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Functional development in clinical high risk youth: Prediction of schizophrenia versus other psychotic disorders

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ABSTRACT

This study evaluates premorbid social and academic functioning in clinical high-risk individuals as predictors of transition to schizophrenia versus another psychotic disorder. Participants were 54 individuals enrolled in phase one of the North American Prodrome Longitudinal Study who over two and a half years of follow-up met criteria for schizophrenia/schizophreniform disorder ($n=28$) or another psychotic disorder ($n=26$). Social and academic functioning in childhood, early adolescence, and late adolescence was assessed at baseline using the Cannon-Spoor Premorbid Adjustment Scale. Social maladjustment in late adolescence predicted significantly higher odds of transition to schizophrenia versus another psychotic disorder independent of childhood and early adolescent adjustment ($OR=4.02$) and conveyed unique risk over academic maladjustment ($OR=5.64$). Premorbid academic maladjustment was not associated with psychotic disorder diagnosis. Results support diagnostic specificity of premorbid social dysfunction to schizophrenia in clinical high-risk youth and underscore an important role for social maladjustment in the developmental pathology of schizophrenia and its prediction.

1. Introduction

Of all psychotic disorders, individuals with schizophrenia experience exceptionally severe and disabling symptoms, limited benefit from available treatments, and restricted independence of living (Bora et al., 2009). If meaningful differences between schizophrenia and other psychoses can be detected prior to the onset of psychosis, this information could aid in earlier identification and treatment of individuals at risk for a particularly severe course of illness (i.e., schizophrenia).

Poor premorbid social functioning is a core feature of schizophrenia (Kraepelin, 1919) and may be promising as an early risk marker for schizophrenia psychosis. Many schizophrenia patients experience a substantial decline in social functioning before their first psychotic episode, including withdrawal from family and peers, suspiciousness, and difficulty communicating (Haas and Sweeney, 1992; MacBeth and Gumley, 2008). The level of social functioning attained prior to psychosis onset is also an important correlate of individual variation in illness characteristics, course, and outcome in schizophrenia (Bromet et al., 1974). For example, deteriorating or chronically poor functioning prior to the onset of schizophrenia psychosis is strongly associated with earlier age

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of psychosis onset, greater severity and treatment refraction of negative symptoms, greater cognitive deficits, and poorer quality of life (Haas and Sweeney, 1992; Bailer et al., 1996; Larsen et al., 1996; Levitt et al., 1996; Addington et al., 2003; Silverstein et al., 2003; Strous et al., 2004; Addington and Addington, 2005; Haim et al., 2006). In addition, premorbid social dysfunction in schizophrenia is typically much more severe and pervasive than functional deficits observed in patients with psychotic mood disorders, patients with non-psychotic psychiatric disorders, non-psychotic siblings of schizophrenia patients, and controls (Strauss and Carpenter, 1972; Cannon et al., 1997; Mueser and Bellack, 1998; Willinger et al., 2001; McClellan et al., 2003; Uzelac et al., 2006). Recent evidence also supports greater premorbid functional deficits in schizophrenia patients compared to patients with schizoaffective disorder, at least in late adolescence (Uzelac et al., 2006; Saracco-Alvarez et al., 2009; Tarbox et al., 2012). This suggests possible diagnostic specificity to schizophrenia even among psychotic disorders, including those in the "schizophrenia-spectrum".

Given the strong connection between premorbid social functioning and schizophrenia pathology, prospective identification of social dysfunction in childhood or adolescence could be informative for prediction of schizophrenia. Early social dysfunction as a marker of liability to schizophrenia is supported by prospective data from birth cohort (Done et al., 1994; Jones et al., 1994; Davidson et al., 1999; Bearden et al., 2000; Rabinowicz et al., 2000; Cannon et al., 2002; Reichenberg et al., 2002), familial high-risk (Hans and Marcus, 1987; Olin et al., 1998; Amminger et al., 1999; Carter et al., 2002; Schiffman et al., 2004; Johnstone et al., 2005; Niemi et al., 2005), psychometric high-risk (Kwapil, 1998), and case-control follow-back (Watt, 1978; Cannon et al., 2001) samples. Association between social dysfunction and future psychosis is also gaining support from prospective research with clinically identified high-risk youth [i.e., presenting with sub-threshold "psychotic-like" positive symptoms indicative of elevated risk for developing a psychotic disorder (Miller et al., 2003; Woods et al., 2009; McGlashan et al., 2010)]. These individuals, typically referred to as "Clinical High-Risk" (CHR) or "Ultra High-Risk" (UHR) in the literature, endorse significantly greater difficulties in social and role functioning at baseline compared to same age non-high-risk controls (Lencz et al., 2004; Cornblatt et al., 2007; Pinkham et al., 2007; Addington et al., 2008; Woods et al., 2009; Corcoran et al., 2011). Furthermore, poor functioning and persistent negative symptoms are among the few predictor variables to make a significant, independent contribution to prediction of psychosis in CHR youth (Yung et al., 2003, 2004; Mason et al., 2004; Dragt et al., 2011; Piskulic et al., 2012), over and above other indicators of risk including positive psychotic-like symptoms (Cannon et al., 2008; Velthorst et al., 2009; Ruhrmann et al., 2010; Thompson et al., 2011; Cornblatt et al., 2012).

In this area of research, baseline functioning of CHR youth has been a primary focus to date. In contrast, only a few studies have examined developmental course of functioning prior to enrollment in a CHR study. Reports from the Dutch Prediction of Psychosis Study (DUPS) (Carr et al., 2000) suggest a possible correlation between deterioration of functioning from childhood to early adolescence and subsequent transition to psychosis in high-risk youth (Mason et al., 2004; Dragt et al., 2011). A pattern of early functional deterioration among CHR individuals is also consistent with results from phase one of the North American Prodrome Longitudinal Study (NAPLS-1) (Addington et al., 2008; Woods et al., 2009), including recent evidence that poor social adjustment in adolescence predicts transition to psychosis in NAPLS-1 CHR youth (Tarbox et al., 2013).

The current study follows from and extends this recent investigation by Tarbox and colleagues. Briefly Tarbox et al. (2013) examined social and academic maladjustment in childhood, early adolescence, and late adolescence (Cannon-Spoor Premorbid Adjustment Scale ratings) in 270 CHR subjects in the NAPLS-1 dataset who (a) were diagnosed with psychosis-risk syndrome at baseline, (b) had at least partial Premorbid Adjustment Scale (PAS) (Cannon-Spoor et al., 1982) data available for childhood, early adolescence, and/or late adolescence, and (c) were followed (in NAPLS-1) for a minimum of 6 months. For analysis, this sample was divided into two outcome groups based on follow-along assessment up to two and a half years: (1) individuals who developed any psychotic illness during the 2.5 year follow-along period ($n=78$) and (2) individuals who did not develop psychosis ($n=192$). Results indicated that early adolescent social maladjustment was a significant predictor of psychosis ($HR=1.30$, $P=0.014$) over and above childhood social dysfunction and independent of baseline severity of most positive and negative psychosis-risk symptoms. Early adolescent social maladjustment also demonstrated moderate positive predictive power (46.0%) and high specificity (72.1%) in predicting psychosis. In contrast, deterioration of academic functioning was observed in CHR youth, but did not predict transition to psychosis.

These findings are consistent with the substantial evidence that poor premorbid social functioning is an important antecedent of schizophrenia. Yet, given the diagnostic heterogeneity of the psychosis outcome group, the previous study could not directly address specificity of premorbid social dysfunction to schizophrenia; in fact, to our knowledge diagnostic specificity of premorbid dysfunction has not been tested in any CHR sample. Thus, it is unknown if premorbid social dysfunction in CHR youth predicts transition to schizophrenia in particular, or predicts psychosis onset more broadly.

The current study therefore focuses solely on CHR youth who developed a psychotic disorder with the primary goal of determining if social maladjustment in childhood, early adolescence, and/or late adolescence predicts outcome diagnosis of schizophrenia versus a non-schizophrenia psychotic disorder. Prediction of outcome diagnosis is also examined for premorbid academic functioning. The current study tests the following hypotheses: (1) premorbid social dysfunction in CHR youth predicts greater odds of transition to schizophrenia compared to odds of another psychotic disorder, (2) premorbid academic dysfunction does not predict outcome diagnosis of schizophrenia versus another psychotic disorder, and (3) premorbid social dysfunction predicts transition to schizophrenia versus other psychotic disorders over and above the effects of academic dysfunction.

2. Method

2.1. Participants

The current study utilized data from phase one of the North American Prodrome Longitudinal Study (NAPLS-1), a collaboration of eight independently conceived, NIMH-funded projects focused on prospectively examining psychosis-risk factors and improving prediction. These projects were granted supplements to create a federated database, and each site obtained IRB approval to contribute anonymous data. The construction of the database has been described previously (Addington et al., 2007).

The NAPLS-1 database consists of data for 860 non-psychotic individuals enrolled across the eight sites between 1998 and 2005. Of this sample, 377 individuals met Criteria for Prodromal Syndromes outlined in the Structured Interview for Psychosis-risk Syndromes (SIPS). A diagnosis of psychosis-risk (prodromal) syndrome requires that one or more of the following criteria are met: (1) new onset or recent worsening of sub-threshold ("Attenuated") Positive psychotic Symptoms (APS), (2) very brief periods of fully psychotic positive symptoms (BIPS), or (3) deterioration in functioning within the last year and having either schizotypal personality disorder or a first degree relative with psychosis (GRD) (Miller et al., 2002, 2003; Hawkins et al., 2004; Lencz et al., 2004; Lemos et al., 2006; McGlashan et al., 2010). The database was closed to follow-up data after September 30, 2006.