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The correlation between metabolic syndrome and neurocognitive and social cognitive performance of patients with schizophrenia

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Abstract

Cognitive impairment is one of the core symptoms of schizophrenia, and patients with schizophrenia are at increased risk of metabolic syndrome (MS). However, the role of MS in cognitive impairment of schizophrenia is not established. This study investigated the correlation between neurocognitive, social cognitive performance and MS with schizophrenia. One hundred and fifty eight (158) schizophrenia patients were divided into 3 groups with ① normal metabolism, ② metabolic disorder (only meeting 1 or 2 MS criteria), and ③ metabolic syndrome (meeting 3 or more MS criteria). MATRICS Consensus Cognitive Battery)MCCB(and the Brief Psychiatric Rating Scale)BPRS(were used to evaluate cognitive performance and clinical symptoms. Blood samples were obtained to detect glucose and lipid metabolic levels. Overall MCCB and subscale T scores in the normal metabolism and metabolic disorder groups were better than in the MS group. After controlling for the confounding factors including age, sex, the usage of hypolipidemic and hypoglycemic drugs, and disease duration, metabolic deficits had effects on the symbol coding and spatial span scores. The results suggest that a defective metabolic state might play a role in neurocognitive performance of schizophrenia patients.

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The correlation between metabolic syndrome and neurocognitive and social cognitive performance of patients with schizophrenia

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ABSTRACT

Cognitive impairment is one of the core symptoms of schizophrenia, and patients with schizophrenia are at increased risk of metabolic syndrome (MS). However, the role of MS in cognitive impairment of schizophrenia is not established. This study investigated the correlation between neurocognitive, social cognitive performance and MS with schizophrenia. One hundred and fifty eight (158) schizophrenia patients were divided into 3 groups with ① normal metabolism, ② metabolic disorder (only meeting 1 or 2 MS criteria), and ③ metabolic syndrome (meeting 3 or more MS criteria). MATRICS Consensus Cognitive Battery)MCCB(and the Brief Psychiatric Rating Scale)BPRS(were used to evaluate cognitive performance and clinical symptoms. Blood samples were obtained to detect glucose and lipid metabolic levels. Overall MCCB and subscale T scores in the normal metabolism and metabolic disorder groups were better than in the MS group. After controlling for the confounding factors including age, sex, the usage of hypolipidemic and hypoglycemic drugs, and disease duration, metabolic deficits had effects on the symbol coding and spatial span scores. The results suggest that a defective metabolic state might play a role in neurocognitive performance of schizophrenia patients.

1. Introduction

Cognitive impairment is one of core symptoms of schizophrenia, mainly neurocognition and social cognition. Cognitive dysfunction significantly affects social performance and overall prognosis (Wu et al., 2016). Many factors can affect cognitive performance; metabolic syndrome (MS) is one of the factors (Chen et al., 2016). In fact, the incidence of metabolic syndrome in schizophrenia is twice that in the general population (Wu et al., 2013).

A number of studies (Boyer et al., 2014, Boyer et al., 2013) have established that MS can impair neurocognitive performance in schizophrenia patients. The latest Meta-analysis (Bora et al., 2017) reported that schizophrenia patients with MS and diabetes had more serious cognitive deficits than those without these metabolic disorders, while MS patients had much poorer memory, poor attention, low processing speed, and poor execution. There is a significant correlation between cognitive dysfunction and MS components including hypertension, dyslipidemia, abdominal obesity, and diabetes in schizophrenia patients. Chinese population studies have also shown much more severe neurocognitive impairment in schizophrenia patients with MS (Li et al., 2014).

However, it is controversial and inconclusive as to which neurocognitive dimensions can be affected more significantly by MS, and whether metabolic syndrome can aggravate social cognition of schizophrenia patients and is still rarely reported. In light of these questions, this study aims to find the possible correlation between MS and overall cognitive performance, and different cognitive dimensions, in schizophrenia patients. This will provide a theoretical basis to answer these questions and help to improve cognitive performance in schizophrenia patients from the perspective of metabolism.

2. Material and methods

2.1. Participants

The study included 158 patients with schizophrenia who were admitted to the psychiatry department at the Third Affiliated Hospital of Sun Yat-sen University, from May 2017 to October 2017, and who were

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receiving antipsychotic medications for 1 year or more. Inclusion criteria for patients with schizophrenia included (1) Meeting diagnostic criteria for schizophrenia (ICD-10); (2) Aged 16 to 55 years, male or female; (3) Having 1 year or longer course of illness and currently in a chronic state; (4) Receiving antipsychotic medications, either as a single agent or as a combination therapy, either with first generation antipsychotics (FGAs) or second generation antipsychotics (SGAs). (5) Have had a period of six or more years of education; (6) Family members or legal guardians of patients fully understood the study contents and had given written, informed consent.

Exclusion criteria for patients with schizophrenia included (1) History of receiving immunosuppressant therapy or taking steroids in the last three months; (2) History of other mental illnesses (such as mood disorders, anxiety, eating disorders, substance abuse, or intellectual disability); (3) Hearing and visual disturbances; (4) Have a history of serious or chronic physical disease (including heart failure, thyroid dysperformance, chronic hepatitis, and metabolic disease history); (5) Pregnancy or lactation in women.

2.2. Diagnostic criteria for metabolic syndrome (MS)

The study employed the unified definition of metabolic syndrome assessed as per the Joint Interim Statement (JIS) definition (Alberti et al., 2009), which requires three out of five of the following risk factors: (1) Abdominal circumference criteria for Asians (Grundy et al., 2005): male ≥ 90 cm, female ≥ 80 cm. (2) Hypertension (≥130 mmHg for systolic blood pressure or ≥85 mmHg for diastolic blood pressure) or on hypertensive medication. (3) Raised fasting blood glucose ≥ 5.6 mmol/L or on diabetic medication. (4) Raised fasting triglyceride ≥1.7 mmol/L. (5) Low high-density lipoprotein cholesterol (HDL-C) [<1.0 mmol/L for men, <1.3 mmol/L for women]. Applying the MS criteria, patients were divided into 3 groups ① normal metabolism (meeting none of the MS diagnostic criteria), ② metabolic disorder (only meeting 1 or 2 MS diagnostic criteria), and ③ metabolic syndrome (meeting 3 or more MS diagnostic criteria).

2.3. Evaluation tools

2.3.1 Survey of Demographic and General Clinical Data. We used a self-made questionnaire to obtain general data including age, sex, ethnicity, illness duration, number of hospitalizations, previous treatment with antipsychotics and type, duration and dose of medication, years of schooling, lifestyle (smoking, drinking history, exercise volume/week), whether taking medications which control blood pressure, blood lipids and glucose and for how long. The weight, height, waist circumference, blood pressure, glucose and lipid metabolism indicators of all subjects were tested and collected by a specific researcher.

2.3.2 MATRICS Consensus Cognitive Battery (MCCB) The MATRICS Consensus Cognitive Battery (MCCB) includes 10 subtests: Continuous Performance Test- Identical Pairs, Trail Marking Test Part A, Category Fluency, Symbol Coding, Hopkins Verbal Learning Test (HVLT), Brief Visuospatial Memory Test (BVMT), The Third Version Wechsler Memory Scale-Spatial Span, Digital Sequence, Neuropsychological Assessment Battery (NBA), and the Managing Emotions of Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT). MCCB includes seven cognitive domains: attention/vigilance, information processing speed, verbal learning, visual learning, working memory, reasoning and problem solving, and social cognition. MCCB is used worldwide, and is recommended by the US Food and Drug Administration (FDA) for assessing cognitive performance of patients with schizophrenia. All subscales were converted to T scores based on the raw score (mean 50, standard deviation 10). The MCCB total score is the sum of the subscales and converted into T points. The higher the T score of subscales and total T score, the better the cognitive performance.

2.3.3 *The Brief Psychiatric Rating Scale (BPRS)* is a scale for assessing the severity of psychotic symptoms and is suitable for the majority of patients with severe psychotic symptoms, especially for patients with schizophrenia. There are 18 items in total and consists of five sub-factors, namely anxiety and depression, lack of vitality, thinking disorder, activation, and hostile suspicion. The total score reflects the severity of the psychotic symptoms. The higher the BPRS score, the more severe the disease.

2.3.4 *ICD-10 and mini-SCID patients/non-patients version* are used to diagnose and recruit schizophrenia patients and healthy controls. Mini-International Neuropsychiatric Interview (MINI) designed by Sheehan and Lecrubier is a short structured interview questionnaire for International Classification of Mental and Behavioural Disorders, 10th Revision (ICD-10). MINI has very good reliability, very good validity, and very good researcher consistency. The interview time is obviously shorter than SCID. The work is in the charge of chief psychiatrist Zili Han. Through case review, all patients had previously been diagnosed with schizophrenia, and at the time of enrollment, the diagnosis of schizophrenia was confirmed again by retrospective evaluation of mini-SCID. All healthy subjects were and are not eligible for any type of mental disorder in ICD-10 after mini-SCID evaluation.

2.4. Research process

The schizophrenia diagnosis process was conducted by an associate chief physician in the Psychiatry Department, who used the mini-SCID procedure according to the ICD-10 diagnostic criteria. In order to accurately study the effects of metabolisms on cognitive performance, all schizophrenia patients in our study were divided according to MS criteria into normal metabolism (meeting none of the MS diagnostic criteria), metabolic disorder (only meeting 1 or 2 items of the MS diagnostic criteria) and metabolic syndrome (meeting 3 items or more of the MS diagnostic criteria). An attending physician evaluated the BPRS of all subjects and used a self-made general data questionnaire to collect demographic data such as age, gender, education, and lifestyle of all study subjects. The weight, height, waist circumference and blood pressure of all subjects were measured by a specific researcher. Finally, MCCB assessment was performed by another attending physician. Metabolic parameters such as fasting blood glucose and lipids for all participants were collected after 10 h fasting on the next morning by a nurse. All participants voluntarily attended this study and gave written informed consent to participating in this study. The Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University approved this study protocol.

2.5. Statistical analysis

The distribution of the variables was assessed using the Shapiro-Wilk test. Normally distributed continuous variables were presented as mean ± standard deviation (SD), demographic and general clinical data were tested by one-way analysis of variance (ANOVA). Skewed distributed continuous variables were tested by a rank-sum test or Kruskal–Wallis H test. The Chi-square test was used for category variables. Fisher's least significant difference (LSD) test was used to perform post-hoc pair-wise comparison between groups of normal metabolism, metabolic disorder and metabolic syndrome. Meanwhile, ANCOVA was used to test the effects of metabolic conditions on cognitive performance, while age, sex, hypolipidemic and hypoglycemic drugs, antipsychotic drug doses, and disease duration were used as confounding factors. Finally, Multiple Linear Regression was used to investigate the effect of individual component of MS on cognitive performance. All statistical analyses were performed using the IBM SPSS 23.0 software package. All *p*-values were two tailed with significance level set at 0.05.

Table 1
Demographic and general clinical data among three groups of patients with schizophrenia.

Variable	Normal metabolism① (n = 37)	Metabolic disorder② (n = 63)	Metabolic syndrome③ (n = 58)	F/χ^2	P	①VS②	①VS③	②VS③
Age(yrs)	23.78(5.07)	28.10(7.82)	31.41(7.59)	23.480	<0.001	0.004	<0.001	0.012
Education(y)	13.43(2.62)	13.21(3.10)	12.90(3.08)	0.804	0.669			
Sex								
Male	17(45.95%)	27(42.86%)	34(58.62%)	3.228	0.199			
Female	20(54.05%)	36(57.14%)	24(41.38%)					
Smoking								
Yes	2(5.41%)	8(12.70%)	13(22.41%)	5.510	0.064	0.407	0.054	0.159
No	35(94.59%)	55(87.30%)	45(77.59%)					
Drinking								
Yes	1(2.70%)	2(3.17%)	5(8.62%)	2.408	0.300			
No	36(97.30%)	61(96.83%)	53(91.38%)					
Exercise								
Yes	16(43.24%)	20(31.75%)	14(24.14%)	3.788	0.150			
No	21(56.76%)	43(68.25%)	44(75.86%)					
Antihypertensive drug	0)0%(	0)0%(	1)1.72%(	1.724	0.422			
Hypolipidemic drug	0)0%(	0)0%(	4)6.90%(	7.031	0.030	0.000	0.154	0.050
Hypoglycemic drugs	0)0%(	1)1.59%(	9)15.52%(	13.206	0.001	1.000	0.011	0.007
Antipsychotic drugs dose(DDD)	330.59(200.57)	425.21(244.15)	402.70(226.70)	2.872	0.238			
Disease duration(m)	65.54(50.46)	76.59(50.10)	93.33(74.76)	2.570	0.080	0.379	0.030	0.130
Drug compliance	6.57(1.63)	6.54(1.72)	6.48(1.43)	0.399	0.819			
BPRS total score	30.03(8.83)	29.73(10.46)	29.60(7.64)	0.637	0.727			

DDD means Drug dose was chlorpromazine equivalence (Gardner et al. 2010).

Table 2
The neurocognitive and social cognitive performance difference between groups of patients with schizophrenia (ANCOVA).

Variable	Groups Normal metabolism① (n = 37) Means(SE)	Metabolic disorder② (n = 63) Means(SE)	Metabolic syndrome③ (n = 58) Means(SE)	①VS②	①VS③	②VS③	F	P
Information processing speed								
TMT	47.51(2.05)	47.57(1.49)	44.99(1.63)	0.980	0.361	0.253	0.735	0.481
SC	38.00(2.03)	35.18(1.48)	31.08(1.62)	0.263	0.012	0.068	3.426	0.035
CF	39.68(1.56)	39.10(1.14)	37.79(1.24)	0.761	0.367	0.446	0.473	0.624
Verbal learning(HVLT)	34.38(2.56)	33.03(1.86)	30.21(2.04)	0.670	0.227	0.318	0.837	0.435
Working memory								
SS	37.30(2.56)	41.96(1.87)	35.20(2.04)	0.143	0.544	0.018	3.112	0.047
DS	40.43(2.34)	41.33(1.70)	37.09(1.86)	0.757	0.287	0.101	1.402	0.249
Reasoning and problem solving(NAB)	40.36(2.89)	40.23(2.10)	40.66(2.30)	0.970	0.940	0.893	0.009	0.991
Visual learnin(BVMT)	38.54(2.48)	39.59(1.81)	35.30(1.98)	0.732	0.333	0.118	1.260	0.287
Attention/vigilance(CPT)	39.83(2.09)	38.82(1.52)	35.36(1.66)	0.694	0.113	0.134	1.603	0.205
Social cognition(MSCEIT)	51.13(2.53)	50.51(1.84)	50.46(2.01)	0.844	0.844	0.985	0.024	0.977
Overall Cognition (MCCB)	33.33(2.61)	34.26(1.90)	28.61(2.08)	0.774	0.181	0.051	2.014	0.137

TMT: trail making A test; SC: symbol coding test; HVLT: Hopkins verbal learning test; SS: spatial span; DS: digital sequence; NAB: Neuropsychological Assessment Battery (NAB); BVMT: brief visual spatial memory test; CF: category fluency; CPT: Continuous Performance; MSCEIT: Mayer-Salovey-Caruso Emotional Intelligence Test; MCCB: MCCB total score.
Age, sex, hypolipidemic, hypoglycemic drugs, antipsychotic drug doses, and disease duration were controlled as covariates in this data analysis.

3. Results

3.1. The comparison of demographic and general clinical data between schizophrenia patients with normal metabolism, metabolic disorder and metabolic syndrome

Table 1. shows the demographic information of all subjects. Among 158 patients with schizophrenia, 37 patients had normal metabolism, 63 patients met the metabolic disorder criteria but did not reach the MS criteria, and 58 patients met the MS criteria. The prevalence of MS was 37.61%. The average age of the normal metabolism group was 23.78 ± 5.07 years, and the average disease duration was 65.54 ± 50.46 months. The average age of the metabolic disorder group was 28.10 ± 7.82 years, and the average disease duration was 76.59 ± 50.10 months. The average age of the metabolic syndrome group was 31.41 ± 7.59, and the average disease duration was 93.33 ± 74.76 months. The use of hypolipidemic and hypoglycemic drugs in patients with metabolic syndrome was higher than in the other two groups (Table 1).

There were significant differences between three groups in age, the usage of hypolipidemic and hypoglycemic drugs, and the disease duration (Table 1). However, there was no significant difference between the three groups in the categories of sex, smoking, drinking, exercise, years of education, antipsychotic drug doses, antihypertensive drug, drug compliance, and the BPRS total score (all $p > 0.05$) (Table 1).

3.2. The comparison of cognitive performance between patients with normal metabolism, metabolic disorder and metabolic syndrome

Overall MCCB total T scores and subscale T scores of the metabolic syndrome group were the lowest, while the metabolic disorder group was much lower than the normal group. Since there were significant differences in age, the use of hypolipidemic and hypoglycemic drugs, and disease duration between the three groups (Table 1), the confounding factors (including age, sex, hypolipidemic, hypoglycemic drugs, antipsychotic drug doses, and disease duration) were controlled for ANCOVA test. ANCOVA showed significant main effects of metabolic factors on SC (F(2155) = 3.426, p = 0.035), and SS (F

Table 3
Multiple Linear Regression analysis of factors affecting cognitive performance in schizophrenia patients.

	TMT		SC		HVLT		SS		DS		NAB		BVMT		CF		MSCEIT		CPT		MCCB	
	B	*P*	*B*	*P*	*B*	*P*	*B*	*P*	*B*	*P*	*B*	*P*	*B*	*P*	*B*	*P*	*B*	*P*	*B*	*P*	*B*	*P*
AC	0.010	0.929	−0.291	0.008	−0.024	0.852	−0.057	0.683	−0.134	0.281	−0.053	0.725	−0.076	0.544	−0.018	0.829	0.016	0.906	−0.140	0.202	−0.142	0.299
SBP	0.017	0.882	0.090	0.412	0.288	0.033	0.058	0.683	0.026	0.840	0.339	0.028	0.222	0.084	0.097	0.248	0.170	0.214	0.243	0.030	0.304	0.029
DBP	−0.026	0.847	−0.042	0.751	−0.393	0.015	−0.104	0.543	0.023	0.879	−0.408	0.028	−0.480	0.002	−0.081	0.425	−0.007	0.966	−0.159	0.234	−0.304	0.070
TG	−1.455	0.210	0.134	0.906	−3.142	0.024	−2.937	0.047	−0.650	0.621	0.027	0.987	−4.007	0.003	−0.985	0.259	−1.473	0.298	−2.194	0.058	−2.847	0.049
HDL-C	−0.301	0.947	2.326	0.602	2.954	0.587	−5.875	0.310	0.819	0.874	3.294	0.598	−10.831	0.039	−1.411	0.680	−1.570	0.777	−3.211	0.478	−1.083	0.848
PFG	−1.669	0.184	−1.491	0.225	−0.167	0.911	0.119	0.940	−3.157	0.027	−2.717	0.115	−0.776	0.588	−2.122	0.025	−2.427	0.113	−2.226	0.075	−1.964	0.207

TMT: trail making A test; SC: symbol coding test; HVLT: Hopkins verbal learning test; SS: spatial span; DS: digital sequence; NAB: Neuropsychological Assessment Battery (NAB); BVMT: brief visual spatial memory test; CF: category fluency; CPT: Continuous Performance; MSCEIT: Mayer-Salovey-Caruso Emotional Intelligence Test; MCCB: MCCB total score; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; AC: Abdominal circumference. TG: Triglycerides; HDL-C: High density lipoprotein cholesterol; PFG: Plasma fasting glucose.

(2155) = 3.112, p = 0.047). Further post-hoc analysis showed that patients with normal metabolism has significant higher SC scores than those with metabolic syndrome (p = 0.012), while patients with metabolic disorder had significant higher SS scores than metabolic syndrome group (p = 0.018) (Table 2).

3.3. The effect of different components of MS on cognitive performance

The total T scores and subscale T scores of MCCB for schizophrenia patients were used as dependent variables, while age, sex, hypolipidemic and hypoglycemic drugs, antipsychotic drug doses, disease duration, and glucose and lipid metabolism parameters were set as independent variables for multiple linear regression analysis (Table 3). We found that systolic blood pressure significantly influenced HVLT, NAB, CPT, and MCCB total score ($p < 0.05$), while diastolic blood pressure had significant impacts on HVLT, NAB, and BVMT ($p < 0.05$). TG had significant impacts on HVLT, SS, and BVMT. Meanwhile, PFG significantly influenced DS and CF. AC and HDL-C had effects on SC and BVMT, respectively ($p < 0.05$) (Table 3).

4. Discussion

This study found that a defective metabolic state played a role in the neurocognitive performances of schizophrenia patients. After controlling the confounding factors (age, sex, antipsychotic dose, disease duration, and the use of hypolipidemic and hypoglycemic drugs), ANCOVA found that metabolic states had effects on SC and SS in chronic schizophrenia patients (Table 2). These results suggested that a defective metabolic state might exacerbate the neurocognitive deficits of schizophrenia, especial in SC and SS. Divergent cognitive impairments have been reported previously in schizophrenia patients with MS compared to those without MS (Boyer et al., 2014, Li et al., 2014, Lindenmayer et al., 2012). For example, Kern (Kern et al., 2011) reported that, while reasoning and problem solving were less impaired, processing speed and working memory were serious damaged in schizophrenia patients. Ojeda et al. (Ojeda et al., 2012) has found that, after controlling information processing speed, working memory is no longer manifested as a unique feature of schizophrenia, suggesting that decreased processing speed may be the core cognitive deficits of schizophrenia. In this study, we also found that MS may have an effect on the symbol coding T score. Therefore, we cautiously speculated that MS slightly possibly affect information processing speed in patients with schizophrenia.

Recently, Eyler and Jeste reported (Eyler and Jeste 2017) that cognitive therapy and MS management may contribute to delay cognitive decline in schizophrenia patients. It is well established that the incidence of MS in chronic schizophrenia patients is 2–4 times that in the general population, while the patient's MS is hard to be reversed, even after stopping antipsychotic treatment (Wu et al., 2014). Evidence from this and previous studies indicates that early management of metabolic risk in schizophrenia patients is beneficial to the improvement of their core cognitive deficits (information processing). Therefore, it is critical in clinical practice to monitor regularly the glucose and lipid metabolic parameters during antipsychotic treatment, to guide for a healthy lifestyle, and to delay or block MS progresses, in order to prevent MS from aggravating cognitive deficits in schizophrenia patients.

The study subjects were divided into three groups according to the items meeting the MS diagnostic criteria. Schizophrenia patients with MS and metabolic disorder had much worse cognitive impairment in symbol coding than that of schizophrenia patients with normal metabolism. Studies on the general population showed that cognitive performance would be worse with the increase of items meeting the MS criteria (Li et al., 2016). At the same time, the accumulation of three or more cardiovascular risk factors (such as, obesity, hypertension, diabetes, and dyslipidemia) can increase the incidence of mild cognitive

impairment in elderly patients by 1.58 times, and the risk from mild cognitive impairment to dementia by 4.92 times (Ng et al., 2016). These studies suggest there is a cumulative effect of metabolic deficits on cognitive impairment. Our further analysis found that with the increase of items meeting MS criteria, cognitive performance also tends to worsen. The result suggests that MS may further worsen cognitive performance in patients with schizophrenia, especially in the SC cognitive dimension.

In order to further explore the effect of different MS parameters on cognitive performance in chronic schizophrenia patients, a multiple linear regression analysis was conducted and showed that neurocognitive performance was correlated with FPG, HDL-C, SBP, DBP, AC and TG. Particularly, the blood pressure (including systolic blood pressure and diastolic blood pressure) had effects on processing speed, working memory, reasoning and problem solving, verbal learning, visual learning and MCCB total scores. These findings were consistent with previous reports that fasting plasma glucose and blood pressure levels were significantly associated with cognitive impairments in processing speed, verbal learning, visual learning, and executive ability in schizophrenia (Goughari et al., 2015, Sabayan et al., 2013, Tsai et al., 2016). In fact, antihypertensive drugs could increase cerebral blood flow and improve neurocognitive performance in the patients with MS (Efimova et al., 2015).

A cross-sectional study reported that differences in social cognitive performance existed between pre-onset, acute phase, and chronic schizophrenia patients, and suggested that social cognitive impairment should occur early in the disease, and later in the disease there should be no further impairment or even improvement (Green et al., 2012). A prospective study conducted a one-year follow-up of first-episode schizophrenia patients and found that they maintained a relatively stable level of social cognitive performance after the acute phase (Horan et al., 2012). Social cognitive impairment in the acute phase was much worse than patients' in remission (Valaparla et al., 2017). This study found no significant effect of defective metabolism on the social cognition performance in chronic schizophrenia patients. Presumably this result may be due to: ① the subjects studied were chronic and stable schizophrenia patients, however social cognitive performance was significantly impaired in an acute phase of first onset and remained relatively stable at chronic phase. ② MS may affect neurocognitive performance, but might have minimal effects on social cognition. Although the MS group had significantly decreased neurocognitive scores including processing speed, digital sequence, working memory, attention, verbal learning, and visual learning, no significant differences were found between MS and non-MS group in terms of social cognition performance. ③ This study subjects were younger, and some patients had a shorter duration of metabolic syndrome, or they had already partially received drugs for intervention. As a result, our study did not find that MS has a widespread role in the deterioration of cognitive performance, especially in social cognition. (Akbaraly et al., 2010) reported that among people aged 33–55 years, the cognitive performance of participants with persistent MS during a 10 year follow-up period was worse than participants without MS, and no significant difference in cognitive performance was observed between those with non-persistent MS and those who never had MS during follow-up. ④ It is also worthy to note that the Managing Emotions of Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) in MCCB is far from a complete picture of social cognition in schizophrenia. Managing emotions is just one of social cognitive domains, including affect perception, social cue perception, theory of mind, empathy, and attribution style. Therefore, a comprehensive tool for social cognitive assessments is important in the future to explore the full picture of social cognition in chronic schizophrenia patients with defective metabolism.

5. Limitations

One limitation of this study is a relatively small sample size which may decrease our study efficiency, but increase the risk of false negative findings. On the other hand, as a cross-sectional study, it cannot easily distinguish the direction of relationships between cognitive performance and MS poor cognitive performance might be also a risk marker for developing MS due to poor decision making. Furthermore, it is worthy to note another significant limitation in this study that, due to lack of correction for multiple comparisons, we could not completely rule out the potential false positive findings reported in this paper. Therefore, a prospective, longitudinal study with adequate power in the future is necessary to confirm the findings in this study.

6. Conclusion

In summary, this study suggests that a defective metabolic state might play a role in neurocognitive performance of patients with schizophrenia, especially in the symbol coding and spatial span scores, either from the point of view of MS or the point of view of individual MS components. This may provide an opportunity for more precise clinical interventions aimed at cognitive deficits in chronic schizophrenia patients.

Author statement

All the authors agree to contribute the article to the journal of psychiatry research, their contributions are as follows.

X.W., J.T. and S.C. designed the experiments. S.C., X.X. and X.W. performed the experiments. S.C., X.W. and C.D. analyzed the data. S.C. and Z.H. prepared the initial draft of the manuscript. C.D. and X.W. revised and edited the manuscript.

There is no conflict of interest in relation to this paper.

CRediT authorship contribution statement

Shengyun Chen: Methodology, Formal analysis, Data curation, Writing - original draft. **Xiaowei Xia:** Methodology, Formal analysis. **Chao Deng:** Data curation, Writing - review & editing. **Xiuhua Wu:** Formal analysis, Data curation, Writing - review & editing. **Zili Han:** Writing - original draft. **Jiong Tao:** Methodology. **Xiaoli Wu:** Methodology, Formal analysis, Data curation, Writing - review & editing.

Declaration of Competing Interest

There is no conflict of interest in relation to this paper.

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Supplementary materials

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