

•Original research article•

Dysfunction of cognition patterns measured by MATRICS Consensus Cognitive Battery (MCCB) among first episode schizophrenia patients and their biological parents

Aiai CAO^{1,2#}, Ting SHEN^{1,#}, Haibin LI¹, Chuangxin WU¹, Marita MCCABE³, David MELLOR⁴, Linda BYRNE⁴, Jie ZHANG¹, Jia HUANG¹, Daihui PENG^{1,*}, Yifeng XU^{*1,5}

Background: Schizophrenia is characterized by abnormal perception, thinking, emotions, and behaviors. Cognitive dysfunction is acknowledged as one of the most pivotal symptoms in schizophrenia. In addition to positive or negative symptoms, which had been proposed by Gallhofer in the early 1970s, schizophrenia patients suffered from cognitive impairments as well. Many studies show that there is genetic susceptibility in the first grading kinship of patients with schizophrenia. Patients with schizophrenia have cognitive impairment not only in the acute phase but also in the stable phase. Studies also show that the healthy first-grading relatives of patients with schizophrenia suffer from cognitive defects. However, there is still a lack of studies about the cognitive features of biological parents of those with schizophrenia. In this study, we speculate the biological parents of schizophrenia patients have specific cognitive dysfunction. And we explore the patterns of cognition among both schizophrenia patients and their biological parents using the Chinese version of MATRICS Consensus Cognitive Battery (MCCB).

Aims: Cognitive features of patients with schizophrenia might be affected by the cognition mode of patients' biological parents. The dysfunctional cognitive patterns need to be characterized among the patients with schizophrenia and their parents.

Methods: We applied the MATRICS Consensus Cognitive Battery (MCCB, a novel measurement tool) to evaluate the cognitive function of 29 first-episode patients with schizophrenia (meeting ICD-10 diagnostic criteria for schizophrenia, aged between 17-45 years old), 58 cases of biological parents of schizophrenia patients (aged between 40-70 years old) and 46 healthy controls (aged between 40-70 years old). Furthermore, we explored the relationship between the cognitive dysfunction in patients with schizophrenia and their biological parents. All data were analyzed using SPSS18.0 statistical software.

Results: 1) Male patients with schizophrenia had obvious cognitive defects in six domains of cognitive function as measured by the MCCB (all except the social cognition domain) compared to their male parents. Female patients showed lower ability on both working memory and problem reasoning than their female parents. 2) The significant differences of both working memory and reasoning problems also existed between the patients' fathers and matched healthy controls. 3) Patients' mothers didn't show any significant difference on the problem reasoning domain compared with healthy controls. However, the visual learning domain appeared abnormal in patients' mothers compared with healthy controls.

Conclusion: There are six dimensions of cognitive impairments in both first-episode schizophrenia patients and their biological parents. Compared with healthy controls, patients' biological parents have conspicuous dysfunction in domains of working memory, problem reasoning and visual learning as well. Further study is needed to explore the underlying mechanisms of similar cognitive dysfunction between first-episode schizophrenia patients and their biological parents.

Key words: first-episode schizophrenia, cognitive function, biological parents, MCCB

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¹Shanghai Mental Health Centre, Shanghai Jiaotong University, Shanghai, China

²Shanghai Changning Mental Health Centre, Shanghai, China

³Institute for Health & Ageing, Australian Catholic University, Melbourne, Australia

⁴School of Psychology, Deakin University, Melbourne, Australia

⁵Shanghai Key Laboratory of Psychotic Disorders, Shanghai, China

joint first author

*joint correspondencing author

*correspondence: Daihui Peng. Mailing address: 600 South Wanping RD, Shanghai, China, Postcode: 200030. E-Mail: pdhsh@126.com; Yifeng Xu. Mailing address: 600 South Wanping RD, Shanghai, China, Postcode: 200030. E-Mail: hyyyb@gmail.com

1. Background

Cognitive dysfunction is acknowledged to be one of the most significant symptoms of schizophrenia^[1], and has a predominant role in the functional outcomes of the illness.^[2] Although the mechanisms underlying this dysfunction remain unclear, prefrontal cortical dysfunction is considered to be a specific pathological basis of abnormality in logical thinking and problem solving^[3] and executive impairment.^[4,5] Thus, relative to controls, patients with schizophrenia have significantly increased errors on the Wisconsin Card Sorting Test^[6], and this may be attributable to difficulties in problem solving rather than physical distractibility.^[6]

Interestingly, patients with schizophrenia exhibit cognitive impairment not only in the acute phase of the illness but also in the stable phase^[1], and many studies show that the healthy first-degree relatives of patients with schizophrenia also suffer from cognitive deficits^[7], suggesting that there is genetic susceptibility for cognitive deficits among patients with schizophrenia.^[8] Cognitive features of patients with schizophrenia might be affected by the cognition mode of patients' biological parents. However, there are few studies to test the issue.^[9] In this study, we explored the patterns of cognition among both schizophrenia patients and their biological parents using the Chinese version of MATRICS Consensus Cognitive Battery (MCCB).

2. Methods

2.1 Subjects

Thirty patients with schizophrenia and both of their parents ($n=60$) were recruited from the inpatient clinics at Shanghai Mental Health Centre, China. In addition, sixty healthy subjects, matched with to the parent group according to age, gender, and education level, were recruited from the general population via advertisement. Written informed consent was obtained from all subjects prior to their participation in the study. All participants were interviewed independently by two psychiatrists to confirm their psychiatric status. Inclusion criteria for schizophrenia were as followed: 1) satisfying DSM-IV diagnosis criteria of schizophrenia, first episode, 2) duration of episode was less than two weeks, 3) aged from 17-45 years, 4) being able to understand and read Chinese, and comprehend test procedures, 5) at least 5-years of schooling, 6) had not completed MCCB or similar cognitive assessments within the previous six months. Exclusion criteria were: 1) more than 2-years course of illness, 2) alcohol and/or psychoactive substance abuse or use, 3) clinical neurological diseases or medical conditions which currently impact the efficacy of assessment.

Inclusion criteria for biological parents of the patients with schizophrenia were: 1) no psychiatric illness identified when screened with the structured Clinical Interview for DSM-IV, 2) aged between 40 and 70 years, 3) at least 5-years education, 4) being able to understand and read Chinese. Exclusion criteria for biological parents were: 1) suffering from schizophrenia,

or other psychotic disorders or pervasive developmental disability, 2) suffering any neurological disorder, loss of consciousness, brain trauma time exceeding one hour, 3) alcohol and/or drug abuse, or use of any psychoactive substance.

Inclusion criteria for the control group matched to the parent participants were: 1) no disorder identified when screened with the SCID, 2) aged from 17-70 years old, 3) at least 5-years education, 4) able to understand and read Chinese. Exclusion criteria were the same as those applied for the biological parents group.

2.2 Assessment Tools

2.2.1 Neuropsychological assessment

The Chinese version of the MATRICS Consensus Cognitive Battery (MCCB) was used in this study. Developed by the U.S. National Institute of Mental Health (NIMH), this test has been found to have good psychometric properties in China. It assesses seven dimensions of cognitive function, including the speed of processing, attention/vigilance, working memory, verbal learning and memory, visual learning and memory, reasoning and problem-solving skills and social cognition. In this study, speed of processing was tested by the Trail Making Test A, attention/vigilance was assessed with Continuous Performance Testing (CPT), working memory was assessed with Spatial Span, verbal learning and memory was assessed with HVLT and BVMT was used to assess visual learning and memory. We used the Mazes Test to assess reasoning and problem-solving ability and the Emotional Test assessed social cognition.

2.2.2 Statistical Analysis

The independent-samples t-tests were used to investigate any differences in the age and length of education of the groups. All the raw scores for the cognitive tests were converted to T-score based on the guidelines of MCCB. First, raw scores on the individual tests were placed on a common metric (normally distributed scaled scores, which have a mean of 10 and a standard deviation of 3 in the Chinese normative group). The scaled scores were then converted into T-scores: the demographic data (age, education, and gender) were used to generate fractional polynomial regression equations to optimally predict the scaled scores. To determine the optimal fractional polynomial equation, the method of Royston and Altman (1994) was employed using the statistical package. The residuals from optimal regression equations were then converted to T-scores with a mean of 50 and a standard deviation of 10.^[10,11] Cognitive index were tested by analysis of covariance.

3. Results

3.1 Demographic data

Due to some missing data on the MCCB measures (two parents) and refusal to complete the MCCB (14 controls

and one patient), the final sample used in the analyses consisted of 29 patients with first episode schizophrenia and 58 parents, and 46 healthy controls. Of the 29 patients with schizophrenia, 13 were male and 16 were female. Their mean age was 26.24 years (SD=5.87), and the mean number of years of education was 12.93 (SD=3.21). The parent group consisted of 30 fathers and 28 mothers with mean age of 50.50 years (SD=7.06) and 9.90 years of education (SD=3.65). Of the 46 healthy participants as the control group of patients' parents: 22 are males and 24 are females at the age of 50.50 (7.06). The demographic details of the three groups are summarized in Table 1. There were no significant differences in the age or education level of the non-patient groups.

3.2 Assessment of Neuropsychological test

3.2.1 Comparison of cognition between schizophrenia patients and control group

To explore the differences in the cognitive functioning of the patient and control groups, we compared scores on the seven psychological dimensions of cognitive function. As shown in Table 2, there were differences in mean scores on the visual learning, reasoning and problem solving, and social cognition tasks, however they were not significant. However, the patient group scored significantly lower than the control group in speed processing, attention, working memory and verbal learning.

3.2.2 Comparison between patients' and control group

As shown in Table 3, the mean scores of patients and their parents differed significantly on only two domains of the MCCB, speed processing and attention.

3.2.3 Comparison between patients' parents and the control group.

As shown in Table 4, patients' parents scored lower than the control group on only one MCCB domains: verbal learning.

4. Discussion

4.1 Main findings

Schizophrenia is likely to have a potential genetic effect. Interestingly, some research showed that social cognitive dysfunction was one of the endophenotypes for schizophrenia and appeared among schizophrenia patients' first grading kinship.^[12] It remains unclear if some domains of cognitive deficits also exist in the first grading kinship of patients with schizophrenia or not.

Previous studies had proved that there is a certain correlation between the negative symptoms of schizophrenia and verbal working memory.^[13, 14, 15] Some studies showed that even if psychotic symptoms disappear, the impairment of verbal memory still exists. Moreover, the impairment also exists in their first grading kinship. In order to explore whether there were differences between schizophrenia patients, their first grading kinship and normal controls in verbal working memory, Sonia investigated 197 cases of schizophrenia, 197 cases of their first-grading relatives, and 200 normal controls by Trail Matching Test. The study showed that the Trail Matching Test level of patients with schizophrenia was lower than that of their first-grading relatives and normal control group. While, there were differences between first-grading relatives and normal control group too. The study suggested that verbal

Figure 1. The flowchart of the study

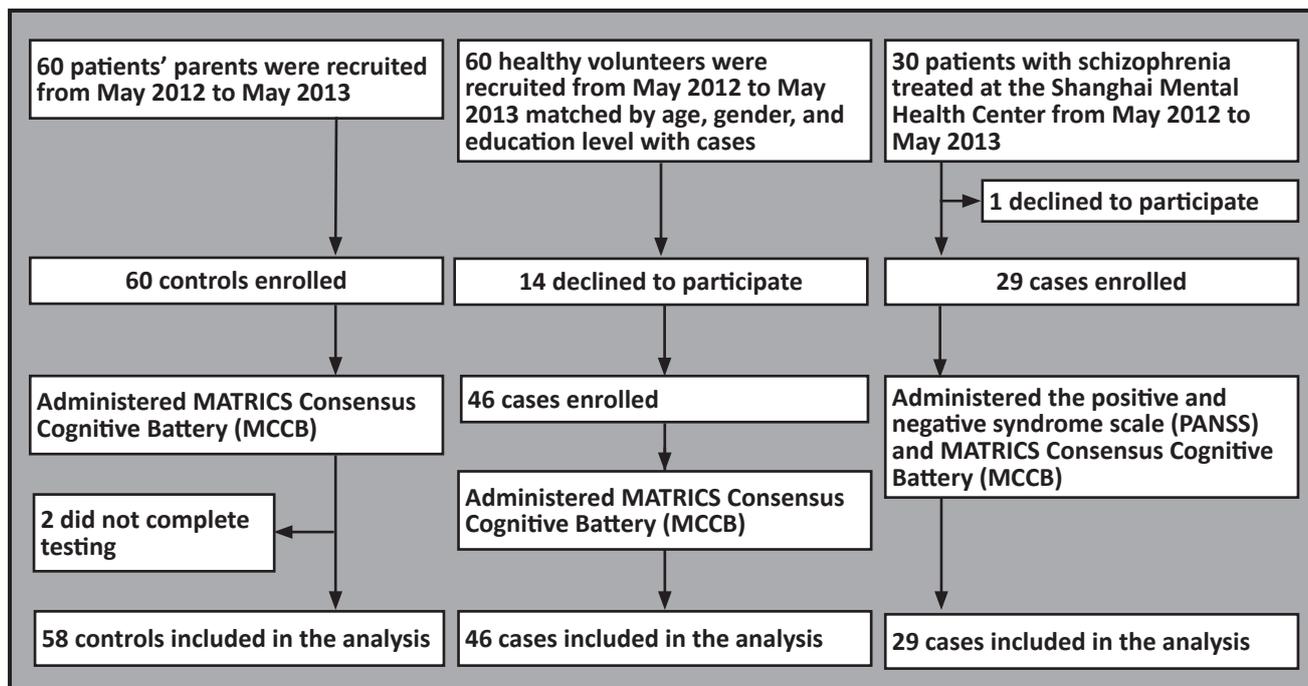


Table 1. Comparison of general information between patients' parents and control group

| | | first-episode schizophrenia (n=29) ① | Patients' parents (n=58)② | Control group (n=46) ③ | ①vs② | | ①vs③ | | ②vs③ | |
|-----------|--------|--|---------------------------------|------------------------------|-------|--------|-------|--------|-------|------|
| | | | | | t | p | t | p | t | p |
| Age | Male | 26.21(5.30) | 53.20(8.07) | 49.41(5.80) | 16.31 | <0.001 | 18.09 | <0.001 | 1.43 | 0.16 |
| | Female | 24.92(6.10) | 48.57(5.27) | 49.42(5.30) | 18.71 | <0.001 | 19.32 | <0.001 | -0.58 | 0.57 |
| Education | Male | 1.87(0.69) | 1.70(0.88) | 1.50(0.74) | 0.91 | 0.370 | 2.24 | 0.027 | 0.00 | 0.39 |
| | Female | 1.90(0.71) | 1.50(0.88) | 1.50(0.66) | 2.12 | 0.037 | 2.60 | 0.011 | 0.87 | 1.00 |

Table 2. Comparison of seven psychological dimensions between patients and control group

| Cognition domain | Patients (n=29) | Control group (n=46) | p | F |
|-------------------|-----------------|----------------------|--------|-------|
| Speed Processing | 32.86(10.64) | 47.67(7.78) | <0.001 | 9.721 |
| Attention | 31.34(11.19) | 46.13(9.83) | <0.001 | 5.212 |
| Working Memory | 35.17(14.64) | 48.83(7.40) | <0.001 | 5.830 |
| Verbal Learning | 34.45(12.46) | 47.98(11.95) | 0.001 | 4.122 |
| Visual Learning | 44.14(8.63) | 46.07(12.15) | 0.631 | 0.750 |
| Problem Reasoning | 39.07(10.47) | 45.24(7.96) | 0.046 | 2.195 |
| Social Cognition | 41.17(12.21) | 45.50(11.69) | 0.070 | 1.989 |

Table 3. Comparison across seven psychological dimensions between patients and their parents

| Cognition domain | Patients (n=29) | Parents (n=58) | p | F |
|-------------------|-----------------|----------------|-------|-------|
| Speed Processing | 32.86(10.64) | 47.36(8.26) | 0.005 | 8.214 |
| Attention | 31.34(11.19) | 45.17(6.94) | 0.005 | 8.200 |
| Working Memory | 35.17(14.64) | 44.15(11.43) | 0.394 | 0.734 |
| Verbal Learning | 34.45(12.46) | 34.45(12.46) | 0.175 | 1.812 |
| Visual Learning | 44.14(8.63) | 53.26(9.47) | 0.012 | 6.586 |
| Reasoning Problem | 39.07(10.47) | 48.55(12.51) | 0.091 | 2.625 |
| Social Cognition | 41.17(12.21) | 45.86(13.95) | 0.100 | 2.764 |

Table 4. Comparison of seven psychological dimensions between patients' parents and control group

| Cognition domain | Parents (n=58) | Control group (n=46) | p | F |
|-------------------|----------------|----------------------|-------|-------|
| Speed Processing | 47.36(8.26) | 47.67(7.78) | 0.124 | 1.677 |
| Attention | 45.17(6.94) | 46.13(9.83) | 0.602 | 0.785 |
| Working Memory | 44.15(11.43) | 48.83(7.40) | 0.231 | 1.360 |
| Verbal Learning | 34.45(12.46) | 47.98(11.95) | 0.001 | 4.122 |
| Visual Learning | 53.26(9.47) | 46.07(12.15) | 0.033 | 2.297 |
| Problem Reasoning | 48.55(12.51) | 45.24(7.96) | 0.081 | 1.881 |
| Social Cognition | 45.86(13.95) | 45.50(11.69) | 0.549 | 0.850 |

working memory might be one of endophenotype manifestations for schizophrenia.^[16]

Electrophysiological studies found that the abnormality of P300 was one index of the cognitive dysfunctions for patients with schizophrenia during the stable period of drug withdrawal. The P300 in frontal brain regions of the patients' healthy relatives dropped, which also suggested that the amplitude of P300 could be used as the endogenous EEG physiological signs to schizophrenia's relatives^[17]. Iconography studies showed that the reduced grey matter on the frontal lobe of the patients with schizophrenia was associated with the impairment of cognitive function. One fMRI study found that the abnormal activation in ventral anteriornucleus and dorsomedial nucleus decreased for schizophrenia group.^[18] Another study on late-onset schizophrenia explored the relative characteristics between rCBF and cognitive impairment, which displayed the relationship between the left frontal lobe dysfunction and memory impairment in late-onset schizophrenia.^[19] These studies demonstrated that there were potential biological mechanisms of cognitive deficits in patients with schizophrenia, relatively independent of clinical symptoms.

4.2 Limitations

The sample size is small, but the disease of the first-episode patients is representative. We hope to increase the sample size in subsequent studies and demonstrate the above result.

4.3 Implications

Based on the current findings, the study tested the cognitive patterns of first-episode patients with schizophrenia and their biological parents using a novel cognition measurement battery. The cognitive assessment tool is the Chinese version of cognitive test battery of schizophrenia (MCCB) developed by the United States MATRICS company. The first interesting result showed that male patients with schizophrenia had obvious cognitive defects in six domains of cognitive function by MCCB tools except the social cognition domain. This result confirmed that social cognition may be one of the endophenotypes for schizophrenia and schizophrenia patients' first grading kinship.^[20] Meanwhile, the female patients showed lower ability on both working memory and problem reasoning than their female parents. The statistically significant differences also existed between the patients' fathers and healthy controls. But the patients' mothers didn't show any significant difference of reasoning problem domain compared with healthy control. Abnormal visual learning domain appeared in patients' mothers compared with healthy controls. Thus, both the first-episode schizophrenia patients and their biological

parents have defects in working memory. The function defect is more significant in the schizophrenia patient group. The genetic susceptibility may be useful to explain the cognitive dysfunction existing in both the schizophrenia patients and their biological parents, especially for domains of verbal learning and reasoning problems.

There are six dimensions of cognitive impairments in both first-episode schizophrenia patients and their biological parents, including speed of processing, attention, working memory, verbal learning, visual learning, and problem reasoning as well. Compared to healthy controls, their biological parents have significant defects in domains of working memory, problem reasoning and visual learning as well. Undoubtedly, the small sample limited the current meaning of this study. However, patients with schizophrenia have significant cognitive dysfunctions, which may be affected by the course of disease, medications, etc. This study analyzed the cognitive patterns in patients with first-episode schizophrenia so as to minimize the effects of medication and course of disease. Future studies need to explore the underlying mechanisms of similar cognitive dysfunction between patients with first-episode schizophrenia and their biological parents.

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Conflict of interest statement

The authors declare no conflict of interest related to this manuscript.

Informed consent

All participants and their legal guardians provided signed informed consent to participate this study

Ethical approval

The ethics committee of the Sixth People's Hospital of Peking University approved this study

Authors' contributions

Cao A, Shen T, and Peng DH chose the study topic and wrote the draft.

Cai A, Li HB, and Wu CX performed the data analysis.

McCabe M and Mellor D provided guidance on data analysis.

Zhang J and Huang J collected cases

MCCB 测定首发精神分裂症患者及其生物学父母存在认知功能障碍

Cao A, Shen T, Li H, Wu C, McCabe M, Mellor D, Byrne L, Zhang J, Huang J, Peng D, Xu Y

背景: 精神分裂症的临床表现为特征性的知觉、思维、情感和行为等障碍。认知障碍也是精神分裂症核心症状之一。20世纪70年代早期 Gallhofer 曾提出过, 精神分裂症除有阳性或阴性症状, 也存在认知障碍。许多研究表明, 精神分裂症的一级亲属中存在遗传易感性。认知障碍不仅急性期存在, 维持巩固期也会有。有研究还显示, 精神分裂症健康的一级亲属亦存在认知缺陷。但对精神分裂症及其生物学父母的认知特征研究仍缺乏。本研究, 我们假设精神分裂症及其生物学父母存在特定的认知功能障碍, 拟采用认知功能成套测验共识版 (MATRICS Consensus Cognitive Battery, MCCB) 中文版, 以探讨精神分裂症患者及其生物学父母的认知模式。

目的: 精神分裂症的认知特征可能受到其生物学父母认知模式的影响。研究旨在描绘精神分裂症患者与其父母之间的功能失调的认知模式。

方法: 采用认知功能成套测验共识版 (MCCB, 一种新的测量工具) 评估 29 例首发精神分裂症 (符合 ICD-10 精神分裂症诊断标准, 年龄 17-45 岁), 58 例精神分裂症

患者的生物学父母 (年龄 40 - 70 岁) 和 46 例健康对照 (年龄 40-70 岁) 的认知功能, 以探讨精神分裂症患者及其生物学父母之间的认知功能障碍之间的关系。所有数据使用 SPSS18.0 统计软件进行分析。

结果: 1) 男性精神分裂症患者与其父亲相比在 MCCB 认知功能测定的 6 个维度有明显认知缺陷 (除社会认知功能外)。女性患者的工作记忆和问题推理能力都低于其母亲。2) 患者父亲和健康对照组之间的工作记忆和推理问题也存在显著差异。3) 与健康对照组相比, 患者母亲在问题推理方面没有明显的差异, 但视觉记忆有异常。

结论: 首发精神分裂症患者及其生物学父母在 6 个维度存在认知功能障碍。患者父母在工作记忆、问题推理和视觉记忆等方面也存在明显功能障碍。仍需深入研究以揭示首发精神分裂症及其生物学父母存在认知功能障碍的潜在机制。

关键词: 首发精神分裂症; 认知功能; 生物学父母; 认知功能成套测验共识版 (MCCB)

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Aiai Cao graduated from Shanghai Jiaotong University School of Medicine in 2010 with her bachelors of medicine and in 2013 with a masters of medicine. Since 2013 she has been working in Shanghai at the women's psychiatric unit of Changning District Mental Health Center. Her research interests include inflammatory factors, cognitive function and genetics of schizophrenia and affective disorders.



Dr. Ting Shen is currently working as a deputy director of physician in the department of emergency and severe case in Shanghai Mental Health Center. She has been engaged in clinical and research work in psychiatry for 18 years. Her research interest is the clinical research of schizophrenia.