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ORIGINAL CONTRIBUTION

Variability of ecological executive function in children and adolescents genetically at high risk for schizophrenia: a latent class analysis

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Abstract
Executive impairments have been observed both in patients with schizophrenia and in their unaffected first-degree relatives. Very few studies have investigated neurocognitive subgroups in unaffected first-degree relatives and in healthy participants using data-driven methods. The study included a high-risk group consisting of 100 unaffected young offspring and siblings of patients with schizophrenia and 198 healthy controls, all aged between 9 and 23 years. Executive function, victimization, and emotional and behavioral problems of participants were assessed by a series of self-report scales. Neurocognitive subgroups were investigated using latent class analysis of executive function measures. Four neurocognitive clusters were identified: a good performance cluster, a good self-control cluster, a low self-control cluster, and a severe impairment cluster. Participants in severe impaired executive function cluster reported a significantly higher level of victimization and had more prominent emotional and behavioral problems than the good performance cluster. Neurocognitive differences between high-risk young people and healthy controls were driven by individuals who have severe and global, rather than selective, executive deficits. Our results may provide clues to an explanation of the mechanisms behind executive impairments in young individuals at genetic risk and help to identify new targets for early interventions.

Keywords Schizophrenia · Executive function · Neurocognitive disorder · Adolescence

Abbreviations

EF	Executive function
HR	High risk
HC	Healthy control
LCA	Latent class analysis
LC	Latent class
SPSS	Statistical Package for Social Sciences

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Introduction

Schizophrenia is a complex behavioral and cognitive syndrome, induced by a variety of genetic and environmental factors [1]. Because it is difficult to define the various types of phenotypic and etiologic heterogeneity, misclassification errors occur in both affected and non-affected participants, reducing the power of the analytical approach [2]. An alternative strategy for improving categorical identification in the context of psychiatric genetics is to use endophenotypes. An endophenotype is a highly heritable characteristic that approximates the genetic liability of a complex disease in unaffected individuals, and may provide a unique opportunity for exploring the relationship between genetic risk loci and the elusive disease phenotype over the life course [3].

In line with the criteria for endophenotypes [4], neurocognitive features are heritable and present prior to the onset of schizophrenia [5]. Additionally, neurocognitive status is more reliable and suitable than symptom profiles for recognizing this illness [6]. Thus, identifying the nature of executive function (EF) among individuals at familial risk for schizophrenia is relevant to the etiology and pathophysiology of the disease, capturing something important and meaningful. The peak risk for schizophrenia usually occurs in late adolescence or early adulthood [7]. Therefore, exploring the neurocognitive characteristics of younger participants (age < 30) at high risk is particularly important [8].

Sufficient evidence has been collected to establish that relatively moderate deficits in executive functioning are widely observed in those genetically predisposed to schizophrenia [9–11]. These EF deficits are generally found to be ubiquitous in studies on schizophrenia families, and their heterogeneity is rarely investigated. Usually, participants are sorted into impaired and unimpaired groups based on total scores or arbitrary cut-off scores [12]. However, there are also some less consistent results suggesting the possibility of the existence of heterogeneity in this area among the unaffected relatives of patients with schizophrenia. Wagshal et al. [13] found that ten adult first-degree relatives of patients with schizophrenia did not differ from healthy controls in accuracy or reaction time on the weather prediction task. Making an attempt to identify the nature and profile of EF in the first-degree relatives of patients with schizophrenia may hasten the discovery of a valid phenotype for cognitive impairment, particularly within those unaffected by the disease. Identifying more specific subgroups with satisfactory discrimination could also help lead clinicians and researchers to the development of more effective and tailored therapeutic strategies instead of a "one size fits all" approach to intervention [14].

Reviewing previous similar studies of EF in the high-risk population, data have commonly been collected using highly structured neuropsychological tasks [6], an approach which increases the risk of underestimating the complexities of EF in real-world settings [15]. Furthermore, to our knowledge, cluster analysis has rarely been conducted in a mixed sample including people both at risk and not at risk of schizophrenia. Without such a sample, it is hard to tell whether any of the clusters are more specifically connected to nonpsychotic participants at familial risk for schizophrenia than to controls. Taking the above into overall account, in the present study, we primarily aimed to investigate subgroups with different EF profiles, assessed from an ecological perspective using self-report rating scales, in a young sample of nonpsychotic first-degree relatives of patients with schizophrenia as well as healthy controls. To our knowledge, no studies on young individuals at high risk for developing schizophrenia have ever analyzed executive functioning using latent class analysis. Our secondary aim was to discuss and interpret distinct characteristics of the latent classes, including demographic profiles and emotional and behavioral problems. These descriptive findings could be useful to enrich the extant theories of familial, genetic, and neurocognitive characteristics associated with schizophrenia.

Methods

Participants

We used data from a cross-sectional study on cognitive function in adolescents genetically at high risk for schizophrenia (i.e., nonpsychotic first-degree relatives of patients with schizophrenia) [12]. All participants included were required to be under 25 years old. Among the 360 families who met the criteria for this study, 256 (71.1%) declined to participate. Of the remaining families, 100 (27.8%) adolescent offspring and siblings of patients diagnosed with schizophrenia provided complete data. In this HR group, 24 participants (24.0%) had a father who had been diagnosed with schizophrenia, 38 (38.0%) a mother, and 38 (38.0%) a sibling. All HR subjects had only one schizophrenia relative.

Inclusion as a schizophrenic parent or sibling of a high-risk participant required meeting a combination of criteria, including being (1) diagnosed with schizophrenia in accordance with the International Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) [16] by child or adult psychiatrists in the Mental Health Center, and (2) without comorbidity of other psychiatric disorders. We recruited the high-risk sample through the inpatient unit of the adult Psychiatry Department and the Child and Adolescent Psychiatry and Psychology Department of the Mental Health Center of Shandong Province between January 2011 and June 2013. The healthy control sample was recruited via fliers posted at an elementary, junior high, and senior high school in a city of Shandong Province.

Identical exclusion criteria were used for both the high-risk and the healthy control groups: any current or past psychiatric disease; head injury with loss of consciousness or neurological disease (including seizure disorder); medical condition or medication known to affect cognitive function; current or past alcohol/substance dependence or abuse; intellectual disability; lifetime exposure to antipsychotic medications or other psychiatric medications; and difficulties with language comprehension.

Procedures

In this study, child and adolescents completed all the measures through telephone or face-to-face survey, which were conducted by research staff who received rigorous training prior to fieldwork. Medical records of the participated children and adolescents were obtained from their healthy parents. Parents and/or siblings of the healthy control group adolescents were also asked whether they had a medical history of any psychiatric disorder.

Ethical considerations

The protocol for this study was approved by the Shandong University School of Nursing ethical review board before data collection. Prior to participation, all relatives, healthy volunteers, and their legal guardians gave their written informed consent.

Measures

Behavior Rating Inventory of Executive Function Self-Report version (BRIEF-SR)

The BRIEF-SR [17] is an 80-item self-report questionnaire that provides valuable ecological insight for identifying EF in everyday environments, including home and school. The Global Executive Composite (GEC) is an overall score, and the items further comprise eight non-overlapping clinical subdomains (inhibit, shift, emotional control, working memory, monitor, plan/organize, organization of materials, and task completion). For analysis in the current study, raw scores were converted to *T* scores for each of the eight subscales [18]; Cronbach's alpha was 0.90 for all subscales and 0.94 for all items.

The Chinese version of the Juvenile Victimization Questionnaire (JVQ)

The Chinese version of the JVQ contains 34 screening items relating to offenses against youth, covering five general areas of victimization: conventional crime, child maltreatment, peer and sibling victimization, sexual victimization, and witnessing and indirect victimization [19]. When administered to school-aged Chinese adolescents, the Chinese JVQ showed acceptable internal consistency ($\alpha = 0.63$–0.97) [20]. In the current study, the sexual victimization module was excluded and the Cronbach's alpha of the remaining items was 0.78. To facilitate analysis, scores were grouped into three victimization levels: no victimization (item scores = 0), low victimization ($4 \geq$ item scores ≥ 1), and high victimization (item scores ≥ 5).

Strengths and difficulties questionnaire (SDQ)

The SDQ is commonly used in screening for DSM-IV behavioral and emotional disorders in children and adolescents. The total difficulties measure used in the present study is obtained by summing the scores of four subscales (emotional symptoms, conduct problems, hyperactivity/inattention, and peer relationship problems). Higher scores on the total difficulties measure reflect more emotional or behavioral difficulties [21]. A satisfactory internal consistency coefficient (Cronbach's alpha) was observed in SDQ total difficulties ($\alpha = 0.77$) and in all subscales ($\alpha = 0.72$–0.76) [22].

Statistical analyses

Statistical analyses were conducted using SPSS (Statistical Package for the Social Sciences, Chicago, IL, USA) version 20.0 and Latent Gold-4.5 software (Statistical Innovation, Belmont, MA, USA). Differences between various groups in relation to demographic variables, JVQ item-level scores, and total difficulties scores were calculated using one-way ANOVAs and Chi-squared tests. The scores of EF were standardized by conversion to *Z* scores relative to the mean and standard deviation (SD) of the healthy control group. All statistical tests were two tailed (significance level of $P < 0.05$).

Latent class analysis

Latent class analysis (LCA) is a person-centered statistical approach for grouping multivariate categorical data into their most likely latent classes and estimating their parameters [23]. Use of LCA in the study of children and adolescents [24] is growing, and Miyake et al. proposed that the latent variable approach has important advantages in testing EF [25]. Compared with traditional clustering techniques such as K-means, LCA yields a lower Type I error rate, a smaller misclassification rate, and a more objective determination of the number of clusters [26, 27]. In this study, we applied LCA in participants who completed all questionnaire items (100 in the high-risk group and 198 in the healthy control group). To present participants' levels of executive functioning in each of the eight aspects in a more intuitively accessible fashion, the levels of participants' executive functioning in each of the eight aspects were given in the form of *T* scores ($M = 50$, $SD = 10$) [28].

Results

Sample characteristics

Table 1 shows the demographic and clinical characteristics of the high-risk and healthy control groups. The groups did not differ in gender, ethnicity, educational background, academic achievement, or socioeconomic status. Compared with their not-at-risk counterparts, participants in the high-risk group were slightly older and more likely to be only children ($P < 0.05$). However, all participants were between 9 and 23 years old, and age was controlled for during our analyses. The high-risk group had a significantly higher mean score than the healthy control group on GEC ($P = 0.037$, Cohen's $d = 0.25$). Regarding the schizophrenic

Table 1 Sample characteristics of the high-risk and healthy control groups

	HR (*n* = 100)	HC (*n* = 198)	t/χ^2	*P*
Age (years), *M* (SD)	14.81 (3.66)	13.79 (3.12)	−2.38*	0.019
Gender: female, *n* (%)	51 (51.0)	104 (52.5)	0.06	0.803
Ethnicity, *n* (%)			0.00	1.000
Han	99 (99.0)	196 (99.0)		
Hui	1 (1.0)	2 (0.01)		
Educational background, *n* (%)			0.88	0.993
Elementary school	35 (35.0)	72 (36.4)		
Junior high school	33 (33.0)	65 (32.8)		
Senior high school	22 (22.0)	41 (20.7)		
University/college	4 (4.0)	8 (4.04)		
Academic achievement, *n* (%)			4.94	0.085
Poor	14 (14.0)	39 (19.7)		
Moderate	37 (37.0)	88 (44.4)		
Good	49 (49.0)	71 (35.9)		
SES[a], *M* (SD)	7.17 (1.86)	7.22 (1.52)	0.24	0.809
GEC[b], *M* (SD)	51.70 (10.93)	49.14 (9.41)	−2.10*	0.037
Total difficulties, *M* (SD)	10.39 (4.87)	10.52 (4.51)	−0.21	0.830
Emotional symptoms, *M* (SD)	2.17 (2.16)	2.42 (2.01)	0.94	0.348
Conduct problems, *M* (SD)	2.10 (1.29)	1.93 (1.43)	−0.89	0.372
Hyperactivity/inattention, *M* (SD)	2.96 (2.00)	3.02 (1.98)	0.20	0.843
Peer relationship problems, *M* (SD)	3.16 (1.48)	3.15 (1.50)	−0.06	0.951

HR high-risk group, *HC* healthy controls

*$P < 0.05$

[a]SES = socioeconomic status, as measured by a composite score of maternal and paternal education, maternal and paternal occupational status, and family economic status

[b]GEC = Global Executive Composite in the BRIEF-SR scale

probands of participants in the high-risk group, the mean duration of illness was 8.59 (7.36) years, and the average age of onset was 26.25 (8.89). More than two-thirds of the patients (70.7%) had no family history of psychosis.

Latent class analysis

We initially estimated LC models containing one to six classes; of these, a four-class solution provided the best fit (see Supplementary Table 1). Supplementary Fig. 1 displays the profiles of the four latent classes with the conditional probabilities of each EF subscale score in the overall sample. Of the 298 individuals, 109 (36.6%) belonged to LC 1, 61 (20.5%) to LC 2, 67 (22.5%) to LC 3, and 61 (20.5%) to LC 4. The distribution of membership across the four clusters by groups did not differ significantly between the high-risk and healthy control groups (Fig. 1).

Table 2 presents means and standard deviations in BRIEF-SR scales by cluster in the overall sample. Significant differences (all $P < 0.001$) were found among the four classes on all the BRIEF-SR subscales. Post hoc analyses with Bonferroni correction are also shown in Table 2.

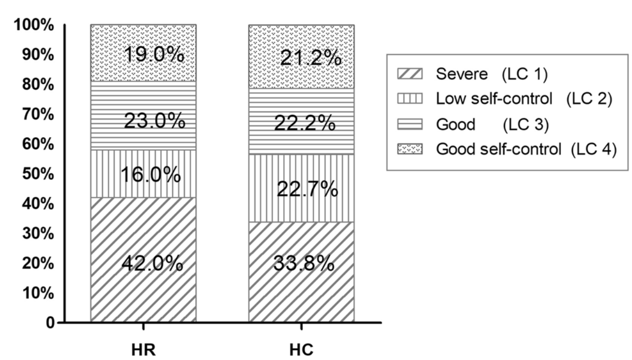

Fig. 1 Percentage membership of each of the four latent classes in the high-risk (HR) and healthy control (HC) groups

The neurocognitive profile of clusters in the HR group is illustrated in Fig. 2. One class (LC 1, $n = 42$, 42.0%) exhibited widespread attenuation in all neurocognitive variables than healthy controls (all $P < 0.05$, Z values ranged from 0.65 to 1.33); we thus labeled this class the "severe impairment class". The cognitive profile of LC 3 (23.0%) showed better performance in all neurocognitive variables than that of controls (all $P < 0.05$, Z values ranged from −2.32 to

Table 2 Cognitive characteristics of four latent classes in overall sample ($N=298$)

M (*SD*)	LC 1 ($n=109$)	LC 2 ($n=61$)	LC 3 ($n=67$)	LC 4 ($n=61$)	*F*	*P*	Post hoc analyses[b]
Inhibit	57.26 (8.91)	52.91 (7.30)	41.12 (6.53)	43.87 (4.59)	85.552	0.000	1 > 2 > 3, 1 > 2 > 4
Shift	57.89 (8.46)	49.08 (7.17)	39.61 (5.25)	48.23 (6.85)	90.506	0.000	1 > 2 > 3, 1 > 4 > 3
Emotional control	55.56 (10.16)	56.23 (6.98)	42.09 (4.98)	42.52 (3.30)	79.870	0.000	1 > 3, 1 > 4, 2 > 3, 2 > 4
Working memory	58.88 (7.53)	48.65 (7.74)	39.98 (5.03)	46.49 (5.92)	117.605	0.000	1 > 2 > 3, 1 > 4 > 3
Monitor	57.43 (8.16)	47.98 (8.28)	40.30 (4.59)	49.39 (8.57)	72.099	0.000	1 > 2 > 3, 1 > 4 > 3
Plan/organize	58.86 (7.79)	46.94 (6.44)	39.97 (4.98)	48.25 (7.04)	115.092	0.000	1 > 2 > 3, 1 > 4 > 3
Organization of materials	56.51 (9.37)	49.76 (8.40)	41.34 (5.95)	48.12 (7.94)	48.694	0.000	1 > 2 > 3, 1 > 4 > 3
Task completion	58.75 (7.47)	47.91 (7.23)	39.30 (4.73)	48.21 (6.56)	122.030	0.000	1 > 2 > 3, 1 > 4 > 3
GEC[a]	59.95 (6.65)	49.93 (3.94)	37.73 (4.29)	45.76 (3.69)	278.114	0.000	1 > 2 > 4 > 3

The raw scores were converted to *T* scores for GEC and eight subscales

[a]GEC = Global Executive Composite in the BRIEF-SR scale

[b]Post hoc analyses with Bonferroni correction

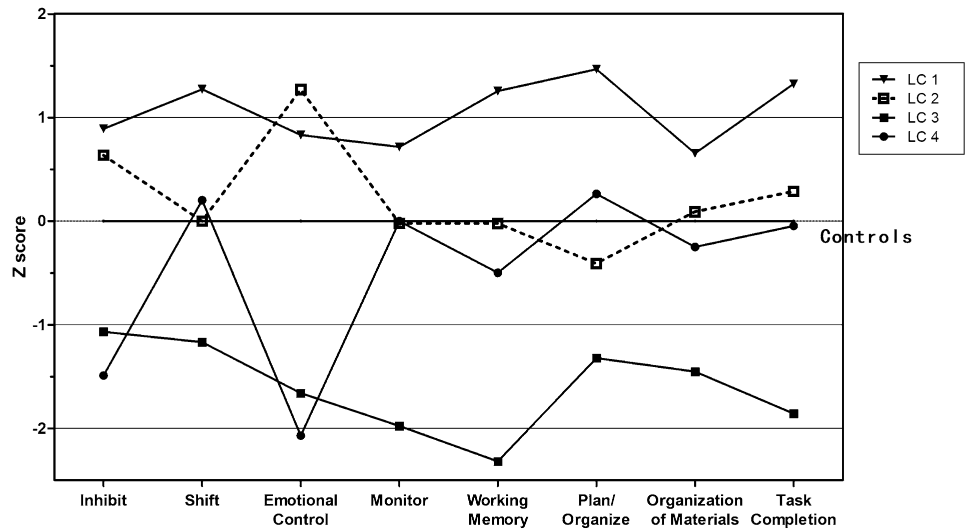

Fig. 2 Executive function profiles of high-risk group clusters (Z scores)

– 1.07); this was, therefore, labeled as "good performance class". Sixteen individuals (16.0%) fell into LC 2, which was labeled the "low self-control class", marked especially by impairments in inhibit and emotional control. Nineteen individuals (19.0%) fell into LC 4, which exhibited higher levels of inhibit and emotional control compared with controls. In line with this profile, we named LC 4 the "good self-control class". The scores of BRIEF-SR scales by cluster in high-risk group and comparisons with healthy controls are shown in Table 3.

Non-cognitive characteristics of HR group clusters

After the profiles had been identified, a series of predictions about potential differences between the groups on the variables were made based on previous research. Non-cognitive features of the four latent classes are reported in Table 4. We did not detect significant differences in demographic characteristics between the classes in the HR group, nor in the clinical characteristics of their ill relatives, such as the duration of their illness.

Among the participants in HR group, we found that total JVQ scores and victimization levels differed significantly between four latent classes ($P=0.006$ and 0.010, respectively). Post hoc analyses with Bonferroni correction ($\alpha=0.05/6=0.0083$) revealed that mean total JVQ score was significantly higher in LC 1 compared with the good performance class (LC 3). 31.6% of participants in LC 1 had a high victimization level, and none of the individuals reporting high-level victimization were members of the good performance class (LC 3).

With respect to scores on the SDQ scale, differences between four clusters were significant in total difficulties, emotional symptoms, conduct problems and hyperactivity/inattention scores. Post hoc analyses with Bonferroni correction showed that the scores of total difficulties, emotional

Table 3 Scores of BRIEF-SR scale by cluster in high-risk group and comparisons with healthy controls

	HR ($n = 100$)				HC ($n = 198$)
	LC 1 ($n = 42$)	LC 2 ($n = 16$)	LC 3 ($n = 23$)	LC 4 ($n = 19$)	*M* (SD)
Inhibit	58.05 (9.60)*	54.82 (8.36)*	41.83 (7.18)*	43.25 (4.20)*	49.50 (9.53)
Shift	59.99 (8.76)*	48.84 (7.84)	42.20 (5.70)*	50.27 (7.07)	48.85 (9.60)
Emotional control	58.44 (10.81)*	54.84 (4.24)*	42.04 (4.47)*	42.57 (3.32)*	49.46 (9.58)
Working memory	60.29 (8.64)*	49.26 (8.28)	39.24 (4.40)*	46.64 (5.64)	49.45 (9.35)
Monitor	56.13 (8.77)*	49.64 (10.02)	40.42 (4.77)*	49.85 (9.02)	49.86 (9.92)
Plan/organize	59.62 (7.15)*	47.23 (4.63)	41.25 (5.97)*	50.76 (6.21)	49.13 (10.04)
Organization of materials	56.26 (9.74)*	50.61 (7.93)	41.30 (5.92)*	47.35 (10.19)	49.89 (9.74)
Task completion	60.37 (8.62)*	50.98 (7.12)	40.66 (4.46)*	48.64 (6.28)	48.94 (9.54)
GEC[a]	61.47 (8.12)*	50.93 (3.44)	38.63 (3.89)*	46.59 (3.03)	49.14 (9.41)

The raw scores were converted to *T* scores for GEC and eight subscales

HR high-risk group, *HC* healthy control

*Significant difference with healthy controls

[a]GEC = Global Executive Composite in the BRIEF-SR scale

Table 4 Non-cognitive characteristics of four latent classes in HR group ($n = 100$)

	LC 1 $n = 42$ (42.0%)	LC 2 $n = 16$ (16.0%)	LC 3 $n = 23$ (23.0%)	LC 4 $n = 19$ (19.0%)	*P*	Post hoc analyses[b]
Age (years), *M* (SD)	15.64 (3.67)	14.69 (3.53)	14.47 (2.87)	13.48 (4.12)	0.179	
Female gender, *n* (%)	22 (52.4)	9 (56.2)	12 (52.2)	8 (42.1)	0.938	
Academic achievement, *n* (%)					0.106	
Poor	11 (26.2)	1 (6.2)	0 (0.0)	2 (10.5)		
Moderate	15 (35.7)	6 (37.5)	9 (39.1)	7 (36.8)		
Good	16 (38.1)	9 (56.2)	14 (60.9)	10 (52.6)		
SES[a], *M* (SD)	6.93 (1.80)	7.06 (2.02)	7.35 (1.75)	7.58 (2.06)	0.604	
Onset age of probands	26.00 (6.76)	27.00 (8.03)	25.00 (14.40)	26.75 (12.63)	0.981	
JVQ, *M* (SD)	3.61 (3.61)	3.06 (2.64)	0.95 (1.17)	2.50 (1.79)	0.006	1 > 3
Victimization level, *n* (%)					0.010	
No	6 (15.8)	2 (12.5)	11 (50.0)	3 (18.8)		
Low	20 (52.6)	11 (68.8)	11 (50.0)	10 (62.5)		
High	12 (31.6)	3 (18.8)	0 (0.0)	3 (18.8)		
The total difficulties	12.88 (4.55)	10.43 (4.57)	6.55 (4.05)	10.00 (3.53)	0.000	1 > 3
Emotional symptoms	3.21 (2.34)	2.29 (2.58)	0.65 (0.88)	1.80 (1.15)	0.000	1 > 3
Conduct problems	2.61 (1.14)	2.00 (1.04)	1.30 (1.13)	2.13 (1.55)	0.004	1 > 3
Hyperactivity/inattention	3.61 (1.75)	2.93 (2.46)	2.00 (2.05)	2.87 (1.55)	0.040	
Peer relationship problems	3.45 (1.20)	3.21 (1.76)	2.60 (1.47)	3.20 (1.70)	0.242	

[a]SES = socioeconomic status, as measured by a composite score of maternal and paternal education, maternal and paternal occupational status, and family economic status

[b]Post hoc analyses with Bonferroni correction

symptoms, and conduct problems in LC 1 were higher than those in LC 3.

General linear model (GLM) was conducted as sensitivity analyses to examine the main effect of cluster and group (HR/HC), as well as the interaction effect of cluster and group on JVQ total score, SDQ total score and four subscales in the total sample. The results showed that the main effect of cluster is significant, while the main effect of HR/HC groups and the interactive effect of cluster and group are not significant (see the Supplementary Table 2). Results indicated that the patterns of associations by cluster hold up in both the HR and HC groups.

Discussion

To our knowledge, this is the first study to represent a step towards understanding meaningful profiles of EF out of a mixed sample including youth genetically at high risk for schizophrenia and healthy controls. LCA was used to identify four substantively meaningful profiles of EF that differed in terms of EF in participants' everyday environment as assessed by the BRIEF-SR. Given the state of current evidence, our preliminary analyses obtained four cognitive phenotypes based on different profiles of EF: (1) a "severe impairment" cluster, (2) a "low self-control" cluster, (3) a "good performance" cluster, and (4) a "good self-control" cluster. These findings support the debated notion that there may be diverse mechanisms producing neurocognitive heterogeneity [29], which deviates from some previous neuropsychological studies of families with schizophrenia [12]. One possible reason is proposed by the neurodevelopmental hypothesis, the dominant paradigm for illuminating environmental risk factors [30]. There is a robust collection of studies observing an increased frequency of obstetric and perinatal complications in schizophrenic patients [31], such as maternal stress [32] and maternal infections [33, 34]. A review by Brown indicated that viral infections during pregnancy can increase the risk for development of schizophrenia in the affected offspring [35].

This study did not find a significant difference in the distribution of membership across the four clusters between the high-risk and healthy control groups. This is consistent with the earlier research finding that EF does not differ significantly between relatives of patients with schizophrenia and normal controls [36]. It is also worth noting that membership in the "good performance class" in our study involved outperforming the average, rather than the EF scores of healthy controls only. This finding suggests that the high-risk participants falling into this cluster have a good level of EF, and perhaps exhibit a different pathophysiology to the most common case of impairment seen in nonpsychotic relatives. Considering that genetic risk factors may be found in essentially all first-degree relatives of patients with schizophrenia, a focus on the participants falling into the good performance class in our study may have relevance beyond simply identifying whether or not these high-risk young individuals have "normal" EF profiles. Our finding may constitute a noteworthy opportunity to extend the field's understanding of the relationship between the genetic risk of schizophrenia and one's practical capacities [37].

The second goal of the present study was to examine differences among the identified classes on four domains that have been associated with EF: demographic characteristics, victimization, behavioral and emotional disorders. Previous studies of both schizophrenic patients and their biological relatives showed that prodromal cognitive deficits are likely related to reduced educational achievement [38–40]. Most often, higher educational achievement contributes independently to cognitive reserve [38, 39]. However, the results in the present study showed that the relationship between academic achievement and EF classes was not statistically significant. A possible explanation for the inconsistent findings may be the lack of adequate sample size in our study. It would benefit from using large cohort designs in high-risk population of schizophrenia to further test the relationship between EF classes and academic performance. This may also be because we measured academic achievements by asking the subjects themselves other than some objective indicators, such as grade retention [40]. The subject may exaggerate his or her self-reported achievements because of vanity.

Our results showed a significant difference in victimization level among the neurocognitive subgroups within the HR group, suggesting that individuals with more exposure to victimization had more severely impaired EF. More specifically, high-risk adolescents in LC 1 showed more experiences of victimization than individuals in LC 3. This finding is in line with other findings of diminished EF in victimized Chinese adolescents [12, 20], indicating that some of the risks to EF are much more likely to be environmental.

Although researchers have long recognized the role of cognitive impairment in psychosis, the past 20 years have seen a resurgence of correlational studies, largely performed in light of the growing evidence that cognitive function is a critical constraint on functional capacity in life [41, 42]. In this study, the participants in LC 1 exhibited the most emotional and behavioral deviance. Such results hold promise for current research suggesting that global cognitive impairment is associated with poorer emotional and behavioral outcomes. It has been emphasized that the persistence of behavioral problems throughout the life course carries implications for concomitant negative life outcomes [43]. For this reason, our latent neurocognitive clusters may reflect longstanding challenges for life outcomes.

The findings from the current study should be considered in light of several limitations. First, the absence of more robust findings in terms of statistical significance may be ascribed to the limited sample size. A large cohort study would be beneficial to test the replicability of our findings. Second, our sample includes children and adolescents, and some participants are already well within the window of risk. The wide age range might overestimate the proportion of 'good performance' cluster. Additionally, it is noteworthy that the data on other proxies for cognitive reserves, such as premorbid IQ and leisure activities, were not available. However, mental retardation was an exclusion criterion in our sample. Third, the onset age of schizophrenia in the probands is relative high, which might affect the distribution of the subtypes of schizophrenic disorders [44]. Further investigation with more comprehensive and balanced subtypes might be warranted. Finally, both HR and HC had a relatively limited sample size, especially when being divided into clusters by performance-based measures of executive function. This might lead to false-negative results due to the lack of statistical power and selection of samples. Hence, a replication study would be needed with a larger sample size.

Despite the above limitations, our findings have a number of theoretical, practical, and policy implications. Our findings may remind primary care practitioners to develop a clear sense of initiative in offering special surveillance for the young people who have parents or siblings with schizophrenia. Moreover, further investigation of those high-risk youth with high-level EF can potentially lead to the elucidation of an underlying protective mechanism.

Conclusion

In conclusion, the current study identified four subgroups which are derived from measures of EF in everyday situations in a sample of young individuals at genetic risk for schizophrenia and healthy controls. Our work goes beyond the previous understanding of potential executive deficits in adolescents at risk of schizophrenia and provides a comparison of characteristics among the derived classes. A particular strength of our study is that we have taken into account the cognitive heterogeneity of healthy controls, which lends further credibility to the results. As a future direction, it is important to investigate biomarkers of neurocognitive subgroupings in HR population. The identification of heterogeneity in genetic and environmental characteristics, stable and valid subtypes may lead to better management as well as early intervention of cognitive deficits and other symptoms of schizophrenia.

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Compliance with ethical standards

Conflict of interest The authors have declared that they have no competing or potential conflicts of interest.

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