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Trajectories of premorbid childhood and adolescent functioning in schizophrenia-spectrum psychoses: A first-episode study

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ABSTRACT

Evidence of social and behavioral problems preceding the onset of schizophrenia-spectrum psychoses is consistent with a neurodevelopmental model of these disorders. Here we predict that individuals with a first episode of schizophrenia-spectrum psychoses will evidence one of three patterns of premorbid adjustment: an early deficit, a deteriorating pattern, or adequate or good social adjustment. Participants were 164 (38% female; 31% black) individuals ages 15–50 with a first episode of schizophrenia-spectrum psychoses. Premorbid adjustment was assessed using the Cannon-Spoor Premorbid Adjustment Scale. We compared the fit of a series of growth mixture models to examine premorbid adjustment trajectories, and found the following 3-class model provided the best fit with: a “stable-poor” adjustment class (54%), a “stable-good” adjustment class (39%), and a “deteriorating” adjustment class (7%). Relative to the “stable-good” class, the “stable-poor” class experienced worse negative symptoms at 1-year follow-up, particularly in the social amotivation domain. This represents the first known growth mixture modeling study to examine premorbid functioning patterns in first-episode schizophrenia-spectrum psychoses. Given that the stable-poor adjustment pattern was most prevalent, detection of social and academic maladjustment as early as childhood may help identify people at increased risk for schizophrenia-spectrum psychoses, potentially increasing feasibility of early interventions.

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1. Introduction

Social, cognitive, and behavioral functioning problems are common among individuals with schizophrenia-spectrum psychotic disorders, during the premorbid phase, after the onset of the prodrome, and comorbid with subsequent clinical symptoms. Premorbid dysfunction in childhood and adolescence could contribute to later impairment during illness by derailing learning necessary for social, educational, and occupational skills (Meehl, 1989). Early detection of deficits may improve public health by identifying people at heightened risk for schizophrenia-spectrum psychoses, thereby increasing the feasibility of preventative early interventions and minimizing symptom severity in vulnerable individuals. However, because schizophrenia-spectrum psychotic

disorders may represent a heterogeneous set of disorders with multiple etiologies and/or pathologies, early identification has proven complex.

Based on a model proposed and presented by the senior author (Haas and Sweeney, 1992), we postulate that poor premorbid functioning may reflect disruption during critical phases of central nervous system development believed to contribute to schizophrenia-spectrum psychoses. For example, neurodevelopmental disruptions during the perinatal and early childhood phases (a “first hit”) may include reduced synaptic plasticity, hippocampal dysgenesis and/or disruption of white matter integrity (Niendam et al., 2009); disruptions during the pubertal phase (a “second hit”) may involve aberrant synaptic pruning, gray and white matter volume reductions, and functional dysconnectivity (Spear, 2000; Mechelli et al., 2011). Thus, disrupted premorbid social maturation and functioning – starting either in the childhood phase or in the adolescent phase, i.e., after the onset of puberty – may indicate abnormal neurodevelopmental processes. Differential patterns of premorbid adjustment and deviations along the course of premorbid development may represent not only the impact of biological changes, but also of social factors. For

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example, a person with a trajectory of early social maladjustment may have reduced opportunities for learning social skills, which could reinforce poor social functioning at later developmental stages. Examining different trajectories of premorbid functioning may have implications for the clinical staging model of psychosis (e.g., McGorry, 2007), a model which highlights the need to distinguish different developmental stages of psychosis with the goals of 1) identifying where an individual exists on that continuum and 2) providing tailored interventions to address functional and clinical impairments at a given stage.

A number of published studies have found associations between poor and/or deteriorating premorbid functioning and clinical and functional outcomes in patients with schizophrenia-spectrum psychoses, including worse social functioning, longer duration of untreated psychosis (DUP), increased negative symptoms, greater cognitive impairment, and poorer quality of life (e.g., Haas and Sweeney, 1992; Larsen et al., 1996; Addington et al., 2003; Strous et al., 2004; Haim et al., 2006). Despite converging research suggesting that a subset of people with schizophrenia-spectrum psychoses have especially poor premorbid functioning, findings are less clear in regards to the number and types of premorbid trajectory patterns across developmental periods, with some studies proposing two patterns (poor or intact functioning across development; Farmer et al., 1983; Sham et al., 1996; Corcoran et al., 2003), and other studies finding three (Haas and Sweeney, 1992) or four (Dickey et al., 1998; Addington et al., 2003) patterns.

In our own previous study (Haas and Sweeney, 1992) we found that total scores on the Premorbid Adjustment Scale (PAS; Cannon-Spoor et al., 1982) differentiated 3 subtypes of patients with first-episode schizophrenia—one with consistent mild-moderate dysfunction, one with stable-poor dysfunction, one with an initially intact premorbid functioning that deteriorated progressively—which capture the variation in onset of poor functioning predicted by a first and second “hit” to neurodevelopmental processes. A recent study by Cole et al. (2012) replicated these three patterns, examining premorbid adjustment of patients with schizophrenia using latent class growth models, however, in that study an initially poor functioning group in childhood decompensated further across development (i.e., “a poor-worsening” group rather than a “stable-poor” group). Thus, the literature on premorbid trajectories suggests that some people with schizophrenia exhibit functional deficits prior to puberty, others after, while others do not exhibit notable behavior changes prior to the onset of the prodrome. Such variance in premorbid patterns of dysfunction is possibly due to heterogeneous neurodevelopmental disruptions in developmentally divergent groups of affected individuals.

Furthermore, several studies – all using the PAS – distinguish between the domains of academic and social premorbid functioning, and find a number of differences between the domains in terms of both their developmental trajectories and associations with clinical and cognitive variables (e.g., Mukherjee et al., 1991; van Kammen et al., 1994; Cannon et al., 1997; Allen et al., 2001; Larsen et al., 2004). In terms of clinical correlates, poor premorbid social functioning has been specifically associated with symptom-related variables, particularly acute and persistent negative symptoms, and longer duration of untreated psychosis (Allen et al., 2001; McClellan et al., 2003; Larsen et al., 2004; Jeppesen et al., 2008; Ruiz-Veguilla et al., 2008; Strauss et al., 2012; Chang et al., 2013), whereas poor premorbid academic functioning has been specifically associated with greater neurocognitive and intellectual impairment, and earlier onset of prodromal symptoms (Allen et al., 2001; Larsen et al., 2004; Norman et al., 2005; Rund et al., 2007). In terms of differential trajectories of academic and social premorbid functioning across development, there is some evidence that premorbid academic functioning deteriorates more steeply from childhood across adolescence, compared to a more stable course of social premorbid adjustment (Monte et al., 2008; Barajas et al., 2013).

Investigations of premorbid adjustment trajectories show promise for detecting meaningful patterns of dysfunction prior to the onset of illness; however, prior studies have some limitations. Relatively few studies have examined these questions in first-episode samples, leaving questions about the potential risks of recall bias, inconsistency of illness phase across participants, and introduction of confounds known to influence psychotic symptomatology such as antipsychotic medications. Only one published investigation used state-of-the-art empirical modeling techniques, which are able to examine *a priori* hypotheses in conjunction with plausible competing models (Cole et al., 2012); however, that study did not examine first-episode samples.

The current investigation sought to extend previous findings by examining trajectories of premorbid functioning in a sample of people seeking treatment for a first episode of a schizophrenia-spectrum disorder. Specifically, we: 1) used growth mixture modeling (GMM) to evaluate competing models of trajectories of premorbid functioning across childhood, early adolescence, and late adolescence in order to better identify and distinguish patterns of premorbid functioning, 2) assessed the clinical and demographic correlates of premorbid patterns at baseline, including their relationship to separate academic and social premorbid adjustment domains, and 3) for the sample for which we had conducted follow-up assessments, assessed the relationship of premorbid patterns to clinical outcomes at a 1-year follow-up. It was hypothesized that a 3-class model would provide the best fit for the data, comprised of stable-good, deteriorating, and stable-poor classes.

2. Methods

2.1. Participants

Participants included 164 first-episode schizophrenia-spectrum psychosis patients who were recruited from inpatient units, outpatient evaluation services, or the emergency room of two separate clinical treatment services: the Payne Whitney Clinic (PWC) of the New York/Cornell University Medical Center (New York City; $n=52$) and the Western Psychiatric Institute and Clinic (WPIC) of the University of Pittsburgh Medical Center (Pittsburgh; $n=112$). Participants were recruited at these two sites consecutively by the senior author (Haas) as part of a National Institute of Mental Health- (NIMH)-funded investigation of first-episode psychosis and, subsequently, as part of an NIMH-funded Conte Center Study of First Episode Psychosis. Protocols were consistent across the two sites, with the exception that follow-up data was collected only at WPIC, where support for multiple follow-up assessments was available. Of the 112 participants at WPIC, approximately half ($n=61$) had available 1-year follow-up data. Participants were included if they met the following inclusion/exclusion criteria: presence of a DSM-IV diagnosis of schizophrenia, schizoaffective disorder (bipolar or depressed type), psychotic disorder NOS, or schizophreniform disorder; no prior hospitalization for a psychotic episode; no prior full criteria for psychotic disorder met (by interview and medical chart review); English as the primary language; $IQ \geq 75$ (assessed using the Ammons Quick Test; Ammons and Ammons, 1962); no medical condition that could produce psychiatric symptoms or neurocognitive deficits (e.g., Alzheimer's disorder); no current or recent (within the last 6 months) substance abuse; and no history of head trauma. The age range of participants was 15–50. Data were collected from 1987 to 2011. For the WPIC sample, 16 participants were not included because they did not meet diagnostic criteria, and 9 were excluded because of incomplete PAS data. For the Cornell sample, 10 participants were excluded because they did not meet diagnostic criteria.

Regarding diagnostic group selection, we wanted to focus on individuals who qualified for diagnoses of schizophrenia-spectrum psychotic disorders. Given that the natural course, treatment response and psychosocial features of delusional disorders and brief psychotic episodes are distinctively different from the schizophrenia-spectrum disorder, we elected to exclude these cases from this study. The few cases that fell into psychotic disorders NOS were cases that had been judged by expert diagnostic consensus review to be sufficiently similar to schizophrenia (and unlike other psychotic disorders) to make it difficult to rule out the DSM diagnosis of schizophrenia and therefore, they fell into the psychotic disorders NOS and were included.

Selection also required availability of Premorbid Adjustment Scale data (PAS; Cannon-Spoor et al., 1982) which were not collected for a series of WPIC participants during a period of reduced funding for collection of PAS data (July 1998 through June 2003). Participants provided written informed consent

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