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Diana I. Simeonova Date

Social and Behavioral Precursors of Conversion to Psychosis:
An Investigation of Youth at Risk for Psychosis

By

Diana I. Simeonova
Doctor of Philosophy

Psychology

_____
Elaine F. Walker, Ph.D.
Advisor

_____
Patricia Brennan, Ph.D.
Committee Member

_____
Linda Craighead, Ph.D.
Committee Member

_____
Stephen Nowicki, Jr., Ph.D.
Committee Member

_____
Stephan Hamann, Ph.D.
Committee Member

Accepted:

_____
Lisa A. Tedesco, Ph.D.
Dean of the Graduate School

_____
Date

Social and Behavioral Precursors of Conversion to Psychosis: An Investigation of Youth at Risk for Psychosis

By

Diana I. Simeonova
M.A., Emory University, 2005
Dipl.-Psych., University of Hamburg, 2000

Advisor: Elaine F. Walker, Ph.D.

An Abstract of
A dissertation submitted to the Faculty of the Graduate School of Emory University in partial fulfillment of the requirements for the degree of Doctor of Philosophy

Psychology

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Abstract

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An Investigation of Youth at Risk for Psychosis

By Diana I. Simeonova

This study explored social and behavioral problems in 122 adolescents ages 12 to 18 with schizotypal personality disorder (SPD), other personality disorders (OPD), and non-psychiatric controls (NC) at baseline and at one year follow-up assessments. Cross-sectional and longitudinal examination of social and behavioral precursors of conversion to psychosis was conducted with a subset of 14 high-risk Converted and 27 high-risk Non-Converted adolescents. Conversion to psychosis was defined as conversion to any Axis I schizophrenia spectrum disorder or affective disorder with psychotic features. SPD adolescents showed a Child Behavior Checklist (CBCL) behavioral profile with more social and behavioral impairments compared to OPD and NC adolescents. At one year follow-up assessment, compared to the Non-Converted subjects, the Converted subjects manifested significantly higher scores on all prodromal symptom scales of the Structured Interview for Prodromal Symptoms (SIPS). There were no differences in social and behavioral problems as a function of conversion status. The findings supported the relationship between positive family history of psychosis or affective disorders and behavioral problems, and were indicative of constitutional vulnerability underlying the risk for psychosis. The CBCL parent-report scale did not show promise as an alternative or adjunctive predictor of conversion to psychosis in high-risk SPD adolescents. The findings provided support for ratings from the SIPS structured interview as more sensitive predictors of conversion to psychosis in high-risk SPD adolescents.

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Psychosis entails one of the most dramatic presentations among the major psychiatric syndromes. Clinically, it is characterized by delusions, hallucinations, disorganized speech and other related symptoms. Psychosis occurs in schizophrenia spectrum disorders (i.e., schizophrenia and schizoaffective disorders), and can also be present in affective disorders, such as depressive and bipolar disorders, and in substance-induced psychosis (APA, 1994). Psychotic syndromes are assumed to vary along a continuum of severity, with co-occuring affective symptoms also varying in severity (Angst & Marneros, 2001; Pillmann & Marneros, 2007).

Social and behavioral precursors of psychosis are well documented in the literature (Cornblatt, 2002; Erlenmeyer-Kimling, 2000; Johnstone et al., 2000; Nuechterlein & Dawson, 1984; Olin & Mednick, 1996). The majority of individuals who succumb to schizophrenia and other psychotic disorders manifest prodromal signs of behavioral disturbance (Larsen, McGlashan, & Moe, 1996; Neumann, Grimes, Walker, & Baum, 1995). As a result, in recent years a series of research findings have generated optimism about the possibility of identifying high-risk individuals who might benefit from early clinical and potentially preventive interventions for psychotic illness (Cornblatt, Lencz, & Obuchowski, 2002; Rakfeldt & McGlashan, 2004; Yung et al., 2007; Salogankas & McGlashan, 2008). Based on this research and a recent emphasis on translational research with clinical utility, currently, a critical need exists for better understanding of the developmental course of social and behavioral precursors to psychosis and their predictive validity and accuracy in the prodromal period.

The purpose of this study is to address some important, but thus far unexplored, research questions about social and behavioral precursors of psychosis in youth at

clinical/behavioral high-risk for the development of psychosis. First, do the developmental behavioral trajectories of clinical high-risk youth who convert to psychosis differ from those who do not convert to psychosis? Second, do high-risk youth who convert to psychosis show a behavioral profile that differentiates them from youth who do not convert to psychosis? Third, is positive family history of psychosis or mood disorders associated with childhood behavioral ratings, and does it add to the prediction of conversion to psychosis? In addressing these questions the present research might also shed light on the diagnostic utility of the Child Behavior Checklist (CBCL) as an adjunctive screening instrument in the identification of high-risk youth converting to psychosis.

First, a brief overview of the nature of the prodrome and the diagnostic specificity of outcome for prodromal individuals is provided. Second, the relevant background literature and the neurodevelopmental theoretical framework guiding the study are reviewed. Third, the purpose of the study, its contribution above and beyond previous investigations, and the importance of the research questions are discussed.

Research Approaches in the Study of the Premorbid and Prodromal Stages

In the present context, the *premorbid* phase refers to the childhood and adolescent periods prior to the prodromal stage. During the premorbid phase subtle impairments (i.e., impairments in social and behavioral skills, and cognitive and neuromotor functions) are often present long before psychosis onset (Keshavan & Cornblatt, 2004). On the other hand, the *prodromal* phase, also called *prodrome*, refers to a developmental period between the premorbid and the psychotic phases. It is characterized by gradual progression of cognitive, affective, and social difficulties as well as subtle pre-psychotic-

like symptoms. The prodrome is typically defined as beginning with the first declines in behavior and lasting up until the onset of psychosis (Beiser, Erickson, Fleming, & Iacono, 1993; McGorry et al., 1995).

Traditionally, the focus of "high-risk" studies has been on identifying premorbid predictors of adult schizophrenia by studying first-degree relatives of affected patients, mostly young offspring of schizophrenic parents at genetic risk of illness development. These studies are typically referred to as "genetic" risk studies, and tend to utilize prospective designs, and begin typically when no clinical symptoms are visible (Cornblatt, 2002; Erlenmeyer-Kimling, 2000; Johnstone et al., 2000; Nuechterlein & Dawson, 1984; Olin & Mednick, 1996). More recently, during the 1990s, a number of high-risk researchers have begun to study the predictor potential of the subtle behavioral precursors that have been reported, retrospectively, to characterize the prodromal period. These "clinical" high-risk studies are considered to be pivotal in efforts to develop secondary prevention programs. The rationale is that this research would contribute to a tangible secondary prevention, which appears more immediately possible and provides an alternative while the search for early premorbid indicators continues to be refined and validated (for review see (Brown & Faraone, 2004; Cornblatt, Lencz, & Obuchowski, 2002; Cornblatt, 2002; Rakfeldt & McGlashan, 2004); Carpenter & Koenig, 2004). Because treatment and high-risk researchers, two traditionally separate fields, have become interested in studying the prodromal precursors of psychosis, this movement has resulted in a paradigm shift and a convergence of two research traditions on the schizophrenia prodrome (Cornblatt, Lencz, & Obuchowski, 2002). Thus, from a high-risk perspective, the search for prodromal risk factors is currently considered "cutting

edge." Although research on the prodromal stage of schizophrenia has experienced a considerable growth, it has also resulted in a great deal of controversy regarding definition of the prodrome, actual risk for psychotic outcome in prodromal individuals, treatment modalities and other related questions (Cornblatt, Lencz, & Obuchowski, 2002).

Notably, because of emerging research providing evidence for classification of disorders based on biological and dimensional approaches, more researchers are beginning to focus on studying the syndrome of psychosis cutting across nosological categories rather than studying separate diagnostic categories.

The Nature of the Prodrome

Most individuals who develop schizophrenia and other psychotic disorders manifest prodromal signs of behavioral disturbance (Larsen, McGlashan, Johannessen, & Vibe-Hansen, 1996). These signs usually begin in adolescence and become progressively worse as the individual approaches young adulthood (Cornblatt, Lencz, & Obuchowski, 2002). It is estimated that at least 70% of patients with schizophrenia manifest premorbid behavioral dysfunction during adolescence (Cannon, Rosso, Bearden, Sanchez, & Hadley, 1999; Neumann, Grimes, Walker, & Baum, 1995), with many showing schizotypal signs, such as social withdrawal and thought abnormalities (Walker, Baum, & Diforio, 1998), deficits in memory and executive function (Silverstein, Mavrolefteros, & Turnbull, 2003), and neurological soft signs (Neumann & Walker, 2003). It is assumed that the heightened risk associated with the postpubertal developmental period stems, in part, from neuromaturational processes that trigger the behavioral manifestation of latent vulnerability (Walker & Diforio, 1997). The prodromal period represents both a viable

point for intervention and a developmental period that, if studied, could shed light on the etiology of schizophrenia and other psychotic disorders.

Two main approaches have been used to measure prodromal symptoms and to diagnose prodromal syndromes (Olsen & Rosenbaum, 2006). One approach focuses on Attenuated Positive Symptoms (APS) and is assumed to measure late prodromal symptoms, while the other approach, the Basic Symptoms (BS) approach is based on a detailed phenomenological way of describing impairment in the pre-onset of psychosis and is assumed to measure early prodromal symptoms. The most frequently used criteria for diagnosis of prodromal states are based on the APS approach, which is the approach used in the present study. They are operationalized either by the Structured Interview for Prodromal Symptoms (SIPS), developed by McGlashan and colleagues at Yale University (Miller et al., 1999; Miller et al., 2002) or by the Comprehensive Assessment of At-Risk Mental States (CAARMS), developed by Yung, McGorry and colleagues at the University of Melbourne, Australia (Yung et al., 1996; Yung et al., 2005).

Extensive genetic and developmental evidence also links schizotypal personality disorder (SPD) with schizophrenia (Siever et al., 2002; Siever, Koenigsberg, & Reynolds, 2003). The diagnostic criteria for SPD entail "subclinical" manifestations of the positive and negative symptoms of schizophrenia. The link is substantiated by research in a number of areas including genetic, psychophysiological, neurological, cognitive and brain abnormalities (Raine & Mednick, 1995; Siever et al., 2002). This constitutes the basis for inclusion of SPD as a prodromal syndrome in standardized measures such as the SIPS. According to DSM-IV-TR criteria for SPD, the symptoms include: ideas of reference, excessive social anxiety, magical thinking, unusual perceptual experiences,

eccentric behavior or appearance, no close friends or confidants, odd speech, constricted affect, and suspiciousness. The disorder can occur in adolescents and in adults. Retrospective, prospective, and archival studies show that most adult patients with schizophrenia manifest SPD traits prior to the development of psychosis (Neumann & Walker, 1995). Further, research evidence suggests that SPD is a risk factor for schizophrenia and psychotic disorders (Walker, Baum, & Diforio, 1998).

A body of literature suggests a diathesis-stress explanation for the relation between SPD and schizophrenia. Under this framework, schizophrenia development involves constitutional vulnerability and environmental stressors. A genetic vulnerability places a person at-risk for schizophrenia, but environmental stress is necessary for the disorder to manifest. It has been suggested that SPD is an indication of vulnerability in the absence of the necessary stressor (Parnas, Schulsinger, Schulsinger, Mednick, & Teasdale, 1982).

The core features of SPD – social withdrawal, unusual perceptual experiences, and ideational abnormalities – parallel the prodromal signs of schizophrenia (Walker, Logan, & Walder, 1999). Adolescents with SPD traits appear to be at a particularly heightened risk for future psychosis development (Chapman, Chapman, Kwapil, Eckblad, & Zinser, 1994; Kwapil, 1998). Research indicates that SPD symptoms increase in severity during the preadolescent and the adolescent periods (Neumann & Walker, 1995; Tyrka et al., 1995). Moreover, about 20% to 40% of individuals meeting criteria for SPD in young adulthood convert to an Axis I psychotic disorder, primarily schizophrenia (Haroun, Dunn, Haroun, & Cadenhead, 2006; Miller et al., 2002; Yung et al., 2003). The remainder either shows other adjustment problems or a complete remission of symptoms

in young adulthood. Thus, studying high-risk adolescents with SPD is a viable research strategy for a better understanding of this developmental period with the possibility to shed light on the etiology of psychosis as well as aid in the formulation of early treatment options for this population.

There are key advantages to the longitudinal study of clinical high-risk adolescents with SPD. For instance, adolescence is the developmental period temporally preceding the peak risk period for onset of Axis I disorders. Also, most adolescents with SPD have not been exposed to psychiatric medications that complicate the interpretations of research results (Walker, Logan, & Walder, 1999).

Diagnostic Specificity of Outcome for Prodromal Individuals

Research indicates that in addition to schizophrenia or schizophrenia spectrum disorders outcome, prodromal individuals are at increased risk for developing affective disorders with psychotic features (i.e., bipolar disorder and unipolar depression) (Haroun, Dunn, Haroun, & Cadenhead, 2006; Miller et al., 2002; Yung et al., 2003). These findings are consistent with a growing evidence of shared etiological factors among schizophrenia spectrum disorders and affective disorders with psychotic features (Cardno, Rijsdijk, Sham, Murray, & McGuffin, 2002; Kelsoe, 2007). Schizophrenia and bipolar disorder, for instance, occur together in the same families more frequently than chance (Dutta et al., 2007). Emerging evidence from molecular studies indicates that at least some of the same genes contribute to both schizophrenia and bipolar disorder (Craddock, O'Donovan, & Owen, 2006; Maier, Hofgen, Zobel, & Rietschel, 2005; Maier, Zobel, & Wagner, 2006; Owen, Craddock, & Jablensky, 2007). The same gene and susceptibility allele may have a variety of phenotypic expressions (Kelsoe, 2007). For

instance, one meta-analysis implicated two regions on chromosomes 13q and 22q in both bipolar disorder and schizophrenia, while a third region on chromosome 8 appeared to be specific to schizophrenia (Badner & Gershon, 2002). Further, research indicates shared limbic lobe circuitry disturbances in schizophrenia and bipolar disorder (Benes, 2004). Thus, this research evidence challenges the current nosological diagnostic classification.

As a result, prodromal researchers have begun to focus their attention on psychosis as the clinical outcome variable in at-risk populations rather than schizophrenia spectrum disorders per se. To remain consistent with the growing prodromal research literature, the outcome variable in the present study is conversion to Axis I psychotic disorder (i.e., encompassing clinical outcome of schizophrenia spectrum disorders and affective disorders with psychotic features).

Within this context, social and behavioral precursors of psychosis are of particular interest because they have the potential to shed light on developmental processes, psychopathological mechanisms of action, and aid in the formulation of early intervention and prevention strategies for high-risk populations.

Social and Behavioral Precursors to Psychosis

Over the past three decades, an extensive body of research has provided evidence of social and behavioral signs of vulnerability to psychosis, especially schizophrenia, long before the illness onset (Cornblatt, 2002; Erlenmeyer-Kimling, 2000; Johnstone et al., 2000; Nuechterlein & Dawson, 1984; Olin & Mednick, 1996). The findings indicate that at least some pre-psychotic youth manifest signs of such problems.

To study social and behavioral precursors of psychosis, researchers have employed number of methods. *Retrospective studies* rely on retrospective accounts by

patients and family members of behaviors preceding the onset of psychosis. *Follow-back studies* examine precursors of illness onset by examining the previous medical and/or academic records and archival data on adults with known clinical outcome of psychosis in adulthood. *Follow-up studies* ascertain the outcome of individuals who either were the subject of previous research, or were treated in a clinical setting for adjustment problems. *High-risk studies* recruit children at different times in the lifespan, utilize mainly prospective design, and follow individuals considered to be at elevated risk for developing psychosis (Walker & Hochman, 2004). In the past, high-risk populations were defined mainly on the basis of family history of psychosis, typically a diagnosis of schizophrenia in the biological mother. More recently, the focus has shifted to populations who manifest behavioral signs of risk. Prodromal research falls in this category, as at-risk subjects are identified on the basis of prodromal symptoms.

The primary sources of information in these studies of youth at risk for psychosis are parent and teacher reports of social and behavioral functioning. The most commonly used instrument in retrospective studies is the Cannon-Spoor Scale (Cannon-Spoor, Potkin, & Wyatt, 1982), rating the patient on global adjustment during childhood and adolescence. In contrast, follow-back and follow-up studies contain less systematic information but address specific behavioral characteristics (Walker, Walder, Lewine, & Loewy, 2002). Recent prospective studies have begun to utilize standardized child behavior rating scales, such as the Child Behavior Checklist (Achenbach, 1991) that cover a broad range of behaviors.

Research indicates that the positive predictive value of behavioral abnormalities may be modest, depending on when the assessment is done and that predictive power

increases with age (Walker & Hochman, 2004). The difference between pre-psychotic individuals and those with healthy adult outcomes is greatest in late adolescence. Thus, studying adolescents at high-risk for psychosis appears to be a viable strategy to address this study's research questions.

What follows is a review of the literature guiding the present study, with focus on research involving preadolescent and adolescent populations. Studies examining precursors to psychosis in childhood are also addressed depending on their relevance to the research questions. Further, because the normative development of behavioral problems in the general population is critical to the understanding of abnormal development in youth, relevant findings from this literature are reviewed.

Retrospective Studies

Retrospective investigations of childhood and adolescent pre-schizophrenic functioning have revealed a pattern of gradually escalating behavior problems across childhood and into adolescence, characterized by sex differences. It has been found that there is a significant increase in adjustment problems in both sexes during adolescence but a more pronounced increase in behavioral problems among pre-schizophrenic males (Fennig, Putnam, Bromet, & Galambos, 1995). Similarly, using the Cannon-Spoor Scale, different developmental trajectories were identified for male and female pre-schizophrenic individuals, with males showing poorer adjustment and deteriorating more rapidly during adolescence than females (Larsen, McGlashan, Johannessen, & Vibe-Hansen, 1996).

To obtain more detailed picture of the premorbid developmental trajectory of psychosis, Walker and colleagues have conducted investigations using retrospective

parental ratings of childhood behavior (Baum & Walker, 1995; Neumann, Grimes, Walker, & Baum, 1995; Walker, Baum, & Diforio, 1998; Walker et al., 1995b; Walker, Grimes, Davis, & Smith, 1993; Walker, Weinstein, & Baum, 1995a). Parents of young adults with schizophrenia were asked to rate the childhood behavior of their children at four age periods: birth to 4 years, 4-8 years, 8-12 years, and 12-16 years using a retrospective version of the CBCL (Walker, Weinstein, & Baum, 1995a). Pre-schizophrenic subjects were compared with their same-sex siblings with healthy adult outcomes. Across all but the first age-period, pre-schizophrenic males showed significantly higher rates of externalizing problems, such as aggressive and delinquent behaviors. They also showed significantly more internalizing behavior problems, such as anxiety, withdrawal, depression and somatic concerns, beginning in the 4-8 age periods. In contrast, pre-schizophrenic females did not differ from their same-sex siblings in externalizing behaviors, but they did manifest more internalizing behaviors, beginning in the 8-12 age period. They also exceeded the pre-schizophrenic males in the rate of internalizing problems, with depression scores differentiating most compared to the other behavior ratings. Specifically, compared to same-sex healthy siblings and pre-schizophrenic males, the pre-schizophrenic females showed higher rates of depression across all age periods and more increase in depression rating during adolescence. This developmental trend indicates that normative sex differences in depressive symptoms are more pronounced in pre-schizophrenic subjects (Walker, Weinstein, & Baum, 1995a).

Walker and colleagues have also tested the hypothesis that pre-schizophrenic children differ from their healthy siblings in facial expressions of emotion by examining home movies of 32 of these patients and 31 of their healthy siblings (Walker, Grimes,

Davis, & Smith, 1993). As with other studies, the researchers divided the retrospective assessment of age periods in four age periods from birth to 16 years. Convergent with the findings examining behavioral ratings, it was found that the pre-schizophrenic females manifested significantly less positive facial emotion than did their same-sex healthy siblings, pre-schizophrenic males, and non-schizophrenic males. They also appeared to show more internalizing behaviors, such as social withdrawal. Those differences were apparent as early as infancy and became more pronounced in adolescence. In contrast, males showed more externalizing behavior problems that may be accompanied by negative affect. Consistent with the findings of increased depression in pre-schizophrenic subjects (Walker, Weinstein, & Baum, 1995a), all pre-schizophrenic subjects showed greater negative affect than their same-sex comparison groups. The effect sizes of facial expression tended to be larger in the birth to 4-year and 12-16 years age periods (Walker, Grimes, Davis, & Smith, 1993).

Another study by Walker and colleagues utilized retrospective CBCL ratings of 29 adults with schizophrenia and their 28 healthy siblings at four age periods to study behavioral precursors of schizophrenia (Neumann, Grimes, Walker, & Baum, 1995). The findings provide evidence for the presence of adjustment problems long before illness onset and indicate that the severity of these problems increases with age. The developmental behavioral trajectories of the pre-schizophrenic participants were compared with their healthy siblings. There was a gradual increase of behavioral problems across childhood and a more dramatic increase during adolescence. As indicated by the standardized CBCL behavioral scales, pre-schizophrenic participants showed a higher rate of Internalizing and Externalizing behavior problems as well as

higher ratings on the Social Problems, Thought Problems, and Attention Problems scales. However, the pattern of age-related changes showed differences between the scales. Social Problems scores were significantly elevated in the pre-schizophrenic subjects at all ages. Attention Problems scores significantly differentiated the two groups as early as the first age period, birth to 4 years, and then became more pronounced in the 12-16 year period. In contrast, Thought Problems emerged in the 4-8 year period and then showed a dramatic increase in the 12-16 year period. Sex was included as a covarite in the analyses and the results indicated that being female was associated with higher Withdrawn and Social Problems scores.

Walker and colleagues also examined the developmental trajectory of behavioral problems in a clinical high-risk group of prodromal youth at risk for psychosis, a group of adolescents diagnosed with SPD (Walker, Baum, & Diforio, 1998). The main research question in the study was whether SPD is preceded by escalating behavioral problems similar to those shown by individuals who are diagnosed with schizophrenia in adulthood. The abovementioned retrospective version of the CBCL, found to be highly sensitive to diagnostic group differences in premorbid behavior (Baum & Walker, 1995), was used to study 14 SPD subjects compared to 17 subjects meeting diagnostic criteria for one or more other personality disorders (OPD) and 26 normal controls (NC). First, the three diagnostic groups were compared cross-sectionally on the mean ratings of the CBCL scales (Internalizing Problems, Externalizing Problems, Social Problems, Thought Problems, and Attention Problems) for the participant's current age period. The results indicated that compared to the OPD and NC groups, the SPD group exhibited more Internalizing Problems, Social Problems, Thought Problems, and Attention Problems.

There were no group differences on the CBCL Externalizing Problems ratings. Second, the groups were compared using retrospective CBCL ratings. The following patterns emerged. For Internalizing Problems, there were no differences between the three diagnostic groups in the first three age periods. At the fourth age period (12-16 years), the SPD group showed significantly more Internalizing Problems relative to both the OPD and NC groups. Similar results were obtained for the Externalizing Problems and for the Thought Problems scales, with the exception that the OPD group did not differ from the SPD or the NC groups. For the Attention Problems scale, the SPD group showed more problems at the first (birth to 4 years) and fourth (12-16 years) age periods compared to the OPD and the NC groups. For the Social Problems scale, at all four age periods, the SPD group had significantly higher scores compared to the OPD and the NC groups. Overall, the study findings suggest parallels in the developmental trajectories of SPD and pre-schizophrenic individuals (Walker, Baum, & Diforio, 1998). It is noteworthy that the same developmental trajectory was not observed in the group of OPD adolescents.

A study utilizing a retrospective version of the CBCL for five age periods (birth to 3 years, 4-7 years, 8-11 years, 12-15 years, and 16-18 years) investigated behavioral problems in 32 subjects with schizophrenia compared to their healthy siblings with no history of mental illness (Rossi et al., 2000). There were significant differences in behavioral problems on all CBCL scales, with higher scores in the patient group. Using cluster analysis the researchers found two subgroups of childhood premorbid behavioral profiles in the patient group. Cluster I pre-schizophrenic patients showed initially low level of problems in childhood and consistent increase over time, while cluster II pre-schizophrenic patients showed a relatively stable high level of problems from childhood

until early adulthood, which were closely related to negative symptoms such as withdrawn and anxious-depressed behaviors (Rossi et al., 2000).

Finally, a study utilizing a retrospective version of the CBCL for two age periods (birth to 3 years and 4-11 years) investigated behavioral problems in 23 adolescents with schizophrenia compared to 23 subjects with anorexia nervosa and 23 healthy controls (Muratori et al., 2005). For both assessed age periods, there were significantly higher levels of behavioral problems in the clinical groups on all CBCL scales compared to healthy controls. No differences were found between schizophrenic and anorectic patients for the age period birth to 3 years. For the age period 4 to 11 years the schizophrenic patients showed significantly higher scores on the scales Social Problems, Thought Problems, Attention Problems and School Competencies.

Overall, the findings from retrospective studies suggest that compared to controls (same-sex healthy siblings or normal controls), pre-schizophrenic males exhibit more externalizing problems, while pre-schizophrenic females exhibit more internalizing problems and more depressive symptoms. Further, pre-schizophrenic subjects (and SPD subjects) show higher ratings on the scales Social Problems, Thought Problems, and Attention Problems. Behavioral problems are noticeable early in childhood, increase with age, and become more pronounced in the adolescent period.

Follow-back Studies

The findings from follow-back studies of schizophrenia patients parallel the results from retrospective reports. Research utilizing data from high school yearbooks from adult males with schizophrenia found that pre-schizophrenic individuals participated in significantly fewer social activities than the normal control group (Barthell

& Holmes, 1968). Interestingly, the groups did not differ on the level of participation in activities. The researchers concluded that the pre-schizophrenic adolescents were more socially isolated than the normal controls.

In the 1970s, Watt and colleagues conducted number of studies by examining school records of adults with schizophrenia and teachers' comments. Those ratings were compared to a same-sex control group (Watt, 1972; Watt, Stolorow, Lubensky, & McClelland, 1970). Pre-schizophrenic males were more likely to be described as moody, unmotivated, abrasive, and noncompliant, while pre-schizophrenic females were described as inhibited, sensitive, and conforming. There was a gradual increase of behavioral problems over time, with a marked rise in adolescence. Moreover, the developmental trajectory differed for males and females. Prior to grade 7 the differentiating factor for pre-schizophrenic children compared to same-sex controls was "emotional instability", with the pre-schizophrenic children being described as less emotionally mature, cheerful, and secure. From grade 7 to grade 12, the pre-schizophrenic females became more introverted and emotionally unstable, while the pre-schizophrenic males became more noncompliant and antisocial compared to same-sex controls. These findings were replicated in an extended study sample (Watt, 1978; Watt & Lubensky, 1976). Within-diagnostic group comparisons revealed that the pre-schizophrenic females were more introverted than all other groups of children, particularly during adolescence. In contrast, the pre-schizophrenic males were never more introverted than any other groups, but were more disagreeable than all other groups during adolescence.

Overall, the findings from follow-back studies suggest that compared to controls, pre-schizophrenic males exhibit more non-compliant and antisocial behaviors, while pre-schizophrenic females are more introverted and socially inhibited. This research provides additional evidence for a marked rise of adjustment problems during the adolescent period.

Follow-up Studies

The findings from follow-up studies parallel the general pattern of findings identified in retrospective and follow-back reports. Those studies are often conducted with general population birth cohorts and are unselected for specific characteristics.

As part of the Medical Research Council National Survey of Health and Development, a study was conducted on the psychiatric outcome data of the 1946 British birth cohort (Jones, Rodgers, Murray, & Marmot, 1994). This general population cohort was repeatedly evaluated between birth and 16 years of age. 30 patients with schizophrenia (10 female) were identified in this cohort. They were compared to 4,716 subjects with no psychiatric diagnosis. Analyses of teacher evaluations indicated that at ages 13 and 15 years the pre-schizophrenic individuals were more anxious, solitary, and gloomy than the comparison group. In terms of sociability, the pre-schizophrenic children preferred to play on their own at ages 4 and 6 years, and showed a statistically significant linear trend for being more socially anxious in adolescence. Using a self-report measure the researchers found that at age 13 the pre-schizophrenic youth reported feeling less socially confident than controls. In contrast with other studies, the researchers failed to find an increase in disruptive or antisocial behaviors in pre-schizophrenic children (Jones, Rodgers, Murray, & Marmot, 1994).

Findings on clinical outcome have been reported on another British birth cohort from 1958 with a similar study design (Done, Crow, Johnstone, & Sacker, 1994). Teachers completed behavior rating scales on the children when they were ages 7 and 11. The ratings for pre-schizophrenic children were compared with those of same-sex individuals with healthy adult outcomes. The pre-schizophrenic males showed more antisocial and hostile behavior ("overreaction "), while pre-schizophrenic females showed heightened "overreaction" and "underreaction" (i.e., social withdrawal and depression) (Done, Crow, Johnstone, & Sacker, 1994). For both sexes, pre-schizophrenic children showed a pattern of escalating adjustment problems with age. Consistent with previous investigations, the developmental trajectory differed depending on sex, such as that the pre-schizophrenic males became more "overreactive", while the pre-schizophrenic females became more "underreactive" with time.

A landmark study was conducted with the Israeli Draft Board Conscript Cohort assessing Israeli males at 16 or 17 years for their eligibility for military service (Davidson et al., 1999). The follow-up was 4 to 10 years. 509 males were admitted and 9,215 males were not admitted with a diagnosis of schizophrenia to a psychiatric hospital during follow-up. Poor social functioning (i.e., fewer social relationships), poor organizational ability, and low intellectual functioning predicted psychiatric hospitalization for schizophrenia. The results suggest that scores measuring social functioning, organizational ability, and intellectual functioning can be used to predict future hospitalization for schizophrenia with positive predictive power of 71.6%. The authors also stress that these findings are consistent with earlier research that points to relatively poor premorbid behavioral and personality adjustment, especially in terms of impaired

social relationships, among those who are later diagnosed with schizophrenia (Davidson et al., 1999). Notably, those findings relate to the late premorbid phase. Other authors have stressed that the impairments subjects in the Israeli draftee study had displayed, if measured prospectively, would have had more predictive power that the impairments noted above from studies of the early premorbid phase (Rakfeldt & McGlashan, 2004). In the Israeli draftee cohort, the intellectual and social deficits of the draftees had the positive predictive value for developing schizophrenia 5 years later (on average) of 75%, as compared to 5% positive predictive value of the teacher's reports of children in the 1946 British cohort (Jones, Rodgers, Murray, & Marmot, 1994).

Another study utilizing data from the Israeli Draft Board Registry compared the premorbid behavioral functioning of patients who were later hospitalized for mental illness. The study groups consisted of 536 patients with schizophrenia, 68 patients with non-psychotic bipolar disorder, and 31 patients with schizoaffective disorder who were compared to healthy controls (Reichenberg et al., 2002). The following behavioral functioning domains were assessed: social functioning, organizational ability, individual autonomy, physical activity, and functioning in structured environments. Subjects with schizophrenia and schizoaffetive disorder showed significant premorbid deficits in all behavioral domains relative to the comparison subjects, while subjects with non-psychotic bipolar disorder were not significantly different from the comparison subjects on any of the behavioral measures.

Overall, the findings from follow-up studies indicate that compared to controls, pre-schizophrenic patients experience significant impairment in social functioning and organizational ability, with females being more socially withdrawn and depressed and

males being more antisocial and hostile over time. As with previous studies, this research provides evidence for escalation of adjustment problems during the adolescent period.

Genetic High-Risk Studies

The trends revealed in retrospective, follow-back, and follow-up studies converge with research utilizing a high-risk prospective paradigm. Traditional high-risk studies focusing on genetic predisposition and the premorbid phase recruit children at different times in the lifespan. Only a few studies thus far have followed genetic high-risk samples into adulthood. As discussed earlier, more recently the focus of high-risk research has shifted to populations who manifest behavioral signs of risk, also called clinical high-risk subjects. Prodromal research falls in this category, as at-risk subjects are identified on the basis of prodromal symptoms. In the following section, findings that pertain to the preadolescent and adolescent developmental periods and are deemed most relevant for the present study are reviewed.

In 1962, Sarnoff Mednick and Fini Schulsinger initiated the Copenhagen High Risk Study of offspring of schizophrenic parents (Mednick & Schulsinger, 1965). This was the first large-scale high-risk study of this population. The study recruited 207 offspring of schizophrenic mothers and 104 offspring of healthy control mothers, when children were on average 15 years of age. The study followed subjects through the risk period, up to 42 years of age on average. Findings based on teacher ratings in the school records of high-risk children indicate that when compared to high-risk males with healthy outcomes, the pre-schizophrenic males were described as being non-compliant, inappropriate and anxious, whereas the pre-schizophrenic females were described as anhedonic and withdrawn. The pre-schizophrenic subjects were isolated from peers

(John, Mednick, & Schulsinger, 1982). Teachers more often judged youth who were later diagnosed with schizophrenia to be emotionally labile and more vulnerable to future psychotic breakdown (Olin & Mednick, 1996). Pre-schizophrenic males were more likely to be rated as disruptive, anxious, lonely and rejected by peers and more likely to have repeated a grade. In contrast, pre-schizophrenic females were rated as nervous and withdrawn. For both sexes, the adjustment problems were greater in older children (Olin & Mednick, 1996) and among the group who later developed schizophrenia teacher ratings predicted prognosis for both sexes (Olin et al., 1998). In a later study with this cohort, the researchers investigated differences among pre-schizophrenic subjects, those with healthy adult outcomes, and those later diagnosed with SPD, or non-psychotic mental illness (Olin et al., 1998; Olin et al., 1997). The findings indicate that 75% of pre-SPD subjects exhibited classroom behaviors that distinguished them from their classmates. The pre-SPD subjects were more passive, socially detached, and hypersensitive to criticism. Premorbid behaviors differentiated between the pre-schizophrenic and the pre-SPD subjects depending on sex. Pre-schizophrenic males were more disruptive and excitable than pre-SPD males, while there were no specific premorbid behaviors differentiating females who later developed schizophrenia vs. SPD.

Another prospective study of high-risk youth with a schizophrenic parent is the Israeli High Risk Study, which begun in 1964 and showed that children at genetic risk for schizophrenia manifest an elevated rate of interpersonal problems, especially social withdrawal, during middle childhood and adolescence (Hans, Marcus, Henson, Auerbach, & Mirsky, 1992). Those children were rated low on social desirability by peers, exhibited low self-esteem, were suspicious and withdrawn, and had poor communication skills. At

follow-up 9 subjects (four female) met diagnostic criteria for schizophrenia or a Cluster A personality disorder. They were compared to high-risk children with healthy adult outcomes. Four subjects, all male, exhibited extreme social isolation and aggressive behavior in childhood. In contrast, the females were shy and withdrawn in childhood and self-reported higher rate of feeling insecure and socially rejected (Hans, Marcus, Henson, Auerbach, & Mirsky, 1992). In addition, childhood attentional problems successfully predicted the development of schizophrenia spectrum disorders (Mirsky & Duncan, 2004). Other relevant findings from this cohort indicate that high-risk youth have poor peer engagement, including failure to relate in age-typical ways with members of the opposite sex. These findings indicate that social withdrawal in this population is characterized by immaturity, social awkwardness, and peer rejection rather than anxiety or shyness (Hans, Auerbach, Asarnow, Styr, & Marcus, 2000).

Other studies of high-risk offspring of schizophrenic parents have yield similar results. The New York High Risk Project (Erlenmeyer-Kimling et al., 1997; Erlenmeyer-Kimling et al., 1995) was designed to investigate endophenotypic markers for the genetic susceptibility to schizophrenia. The first recruitment phase was in 1977-1979. Data on childhood behavioral problems of 185 subjects were obtained in a parent interview when children were 7-12 years of age (mean age = 9.5 years) (Amminger et al., 1999). A childhood behavior measure, mainly reflecting externalizing behaviors, was derived by a factor analysis. Because of insufficient factor loading, other items (i.e. reflecting social withdrawal) were not included in the analyses. Subjects with adult outcomes of schizophrenia-related psychoses exhibited significantly more behavioral problems than those with adult outcomes of affective disorders or anxiety disorders or those with

substance abuse only or no disorder. Other relevant findings from this cohort relate to impaired attention (Cornblatt, Obuchowski, Roberts, Pollack, & Erlenmeyer-Kimling, 1999; Cornblatt & Erlenmeyer-Kimling, 1985). In high-risk children impaired attention seems to remain stable throughout childhood and into adulthood. For instance, unaffected offspring in this cohort showed impaired attention in childhood, which was associated with later personality traits of social indifference and insensitivity (Cornblatt, Lenzenweger, Dworkin, & Erlenmeyer-Kimling, 1992). Offspring of parents with affective psychoses displayed attentional impairment, but not to the same degree as children at high-risk for schizophrenia. Overall, attentional problems have been proposed to play a mediating role. Researchers have suggested that attentional impairments may affect social interactions leading to anxiety, social withdrawal, and increased stress related to social situations, thus creating a possible feedback loop making psychosis outcome in susceptible individuals more likely (Cornblatt, Obuchowski, Schnur, & O'Brien, 1997).

The Edinburgh High Risk Study recruited a total sample of 228 subjects with at least two family members with a diagnosis of schizophrenia (Johnstone et al., 2000). While this is a prospective study, the researchers examined behavioral problems and their association with psychosis and later schizophrenic illness via retrospective CBCL ratings prior to age 13 and for ages 13-16 (Miller, Byrne, Hodges, Lawrie, & Johnstone, 2002). Two sets of data analyses were conducted in this study. For the first set of findings CBCL scores at study entry were available for 162 subjects. Those subjects included control group, subjects without psychotic symptoms, subjects with psychotic symptoms, and subjects with schizophrenia. CBCL scores for the children prior to age 13 did not

distinguish any of the study groups at entry to the study, while CBCL scores for ages 13 to 16 for the scales Delinquent Behavior and other problems distinguished significantly between controls and subjects with psychotic symptoms and controls and subjects with schizophrenia, respectively. The second set of analyses included two comparison groups: high-risk subjects with schizophrenia and well high-risk subjects. With the exception of the scales Somatic Symptoms and Thought Problems, all scale scores for ages 13-16 were significant predictors of later schizophrenia with subjects with schizophrenia showing significantly higher scores. This was also true for the scales Aggressive Behavior and Total Problems prior to age 13, with subjects with later schizophrenia showing higher scores (Miller, Byrne, Hodges, Lawrie, & Johnstone, 2002).

In contrast to the abovementioned studies, some studies examining sex-related differences in genetic high-risk samples have shown inconsistent findings regarding social and behavioral problems in this population. While a number of research reports have indicated that high-risk males exhibit more externalizing and disruptive behaviors and high-risk females exhibit more passivity and social withdrawal relative to controls, some studies have reported converse findings. With respect to premorbid social adjustment, one study found that schizophrenic males had significantly higher premorbid social impairment scores compared to schizophrenic females and males with affective disorders with psychotic features (Foerster, Lewis, Owen, & Murray, 1991a). Another study utilizing data from The New York High Risk Project described above reported high levels of physical anhedonia in males compared to females (Freedman, Rick, Roberts, Cornblatt, & Erlenmeyer-Kimling, 1998). Further, a recent study examined sex-differences in aggressive behavior in a high-risk sample of offspring of mothers with

schizophrenia reported that compared to high-risk females, high-risk males had significantly lower scores of aggressive behavior as measured by CBCL (Gutt et al., 2008). No sex-related differences in aggressive behavior were found in the control group of offspring of non-schizophrenic mothers. Another finding from this study showed that being a high-risk male was a protective factor against the presence of aggressive behavior in this population (Gutt et al., 2008).

Overall, the findings from genetic high-risk studies converge with findings from retrospective, follow-back, and follow-up studies. Although some inconsistent sex-related findings were reported in the literature, overall genetic high-risk studies indicate that compared to high-risk subjects with healthy outcomes, pre-schizophrenic males exhibit more externalizing behavior problems, while pre-schizophrenic females exhibit more internalizing behavior problems. Pre-schizophrenic subjects have an elevated rate of interpersonal problems and are more socially isolated and withdrawn, have poor peer engagement, and show more social awkwardness. They also have higher levels of impaired attention, which remain stable and elevated from childhood to adolescence, and are assumed to negatively affect social interactions leading to increased stress related to social situations.

Clinical High-Risk Studies

Consistent with findings from traditional genetic high-risk studies, findings from clinical high-risk studies reveal social and behavioral problems in this population. Studies conducted with a prodromal population at the Personal Assessment and Crisis Evaluation (PACE) clinic in Melbourne, Australia indicate a pattern of pre-psychotic behavioral deficits. In this study, patients (age range = 14-28 years) with either family history of

psychotic disorder, SPD, subthreshold psychotic symptoms, or brief transient psychotic symptoms were assessed. 20 of 49 subjects converted to psychosis within 12 months. Long duration of prodromal symptoms, poor overall functioning at intake, low level psychotic-like symptoms, depressive symptoms, apathy/avolition, anxiety symptoms, decreased attention, and disorganization were significant predictors of conversion to psychosis (Yung et al., 2003). A strategy of psychosis prediction was identified by using a combination of risk factors. A continuation of this study with a larger samples size of 104 subjects was conducted (Yung, Phillips, Yuen, & McGorry, 2004) and similar results were obtained.

The Recognition and Prevention (RAP) program was initiated in New York in 1998 to study a clinical high-risk population of adolescents and young adults. Based on analyses of structured instruments, recent findings from baseline data identified three different clinical groups: 20 clinical high-risk subjects characterized by attenuated negative symptoms (in particular, social withdrawal/isolation and school withdrawal/difficulties) or attenuated disorganized symptoms (odd behaviors or poor hygiene), 42 clinical high-risk subjects with attenuated positive symptoms without psychosis, and 20 schizophrenia-like psychosis subjects, but without meeting DSM-IV criteria for schizophrenia (Cornblatt et al., 2004; Lencz et al., 2004). The RAP program is a systematic attempt to teas apart different characteristics and prodromal symptoms often monitored as one group. The most commonly presenting symptom in all three groups was social isolation/withdrawal. Positive symptoms were reported as commonly as non-specific behavioral deficits, such as decline in school functioning, depressed mood, and anxiety symptoms (Lencz et al., 2004).

A recent study from this research group reported on the social and role functioning of high-risk prodromal subjects based on baseline and prospective 6 and 12 months data (Cornblatt et al., 2007). The social functioning scale in the study measured quantity and quality of peer relationships, level of peer conflict, age-appropriate intimate relationships, and relationships with family members. The role functioning scale measured age-appropriate level of functioning in school, work, home, and other settings. Relative to normal controls, the prodromal group displayed impaired social and role functioning at baseline. Role functioning declined before ascertainment and then it improved over a 12-month period. The researchers interpreted this finding as perhaps role functioning being a more sensitive indicator of clinical change and more responsive to environmental and treatment effect (Cornblatt et al., 2007). On the other hand, social impairment was consistent over time and predicted later onset of psychosis. This finding indicated that social functioning might represent a stable trait and be a potential vulnerability marker for psychosis development in high-risk prodromal subjects (Cornblatt et al., 2007).

Another research program for the study of the prodromal period is the Cognitive Assessment and Risk Evaluation (CARE) program at the University of California, San Diego (Seeber & Cadenhead, 2005). The at-risk sample is heterogeneous and subjects meet criteria for one of the following groups: brief intermittent psychosis group, subsyndromal group, genetic risk and deterioration group, psychotic syndrome/first episode group. A study on social functioning compared 55 at-risk adolescents and young adults, 16 first episode patients with schizophrenia, and 45 normal controls (Ballon et al., 2007). Consistent with results from other genetic and clinical high-risk samples, the at-

risk and the first-episode schizophrenia groups showed significant social functioning impairment with regard to family, peer, school, and work relationships compared to controls. No differences were reported between the two clinical groups, and data on prediction of psychosis were not reported.

Further, recent findings from the North American Prodrome Longitudinal Study (NAPLS), a collaborative, multisite research project with 8 participating research sites and baseline and follow-up aggregated data for 888 at risk and comparison subjects, are beginning to shed light on the characterization and the development of prodromal stages of psychotic illness. To date three NAPLS reports have been published in the literature. The first study addressed the rationale and design of this multisite research collaboration formed to explore a series of research questions with the aim to gain a better understanding of the psychosis prodrome and to improve the accuracy of prospective prediction of initial psychosis (Addington at al., 2007). The second study's objective was to determine the risk of conversion to psychosis within 30 months follow-up and to investigate a set of uniquely contributing predictor variables combined into a multivariate algorithm with higher positive predictive power to predict conversion to psychosis (Cannon et al., 2008). The findings were based on the largest worldwide dataset of 291 prodromal cases followed-up longitudinally and revealed that five baseline variables contributed uniquely to the prediction of psychosis: genetic risk for schizophrenia with recent deterioration in functioning, higher levels of unusual thought content, higher levels of suspiciousness and paranoia, greater social impairment, and history of any substance abuse. The risk of conversion to psychosis was 35% with an overall decelerating rate during the 30 month follow-up period (Cannon et al., 2008). The third and most recently

published NAPLS study (Woods et al., 2009) provided strong evidence for the diagnostic validity of the "prodromal risk syndrome" (patients both currently symptomatic and at risk for getting worse in the future) for first psychosis. The findings raised the possibility of the use of translational/time-limited diagnoses in the upcoming DSM-V for prodromal patients. With respect to the present research, the following results are noteworthy. Prodromal patients were significantly different from normal controls, help-seeking controls, and a group of familial high-risk subjects on many of the assessed areas of functioning (i.e., social and role functioning, premorbid adjustment, and other variables). Individuals, who met SIPS criteria for the prodrome, but not SPD, were also compared to adolescents and young adults who also met criteria for SPD. The findings indicated that the prodromal and SPD patients were impaired to a similar degree on measures of role functioning, psychological, and current global functioning. However, SPD patients showed significantly greater overall social functioning impairment and significantly poorer premorbid adjustment beginning in early adolescence. Findings based on the administration of the SIPS indicated that the SPD group was more severely impaired than the prodromal group on the disorganization scale and on several individual items such as disorganized speech, social anhedonia, emotion expression, odd behavior, and personal hygiene. In addition, family history of psychosis as defined by definite psychosis in first- or second-degree relatives distinguished the two groups in that SPD participants showed lower score for illness density compared to prodromal individuals (Woods et al., 2009).

Findings from clinical high-risk studies parallel the results from genetic high-risk studies. This relates especially to findings of significant decline in social functioning in

multiple domains and findings of depressive symptoms, anxiety symptoms, decreased attention, and disorganization as significant predictors of conversion to psychosis.

Family History of Psychosis. Within the context of high-risk studies with this population and the relation to social and behavioral problems, it is important to address the role of family history. Family and twin studies of schizophrenia and affective psychoses indicate that psychosis aggregates in families (Ivleva, Thaker & Tamminga, 2008). For instance, the lifetime risk for schizophrenia development increases 8- to 12-folds in first-degree biological relatives of schizophrenia probands. Research evidence suggests that there might be important differences between patients with positive family history and those without family history. While a number of large epidemiological studies show that that the familial risks for schizophrenia and bipolar disorders are mainly independent from each other (Kendler, & Gardner, 1997; Laursen et al., 2005), there are also studies indicating coaggregation of these disorders in families with bipolar disorder and schizophrenia patients (Arajarvi et al., 2006; Henn, Bass, Shields, Crow, & DeLisi, 2006; Lichtenstein et al., 2009). Some family studies have also suggested that there could be a familial relationship between the predispositions to schizophrenia and unipolar depression (Maier et al., 1993; Bralckwood et al., 2001). With respect to premorbid functioning, one study found family history of schizophrenia to be associated with poor overall premorbid adjustment during ages 5 to 11 in patients with schizophrenia (Foerster, Lewis, Owen, & Murray, 1991b). Another family study comparing patients with and without family history of schizophrenia found family history to be associated with worse premorbid adjustment related to attention problems and social problems (St. Hilaire et al., 2005). A third study with similar design examined

differences in the premorbid adjustment, symptoms, and intellectual functioning between 28 first-episode schizophrenia spectrum patients (with diagnoses of schizophrenia, schizoaffective, and schizopreniform disorders) with positive family history and 28 matched patients without family history (Norman, Manchanda, Ashok, Harricharan, & Northcott, 2007). The findings indicated that the patients with positive family history showed poorer intellectual functioning, less reduction in clinical symptoms at 24 and 36 months follow-up, and more severe form of the illness. Similarly, a study examining the contribution of familial liability for schizophrenia found that patients from multiply affected families (i.e., with two or more first- and/or second-degree relatives with a psychotic disorder) had poorer premorbid social and academic functioning compared to patients from non-affected families and controls (Walshe et al., 2007). A significant decline of social functioning between childhood and adolescence was found only for the group of patients with familial schizophrenia. In addition, unaffected siblings of patients with familial schizophrenia demonstrated significantly worse academic functioning than controls during adolescence, and a significant decline in academic functioning between childhood and adolescence. Notably, the unaffected siblings of patients with familial schizophrenia had significantly greater deterioration in academic functioning compared to siblings from non-affected families, which the researchers interpreted as possibly related to a genetic risk for schizophrenia (Walshe et al., 2007). Overall, the findings from studies examining family history suggest that further investigation of the familial effect of psychosis in the present study might contribute to a better understanding of social and behavioral problems in high-risk youth.

Normative Development of Child and Adolescent Behavioral Problems

A limited number of studies have examined the normative development of child and adolescent behavioral problems in the general population. Several studies have utilized multilevel analytic methods to examine normative developmental trajectories (Bongers, Koot, van der Ende, & Verhulst, 2003, 2004; Dekker et al., 2007; Keiley, Bates, Dodge, & Pettit, 2000; Stanger, Achenbach, & Verhulst, 1997), revealing age- and sex-related changes in behavioral problems over time. There is also evidence of age- and sex-related changes from cross-sectional or birth-cohort studies (Campbell, 1995; Cicchetti & Toth, 1998; Fergusson, 1998). In the present context, understanding the normative development of behavioral problems provides a "baseline" for defining deviation and for understanding how behavioral trajectories of youth at high-risk for psychosis compare to healthy individuals.

One study of 2076 children and adolescents aged 4 to 18 years examined normative developmental trajectories of behavioral problems using parent-reported CBCL ratings (Bongers, Koot, van der Ende, & Verhulst, 2003). The researchers studied multiple cohorts and used a multilevel growth curve analysis taking into account time-related changes in trajectories. There were 5 time points of prospective assessment. Most CBCL scales showed linear increase or decrease with age. There were significant differences between males and females on all scales except the Withdrawn, Social Problems, and Thought Problems clinical scales. Also, the Thought Problems trajectory did not indicate significant change over time. The Withdrawn, Internalizing Problems, and Somatic Complaints scales showed an increase over time, and females exhibited higher Internalizing Problems and Somatic Complaints scores than males during adolescence. On the other hand, interestingly, the developmental trajectories for

Externalizing Problems and Aggressive Behavior indicated a decrease over time, with males showing more problems that females during the entire measurement period and a much faster rate of decrease with age, with nearly no sex difference remaining at 18 years of age. For the Anxious/Depressed scale, the findings indicated a trajectory with an initial increase for males then decrease after adolescence while females showed a similar trajectory but with higher level of problems overall. For the Delinquent Behavior scale, the change over time was curvilinear, with an initial decrease and then increase of problems, with males exhibiting more deviant behavior than females. Finally, Attention Problems and Social Problems increased until age 11 and decreased thereafter. Males showed greater attentional difficulties than females, whereas there was no sex difference on the Social Problems scale.

A second study with the same sample of children and adolescents aimed to identify groups of individuals who show different developmental trajectories within the Externalizing Problems category (Bongers, Koot, van der Ende, & Verhulst, 2004). Trajectories were estimated from multilevel growth curve analyses and semiparametric mixture models. Four clusters of behavioral problems – aggression, opposition, property violations, and status violations – were examined within Externalizing Problems. Aggression, opposition, and property violations decreased over time, while status violations increased. Within each cluster, three to six group-based developmental pathways were identified, most of which followed the shape of the average trajectories. Overall, males exhibited higher levels of behavioral problems compared to females.

Stanger and colleagues (Stanger, Achenbach, & Verhulst, 1997) also examined aggressive behavior trajectories. They studied 1139 children and adolescents aged 4 to 18

using a longitudinal design with five repeated measurements. The findings indicated that the scores for both aggressive and delinquent behaviors declined between 4 and 10 years of age. After 10 years of age, scores for aggressive behavior continued to decline, while delinquent behaviors increased until age 17. For both behaviors, males had higher scores than females. Those findings are consistent with the findings reported by Bongers and colleagues (Bongers, Koot, van der Ende, & Verhulst, 2003, 2004).

Finally, a third study with the abovementioned data-set of 2076 participants (Dekker et al., 2007) examined different trajectories of depressive symptoms from early childhood to late adolescence. An Affective Problems scale was constricted from CBCL items and scores from the Young-Adult Behavior Checklist (YABCL) and the Young-Adult Self-Report (YASR) were used. In both sexes, six distinct trajectories were identified. The findings indicated that sex differences exist not only in the level, but also in shape and timing of onset of deviant levels of depressive problems.

Taken together, the findings of these studies of CBCL scores in normal youth indicate a number of group-based developmental pathways existing within average trajectories for individual behaviors. In general, the level of behavioral problems tends to rise in the adolescent period, followed by a normative decrease in the post-adolescent period for some behaviors. Finally, this emerging literature indicates that sex-related differences in levels of behavioral problems and developmental trajectories may vary depending on the developmental period studied.

Summary

In summary, there is rich literature providing evidence for social and behavioral precursors of psychosis in youth at risk for the development of psychosis. As evident, a

number of methodologies and measures have been used in this area of research, adding to its complexity. Although each paradigm has limitations as well as strengths, methodological diversity in this instance presents an advantage. When the same general pattern emerges across studies employing different methodology and data sources, inferences can be made with more confidence in the findings (Walker, Walder, Lewine, & Loewy, 2002). The general pattern of findings suggest that pre-psychotic youth are more socially isolated, withdrawn, emotionally labile, anxious, and aggressive than their healthy siblings and/or age-matched comparison subjects. The divergence in developmental trajectories becomes more pronounced with age and is especially apparent in the adolescent period. Although some inconsistent sex-related findings were reported in the literature, overall the research evidence indicates that the behavioral expression of vulnerability to psychosis is characterized by sex differences, with males exhibit more externalizing behavior problems, while females exhibit more internalizing behavior problems. The development of social and behavioral problems in youth at risk for psychosis seems to follow an expected normative developmental trajectory, but with a more pronounced elevation during adolescence.

Theoretical Framework Guiding the Present Study

The general theoretical framework guiding the present study assumes that neurodevelopmental changes that occur during reproductive maturation can trigger the expression of genes that are involved in both normal and abnormal development (Walker, 2000). This diathesis-stress model postulates that constitutional vulnerability arises from hereditary and prenatal factors that influence development of the central nervous system (Walker & Diforio, 1997). Further, vulnerability is expressed in multiple domains of

behavior, and subclinical manifestations, such as schizotypal signs, can be detected long before the onset of clinical symptoms (Cornblatt, Lencz, & Obuchowski, 2002).

Purpose of the Present Study

The primary purpose of this study is to examine social and behavioral precursors of psychosis in adolescents at high-risk for the development of psychosis. Of significant importance is the examination of the developmental behavioral trajectories and behavioral profiles of high-risk youth compared to controls, and of high-risk youth who convert to psychosis compared to those who do not convert to psychosis. First, a critical need exists currently in the field for a better understanding of the predictive validity and accuracy and the developmental course of behavioral precursors of psychosis in the prodromal period. The present study has the potential to yield information that will aid in the identification of youth who are likely to develop psychosis and thus might have substantial implications for preventive intervention. The latter is a particularly important issue for prevention clinical trails involving pharmacotherapy, which is accompanied by side effects of varying severity. False positives are of concern, because individuals in this category are especially vulnerable to the costs rather than benefits of intervention. Therefore, this research would add evidence to the growing debate over detection and clinical intervention at the prodromal high-risk stage of the development of psychosis. Moreover, this study will examine social and behavioral antecedents of psychosis with a prospective design in a population of high-risk adolescents with SPD. Given that there is very limited research examining the developmental course of the psychosis prodrome, and that there have been no published studies characterizing the longitudinal trajectories

of SPD youth who convert to psychosis, the findings would contribute knowledge to the field above and beyond previous investigations.

The secondary purpose of this study is to examine the potential interactive effects of positive family history of psychosis or affective disorders on social and behavioral problems. According to the diathesis-stress model (Walker & Diforio, 1997), hereditary factors serve to trigger constitutional vulnerability for psychosis, which is expressed in multiple domains of behavior before the onset of psychosis. Thus, the high-risk SPD adolescents would be expected to be more sensitive to the potential moderating effect of genetic predisposition and family history of psychosis or affective disorders.

Finally, this study will shed light on the clinical and diagnostic utility of the CBCL as an adjunctive screening instrument in the identification of high-risk youth. The CBCL is the most widely used parent rating scale for behavioral problems currently used in clinical settings in the U.S. It is easily completed by parents within 15 to 30 minutes. Although, rating scales like the CBCL were not intended to predict specific clinical outcome, they have the potential to become a practical and inexpensive adjunctive screening measure for identifying individuals likely to develop psychosis. Current standardized measures of prodromal symptoms (e.g., the SIPS) and SPD (e.g., the SIDP-IV) are administered in the context of an individual diagnostic interview by a trained clinician. These are time consuming and costly screening measures, and therefore have limited utility for large-scale screening of youth. If the parent-report CBCL proves capable of differentiating among youth as a function of their risk for psychosis, it will constitute a significant advance for the field. In particular, it would mean that the CBCL can serve as a brief, low-cost screening measure for identifying youth who are most

likely to benefit from preventive interventions. From a public health standpoint, this would be a significant step forward. Moreover, the CBCL is applicable to a broad age range, including preadolescent children, and there are normative data available from large samples. Thus the CBCL offers the possibility of identifying at-risk subjects at a younger age than standard clinical interview measures.

Research Questions and Hypotheses

This study addresses several important, but thus far unexplored, research questions related to social and behavioral precursors of psychosis in youth at high-risk for the development of psychosis.

The first research question concerned the social and behavioral problems of high-risk SPD adolescents; specifically, would these high-risk SPD adolescents differ significantly from non-psychiatric controls (NC) and youth with other personality disorders (OPD)? It was hypothesized that high-risk adolescents with SPD will exhibit more CBCL behavioral problems than controls and OPD adolescents. The behavioral differences between the SPD group and healthy controls will be present on all CBCL scales. This prediction was based on the evidence that youth at risk for psychosis, as well as other mental health problems, show a generalized increase in adjustment problems, relative to healthy controls, that spans both internalizing and externalizing behavior problems. In contrast, it was hypothesized that the behavioral differences between the SPD group and the OPD group will be present on the CBCL scales Anxious/Depressed, Social Problems, Thought Problems, and Attention Problems. Thus, relative to OPD youth who are not at specific risk for psychosis, it was predicted that the SPD group will

manifest more severe impairment on scales that tap into the behavioral deficits that characterize prodromal subjects.

A related research question was whether high-risk SPD adolescents would exhibit changes in CBCL behavioral problems over time that would distinguish them from controls and OPD youth. It was hypothesized that high-risk adolescents with SPD would evidence a shift in behavior toward greater social and behavioral problems compared to the NC and the OPD youth. This hypothesis draws on theoretical assumptions and research evidence that youth at risk for psychosis show a longitudinal escalation in adolescent behavior problems relative to controls.

The second research question pertained to cross-sectional and longitudinal differences in social and behavioral problems in high-risk SPD adolescents who converted to psychosis and those who did not convert to psychosis. It was hypothesized that the high-risk Converted group will exhibit more pronounced problems in social and behavioral domains that have been shown to be predictive of conversion to psychosis in prodromal individuals. It was hypothesized that SPD youth who convert to psychosis will show higher scores on the CBCL scales Anxious/Depressed, Withdrawn, Social Problems, Thought Problems, Attention Problems, and Internalizing Problems. Further, it was predicted that these differences will become more pronounced over time.

The third research question pertained to the nature of the relationship between social and behavioral problems at baseline and changes in prodromal symptomatology at one year follow-up assessment. It was hypothesized that CBCL behavioral problems will predict a poor outcome as measured by increased prodromal symptomatology at one year follow-up.

Further, given the research evidence that positive family history of psychosis is linked with risk for conversion, this study also sought to determine whether family history of psychosis or mood disorder in first-or second-degree relatives is associated with CBCL social and behavioral problems. Related to this is the question of whether family history adds to the prediction of conversion to psychosis. It was hypothesized that participants with positive family history will exhibit more behavioral problems than participants without a family history. The potential moderating effect of family history on social and behavioral problems was also examined.

Finally, as discussed previously, research has provided evidence for sex-related differences in social and behavioral problems in this population. Some inconsistent findings were also reported. Therefore, sex was considered as a variable in the analyses and the potential interactive effect of sex was examined.

Method

Participants

This study utilized data from 122 participants enrolled in a prospective study of high-risk adolescents at Emory University. Recruitment was conducted through announcements directed at parents and clinicians. The announcements targeted to recruit adolescents with personality disorders and described, in lay terms, the key diagnostic features of SPD. Although personality disorders are not routinely diagnosed in individuals younger than 18 years of age, studying SPD in adolescents is a well-defined and established research strategy for identifying pre-psychotic and prodromal individuals at risk for the development of psychosis.

The subject groups included 40 high-risk adolescents with SPD, 48 adolescents with OPD, and 34 non-psychiatric controls, ranging in age from 12 to 18 years (mean age = 14.2; SD = 1.8), who underwent an initial assessment. A follow-up of 90 participants (30 SPD, 36 OPD, 24 NC) was conducted at one year after the initial assessment. Demographic characteristics of the sample are presented in Table 1.

Insert Table 1

Assent and written consent were obtained from all participants and a parent in accordance with the guidelines of the Emory University Human Subjects Review Committee. Exclusion criteria at study entry were neurological disorder, mental retardation, substance abuse or addiction, and current Axis I disorder as described by DSM-IV-TR with the exception of learning disorders, attention-deficit/hyperactivity disorder, and other disruptive behavior disorders. The latter disorders show a high rate of comorbidity with psychosis (Schaeffer & Ross, 2002).

Priority was given to the recruitment of adolescents who had never received psychotropic medications. Nevertheless, 29% of the participants were receiving one or more psychotropic medications at the baseline assessment. This is consistent with national trends in prescription increase of psychiatric medications in pediatric populations (Zito et al., 2003). The psychotropic drugs for which increased prescriptions to children have been most clearly documented are stimulants, antidepressants, and antipsychotics. The current sample reflected this trend in that the most common class of medication was stimulants (19%), followed by antidepressants (14%), and antipsychotics (9%). Most

psychotropic medications were prescribed off-label by pediatricians and primarily targeted conduct and disruptive behavior problems.

Diagnosis and Assessment

During the initial and one year follow-up assessments participants were administered a series of structured interviews and assessment instruments. All interviews were conducted by either the principal investigator of the study or an advanced doctoral student (4th year or beyond). Following standard procedure, training of doctoral students was conducted over 2-months in weekly meetings through the use of practice interviews and observation of interview videotapes. Because developmental changes were a central focus of this research, it was important to maintain uniform procedures across the initial and follow-up assessments. All interviews were videotaped for the purpose of establishing inter-rater reliability. Inter-rater reliabilities exceeded the minimum study criterion of Kappa equal to or greater than .80. Diagnostic decisions were ultimately made by the principal investigator, a licensed clinical psychologist, based on discussion with the interviewer, written notes of responses to interview questions, and reviewing a videotaped interview. Subjects were then assigned a DSM-IV-TR diagnosis.

Structured Interview for DSM-IV Personality Disorders (SIDP-IV). The Structured Interview for DSM-IV Personality Disorders (Pfohl, Blum, & Zimmerman, 2001) was administered for two reasons: 1) it provides a comprehensive assessment of the symptoms for DSM-IV Axis II disorders, and 2) it is appropriate for use with a broad age range, including adolescents. The assessment of personality disorders during the adolescent period has been shown to be valid (Johnson et al., 1995) and broadly reliable

(Bernstein et al., 1993). Furthermore, the SIDP-IV, has been shown to have good inter-rater reliability (Brent, Zelenak, Bukstein, & Brown, 1990).

Structured Clinical Interview for DSM-IV Disorders (SCID-I). The Structured Clinical Interview for Axis I DSM-IV Disorders (First, Spitzer, Gibbon, & Williams, 1995) was used to determine whether participants met criteria for an Axis I disorder. The SCID-I was chosen because it provides a comprehensive assessment of the symptoms criteria for DSM-IV Axis I disorders. This instrument has been shown to have excellent inter-rater reliability in adolescent populations (Martin, Pollock, Bukstein, & Lynch, 2000). The SCID-I has also been used in several studies focusing on adolescent populations with schizophrenia spectrum disorders (Mittal et al., 2006; Walker, Logan, & Walder, 1999; Weinstein, Diforio, Schiffman, Walker, & Bonsall, 1999).

Structured Interview for Prodromal Symptoms (SIPS). The Structured Interview for Prodromal Symptoms (Miller et al., 2002) was used to assess prodromal symptomatology in the study participants. The SIPS contains an instrument, the Scale of Prodromal Symptoms (SOPS), designed to rate the severity of 19 symptoms along a six point scale ranging from "absent" to "severe." The SOPS is comprised of symptoms that are classified into positive (unusual thoughts/ideas, suspiciousness, grandiosity, perceptual abnormalities, conceptual disorganization), negative (social isolation, avolition, decreased expression of emotion, decreased experience of emotion, decreased ideational richness, deteriorated role function), disorganized (odd behavior, bizarre thinking, trouble with focus and attention, impairment in personal hygiene or social attention), and general (sleep disturbance, dysphoric mood, motor disturbance, impaired stress tolerance) categories. The mean of the combined category scores was used as an

indicator of total symptomatology. This instrument has been shown to yield reliable ratings of prodromal symptoms and predicts risk for conversion to Axis I psychotic disorders, particularly schizophrenia (Miller et al., 2002). In the present study, the instrument served as a measure of Attenuated Positive Syndrome (APS) symptoms defined by the presence of moderate to severe positive symptoms in the study participants. Raters were trained in a comprehensive workshop to reach the minimum criteria of reliability of .85 in SIPS/SOPS ratings.

Child Behavior Checklist (CBCL). The CBCL parent-report scale (Achenbach, 1991) was used to asses multiple behavioral problems and competencies of participants. The measure includes 118 items rated from 0 (not at all typical of the child) to 2 (often typical of the child) and is appropriate for ages 4 to 18 years. The CBCL clinical scales contain the Total Problems scale, two broadband dimensions (Internalizing Problems and Externalizing Problems) and eight cross-informant syndromes (Anxious/Depressed, Withdrawn, Somatic Complaints, Social Problems, Thought Problems, Attention Problems, Delinquent Behavior, and Aggressive Behavior). The Total Problems scale is composed of the Internalizing and Externalizing Problems scales. The Internalizing Problems scale is composed of the Anxious/Depressed, Withdrawn, and Somatic Complaints subscales. The Externalizing Problems scale is composed of the Delinquent Behavior and Aggressive Behavior subscales. The CBCL also yields a measure of social competencies, the Total Competence scale. The items included in this measure tap into the amount and quality of involvement in sports, organizations, jobs and chores, social relationships, and school performance. The Total Competence scale is composed of the Activities, Social, and School subscales. Scores on the behavioral problems CBCL scales

are reported in the form of *T* Scores. The mean *T* score on each scale is 50 with a standard deviation of 10. Scores of less than 67 are considered within the normal range, 67 to 70 are considered to be in the borderline clinical range, and 70 or above are considered to be clinically significant (Achenbach, 1991). Unlike the behavioral problems scales, high scores on the social competence scales indicate more competencies. The CBCL was completed by one of the parents, most frequently the mother. The Achenbach Data Manager Software (Achenbach System of Empirically Based Assessment, Burlington, VT) was used to score all completed checklists. Research has demonstrated the validity and reliability of the CBCL (Achenbach, 1991; Crijnen, Achenbach, & Verhulst, 1999; Ivanova et al., 2007).

Family History Assessment. To index the occurrence of mental illness and the rate of mental illness in first- and second-degree relatives of study participants, data on family history of mental disorders was collected. Although relatives were not directly interviewed, general information on mental disorders in first-and second-degree relatives was obtained from parents of participants. Specifically, the occurrence of psychosis, depression, and bipolar disorder were of critical interest. A broad definition of positive family history was employed in the present study, defined as having at least one first-or second-degree relative with diagnosis of psychosis spectrum disorder or affective disorder.

Results

Preliminary analyses

Preliminary analyses were conducted to examine whether the distributions of the dependent measures met statistical assumptions for parametric statistics. Some of the

CBCL scales revealed non-normal distribution. Therefore, analyses for each dependent measure were run with non-transformed and with log transformed data. Overall, the results from analyses with the non-transformed data paralleled the results from analyses with the log transformed data. Therefore, the findings reported in the present study were based on analyses with the non-transformed data.

The cross-temporal stability of the CBCL scales was examined with correlational analyses. The analyses revealed significant positive inter-correlations across assessment periods (baseline and one year follow-up) within each CBCL scale. All *p* values were less than .05. These results suggest longitudinal stability of the ratings.

Some participants in the study were taking psychotropic medications. These participants were observed under a naturalistic paradigm as medication treatment was not a component of the present study. Correlational analyses were conducted to determine the effects of medications on social and behavioral ratings. The same analytic approach was used to examine the relationship between psychotropic medications and prodromal symptomatology. There were significant correlations between medication status and CBCL scales. There were also significant correlations between medication status and prodromal symptomatology. Therefore, analyses with general medication status (dummy coded: present/absent) as a covariate were conducted. It should be noted that the inclusion of medication as a covariate has the potential to alter the pattern of findings, not only because of the effects of psychotropics on behavior, but also because those with elevated symptoms and behavior problems are more likely to be administered medication. Thus controlling for medication may constrict variance in symptoms and behavior

problems, and constrain diagnostic group differences. The results should, therefore, be interpreted with caution.

Diagnostic group differences between SPD, OPD, and NC adolescents

Group demographics. Analyses were conducted to test for differences between the three groups of SPD, OPD, and NC participants. There were no significant age ($F(2,119) = .46$, $p = .631$) or sex differences ($\chi^2 = 2.10$, $p = .349$) between the groups.

Prodromal symptomatology at baseline and follow-up assessments. A series of univariate analyses of variance (ANOVA) were conducted on the baseline diagnostic group differences in positive, negative, disorganized, general, and total prodromal symptomatology as measured by the five symptom domains of the SIPS. Table 2 contains the means and standard deviations for each diagnostic group. Consistent with expectations, post-hoc tests showed that for each scale the SPD group had significantly higher scores compared to both, the OPD group and the NC group. There were no significant differences between the OPD and the NC participants. To clarify the role of psychotropic medications, the same series of analyses were also conducted with medication status as a covariate (ANCOVA). The medication covariate was significant only for the general symptoms domain.

Insert Table 2

A series of ANOVA analyses were also conducted on the follow-up (one year after the initial assessment) diagnostic group differences in positive, negative,

disorganized, general, and total prodromal symptomatology. Overall, the results paralleled the findings of the baseline analyses (see Table 3). Compared to the OPD and the NC groups, the SPD group showed significantly higher scores for each of the symptom domains. There were no significant differences between the OPD and the NC participants. ANCOVA analyses showed that medication status was not a significant covariate.

Insert Table 3 and Figure 1

Group differences between high-risk Converted and high-risk Non-Converted adolescents

Within the total follow-up timeframe of four years, 14 high-risk adolescents assessed at baseline converted to an Axis I psychotic disorder. The Converted group was comprised of 13 high-risk SPD participants and one OPD participant, while the Non-Converted group was comprised of 27 high-risk SPD participants. Conversion was defined as conversion to any Axis I schizophrenia spectrum disorder or affective disorder with psychotic features. The conversion rate of 35% in our sample corresponded to the conversion rate of other prospective studies of prodromal youth (Haroun, Dunn, Haroun, & Cadenhead, 2006; Miller et al., 2002; Yung et al., 2003). The DSM-IV-TR Axis I clinical outcomes in the high-risk SPD participants who converted to psychosis were as follow: schizoaffective disorder (n = 5), schizophrenia undifferentiated type (n = 4), bipolar I disorder most recent episode mixed with severe psychotic features (n = 3), and major depressive disorder recurrent severe with psychotic features (n=1). The OPD

participant who converted to psychosis had a clinical outcome diagnosis of psychotic disorder not otherwise specified. Chi^2 analyses comparing the rate of conversions among the groups showed, as expected, that there were significantly more conversions among the SPD group. It should be noted that all but three of these conversions occurred after the one year follow-up.

Group demographics. Analyses were conducted to test for differences between high-risk Converted and high-risk Non-Converted adolescents to an Axis I psychotic disorder. There were no significant age ($F(1,39) = .77$, $p = .385$) or sex differences ($\chi^2 = .36$, $p = .548$) between the two groups. Given that one subject with a baseline diagnosis of OPD converted to an Axis I psychotic disorder, the subject was included in the Converted group. Nevertheless, subsequent statistical analyses were conducted with and without inclusion of this subject. There were no significant age ($F(1,38) = .44$, $p = .510$) or sex differences ($\chi^2 = .10$, $p = .750$) between the Converted group and the Non-Converted group when the converted OPD participant was excluded.

Prodromal symptomatology at baseline and follow-up assessments. The same analytic approach described above was used to test group differences in the five prodromal composite scales between Converted and Non-Converted high-risk participants at baseline. Table 4 contains the means and standard deviations for each outcome group. There were no significant differences between the two groups on any of the scales at baseline. ANCOVA analyses showed that the medication covariate was significant only for the general symptoms domain.

Insert Table 4

However, ANOVA conducted on follow-up SIPS ratings revealed notably divergent scores. Consistent with expectations, the Converted group showed significantly more positive, negative, disorganized, general, and total prodromal symptomatology (see Table 5). ANCOVA showed that medication status was not a significant covariate.

Insert Table 5 and Figure 2

ANOVA and ANCOVA analyses, with medication status as a covariate, were also conducted with baseline and follow-up data by excluding one OPD subject who converted to an Axis I psychotic disorder. The pattern of findings paralleled the findings described above.

Results of hypothesis testing

Diagnostic group differences between SPD, OPD, and NC adolescents

CBCL scores at baseline assessment. To test the hypothesis that high-risk adolescents with SPD have more social and behavioral problems than controls and OPD adolescents, multivariate analyses of variance (MANOVA) were conducted with the baseline CBCL data.

First, analyses with the CBCL individual scales scores (Activities, Social, School, Anxious/Depressed, Withdrawn, Somatic Complaints, Social Problems, Thought Problems, Attention Problems, Delinquent Behavior, and Aggressive Behavior) as the

dependent variables and diagnostic status as the independent variable were conducted. Second, analyses with the CBCL composite scales scores (Total Competence, Internalizing Problems, and Externalizing Problems) as the dependent variables were conducted.

Consistent with the hypothesis, there were significant diagnostic group differences between the SPD group and the comparison groups at baseline assessment. MANOVA with the CBCL individual scales revealed a significant main effect for diagnostic status, Wilks's $\Lambda = .50$, $F(22, 210) = 3.86$, $p = .000$, $\eta^2 = .28$. MANOVA with the CBCL composite scales yielded similar findings with a significant main effect for diagnostic status, Wilks's $\Lambda = .58$, $F(6, 228) = 11.66$, $p = .000$, $\eta^2 = .23$. Univariate tests results were consisted with predictions. The findings showed that diagnostic groups differed on all CBCL individual scales, except for Activities. Similarly, diagnostic groups differed on all CBCL composite scales. Planned post-hoc comparisons were conducted to determine the nature of the diagnostic group differences. To provide an estimate for the degree of association between the effect and the dependent variable, η^2 was computed.

As predicted, when compared with OPD participants, SPD participants showed significantly higher scores on the Anxious/Depressed, Social Problems, and Thought Problems scales. Although the trends were in the predicted direction, there were no significant differences between the two groups on Attention Problems. In sum, these findings demonstrate that the CBCL can distinguish between high-risk SPD youth and youth with other behavioral syndromes.

Also as predicted, when compared with the NC group, the SPD group showed significantly lower scores on the Social and School scales, and significantly higher scores

on the Anxious/Depressed, Withdrawn, Somatic Complaints, Social Problems, Thought Problems, Attention Problems, and Aggressive Behavior scales. Compared with NC participants, the OPD participants had significantly lower scores on the scales Social and School, and significantly higher scores on the scales Anxious/Depressed, Withdrawn, Somatic Complaints, Social Problems, Attention Problems, Delinquent Behavior, and Aggressive Behavior.

In the analyses with the CBCL composite scales, when compared with the OPD group, the SPD group showed higher scores on the scale Internalizing Problems. When compared with the NC group, the SPD group showed lower scores on the scale Total Competence and higher scores on the scales Internalizing Problems and Externalizing Problems. When compared with the NC group, the OPD group showed lower scores on the scale Total Competence, and higher scores on the scales Internalizing Problems and Externalizing Problems. The means and standard deviations for all individual and composite CBCL scales are presented in Table 6.

Insert Table 6 and Figure 3

Consistent with previous research (Walker et al., 1998), these results indicate that adolescents with SPD have more social and behavioral problems than normal control adolescents as well as adolescents with other personality disorders.

To clarify the role of psychotropic medications, the same series of multivariate analyses of variance were conducted with medication status as a covariate (MANCOVA).

MANCOVA with the CBCL individual scales revealed a significant main effect for medication status, Wilks's $\Lambda = .80$, $F(11, 104) = 2.28$, $p = .015$, $\eta^2 = .19$. Similarly, MANCOVA with the CBCL composite scales yielded a significant main effect for medication status, Wilks's $\Lambda = .90$, $F(3, 113) = 4.04$, $p = .009$, $\eta^2 = .09$.

The medication covariate was significant for the individual and composite scales Anxious/Depressed, $F(1, 114) = 5.82$, $p = .017$, $\eta^2 = .04$, Social Problems, $F(1, 114) = 13.08$, $p = .000$, $\eta^2 = .10$, Thought Problems, $F(1, 114) = 4.89$, $p = .029$, $\eta^2 = .04$, Aggressive Behavior, $F(1, 114) = 15.75$, $p = .000$, $\eta^2 = .12$, Internalizing Problems, $F(1, 115) = 3.96$, $p = .049$, $\eta^2 = .03$, and Externalizing Problems $F(1, 115) = 11.48$, $p = .001$, $\eta^2 = .09$.

Overall, the pattern of results paralleled the results without the inclusion of the covariate. However, the following differences emerged with this set of analyses. SPD and OPD adolescents no longer had significantly different scores on the scales Social Problems, Thought Problems, and Internalizing Problems. Also, compared to the OPD group, the SPD group showed significantly lower scores on Externalizing Problems. SPD and NC adolescents no longer had significantly different scores on the scales Aggressive Behavior and Externalizing Problems. Finally, OPD and NC adolescents no longer had significantly different scores on the scales Social, School, and Social Problems.

Given the literature on sex-related differences in behavioral problems in youth, exploratory MANOVA analyses were conducted with sex as an independent variable aiming to examine the potential moderating effect of this variable. The addition of sex to the analyses did not alter the overall pattern of findings. There was no significant main

effect or interaction effect of sex with diagnostic group on the CBCL individual or composite scores.

CBCL scores at follow-up assessment. To further test the hypothesis that high-risk adolescents with SPD have more social and behavioral problems than controls and OPD adolescents, MANOVAs were conducted with the follow-up assessment data.

Consistent with the hypothesis, there were significant diagnostic group differences at follow-up assessment. First, MANOVA with the CBCL individual scales revealed a significant main effect for diagnostic status, Wilks's $\Lambda = .59$, $F(22, 144) = 1.93$, $p = .011$, $\eta^2 = .22$. Second, MANOVA with the CBCL composite scales yielded similar findings with a significant main effect for diagnostic status, Wilks's $\Lambda = .72$, $F(6, 160) = 4.56$, $p = .000$, $\eta^2 = .14$. Univariate tests, conducted to determine which social and behavioral scales differentiated the groups, were overall consisted with predictions. The findings showed that diagnostic groups differed on all CBCL individual and composite scales. Planned post-hoc comparisons were conducted to determine the nature of the diagnostic group differences.

Similarly to the baseline results, in the analyses with the CBCL individual scales when compared with OPD participants, SPD participants showed higher scores on the scales Anxious/Depressed and Social Problems. Although the findings were in the predicted direction, there were no significant differences between the two groups on Thought Problems and Attention Problems. When compared with the NC group, the SPD group showed significantly lower scores on the scales Social and School, and significantly higher scores on the scales Anxious/Depressed, Withdrawn, Somatic Complaints, Social Problems, Thought Problems, and Attention Problems, Delinquent

Behavior, and Aggressive Behavior. Compared with NC participants, the OPD participants had significantly lower scores on the scales Activities and Social. No other significant differences emerged between the NC group and the OPD group.

In the analyses with the CBCL composite scales, when compared with the OPD group, the SPD group did not show significantly higher scores on any of the scales. When compared with the NC group, the SPD group showed lower scores on the scale Total Competence and higher scores on the scales Internalizing Problems and Externalizing Problems. When compared with the NC group, the OPD group showed lower scores on the scale Total Competence, and higher scores on the scale Externalizing Problems. The means and standard deviations for CBCL scales at follow-up are presented in Table 7.

Insert Table 7

To clarify the role of psychotropic medications, the same analyses were conducted with medication status as a covariate. MANCOVA with the CBCL individual scales revealed a significant main effect for medication status, Wilks's $\Lambda = .74$, $F(11, 71) = 2.26$, $p = .020$, $\eta^2 = .26$. The medication covariate was significant for the scales Anxious/Depressed, $F(1, 81) = 8.81$, $p = .004$, $\eta^2 = .09$, Social Problems, $F(1, 81) = 12.17$, $p = .001$, $\eta^2 = .13$, Attention Problems, $F(1, 81) = 4.19$, $p = .044$, $\eta^2 = .04$, and Aggressive Behavior, $F(1, 81) = 4.47$, $p = .038$, $\eta^2 = .05$. MANCOVA with the CBCL composite scales did not show a significant main effect for medication status.

The following differences in findings emerged compared to the analyses without medications as a covariate. The multivariate F value for diagnostic status was no longer significant for the analyses with the individual CBCL scales. The univariate tests no longer indicated significant differences between the SPD and the OPD adolescents. The univariate tests indicated only significant differences between the SPD and the NC adolescents on the scales Social and Thought Problems, and between the OPD and the NC adolescents on the scale Social.

For the covariate analyses with the composite CBCL scales, the multivariate F value for diagnostic status remained significant. However, the following differences emerged regarding the univariate tests. SPD and NC adolescents no longer had significantly different scores on the scales Internalizing Problems and Externalizing Problems. Also, OPD and NC adolescents no longer differed on the Externalizing Problems scale.

Similarly to the baseline results, exploratory MANOVA analyses examining the potential moderating effect of sex yielded the same overall pattern of results. There was no significant main effect or interaction effect of sex with the CBCL individual or composite scores.

Temporal progression of social and behavioral characteristics. To test the hypothesis that over time high-risk adolescents with SPD exhibit a shift in behavior toward greater social and behavioral problems compared to controls and OPD youth, and to determine the nature of the developmental behavioral trajectories of the diagnostic groups, repeated measures ANOVAs were conducted for each CBCL scale. A series of 2 (time) x 3 (diagnostic group) repeated measures ANOVAs were conducted. The CBCL

scores for each time of assessment (baseline vs. follow-up) were the within-subject factor (dependent variable) and diagnostic status (SPD vs. OPD vs. NC) was the between-subject factor (independent variable).

There was a main effect for diagnostic status for the following individual and composite CBCL scales: Social, $F(2, 85) = 12.96$, $p = .000$, $\eta^2 = .23$, School, $F(2, 85) = 7.48$, $p = .001$, $\eta^2 = .15$, Anxious/Depressed, $F(2, 86) = 12.82$, $p = .000$, $\eta^2 = .23$,Withdrawn, $F(2, 87) = 8.33$, $p = .000$, $\eta^2 = .16$, Somatic Complaints, $F(2, 87) = 7.39$, $p = .001$, $\eta^2 = .14$, Social Problems, $F(2, 87) = 11.33$, $p = .000$, $\eta^2 = .20$, Thought Problems, $F(2, 87) = 12.67$, $p = .000$, $\eta^2 = .22$, Attention Problems, $F(2, 87) = 12.28$, $p = .000$, $\eta^2 = .22$, Delinquent Behavior, $F(2, 87) = 5.83$, $p = .004$, $\eta^2 = .11$, Aggressive Behavior, $F(2, 87) = 7.65$, $p = .001$, $\eta^2 = .15$, Total Competence, $F(2, 82) = 11.49$, $p = .000$, $\eta^2 = .21$, Internalizing Problems, $F(2, 87) = 17.26$, $p = .000$, $\eta^2 = .28$, and Externalizing Problems, $F(2, 87) = 9.16$, $p = .000$, $\eta^2 = .17$.

Consistent with the results above, compared with the OPD adolescents, the SPD adolescents had significantly higher scores on the scales Anxious/Depressed, Social Problems, Thought Problems, and Attention Problems. Compared with the NC group, the SPD group had significantly lower scores on the scales Social, School, and Total Competence, and significantly higher scores on the scales Anxious/Depressed, Withdrawn, Somatic Complaints, Social Problems, Thought Problems, Attention Problems, Delinquent Behavior, Aggressive Behavior, Internalizing Problems, and Externalizing Problems. Finally, compared to the NC group, the OPD group had significantly lower scores on the scales Social, School, and Total Competence, and significantly higher scores on all other scales. Also, overall the OPD youth showed

highest scores for the individual scales Delinquent Behavior and Aggressive Behavior, and the composite scale Externalizing Problems.

Insert Figures 4, 5, 6, and 7

There was a main effect for time for the following individual and composite CBCL scales: Anxious/Depressed, Wilks's $\Lambda = .89$, $F(1, 86) = 10.23$, $p = .002$, $\eta^2 = .10$, Withdrawn, Wilks's $\Lambda = .95$, $F(1, 87) = 4.47$, $p = .037$, $\eta^2 = .04$, Somatic Complaints, Wilks's $\Lambda = .86$, $F(1, 87) = 13.52$, $p = .000$, $\eta^2 = .13$, Social Problems, Wilks's $\Lambda = .89$, $F(1, 87) = 10.48$, $p = .002$, $\eta^2 = .10$, Thought Problems, Wilks's $\Lambda = .92$, $F(1, 87) = 6.62$, $p = .012$, $\eta^2 = .07$, Aggressive Behavior, Wilks's $\Lambda = .87$, $F(1, 87) = 12.10$, $p = .001$, $\eta^2 = .12$, and Internalizing Problems, Wilks's $\Lambda = .86$, $F(1, 87) = 13.14$, $p = .000$, $\eta^2 = .13$. The effect of time was due to decreasing social and behavioral problems over time. Although the time effect was not significant for the other CBCL scales, the overall trend across scales was toward a decline of problems over time.

These main effects were qualified by a significant Time X Diagnostic Status interaction for the following CBCL scales: Activities, Wilks's $\Lambda = .93$, $F(2, 88) = 3.31$, $p = .041$, $\eta^2 = .07$, Aggressive Behavior, Wilks's $\Lambda = .87$, $F(2, 87) = 6.15$, $p = .003$, $\eta^2 = .12$, and Externalizing Problems, Wilks's $\Lambda = .87$, $F(2, 87) = 6.24$, $p = .003$, $\eta^2 = .12$. Paired sample *t* tests were conducted to follow-up on the significant interactions. Differences in mean ratings were significantly different between baseline and follow-up assessments, where OPD participants showed significant decreases on the scales

Aggressive Behavior, t (36) = 2.07, p = .046 and Externalizing Problems, t (35) = 5.48, p = .000, and decrease in functioning over time on the scale Activities, t (35) = 4.86, p = .000. Similarly, although not significant, the SPD participants' scores on the three scales followed this trend.

To clarify the role of psychotropic medications as it relates to the developmental trajectories of social and behavioral problems in this population, the same series of repeated measures analyses were conducted by controlling for medication status. 2 x 3 repeated measures ANCOVAs were conducted. The medication covariate was significant for the scales Anxious/Depressed, F(1, 85) = 11.12, p = .001, η^2 = .11, Social Problems, F(1, 86) = 17.60, p = .000, η^2 = .17, Attention Problems, F(1, 86) = 8.50, p = .005, η^2 = .09, Delinquent Behavior, F(1, 86) = 5.96, p = .017, η^2 = .06, Aggressive Behavior, F(1, 86) = 17.69, p = .000, η^2 = .17, Internalizing Problems, F(1, 86) = 7.58, p = .007, η^2 = .08, and Externalizing Problems, F(1, 86) = 14.63, p = .000, η^2 = .14. There was also a significant Time X Medication Status interaction for the scales Thought Problems, Wilks's Λ = .94, F(1, 86) = 5.38, p = .023, η^2 = .05, and Aggressive Behavior, Wilks's Λ = .94, F(1, 86) = 4.86, p = .030, η^2 = .05.

The following differences emerged compared to the analyses over time without medications as a covariate. In regard to diagnostic group differences, SPD and OPD adolescents no longer had significantly different scores on the scales Anxious/Depressed, Social Problems, Thought Problems, and Attention Problems. Also, SPD and NC adolescents no longer had significantly different scores on the scales Delinquent Behavior, Aggressive Behavior, and Externalizing Problems. In addition, OPD and NC adolescents no longer had significantly different scores on the scales Social Problems and

Attention Problems. Finally, the covariate analyses no longer indicated significant main effect for time for the scales Withdrawn, Thought Problems, and Aggressive Behavior.

Exploratory repeated measures ANOVAs were conducted with diagnostic status and sex as between-subject factors. The overall pattern of results remained consistent with the results outlined above in the first set of analyses. There was no significant main effect or interaction effect of sex with the CBCL individual or composite scores.

Group differences between high-risk Converted and high-risk Non-Converted adolescents

CBCL scores at baseline assessment. To test the hypothesis that high-risk adolescents who convert to psychosis have more social and behavioral problems than high-risk adolescents who do not convert to psychosis, MANOVAs were conducted with the baseline assessment data. The means and standard deviations for all CBCL scales are presented in Table 8.

Insert Table 8 and Figure 8

Contrary to the prediction, no significant main effect for conversion status was found with the CBCL individual or composite scales. Although the multivariate F value was not significant, the univariate test for the scale Aggressive Behavior was significant, $F(1, 38) = 4.23$, $p = .046$, $\eta^2 = .10$, indicating higher scores in the Non-Converted group.

Further, MANCOVAs with medication status as a covariate, showed no significant main effect for medication for individual or composite scales. However, in those analyses the univariate test for the scale Aggressive Behavior was no longer

significant. Also, exploratory analyses examining the potential moderating effect of sex were conducted. Similarly, there was no significant main effect or interaction effect of sex with any of the CBCL scales.

All of the analyses were also conducted by excluding one OPD subject from the Converted group. Although the multivariate F values were not significant, overall the findings paralleled the findings outlined above. However, the following differences emerged. In addition to a significant univariate test for the scale Aggressive Behavior, compared to the Converted group, the Non-Converted group also showed significantly higher scores on the composite scale Externalizing Problems, $F(1, 37) = 4.48$, $p = .041$, $\eta^2 = .10$.

The MANCOVAs with medication status as a covariate showed no significant effect for medication for individual or composite scores. The findings paralleled the findings without the medication covariate. Exploratory analyses including sex as a variable indicated a significant main effect of sex for Thought Problems, $F(1, 35) = 4.80$, $p = .035$, $\eta^2 = .12$, with female adolescents showing higher scores. There were also significant Conversion Status X Sex interactions for the scales Thought Problems, $F(1, 35) = 4.72$, $p = .037$, $\eta^2 = .11$, and Delinquent Behavior, $F(1, 35) = 4.10$, $p = .050$, $\eta^2 = .10$. Univariate tests within sex for the Thought Problems scale revealed significant differences only for females, in that Converted females showed higher scores than Non-Converted females whereas there were no differences between the Converted and Non-Converted males. For the Delinquent Behavior scale Non-Converted females showed higher scores compared to Converted females. There were no differences between males.

Insert Figure 9 and Figure 10

CBCL scores at follow-up assessment. Similar to the baseline findings, no significant main effect for conversion status was found with MANOVAs of the follow-up CBCL individual or composite scales. While in the baseline data analyses there were some significant unvariate tests, no univariate tests were significant in this set of analyses. The means and standard deviations for all CBCL scales are presented in Table 9.

Insert Table 9

Analyses with medication status as a covariate, yielded similar results and no significant main effect for medication was found for individual or composite scales. Further, exploratory analyses with sex as a potential moderating variable showed no significant main effect or interaction effect of sex with the CBCL individual scores. However, similarly to the baseline results, although the multivariate F value was not significant, the univariate test for the scale Aggressive Behavior was significant, $F(1, 24) = 4.82$, $p = .038$, $\eta^2 = .16$, indicating higher scores for female adolescents. Also, there was a significant main effect of sex with the CBCL composite scales, Wilks's $\Lambda = .70$, $F(3, 22) = 3.06$, $p = .049$, $\eta^2 = .29$, indicating more problems for female adolescents. Analyses conducted by excluding one OPD subject from the Converted group showed

similar results, but in these analyses there no longer was a significant main effect of sex for the CBCL composite scales.

Temporal progression of social and behavioral characteristics. To test the hypothesis that over time high-risk adolescents who convert to psychosis exhibit a shift in behavior toward greater social and behavioral problems compared to high-risk adolescents who do not convert to psychosis and to determine the nature of the developmental behavioral trajectories, a series of 2 (time) x 2 (outcome group) repeated measures ANOVAs were conducted for each CBCL scale. The CBCL scores for each time of assessment (baseline vs. follow-up) were the within-subject factor and diagnostic status (Converted vs. Non-Converted) was the between-subject factor.

Contrary to the prediction, there was no main effect for conversion status and no significant Time X Conversion Status interactions for any of the fourteen CBCL scales.

There was a main effect for time for the following individual and composite scales: Anxious/Depressed, Wilks's $\Lambda = .83$, $F(1, 29) = 5.61$, $p = .025$, $\eta^2 = .16$, Somatic Complaints, Wilks's $\Lambda = .77$, $F(1, 29) = 8.32$, $p = .007$, $\eta^2 = .22$, and Internalizing Problems, Wilks's $\Lambda = .80$, $F(1, 29) = 6.82$, $p = .014$, $\eta^2 = .19$. The effect of time was due to decreasing social and behavioral problems over time. Although the time effect was not significant for the remaining CBCL scales, the overall trend across scales was towards a decline of problems over time.

The same set of analyses was conducted by controlling for medication status. The medication covariate was significant for the scale Social Problems, $F(1, 27) = 5.41$, $p = .027$, $\eta^2 = .16$, and there were no significant Time X Medication Status interactions. When controlling for medication status however, the previously significant main effects

for time for Anxious/Depressed, Somatic Complaints, and Internalizing Problems were no longer significant.

In addition, exploratory repeated measures ANOVAs examining the potential moderating effect of sex were conducted. Overall**,** the pattern of findings paralleled the findings outlined above. The following differences emerged compared to the analyses without sex. There was a significant main effect of time for the individual scale Thought Problems, Wilks's $\Lambda = .84$, $F(1, 27) = 5.04$, $p = .033$, $\eta^2 = .15$, due to a significant decrease of problems over time. There was also a significant Time X Sex interaction for the scale Thought Problems, Wilks's $\Lambda = .66$, $F(1, 27) = 13.35$, $p = .001$, $\eta^2 = .33$, with female adolescents showing significant decrease of problems over time.

All of the analyses were conducted by excluding one OPD subject from the Converted group. Overall, the findings paralleled the findings outlined above. The only difference was in the medication covariate analyses. The results indicated that in addition to Social Problems, the medication covariate was also significant for the scales Aggressive Behavior, $F(1, 27) = 6.15$, $p = .020$, $\eta^2 = .18$, and Externalizing Problems, $F(1, 27) = 5.03$, $p = .034$, $\eta^2 = .15$.

In summary, there were no differences in CBCL scores as a function of conversion status and the findings did not indicate a differential behavioral profile between high-risk Converted and high-risk Non-Converted adolescents. Therefore, no further analyses on CBCL prediction of conversion were conducted.

CBCL scores predicting severity of prodromal symptomatology at one year follow-up assessment with entire sample

To test the hypothesis that social and behavioral problems predict a poor outcome as measured by increase in prodromal symptomatology at one year follow-up, a series of hierarchical regression analyses were conducted with positive, negative, disorganized, general, and total symptoms at one year follow-up assessment as the dependent variables. Because prodromal symptoms were rated on a continuous scale, it was possible for OPD and NC subjects to endorse prodromal items and be at a sub-threshold level for inclusion in the SPD group. Thus, regression analyses were conducted on the entire sample. Separate analyses were conducted to test the relation of positive, negative, disorganized, general, and total symptomatology with individual and composite CBCL scales. To control for baseline differences, positive, negative, disorganized, general, and total prodromal symptoms at baseline assessment were entered in Block 1. CBCL scores were entered in Block 2. With each respective analysis, the social and behavioral problems observed during baseline assessment were entered as predictor variables, and the magnitude of R^2 change was tested for significance. This analytic approach tested the hypothesis that controlling for prodromal symptoms at baseline assessment, social and behavioral problems at baseline assessment predict prodromal symptom severity at follow-up assessment.

Contrary to the prediction, overall social and behavioral problems did not account for a significant amount of the variance in positive, negative, general, and total prodromal symptomatology at one year follow-up assessment. Nevertheless, in the analyses with disorganized symptoms at follow-up as a dependent variable, there was a significant increment in R^2 for the CBCL individual scales, $R^2 = .48$, adjusted $R^2 = .47$, $F(1, 85) = 6.04$, $p = .016$. The scale Anxious/Depressed significantly predicted disorganized

symptoms at follow-up, β = .20, $t(85) = 2.45$, $p = .016$. Similarly, there was a significant increment in R^2 for the CBCL composite scales, $R^2 = .49$, adjusted $R^2 = .47$, $F(1, 85) = 4.22$, $p = .043$. Higher scores on the scale Internalizing Problems, β = .30, $t(85) = 2.99$, $p = .004$, and lower scores on the scale Externalizing Problems, β = -.198, $t(85) = -2.05$, $p = .043$, predicted disorganized symptoms at follow-up. Finally, in these series of analyses, prodromal symptomatology at baseline assessment accounted for a significant amount of the variance for Block 1 for all five prodromal scales (see Tables 10 and 11).

Insert Table 10 and Table 11

To clarify the role of psychotropic medications, a second set of analyses was conducted, controlling for medication status. The pattern of findings paralleled the findings outlined above and medication status was not a significant covariate. Also, exploratory analyses examining the potential moderating effect of sex were conducted. No significant interaction effect of sex was found and no differences in the results emerged.

The relation between social and behavioral characteristics and family history in entire sample

To test the hypothesis that participants with positive family history of psychosis or mood disorders in first-or second-degree relatives have more social and behavioral problems than participants without family history and to test for potential interactive

effects of this variable, a series of cross-sectional and longitudinal analyses were conducted examining the role of family history.

Social and behavioral characteristics and family history at baseline assessment. MANOVA analyses were conducted with diagnostic status and family history as independent variables and CBCL individual and composite scores at baseline as dependent variables. The main effects for diagnostic groups were as described above.

Although no significant main effect or interaction effect for family history was found with the CBCL individual scales and the multivariate F value was not significant, a number of univariate tests were significant. The findings indicated significantly higher CBCL scores for adolescents with family history on the scales Anxious/Depressed, $F(1, 98) = 4.35$, $p = .040$, $\eta^2 = .04$, Thought Problems, $F(1, 98) = 6.64$, $p = .011$, $\eta^2 = .06$, Delinquent Behavior, $F(1, 98) = 4.35$, $p = .040$, $\eta^2 = .04$, and Aggressive Behavior, $F(1, 98) = 6.61$, $p = .012$, $\eta^2 = .06$. In addition, the univariate tests showed a significant Diagnostic Status X Family History interaction effect for the individual scales Anxious/Depressed, $F(2, 98) = 3.59$, $p = .032$, $\eta^2 = .06$, Social Problems, $F(2, 98) = 9.27$, $p = .000$, $\eta^2 = .16$, Thought Problems, $F(2, 98) = 5.63$, $p = .005$, $\eta^2 = .10$, Attention Problems, $F(2, 98) = 3.39$, $p = .037$, $\eta^2 = .06$, and Aggressive Behavior, $F(2, 98) = 5.04$, $p = .008$, $\eta^2 = .09$. As expected, family history moderated the relationship between diagnostic status and social and behavioral problems. Univariate tests within family history groups revealed significant diagnostic group differences only for adolescents with positive family history: Anxious/Depressed, $F(2, 63) = 23.15$, $p = .000$, $\eta^2 = .42$, Social Problems, $F(2, 63) = 33.30$, $p = .000$, $\eta^2 = .51$, Thought Problems, $F(2, 63) = 17.98$, $p = .000$, $\eta^2 = .36$, Attention Problems, $F(2, 63) = 13.50$, $p = .000$, $\eta^2 = .30$, Aggressive

Problems, $F(2, 63) = 15.32$, $p = .000$, $\eta^2 = .32$. When compared with OPD adolescents, SPD adolescents showed significantly higher scores on the scale Social Problems. When compared with the NC group, both the SPD group and the OPD group showed significantly higher scores on all of the above scales.

Insert Figures 11, 12, 13, 14 and 15

In the analyses with the composite CBCL scales, there was a significant main effect for family history, Wilks's $\Lambda = .91$, $F(3, 96) = 3.01$, $p = .034$, $\eta^2 = .08$. Adolescents with presence of family history had higher scores on the scale Externalizing Problems, $F(1, 98) = 8.91$, $p = .004$, $\eta^2 = .08$. Although the multivariate F value was not significant for the diagnostic status x family history interaction, the univariate test for the scale Total Competence was significant, $F(2, 98) = 3.13$, $p = .048$, $\eta^2 = .06$.

Social and behavioral characteristics and family history at follow-up assessment. Similar to the baseline data analyses, MANOVA analyses with the follow-up data were conducted to examine the potential moderating effect of family history. There was no significant main effect or interaction effect of family history with the CBCL individual scales.

In the analyses with the CBCL composite scales, although the multivariate F value was not significant, the univariate test for the Externalizing Problems scale was significant, $F(1, 66) = 6.15$, $p = .016$, $\eta^2 = .08$, indicating higher scores for participants with positive family history of psychosis or affective disorders.

Social and behavioral characteristics and family history over time. To clarify the role of family history as related to the developmental trajectories of social and behavioral problems, repeated measures ANOVAs were conducted. CBCL scores of each time of assessment (baseline vs. follow-up) were the within-subject factor and diagnostic status and family history were the between-subject factors. The overall pattern of findings was consistent with the repeated measures ANOVA findings described earlier.

The findings indicated a significant Time X Family History interaction for the competence scale Social, Wilks's $\Lambda = .91$, $F(1, 69) = 7.29$, $p = .009$, $\eta^2 = .09$, with scores of adolescents without family history decreasing significantly over time. There was a significant main effect for family history for the following individual and composite scales: Delinquent Behavior, $F(1, 71) = 5.04$, $p = .028$, $\eta^2 = .07$, Aggressive Behavior, $F(1, 71) = 5.26$, $p = .025$, $\eta^2 = .07$, and Externalizing Problems, $F(1, 71) = 9.14$, $p = .003$, $\eta^2 = .11$. Adolescents with positive family history on those scales exhibited significantly higher scores compared to adolescents without family history. Further, there were significant Diagnostic Status X Family History interactions for the individual scales Social Problems, $F(2, 71) = 5.37$, $p = .007$, $\eta^2 = .13$, Thought Problems, $F(2, 71) = 3.51$, $p = .035$, $\eta^2 = .09$, and Aggressive Behavior, $F(2, 71) = 4.77$, $p = .011$, $\eta^2 = .12$. Paired samples *t* tests were conducted to follow-up on the significant interactions. Differences in mean ratings were significantly different between baseline and follow-up assessments, where OPD participants showed decrease over time in behavioral problems on the scales Social Problems, t (35) = 3.46. $p = .001$, Thought Problems, t (35) = 2.51. $p = .017$, and Aggressive Behavior, t (35) = 5.48. $p = .000$. Additionally, SPD participants showed

significant decrease over time in behavioral problems on the scale Social Problems, t (29) = 2.12. p = .043.

Discussion

The primary purpose of this study was to investigate social and behavioral precursors of psychosis in adolescents at clinical high-risk for the development of psychosis. This research focused on the cross-sectional and longitudinal examination of social and behavioral problems in high-risk SPD adolescents, a population that manifests prodromal signs and is at a heightened risk for future development of a psychotic disorder. Given that very limited research has been conducted in this area, a critical need exists currently in the field for a better understanding of the predictive validity and accuracy of precursors of psychosis in the prodromal period. This is the first study to examine social and behavioral antecedents of psychosis with a prospective design in a population of high-risk SPD adolescents.

Diagnostic group differences in social and behavioral problems

A primary goal of the study was to examine parent-reported social and behavioral problems of high-risk SPD adolescents compared to controls with and without other psychopathology. Consistent with previous research (Walker, Baum, & Diforio, 1998; Walker, Downey, & Bergman, 1989; Bergman & Walker, 1995; Olin et al., 1998) these findings indicated that adolescents with SPD have more social and behavioral problems than normal controls as well as adolescents with OPD. The baseline and follow-up findings supported the hypothesis that compared to the OPD group, the SPD group manifests more severe impairment on scales that tap into the behavioral deficits characterizing prodromal subjects; namely, higher baseline scores on the

Anxious/Depressed, Social Problems, and Thought Problems scales and higher follow-up scores on the Anxious/Depressed and Social Problems scales. While not all predicted differences between the two groups were significant in the cross-sectional analyses, the longitudinal findings demonstrated a shift in behavior toward greater impairment for SPD adolescents on all the hypothesized scales: Anxious/Depressed, Social Problems, Thought Problems, and Attention Problems.

It is noteworthy to mention that the behavioral findings with the high-risk SPD group were also consistent with the developmental course and pattern observed in pre-schizophrenic individuals (Neumann & Walker, 1995; Walker, Grimes, Davis, & Smith, 1993; Olin & Mednick, 1996; Miller at al., 2002), which provides further evidence for the link between SPD and psychosis. Additionally, it is interesting that the OPD group showed the highest scores on the Externalizing Problems scale. This makes sense given that this group consisted of a number of individuals presenting with conduct problems.

The ability of the CBCL to distinguish among the diagnostic groups indicates that this scale has potential to contribute to the identification of youth at risk for psychosis. Thus, based on the present findings, scores on the Anxious/Depressed, Social Problems, Thought Problems, and Attention Problems scales of the CBCL could be used to identify youth who are likely to meet diagnostic criteria for SPD, and, therefore, likely to be at risk for subsequent psychosis. Further, based on the conversion rate of 35% observed in the present and previous samples of clinical at-risk subjects, it appears that the CBCL may be useful for significantly improving prediction beyond the base rate of 1-2% for psychosis in the general population.

The relation of social and behavioral problems with conversion to psychosis

Another goal of the study was to examine the nature and developmental course of CBCL scores of high-risk adolescents who converted to an Axis I psychotic disorder compared to those who did not convert. Consistent with expectations, significantly more of the SPD subjects converted to psychosis within the total follow-up period of 4 years. Further, although the Converted SPD subjects did not differ from Non-Converted subjects in baseline scores on the SIPS prodromal symptoms, at the one-year follow-up the Converted subjects manifested significantly higher scores on the positive, negative, disorganized, general, and total prodromal symptom scales.

However, contrary to predictions, there were no differences in CBCL scores as a function of conversion status, and the findings did not indicate a differential behavioral profile between high-risk Converted and high-risk Non-Converted youth. Surprisingly, although the multivariate F value was not significant, the only significant univariate test at baseline pointed to a higher score on the scale Aggressive Behavior for the Non-Converted group. In contrast, the SIPS prodromal symptoms ratings showed a trend toward higher scores for the Converted subjects at baseline, and by follow-up all of the scores were significantly higher for the Converted group.

Given that this is the first study in the literature examining parent-reported behavior problems in a prospective study of high-risk SPD adolescents, direct comparison with other studies is not possible. Nevertheless, on the surface, the present results would seem inconsistent with findings from studies of individuals classified as prodromal, based on criteria other than SPD diagnosis (i.e., brief intermittent psychosis criteria, brief limited intermittent psychotic symptoms, attenuated psychotic symptoms, genetic risk and functional decline prodromal syndrome). Specifically, studies of clinical

high-risk youth that compared converted to non-converted subjects have reported findings of significant decline in social functioning in multiple domains and findings of depressive symptoms, anxiety symptoms, decreased attention, and disorganization as predictors of conversion to psychosis (Yung, Phillips, Yuen, & McGorry, 2004; Cornblatt et al., 2007; Ballon et al., 2007; Cannon et al., 2008; Woods et al., 2009).

It is plausible that the present results point to the advantage of direct clinical assessment of prodromal symptoms. In other words, although parents have observed their child throughout his life time in a variety of contexts, this may not outweigh the advantages of the clinical interview for obtaining reliable and valid information about prodromal indicators. The advantages of the clinical interview may be a function of both clinical training of the rater and the probing questions that are contained in clinical interviews. First, with respect to clinician training, preparation of interviewers to administer the SIPS, SIDP-IV and SCID entails many hours of viewing experienced interviewers and practicing administration. Interviewers must achieve consistency in the procedures they utilize, and reliability in the scores they apply to each symptom rating. Thus, compared to untrained individuals, clinical interviewers have greater skills in behavioral observation and perception of more subtle distinctions. These skills undoubtedly enhance the reliability and validity of their behavioral ratings. Further, structured clinical interviews include follow-up and probe questions that are aimed at eliciting information that individuals might ordinarily not be inclined to reveal. For example, the SIPS contains numerous questions about unusual sensory experiences in the auditory, visual, and tactile domains. Although only one SIPS rating is made for perceptual abnormalities, this rating is informed by the subject's responses to numerous

probe and follow-up questions. It would be uncommon for parents to pursue such lines of questioning with their child.

Past research comparing the predictive power of structured diagnostic interviews with parent-reported behavior problems indicates that structured interviews have higher positive predictive power and greater validity (Wassenberg, Max, Koele, & Firme, 2004; Reitman, Hummel, Franz, & Gross, 1998). Also, the validity of parent report varies by type of behavioral problem. Past research has revealed a greater parent –child agreement regarding externalizing problems compared to internalizing problems (Berg-Nielsen, Vika, & Dahl, 2003; Seiffge-Krenke & Kolmar, 1998). It has been argued that while externalizing problems are more readily observable because the problem behaviors are directed towards others, internalizing problems are only poorly recognized by parents (Bird, Gould, & Staghezza, 1992; Sourander, Helstela, & Helenius, 1999). In line with this, it is possible that especially CBCL ratings taping into negative prodromal symptoms (e.g., decreased expression or experience of emotion, social isolation, decreased role functioning) might be more difficult for parents to observe and to report accurately. Further, research has substantiated the utility of structured assessments in the prediction of psychotic disorders. Findings from recent prodromal studies indicate that the prediction of conversion to psychosis is greatly improved and maximized by combining predictive variables, including clinician-based SIPS ratings, into specific predictive algorithms. One study found that a combination of five baseline variables significantly increased positive predictive power (i.e., 68%-80%) compared with the SIPS prodromal criteria alone (35%) (Cannon et al., 2008).

It is also important to consider the possibility that the predictive power of the parent-report CBCL will improve when more long-term psychiatric outcome data are obtained. It is likely that more high-risk individuals will convert to psychosis in future follow-up assessments. Compared to the mean age of clinical and ultra high-risk prodromal samples in other studies (mid to late teens/early twenties) (Yung et al., 2003; Yung, Phillips, Yuen, & McGorry, 2004; Klosterkotter et al., 2001; Woods et al., 2009), this sample has a younger mean age (early teens). Thus, adolescents in this study are just entering the highest risk period for onset of psychosis in late adolescence/early adulthood. It is possible that the baseline or one-year follow-up CBCL will yield significant differences between the Converted and the Non-Converted adolescents as the high-risk individuals move more closer to the age of conversion to psychosis. Support for this possibility is provided from studies showing evidence for increased positive predictive power temporally closer to the onset of psychosis (Rackfield & McGlashan, 2004; Salokangas & McGlashan, 2008). Along similar lines, positive predictive power is affected by the duration of the follow-up period.

In addition, it is also possible that limited statistical power due to a small sample size reduced the likelihood of detecting a significant difference. Thus, future longitudinal high-risk studies with larger sample sizes may detect CBCL profile differences between Converted and Non-Converted subjects. Nonetheless, the present results indicate that the effect size for prediction of conversion with the CBCL is likely to be much smaller than that of the SIPS prodromal ratings. Therefore, even if larger sample sizes yielded a significant difference, it would not necessarily indicate adequate predictive power to

justify even the adjunctive use of the CBCL in predicting psychosis risk for psychosis conversion in clinical risk groups.

Another potential explanation for the absence of a relation between CBCL rating and conversion to psychosis is that unexplored moderators may have contributed to the inability to detect significant differences between Converted and Non-Converted adolescents. While it is not possible to incorporate all potential risk-modifying factors in any one study of child behavior, research indicates that there are sometimes interactive effects among risk factors. For instance, in applying this strategy past studies have directly tested assumptions implicit in the diathesis-stress model and have identified main and interactive effects of parental psychopathology and maltreatment on CBCL behavioral ratings (Walker, Downey, & Bergman, 1989). Therefore, future research should aim to investigate simultaneously main and interactive effects of relevant variables on social and behavioral problems in high-risk youth. Again, however, the potential for such interactive effects does not mitigate the present findings that the SIPS ratings proved better at predicting conversion than the CBCL ratings.

It is of interest to note the finding of a higher score on the CBCL Aggressive Behavior scale in the high-risk Non-Converted group. This finding is inconsistent with studies indicating that delinquent or aggressive behavior in pre-schizophrenic adolescents significantly predicts later onset of schizophrenia (Miller et al., 2002; Gosden, Kramp, Gabrielsen, Andersen, & Sestoft, 2005). However, in those past studies the pre-schizophrenic subjects were not compared to individuals who met clinical risk criteria. Instead, the comparison was with genetic high-risk subjects who did not develop a psychotic disorder, or to low-risk control subjects. It cannot be ruled out, however, that

levels of behavioral problems and developmental trajectories in the Converted and the Non-Converted group may vary depending on the specific psychotic outcome (in the Converted group) or the heightened risk for a specific psychotic outcome (in the Non-Converted group) in this study. Related to this, very limited research has been conducted comparing similarities and differences among different subtypes of psychotic disorders in adolescents. Nevertheless, a recent longitudinal study of 41 adolescents diagnosed with a psychotic disorder (n = 17 schizophrenia, n = 11 schizoaffective, n = 13 bipolar disorder with psychotic features) and followed-up over a 5-year period provides support for a differential developmental course and outcome in adolescents with different psychotic disorders (Ledda, Fratta, Pintor, Zuddas, & Cianchetti, 2009). Significantly better outcome at 12 months, 3 years, and 5years follow-up was reported for individuals with bipolar disorder, while more substantial deterioration in longitudinal course was reported for individuals with schizophrenia and schizoaffective disorder. The latter two diagnostic groups were very similar in regard to the level of impairment. At 3 year follow-up compared to bipolar patients, the schizophrenic patients showed significantly worse functioning in conceptual disorganization, mannerism and posturing, uncooperativeness, lack of judgment and insight, active social avoidance, and self-neglect. At 5 year follow-up the findings were similar, but with worsening of schizophrenic patients related to negative symptoms. It is also important to note that the following diagnostic changes occurred prospectively from initial assessment to 5-year follow-up: 2 of 13 schizophrenic patients became bipolar, 6 of 18 schizoaffective patients became schizophrenic and 4 bipolar; 3 of 10 bipolar patients became schizoaffective (Ledda, Fratta, Pintor, Zuddas, & Cianchetti, 2009). This study provides support for a differential developmental course

and clinical outcome for adolescents with different psychotic disorders. It is possible that similar neurobehavioral mechanisms contribute to differential risk profiles in high-risk Converted and high-risk Non-Converted adolescents in the present study, thus impacting the presentation of social and behavioral precursors of psychosis during the prodromal period. Therefore, future research should aim to examine the relationship between behavioral problems and conversion to specific subtypes of psychotic disorder.

Consistent with the findings of lack of significant association between CBCL and conversion, baseline CBCL behavioral ratings for the most part were not associated with prodromal symptomatology at one year follow-up. Only two significant findings emerged from these analyses. First, the individual scale Anxious/Depressed and the composite scale Internalizing Problems predicted disorganized symptoms and second, there was an inverse relationship between Externalizing Problems and disorganized symptoms. Given that CBCL scores did not predict conversion, it was expected that behavioral ratings will likely not be linked to prodromal symptomatology.

Longitudinal trend across CBCL scales

The findings of this study also indicated that the mean longitudinal trend across CBCL scales and within the three diagnostic groups was toward a decrease of social and behavioral problems over time. This finding is consistent with the literature on normative decrease of social and behavioral problems in the post-adolescent period (Bongers, Koot, van der Ende, & Verhulst, 2003, 2004; Dekker et al., 2007). Additionally, however, findings from studies of CBCL scores in normal youth indicate a number of group-based developmental pathways existing within average trajectories for individual behaviors (Dekker et al., 2007). These studies show that the nature of developmental behavioral

trajectories is highly dynamic and is impacted by number factors (i.e., sex, nature and timing of onset of deviant levels of behavioral problems, and other). Nevertheless, it is important to keep in mind that although the prospective analyses did not show a shift in behavior toward greater social and behavioral problems in high-risk adolescents over time, behavioral problems exhibited by high-risk SPD adolescents remained significantly higher than the other groups throughout the study. Furthermore, significant Time X Diagnostic Status interactions were found for the individual scales Activities and Aggressive Behavior, and for the composite scale Externalizing Problems. This was due to the magnitude of differences between the OPD group and the other groups, which grew over the period of one year. Similarly, although not significant, the SPD participants' scores followed this trend.

Sex differences

To examine the role of sex differences in the study, exploratory analyses were conducted investigating the potential main and interactive effects of sex on CBCL behavioral ratings. Overall, some mixed findings emerged. In contrast with research evidence indicating that the behavioral expression of vulnerability to psychosis is characterized by sex differences (Watt, 1978; Walker, Downey, & Bergman, 1989; Olin & Mednick, 1996; Done, Crow, Johnstone, & Sacker, 1994), cross-sectional and longitudinal analyses with the entire sample of adolescents did not demonstrate main or interactive effects of sex on CBCL behavioral ratings. This parallels some results from studies reporting inconsistent findings or absence of sex differences (Freedman et al., 1998; Gutt et al., 2008). The analyses with the high-risk Converted and high-risk Non-Converted adolescents provided some preliminary evidence for the effect of sex on

CBCL behavioral ratings. Specifically, in the analyses excluding one OPD subject from the high-risk Converted group, female adolescents showed higher baseline scores on the scale Thought Problems. This finding, however, was qualified by a significant Conversion Status X Sex interaction. Thus, sex was a moderator of the relation between conversion status and the scale Thought Problems at baseline assessment. Converted females showed higher scores than Non-Converted females whereas there were no differences between the Converted and Non-Converted males. Surprisingly, a significant Conversion Status X Sex interaction for the Delinquent Behavior scale indicated that Non-Converted females showed higher scores compared to Converted females. There were no differences between males. Additionally, a significant Time X Sex interaction demonstrated a decrease of problems over time on the scale Thought Problems for female adolescents. Also, females had significantly higher scores on the scale Aggressive Behavior at follow-up assessment. The findings on some of the CBCL behavioral ratings seem to be in line with past research providing evidence for female sex as a significant predictor of psychosis and indicating that female adolescents with prodromal symptoms have the highest risk for developing a psychosis (McGorry et al., 2002). However, given that there is an issue of limited statistical power in these analyses, these results should be interpreted with caution. Related to this, it is important to note that the results of a recent study with this sample of high-risk Converted and high-risk Non-Converted adolescents, pointed to sex-related differences in baseline neurocognitive functioning (Walder, Mittal, Trotman, McMillan, & Walker, 2008). In this study, within-sex comparisons revealed a relation between conversion status and neurocognitive performance among females, with more impairment in neurocognition in high-risk Converted females compared with high-

risk Non-Converted females. There were no significant within-sex differences for males. Overall, however, the sex-related findings in the present study are mixed, should be viewed as preliminary, and should be interpreted with caution.

Psychotropic medications

Some adolescents in the study were being treated with psychotropic medications. This represents a methodological challenge. For ethical reasons, medications, particularly those that appear to have some efficacy for the individual, cannot be changed for research purposes. On the other hand, there is reason to be concerned about the potential effects of psychotropic medication on the behavioral measures of interest in the study. One approach to addressing this is to include medication status as a covariate. However, this approach does not take into account the fact that behavioral abnormalities also serve to precipitate psychotropic medication; subjects who manifested the most pronounced behavioral problems prior to baseline would be more likely to receive medication. Consistent with this assumption, medication was associated with higher CBCL ratings at baseline and follow-up. Therefore, treating medication as a covariate also constrains variance in baseline CBCL ratings. For this reason, analyses were conducted with and without psychotropic medication (present/absent) as a covariate. The effect of medication status seemed to be manifested largely in the analyses with the entire sample of adolescents. There was a main effect for medication status in both the cross-sectional and the longitudinal analyses. The main difference in findings compared to the analyses without medication as a covariate was that several of the statistically significant group differences between the high-risk SPD adolescents and the OPD adolescents were no longer significant. The two groups no longer had different baseline CBCL scores on the

scales Social Problems, Thought Problems, and Externalizing Problems and different follow-up CBCL scores on the scales Anxious/Depressed and Social Problems. The medication effects also altered some of the previously significant cross-sectional differences between the SPD group and the NC group. Moreover, the longitudinal analyses followed the same pattern of findings. There were no longer any differences between the SPD group and the OPD group on any of the CBCL scales. Similar to the cross-sectional analyses, some of the previously reported differences between SPD and NC adolescents were no longer significant. Although, fewer medication effects emerged in the analyses with the high-risk Converted and high-risk Non-Converted adolescents, the following results are noteworthy. The longitudinal analyses showed that medication status was a significant covariate for the scale Social Problems. In addition, there no longer was a significant main effect for time for the scales Anxious/Depressed, Somatic Complaints, and Internalizing Problems. Overall, it appears that medication status showed little association with conversion to psychosis. While this study was not intended to address directly questions about medication effects, the findings underscore the effect of psychotropic medications on behavior. Taken together, the findings demonstrate that psychotropic medications should be examined further in future research on social and behavioral problems in high-risk youth. Also, future studies should focus on examining different classes of medications to better parse out the relationship to behavioral ratings.

Family history of psychosis

In terms of family history, the results were consistent with the hypothesized relationship and with previous research (Walker, Downey, & Bergman, 1989; Foerster et al., 1991; St. Hilaire et al., 2005; Walsche et al., 2007). The findings were also indicative

of constitutional vulnerability underlying the risk for psychosis and provided support for the neural diathesis-stress model (Walker & Diforio, 1997). As predicted, there was a main effect of family history for a number of CBCL scales indicating higher scores for adolescents with positive family history of psychosis or affective disorders. Notably, the findings also demonstrated significant Diagnostic Status X Family History interactions for several behavioral scales providing support for family history as a moderator of the relation between diagnostic status and CBCL scales. One research question of interest was whether family history adds to the prediction of conversion to psychosis beyond that achieved with the CBCL. However, given that there were no differences in CBCL scores as a function of conversion status, no further analyses on family history prediction of conversion were undertaken.

Limitations of the present study

A number of limitations should be mentioned and should be considered in interpreting the present findings. First, because of the small sample size of individuals in the Converted group the conclusions offered by this study should be viewed as preliminary. It is likely that the small sample size limited statistical power and also constricted the ability to detect more sex-related differences in this population. Second, the presence of adolescents taking psychotropic medications represented a methodological challenge. Third, some adolescents in the study were participating in psychotherapy, which may have an impact on social and behavioral problems. Fourth, high-risk adolescents with SPD constitute a subgroup of those at risk for psychosis. Although most individuals who develop a psychotic disorder show premorbid behavioral abnormalities and prodromal signs as the illness approaches, a minority manifest minimal

or no behavioral abnormality. Further, although, SPD appears to be on a continuum with schizophrenia, there is lack of research on its relationship to other psychotic illnesses and affective disorders with psychotic features. Therefore, SPD individuals might have a different genetic make-up and heritability for psychosis compared to those individuals exhibiting other high-risk signs or syndromes. Therefore, caution should be used when generalizing the findings of the study to psychosis in general. Finally, multilevel growth curve analytical approaches are useful for the investigation of developmental behavioral trajectories, allowing for examination of trajectories by sex and allowing for the identification of group-based developmental pathways within behavioral clusters. Therefore, future research with large sample sizes and addressing both number and shape of latent developmental trajectories is warranted.

Conclusions

Taken together, the findings of this study suggest the following main conclusions. First, consistent with previous research youth with SPD showed a behavioral profile that was distinguishable from OPD and NC adolescents. Thus, the CBCL is capable of differentiating among groups at varying levels of risk for psychosis. Second, consistent with prediction, a significant subgroup of the SPD adolescents eventually converted to an Axis I psychotic disorder, and ratings from the SIPS prodormal scales distinguished these two groups. However, contrary to prediction, the CBCL behavioral profiles of high-risk Converted participants did not differ from high-risk Non-Converted participants. Thus, the CBCL does not show promise as an alternative or adjunctive predictor of conversion among those at risk for psychosis. Instead, it appears that ratings from the SIPS structured interview are more sensitive predictors of conversion to psychosis.

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Table 1. Demographic Characteristics of Samples

	SPD			OPD	NC	Total
		Converted (SPD + one OPD)	Non-Converted (SPD)			
Total	40	14	27	48	34	122
Males	26	8	18	25	17	68
Females	14	6	9	23	17	54
Age (yrs.)						
M	14.20	14.57	14.07	14.44	14.06	14.25
(SD)	(1.71)	(1.55)	(1.79)	(1.78)	(1.95)	(1.80)
Race						
Caucasian	25	11	19	28	23	76
African American	23	3	5	7	15	45
Asian American	0	0	2	1	3	4
Other	1	0	1	1	1	3

Table 2. Means and Standard Deviations of Prodromal Symptoms by Diagnostic Group at Baseline Assessment

	1 SPD	2 OPD	3 NC	Total	Group Differences
			Prodromal Symptoms		
Positive					
M	2.43	.70	.51	1.23	1 > 2,3**
(SD)	(.93)	(.56)	(.54)	(1.10)	
Negative					
M	1.82	.79	.41	1.01	1 > 2,3**
(SD)	(1.15)	(.76)	(.56)	(1.03)	
Disorganization					
M	1.75	.44	.25	.82	1 > 2,3**
(SD)	(.97)	(.49)	(.35)	(.93)	
General					
M	1.66	.76	.33	.94	1 > 2,3**
(SD)	(1.09)	(.73)	(.41)	(.96)	
Total					
M	1.89	.67	.37	.99	1 > 2,3**
(SD)	(.82)	(.48)	(.37)	(.87)	

** $p \leq .01$.

Table 3. Means and Standard Deviations of Prodromal Symptoms by Diagnostic Group at Follow-Up Assessment

	1 SPD	2 OPD	3 NC	Total	Group Differences
			Prodromal Symptoms		
Positive					
M	2.00	.64	.36	1.03	1 > 2,3**
(SD)	(1.05)	(.61)	(.43)	(1.03)	
Negative					
M	1.79	.89	.52	1.10	1 > 2,3**
(SD)	(1.21)	(.83)	(.73)	(1.08)	
Disorganization					
M	1.49	.52	.28	.79	1 > 2,3**
(SD)	(.92)	(.52)	(.40)	(.83)	
General					
M	1.35	.59	.39	.80	1 > 2,3**
(SD)	(1.13)	(.62)	(.62)	(.92)	
Total					
M	1.66	.66	.39	.93	1 > 2,3**
(SD)	(.84)	(.42)	(.48)	(.81)	

** $p \leq .01$

Table 4. Means and Standard Deviations of Prodromal Symptoms for High-Risk Converted (SPD + one OPD subject) and High-Risk Non-Converted (SPD) Adolescents at Baseline Assessment

	1 Converted	2 Non-Converted	3 Total	Group Differences
		Prodromal Symptoms		
Positive				
M	2.28	2.45	2.40	1, 2 = n.s.
(SD)	(.98)	(.94)	(.94)	
Negative				
M	2.10	1.62	1.77	1, 2 = n.s
(SD)	(1.48)	(.98)	(1.17)	
Disorganization				
M	1.91	1.64	1.73	1, 2 = n.s.
(SD)	(1.17)	(.84)	(.96)	
General				
M	1.83	1.55	1.65	1, 2 = n.s.
(SD)	(1.26)	(.98)	(1.08)	
Total				
M	1.98	1.82	1.87	1, 2 = n.s.
(SD)	(1.11)	(.67)	(.83)	

Table 5. Means and Standard Deviations of Prodromal Symptoms for High-Risk Converted (SPD + one OPD subject) and High-Risk Non-Converted (SPD) Adolescents at Follow-Up Assessment

	1 Converted	2 Non-Converted	3 Total	Group Differences
		Prodromal Symptoms		
Positive				
M	2.60	1.48	1.97	1 > 2**
(SD)	(.87)	(.91)	(1.04)	
Negative				
M	2.36	1.27	1.75	1 > 2**
(SD)	(1.30)	(.92)	(1.21)	
Disorganization				
M	1.92	1.12	1.47	1 > 2**
(SD)	(.74)	(.89)	(.91)	
General				
M	1.82	.93	1.32	1 > 2*
(SD)	(1.45)	(.60)	(1.13)	
Total				
M	2.17	1.20	1.63	1 > 2**
(SD)	(.80)	(.61)	(.84)	

** $p \leq .01$; * $p \leq .05$

Table 6. CBCL Scales Mean *T* Scores, Standard Deviations, and MANOVA Tests of Between-Subjects Effects by Diagnostic Group at Baseline Assessment

	1 SPD Mean (SD)	2 OPD Mean (SD)	3 NC Mean (SD)	Group Differences	MANOVA Results Tests of Between-Subjects Effects
			CBCL Individual Scales		
Activities▲	42.95 (8.17)	43.31 (9.53)	44.35 (9.83)	1, 2, 3 = n.s.	$F(2, 115) = .22$, $p = .798$, $\eta^2 = .01$
Social ▲	35.85 (8.25)	38.18 (9.41)	45.41 (11.82)	1 < 3**, 2 < 3**	$F(2, 115) = 9.25$, $p = .000$, $\eta^2 = .14$
School ▲	37.87 (8.75)	39.84 (9.39)	44.85 (8.56)	1 < 3**, 2 < 3**	$F(2, 115) = 5.80$, $p = .004$, $\eta^2 = .09$
Anxious/Depressed	71.36 (11.73)	63.40 (9.94)	55.97 (8.24)	1 > 2, 3**, 2 > 3**	$F(2, 115) = 21.00$, $p = .000$, $\eta^2 = .27$
Withdrawn	67.33 (11.76)	63.71 (9.23)	56.32 (7.88)	1 > 3**, 2 > 3**	$F(2, 115) = 11.77$, $p = .000$, $\eta^2 = .17$
Somatic Complaints	63.85 (11.39)	60.82 (8.11)	55.15 (6.91)	1 > 3**, 2 > 3**	$F(2, 115) = 8.58$, $p = .000$, $\eta^2 = .13$
Social Problems	70.74 (11.23)	63.04 (9.95)	56.82 (9.52)	1 > 2, 3**, 2 > 3**	$F(2, 115) = 16.85$, $p = .000$, $\eta^2 = .23$
Thought Problems	69.28 (10.12)	63.71 (9.33)	58.41 (9.66)	1 > 2, 3**, 2 > 3**	$F(2, 115) = 11.45$, $p = .000$, $\eta^2 = .17$
Attention Problems	67.85 (8.97)	63.60 (9.35)	57.47 (8.68)	1 > 3**, 2 > 3**	$F(2, 115) = 12.02$, $p = .000$, $\eta^2 = .17$
Delinquent Behavior	61.08 (7.96)	64.42 (10.28)	56.53 (6.69)	2 > 3**	$F(2, 115) = 8.12$, $p = .001$, $\eta^2 = .12$
Aggressive Behavior	65.26 (10.58)	67.76 (11.13)	57.38 (10.05)	1 > 3**, 2 > 3**	$F(2, 115) = 9.62$, $p = .000$, $\eta^2 = .14$
			CBCL Composite Scales		
Total Competence ▲	35.49 (7.87)	37.17 (9.71)	45.15 (10.04)	1 < 3**, 2 < 3**	$F(2, 116) = 11.19$, $p = .000$, $\eta^2 = .16$
Internalizing Problems	69.62 (9.99)	63.61 (10.01)	51.62 (12.65)	1 > 3**, 2 >3**	$F(2, 116) = 25.80.19$, $p = .000$, $\eta^2 = .31$
Externalizing Problems	62.33 (11.62)	66.39 (10.17)	53.24 (12.30)	1 > 3**, 2 >3**	$F(2, 116) = 13.52$, $p = .000$, $\eta^2 = .19$

Note: ▲ high scores indicate more social competencies; ** $p \leq .01$;

Table 7. CBCL Scales Mean *T* Scores, Standard Deviations, and MANOVA Tests of Between-Subjects Effects by Diagnostic Group at Follow-Up Assessment

	1 SPD Mean (SD)	2 OPD Mean (SD)	3 NC Mean (SD)	Group Differences	MANOVA Results Tests of Between-Subjects Effects
			CBCL Individual Scales		
Activities▲	43.48 (7.12)	40.68 (9.76)	46.96 (7.73)	2 < 3*	$F(2, 82) = 3.89$, $p = .024$, $\eta^2 = .09$
Social▲	37.30 (7.17)	39.62 (7.86)	46.00 (8.69)	1 < 3**, 2 < 3**	$F(2, 82) = 8.22$, $p = .001$, $\eta^2 = .17$
School▲	36.81 (8.52)	40.82 (7.62)	45.42 (8.92)	1 < 3**	$F(2, 82) = 6.83$, $p = .002$, $\eta^2 = .14$
Anxious/Depressed	64.07 (11.06)	57.91 (8.79)	54.54 (7.96)	1 > 2, 3**	$F(2, 82) = 6.90$, $p = .002$, $\eta^2 = .14$
Withdrawn	61.37 (10.67)	58.06 (10.96)	54.17 (6.72)	1 > 3*	$F(2, 82) = 3.39$, $p = .038$, $\eta^2 = .08$
Somatic Complaints	59.81 (11.89)	57.18 (8.97)	53.00 (5.74)	1 > 3*	$F(2, 82) = 3.44$, $p = .036$, $\eta^2 = .08$
Social Problems	66.56 (12.52)	58.26 (9.03)	55.88 (8.99)	1 > 2, 3**	$F(2, 82) = 7.91$, $p = .001$, $\eta^2 = .16$
Thought Problems	65.04 (9.48)	59.09 (10.24)	54.71 (9.02)	1 > 3**	$F(2, 82) = 7.36$, $p = .001$, $\eta^2 = .15$
Attention Problems	66.48 (11.13)	60.21 (9.85)	56.50 (8.73)	1 > 3**	$F(2, 82) = 6.59$, $p = .002$, $\eta^2 = .14$
Delinquent Behavior	62.63 (9.11)	60.15 (8.06)	55.83 (7.93)	1 > 3*	$F(2, 82) = 4.25$, $p = .017$, $\eta^2 = .09$
Aggressive Behavior	62.56 (10.40)	59.88 (10.68)	54.75 (7.21)	1 > 3*	$F(2, 82) = 4.19$, $p = .000$, $\eta^2 = .19$
			CBCL Composite Scales		
Total Competence▲	36.41 (7.43)	37.88 (9.68)	46.88 (10.51)	1 < 3**, 2 < 3**	$F(2, 82) = 9.47$, $p = .000$, $\eta^2 = .19$
Internalizing Problems	62.48 (13.74)	55.56 (12.00)	48.67 (11.43)	1 > 3**	$F(2, 82) = 7.85$, $p = .001$, $\eta^2 = .16$
Externalizing Problems	62.63 (12.54)	58.68 (11.09)	50.88 (11.86)	1 > 3**, 2 > 3**	$F(2, 82) = 6.49$, $p = .002$, $\eta^2 = .14$

Note: ▲ high scores indicate more social competencies; ** $p \leq .01$,* $p \leq .05$;

Table 8. CBCL Scales Mean *T* Scores, Standard Deviations, and MANOVA Tests of Between-Subjects Effects by Outcome Group at Baseline Assessment

	1 Converted Mean (SD)	2 Non-Converted Mean (SD)	Group Differences	MANOVA Results Tests of Between-Subjects Effects
		CBCL Individual Scales		
Activities▲	43.36 (10.15)	42.04 (7.73)	1, 2 = n.s.	$F(1, 38) = .21$, $p = .648$, $\eta^2 = .01$
Social▲	36.93 (7.04)	35.12 (8.78)	1, 2 = n.s	$F(1, 38) = .44$, $p = .510$, $\eta^2 = .01$
School▲	37.79 (8.36)	37.96 (8.95)	1, 2 = n.s	$F(1, 38) = .01$, $p = .952$, $\eta^2 = .00$
Anxious/Depressed	69.79 (14.30)	72.58 (10.17)	1, 2 = n.s	$F(1, 38) = .51$, $p = .478$, $\eta^2 = .01$
Withdrawn	66.29 (10.61)	67.38 (12.58)	1, 2 = n.s	$F(1, 38) = .07$, $p = .783$, $\eta^2 = .00$
Somatic Complaints	65.43 (12.30)	63.54 (11.18)	1, 2 = n.s	$F(1, 38) = .24$, $p = .625$, $\eta^2 = .01$
Social Problems	66.14 (12.27)	72.96 (9.91)	1, 2 = n.s	$F(1, 38) = 3.64$, $p = .064$, $\eta^2 = .09$
Thought Problems	67.79 (12.99)	69.85 (8.25)	1, 2 = n.s	$F(1, 38) = .37$, $p = .543$, $\eta^2 = .01$
Attention Problems	67.71 (10.13)	67.96 (8.31)	1, 2 = n.s	$F(1, 38) = .007$, $p = .934$, $\eta^2 = .00$
Delinquent Behavior	60.14 (6.81)	61.85 (8.55)	1, 2 = n.s	$F(1, 38) = 4.13$, $p = .524$, $\eta^2 = .01$
Aggressive Behavior	61.07 (10.49)	68.12 (13.23)	1 < 2*	$F(1, 38) = 4.23$, $p = .046$, $\eta^2 = .10$
		CBCL Composite Scales		
Total Competence▲	36.43 (7.93)	34.62 (7.99)	1, 2 = n.s	$F(1, 38) = .47$, $p = .497$, $\eta^2 = .01$
Internalizing Problems	69.00 (12.24)	70.19 (8.65)	1, 2 = n.s	$F(1, 38) = .12$, $p = .722$, $\eta^2 = .00$
Externalizing Problems	58.29 (13.12)	65.00 (10.27)	1, 2 = n.s	$F(1, 38) = 3.19$, $p = .082$, $\eta^2 = .08$

Note: ▲ high scores indicate more social competencies; * $p \leq .05$;

Table 9. CBCL Scales Mean *T* Scores, Standard Deviations, and MANOVA Tests of Between-Subjects Effects by Outcome Group at Follow-Up Assessment

	1 Converted Mean (SD)	2 Non-Converted Mean (SD)	Group Differences	MANOVA Results Tests of Between-Subjects Effects
		CBCL Individual Scales		
Activities▲	41.25 (9.10)	43.69 (7.74)	1, 2 = n.s.	$F(1, 26) = .58$, $p = .451$, $\eta^2 = .02$
Social ▲	36.75 (5.10)	37.69 (8.35)	1, 2 = n.s.	$F(1, 26) = .12$, $p = .735$, $\eta^2 = .01$
School▲	37.00 (7.13)	36.38 (9.48)	1, 2 = n.s.	$F(1, 26) = .04$, $p = .850$, $\eta^2 = .00$
Anxious/Depressed	64.17 (9.02)	63.88 (12.35)	1, 2 = n.s.	$F(1, 26) = .01$, $p = .946$, $\eta^2 = .00$
Withdrawn	61.33 (7.53)	60.69 (12.80)	1, 2 = n.s.	$F(1, 26) = .02$, $p = .878$, $\eta^2 = .00$
Somatic Complaints	59.58 (9.27)	59.75 (13.52)	1, 2 = n.s.	$F(1, 26) = .01$, $p = .971$, $\eta^2 = .00$
Social Problems	62.58 (11.52)	69.38 (12.39)	1, 2 = n.s.	$F(1, 26) = 2.18$, $p = .152$, $\eta^2 = .08$
Thought Problems	63.58 (8.86)	65.19 (10.56)	1, 2 = n.s.	$F(1, 26) = .18$, $p = .674$, $\eta^2 = .01$
Attention Problems	62.92 (10.22)	69.31 (10.94)	1, 2 = n.s.	$F(1, 26) = 2.47$, $p = .128$, $\eta^2 = .09$
Delinquent Behavior	62.67 (9.28)	63.19 (9.29)	1, 2 = n.s.	$F(1, 26) = .02$, $p = .884$, $\eta^2 = .00$
Aggressive Behavior	60.92 (9.75)	65.00 (11.59)	1, 2 = n.s.	$F(1, 26) = .97$, $p = .334$, $\eta^2 = .04$
		CBCL Composite Scales		
Total Competence▲	35.17 (6.14)	36.56 (8.78)	1, 2 = n.s.	$F(1, 26) = .22$, $p = .642$, $\eta^2 = .01$
Internalizing Problems	61.75 (11.60)	62.63 (15.19)	1, 2 = n.s.	$F(1, 26) = .03$, $p = .869$, $\eta^2 = .01$
Externalizing Problems	59.92 (12.74)	65.56 (12.35)	1, 2 = n.s.	$F(1, 26) = 1.39$, $p = .248$, $\eta^2 = .05$

Note: ▲ high scores indicate more social competencies; * $p \leq .05$;

Table 10. Results of Regression Analyses of the Relation of CBCL Individual Scales at Baseline Assessment with SIPS Symptom Severity at One Year Follow-Up Assessment for the Entire Sample

Dependent variable Step and Model	R^2	ΔR^2	*B*	*SE B*	β
Positive Symptoms					
Step 1	.437	.430			
Positive Symptoms-Baseline			.685	.084	.661
Model F (1,86)= 66.68, p = .000					
Negative Symptoms					
Step 1	.375	.368			
Negative Symptoms-Baseline			.641	.090	.621
Model F (1,85)= 50.97, p = .000					
Disorganization					
Step 1	.443	.436			
Disorganization-Baseline			.598	.072	.665
Step 2	.480	.467			
Disorganization-Baseline			.536	.075	.597
Anxious/Depressed			.015	.006	.204
Model F (2,85)= 39.17, p = .000					
General Symptoms					
Step 1	.312	.304			
General Symptoms-Baseline			.590	.095	.559
Model F (1,85)= 38.54, p = .000					
Total Symptoms					
Step 1	.544	.539			
General Symptoms-Baseline			.729	.073	.738
Model F (1,85)= 100.25, p = .000					

Table 11. Results of Regression Analyses of the Relation of CBCL Composite Scales at Baseline Assessment with SIPS Symptom Severity at One Year Follow-Up Assessment for the Entire Sample

Dependent variable Step and Model	R^2	ΔR^2	*B*	*SE B*	β
Positive Symptoms					
Step 1	.441	.434			
Positive Symptoms-Baseline			.687	.083	.664
Model F (1,87)= 68.55, p = .000					
Negative Symptoms					
Step 1	.379	.372			
Negative Symptoms-Baseline			.646	.089	.616
Model F (1,86)= 52.46, p = .000					
Disorganization					
Step 1	.440	.433			
Disorganization-Baseline			.593	.072	.663
Step 2	.469	.457			
Disorganization-Baseline			.538	.075	.601
Internalizing Problems			.012	.005	.182
Step 3	.494	.476			
Disorganization-Baseline			.533	.073	.595
Internalizing Problems			.019	.007	.303
Externalizing Problems			-.013	.006	-.198
Model F (3,85)= 27.66, p = .000					
General Symptoms					
Step 1	.317	.309			
General Symptoms-Baseline			.594	.094	.563
Model F (1,86)= 39.90, p = .000					
Total Symptoms					
Step 1	.548	.543			
General Symptoms-Baseline			.730	.072	.740
Model F (1,85)= 102.99, p = .000					

Figure1. SIPS Prodromal Symptoms by Diagnostic Group at Baseline and Follow-Up Assessments

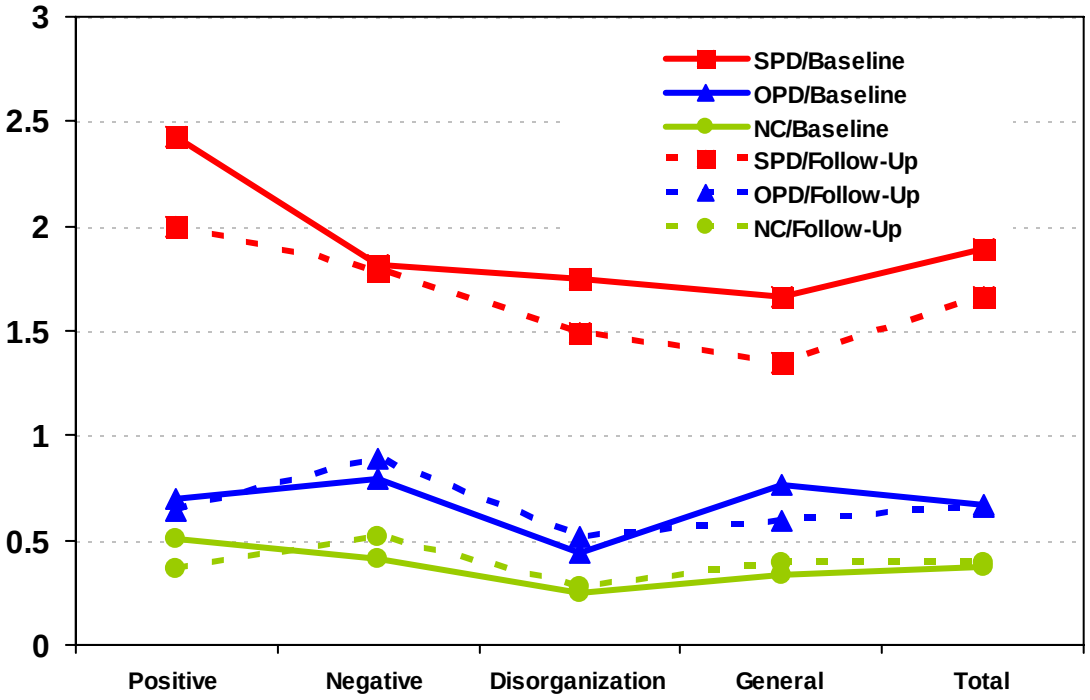

Figure 2. SIPS Prodromal Symptoms by Outcome Group at Baseline and Follow-Up Assessments

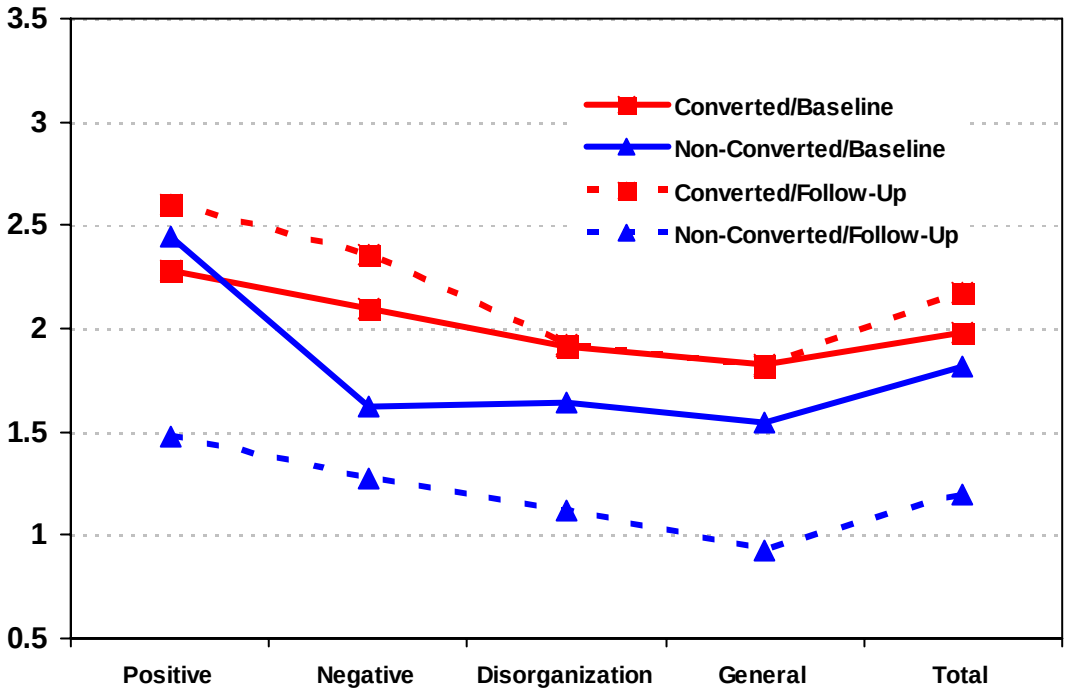

Figure 3. CBCL Composite Scores by Diagnostic Group at Baseline and Follow-Up Assessments

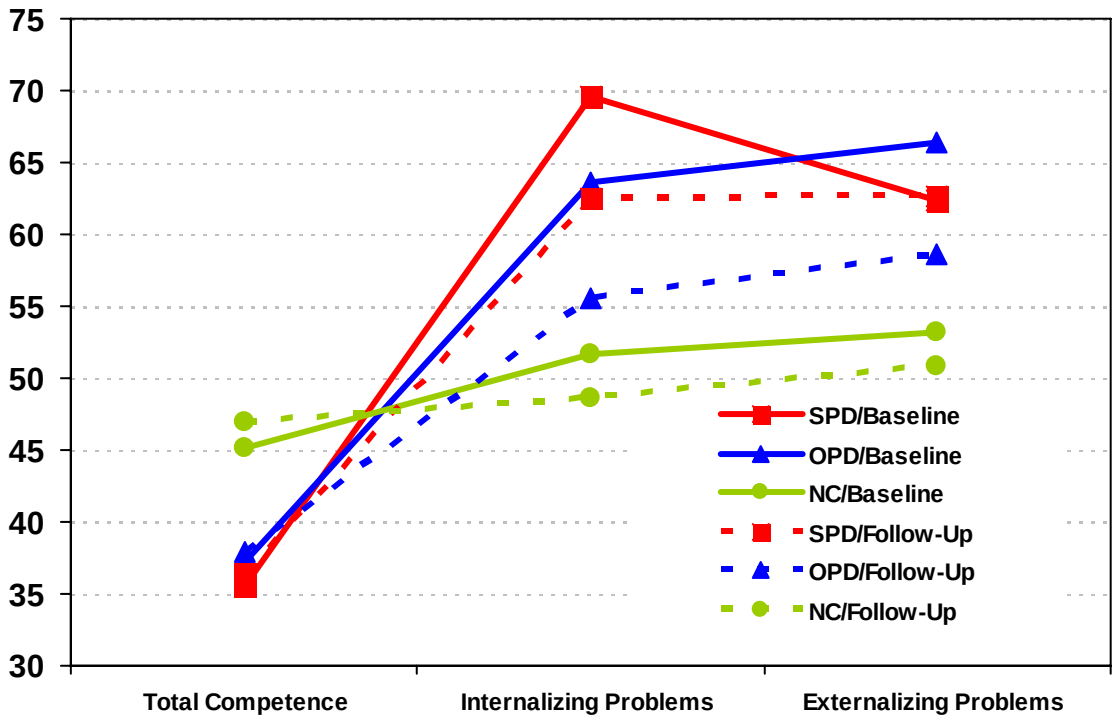

Figure 4. Behavioral Ratings for the CBCL Scale Anxious/Depressed by Diagnostic Group Over Time

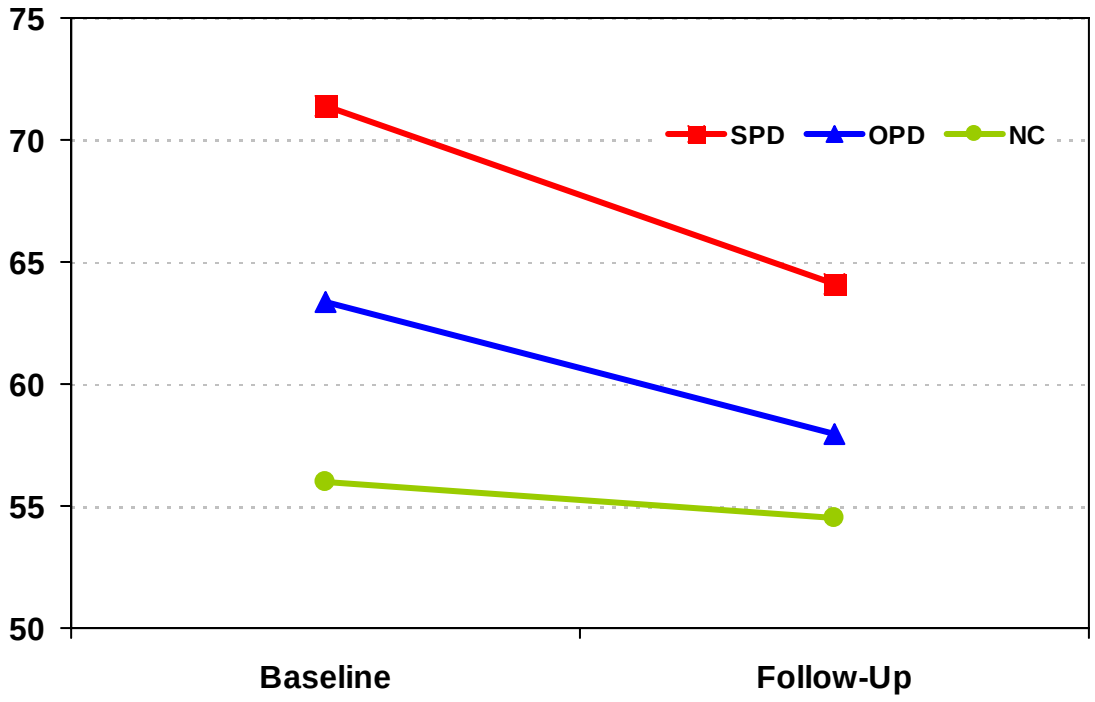

Figure 5. Behavioral Ratings for the CBCL Scale Social Problems by Diagnostic Group Over Time

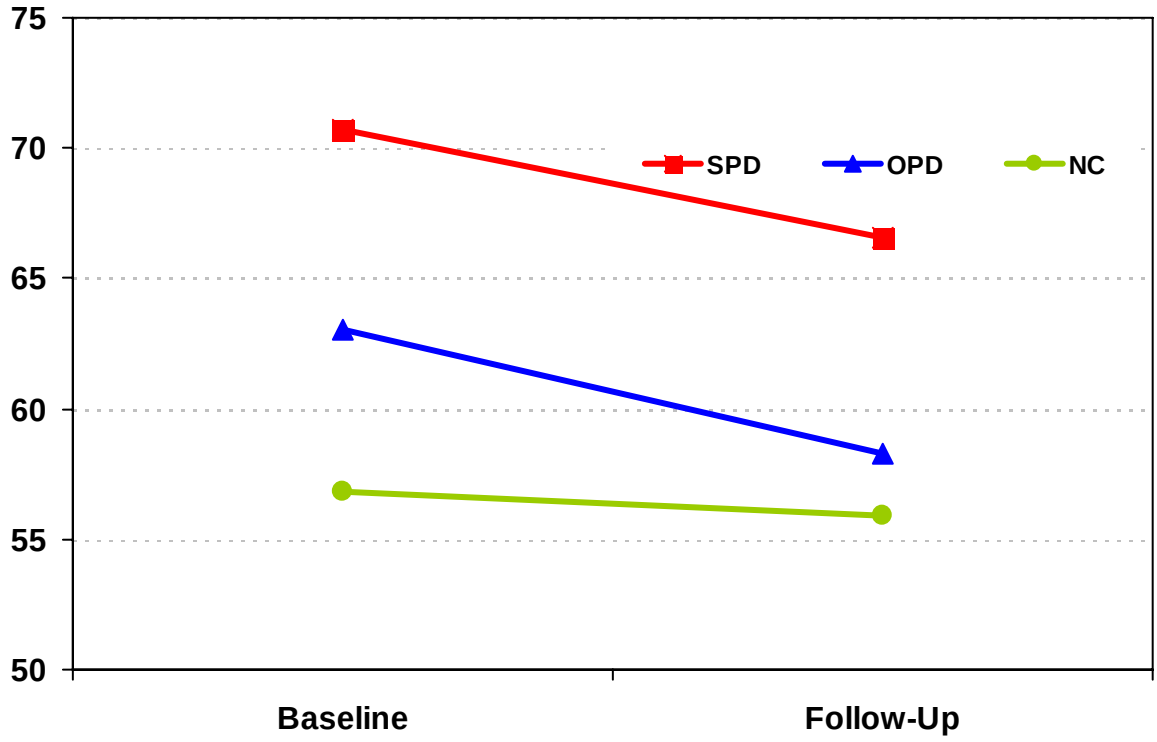

Figure 6. Behavioral Ratings for the CBCL Scale Thought Problems by Diagnostic Group Over Time

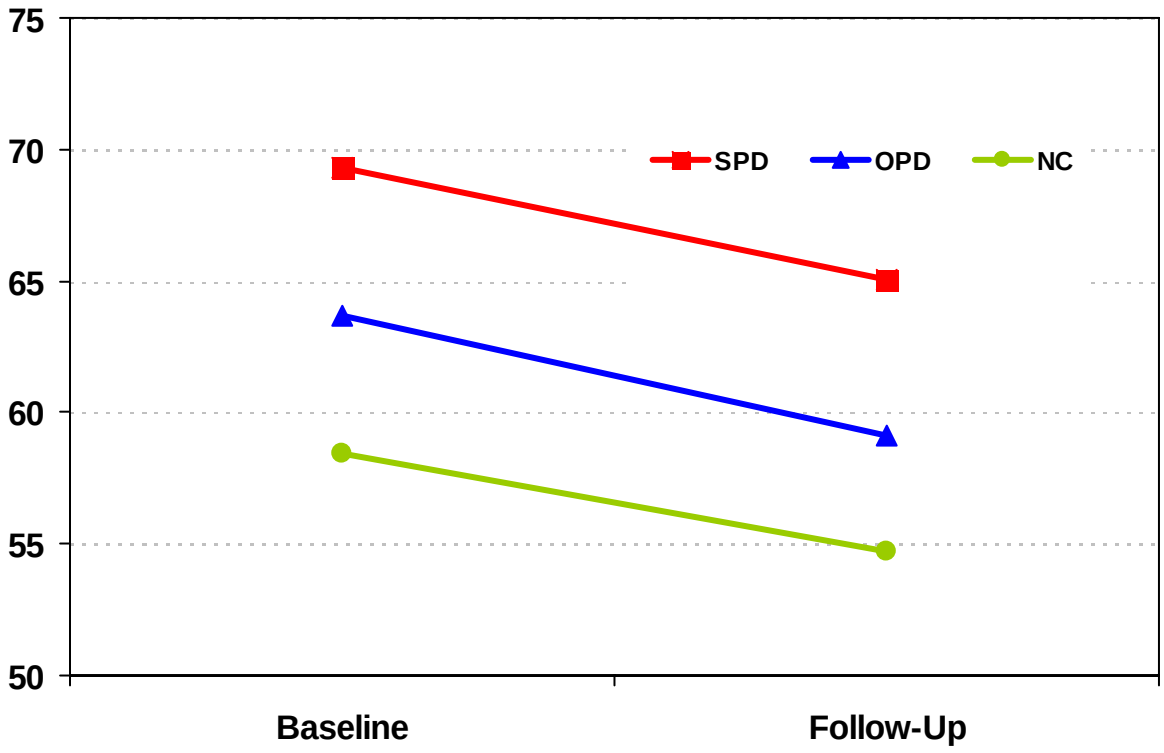

Figure 7. Behavioral Ratings for the CBCL Scale Attention Problems by Diagnostic Group Over Time

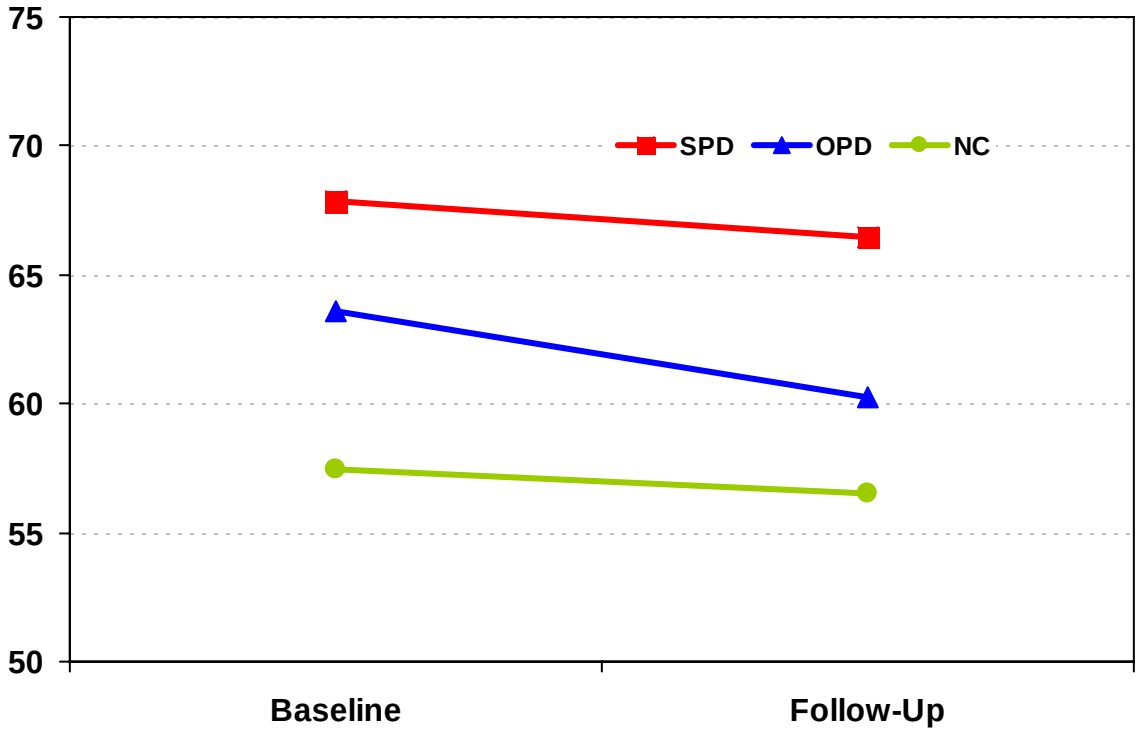

Figure 8. CBCL Composite Scores by Outcome Group at Baseline and Follow-Up Assessments

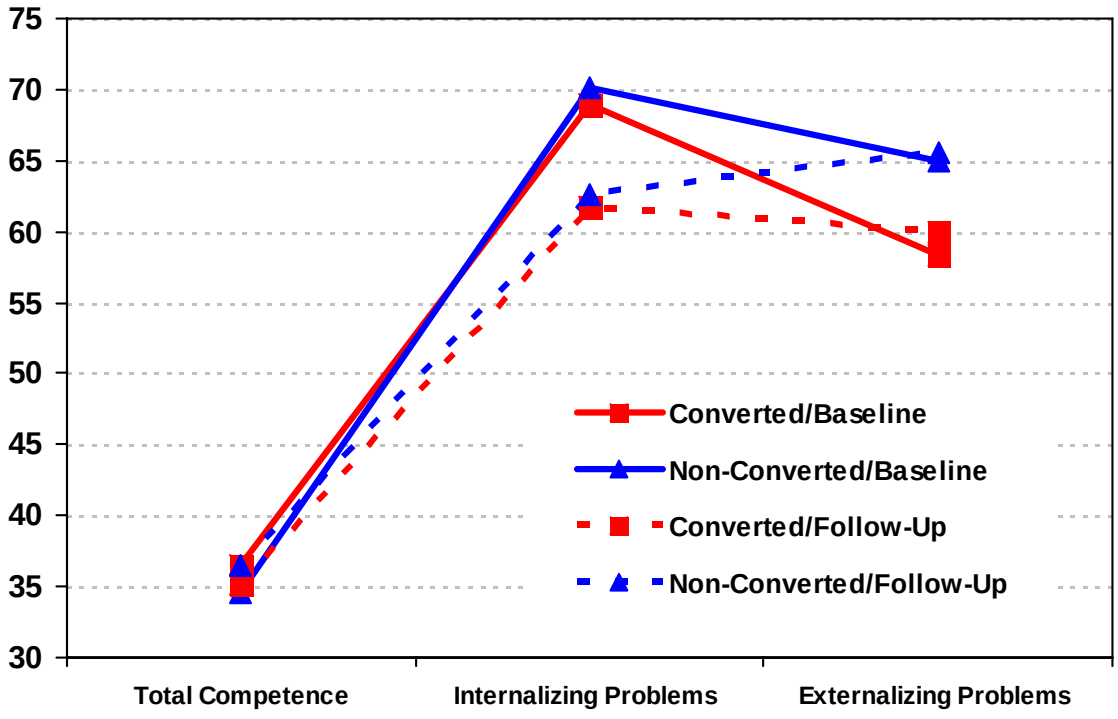

Figure 9. Conversion Status X Sex Interaction for the CBCL Scale Thought Problems

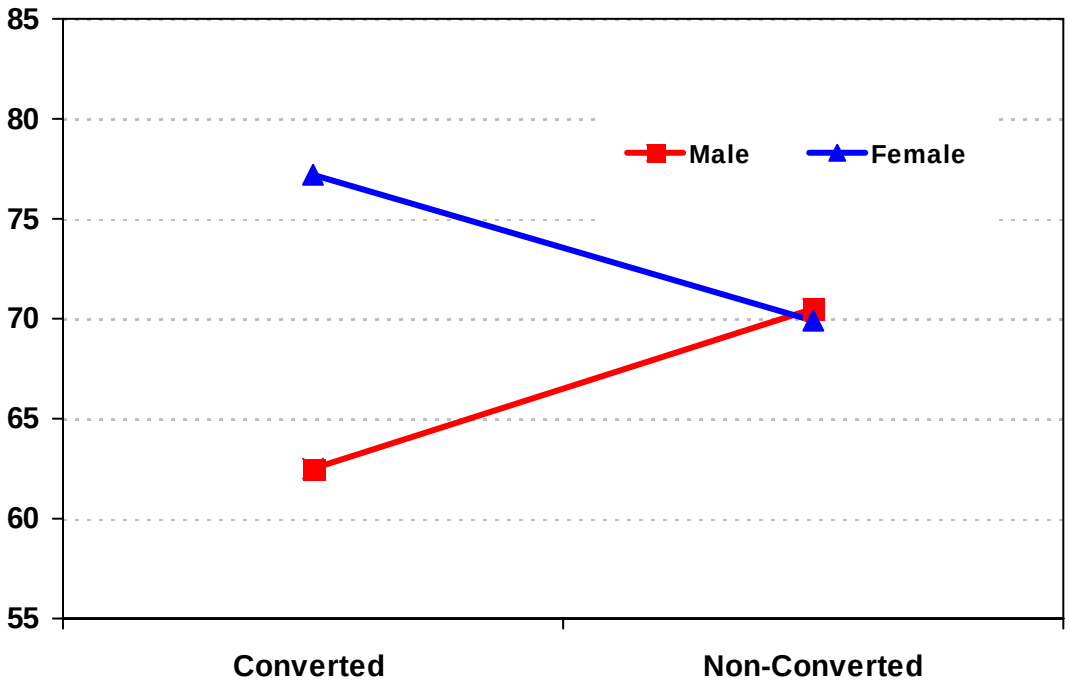

Figure 10. Conversion Status X Sex Interaction for the CBCL Scale Delinquent Behavior

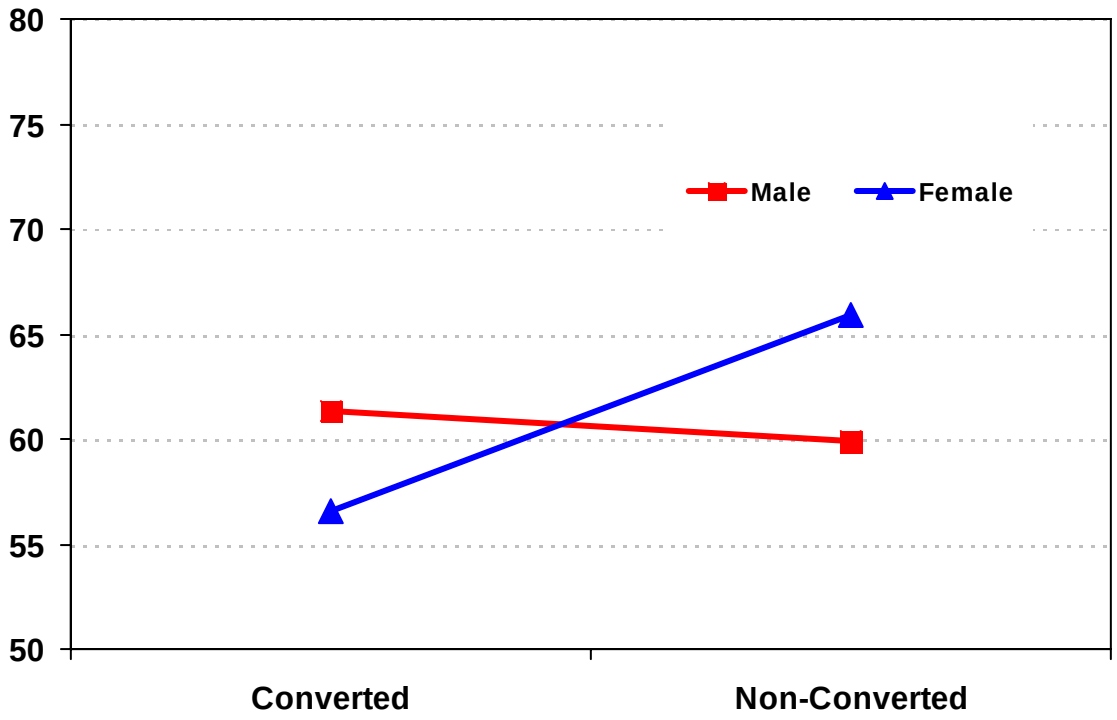

Figure 11. Diagnostic Status X Family History Interaction for the CBCL Scale Anxious/Depressed

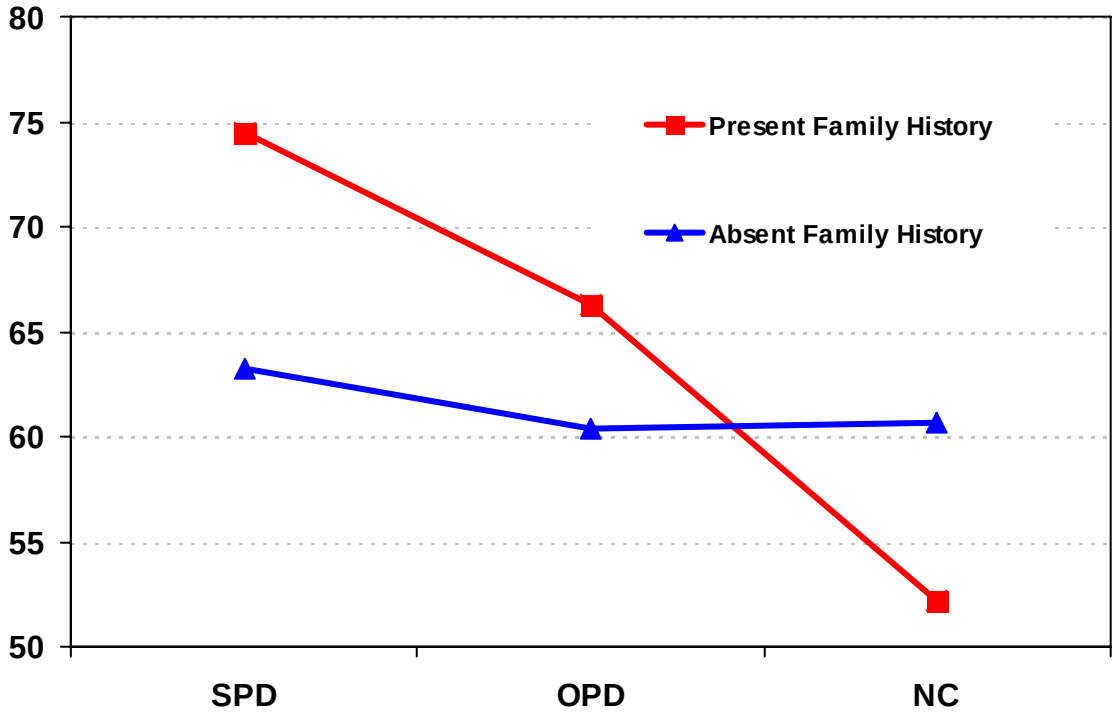

Figure 12. Diagnostic Status X Family History Interaction for the CBCL Scale Social Problems

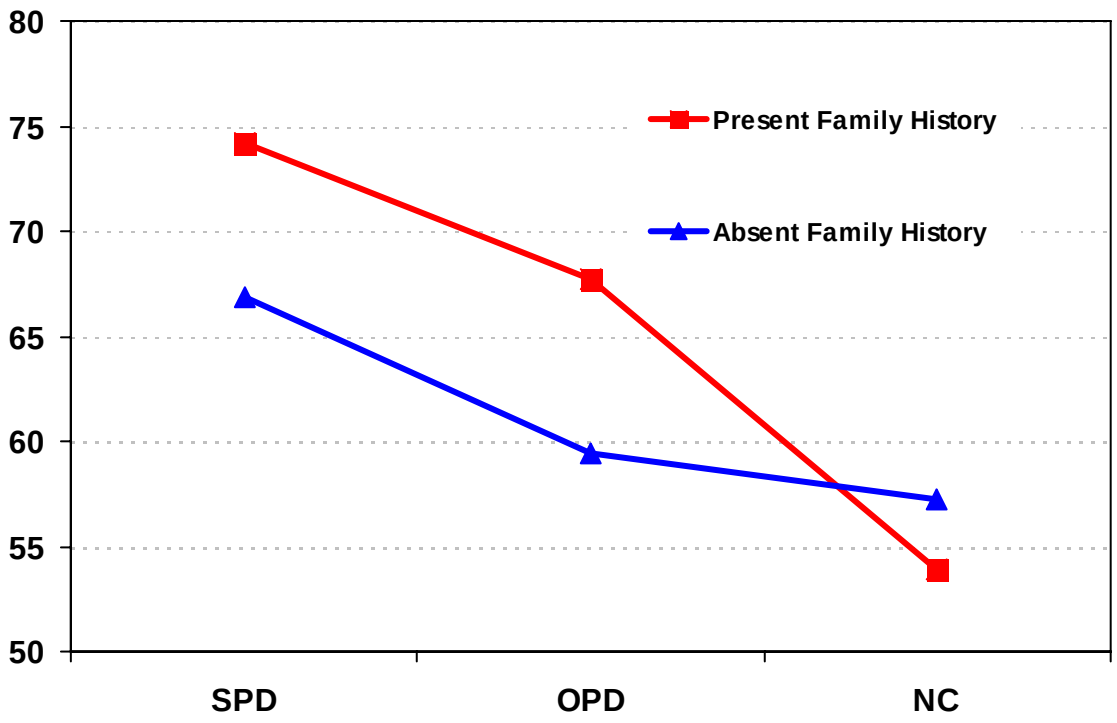

Figure 13. Diagnostic Status X Family History Interaction for the CBCL Scale Thought Problems

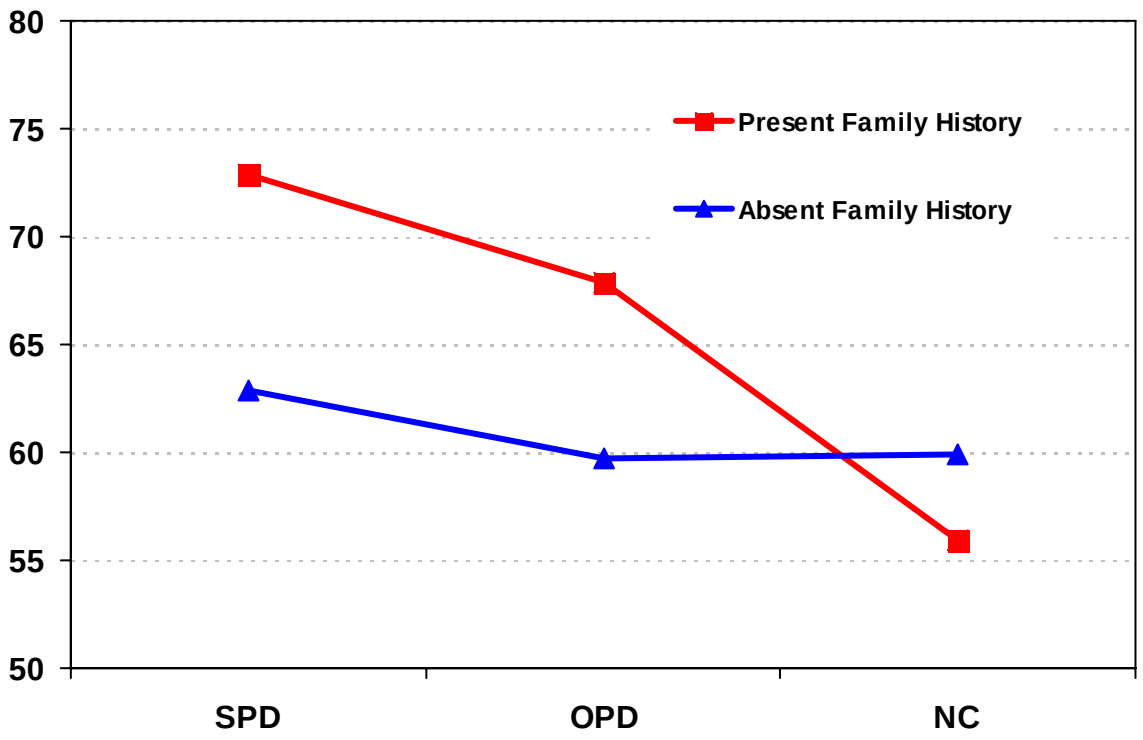

Figure 14. Diagnostic Status X Family History Interaction for the CBCL Scale Attention Problems

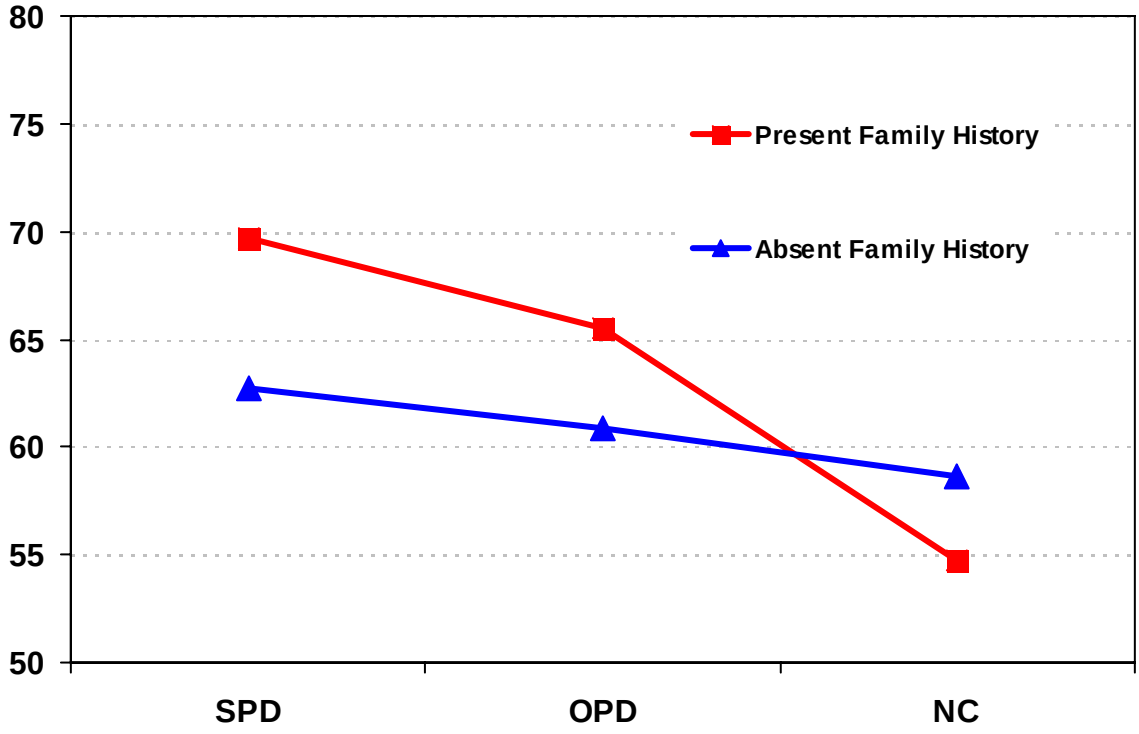

Figure 15. Diagnostic Status X Family History Interaction for the CBCL Scale Aggressive Behavior