have an observed count of less than five.
*Represents a significant difference between the three diagnostic groups (p<0.05)

Table 2

SRS Total and Subscale Alpha Coefficients for the Overall Sample and by Diagnostic Group

Variable	Overall Sample	Healthy Controls	Psychiatric Controls	Clinical High Risk
SRS Total Score	0.96	0.96	0.88	0.94
Social Awareness Subscale Score	0.47	0.41	0.28	0.57
Social Cognition Subscale Score	0.84	0.89	0.58	0.80
Social Communication Subscale Score	0.90	0.92	0.80	0.85
Social Motivation Subscale Score	0.80	0.73	0.72	0.82
Autistic Mannerisms Subscale Score	0.86	0.89	0.55	0.84

Table 3

SRS Total and Subscale Scores for Overall Sample and by Diagnostic Group (mean ± SD)

Variable	Overall Sample (n = 122)	Healthy Controls (n = 45)	Other Disorders (n = 28)	Clinical High Risk (n = 49)	Statistics [a]
SRS Total Score*	67.2 ± 32.7 (range: 3.0 – 156.0)	51.9 ± 34.0 (range: 3.0 – 131.0)	67.2 ± 21.3 (range: 25.0 – 99.0)	81.3 ± 31.0 (range: 27.0 – 156.0)	$F_{2,119}$=11.07, p<0.001[b]
Social Awareness Subscale Score	9.2 ± 3.5 (range: 0.0 – 18.0)	8.4 ± 3.5 (range: 0.0 – 16.0)	9.8 ± 3.2 (range: 4.0 – 18.0)	9.8 ± 3.6 (range: 3.0 – 18.0)	$F_{2,114}$=2.35, p=0.100
Social Cognition* Subscale Score	13.0 ± 7.5 (range: 0.0 – 29.0)	9.9 ± 8.1 (range: 0.0 – 29.0)	13.1 ± 5.0 (range: 3.0 – 25.0)	16.0 ± 6.9 (range: 5.0 – 28.0)	$F_{2,106}$=7.88, p=0.001[b]
Social Communication* Subscale Score	24.1 ± 12.9 (range: 1.0 – 54.0)	17.6 ± 13.3 (range: 1.0 – 48.0)	24.1 ± 9.9 (range: 8.0 – 40.0)	29.9 ± 11.1 (range: 8.0 – 54.0)	$F_{2,105}$=11.79, p<0.001
Social Motivation* Subscale Score	11.0 ± 6.1 (range: 0.0 – 24.0)	7.8 ± 4.9 (range: 0.0 – 18.0)	11.7 ± 5.6 (range: 3.0 – 23.0)	13.4 ± 6.2 (range:)	$F_{2,109}$=10.96, p<0.001
Autistic Mannerisms* Subscale Score	10.4 ± 7.6 (range: 0.0 – 34.0)	7.5 ± 7.4 (range: 0.0 – 29.0)	9.2 ± 4.5 (range: 0.0 – 20.0)	14.4 ± 7.6 (range: 1.0 – 34.0)	$F_{2,101}$=10.49, p<0.001[b]

[a] One-way analysis of variance comparisons between diagnostic groups.
[b] Significant Levene's test of homogeneity of variances results required that equal variances not be assumed in paired comparisons.
*Represents a significant difference between the three diagnostic groups (p<0.05).

Table 4

SRS Total and Subscale Scores by Sex within the Clinical High Risk Group

Variable	Mean ± SD	Gender	*n*	*t*	*p*	*d*
SRS Total Score	83.3 ± 31.4	Male	32	0.62	0.536	0.19
	77.5 ± 30.7	Female	17			
Social Awareness Subscale Score	9.9 ±3.7	Male	30	0.42	0.677	0.11
	9.5 ± 3.6	Female	17			
Social Cognition Subscale Score	16.3 ± 6.9	Male	27	0.34	0.732	0.11
	15.5 ± 7.1	Female	16			
Social Communication Subscale Score	30.4 ± 11.7	Male	30	0.37	0.716	0.12
	29.1 ± 10.1	Female	15			
Social Motivation Subscale Score	13.2 ± 5.8	Male	30	0.25	0.805	0.08
	13.7 ± 7.0	Female	17			
Autistic Mannerisms Subscale Score	15.0 ± 8.0	Male	25	0.63	0.535	0.21
	13.4 ± 7.1	Female	14			

Table 5

SRS Total and Subscale Correlations with SIPS Symptoms within the Clinical High Risk Group

	SIPS Symptom Subscales			
Variable	Positive	Negative	Disorganized	General
SRS Total Score	0.30*	0.64**	0.37**	0.62**
Social Awareness Subscale Score	0.22	0.37*	0.33*	0.39**
Social Cognition Subscale Score	0.20	0.42**	0.34*	0.51**
Social Communication Subscale Score	0.33*	0.64**	0.39**	0.58**
Social Motivation Subscale Score	0.34*	0.60**	0.27	0.65**
Autistic Mannerisms Subscale Score	0.09	0.52**	0.24	0.41**

* Correlations significant at the $p<0.05$ level

** Correlations significant at the $p<0.01$ level

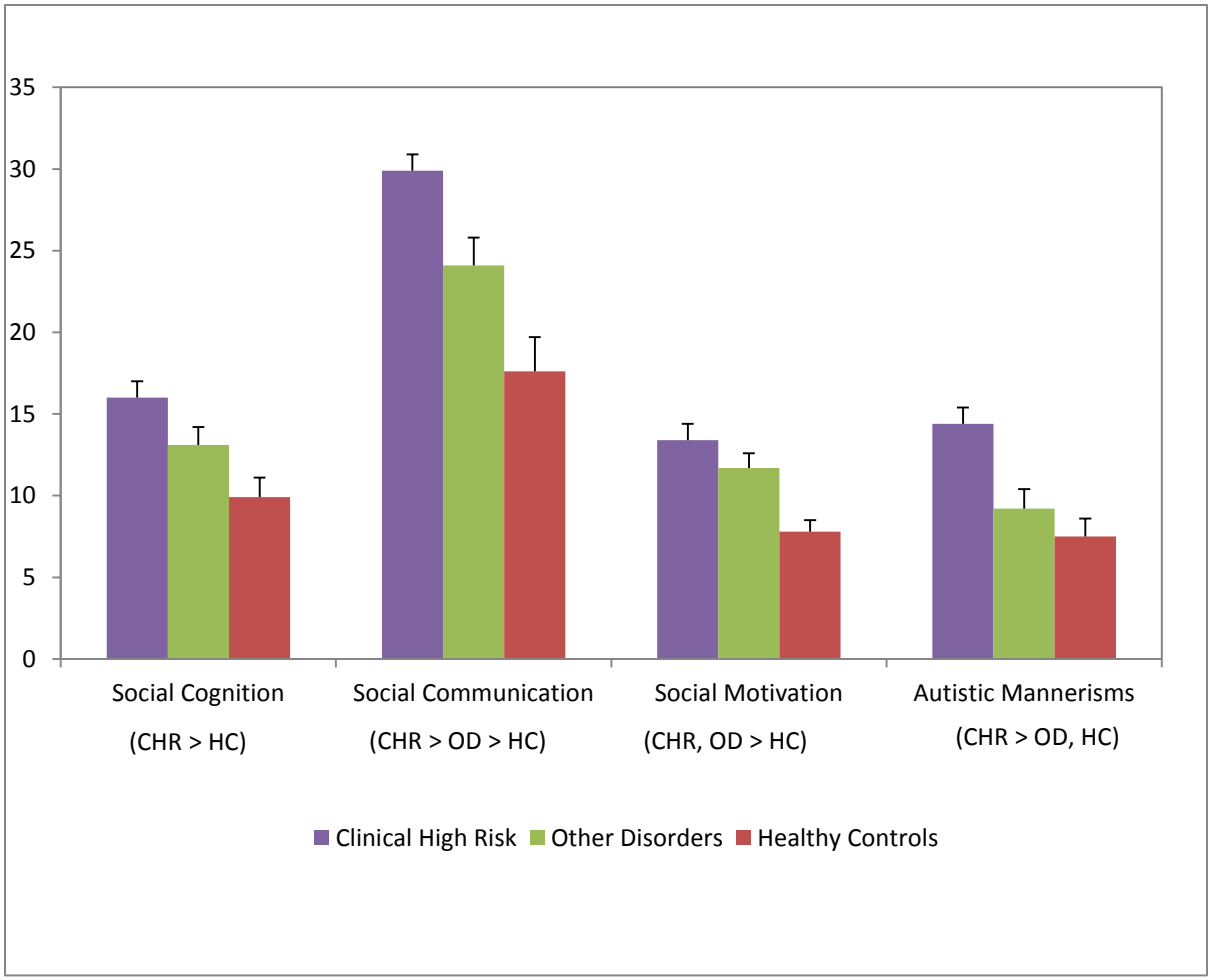

Figure 1. Mean SRS Subscale Scores by Diagnostic Group.

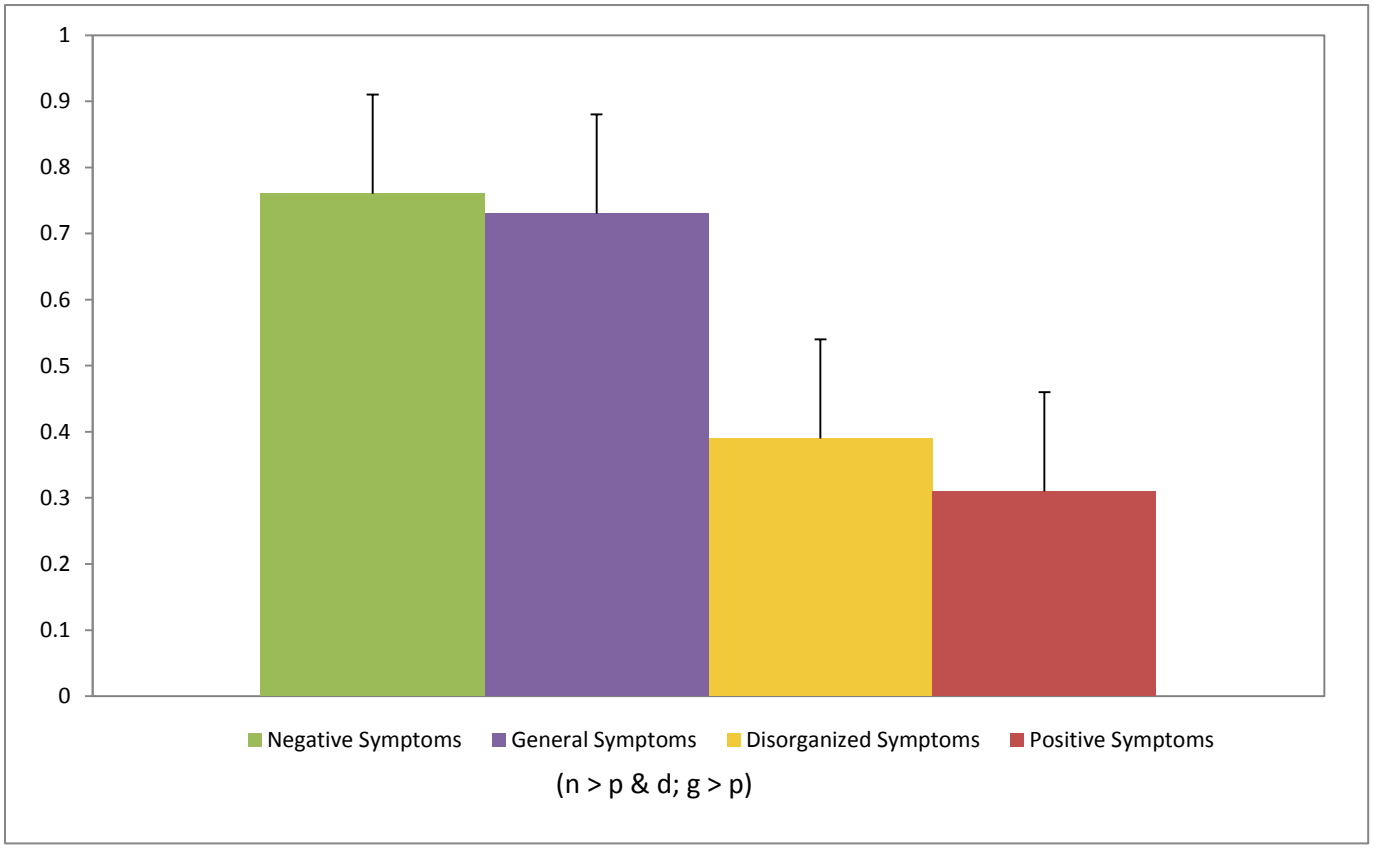

Figure 2. Standardized Comparisons of Differences in Associations between SRS Total Score and SIPS Symptom Domains.

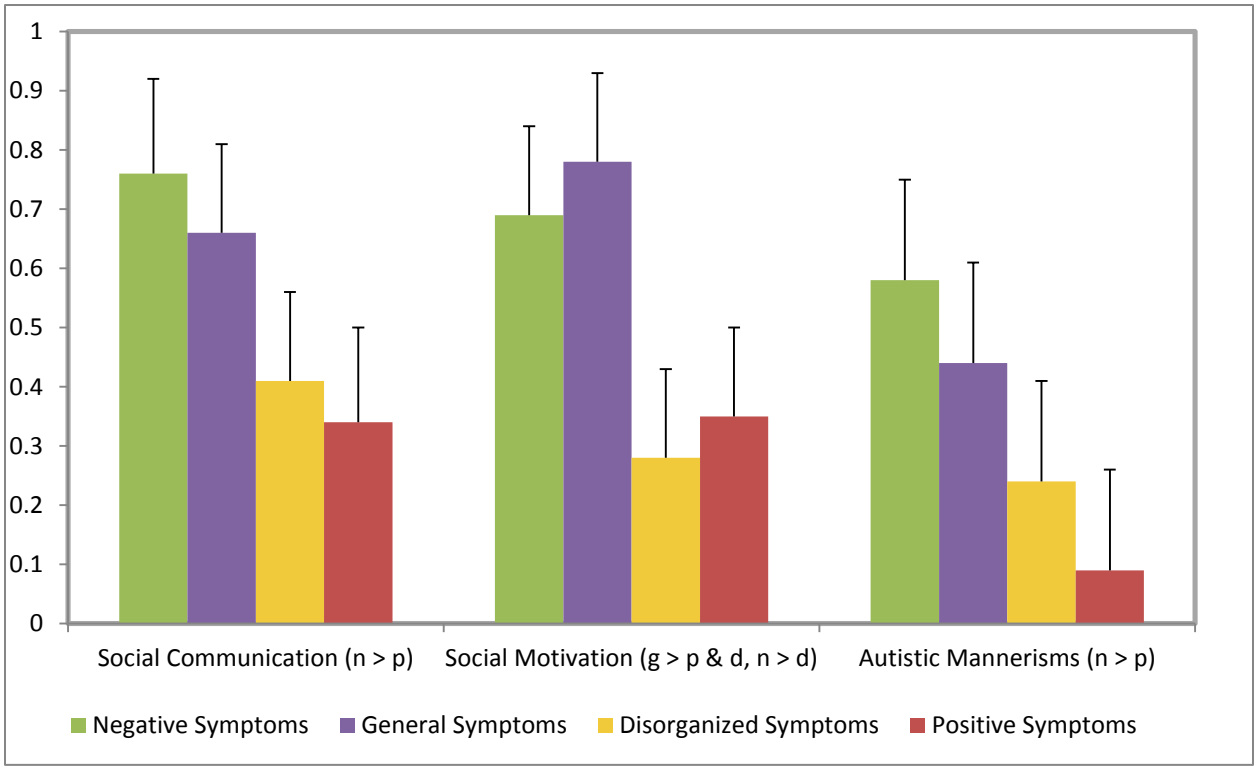

Figure 3. Standardized Comparisons of Differences in Associations between SRS Subscales and SIPS Symptom Domains.

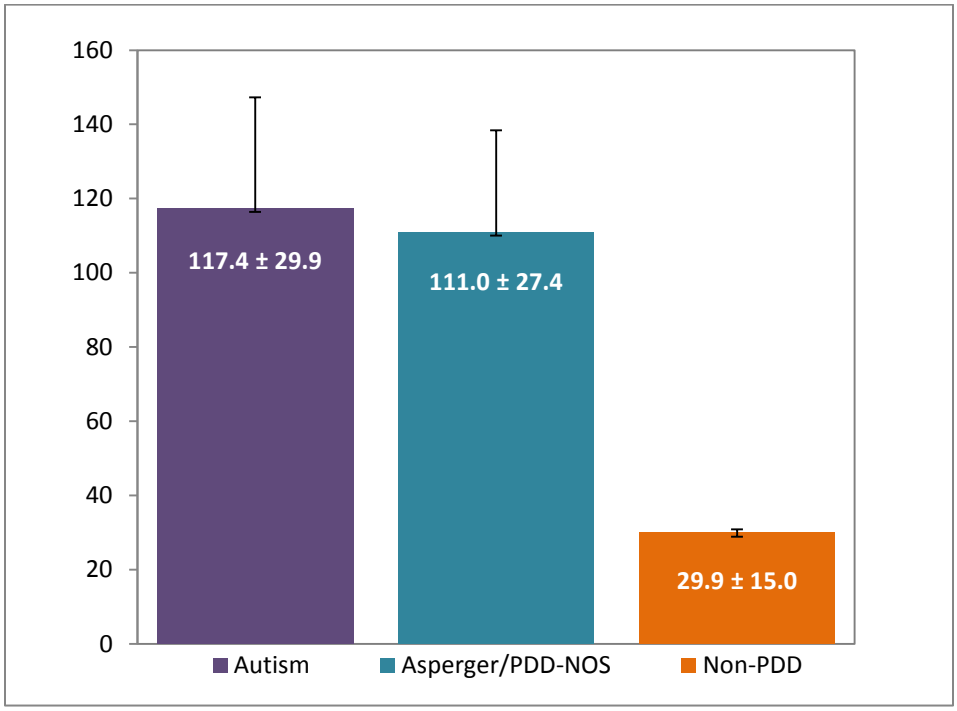

Figure 4. Average SRS Total Scores, as published in Constantino and colleagues, 2003.