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Neurocognitive Assessments Are More Important Among Adolescents Than Adults for Predicting Psychosis in Clinical High Risk

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ABSTRACT

BACKGROUND: Few studies have examined the effects of age on neurocognition to predict conversion to psychosis in individuals at clinical high risk (CHR). This study aimed to compare the extent and predictive performance of cognitive deficits between adolescents and adults at CHR.

METHODS: A comprehensive neuropsychological battery was performed on 325 CHR individuals and 365 healthy control (HC) subjects. The subjects were first divided into 189 CHR adolescents (age 12−17 years), 136 CHR adults (age 18−45 years), 88 HC adolescents, and 277 HC adults. CHR subjects were then divided into converters (CHR-Cs) (adolescents, n = 43; adults, n = 34) and nonconverters (CHR-NCs) (adolescents, n = 146; adults, n = 102) based on their 2-year follow-up clinical status.

RESULTS: The adolescents and adults at CHR performed significantly worse than their control groups on all neurocognitive tests, except for performance on the continuous performance test in adolescents. In the comparison between adolescents and adults, patterns of neurocognitive deficits seemed to vary in HC subjects rather than in CHR subjects. In the comparison between CHR and HC subjects, the rank order of effect sizes across the neurocognitive tests was similar for the top two tests of symbol coding and verbal learning. Comparison between CHR-Cs and CHR-NCs revealed that adolescent CHR-Cs performed significantly worse than CHR-NCs on seven of eight neurocognitive tests; however, adult CHR-Cs performed significantly worse than CHR-NCs only in the visuospatial memory test.

CONCLUSIONS: The role of neurocognitive dysfunction may have different patterns and weights during the onset of psychosis in adolescents and adults at CHR, implicating the development of specific strategies that could monitor and improve cognitive function in CHR adolescents.

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Neurocognitive dysfunction has been considered a critical characteristic of individuals at clinical high risk (CHR) for psychosis, with greater impairment seen in those who eventually develop psychosis. Although there have been several studies (1–3) and meta-analyses (4,5) that demonstrate impairments of typically small to medium effects across a range of neurocognitive functions in those with CHR syndrome, an important question that has not been fully addressed in the literature is whether neuropsychological deficits among adolescents in the CHR phase have better early warning effects and greater predictive power than among adults at CHR. It would be beneficial to know whether pre-illness neurocognitive deficits in adolescents were different from adults in terms of the later conversion to psychosis.

Several studies (6–8) have shown that adolescent-onset (onset age <18 years) psychosis may be associated with more neurocognitive deficits than adult-onset psychosis. These studies included samples in the post-illness phase, thereby not addressing whether greater cognitive deficits in adolescents were the cause or effect of early-onset psychosis. In addition, the majority of individuals at CHR ages 14 to 25 years (9,10) generally covered adolescent and early adult stages, which differed greatly in the trajectory of neuropsychological development (11,12). Therefore, a decline or cessation of neurocognitive functions at different stages of the individual trajectory may lead to different outcomes. If CHR states initiated in the adolescent phase are associated with a broader range and greater severity of neurocognitive deficits, then more disruptions in developmental processes are implicated (13). A better understanding of such differences may improve the efficiency of early identification and accuracy of prediction in early psychosis.

Although the age effects on neurocognitive functions in psychosis have been widely reported (14,15), the existing literature (1,16,17) that has studied neurocognition in the CHR population treats adolescents and adults in the same way, assuming that cognitive deficits in both groups have identical meanings in either risk factor identification or prediction of

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conversion to psychosis. This study addresses these issues by assessing and comparing a wide range of neurocognitive domains between adolescents and adults in the premorbid phase of psychosis and well-matched healthy control (HC) subjects to better understand the age effects of cognitive deficits in CHR individuals. More specifically, our aims were as follows: 1) to compare the cognitive performances between adolescents and adults at CHR and HC subjects; 2) to compare the cognitive performances between CHR converter (conversion to psychosis) and nonconverter groups in adolescents and adults; and 3) to examine the predictive power of specific neurocognitive functions in adolescents and adults at CHR.

METHODS AND MATERIALS

Participants and Procedures

A total of 447 participants at CHR and 365 HC subjects aged 12 to 45 years were recruited through the extended phase of ShangHai At Risk for Psychosis (SHARP-extended) between 2016 and 2019. Of all individuals at CHR, 76 did not complete baseline neurocognitive tests, while 46 were lost to follow-up by the 2-year follow-up visit. The remaining 325 CHR participants completed neurocognitive assessments using the Chinese version of the MATRICS Consensus Cognitive Battery (MCCB) (18–20) at baseline and clinical follow-up at least 2 years later. Participants included in this analysis and those lost to attrition or without baseline neurocognitive data showed no significant differences (Table S1). Participants initially sought mental health services at the Shanghai Mental Health Center (SMHC). All participants were psychotropically naive when they were recruited. None of the participants had received any treatment for a psychiatric disorder before inclusion, and a history of drug (such as methamphetamine) abuse was an exclusion criterion in this study.

SHARP-extended followed similar procedures and criteria as SHARP (9,21,22). Potential participants were referred to the study group by the clinicians of SMHC. All procedures and consent forms were approved by the Research Ethics Committee of SMHC. Written informed consent was obtained from all participants at the recruitment stage of the study. Subjects younger than 18 years of age had their consent forms signed by their parents and provided written assent. Participants were informed that this part of the study involved a group of clinical and cognitive assessments at baseline with a naturalistic follow-up. This study did not impact routine clinical treatment procedures at SMHC. All participants from the first visit were followed up for at least 2 years after consent was obtained. Both CHR participants and their caregivers were informed that they could contact the interviewer and study clinicians any time for questions and progress reports regarding the patients' medical conditions. Except for those who did not desire any further contact, CHR participants were reassessed by telephone or face-to-face interviews every 6 months.

Measurements and Outcome

The Structured Interview for Prodromal Syndromes (SIPS) (23), followed by diagnostic consensus of the study team, was used to identify participants at CHR. In our previous studies (9,10), the Chinese version of SIPS (24), which was developed by the SHARP team, demonstrated good interrater reliability (intraclass correlation coefficient: $r = 0.96$, $p < .01$; SIPS total score) and validity (26.4% of the subjects converted to psychosis in the following 2 years) in China. The first author received SIPS certification at Yale University–sponsored SIPS training and has developed extensive expertise in its use by managing clinical assessments since the initiation of the first SHARP Chinese CHR research project.

The Chinese version of MCCB (18) was used to assess neurocognition and was administered according to the standardized guidelines provided in the test manual. Consistent with the original version of MCCB (20,25), the Chinese version of the following eight subtests were included in this study: 1) part A of the Trail Making Test (Trail Making A) (26); 2) the symbol coding of the Brief Assessment of Cognition in Schizophrenia (BACS) (27); 3) the category fluency test (28); 4) the Continuous Performance Test–Identical Pairs (CPT-IP) (29); 5) the spatial span of the Wechsler Memory Scale-III (30); 6) the revised Hopkins Verbal Learning Test (HVLT-R) (31); 7) the revised Brief Visuospatial Memory Test (BVMT-R) (32); and 8) the Neuropsychological Assessment Battery: mazes (NAB mazes) (33). Test-retest reliability in a previous Chinese psychosis sample ranged from 0.73 to 0.94 (18). Neurocognitive tests cover six domains: speed of processing (Trail Making A, BACS symbol coding, and category fluency), attention/vigilance (CPT-IP), working memory (WMS-3 spatial span), verbal learning (HVLT-R), visual learning (BVMT-R), and reasoning and problem solving (NAB mazes). A composite T score was generated using the MCCB computer program, which converts raw scores to T scores representing overall neurocognitive performance. Age- and sex-corrected Chinese norms were used according to guidelines outlined in the Chinese version of the MCCB manual. Due to the MCCB being used here for assessing neurocognition, the Mayer-Salovey-Caruso Emotional Intelligence Test, which was designed for social cognition, was not included.

Conversion to psychosis was the primary outcome used in the SHARP-extended study, based on the criteria for the presence of psychotic symptoms syndrome (34), as identified by the SIPS/Scale of Prodromal Symptoms. Conversion was identified when the subject showed a level-6 positive symptom (severe and psychotic, present with full conviction) that was either dangerous, disorganized, or occurring at an average of at least 1 hour/day more than 4 days in a week. Outcome determination was based mainly on face-to-face ($n = 227$) or telephone interviews ($n = 98$), depending on the wishes of the participant. Individuals cited three main reasons for being reluctant to visit the hospital for a face-to-face interview: 1) the hospital reminded them of unpleasant past experiences and stigma ($n = 56$); 2) they lacked time or lived a long way from the hospital ($n = 32$); and 3) they considered it unnecessary to see a doctor once symptoms remitted ($n = 8$). Two individuals gave no reason to refuse their face-to-face interviews.

Data Analysis

We attempted to compare cognitive performance between adolescents and adults. CHR and HC individuals were first divided into four groups: CHR adolescents or HC adolescents (12–17 years) and CHR adults or HC adults (18–45 years).

Table 1. Baseline Demographic, Clinical, and Cognitive Variables, Comparison Between Adolescents and Adults

Variables	HC Adolescents	HC Adults	HC Adolescents vs. HC Adults		CHR Adolescents	CHR Adults	CHR Adolescents vs. CHR Adults	
			t/χ^2	p			t/χ^2	p
Participants, *n*	88	277	–	–	189	136	–	–
Demographic Variables								
Age, years, mean (SD)	15.9 (1.2)	24.5 (5.3)	t = 15.115	<.001	15.6 (1.3)	23.5 (5.0)	t = 20.673	<.001
Male, *n* (%)	43 (48.9%)	140 (50.5%)	χ^2 = .075	.784	82 (43.4%)	68 (50.0%)	χ^2 = 1.392	.238
Clinical Variables, Mean (SD)								
Positive symptoms	–	–	–	–	10.1 (3.5)	9.8 (3.3)	t = 0.935	.351
Negative symptoms	–	–	–	–	12.7 (5.8)	11.6 (6.0)	t = 1.646	.101
Disorganized symptoms	–	–	–	–	6.7 (3.3)	6.2 (2.9)	t = 1.249	.213
General symptoms	–	–	–	–	9.0 (3.2)	9.2 (2.7)	t = 0.697	.486
Cognitive Variables, Mean (SD)								
Trail making A	27.7 (9.3)	27.6 (9.8)	t = 0.157	.875	33.5 (14.8)	34.0 (11.9)	t = 0.345	.730
BACS symbol coding	64.5 (9.6)	64.1 (10.6)	t = 0.367	.714	58.0 (10.3)	55.9 (10.6)	t = 1.749	.081
Category fluency	21.6 (5.0)	23.0 (5.4)	t = 2.308	.022	19.2 (5.1)	19.7 (5.5)	t = 0.938	.349
CPT-IP	2.6 (0.7)	2.9 (0.6)	t = 3.929	<.001	2.4 (0.8)	2.5 (0.8)	t = 1.067	.287
WMS-3 spatial span	17.5 (3.3)	16.7 (2.9)	t = 2.242	.026	15.6 (3.2)	15.5 (2.9)	t = 0.434	.664
HVLT-R	26.9 (3.6)	26.2 (4.3)	t = 1.434	.153	23.8 (5.4)	23.1 (4.7)	t = 1.133	.258
BVMT-R	30.1 (4.4)	28.1 (5.3)	t = 3.163	.002	27.3 (6.1)	24.8 (6.6)	t = 3.499	.001
NAB mazes	19.7 (4.8)	19.0 (5.4)	t = 1.216	.225	16.8 (6.6)	15.7 (6.2)	t = 1.511	.132
Cognitive Domains T Scores, Mean (SD)								
Speed of processing	57.7 (7.9)	58.7 (8.0)	t = 1.057	.291	53.4 (8.2)	52.6 (8.1)	t = 0.855	.393
Attention/vigilance	51.7 (9.3)	55.4 (7.6)	t = 3.814	<.001	50.1 (9.5)	51.3 (9.9)	t = 0.950	.343
Working memory	51.7 (10.4)	49.1 (9.4)	t = 2.200	.028	46.3 (10.0)	45.9 (9.1)	t = 0.410	.682
Verbal learning	53.1 (6.8)	51.8 (8.2)	t = 1.357	.176	48.4 (9.5)	47.2 (8.4)	t = 1.141	.255
Visual learning	59.6 (6.7)	56.8 (7.7)	t = 3.074	.002	56.4 (8.2)	53.2 (9.0)	t = 3.400	.001
Reasoning and problem-solving	58.9 (8.2)	57.8 (8.6)	t = 1.101	.272	55.3 (10.0)	53.5 (9.5)	t = 1.606	.109
Composite score	57.0 (7.0)	56.4 (7.2)	t = 0.625	.532	52.2 (8.5)	51.0 (7.6)	t = 1.231	.219

BACS, Brief Assessment of Cognition in Schizophrenia; BVMT-R, Brief Visuospatial Memory Test–Revised; CHR, clinical high risk for psychosis; CPT-IP, Continuous Performance Test–Identical Pairs; HC, healthy control; HVLT-R, Hopkins Verbal Learning Test–Revised; NAB, Neuropsychological Assessment Battery; WMS-3, Wechsler Memory Scale–Third Edition.

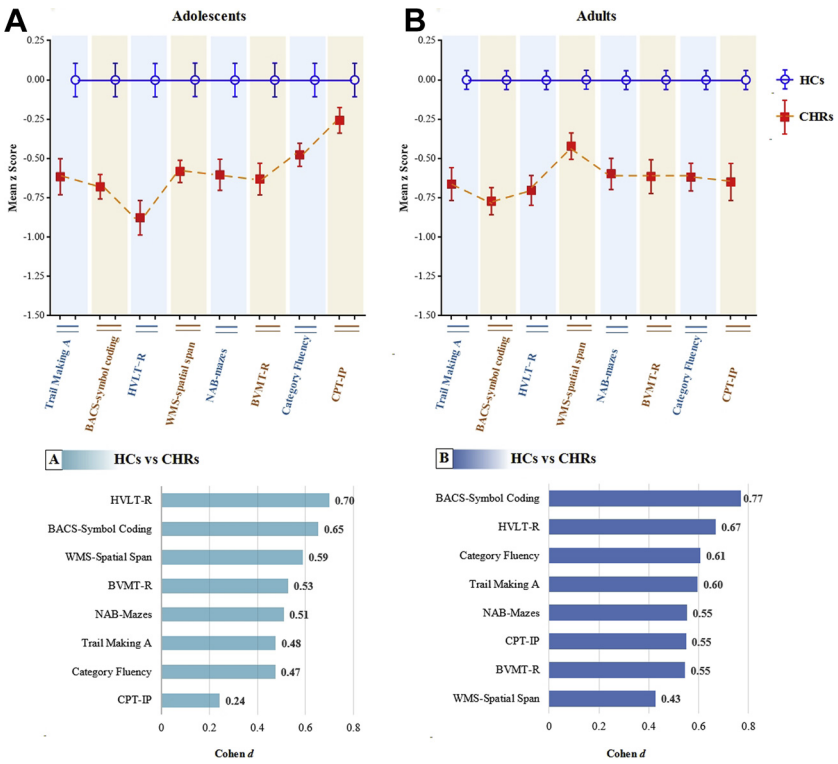

Figure 1. Neuropsychological profile and effect sizes (Cohen's *d*) for comparisons of **(A)** adolescent and **(B)** adult groups of clinical high risk (CHR) and healthy control (HC) subjects. Mean scores were standardized with HC subjects' mean (SD) to convert to *z* score. Effect sizes are rank ordered from largest to smallest. BACS, Brief Assessment of Cognition in Schizophrenia; BVMT-R, Brief Visuospatial Memory Test–Revised; CPT-IP, Continuous Performance Test–Identical Pairs; HVLT-R, Hopkins Verbal Learning Test–Revised; NAB, Neuropsychological Assessment Battery; WMS, Wechsler Memory Scale.

Demographic, baseline clinical features, and neurocognitive performance are presented and compared separately. The metric of each neurocognitive test score is as follows: Trail Making A, time to completion; BACS symbol coding, total number correct; category fluency, total number of animals named in 60 seconds; CPT-IP, mean d′ value across 2-, 3-, and 4-digit conditions; WMS-3 spatial span, sum of raw scores on forward and backward conditions; HVLT-R, total number of words recalled correctly over three learning trials; BVMT-R, total recall score over three learning trials; and NAB mazes, total raw score (25). First, neurocognitive performance was compared between adolescents and adults at CHR and HC subjects (Table 1). Second, comparisons between CHR participants and HC subjects were conducted in the adolescent and adult groups (Figure 1). Mean scores of CHR were standardized with mean (SD) of adolescent/adult HC groups separately to convert to the *z* score. Third, comparisons between converters and nonconverters were conducted separately for adolescents and adults at CHR (Table 2). Effect sizes were calculated using Cohen's *d* for mean comparisons (Figure 2). Fourth, considering the differences in scores of negative and disorganized symptoms identified in the comparisons between converters and nonconverters, these potential confounders were controlled for using multivariate analysis of variance. Corrected scores of cognitive variables were further compared, and marginal means were presented in the radar map (Figure 3). Finally, receiver operating characteristic (ROC) analysis was used to test whether the individual neurocognitive test distinguished between converters and nonconverters. The predictive value of these tests was determined according to the area under the ROC curve (Figure 4).

RESULTS

Demographic, Clinical, and Cognitive Characteristics

Within the HC group, adolescents performed significantly worse than the adult group on category fluency and CPT-IP but significantly better on WMS-3 spatial span and BVMT-R (Table 1). Within the CHR group, adults performed significantly worse than the adolescent group on the BVMT-R test.

Neuropsychological Profile and Comparisons Between CHR Participants and HC Subjects

Both the CHR adolescents and CHR adults demonstrated significantly poorer performances than the HC subjects on all eight neurocognitive tests (Figure 1), except for performance on the CPT-IP test in adolescents (t = 1.846, p = .066). The effect sizes across the eight neurocognitive tests for comparisons between HC and CHR participants from adolescent and adult groups are presented in Figure 1. The top two tests of BACS symbol coding and HVLT-R with maximum effect size were identical in the adolescent and adult groups.

Neuropsychological Profile and Comparisons Between CHR-Cs and CHR-NCs

Overall, the conversion rate was 23.7% (77/325) in the overall sample, 22.8% (43/189) in CHR adolescents, and 25.0%

Table 2. Baseline Demographic, Clinical, and Cognitive Variables, Comparison Between CHR-Cs and CHR-NCs

	Adolescents				Adults			
			CHR-Cs vs. CHR-NCs				CHR-Cs vs. CHR-NCs	
Variables	CHR-Cs	CHR-NCs	t/χ^2	p	CHR-Cs	CHR-NCs	t/χ^2	p
Participants, *n*	43	146	–	–	34	102	–	–
Demographic Variables								
Age, years, mean (SD)	15.7 (1.1)	15.6 (1.4)	$t = 0.062$	.951	22.6 (5.1)	23.8 (4.9)	$t = 1.240$	.217
Male, *n* (%)	23 (53.5%)	59 (40.4%)	$\chi^2 = 2.313$	.1284	20 (58.8%)	48 (47.1%)	$\chi^2 = 1.412$	.235
Clinical Variables, Mean (SD)								
Positive symptoms	10.7 (3.4)	10.0 (3.6)	$t = 1.240$	.216	10.4 (2.8)	9.6 (3.4)	$t = 1.326$	.187
Negative symptoms	15.2 (5.4)	11.9 (5.6)	$t = 3.432$	.001	12.7 (6.8)	11.2 (5.7)	$t = 1.314$	.191
Disorganized symptoms	7.7 (2.8)	6.3 (3.3)	$t = 2.473$	.014	6.3 (2.9)	6.2 (2.9)	$t = 0.103$	.918
General symptoms	9.0 (3.0)	9.0 (3.2)	$t = 0.022$	.982	8.8 (2.4)	9.3 (2.8)	$t = 0.996$	.321
Cognitive Variables, Mean (SD)								
Trail making A	38.0 (17.3)	32.2 (13.7)	$t = 2.316$	.022	34.4 (10.7)	33.9 (12.4)	$t = 0.219$	.827
BACS symbol coding	56.2 (10.9)	58.5 (10.1)	$t = 1.271$	.205	53.5 (11.2)	56.7 (10.4)	$t = 1.519$	.131
Category fluency	19.2 (5.1)	19.1 (5.1)	$t = 0.101$	.920	19.4 (6.0)	19.8 (5.4)	$t = 0.338$	.736
CPT-IP	2.3 (0.7)	2.4 (0.8)	$t = 1.169$	.244	2.6 (0.9)	2.5 (0.8)	$t = 0.454$	.650
WMS-3 spatial span	16.1 (3.3)	15.5 (3.3)	$t = 1.049$	.295	15.3 (2.5)	15.5 (3.0)	$t = 0.362$	.718
HVLT-R	23.2 (5.8)	23.9 (5.2)	$t = 0.801$	.424	23.1 (4.6)	23.1 (4.8)	$t = 0.031$	.975
BVMT-R	24.9 (6.6)	28.0 (5.8)	$t = 2.972$	.003	22.0 (7.4)	25.8 (6.1)	$t = 2.904$	.004
NAB mazes	14.6 (7.0)	17.5 (6.3)	$t = 2.621$	.009	15.6 (6.5)	15.8 (6.1)	$t = 0.127$	.899
Cognitive Domains T Scores, Mean (SD)								
Speed of processing	51.9 (8.7)	53.8 (8.0)	$t = 1.372$	.172	51.5 (9.4)	53.0 (7.6)	$t = 0.922$	.358
Attention/vigilance	48.7 (8.6)	50.7 (9.8)	$t = 1.201$	.231	52.1 (11.0)	51.1 (9.5)	$t = 0.504$	.615
Working memory	47.7 (8.4)	45.9 (10.4)	$t = 1.038$	.301	45.3 (8.0)	46.1 (9.4)	$t = 0.419$	.676
Verbal learning	47.4 (10.3)	48.7 (9.2)	$t = 0.764$	.446	47.2 (8.1)	47.3 (8.6)	$t = 0.032$	.974
Visual learning	53.2 (8.9)	57.4 (7.8)	$t = 2.997$	.003	49.3 (10.0)	54.5 (8.3)	$t = 2.985$	.003
Reasoning and problem solving	51.7 (10.8)	56.3 (9.6)	$t = 2.680$	.008	53.4 (10.0)	53.6 (9.4)	$t = 0.109$	.913
Composite score	50.1 (8.3)	52.8 (8.4)	$t = 1.812$	.072	50.1 (8.9)	51.3 (7.2)	$t = 0.811$	.419

BACS, Brief Assessment of Cognition in Schizophrenia; BVMT-R, Brief Visuospatial Memory Test–Revised; C, converter; CHR, clinical high risk for psychosis; CPT-IP, Continuous Performance Test–Identical Pairs; HVLT-R, Hopkins Verbal Learning Test–Revised; NAB, Neuropsychological Assessment Battery; NC, nonconverter; WMS-3, Wechsler Memory Scale–Third Edition.

(34/136) in CHR adults. In the adolescents, the CHR-C group performed significantly worse than the CHR-NC group on the Trail Making A ($t = 2.316$, $p = .022$), NAB-maze ($t = 2.621$, $p = .009$), and BVMT-R ($t = 2.972$, $p = .003$) tests. In adults, the CHR-C group performed significantly worse than the CHR-NC group only on the BVMT-R ($t = 2.904$, $p = .004$) test (Table 2 and Figure 2). The top test of the BVMT-R with maximum effect size for comparisons between converters and nonconverters was identical in adolescents and adults.

For further comparison, scores of negative symptoms and disorganized symptoms were controlled using multivariate analysis of variance because CHR-Cs and CHR-NCs differed at baseline. In CHR adolescents, CHR-Cs demonstrated significantly poorer performance than CHR-NCs on neurocognitive tests, except for the WMS-3 spatial span test (Figure 3A). However, in CHR adults, CHR-Cs demonstrated significantly poorer performances than CHR-NCs on the BVMT-R tests (Figure 3B).

Discrimination of the Conversion Outcome

After adjusting for the clinical symptoms, the ROC analysis for each cognitive test resulted in an area under the ROC curve ranging from 0.661 to 0.707, which were all significant in the discrimination of the conversion outcome in CHR adolescents (Figure 4). None of the cognitive tests reached a significant level in the ROC analysis of CHR adults.

DISCUSSION

Although neurocognitive deficits have been widely used to predict psychosis from CHR status, very few studies have been conducted specifically for comparisons of cognitive performance between adolescents and adults at CHR. To our knowledge, this study is one of the largest sample sizes in which both the adolescent and adult CHR groups were matched to adolescent and adult HC groups, respectively. This study was based on a drug-naive CHR cohort sample at their first contact with mental health service, which is another strength of this study. This avoided the significant impact on neurocognition due to confounding factors of medications. Furthermore, this CHR sample excluded psychotic symptoms caused by substance abuse, such as methamphetamine, which can better reflect the neurocognitive functions of primary psychotic disorders.

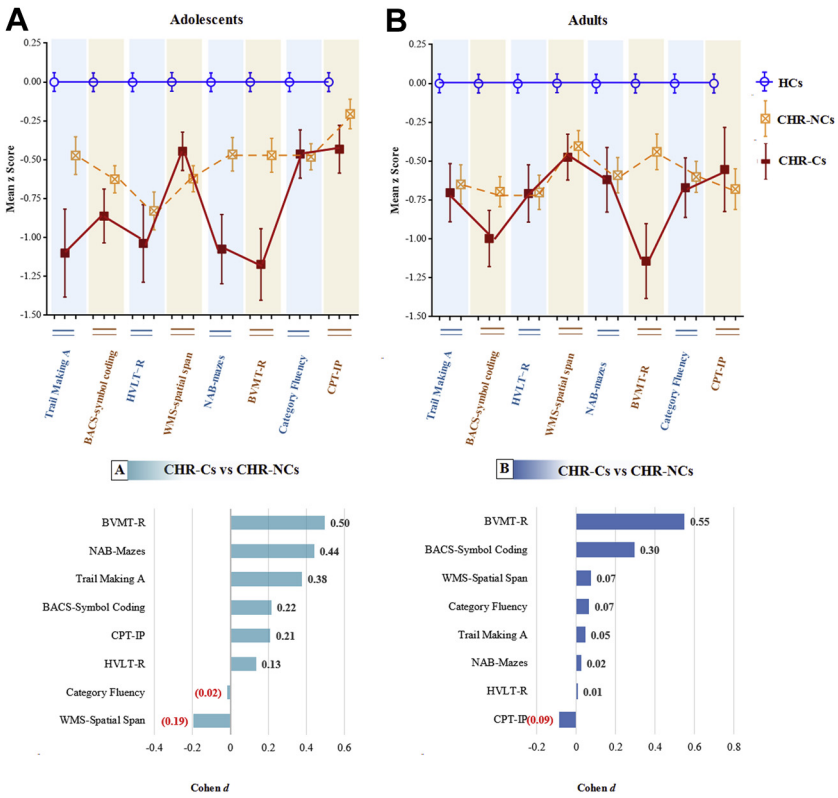

Figure 2. Neuropsychological profile and effect sizes (Cohen's *d*) for comparisons of **(A)** adolescent and **(B)** adult clinical high-risk converters to psychosis (CHR-Cs), clinical high-risk nonconverters (CHR-NCs), and healthy control (HC) subjects. Mean scores were standardized with HC subjects' mean (SD) to convert to *z* score. Effect sizes are rank ordered from largest to smallest. BACS, Brief Assessment of Cognition in Schizophrenia; BVMT-R, Brief Visuospatial Memory Test–Revised; CPT-IP, Continuous Performance Test–Identical Pairs; HVLT-R, Hopkins Verbal Learning Test–Revised; NAB, Neuropsychological Assessment Battery; WMS, Wechsler Memory Scale.

Key Findings

The first aim of this study was to compare a wide range of neurocognitive functions in two groups of CHR adolescents and CHR adults at their first admission to mental health services. The two groups varied in the level of severity and the affected domains when comparing CHR participants with HC subjects, especially in the comparison between CHR converters and nonconverters. The neurocognitive functions in adolescents at CHR showed more significant impairments and were associated with a higher risk of conversion to psychosis. The results of this comparative analysis were consistent between the two groups that declined performance on the BVMT-R test and may be considered particularly important markers for predicting psychosis in the CHR stage. This result was highly consistent with the results of the NAPLS-2 (North American Prodromal Longitudinal Study phase 2) (35), suggesting a central role for visual learning abilities in the development of psychosis from the CHR stage. The results were also consistent with our recent findings that the BVMT-R test is a significant independent predictor of psychosis prediction when included in a risk calculator algorithm (36).

Adolescents Versus Adults

The comparison of neurocognitive functions between adolescents and adults in the HC and CHR groups separately reflects the age effects in the two groups. Patterns of neurocognitive deficits seemed to vary in the HC group rather than in the CHR group. Such variation in HC subjects is not simply because one group is better than the other group, but because adolescents and adults show advantages in different neurocognitive domains. However, we found that only the BVMT-R test differed significantly between the two groups, and CHR adolescents performed better than CHR adults. Our findings revealed an age effect in the development of neurocognitive functions, which were dynamic (37) and not balanced over all domains (38). A possible explanation for such diverse neurocognitive performances between adolescent and adult HC subjects were not replicated in CHR participants, which may be due to floor effects caused by the broad and significant neurocognitive deficits in the CHR sample. Consistent with findings from an adolescent HC sample (ages 12–19 years) of NAPLS-2, adolescents generally showed improvement with age in most MCCB cognitive domains, except BVMT-R and HVLT-R (39). The BVMT-R score did not change significantly in adolescent HC subjects of NAPLS-2, contrary to our adolescent HC subjects who performed significantly better than the adult group in the BVMT-R test. BVMT-R performance can show a different or even opposite trend of age change compared with other tests.

CHR Versus HC Subjects

The comparison of neurocognitive functions between CHR and HC participants reflects the neurocognitive characteristics of individuals during CHR. As expected, neurocognitive deficits were present in the entire CHR sample and suggested that

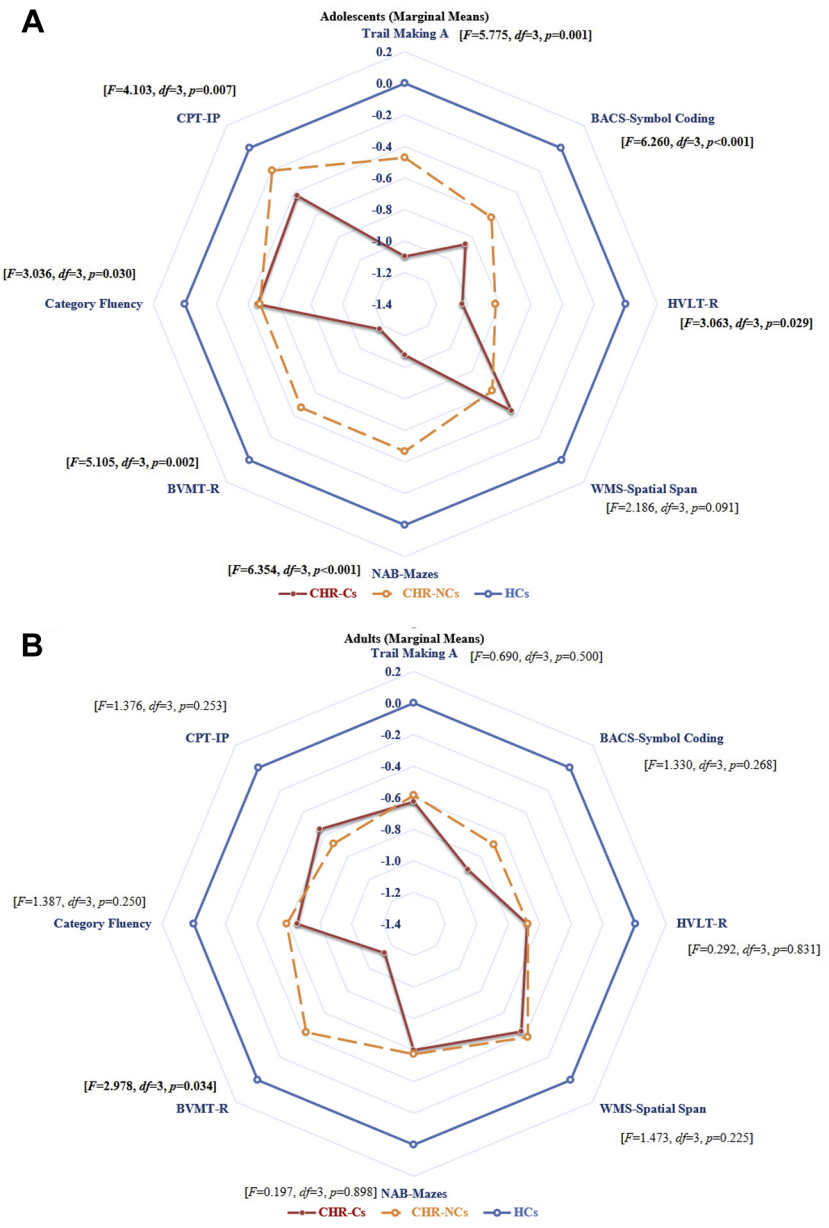

Figure 3. Neuropsychological comparisons between **(A)** adolescent and **(B)** adult groups of clinical high-risk converters to psychosis (CHR-Cs) and clinical high-risk nonconverters (CHR-NCs) adjusted for scores of negative and disorganized symptoms. Marginal means from multivariate analysis of variance were standardized with healthy control (HC) subjects' means (SDs) to convert to *z* score. BACS, Brief Assessment of Cognition in Schizophrenia; BVMT-R, Brief Visuospatial Memory Test–Revised; CPT-IP, Continuous Performance Test–Identical Pairs; HVLT-R, Hopkins Verbal Learning Test–Revised; NAB, Neuropsychological Assessment Battery; WMS, Wechsler Memory Scale.

neurocognitive decline may not only be a consequence of psychosis but also precedes psychotic development and contributes to the onset of psychosis (40,41). Although the patterns of neurocognitive deficits were not consistent between adolescents and adults in the comparisons of CHR and HC participants, the performances in the BACS symbol coding and HVLT-R tests were the top two poorest neurocognitive deficits that were identical in both age groups (Figure 1). BACS symbol coding and HVLT-R, included in the speed of processing and verbal learning domains, represent executive functioning and working memory abilities. In agreement with previous research (42–47), these neurocognitive domains represent major features of cognitive dysfunction among patients with schizophrenia. Our findings suggest that executive functioning and working memory abilities, as measured by BACS symbol coding and HVLT-R, may be particularly valuable in capturing CHR states, which may be more associated with state markers, while BVMT-R may be more associated with a trait marker.

Converter Versus Nonconverter

In both adolescents and adults at CHR in the comparison of CHR-Cs and CHR-NCs, our results showed that BVMT-R may be considered a particularly important trait marker of risk in the CHR stage for predicting psychosis. Our findings are in line with

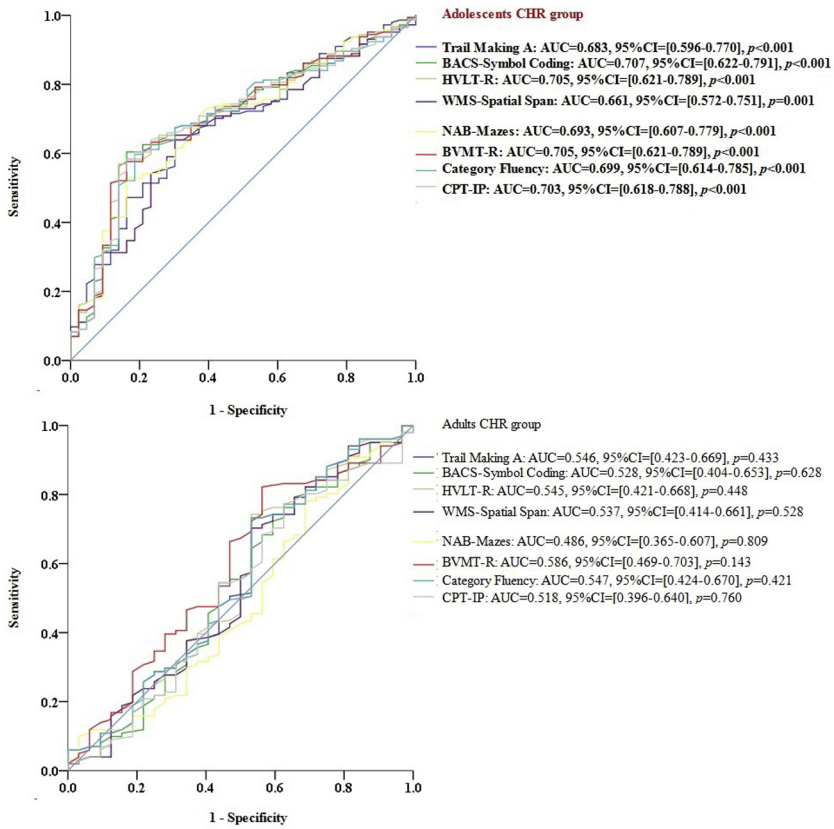

Figure 4. Receiver operating characteristic curve profiles for neurocognitive tests in terms of discrimination of the conversion outcome. The scores of cognitive variables were adjusted for scores of negative and disorganized symptoms. AUC, area under the receiver operating characteristic curve; BACS, Brief Assessment of Cognition in Schizophrenia; BVMT-R, Brief Visuospatial Memory Test–Revised; CHR, clinical high risk; CPT-IP, Continuous Performance Test–Identical Pairs; HVLT-R, Hopkins Verbal Learning Test–Revised; NAB, Neuropsychological Assessment Battery; WMS, Wechsler Memory Scale.

some previous study results (17,35,36), showing a worse performance for CHR-Cs than for CHR-NCs in the BVMT-R test. The CHR-C adolescents had more severe negative and disorganized symptoms than the CHR-NC adolescents. Thus, when clinical symptoms were accounted for, our results (Figure 3) showed a clearer picture of neurocognitive heterogeneity between adolescents and adults for comparisons of CHR-Cs and CHR-NCs. Compared with adults, adolescents at CHR show a broader range of neurocognitive dysfunction. In contrast, differences between CHR-C and CHR-NC adults were limited to BVMT-R. Consistently, in the ROC method, all neurocognitive tests contributed significantly to the discrimination of conversion in CHR adolescents, but none of them was significant in adults (Figure 4). Overall, neurocognitive assessments for predicting conversion are much better in adolescents than in adults, possibly indicating that neurocognitive developmental trajectories play a more important role in adolescent-onset psychosis. Inconsistent with the finding of Carrion *et al.* (48), they found that the CHR-C group performed significantly poorer in BVMT-R than the CHR-NC group, and only the HVLT-R test predicted conversion. The main reason for this inconsistency may be the different severities of CHR samples. In Carrion's study, only 12 patients at CHR progressed to psychosis (12/175, 6.85%), showing a significantly lower conversion rate than reported in our sample (23.7%). The low conversion rate may be attributable to the greater number of CHR individuals who were identified as false positives (49).

Limitations

There are several limitations to this study. First, our sample was recruited from a single site; although it has the advantage of homogeneity, the generalizability of the findings is limited. Second, it is also important to note that the SHARP-extended cohort was surveyed naturalistically, meaning that the various medications individuals took with varying compliance during the follow-up period may have affected the natural trajectory of illness and the presentation of symptoms and syndromes measured during clinical outcome assessments. Third, our sample was psychotropically naive when they entered the study, with no history of drug abuse or dependence. This may limit the generalizability of our findings to CHR individuals with a history of drug abuse or prior psychotropic medication use. Fourth, the specific effects of cultural variation on performance on these tasks are not sufficiently known, highlighting the possibility of cultural bias. Finally, no objective intelligence quotient test was performed during the screening procedure. Whether or not this limitation affects these findings of discrepancies in cognitive deficits is unknown.

Conclusions

In summary, this study further demonstrates that neurocognitive deficits in CHR adolescents are more associated with conversion to psychosis than in adults. Age-related differences should be considered when using cognitive variables

in psychosis prediction. Therefore, clinicians may need to be particularly vigilant to cognitive decline as early signs of psychosis, especially in adolescents at CHR. This may also be an important clue to develop specific strategies that could monitor and improve cognitive functions in adolescents who are at high risk of psychosis.

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ARTICLE INFORMATION

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