Schizophrenia Research 169 (2015) 209–213

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Patterns of premorbid functioning in individuals at clinical high risk of psychosis

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ARTICLE INFO

Article history:
Received 14 August 2015
Received in revised form 2 November 2015
Accepted 3 November 2015
Available online 14 November 2015

Keywords:
Clinical high risk
Conversion
Premorbid functioning
Schizophrenia
Social functioning
Symptoms

ABSTRACT

In schizophrenia, four typical patterns of premorbid functioning have been observed: stable-good, stable-intermediate, poor-deteriorating and deteriorating. However, it is unknown whether similar patterns exist in those who are at clinical high risk (CHR) of psychosis. The aim of this study was to examine patterns of premorbid functioning in a large sample of individuals at CHR of psychosis and its association with symptoms, functioning, and conversion to psychosis. One-hundred sixty people at CHR of psychosis were assessed on premorbid functioning using the Premorbid Adjustment Scale. Poorer premorbid functioning was significantly correlated with worse negative symptom severity and lower social functioning. Cluster analysis was used to identify patterns of premorbid functioning. Results indicated three patterns of premorbid functioning in our CHR sample: stable-intermediate, stable-good, and deteriorating. The deteriorating group had more severe disorganization, worse negative symptoms, and poorer social functioning than the other groups. Participants who made the conversion to psychosis had significantly poorer premorbid functioning during adolescence compared to those who did not convert. These results suggest that those at a clinical high risk for psychosis display similar patterns in premorbid functioning as have been observed in those with a psychotic illness and that poor premorbid functioning may be a predictor of psychosis.

1. Introduction

It has been well-documented in many studies over the past fifty years that poor premorbid functioning in people with schizophrenia is associated with an earlier age at psychosis onset, increased negative symptom severity, neurocognitive deficits, and poor clinical outcome and psychosocial functioning (Silverstein et al., 2003; Addington and Addington, 2005; Haim et al., 2006). Furthermore, males with schizophrenia tend to show poorer premorbid functioning relative to female patients (Bailer et al., 1996). In studies of individuals experiencing a first episode of psychosis, premorbid functioning has been examined by using cluster analysis (Addington et al., 2003). This method identified specific courses of premorbid functioning across four developmental stages, namely childhood, early and late adolescence and adulthood. Typical patterns were stable-good, stable-intermediate, poor-deteriorating and deteriorating. Those with a deteriorating pattern were significantly younger at onset of psychosis, had increased levels of positive and negative symptoms and poorer quality of life than the two stable groups (Addington and Addington, 2005). This suggests that in schizophrenia different patterns of premorbid functioning developmentally may have different outcomes.

Premorbid functioning has also been examined in those at clinical high risk (CHR) of psychosis, that is, people who experience attenuated positive symptoms, brief intermittent psychotic symptoms, or have a genetic risk for the disorder and a recent decline in functioning (McGlashan et al., 2010). CHR individuals show poorer premorbid functioning compared to healthy controls (Tikka et al., 2013; Morcillo et al., 2015; Tarbox et al., 2013) and similar premorbid functioning to patients with psychosis (Addington et al., 2008). Consistent with findings in schizophrenia, males at CHR of psychosis tend to show poorer premorbid functioning than CHR females (Tarbox et al., 2013; Salokangas et al., 2014). Furthermore, poor premorbid functioning has been shown to be associated with later poorer outcome such as increased disorganization and negative symptom severity (Quijada et al., 2012) and low functional outcome (Salokangas et al., 2014).

Poor premorbid functioning has been associated with conversion to psychosis (Dragt et al., 2011) or in conjunction with reduced P300 parietal amplitude (Nieman et al., 2014). However, poor premorbid social

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http://dx.doi.org/10.1016/j.schres.2015.11.004
0920-9964/

functioning in early adolescence significantly predicted conversion to psychosis, but not poor academic and overall premorbid functioning (Tarbox et al., 2013).

The CHR studies reported above typically used overall premorbid functioning scores or mean scores at different developmental periods. However a with these at-risk young people it may be more useful to evaluate whether there are different patterns of premorbid functioning developmentally, and whether these patterns associate differentially with clinical characteristics as has been observed in schizophrenia (Haas et al., 2001; Addington et al., 2003).

The aim of this study was to examine premorbid functioning in a large sample of individuals at CHR including the association with conversion to psychosis. More specifically our hypotheses were that, first, poorer premorbid functioning would be associated with worse symptom severity and poorer social functioning. Secondly, using cluster analysis to determine specific courses of premorbid functioning across the developmental stages: childhood, early and late adolescence, we hypothesized that four groups representing distinct patterns of premorbid functioning would emerge, namely stable-good, stable-intermediate, poor-deteriorating and deteriorating. Third, we hypothesized that those with a deteriorating course or those with a poor-deteriorating course would present with worse negative symptoms and lower functioning. The fourth hypothesis was that those who made the transition to psychosis would show poorer premorbid functioning compared to those who did not.

2. Method

2.1. Participants

One-hundred and sixty (88 males, 72 females) individuals at CHR of psychosis participated as part of a multi-site NIMH funded study "Enhancing the Prospective Prediction of Psychosis" (PREDICT). This was a 4-year longitudinal observational study to determine predictors of conversion to psychosis in individuals at CHR of developing psychosis with participants having follow-ups of 6 months to 4 years. Approximately 30% were lost to follow-up by year one. The study was conducted at the Universities of Toronto, North Carolina, and Yale. All CHR individuals met the Criteria of Psychosis-risk Syndromes (COPS) based on the Structured Interview for Psychosis-risk Syndromes (SIPS). 154 CHR participants met attenuated positive symptom syndrome (APSS) criteria, which includes the emergence or worsening of a non-psychotic level disturbance in thought content, thought process or perceptual abnormality over the past year, 4 participants met criteria for genetic risk and deterioration (GRD), which required either a first degree relative with a psychotic disorder or the subject having schizotypal personality disorder plus at least a 30% drop in functioning on the General Assessment of Functioning (GAF) scale in the past 12 months, and 2 participants met both APSS and GRD.

Participants were excluded if they met criteria for any current or lifetime axis I psychotic disorder, prior history of treatment with an antipsychotic, IQ < 70, or past or current history of a clinically significant central nervous system disorder that may confound or contribute to clinical high risk symptoms, or using antipsychotics at baseline. DSM-IV diagnoses of substance dependence and abuse were exclusion criteria. Antipsychotics were not used at any later points in this study.

2.2. Measures

Criteria for a psychosis-risk syndrome and for conversion to psychosis were determined using the SIPS (McGlashan et al., 2010). Conversion meant that at least one of the five attenuated positive symptoms reached a psychotic level of intensity (rated 6) for a frequency of ≥1 h/day for 4 days/week during the past month or that attenuated psychotic symptoms that reached a psychotic level of intensity that seriously impacted functioning (e.g. severely disorganized or dangerous to self or others). Symptoms were assessed with the Scale of Prodromal Symptoms (SOPS), which consists of 19 items in four symptom domains: positive, negative, general, and disorganized.

Participants were rated on premorbid functioning with the Premorbid Adjustment Scale (PAS) (Cannon-Spoor et al., 1982). The PAS measures premorbid functioning in four areas of development: (i) sociability/withdrawal, (ii) peer relationships, (iii) ability to function outside the nuclear family and (iv) capacity to form intimate sociosexual ties, at each of four developmental stages, namely, childhood (up to age 11), early adolescence (12–15 years), late adolescence (16–18 years), and adulthood (19 and up) (van Mastrigt and Addington, 2002). Premorbid functioning was defined as the period up until the onset of the first attenuated psychotic symptom that contributed to the participant meeting COPS criteria.

Social functioning was assessed using the Social Functioning Scale (SFS), a self-report questionnaire developed for outpatients with schizophrenia and has excellent psychometric properties (Birchwood et al., 1990). The SFS has a total score and seven sub-scores: Withdrawal/social engagement, Interpersonal communication, Independence-performance, Independence-competence, Recreation, Prosocial, and Employment/occupation. Only the total score was used in this study.

2.3. Procedures

All three sites involved in this longitudinal study of predictors of conversion to psychosis recruited CHR individuals. Raters were experienced research clinicians who demonstrated adequate reliability at routine reliability checks. Gold standard post-training agreement on the critical threshold for determining initial eligibility and subsequent conversion status based on the SIPS was excellent (kappa = .90). The PI or clinical psychiatrist or psychologist at each site conducted a comprehensive clinical assessment to determine if entry criteria were met. Dr. Jean Addington chaired weekly conference calls to review criteria for all individuals admitted to the study. The study protocols and informed consents were reviewed and approved by the ethical review boards of all three study sites. All ratings were acquired at the baseline assessment.

2.4. Statistical analysis

Due to the young age of the sample and the fact that only a small proportion completed the adult subscale for the cluster analysis, we only used three developmental stages, childhood, early adolescence and late adolescence in all of our statistical analyses.

T-tests were used to compare CHR males and females on premorbid functioning variables and those who converted and those who did not on premorbid functioning. Spearman's correlations were used to measures associations between premorbid functioning and symptoms and social functioning. Cluster analysis was used to identify distinct patterns of premorbid functioning. *K*-means cluster analysis was used to assign

Table 1
Premorbid functioning, social functioning, and symptom scores.

	Mean (SD)	Range
Social Functioning Scale	125.8 (20.9)	45.0–175.0
Premorbid functioning		
Childhood	0.19 (0.17)	0.0–1.0
Early adolescence[a]	0.26 (0.18)	0.0–0.8
Late adolescence[b]	0.28 (0.19)	0.0–1.0
SOPS subscales		
Positive	11.0 (3.2)	4.0–22.0
Negative	8.7 (5.8)	0.0–22.0
Disorganization	4.1 (2.8)	0.0–13.0
General	7.1 (3.9)	0.0–18.0

[a] Only 157 participants had reached early adolescence.
[b] Only 119 participants had reached late adolescence.