Negative symptoms in individuals at clinical high risk of psychosis

Danijela Piskulic [a,*], Jean Addington [a], Kristin S. Cadenhead [b], Tyrone D. Cannon [c], Barbara A. Cornblatt [d], Robert Heinssen [e], Diana O. Perkins [f], Larry J. Seidman [g], Ming T. Tsuang [b,g], Elaine F. Walker [h], Scott W. Woods [i], Thomas H. McGlashan [i]

[a] Department of Psychiatry, University of Calgary, Calgary, Alberta, Canada
[b] Department of Psychiatry, University of California, San Diego, CA, USA
[c] Department of Psychology and Psychiatry and Biobehavioral Sciences, University of California, Los Angeles, CA, USA
[d] Department of Psychiatry, Zucker Hillside Hospital, Long Island, NY, USA
[e] Schizophrenia Spectrum Disorders Research Program, Division of Adult Translational Research, National Institute of Mental Health, Bethesda, MD, USA
[f] Department of Psychiatry, University of North Carolina, Chapel Hill, NC, USA
[g] Department of Psychiatry, Harvard Medical School, Boston, MA, USA
[h] Departments of Psychology and Psychiatry, Emory University, Atlanta, GA, USA
[i] Department of Psychiatry, Yale University, New Haven, CT, USA

ARTICLE INFO

ABSTRACT

Negative symptoms are present in the psychosis prodrome. However, the extent to which these symptoms are present prior to the onset of the first episode of psychosis remains under-researched. The goal of this study is to examine negative symptoms in a sample of individuals at clinical high risk (CHR) for psychosis and to determine if they are predictive of conversion to psychosis. Participants ($n = 138$) were all participants in the North American Prodrome Longitudinal Study (NAPLS 1) project. Negative symptoms were assessed longitudinally using the Scale of Prodromal Symptoms. The mean total negative symptom score at baseline was 11.0, with 82.0% of the sample scoring at moderate severity or above on at least one negative symptom. Over the course of 12 months, the symptoms remained in the above moderate severity range for 54.0% of participants. Associations between individual symptoms were moderate, and a factor analysis confirmed that all negative symptoms loaded heavily on one factor. Negative symptoms were more severe and persistent overtime in those who converted to psychosis, significantly predicting the likelihood of conversion. Thus, early and persistent negative symptoms may represent a vulnerability for risk of developing psychosis.

© 2012 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Recent advances in research in early detection of psychosis have led to the development of reliable criteria to identify individuals who may be at risk of developing psychosis and thus potentially experiencing a prodrome for psychosis (Yung and McGorry, 1996b; McGlashan et al., 2010). These prospective studies rely primarily on the presence of attenuated positive symptoms and decreased functioning (Yung and McGorry, 1996b; McGlashan et al., 2010). However, significant proportions of these individuals have non-specific symptoms (e.g. depression and anxiety) as well as negative symptoms, such as social isolation/withdrawal, and reduced motivation (Lencz et al., 2004). This finding pertaining to the construct of amotivation or avolition is in agreement with findings from patients with schizophrenia (Faerden et al., 2009). Interestingly, it is these behavioural and functional changes that are often the first reasons for seeking help (Yung and McGorry, 1996a; Lencz et al., 2004). Relative to attenuated positive symptoms, the prevalence of negative symptoms is high (Yung et al., 2003; Lencz et al., 2004; Velthorst et al., 2009), among of which social isolation and deterioration in role (school) functioning are most frequently reported (Lencz et al., 2004). Furthermore, negative symptoms, especially increased social isolation and withdrawal, have been reported to be predictive of transition to psychosis (Kwapil, 1998; Mason et al., 2004; Yung et al., 2005; Velthorst et al., 2009). In the Edinburgh longitudinal study of individuals at genetic high risk of psychosis (Johnstone et al., 2005), social withdrawal and isolation, as measured on the Structural Interview for Schizotypy, emerged as the strongest discriminator between those who converted and those who did not.

Typically, negative symptoms are examined as one construct, although there are reports of negative symptoms clustering into two domains of diminished expression (i.e. affective flattening and poverty of speech) and amotivation (i.e. avolition/apathy and anhedonia/asociality) (Mueser et al., 1994; Sayers et al., 1996). More recently

there has been a focus on differences among individual negative symptoms with suggestions that "avolition" is a core negative symptom with a direct impact on both functional outcome and cognitive function (Foussias and Remington, 2010).

Previous studies of the psychosis prodrome that explored the predictive value of negative symptoms to psychosis conversion have done so using different instruments to assess prodromal symptoms. Whereas some studies used scales designed to rate the severity of sub-psychotic level symptoms (Yung et al., 2005; Velthorst et al., 2009) others used conventional rating scales for psychotic-level symptoms (Mason et al., 2004) or a scale designed to assess a single symptom (Kwapil, 1998). Furthermore, none of the studies included longitudinal examination of negative symptoms. Thus, the goal of the present investigation was to examine in more detail negative symptoms in a sample of individuals described as being at clinical high risk (CHR) of developing psychosis. The specific aims were: 1) to determine the prevalence of individual negative symptoms; 2) to determine the stability of negative symptoms, 3) to explore the factor structure of positive and negative symptoms of the SOPS, and 4) to explore longitudinally the role of negative symptoms in conversion to psychosis.

2. Methods

2.1. Participants

The North American Prodrome Longitudinal Study (NAPLS-1) project is a consortium of eight research sites that investigated the earliest phase of psychotic illness, with the goal of improving the accuracy of prospective prediction of psychosis (Addington et al., 2007; Cannon et al., 2008). All sites recruited CHR individuals and followed them up for a period of up to 2.5 years during the period 2000–2006. Although initially developed as independent studies, the investigations at eight sites employed similar ascertainment and diagnostic methods (i.e. Structured Interview for Prodromal Symptoms - SIPS; McGlashan et al., 2010) making it possible to form a standardised protocol for mapping data into a new scheme representing the common components across sites (Addington et al., 2007). The study protocols and informed consents were reviewed and approved by the ethical review boards of all eight study sites. Methods and details of the NAPLS-1 are reviewed in detail elsewhere (Addington et al., 2007; Cannon et al., 2008).

Three hundred and seventy-two participants met one of the three established criteria for a psychosis risk syndrome, namely: attenuated psychotic symptom state (APSS), brief intermittent psychotic symptom state (BIPS) and genetic risk with deterioration (GRD). Criteria for a prodromal syndrome and criteria for conversion to psychosis were determined using the Structured Interview for Prodromal Syndromes (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 symptoms seriously impacting functioning (e.g. severely disorganised or dangerous to self or others) (McGlashan et al., 2010). All NAPLS sites demonstrated reliability in rating criteria (κ's ranged from 0.80 to 1.00 across sites) (Addington et al., 2007).

The Structured Clinical Interview for DSM-IV (SCID-I) (First et al., 1995) was used to determine the presence of any axis I disorders. Participants were excluded if they met criteria for any current or lifetime axis I psychotic disorder, IQ <than 70 or past or current history of a clinically significant central nervous system disorder which may confound or contribute to prodromal symptoms.

For this project we included only participants who had completed the negative symptom ratings at both 6- and 12-month follow-up. Thus, participants were 50 females and 88 males. At ascertainment, the mean age was 18.6 years (S.D.=4.88). On average participants had 10.7 years of education (S.D.=3.25) with 91 participants (66.0%) attending high school and 18 (13.0%) attending college. Twenty-six participants (19.0%) were employed full-time. Sixty-six participants (48.0%) met DSM-IV criteria for a mood disorder, 12 (9.0%) met criteria for an anxiety disorder and 5 (3.5%) met criteria for substance abuse disorders. All participants met the criteria for attenuated psychotic symptom syndrome (APSS). This sample of 138 did not differ on demographic or symptom variables from the 234 participants excluded from the analysis who did not have follow-up data on negative symptoms.

2.2. Assessments

The Structured Interview for Prodromal Syndromes (SIPS) (McGlashan et al., 2010) criteria were used at the study entry. Attenuated positive symptoms and negative symptoms were assessed using the Scale of Prodromal Symptoms (SOPS).[1]

---

[1] Descriptions of negative symptoms are available in the Supplementary Material

2.3. Statistical analyses

Demographic variables and negative symptom ratings were summarised using descriptive statistics. Difference in prevalence of negative symptoms over time was assessed using the two-proportions Z-test. Stability of negative symptoms over time was assessed using repeated measures analysis of variance ANOVA with the Bonferroni correction for multiple comparisons. Principal component analysis (PCA) was used to explore the factor structure of positive and negative symptoms of the SOPS. Participants who received a diagnosis of a psychotic disorder during the course of the study were classified as converters. Group differences between converters and non-converters, as well as gender differences, were assessed using the Mann–Whitney U test (MWU). Direct logistic regression was performed to evaluate the predictive value of negative symptoms on conversion. This method was chosen because it allows evaluation of the contribution made by each negative symptom over and above contribution of other predictors (Tabachnik and Fidel, 2001). Furthermore, it was an appropriate model given that we had no specific hypotheses about the order or importance of individual negative symptoms. All assumptions for the different analyses were met prior to interpretation of the results.

3. Results

3.1. Baseline negative symptoms

A majority of participants (82.0%) at the start of the study endorsed at least one negative symptom rated ≥3 on the SOPS (i.e. moderate to above moderate severity). Sixty-one (44.0%) participants reported at least one symptom in the moderate to above moderate range (i.e. SOPS ratings of 3 and 4), and 52 (38.0%) participants reported symptoms in the severe range (i.e. SOPS ratings of 5 and 6). Males had more severe negative symptoms ($M=13.60$, S.D.$=7.25$) compared to females ($M=8.86$, S.D.$=6.58$, $t=-3.81$, $P<0.001$). Reported prevalence for specific negative symptoms of ≥3 severity rating at baseline 6- and 12-month follow-up are displayed in Fig. 1. At baseline, "deterioration in role functioning", "avolition" and "social withdrawal" were the most frequently reported negative symptoms whereas "decreased ideational richness" was the least reported symptom.

3.2. Change over time

Repeated measures ANOVAs revealed that there was a significant decrease in severity of negative symptoms over time ($F (2, 274)= 43.72$, $P<0.001$). Table 1 displays the results of within-subjects contrasts for changes in the severity of each negative symptom over time. At 12 months, seventy-four participants (54%) continued to score in the moderate to above moderate severity (i.e. ≥3) on at least one negative symptom. Significant decrease in prevalence of
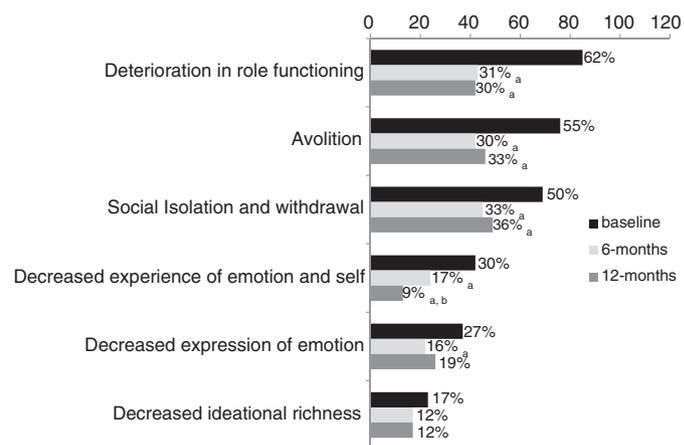
Note: a, significantly different from baseline at P<0.05 level
b, significantly different from 6-months at P<0.05 level

Fig. 1. Prevalence of reported negative symptoms rated ≥3 at baseline, 6 and 12 months.