Published in final edited form as:

Schizophr Res. 2015 August ; 166(0): 322–327. doi:10.1016/j.schres.2015.05.037.

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

Raquel E. Gur^a, Mary March^a, Monica E. Calkins^a, Lauren Weittenhiller^a, Daniel H. Wolf^a, Bruce I. Turetsky^a, and Ruben C. Gur^a

^aDepartment of Psychiatry, Neuropsychiatry Section, Perelman School of Medicine, University of Pennsylvania, 10 Gates, 3400 Spruce Street, Philadelphia, PA 19104, USA

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.

Keywords

Negative symptoms; psychosis; clinical risk; neurocognition

Corresponding author: Raquel E. Gur, M.D. Ph.D. Neuropsychiatry Section, Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, 3400 Spruce, Philadelphia PA, USA. Tel: 215 662 2915, fax: 215 662 7903. raquel@upenn.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Contributors

All authors significantly contributed to study design, data collection and reviewed and approved this manuscript.

Conflict of interest

Raquel E. Gur participated in an advisory board for Otsuka unrelated to the study. All other authors declare no conflicts.

1.0 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 (Cornblatt et al., 2012; Demjaha et al., 2012; Johnstone et al., 2005; Kwapil et al., 2013; Murphy et al., 2008; Nieman et al., 2013; Schultze-Lutter et al., 2012; Yung et al., 2004), 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 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. 0 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

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 hours). 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.

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.

The Penn Computerized Neurocognitive Battery (CNB)—The 1-hour computerized neurocognitive battery included 14 tests assessing 5 domains (Gur et al., 2012, 2014): executive functions (abstraction and mental flexibility, attention, working memory), episodic memory (words, faces, shapes), complex cognition (verbal reasoning, nonverbal reasoning, spatial processing), social cognition (emotion identification, emotion intensity differentiation, age differentiation), sensorimotor speed (motor, sensorimotor). Except for tests designed exclusively for measuring speed, each test provides measures of both accuracy and speed. The Reading subtest of the Wide Range Achievement Test, version 4 (Wilkinson and Robertson, 2006) was administered to determine ability to complete the battery and provide an IQ estimate.

After complete description of the study, written informed consent was obtained for participants aged ≥ 18. For participants <18, written assent and parental permission were obtained. The procedures were approved by the University of Pennsylvania Institutional Review Board.

2.3 Data Analysis

The ratings of the 13 CAINS items, 19 SOPS items, and two GAF measures (current, highest) were the dependent measures in a MANCOVA (SAS Proc GLM), with Diagnosis (SZ, CHR, NC) as a between-group factor, item as a repeated-measures factor, and age and education as covariates. The overall MANCOVA was followed by two-group contrasts (SZ vs. NC, CHR vs. NC, SZ vs. CHR). The relationships among the CAINS and SOPS measures were examined by Pearson correlations across the whole sample, and then separately in the SZ and CHR samples (there was not enough variability on the SOPS in the NC group). To reduce the number of correlations, we averaged the subscale items within the CAINS factors (Motivation and pleasure = items 1–9 and Expression = items 10–13) and SOPS (Negative, Positive, Disorganized, General).

CNB domains were examined for performance accuracy and speed and transformed to their standard equivalents (Z-scores) using the NC group as a reference. Domain scores were entered as dependent measures in mixed model repeated measures (MMRM, Proc Mixed in SAS) analyses. Diagnostic group (NC, CHR, SZ) served as a between-group factor, domain as a within-group factor and age as a covariate. Analyses were performed separately for accuracy and speed scores.

3.0 Results

Means for each of the CAINS, SOPS and GAF items for the three groups, as well as effect sizes for group differences, are presented in Table 2. The groups differed on all items, with most effects sizes ranging from moderate to large. The exceptions are small effect sizes on some SOPS items in differentiating CHR from SZ. These results indicate good ability of all scales in differentiating the three groups. Indeed, the MANCOVA (Table 3) indicates robust group effects on all contrasts. The Group × item interactions were significant only for the CHR vs. SZ contrast on the CAINS, all contrasts on the SOPS, and all but the CHR vs. SZ contrast on the GAF. These interactions indicate within instrument variability in sensitivity to clinical grouping.

Correlations among scale items are shown in Table 4a, and for the SZ and CHR subsamples in Table 4b. The overall correlations among items within scales are moderate to high for the entire sample, and the two scales correlate with each other as well and in the expected direction of negative correlations between the CAINS and SOPS and the GAF. These correlations are somewhat moderated within SZ and CHR (Table 4b), perhaps due to reduced power and range of scores. However, they remain moderate to high and still in the expected directions.

Neurocognitive performance is presented in Figure 1. The MMRM analysis on the accuracy scores showed a main effect of diagnosis, $F = 6.43$, $df = 2, 75$, $p = 0.0027$, a main effect of

domain, $F=2.27$, $df=11,728$, $p=0.0101$, and no interaction. For the speed scores, there was a main effect of diagnosis ($F=5.21$, $df=2,75$, $p=0.0076$), a main effect of domain ($F=5.51$, $df=13,874$, $p<0.001$), and a diagnosis $\times$ domain interaction ($F=1.79$, $df=26,874$, $p=0.0090$). As can be seen, both patients with schizophrenia and those at clinical risk were impaired in accuracy, relative to healthy controls. Lower performance accuracy was noted for episodic memory tests, whereas performance speed was generally lower in both groups with the exception that working memory performance speed as well as two of the social cognition domains were better in clinical risk compared to the schizophrenia group.

4.0 Discussion

In the first administration of the CAINS to a normative sample of youth compared to clinical risk for psychosis and with schizophrenia, we found robust differences among the groups. Notably, we observed some low level negative symptoms in the normative sample, consistent with a CAINS report in adults of meaningful variation in healthy people (Wolf et al., 2014). Nonetheless, the CAINS distinguished clinical risk from healthy controls with effect sizes ranging from moderate to large. This effect was obtained even though negative symptoms are not typically prominent in CHR and clinical ratings are largely based on attenuated positive symptoms. The schizophrenia group had higher scores than controls with effect sizes in the large range on all items. The schizophrenia sample also scored higher compared to CHR, with effect sizes ranging from small to large. Both groups had similarly lower motivation for friends, decreased frequency of experienced pleasure in the immediate past and decreased anticipatory pleasure in the immediate future. Large effect sizes differentiating CHR from SZ were observed for motivation for close relationships with family, motivation for recreational activities, and facial expressivity. These symptoms were more prominent in SZ than CHR, suggesting a progression toward less engagement with family and recreational activities.

Comparison between CAINS and SOPS ratings permit evaluation of the presence of positive and disorganized symptoms and the comparability of negative symptom ratings of the SOPS with CAINS ratings. The SOPS results indicated a prominent presence of positive symptoms both in CHR and SZ, with large effect sizes for all positive items as well as disorganized and general items, except motor disturbance. The SOPS negative symptoms likewise distinguished both CHR and SZ from controls, with large effect sizes for nearly all items and contrasts. As with the CAINS, the negative items on the SOPS also distinguished CHR from SZ with moderate to large effect sizes. The exception is ideational richness in which CHR were scored more severely than SZ. This unanticipated finding merits further evaluation. GAF scores indicated decreased global functioning in both CHR and SZ compared to controls with very large effect sizes among the groups. These effects were both for current level of functioning and for the highest level of functioning obtained in the past year, suggesting poorer recent functioning in both clinical groups.

Further supporting the utility and construct validity of the CAINS, we found moderate intercorrelations among its subscales and higher correlations of the CAINS subscales with the SOPS negative measures, compared to the positive, disorganized and general measures.

This pattern is consistent with results of the validation study in adults with chronic schizophrenia with scales tapping similar domains (Kring et al., 2013).

In contrast to the CAINS, SOPS and GAF, where SZ showed more severe symptoms than CHR, both groups showed comparable impairment on the neurocognitive measures. The level of impairment for accuracy is similar to that we reported in a larger sample of youths with psychosis spectrum features and here too we observed the most pronounced impairment in speed of language and of emotion processing (Calkins et al., 2014). The SZ and CHR groups had a nearly identical pattern and level of deficits, which is generally less severe than that reported for samples of chronic SZ (Calkins et al., 2010, 2013; Gur et al., 2007b, in press). Presence of neurocognitive deficits early in illness supports the conceptualization of psychosis as reflecting underlying brain dysfunction present before a symptom-based clinical diagnosis can be made (Kahn and Keefe, 2013). Milder level of deficits in the CHR group may reflect inclusion of some individuals who may never develop psychosis. However, the milder impairment of our SZ group compared to that seen in chronic patients is consistent with the notion of disease-related progression. Notably, greater abnormality in speed compared to accuracy has also been observed in first-degree family members of SZ patients and was interpreted as compensatory effort to maintain performance accuracy by reducing speed (Gur et al., 2007b, in press). In more chronic stages of illness, both accuracy and speed are reduced in SZ. While performance on the CNB was correlated with greater symptom severity and lower functioning, these correlations were small to moderate, indicating that cognition and symptoms associated with psychosis proneness and schizophrenia exert independent influences on functional disability in patients. The slower response time on social cognition tests, evident in schizophrenia and, to a lesser extent, in CHR, is consistent with growing literature on deficits in emotion processing (Kohler et al., 2014) and other measures of social cognition in SZ and CHR (Allott et al., 2014; Amminger et al., 2012; Irani et al., 2012; Meyer et al., 2014; Walther et al., 2015). Such effects support recent emphasis on social neuroscience as offering unique pathways to elucidating neuropsychiatric disorders (Adolphs and Anderson, 2013; Cacioppo et al., 2014).

Our study has several limitations. While the sample size is sufficiently powered for detecting group differences in the ratings, its power is marginal for examining correlations among measures. Thus, correlations calculated within subsamples show some fluctuations that could be related to low power. Another limitation is that although all other clinical ratings were done by consensus of investigators, the CAINS ratings were obtained by clinical assessors. However, the raters were highly reliable against the gold standard in the original study (Kring et al., 2013). Finally, the groups were comparable for parental education, significant age and education differences could account for some of the effects. However, effects sustained covarying by age and education.

Positive symptoms have been the focus of clinical diagnosis and treatment in schizophrenia and have received considerable attention in studies of CHR. Our study is the first to describe a comprehensive assessment of the range of symptoms of CHR individuals including both a standard scale for assessment of negative symptoms and a new scale with a more detailed probe of negative symptoms. The results indicate that negative symptoms, while less prominent than positive symptoms, can be reliably identified in CHR and are associated

with deficits in neurocognitive performance and functioning. This pattern of results is consistent with the growing literature on clinical risk and the established literature of schizophrenia, which also indicates stronger link between negative symptoms and neurocognition. Further longitudinal studies are needed to document the course of negative symptoms in relation to other features of the illness in individuals with and without persistent symptoms (Yung et al., 2008), as well as a broader range of psychosis spectrum disorders.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

We thank Amy Cassidy MA for assistance in project management, Christina Hays BA for help with data collection, Noemi Cagagianian for assistance compiling the literature and the research participants for their time and effort.

Role of funding source

The study was supported by the National Institute of Mental Health Conte Center grant P50-MH096891.

References

1. Adolphs R, Anderson D. Social and emotional neuroscience. *Curr. Opin. Neurobiol.* 2013; 23(3): 291–293. [PubMed: 23669616]
2. Allott KA, Schäfer MR, Thompson A, Nelson B, Bendall S, Bartholomeusz CF, Yuen HP, McGorry PD, Schlögelhofer M, Bechdolf A, Amminger GP. Emotion recognition as a predictor of transition to a psychotic disorder in ultra-high risk participants. *Schizophr. Res.* 2014; 153(1–3):25–31. [PubMed: 24552619]
3. Amminger GP, Schäfer MR, Papageorgiou K, Klier CM, Schlögelhofer M, Mossaheb N, Werneck-Rohrer S, Nelson B, McGorry PD. Emotion recognition in individuals at clinical high-risk for schizophrenia. *Schizophr. Bull.* 2012; 38(5):1030–1039. [PubMed: 21422108]
4. Andreasen, N. The Scale for the Assessment of Negative Symptoms (SANS). Iowa City, IA: University of Iowa; 1983.
5. Cacioppo JT, Cacioppo S, Dulawa S, Palmer AA. Social neuroscience and its potential contribution to psychiatry. *World Psychiatry.* 2014; 13(2):131–139. [PubMed: 24890058]
6. Calkins ME, Tepper P, Gur RC, Ragland JD, Klei L, Wiener HW, Richard J, Savage RM, Allen TB, O’Jile J, Devlin B, Kwentus J, Aliyu MH, Bradford LD, Edwards N, Lyons PD, Nimgaonkar VL, Santos AB, Go RC, Gur RE. Project among African-Americans to explore risks for schizophrenia (PAARTNERS): evidence for impairment and heritability of neurocognitive functioning in families of schizophrenia patients. *Am. J. Psychiatry.* 2010; 167(4):459–472. [PubMed: 20194479]
7. Calkins ME, Ray A, Gur RC, Freedman R, Green MF, Greenwood TA, Light GA, Nuechterlein KH, Olincy A, Radant AD, Seidman LJ, Siever LJ, Silverman JM, Stone WS, Sugar C, Swerdlow NR, Tsuang DW, Tsuang MT, Turetsky BI, Braff DL, Lazzaroni LC, Gur RE. Sex differences in familiarity effects on neurocognitive performance in schizophrenia. *Biol. Psychiatry.* 2013; 73(10): 976–984. [PubMed: 23395246]
8. Calkins ME, Moore TM, Merikangas KR, Burstein M, Satterthwaite TD, Bilker WB, Ruparel K, Chiavacci R, Wolf DH, Mentch F, Qiu H, Connolly JJ, Sleiman PA, Hakonarson H, Gur RC, Gur RE. The psychosis spectrum in a young U.S. community sample: findings from the Philadelphia Neurodevelopmental Cohort. *World Psychiatry.* 2014; 13(3):296–305. [PubMed: 25273303]
9. Cornblatt BA, Carrión RE, Addington J, Seidman L, Walker EF, Cannon TD, Cadenhead KS, McGlashan TH, Perkins DO, Tsuang MT, Woods SW, Heinssen R, Lencz T. Risk factors for

- psychosis: impaired social and role functioning. *Schizophr. Bull.* 2012; 38(6):1247–1257. [PubMed: 22080497]
10. Demjaha A, Valmaggia L, Stahl D, Byrne M, McGuire P. Disorganization/cognitive and negative symptom dimensions in the at-risk mental state predict subsequent transition to psychosis. *Schizophr. Bull.* 2012; 38(2):351–359. [PubMed: 20705805]
 11. Erhart SM, Marder SR, Carpenter WT. Treatment of schizophrenia negative symptoms: future prospects. *Schizophr. Bull.* 2006; 32(2):234–237. [PubMed: 16492797]
 12. Gur RE, Kohler CG, Ragland JD, Siegel SJ, Lesko K, Bilker WB, Gur RC. Flat affect in schizophrenia: relation to emotion processing and neurocognitive measures. *Schizophr. Bull.* 2006; 32(2):279–287. [PubMed: 16452608]
 13. Gur RE, Loughhead J, Kohler CG, Elliott MA, Lesko K, Ruparel K, Wolf DH, Bilker WB, Gur RC. Limbic activation associated with misidentification of fearful faces and flat affect in schizophrenia. *Arch. Gen. Psychiatry.* 2007a; 64(12):1356–1366. [PubMed: 18056543]
 14. Gur RE, Nimgaonkar VL, Almasy L, Calkins ME, Ragland JD, Pogue-Geile MF, Kanes S, Blangero J, Gur RC. Neurocognitive endophenotypes in a multiplex multigenerational family study of schizophrenia. *Am. J. Psychiatry.* 2007b; 164(5):813–819. [PubMed: 17475741]
 15. Gur RC, Richard J, Hughett P, Calkins ME, Macy L, Bilker WB, Brensinger C, Gur RE. A cognitive neuroscience-based computerized battery for efficient measurement of individual differences: standardization and initial construct validation. *J. Neurosci. Methods.* 2010; 187(2): 254–262. [PubMed: 19945485]
 16. Gur RC, Richard J, Calkins ME, Chiavacci R, Hansen JA, Bilker WB, Loughhead J, Connolly JJ, Qiu H, Mentch FD, Abou-Sleiman PM, Hakonarson H, Gur RE. Age group and sex differences in performance on a computerized neurocognitive battery in children age 8–21. *Neuropsychology.* 2012; 26(2):251–265. [PubMed: 22251308]
 17. Gur RC, Calkins ME, Satterthwaite TD, Ruparel K, Bilker WB, Moore TM, Savitt AP, Hakonarson H, Gur RE. Neurocognitive growth charting in psychosis spectrum youths. *JAMA Psychiatry.* 2014; 71(4):366–374. [PubMed: 24499990]
 18. Gur RC, Braff DL, Calkins ME, Dobie DJ, Freedman R, Green MF, Greenwood TA, Lazzeronia LC, Light GA, Nuechterlein KH, Olincy A, Radant AD, Seidman LJ, Siever LJ, Silverman JM, Sprock J, Stone WS, Sugar CA, Swerdlow NR, Tsuang DW, Tsuang MT, Turetsky BI, Gur RE. Neurocognitive performance in family-based and case-control studies of schizophrenia. *Schizophr. Res.* In press.
 19. Irani F, Seligman S, Kamath V, Kohler C, Gur RC. A meta-analysis of emotion perception and functional outcomes in schizophrenia. *Schizophr. Res.* 2012; 137(1–3):203–211. [PubMed: 22341200]
 20. Johnstone EC, Ebmeier KP, Miller P, Owens DG, Lawrie SM. Predicting schizophrenia: findings from the Edinburgh High-Risk Study. *Br. J. Psychiatry.* 2005; 186:18–25. [PubMed: 15630119]
 21. Kahn RS, Keefe RS. Schizophrenia is a cognitive illness: time for a change in focus. *JAMA Psychiatry.* 2013; 70(10):1107–1112. [PubMed: 23925787]
 22. Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, Williamson D, Ryan N. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. *J. Am. Acad. Child. Adolesc. Psychiatry.* 1997; 36(7):980–988. [PubMed: 9204677]
 23. Kay SR, Flszbein A, Opfer LA. The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophr. Bull.* 1987; 13(2):261–276. [PubMed: 3616518]
 24. Kohler CG, Richard JA, Brensinger CM, Borgmann-Winter KE, Conroy CG, Moberg PJ, Gur RC, Gur RE, Calkins ME. Facial emotion perception differs in young persons at genetic and clinical high-risk for psychosis. *Psychiatry Res.* 2014; 216(2):206–212. [PubMed: 24582775]
 25. Kring AM, Gur RE, Blanchard JJ, Horan WP, Reise SP. The Clinical Assessment Interview for Negative Symptoms (CAINS): final development and validation. *Am. J. Psychiatry.* 2013; 170(2): 165–172. [PubMed: 23377637]
 26. Kwapil TR, Gross GM, Silvia PJ, Barrantes-Videl N. Prediction of psychopathology and functional impairment by positive and negative schizotypy in the Chapmans' ten-year longitudinal study. *J. Abnorm. Psychol.* 2013; 122(3):807–815. [PubMed: 24016018]

27. Lyne J, Renwick L, Madigan K, O'Donoghue B, Bonar M, Grant T, Kinsella A, Malone K, Turner N, O'Callaghan E, Clarke M. Do psychosis prodrome onset negative symptoms predict first presentation negative symptoms? *Eur. Psychiatry*. 2014; 29(3):153–159. [PubMed: 23523737]
28. Mason O, Startup M, Halpin S, Schall U, Conrad A, Carr V. Risk factors for transition to first episode psychosis among individuals with 'at-risk mental states'. *Schizophr. Res*. 2004; 71(2–3): 227–237. [PubMed: 15474894]
29. Maxwell, ME. Manual for the FIGS. Bethesda, MD: National Institute of Mental Health; 1992.
30. McGlashan, TH.; Miller, TJ.; Woods, SW.; Rosen, JL.; Hoffman, RE.; Davidson, L. Structured Interview for Prodromal Syndromes, (Version 4.0) Prime Clinic Yale School of Medicine, New Haven, CT. New Haven: Prime Clinic Yale School of Medicine; 2003. 2003.
31. Meyer EC, Carrión RE, Cornblatt BA, Addington J, Cadenhead KS, Cannon TD, McGlashan TH, Perkins DO, Tsuang MT, Walker EF, Woods SW, Heinssen R, Seidman LJ. The relationship of neurocognition and negative symptoms to social and role functioning over time in individuals at clinical high risk in the first phase of the North American Prodrome Longitudinal study. *Schizophr. Bull*. 2014; 40(6):1452–1461. [PubMed: 24550526]
32. Miller TJ, McGlashan TH, Rosen JL, Cadenhead K, Cannon T, Ventura J, McFarlane W, Perkins DO, Pearlson GD, Woods SW. Prodromal assessment with the structured interview for prodromal syndromes and the scale of prodromal symptoms: predictive validity, interrater reliability, and training to reliability. *Schizophr. Bull*. 2003; 29(4):703–715. [PubMed: 14989408]
33. Murphy BP, Stuart AH, McGorry PD. Duration of untreated negative symptoms and duration of active negative symptoms: proof of concepts. *Early Interv Psychiatry*. 2008; 2:27–33. [PubMed: 21352128]
34. Nieman DH, Velthorst E, Becker HE, de Haan L, Dingemans PM, Linszen DH, et al. The Strauss and Carpenter Prognostic Scale in subjects clinically at high risk of psychosis. *Acta Psychiatr. Scand*. 2013; 127:53–61. [PubMed: 22775300]
35. Piskulic D, Addington J, Cadenhead KS, Cannon TD, Cornblatt BA, Heinssen R, Perkins DO, Seidman LJ, Tsuang MT, Walker EF, Woods SW, McGlashan TH. Negative symptoms in individuals at clinical high risk of psychosis. *Psychiatry Res*. 2012; 196(2–3):220–224. [PubMed: 22445704]
36. Schultze-Lutter F, Ruhrmann S, Berning J, Maier W, Klosterkötter J. Basic symptoms and ultrahigh risk criteria: symptom development in the initial prodromal state. *Schizophr. Bull*. 2010; 36(1):182–191. [PubMed: 18579555]
37. Schultze-Lutter F, Ruhrmann S, Fusar-Poli P, Bechdolf A, Schimmelmann BG, Klosterkötter J. Basic symptoms and the prediction of first-episode psychosis. *Curr. Pharm. Des*. 2012; 18(4):351–357. [PubMed: 22239566]
38. Walther S, Stegmayer K, Sulzbacher J, Vanbellingen T, Müri R, Strik W, Bohlhalter S. Nonverbal social communication and gesture control in schizophrenia. *Schizophr. Bull*. 2015; 41(2):338–345. [PubMed: 25646526]
39. Wilkinson, GS.; Robertson, GJ. Psychological Assessment Resources. In: Lutz, FL., editor. Wide Range Achievement Test, Fourth edition. WRAT4 Introductory Kit. 2006.
40. Wolf DH, Satterthwaite TD, Kantrowitz JJ, Katchmar N, Vandekar L, Elliott MA, Ruperal K. Amotivation in schizophrenia: integrated assessment with behavioral, clinical, and imaging measures. *Schizophr. Bull*. 2014; 40(6):1328–1337. [PubMed: 24657876]
41. Yung AR, Nelson B, Stanford C, Simmons MB, Cosgrave EM, Killackey E, et al. Validation of "prodromal" criteria to detect individuals at ultra high risk of psychosis, 2 year follow-up. *Schizophr. Res*. 2008; 105:10–17. [PubMed: 18765167]
42. Yung AR, Phillips LJ, Yuen HP, McGorry PD. Risk factors for psychosis in an ultra high-risk group: psychopathology and clinical features. *Schizophr. Res*. 2004; 67:131–142. [PubMed: 14984872]

Figure 1.

Computerized Neurocognitive Battery profiles of clinical high risk (CHR), schizophrenia (SZ) and normal controls (NC). ABF – abstraction/flexibility, ATT – attention, WM – working memory, VME – verbal memory, FME – face memory, SME – spatial memory, LAN – language, NVR – non-verbal reasoning, SPA – spatial processing, EMI – emotion identification, EMD – emotion differentiation, AGD – age discrimination, MOT – motor, SM – sensorimotor

Table 1

Demographic characteristics of the sample

	SZ	21 M	10 F	CHR	15 M	14 F	NC	13 M	19 F	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

Table 2

Means for the three groups of subjects on all items of the CAINS, SOPS and GAF with effect sizes for all group contrasts *

CAINS	NC			CHR			SZ			Effect Size (Cohen's d)		
	Mean	SD		Mean	SD		Mean	SD		CHR v	NC SZ v NC	CHR v SZ
S1 - MOT FOR CLOSE FAM/SPOUSE/PARTNER REL	0.30	0.65		0.73	0.87		1.60	1.22		0.55	1.32	0.81
S2 - MOT FOR CLOSE FRIENDS & ROM REL	0.23	0.50		1.50	1.03		1.83	1.23		1.53	1.68	0.29
S3 - FREQ PLEASUR SOCIAL ACT - PAST WEEK	0.10	0.40		0.85	1.08		1.43	1.36		0.89	1.32	0.47
S4 - FREQ EXPECT PLEASUR SOCIAL ACT - NEXT WEEK	0.07	0.25		0.73	1.19		1.73	1.57		0.76	1.47	0.71
W5 - MOTIVATION FOR WORK & SCHOOL ACTIVITIES	0.47	0.68		1.23	1.18		1.90	1.32		0.78	1.35	0.53
W6 - FREQ EXP PLEA WRK & SCHL ACT - NEXT WEEK	0.93	1.23		2.08	1.49		2.30	1.62		0.82	0.94	0.14
R7 - MOTIVATION FOR RECREATIONAL ACTIVITIES	0.23	0.50		0.77	1.11		1.73	1.23		0.61	1.58	0.81
R8 - FREQ PLEASUR RECREAT ACT - PAST WEEK	0.70	0.88		1.38	1.06		1.63	1.16		0.69	0.90	0.22
R9 - FREQ EXP PLEASUR RECR ACT - NEXT WEEK	0.10	0.40		0.54	0.99		0.90	1.40		0.57	0.77	0.29
E10 - FACIAL EXPRESSION	0.07	0.25		0.58	0.90		1.47	1.31		0.75	1.48	0.78
E11 - VOCAL EXPRESSION	0.07	0.25		0.46	0.90		1.30	1.42		0.58	1.20	0.70
E12 - EXPRESSIVE GESTURES	0.10	0.31		0.46	0.95		1.30	1.44		0.50	1.14	0.68
E13 - QUANTITY OF SPEECH	0.03	0.18		0.35	0.89		0.77	1.01		0.47	1.01	0.44
SOPS												
P1 - Unusual Thought Content/Delusional Ideas	0.25	0.57		2.54	1.88		5.42	1.52		1.61	4.46	1.66
P2 - Suspiciousness/Persecutory Ideas	0.22	0.49		1.89	1.50		4.06	2.26		1.47	2.33	1.12
P3 - Grandiosity	0.13	0.49		1.07	1.33		1.90	2.41		0.92	1.01	0.42
P4 - Perceptual Abnormalities/Hallucinations	0.31	0.64		2.04	1.91		4.52	2.42		1.18	2.35	1.12
P5 - Disorganized Communication	0.06	0.25		1.54	1.40		1.71	2.08		1.43	1.10	0.10
N1 - Social Anhedonia	0.16	0.37		2.00	1.68		3.68	1.92		1.48	2.52	0.92
N2 - Avolition	0.16	0.37		1.36	1.39		3.23	1.80		1.15	2.34	1.14
N3 - Expression of Emotion	0.00	0.00		1.21	1.47		2.55	2.05		1.14	1.75	0.74
N4 - Experience of Emotions and Self	0.03	0.18		0.64	1.28		1.74	2.08		0.65	1.15	0.63
N5 - Ideational Richness	0.19	0.47		1.61	1.47		1.03	1.60		1.27	0.71	-0.37
N6 - Occupational Functioning	0.47	0.76		1.61	1.77		4.13	1.98		0.82	2.42	1.32
D1 - Odd Behavior or Appearance	0.13	0.42		0.82	1.25		2.19	1.94		0.73	1.46	0.83

CAINS	NC			CHR			SZ			Effect Size (Cohen's d)			
	Mean			Mean			Mean			CHR v	NC SZ v NC	CHR v SZ	
	Mean	SD	SD	Mean	SD	SD	Mean	SD	SD				
D2 - Bizarre Thinking	0.00	0.00	1.43	1.04	1.43	2.03	3.16	2.03	1.00	2.18	1.19		
D3 - Trouble with Focus and Attention	0.28	0.63	1.39	1.68	1.39	1.56	2.23	1.56	1.26	1.61	0.36		
D4 - Personal Hygiene	0.03	0.18	1.10	0.79	1.10	1.68	1.03	1.68	0.93	0.83	0.17		
G1 - Sleep Disturbance	0.38	0.61	1.33	2.00	1.33	1.98	1.74	1.98	1.53	0.92	-0.15		
G2 - Dysphoric Mood	0.28	0.63	1.07	1.07	1.51	2.12	2.71	2.12	0.67	1.54	0.88		
G3 - Motor Disturbances	0.00	0.00	0.26	0.07	0.26	0.65	0.19	0.65	0.38	0.41	0.24		
G4 - Impaired Tolerance to Normal Stress	0.16	0.45	1.24	0.71	1.24	1.96	2.10	1.96	0.58	1.36	0.83		
GAF													
Current	86.88	6.88	60.61	60.61	12.80	10.13	42.32	10.13	-2.50	-5.10	-1.55		
Highest	87.38	6.53	65.11	65.11	10.44	12.75	46.13	12.75	-2.50	-4.04	-1.60		

* All effect sizes 0.5 are significant at $p < .01$ two-tailed.

Table 3

Group $\times$ Subscale MANCOVA results

CAINS	Diag		Diag*Subscale			
	F	df	p	F	df	p
Across groups	26.75	2,77	<.0001	1.91	24, 110.27	0.013
NC vs CHR	23.95	1,49	<.0001	1.33	12,38	0.2426
NC vs SZ	44.76	1,53	<.0001	1.78	12,42	0.0839
CHR vs SZ	14.35	1,49	0.0004	2.42	12,38	0.0191
SOPS						
Across groups	106.80	2,76	<.0001	6.89	36,102.15	<.0001
NC vs CHR	97.16	1,49	<.0001	10.19	18,32	<.0001
NC vs SZ	232.53	1,52	<.0001	28.43	18,35	<.0001
CHR vs SZ	33.80	1,48	<.0001	2.71	18,31	0.0072
GAF						
Across groups	120.23	2,76	<.0001	5.80	2,76	0.0045
NC vs CHR	96.59	1,49	<.0001	10.18	1,49	0.0025
NC vs SZ	268.54	1,52	<.0001	7.59	1,52	0.0081
CHR vs SZ	45.19	1,48	<.0001	0.55	1,48	0.4613

Table 4

a: Intercorrelations among the CAINS, SOPS and GAF subscales for the whole sample

WHOLE SAMPLE	CAINS	SOPS			GAF			CNB		
		Mot/Pleas	Expression	Negative	Positive	Disorganized	General	Current	Highest	SQ
CAINS	Mot/Pleas	-	0.486	0.674	0.600	0.614	0.555	-0.671	-0.706	-0.243
	Expression		-	0.650	0.269	0.383	0.177	-0.466	-0.521	-0.190
SOPS	Negative			-	0.706	0.697	0.663	-0.882	-0.844	-0.413
	Positive				-	0.727	0.651	-0.818	-0.776	-0.246
	Disorganized					-	0.561	-0.673	-0.622	-0.134
	General						-	-0.734	-0.720	-0.295
GAF	Current							-	0.940	0.392
	Highest								-	0.360
AQ										0.108
SQ										-

b: Intercorrelations among the CAINS, SOPS and GAF subscales for the SZ sample (upper half of matrix) and the CHR sample (lower half of matrix)

SZ CHR		SOPS				GAF				CNB			
		Mot/Pleas	Expression	Negative	Positive	Disorganized	General	Current	Highest	AQ	SQ		
CAINS	Mot/Pleas	-	0.353	0.632	0.232	0.423	0.239	-0.487	-0.538	-0.064	-0.112		
	Expression	0.238	-	0.583	-0.114	0.094	-0.063	-0.188	-0.282	0.05	-0.028		
SOPS	Negative	0.217	0.357	-	0.058	0.185	0.158	-0.552	-0.436	-0.128	-0.216		
	Positive	0.159	-0.230	0.196	-	0.635	0.263	-0.422	-0.269	-0.112	0.053		
	Disorganized	0.184	0.030	0.565	0.196	-	0.082	-0.311	-0.242	0.030	0.178		
	General	0.319	-0.104	0.440	0.253	0.386	-	-0.515	-0.254	-0.264	-0.020		
GAF	Current	-0.314	-0.279	-0.758	-0.507	-0.437	-0.438	-	0.813	0.445	0.149		
	Highest	-0.379	-0.315	-0.612	-0.380	-0.303	-0.499	0.744	-	0.476	0.203		
CNB	AQ	-0.129	0.115	-0.073	0.057	0.205	0.133	0.164	0.118	-	0.037		
	SQ	-0.126	-0.177	-0.499	-0.009	-0.144	-0.225	0.493	0.383	0.264	-		