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Various Neurocognitive Deficits and Conversion Risk in Individuals at Clinical High Risk for Psychosis

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Abstract

Aim—Individuals at clinical high risk for psychosis (CHR) exhibit neurocognitive deficits in multiple domains. The aim of this study is to investigate whether several components of neurocognition are predictive of conversion to psychosis.

Methods—Fifty-two CHR individuals were assessed with the Structured Interview for Psychosis Risk Syndromes and completed a battery of neurocognitive tests at baseline including measures of executive functioning, attention, working memory, processing speed, and reaction time. Neurocognitive functioning at baseline was scored based on an external normative control group. Most subjects were followed for 2.5 years to determine conversion status.

Results—Significant differences in neurocognitive functioning between CHR individuals and the control group were present in all domains. Twenty-six percent of the participants converted to psychosis within 9.8 (standard deviation=8.0) months on average (median 9 months), but there were no significant differences in neurocognition converters and non-converters.

Conclusions—Individuals at CHR have deficits in neurocognitive functioning, but such deficits do not appear to be related to conversion risk.

Keywords

Cognition; conversion; neurocognition; prodromal; psychosis

Introduction

Previous studies have shown that individuals who are at clinical high risk (CHR) for psychosis have overall neurocognitive impairment compared to healthy controls (HC) ¹⁻⁶, including deficits in attention ^{3, 5, 7}, verbal memory ^{1, 3, 5, 7-9}, processing speed ^{3, 5, 8, 9}, working memory ^{1, 5, 7, 8, 10}, and executive functioning ^{1, 2, 5, 8}. Moreover, a number of longitudinal studies have identified several baseline neurocognitive deficits that are

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predictive of conversion to psychosis, including verbal memory ^{1, 3} and an overall impaired cognition in comparison with non-converters ²⁻⁴.

The first aim of this study was to examine the baseline neurocognitive functioning of individuals at CHR for psychosis at The Center of Prevention and Evaluation (COPE), a research clinic working with CHR individuals at Columbia University Medical Center and New York State Psychiatric Institute (NYSPI). The second aim of this study was to compare converters (CHR+) with non-converters (CHR-). Our first hypothesis was that CHR individuals would have baseline neurocognitive impairments across all domains tested. Secondly, we hypothesized that the CHR+ subgroup would perform more poorly than CHR- individuals.

Methods

Participants

Subjects were recruited via the Internet (copeclinic.org), brochures and mailings to clinicians and schools, presentations throughout the New York City metropolitan area and from other programs within Columbia University/NYSPI. We recruited subjects age 13-30 who met CHR criteria as assessed by the Structured Interview for Psychosis Risk Syndromes (SIPS) ¹¹. Participants were recruited between the period of April 2009 and April 2014.

Exclusion criteria included a history of psychotic symptoms beyond BIPS criteria (e.g., schizophrenia). Participants were also excluded if their symptoms were better accounted for by a non-psychotic diagnosis (e.g., borderline personality disorder), or if their symptoms only occurred in the context of substance use. Further, participants with an IQ <70 or any medical or neurological disorder that could significantly affect functioning of the brain were excluded. Subjects were also excluded if they were acutely suicidal or homicidal and needed emergent care. COPE's patients are primarily referred from academic counseling centers and mental health professionals throughout the tri-State area, which included New York state, New Jersey, and Connecticut. We included 52 CHR participants for this study. Subjects received longitudinal follow up for 2.5 years (range: 1-5 years) to determine conversion status, which was assessed by face-to-face interview on a trimonthly basis using the SIPS.

An external normative healthy control group (EN-HC) was included for our calculation of CHR Z-scores on neurocognitive assessments ^{12, 13}. These participants were recruited by advertisement and they received compensation for participation in the study. Exclusion criteria were a history of any psychiatric conditions including substance use disorders, neurological diseases and major medical illness.

The Institutional Review Board at NYSPI approved this study. Before beginning any research, informed consent was obtained (informed assent and parental consent if the participant was under 18 years of age).

Assessments

Demographic information was acquired at baseline. The demographic questionnaire administered prior to the neurocognitive assessments prompted participants to choose from the following options for education level: completed less than high school; high school; technical; some college; BA/BS; or graduate school. Adjustment for education level for the neurocognitive assessments required a number of years of education. Therefore, the numbers of years of education were estimated for some of the participants. The following estimates were used: 10 years of education for “less than high school;” 12 years for “high school;” 13.5 years for “technical;” 14 years for “some college;” 16 years for “BA/BS;” and 18 years for “graduate level.”

Our neurocognitive battery assessed the following domains of neurocognitive functioning: executive functioning (computerized Stroop), attention (Continuous Performance Test-Identical Pair (CPT-IP)), working memory (computerized N-Back), processing speed (choice reaction time (CHRT)) and reaction time (simple reaction time (SRT))¹². During the SRT task, participants were instructed to react as fast as possible to visual stimuli. During the CHRT task, participants were instructed to detect in which of four boxes the stimulus was presented and to react according to specific task instructions.

The neurocognitive assessments were completed in a fixed order after subjects were assessed by the SIPS. The analyzed variables are as follows: reaction time for the SRT and CHRT, the number of correct responses on the CHRT, d-prime (measures overall sensitivity) on CPT-IP and N-back, and the interference score for Stroop.

Statistical analysis

Independent t-tests and chi-square analyses were used to assess demographic comparability between the CHR+ individuals and CHR- individuals. Subscores from SRT, CHRT, CPT-IP, N-back and Stroop were first converted into Z-scores based on normative data and adjusted for gender, age and education, and then compared in the same fashion. The scores were adjusted based on regression formulas from the EN-HC sample. Each variable had various weights for age, sex and education to create a predicted score. The predicted score was then subtracted from the actual score and divided by the standard deviation (SD) of the sample within various age groups^{12, 13}. Group comparisons of the neurocognitive tests were carried out with independent t-tests based on the normative-adjusted z-scores. The CHR Z-scores were based on the EN-HC; therefore the Z-score of the EN-HC group was 0 with an SD of 1. An index of overall neurocognitive performance was calculated by converting the each Z-scores to a negative value and then averaging these values for each participant on the six subscores.

Higher positive Z-scores for SRT, Choice Reaction Time-Reaction Time (CHRT-RT) and Stroop indicate poorer performance. Lower negative Z-scores for Choice Reaction Time-Numbers Correct (CHRT-NC), CPT-IP, N-back and overall performance indicate poorer performance.

Results

Demographics and clinical characteristics of the participants are summarized in Table 1. Group comparisons between CHR+ and CHR- revealed no significant differences for age ($p=0.13$) and gender ($\chi^2(1)=0.29$, $p=0.59$), but did reveal a significant difference for years of education ($p=0.008$; CHR- > CHR+). We estimated the years of education for 18 of the 52 participants (34.6%). During follow-up, 14 CHR participants (26.9%) converted to psychosis within 9.8 (SD=8.0) months on average, with a range of 1 to 32 months and median 9 months (Supplementary figure 1). Of the CHR+, eight converted to schizophrenia, two to a schizoaffective disorder, two to psychotic disorder NOS, one had a delusional disorder and the diagnosis of one CHR+ was missing. One of the CHR+ participants had missing time to conversion data and the diagnosis of one CHR+ is unknown. After correcting for multiple comparisons, group comparisons between CHR+ and CHR- showed no baseline differences in positive, negative, or disorganized symptoms or symptoms of general psychopathology; there were also no baseline differences in social and occupational functioning, as assessed by the Global Assessment of Functioning (modified scale).

Of the 52 CHR participants, two did not have CPT-IP data and one had missing N-back data. There was one extreme outlier (>50 SD) on the Choice RT number of correct answers, which was also omitted from the analysis. Consequently, the baseline CPT-IP consisted of 50 measurements, the N-back of 51 and the Choice RT number correct consisted of 51 measurements, instead of 52.

Table 2 shows the results of the neurocognitive measures for the different CHR groups. Overall, CHR individuals performed significantly worse on all measures in comparison to the EN-HC: SRT ($p<0.0001$), CHRT-RT ($p<0.0001$), CHRT-NC ($p<0.02$), CPT-IP ($p<0.001$), Stroop ($p<0.005$), N-back ($p<0.02$) and Overall ($p<0.0001$). There were no significant differences between the CHR+ and CHR- participants after correcting for multiple comparisons (Bonferroni). CHR+ individuals performed more poorly than the CHR- individuals on the SRT, CHRT-RT, CHRT-NC, N-back and on overall neurocognitive performance. CHR- individuals performed more poorly than CHR+ individuals on the Stroop and CPT-IP (see Figure 1 for the neurocognitive profile of the CHR groups).

Discussion

The aim of this study was to determine whether neurocognitive functioning is predictive of conversion to psychosis. Our results indicate that our CHR cohort had cognitive impairments similar to what has been reported in other CHR samples¹⁻¹⁰. However, none of the neurocognitive domains assessed at baseline (reaction time, processing speed, executive functioning, working memory, attention and overall performance) were significantly different between subjects who converted to a psychotic disorder and subjects who did not. This finding is consistent with prior findings for executive functioning and working memory in CHR subgroups^{8, 14}.

Our study was limited by its small sample size and modest conversion rate, both of which decrease the power of this study. The low conversion rate could be due to the help-seeking

nature of COPE's participants; most participants were referred from academic (school-based) settings and private clinicians for early assessment and potential intervention. Additionally, we did not examine performance on all neurocognitive domains, such as verbal memory, which has been shown to most consistently predict conversion in comparison to other domains that have more variable predictive power^{4, 15}.

In addition, although our hypotheses were made a priori to the analysis, the participants were not specially recruited for neurocognitive assessment and not all subjects recruited by COPE received the neurocognitive battery. As a result our sample was small and was not recruited to observe an effect on neurocognitive performance.

In summary, consistent with the literature, the CHR population did show overall neurocognitive deficits compared to the healthy control external comparison group. We did not find a significant neurocognitive predictor for conversion in this study.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflict of Interest: RRG is disclosing that he receives research support from Otsuka and Genentech.

References

1. Lencz T, Smith CW, McLaughlin D, et al. Generalized and specific neurocognitive deficits in prodromal schizophrenia. *Biol Psychiatry*. 2006; 59:863–71. [PubMed: 16325151]
2. Giuliano AJ, Li H, Mesholam-Gately RI, Sorenson SM, Woodberry KA, Seidman LJ. Neurocognition in the psychosis risk syndrome: a quantitative and qualitative review. *Curr Pharm Des*. 2012; 18:399–415. [PubMed: 22239571]
3. Seidman LJ, Giuliano AJ, Meyer EC, et al. Neuropsychology of the prodrome to psychosis in the NAPLS consortium: relationship to family history and conversion to psychosis. *Arch Gen Psychiatry*. 2010; 67:578–88. [PubMed: 20530007]
4. Fusar-Poli P, Borgwardt S, Bechdolf A, et al. The psychosis high-risk state: a comprehensive state-of-the-art review. *JAMA Psychiatry*. 2013; 70:107–20. [PubMed: 23165428]
5. Carrion RE, Goldberg TE, McLaughlin D, Auther AM, Correll CU, Cornblatt BA. Impact of neurocognition on social and role functioning in individuals at clinical high risk for psychosis. *Am J Psychiatry*. 2011; 168:806–13. [PubMed: 21536691]
6. Pukrop R, Klosterkötter J. Neurocognitive indicators of clinical high-risk states for psychosis: a critical review of the evidence. *Neurotox Res*. 2010; 18:272–86. [PubMed: 20405352]
7. Fusar-Poli P, Deste G, Smieskova R, et al. Cognitive functioning in prodromal psychosis: a meta-analysis. *Arch Gen Psychiatry*. 2012; 69:562–71. [PubMed: 22664547]
8. Eastvold AD, Heaton RK, Cadenhead KS. Neurocognitive deficits in the (putative) prodrome and first episode of psychosis. *Schizophr Res*. 2007; 93:266–77. [PubMed: 17467955]
9. Niendam TA, Bearden CE, Johnson JK, et al. Neurocognitive performance and functional disability in the psychosis prodrome. *Schizophr Res*. 2006; 84:100–11. [PubMed: 16563699]

10. Keefe RS, Perkins DO, Gu H, Zipursky RB, Christensen BK, Lieberman JA. A longitudinal study of neurocognitive function in individuals at-risk for psychosis. *Schizophr Res.* 2006; 88:26–35. [PubMed: 16930949]
11. Miller TJ, McGlashan TH, Rosen JL, et al. 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; 29:703–15. [PubMed: 14989408]
12. Keilp JG, Gorlyn M, Russell M, et al. Neuropsychological function and suicidal behavior: attention control, memory and executive dysfunction in suicide attempt. *Psychological medicine.* 2013; 43:539–51. [PubMed: 22781400]
13. Keilp JG, Sackeim HA, Mann JJ. Correlates of trait impulsiveness in performance measures and neuropsychological tests. *Psychiatry research.* 2005; 135:191–201. [PubMed: 15996748]
14. Frommann I, Pukrop R, Brinkmeyer J, et al. Neuropsychological profiles in different at-risk states of psychosis: executive control impairment in the early--and additional memory dysfunction in the late--prodromal state. *Schizophr Bull.* 2011; 37:861–73. [PubMed: 20053865]
15. Addington J, Barbato M. The role of cognitive functioning in the outcome of those at clinical high risk for developing psychosis. *Epidemiol Psychiatr Sci.* 2012; 21:335–42. [PubMed: 23174394]

Figure 1. Neurocognitive profiles

Neurocognitive profiles of the clinical high risk groups for psychosis. All Z-scores are transformed to a negative value. Error bars represent 95% SD. CHR, Clinical high risk; CHR+, converter CHR; CHR-, non-converter CHR; EN-HC, external normative healthy control group; SRT, Simple Reaction Time; CHRT-RT, Choice Reaction Time-Reaction Time; CHRT-NC, Choice Reaction Time-Number Correct; CPT-IP, Continuous Performance Test-Identical Pair; Overall, overall neurocognitive performance.

Table 1
Demographics and clinical characteristics

	CHR (N=52)	CHR+ (N=14)	CHR- (N=38)	P-value [†]
Age, mean (SD)	20.27 (3.47)	19.07 (3.29)	20.71 (3.46)	0.13
Gender (%male)	0.73	0.79	0.71	0.59
Education, mean (SD)	13.13 (2.14)	11.86 (2.51)	13.59 (1.80)	0.008
SIPS Total Positive, mean (SD)	14.83 (3.68)	15.64 (3.34)	14.53 (3.79)	0.34
SIPS Total Negative, mean (SD)	18.73 (5.90)	21.86 (5.52)	17.58 (5.68)	0.02
SIPS Total Disorganization, mean (SD)	10.81 (3.32)	11.93 (3.03)	10.40 (3.37)	0.14
SIPS Total General, mean (SD)	12.50 (3.86)	13.50 (3.59)	12.13 (3.93)	0.26
SIPS GAF, mean (SD), N	45.27 (5.65)	43.93 (6.70)	45.76 (5.23)	0.30

[†] CHR+ versus CHR-.

CHR, clinical high risk; CHR+, converter CHR; CHR-, non-converter CHR; GAF, Global Assessment of Functioning (modified scale); SD, standard deviation; SIPS, Structured Interview for Psychosis Risk Syndromes; bold, significant difference.

Table 2

Neurocognitive measures

	EN-HC (N=58)	CHR (N=52)	CHR+ (N=14)	CHR- (N=38)	P-value [‡]	P-value [§]
SRT [‡]	0 (1.00)	2.04 (2.18)	2.49 (2.16)	1.87 (2.19)	<0.0001	0.36
CHRT-RT [‡]	0 (1.00)	0.97 (1.46)	1.17 (1.54)	0.89 (1.44)	<0.0001	0.55
CHRT-NC [‡]	0 (1.00)	-1.09 (3.32)	-1.82 (4.85)	-0.84 (2.65)	<0.02	0.36
CPT-IP [‡]	0 (1.00)	-0.66 (0.99)	-0.21 (1.15)	-0.83 (0.88)	<0.001	<0.05
Stroop [‡]	0 (1.00)	0.67 (1.33)	0.59 (1.11)	0.70 (1.41)	<0.005	0.81
N-back [‡]	0 (1.00)	-0.59 (1.39)	-0.76 (1.76)	-0.54 (1.26)	<0.02	0.63
Overall [‡]	0 (1.00)	-1.01 (0.93)	-1.18 (1.16)	-0.96 (0.85)	>0.0001	0.46

[‡]Mean z-score (standard deviation) adjusted for years of education, age and gender.

[‡]EN-HC versus CHR.

[§]CHR+ versus CHR-.

CHR, clinical high risk; CHR+, converter CHR; CHR-, non-converter CHR; SRT, simple reaction time; CHRT-NC, choice reaction time-number correct; CHRT-RT, choice reaction time-reaction time; CPT-IP, continuous performance test-identical pair; EN-HC, external normative healthy control group; SRT, simple reaction time; bold, significant difference.