Study investigating executive function in schizophrenia patients and their unaffected siblings

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Abstract

Background: Schizophrenia (SCZ) is a serious genetic mental illness. Most research indicates that executive impairment has a certain genetic predisposition. The shared neuropathological characteristics of patients with schizophrenia and their siblings might reveal intermediate phenotypes in behavior that could be used to further characterize the illness.

Methods: Our study involved 32 schizophrenia patients, 32 unaffected siblings,and 33 healthy controls. The three groups underwent a computerized version of the Wisconsin Card Sorting Test (WCST) and a battery of cognitive neuropsychological assessments. These tests evaluated executive function and several cognitive domains.

Results: In this study, the WCST results demonstrate that the total correct (TC), total error (TE), perseverative response (PR) and perseverative error (PE) scores in the SZ group were significantly lower than those in the HC group (TC ($p=0.011$), TE ($p<0.001$), PR ($p=0.007$) and PE ($p=0.002$)), and compared to the unaffected siblings, we found significant differences in TE ($p=0.003$). Moreover, significant differences were observed between the unaffected siblings and healthy controls as follows: TC ($p=0.034$), TE ($p=0.008$), PR ($p=0.016$) and PE ($p=0.013$).

Conclusion: The schizophrenia patients and their siblings performed worse in the WCST test than the healthy controls. This result supports the claim that the development of functional impairment is not unique to schizophrenia patients and that unaffected siblings may have a certain level of abnormal brain function.Neurological abnormalities lead to abnormal functioning in siblings and patients,suggesting that genetics plays a considerable role in such results.

Background

Schizophrenia is a serious genetic mental illness with positive symptoms [1] and negative symptoms [2]. Furthermore,cognitive impairment is a core symptom of schizophrenia that affects the individual's daily life or social abilities [3].Most research indicates that executive impairment is a core feature of cognitive impairment [4], which has three dimensions, namely, abstract generalization, cognitive transfer, and attention; patients cannot make plans, perform innovative work, adjust themselves according to rules, and make multiple arrangements [5]. For various reasons, executive function has become an attractive intermediate phenotype of schizophrenia, including its objective measurement, relative clinical stability in disease processes, heritability to disability, and association with genetic risk [6]. Recent studies have also found that schizophrenia patients are similar to their unaffected siblings in many ways, especially in abnormal brain regions, language dysfunctions and emotional cognition [7].

Many brain imaging studies have shown that this abnormality is closely related to dorsolateral prefrontal cortex (DLPFC) regions [8]. In some studies investigating response inhibition, abnormalities were found in the anterior cingulate cortex (ACC) and PFC connectivity in unaffected siblings and SCZ patients [9]. Although evidence suggests that executive impairment is consistent with disease progression, the current

damaging mechanism is still unclear. Decades of family, twin, and adoption studies have shown that the effects of substantial genetic components on risk have a certain contribution to environmental impact, but how schizophrenia is transmitted is complex, and convergence evidence supports highly polygenic structures [10, 11].Both patients and their unaffected siblings exhibit cognitive function impairments, such as social cognition, working memory, and attention [12, 13]. Since early intervention can help prevent and delay the onset of psychosis, it is necessary to identify a biomarker that can identify individuals at a higher risk of developing schizophrenia early [14].

However, research often compares people with schizophrenia to healthy people; thus, whether executive dysfunction is unique to patients with schizophrenia is unclear. Few studies attempted to explore executive deficits in patients with schizophrenia and unaffected siblings. Furthermore, the manifestations of the neurobiological abnormalities are quite heterogeneous, and the differences in the degree of family transmission in a particular cognitive function domain, especially executive function, have not been systematically addressed [15]. Therefore, we need to explore the executive function of schizophrenia patients and their unaffected siblings to clarify this relationship. Executive dysfunction can be used to predict a patient's daily performance [16], especially in prospective memory, work performance and emotional abnormality [17]. Despite the strong evidence of neurocognitive dysfunction in mentally ill patients, the degree of similarity in the cognitive structure of mental disorders between patients and their unaffected siblings is not well described [18]. Clarifying the functional link between patients and unaffected siblings could provide great benefits for disease prevention and prognosis. Thus, finding the link between patients and their siblings could provide important evidence for studies investigating schizophrenia.

In the current study, we use a computerized version of the WCST to indirectly assess the participants' executive function. Evidence suggests that schizophrenia patients perform worse on the WCST than normal control and other psychiatric patients [19]. However, in many studies, participants have a greater age at onset.Currently, many studies focus only on the difference between patients and normal people and do not conduct in-depth research involving the patients' unaffected siblings [20]. To render the research results more applicable, first, in our study, we choose patients with an earlier onset age, and the ages of the siblings were similar. Studies have suggested that the earlier the age at onset is, the more severe the executive function impairment, and the WCST scores may be sensitive to these groups; this study combined the WCST with neuropsychological tests to further explore the performance impairment in the unaffected siblings.Second, our objective is to reveal the possible connections between executive function in schizophrenia patients and the performance of their unaffected siblings. In the current study, we focus on performance differences on the WCST between patients and their unaffected siblings and between these groups and healthy people to determine whether executive function is influences by genetics. We hypothesized that both the patients and their unaffected siblings have cognitive function damage, especially executive function, compared with the healthy control group and that the unaffected siblings perform better than the patients.

Methods

Study design

In this study, the participants were selected according to the inclusion and exclusion criteria. The neuropsychological test was performed before the test was started. The WCST test was performed one day after the test was completed to evaluate the participants' executive function. The Institutional Review Board of Anhui Medical University approved the study protocol. All participants provided written informed consent. All participants were unaware of the purpose of the study and remained in good health prior to testing.

Participants

In total, 106 subjects were included in our study, including 34 schizophrenia patients, 34 unaffected siblings of the schizophrenia patients, and 38 unrelated healthy control subjects. The patients' symptoms were evaluated by two psychiatrists from the Fourth People's Hospital of Hefei City. All participants met our inclusion and exclusion criteria. The Institutional Review Board of Anhui Medical University approved the study protocol. All participants provided written informed consent. All participants were unaware of the purpose of the study and remained in good health prior to testing.

Schizophrenia outpatients were recruited from the clinic of the Fourth People's Hospital of Hefei City, and the subjects were selected according to the enrollment and exclusion criteria. The enrollment criteria were as follows: (1) meeting the diagnostic criteria of the DSM-IV and a comprehensive international diagnostic interview conducted by a psychiatric consultant; (2) no change in psychotropic substances for at least two months before participating in the study; and (3) no obvious visual impairment. The exclusion criteria were as follows: (1)severe head trauma or history of nervous system disease, severe physical illness, noncooperators, etc.; (2) drug abuse or alcohol addiction within the past six months; and (3) a more stable emotional state or a Hamilton Anxiety/Depression Rating Scale (HAMA/HAMD) score > 7 points. All patients were defined as clinically stable for a period of 2 weeks without drug replacement or rehospitalization.

The unaffected siblings were the brothers or sisters of the patients. The inclusion criteria for the siblings were as follows: (1) no mental disorder according to the DSM-IV; (2) intact general cognitive function as measured using the Beijing Version of the Montreal Cognitive Assessment (MoCA) test scores > 22 points; and (3) HAMA or HAMD < 7 points.The exclusion criteria were as follows: (1) a lifetime history of substance abuse; (2) history of head trauma or nervous system or other serious physical illness; and (3) a history of the long-term use of drugs or mental disorders among the family members. The healthy subjects were recruited from the nearby community for comparison and matched with the patients by gender and age. There are no cognitive impairments or mental problems among the healthy subjects.

Neuropsychological assessment

Standardized neurological tests were used to investigate the participants' basic cognitive status and emotions, such as anxiety and depressive symptoms. In this study, we used the MoCA test to measure the overall cognitive function of the participants; this test requires less time and can be used to assess general cognitive function. The other tests used include the following: the digital span forward (DST F/B)/backward test is used to assess the participants' attention and short-term memory; the Stroop color-word test includes three tests, namely, the Stroop color test (SCT), the Stroop word test (SWT), and the Stroop inference test (SIT), and is used to assess the participants' executive control; and the Trail making test A and B (TMT A/B) was used to observe the participants' cognitive flexibility. The symptoms of depression and anxiety were assessed using HAMD and HAMA. The patients' symptoms were assessed using the Positive and Negative Symptoms Scale (PANSS). These tests are evaluated by experienced psychologists and psychiatrists. All participants were provided a brief overview of the results after the test was completed.

Wisconsin Card Sorting Test (WCST)

Executive function is measured by the WCST, which has been applied to patients and healthy people. The WCST Computer Edition measures executive function, mainly the ability to abstract reasoning and transform cognitive and concept formation. The WCST displays 4 stimulating cards and a response card (64response cards displayed one at a time) on the screen. The participants find the card from the stimulus cards that match the card, and the participants need to continue to attempt, analyze, and reason to find the classification rules set by the computer and make ten choices according to the correct classification rules; then, the computer proceeds to the next classification rule when the classification is completed or eliminated 6 times in a row. After the 64 response cards, the test ends. This study counts the total number of correct responses (TC), the total number of error responses (TE), the number of persistent responses (PR), the number of persistent errors (PE), and the number of trials to complete the first category (TCFC) [21, 22]. The greater the number of TC, the stronger the abstract generalization, working memory, attention, and executive control ability[22]; greater TE and PE reflect the cognitive transfer and executive control functions of the subjects, and the cognitive flexibility is reduced; the greater the number of classifications completed is, the greater the concept conversion, classification initiative, and diversity concept [23] (Fig. 1).

Statistics

A data analysis was performed using SPSS 18.0 (IBM, Armonk,NY, USA). A one-way analysis of variance (ANOVA) and χ^2 analyses were used to compare the demographic data across the three groups. The results of the WCST task were analyzed as a between-subjects variable by one-way ANOVAs of each of the three groups of results. Post hoc comparisons were performed using LSD or Tamhane's test in the presence of significant differences or interaction effects among the three groups. The degree of

correlation between the variables is analyzed by Pearson's correlation. The test scores are expressed as an average with standard errors, and in the current experiment, $p < 0.05$ (two-tailed) was set at the level of significance.

Results

Two patients and two unaffected siblings did not complete the initial neuropsychological test, and the WCST was not completed. Five healthy people were tested by the WCST in the past year. Finally, data from only 97 participants were used in the analysis. Here, the demographics and corresponding clinical information of the participants are shown in Table 1. Similarly, the clinical symptoms and neuropsychological assessments are included in Table 1. The patients with schizophrenia, their unaffected siblings, and healthy controls matched by gender and level of education required approximately 2 hours to complete all tests (neuropsychological testing and WCST tasks).

Demographic characteristics and clinical information,and neuropsychological tests of three groups

The average age of the 32 patients (17 females and 15 males) with schizophrenia is 22.4 years, and on average, the patients had 14.46 years of education. Thirty two (15 females and 17 males) unaffected siblings (M_{age} = 23.03, $M_{education}$ = 14.21) were recruited. The siblings are all the patients' brothers or sisters. The healthy control group included 33 participants (16 females and 17 males) with an average age of 22.5 years and an education level of 14 years. No significant differences were found among the three groups in terms of age, education, and gender (Table. 1).

The neuropsychological assessment and the study variables were assessed using a one-way analysis of variance (ANOVA) and χ^2 tests. When a difference was observed among the three groups, a post hoc comparison using LSD or Tamhane was performed (Table 1). There was a significant difference among theschizophrenia, sibling, and healthy control groups in certain parts of the neuropsychological tests (Table.1). Significant group differences were found in the following parameters: SCT [$F(2,95) = 9.196$, $p < 0.001$], SWT [$F(2,95) = 11.01$, $p < 0.001$], SIT [$F(2,95) = 13.758$, $p < 0.001$]; DSTF ($F(2, 95) = 10.09$,$p < 0.001$), DSTB [$F(2, 95) = 7.689$, $p < 0.001$]; and TMT A [$F(2, 95) = 9.767$, $p < 0.001$] and B [$F(2, 95) = 14.308$, $p < 0.001$]). Significant differences were found in the other variables. Regarding the MOCA total score [$F(2, 95) = 29.831$, $p < 0.001$], the schizophrenia patients has lower scores (25.31±3.14) than the healthy controls (29.51±1). However, the HAMA (4.09±1.8)and HAMD (3.75±1.41) scores are lower than those of the healthy controls (4.33±1.93; 4.24±1.78); furthermore, all participant test scores are within the scope of the study requirements. The post hoc analyses revealed significant differences between the schizophrenia patients and healthy controls as follows: SCT [$p<0.001$], SWT [$p < 0.001$], SIT [$p < 0.001$]; DST A ($p < 0.001$), DSTB ($p < 0.001$); and TMT A [$p < 0.001$] and B [$p < 0.001$]). In these tests, the patients' performance was also worse than that in the control group. Compared with their siblings, we found significant differences in the patients in some variables as follows: SCT [$p = 0.037$] and SWT [$p = 0.034$];

TMT B [p = 0.028]), SCT [p = 0.033], SWT [p = 0.013], SIT [p = 0.001], DSTF (p < 0.001), DSTB (p = 0.004), TMT A [p = 0.008] and TMT B [p = 0.003] showed differences between the healthy controls and unaffected siblings. In addition, the HAMA, HAMD, and VFT scores did not significantly differ among the three groups as follows: HAMA (F = 0.931, p = 0.398), HAMD (F = 1.723, p = 0.184), and VFT [F = 1.242, p = 0.293].

Assessment of executive function in three groups

The data displayed in Table 2 show the results of the WCST. The results show that executive function performance, the total correct, the total errors, perseverative responses and perseverative errors significantly differed among the three groups as follows: TC [F(2,95) = 3.862, p = 0.024], TE [F(2,95) = 16.826, p<0.001],PR [F(2,95) = 4.595, p<0.012], PE [F(2,95) = 5.710, p <0.005]; the post hoc analyses show differences in four variables between the patients with schizophrenia and the control group as follows: TC (p = 0.011), TE (p<0.001), PR (p = 0.007) and PE (p = 0.002). There are significant differences between the unaffected siblings and the healthy controls as follows: TC (p = 0.034), TE (p = 0.008), PR (p = 0.016) and PE (p = 0.013). By comparing the siblings with the patients, we found that TE (p = 0.003) has significant differences. In addition, the trial to complete the first category did not reveal significant differences (F = 1.15, P = 0.321) among the patients (16.03±12.85), their unaffected siblings (13±4.37), and the healthy controls (13.71±5.18)(Table 2;Fig. 2)

Correlation analysis between WCST and neuropsychological tests between patients and unaffected slibings

To explore whether the WCST performance of the patients and their siblings is related to the neuropsychological tests (MOCA, Stroop test, TMT A and B), we used Pearson's correlation analyses. The results show that there is a significant correlation between the trial to complete the first category and all neuropsychology indicators. The trial to complete the first category is significantly negatively correlated with MOCA (r = -.0.27, p = 0.031) and TMT B (r = −0.27, p<0.001).Furthermore, there is a significant positive correlation with SCT (r = 0.424, p<0.001), SWT (r = 0.297, p = 0.017), and SIT (r = 0.402, p<0.001). No significant relationships were found between the remaining aspects of the WCST (TC, TE, PE and PR) and the neuropsychological test. In any of the three groups, no relationship was found between the WCST performance and the demographic information (Table 3).

Discussion

Schizophrenia patients often have executive dysfunction. Executive function is an advanced cognitive function, and cognitive dysfunction is a manifestation of positive and negative symptoms independent of schizophrenia, which affects patients' daily life, social interaction, employment, etc.[24]. Related studies have shown that cognitive dysfunction often precedes other symptoms of schizophrenia [25], suggesting that cognitive deficits may be a hallmark of neurodevelopmental abnormalities and are

somewhat associated with heredity [26]. Therefore, patients' unaffected siblings may also have functional impairment.

In the current study, the schizophrenia patients and their unaffected siblings showed worse WCST performance than the healthy subjects, further indicating that unaffected siblings have functional impairment, and they also performed worse on the neuropsychological assessment than the healthy controls. The data of the patients and siblings show that there is a significant negative correlation between the TCFC and MOCA scores and a significant positive correlation between the TCFC and Stroop test, suggesting that not only the patients but also their unaffected siblings have damage to the executive function (PR and PE) [27].

Cognitive impairment is widely recognized as an important feature of SCZ and is closely related to long-term functional outcomes [28]. Executive function refers to the ability to establish goals, formulate and revise plans, implement plans, and carry out purposeful activities. Executive function is a comprehensive ability to use knowledge and information [29, 30]. Patients with schizophrenia have defects in executive function. Performing functional impairment is a key dysfunction in patients with schizophrenia [31]. In our study, the neuropsychological assessment data suggest that patients with schizophrenia have low scores relative to the healthy controls, suggesting that patients with schizophrenia have impairments in cognitive function, attention, and cognitive flexibility. Most studies have found cognitive impairment in schizophrenia [32]. As expected, the patients' executive function (TC, TE, PR, and PE) is also significantly worse than that of the healthy people here, and the WCST is used to evaluate executive functions.

The results of this study confirm previous research; the patients showed poorer WCST performance, and the control group performed normally [33]. These patients show a diminished capacity to generate or apply cognitive inhibition [34].WCST is a more complex neuropsychological test that tests participants' abstract summative capabilities, strategy shifts, and the ability to adapt to environmental changes to achieve higher goals [35]. These findings have important implications suggesting that WCST performance defects can serve as an internal endophenotypic marker of schizophrenia [36]. Impaired executive function is the most extensive and consistent finding observed in cognitive studies involving SCZ patients.

Evidence from several studies suggests that reduced activation abnormalities in the PFC are associated with the performance of executive functional deficits in schizophrenia [37]. Executive function heavily depends on the frontal lobes, and an important region is the anterior cingulate cortex (ACC) [38]. A large amount of converging evidence indicates that abnormalities in the DLPFC are the prototype centers for higher-order cognitive processing in the pathophysiology of schizophrenia. Importantly, through the Wisconsin card classification test, in patients with cognitive dysfunction, the gray matter volume in the DLPFC is significantly reduced [39]. In addition, in related imaging studies involving schizophrenia patients, this result is consistently observed [40]. The DLPFC plays a very important role in the WCST and may be related to perseverative responses and perseverative errors [41].

Our study suggests that schizophrenic patients have poor performance in the WCST. The patients have lower TC scores, suggesting that patients may have certain cognitive dysfunction as cognitive dysfunction affects the overall score, speed of processing, attention/vigilance, short-term memory, etc [42]. This finding is also consistent with our results as the patients' MOCA scores are significantly lower than those of the healthy subjects. The total error data of the patients with schizophrenia is significantly higher than normal, showing that there is poor cognitive flexibility; cognitive flexibility bias implies that patients have a poor ability to transfer strategies, which, in turn, affects their daily thinking, such as multitasking and finding new, adaptable solutions for changing needs [43].

Patients with schizophrenia usually have abnormalities in persistent responses,which is among the best indicators of all WCST indicators of brain damage and whether focal damage exists in the frontal lobe. This finding also suggests that abnormal brain function is the cause of the poor performance [44]. The higher the number of persistent errors in the patient shows problems in concept formation, use of correction, and plasticity of the concept, i.e.brain frontal lobe impairment. These findings are consistent with previous results [45]. The poor performance of the schizophrenia patients in the WCST has been reported in recent years. In particular, the schizophrenia patient sample showed significantly worse WCST performance than the control group, which is consistent with previous results indicating impaired cognitive ability involved in performing function in schizophrenia [46, 47]. In our study, some results are in consistent with previous studies. We found that the patients' trial to complete the first category showed no abnormalities, indicating that the patients' abstract generalization ability was not impaired. Many factors impact this performance. There is areas on explaining that the patient recovered to some extent in the abstract generalization ability during the recovery period. Furthermore, compared with the previous study, our healthy controls performed normally, and the patients did not differ from the healthy controls. Normally, patients should be abnormal on this indicator, but this does not match the results. We found that this finding maybe related to the patients' course of illness and education, and a high education level also has a great impact on this result. In patients with higher levels of function and education, their cognitive dysfunction is not particularly prominent [48]. Furthermore, the stability of the outpatient, the duration of the disease, and the dose of antipsychotics may differing, which may cause the discrepancy from previous results. We chose stable outpatients who had not changed their medications within eight weeks. In addition, at the educational level, we also sought healthy groups that were comparable to the patient level to ensure the reliability of the results.

Schizophrenia is a complex disease that affects perception, thought and behavior. Family studies have shown that various genes and the external environment play an important role in the development of the disease, but the pathogenesis of this disease remains ambiguous [49]. Since SCZ is a heterogeneous syndrome, markers of the genetic risk or intermediate phenotype in siblings may represent a useful strategy because they are not affected by other nonspecific variables associated with family stress and lifestyle changes [50]. Previous studies using fMRI reported that siblings had reduced DLPFC, left middle frontal gyrus, inferior frontal gyrus (IFG) regions, and ACC compared to healthy groups[51].These brain regions affect executive function, which, in turn, affects performance on the WCST. Our study suggests that the unaffected siblings' WCST performance is significantly weaker than that of the healthy controls,

and a slight difference from the patient scores was observed. Our findings are consistent with those of our predecessors and echo the imaging data. Abnormal brain regions affect performance on the WCST. The DLPFC affects executive function, performs abnormal functions, and is expressed in the WCST.

According to our findings, patients and their unaffected siblings performed poorly on the WCST, suggesting that executive dysfunction is not unique to patients but rather is greatly related to heredity and family. Schizophrenic patients have impairments in certain abilities, such as cognitive flexibility and abstract generalization skills; thus, when completing WCST tasks, there will be more persistent errors, and ultimately, it is difficult to achieve high scores. By exploring the commonality among family members by comparing patients with unaffected siblings, the results provide primary evidence of a specific phenotype. The unaffected siblings performed slightly better that the patients on the WCST but significantly differed from the normal controls. This finding also indicates that unaffected siblings have impairments in certain functions, such as reaction inhibition, short-term memory, attention, and abstract generalization. This finding also shows that heredity plays a great role in the occurrence of the disease. The internal phenotypic method has always been a concern in related research. In a family, a certain type of functional damage is related to heredity to a certain extent and eventually becomes a factor affecting disease conversion [52]. An abnormality in executive function usually precedes patients' psychiatric symptoms [53], and cognitive impairment accelerates the development of symptoms and ultimately leads to disease. These defects lead to social or occupational dysfunction and poor life outcomes. In addition, in our study, both the Stroop test and MOCA were significantly associated with the WCST, further confirming the existence of cognitive dysfunction between the patients and their unaffected siblings.

Limitations

Here, some limitations of this study should be noted. First, we use the WCST and a series of neuropsychological tests to discover the existence of executive control defects; this analytical strategy allowed us to obtain evidence supporting our hypothesis. However, the results may be inaccurate due to some subjective factors. Therefore, behaviors (e.g. presenting multiple sensory cues and goals) and physiological (e.g. brain imaging) studies should be performed to provide more reliable basis. Second, compared with previous studies using the WCST, our research selected relatively fewer indicators; thus, the results need to be further explored [37, 54]. Third, the average age of the unaffected siblings in our sample is 23 years, suggesting that some siblings have not passed the risk of schizophrenia, which may result in inconsistent results compared with previous studies. Fourth, many patients are still in the medication phase in our study, which may affect our results as some antipsychotics may be associated with WCST performance. In future research, we plan to combine neuroimaging to explore changes in the participants' brains. Furthermore, the age distribution will be expanded to maximize the research's scalability.

Conclusions

In summary, schizophrenia patients and unaffected siblings perform poorly on the WCST, and the neuropsychological tests confirmed this result. The patients and their siblings have significant correlations with general cognitive tasks in WCST scores. We found that both the patients and their first-degree relatives have cognitive function damage compared with the healthy control group and that the unaffected siblings perform better than the patients. Unaffected siblings may have a certain level of abnormal brain function. Neurological abnormalities lead to abnormal functioning in siblings and patients, suggesting that genetics plays a considerable role in such results.

Abbreviations

M:male; F:female; PANSS:Positive and Negative Syndrome Scale; NA:not applicable; HAMA:Hamilton Anxiety Rating Scale; HAMD:Hamilton Depression Rating Scale; MoCA:Montreal Cognitive Assessment Test; VFT:Verbal Fluency Test; WCST:Wisconsin Card Sorting Test; DLPFC:dorsolateral prefrontal cortex; ACC:anterior cingulate cortex; TC:the total correct;TE:total error;PR:perseverative response;PE:perseverative error; TCFC:the number of trials to complete the first category.

Declarations

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Authors' contributions

FFX and and KLH conceived and designed the research. PPH and CYZ collected the research data and prepared the draft of the manuscript. XMB, LW,GXX,FQY,XGC and KW performed the statistical analysis and drafted the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and analysed during the current study are available

from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study was approved by the Medical Ethics Committee of Anhui Medical University, Hefei, China.The patient's parents signed the informed consent on behalf of the patient. The remaining participants provided written informed consent for participation in this study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Tables

[Due to technical limitations, tables could not be displayed here. Please see the supplemental files section to access the tables.]

Figures

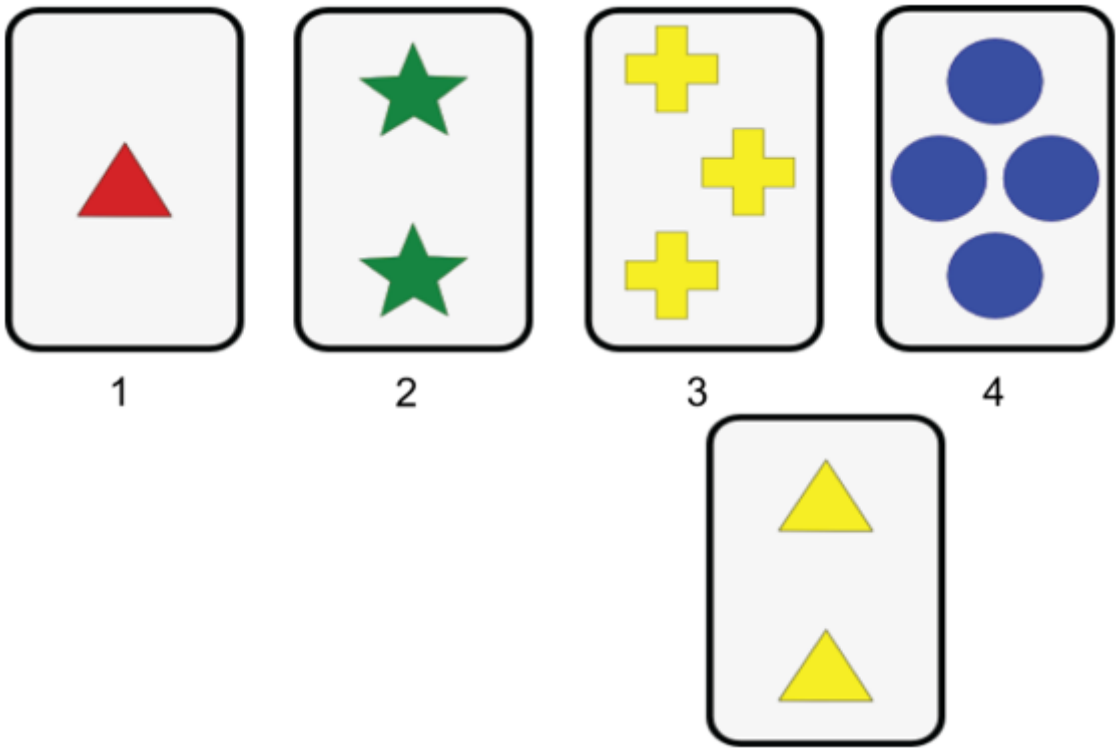

Figure 1

Wisconsin Card Sorting Test（WCST）

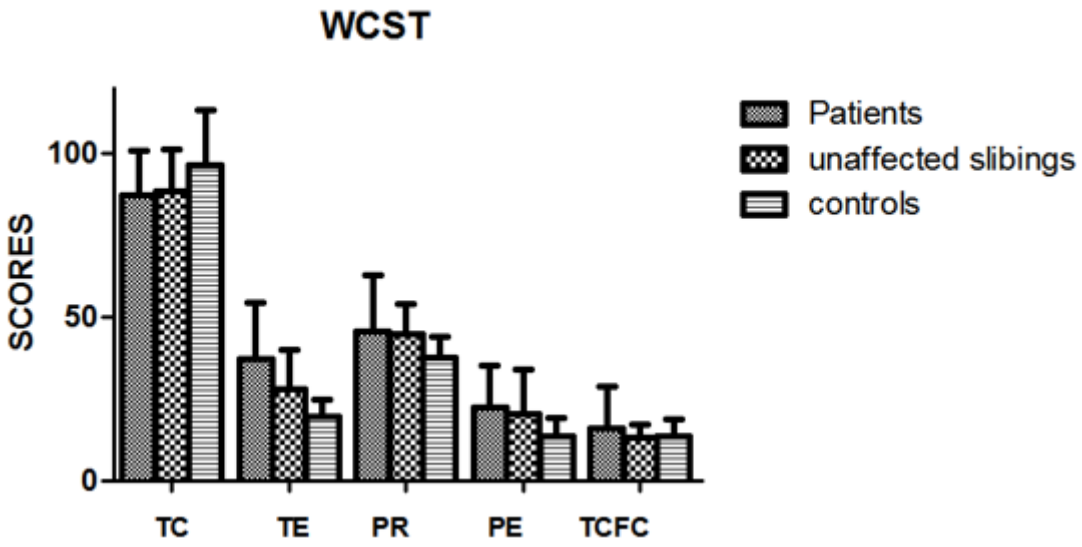

Figure 2

Assessment of executive functions for Schizophrenia, Unaffected siblings and Healthy controls groups.