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# Negative symptoms in youths with psychosis spectrum features: Complementary scales in relation to neurocognitive performance and function

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ABSTRACT

*Background:* Negative symptoms in schizophrenia are related to impaired functioning. The presence of negative symptoms in early phases of psychosis in individuals at clinical risk is receiving increased attention.
*Methods:* We evaluated comprehensively a sample of 92 young people (age range 15–25) applying the Clinical Assessment Interview for Negative Symptoms (CAINS), adapted for youth. Individuals at clinical high risk (CHR, n = 29) were compared to individuals with schizophrenia (SZ, n = 31) and normal controls (NC, n = 32). In addition to the CAINS, participants were assessed with the Structured Interview for Prodromal Syndromes (SIPS), enabling examination of the relations among scales, as well as the Penn Computerized Neurocognitive Battery (CNB), to examine association with cognitive performance, and the Global Assessment of Function (GAF) to assess overall functioning.
*Results:* The CHR group was intermediate to SZ and NC on nearly all clinical measures. Negative symptoms on the CAINS correlated better with negative than with other symptoms on the SIPS and were associated with neurocognitive deficits and poorer functioning.
*Conclusions:* This study illustrates the feasibility of in-depth evaluation of negative symptoms in youth and indicates that these symptoms are present already in the at-risk state and relate to impaired cognition and functioning.



## 1. Introduction

Negative symptoms in schizophrenia are associated with impaired functioning and are a treatment challenge (Erhart et al., 2006). An extensive literature has examined the relation of negative symptoms to cognitive and affective processes (Gur et al., 2006) and to brain parameters (Gur et al., 2007a). Most studies on negative symptoms have been conducted in people with chronic schizophrenia. Effort to identify individuals at clinical risk has centered on attenuated positive symptoms, with some including particular aspects of negative symptoms such as impaired abstract thinking (Schultze-Lutter et al., 2010). However, a broader range of negative symptoms occurs prior to the onset of psychosis (Lyne et al., 2014) and transition to schizophrenia has been related to anhedonia, asociality and blunted affect (Mason et al., 2004). Negative symptoms may be more severe and persistent in adults presenting with attenuated positive symptoms who convert to psychosis (Piskulic et al., 2012). Despite evidence for the importance of negative symptoms in early phases of psychosis (Yung et al., 2004; Johnstone et al., 2005; Murphy et al., 2008; Cornblatt et al., 2012; Demjaha et al., 2012; Schultze-Lutter et al., 2012; Kwapil et al., 2013; Nieman et al., 2013), little work has evaluated their full range among psychotic, clinical high risk, and typically developing youth.

Instruments employed to assess severity of negative symptoms in schizophrenia, include the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) and the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1983). The SANS is the only instrument that exclusively assesses negative symptoms and it has not been applied in the prodromal population.

The Clinical Assessment Interview for Negative Symptoms (CAINS) is a semi-structured interview with 13 items representing two factors: motivation-pleasure and expression. It has been validated in adults with schizophrenia demonstrating strong internal consistency and convergent validity (Kring et al., 2013). The CAINS factors are rated based on self-report of internal experience and actual behavior within the past week, and interviewer rating of expressiveness. The CAINS uniquely probes consummatory (past week) and anticipatory (future week) pleasure. The clearly specified anchors and the readily available

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online training materials result in high inter-rater reliability (Kring et al., 2013). However, it has been aimed at an adult population and requires adaptation for adolescents.

To advance research on negative symptoms in at-risk cohorts, we adapted the CAINS to adolescents. The goal of the study was to examine the presence and severity of negative symptoms in young people at clinical risk for psychosis, those with schizophrenia and normative comparisons. We were interested in establishing whether the CAINS can detect negative symptoms in youth at clinical risk, the extent to which it relates to symptoms measured by other scales and to functioning. We related the clinical measures to performance on the Penn computerized neurocognitive battery (Gur et al., 2010, 2012) where we observed deficits in a community-based sample with psychosis spectrum features (Calkins et al., 2014; Gur et al., 2014).

## 2. Materials and methods

### 2.1. Participants

The sample included three groups of research volunteers who presented consecutively to the Conte Center and met clinical and neuroimaging criteria. Participants, consisting of self, clinician or community referrals, were comprehensively screened for suitability to the study before intake. To capture the early phases of psychosis, age range was 12–30 years. Participants were proficient in English since the assessment instruments and norms for the neurocognitive tests are available for English speakers. The assessment was accomplished in 1–2 visits and participants were classified as follows:

1. Patients (n = 31) met DSM-IV criteria for schizophrenia (SZ). We did not include in this group individuals with other psychoses diagnoses. Exclusion criteria: current substance abuse and history of substance dependence in past 6 months; history of any neurologic event or disease; medical diseases that may affect brain function or interfere with participation; orthopedic circumstances and metallic inserts interfering with MR scanning; pregnancy determined by urine test; neurodevelopmental disorders. Of the sample that met diagnostic criteria for SZ, 24 were treated with second-generation antipsychotics at study entry, one was treated with an antidepressant and 6 were not treated yet.
2. Clinical High Risk (CHR; n = 29) met standardized criteria as at-risk for psychosis, operationally defined as at least one current positive symptom (P1–P5) rated 3, 4 or 5, or at least two current negative and/or disorganized symptoms rated 3, 4, 5 or 6 within the past 6 months, on the Scale of Prodromal Symptoms (SOPS; McGlashan et al., 2003), but did not meet criteria for a DSM-IV psychotic disorder. We also applied the Structured Interview for Prodromal Syndromes (SIPS; Miller et al., 2003) summary criteria for comparability to studies in our center and the field. Exclusion criteria were the same as for the SZ. CHR participants were not treated with antipsychotics at study enrollment, except one recently started on a second-generation antipsychotic.
3. Normal Controls (NC; n = 32) were healthy participants sociodemographically balanced to patient and psychosis risk groups, free of any psychiatric or medical disorders, without history of psychotic and mood disorders in first-degree relatives, and passed the exclusionary criteria specified for SZ and CHR groups. Healthy participants are recruited by the center continuously and undergo the same assessment procedures as SZ and CHR. Sample characteristics are summarized in Table 1. While generally similar, there were significant differences between some groups on age and education, but not on parental education. Therefore, age and education were entered as covariates in the statistical analysis of group effects on the main variable of interest.

### 2.2. Procedures

#### 2.2.1. Clinical assessment

Participants underwent a standard assessment designed to evaluate behavioral, psychiatric, medical, developmental and psychosocial concomitants of psychotic disorders. Collateral informants (parent or guardian) were required for participants ≤ 18, and requested for individuals ≥ 18. At the time of evaluation all SZ and CHR participants were stable and able to complete the study procedures. The assessment, administered on a laptop computer, used an interface validated in the Penn Schizophrenia Research Center and included semi-structured interviews based on the Kiddie-Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997), Structured Interview for Prodromal Syndromes (SIPS; Miller et al., 2003), and Family Interview for Genetic Studies (FIGS; Maxwell, 1992). The K-SADS allows differential diagnosis and understanding of the context of reported sub-psychotic symptoms. The SIPS is integrated into the psychosis section of the K-SADS. The SOPS, embedded within the SIPS, describes and provides established anchors for prodromal and other symptoms occurring within the past 6 months. Symptom domains include positive, negative, disorganization, and general. The SIPS Global Assessment of Function (GAF) rated overall severity of symptoms and impact on functioning in the past year. Assessments were conducted by trained research coordinators, blind to the preliminary group status (time: ~2–4 h). Cases with SOPS ratings > = 3 were presented to a consensus conference with doctoral level clinicians, where diagnoses and consensus SOPS and GAF ratings were achieved. Other cases were reviewed by a doctoral level clinician to confirm ratings or submit to consensus conference.

#### 2.2.2. The Clinical Assessment Interview for Negative Symptoms (CAINS)

CAINS was adapted to activities and lifestyles of young people and administered by trained assessors. Adaptations were done by investigators and research staff with expertise in assessment of youth and included 1) revised language to increase understandability, 2) incorporated probes on social media, 3) added probes to accommodate for living situations of young people (i.e. assessing for motivation to be around family while living at home) and 4) added a general rule, not applicable in this study, to only probe about romantic relationships if over the age of 11 (see modified CAINS in Supplement). The CAINS provides information on motivation and pleasure for social, school and work and recreation. Assessment of expression includes facial, vocal, gestures and speech quantity. Item are scored on Likert type scale: 0 = no impairment, 1 = mild deficit, 2 = moderate deficit, 3 = moderately severe deficit, 4 = severe deficit.

**Table 1**
Demographic characteristics of the sample.

| | SZ (21M, 10F) | | | CHR (15M, 14F) | | | NC (13M, 19F) | | | SZ vs CHR | SZ vs NC | CHR vs NC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Range | Mean | SD | Range | Mean | SD | Range | p | p | p |
| Age | 23.21 | 3.89 | 14 to 29 | 18.94 | 2.93 | 14 to 24 | 19.94 | 3.71 | 12 to 29 | <.0001 | 0.0017 | NS |
| Education | 13.28 | 2.41 | 7 to 20 | 11.18 | 2.86 | 6 to 16 | 13.10 | 3.34 | 5 to 18 | 0.0029 | NS | 0.0312 |
| Parental education | 14.88 | 3.12 | 7 to 20 | 13.87 | 2.62 | 10 to 20 | 15.08 | 2.68 | 10 to 20 | NS | NS | NS |