



Symptom dimensions and functional impairment in early psychosis: More to the story than just negative symptoms

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ABSTRACT

Functional impairment is a defining feature of psychotic disorders and usually appears well before their onset. Negative symptoms play a prominent role in the impaired functioning of individuals with schizophrenia and those at clinical-high-risk (CHR) for psychosis. Despite high rates of depression and anxiety in early psychosis, few studies have examined the contribution of these symptoms to functioning in the putative 'prodrome.' In the current study, we tested the hypotheses that 1) worse negative and disorganized, but not positive, symptoms would be significantly related to impaired social and role functioning in two cohorts of CHR individuals (combined $N = 98$) and a separate sample of individuals with recent-onset (RO) psychotic disorders ($N = 88$); and 2) worse anxiety and depression would be significantly related to impaired functioning in both samples, above and beyond the contributions of negative and disorganized symptoms. Findings largely supported our hypotheses that more severe negative and disorganized symptoms were related to poorer social and role functioning in both samples. Anxiety and depression severity were significantly related to poorer functioning in both samples. In addition, depression, but not anxiety, predicted poorer global and social functioning above and beyond that explained by negative symptoms in the CHR sample. These results suggest the need for phase-specific treatment in early psychosis, with a focus on symptom dimensions to improve functional outcomes for CHR individuals.

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1. Introduction

The longer individuals with schizophrenia are left without adequate treatment, the worse their symptoms and functioning become (McGlashan and Johannessen, 1996; Keshavan et al., 2003). These findings prompted research addressing the urgent need to identify those at clinical high risk (CHR) for psychosis. Longitudinal studies of adolescents and young adults with CHR syndromes, primarily those with attenuated psychotic symptoms, show a mean transition rate to full psychosis of 29% over two years (Fusar-Poli et al., 2012). Given that the majority of CHR individuals do not convert within this time period, however, researchers have discussed the risk-to-benefit ratio associated with treatment during this phase (Haroun et al., 2006).

Recently, CHR studies have moved beyond a singular focus on psychotic transition outcomes, exploring the relationship of clinical symptoms and other risk factors to real-world functioning. Functional impairment is present in CHR individuals compared to healthy

controls (Cornblatt et al., 2007; Addington et al., 2011) and predicts later psychosis (Cannon et al., 2008; Velthorst et al., 2010; Dragt et al., 2011), but is also present to a significant degree in CHR individuals who do not go on to convert over time (Schlosser et al., 2012). Moreover, poor functioning may be relatively stable in a subset of CHR individuals regardless of changes in their positive symptoms. That is, some CHR individuals who begin follow-along studies with poor functioning continue to show poor functioning after several years, even when their positive symptoms never cross the threshold into full psychotic severity (Yung et al., 2007; Addington et al., 2011; Schlosser et al., 2012). Thus, although they do not convert to full-blown psychosis over brief follow-up periods, these 'false positives' are still in need of clinical intervention.

Numerous studies have shown that symptoms contribute significantly to impairment in individuals with schizophrenia (Norman et al., 2000; Pinikahana et al., 2002), with negative symptoms accounting for up to 18% of the variance in functioning (Ventura et al., 2009). Similar findings have been replicated in CHR individuals (Niendam et al., 2006b; Cornblatt et al., 2007; Niendam et al., 2007; Svriskis et al., 2007; Corcoran et al., 2011), and negative symptoms are a significant predictor of conversion to psychotic disorder (Piskulic et al., 2012). In addition, disorganized symptoms are related

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to impaired functioning in psychosis (Norman et al., 1999; Sakiyama et al., 2002; Takahashi et al., 2005). A recent study on a small sample of CHR individuals showed that disorganized symptoms were a significant predictor of declines in social functioning over a one-year follow-up (Eslami et al., 2011).

Depression and anxiety are also highly common in schizophrenia, with an estimated 30 to 40% of individuals meeting criteria for a major depressive episode and 11 to 15% with a diagnosed anxiety disorder (Sands and Harrow, 1999; Achim et al., 2011). Depression and anxiety often precede the disorder (Yung and McGorry, 1996; Häfner et al., 2002), and are associated with poorer functioning (Dickerson et al., 1998; Häfner et al., 1999; Braga et al., 2005; Saarni et al., 2010). High rates of comorbidity have been a recent focus of CHR research (Salokangas et al., 2012; Fusar-Poli et al., 2013). One common finding across research clinics has been the high prevalence of depression and anxiety, with rates of major depressive disorder ranging from 17 to 50% and anxiety disorders from 24 to 58% (Meyer et al., 2005; Rosen et al., 2006; Salokangas et al., 2012), and these symptoms are related to less functional recovery over time (Schlosser et al., 2012). Thus, it is possible that the functional impairment in this population may be related, at least partly, to symptoms of depression and anxiety. No studies to date, however, have examined the relationship of both depression and anxiety to functioning in the context of other symptom domains in early psychosis.

In the current study we examined the impact of various symptom domains on functioning in two cohorts of CHR participants—one assessed at the UCSF Prodrome Assessment, Research and Treatment (PART) and the other at the UC Davis Early Diagnosis and Preventive Treatment of Psychotic Illness (EDAPT) programs. We also examined the relationship between symptoms and functioning in a sample of participants at UCSF with a recent onset of psychotic disorder (RO), for context and comparison. We hypothesized the following for both CHR and RO samples: (a) more severe negative and disorganized, but not positive, psychotic symptoms would be negatively related to functioning; and (b) symptoms of depression and anxiety would explain unique variance in functioning, above and beyond the variance explained by negative and disorganized symptoms. Of note, these data were originally collected in separate studies (CHR vs. RO) for separate purposes by the authors as part of an established collaboration. Hypotheses were developed prior to examining any data or conducting analyses, based on available measures.

2. Materials and methods

2.1. Participants

We recruited 186 participants aged 12 to 28 years from the community via advertisements and referrals at the UCSF PART (CHR $n = 65$; RO $N = 88$) and UCD EDAPT ($n = 33$) programs for a variety of research studies. The majority of participants are referred by treatment providers, educators, hospitals, or family members who have been made aware of our programs by word of mouth, through our websites, and regular community outreach presentations we provide for schools, clinics, and other treatment programs. The socio-economic makeup and ethnic makeup of the PART and EDAPT programs are representative of the diversity of the larger San Francisco and Sacramento communities. The PART and EDAPT programs are largely parallel programs in terms of study criteria and procedures. We included two sites of CHR participants to achieve adequate statistical power through a sufficiently large sample size to detect significant effects in the proposed regression analyses. Inclusion as a CHR participant at either site was defined as meeting criteria of a prodromal syndrome on the Structured Interview for Prodromal Syndromes (SIPS; McGlashan et al., 2001). These criteria include one or more of the following: 1) Attenuated Positive Symptom syndrome (APS: attenuated symptoms of psychosis with recent

onset or worsening; 94.9%), 2) Brief Intermittent Psychotic Symptom syndrome (BIPS: fully psychotic symptoms of brief duration and with full recovery; 5.1%), or 3) Genetic Risk and Deterioration syndrome (GRD: a decline in role functioning and either a diagnosis of Schizotypal Personality Disorder or a first-degree relative with a psychotic disorder; 2.0%). CHR individuals are recruited at both UCSF and UCD to participate in ongoing studies examining the longitudinal course of psychosis risk, with conversion to psychosis (defined as both affective and non-affective psychotic disorders) as a primary outcome. Inclusion as an RO participant at UCSF was defined as meeting DSM-IV-TR criteria for schizophrenia (70.5%), schizoaffective (26.1%), or schizophreniform (3.4%) disorder with onset within the last 5 years (median number of months since onset = 13.5; range = 0–57). Exclusion criteria were the following: significant current substance use disorder, neurological disorder, or IQ below 70. In general, RO participants were symptomatically stable. That is, current symptoms were in the low-to-moderate range on all measures, no participant had been hospitalized within the past three months, and those taking psychotropic medications were all on a stable dose. Table 1 lists the demographic information for both samples, as well as tests of differences in demographic and symptom variables between the two CHR samples.

2.2. Measures

We assessed CHR status using the SIPS and baseline Axis I diagnoses using the Structured Clinical Interview for DSM-IV (SCID-I/P; First et al., 2002) or, for participants under age 16, the Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS; Kaufman et al., 1996). To assess for psychotic symptom severity in the RO participants, we used the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1983) and Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984). To assess for symptoms of attenuated psychosis in CHR participants, we used the Scale of Prodromal Symptoms (SOPS; McGlashan et al., 2001). The SOPS is embedded within the SIPS and yields a total score for positive, negative, disorganized and general symptoms. In line with the work of Liddle (1987), and consistent with previous research (Brekke et al., 1994; Andreasen et al., 1995; Barch et al., 2003; Klaassen et al., 2011), we separated the SANS, SAPS, and SOPS psychosis symptoms into the three major factors: 1) Reality Distortion/Positive Symptoms; 2) Disorganization; and 3) Poverty/Negative Symptoms. We used the Brief Psychiatric Rating Scale Depression and Anxiety items (BPRS; Overall and Gorham, 1962) to assess for depression and anxiety in both samples of participants.

Social functioning and occupational functioning were measured using two of the four original items of the Strauss Carpenter Outcome Scales (SCOS; Strauss and Carpenter, 1972): Social Contacts – contact with friends/acquaintances over the past month (SCOS-S), and Useful Employment – time spent employed or enrolled in school over the past month (SCOS-E). We also used the Global Functioning: Social (GFS; Auther et al., 2006) and Global Functioning: Role (GFR; Niendam et al., 2006a) scales, which were developed specifically to capture the range of functioning in CHR or younger psychosis populations. Finally, we used a modified version of the Global Assessment of Functioning scale (GAF; Hall, 1995) as a well-validated, broad measure of functioning. This modified version uses clearly defined anchors to improve reliability and minimize rater bias when making global functioning ratings. Both samples were administered all four functioning measures.

2.3. Procedure

Referred individuals completed a phone screen and, if eligible, were scheduled for an in-person intake interview at the PART lab at UCSF or EDAPT clinic at UCD. After study eligibility was determined via clinical interview with the SIPS (for CHR samples) or SCID-I/P (for RO sample), participants returned to complete the remainder of

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