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Analysis of influencing factors of visual working memory in young adult patients with schizophrenia

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ABSTRACT

Background Patients with schizophrenia have general cognitive impairments, and the impairment of working memory is considered to be the basis of cognitive impairments. The research on visual working memory, one of the subcomponents, is getting more and more attention. However, the influencing factors which cause the deficits of visual working memory in patients with schizophrenia have not been clearly explained. To provide evidence for cognitive impairment interventions, the present study explored the factors influencing the deficits of patients' visual working memory.

Aim The present study discussed the relevant factors influencing the visual working memory of patients with schizophrenia by measuring the accuracy of the visual working memory of patients with schizophrenia and healthy controls.

Methods Colour-recall paradigm was employed to measure the accuracy of the visual working memory of 61 healthy controls and 61 patients who met the International Classification of Diseases, Tenth Revision diagnostic criteria for schizophrenia. The age range of subjects was 18–50. Scale for the Assessment of Positive Symptoms (SAPS) and Scale for the Assessment of Negative Symptoms (SANS) were used to evaluate the patients' clinical symptoms.

Results Compared with the healthy control group, the accuracy of visual working memory of patients with schizophrenia was significantly impaired (t=3.062, p=0.003). The accuracy of visual working memory of patients with schizophrenia was not related to age (r=0.023, p=0.860), the age of onset (r=−0.003, p=0.979), the duration of illness (r=−0.038, p=0.769), education level (r=−0.181, p=0.162), continuous working time before illness (r=−0.107, p=0.413) or the daily dose of antipsychotic drugs (r=0.062, p=0.635); however, it was positively related to the number of hospitalisations (r=0.471, p<0.001). The total score of Scale for the Assessment of Positive Symptoms (SAPS) was negatively related to the accuracy of visual working memory (r=−0.388, p=0.005), while the total score of Scale for the Assessment of Negative Symptoms (SANS) (r=0.416, p=0.001), the total score of diminished emotional expressiveness (r=0.352, p=0.005) and the total score of attention disorder (r=0.310, p=0.015) were positively related to the accuracy of visual working memory. Patients using a single drug and those using multiple drugs were compared with each other. They were not significantly different in age (t=0.010, p=0.992), the number of hospitalisations (t=0.656, p=0.514), the duration of illness (t=0.701, p=0.486), the total score of SANS (t=0.078, p=0.938), the total score of SAPS (t=1.815, p=0.079) and the daily dose of antipsychotic drugs (t=1.794, p=0.078). However, in order to explore whether single or combined drug use would affect the accuracy of visual working memory of patients with schizophrenia, the present study also compared these two groups' different S0 values of the accuracy of visual working memory. The results showed that the accuracy of visual working memory of patients with schizophrenia with combined drug use was significantly better than that of patients with single drug use (t=2.515, p=0.015, independent sample t-test).

Conclusion The present study indicates that the visual working memory of young adult patients with schizophrenia is impaired compared with the healthy people within the same age range. The impairment is more obvious in patients who have multiple hospitalisations and suffer from severe negative symptoms. The impairment in patients with more severe positive symptoms is not very obvious. Combined drug use is likely to alleviate the impairment.

INTRODUCTION

Patients with schizophrenia have extensive cognitive impairments, and it significantly influences patients' functional prognosis.[1 2] How to evaluate patients' cognitive functions as the basis for the clinical intervention has become a hot topic in research in recent years. The impairment of working memory is considered as the basis of the cognitive impairments of patients with schizophrenia.[3] Therefore, as a subcomponent of working memory, visual working memory appears to be very important. Visual working memory is the activation of the maintained visual information in order to complete the ongoing task. Among many cognition theories, the concept of visual working memory is a dominant one, and it is used to explain the individual difference of fluid intelligence and multiple cognitive abilities.[4 5] Visual working memory's capacity is extremely limited with a maximum capacity of four items.[6] In recent

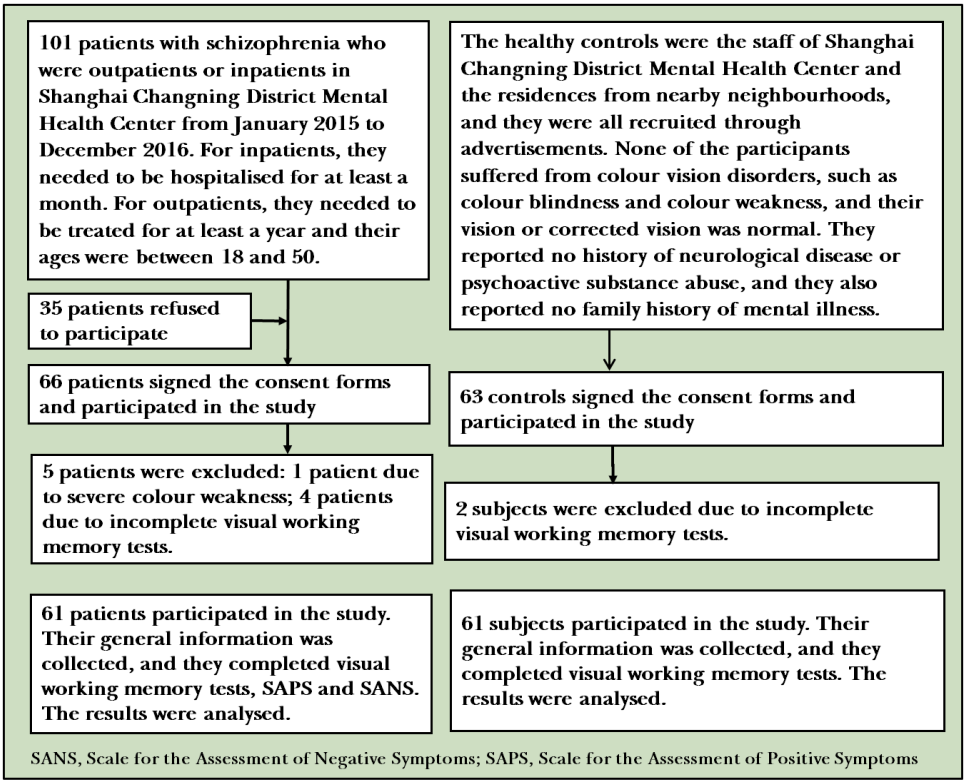

Figure 1 Flowchart of the study.

years, research has indicated that the accuracy of every piece of visual information in visual working memory is limited as well, and the characterisation accuracy of visual working memory is considered to be a more sensitive measurable index than the capacity.[7 8] Even though the importance of the role played by visual working memory on research about schizophrenia has been recognised, the explanation on influencing factors of visual working memory impairments in patients with schizophrenia has not been clear yet. Therefore, the present study employed the colour-recall paradigm,[8] which can measure the accuracy of visual working memory to measure and compare the visual working memory of young adult patients with schizophrenia and healthy controls. In the meantime, in order to provide evidence for interventions, the present study also tried to discuss the influencing factors of patients' visual working memory.

SUBJECTS AND METHODS

Subjects

The patients with schizophrenia who participated in the present study were outpatients and inpatients at the Shanghai Changning District Mental Health Center from January 2015 to December 2016 (figure 1). For inpatients, they needed to be hospitalised for at least a month; for outpatients, they needed to be treated for at least 1 year. Inclusion criteria: (1) subjects who met the diagnostic criteria of schizophrenia according to International Classification of Diseases, Tenth Revision; (2) aged between 18 and 44; (3) subjects who were able to complete the working memory test and clinical symptom evaluation; (4) subjects with no colour vision disorders such as colour blindness or colour weakness, and normal vision or corrected vision; (5) subjects whose education levels were equal to or above 9 years. Exclusion criteria: (1) subjects with mental retardation or organic brain diseases; (2) subjects with severe depression or impulsivity; (3) subjects with comorbid depression. Among 101 patients with schizophrenia who met the inclusion criteria, 35 of them declined to participate in the study, and one of them was found to have visual impairment. Four subjects completed the visual working memory simulation test. A total of 61 patients' cognitive and clinical evaluations were collected (29 males and 32 females). The age range was 23–48 years old with a median age of being 35 years old and a mean (SD) of 35.84 (6.65) years old. The duration of illness' range was 3–30 years with a median of 12 years and a mean (SD) of 13.13 (2.52) years. The range of education level was 9–16 years with a median of 12 years and a mean (SD) of 12.02 (2.24) years. The range of the number of hospitalisations was 0–14 times with a median of 3 times and a mean (SD) of 3.5 (2.7) times. The range of the continuous working time before illness was 0–22 years with a median of 0.5 years and a mean (SD) of 2.6 (4.4) years. The range of the total score of SAPS was 0–30 with a median of 4 and a mean (SD) of 5.67 (7.01). The range of the total score of SANS was 5–53 with a median of 23 and a mean (SD) of 24.87 (12.26). The use of antipsychotic drugs was the following: 35 subjects were using a single drug with 2 using a typical

antipsychotic drug and 33 using atypical antipsychotic drugs. Twenty-six participants were using multiple drugs with 12 of them employing a combined different atypical antipsychotics use, 14 of them employing a combined atypical and typical antipsychotics use and no combined typical antipsychotics use cases. According to the antipsychotics DDD value updated by the WHO on 20 December 2017, the range of the converted daily dose of patients was 0.2–3.5 with a median of 1.5 and mean (SD) of 1.63 (0.86).

The healthy controls were the staff of Shanghai Changning District Mental Health Center and residents from nearby neighbourhoods, and they were all recruited through advertisements. A total of 61 healthy controls participated in the study (32 males and 29 females). The age range was 18–50 years old with a median age of 31 years old and a mean (SD) of 33.82 (9.89) years old. None of the participants suffered from colour vision disorders, such as colour blindness or colour weakness, and their vision or corrected vision was normal. They reported no history of neurological disease or psychoactive substance abuse, and they also reported no family history of mental illness. The two groups were not significantly different in age (t=1.310, p=0.193) or gender (t=0.295, p=0.587).

Methods

Visual working memory test

The test for visual working memory in the present study was programmed with PsychToolbox software package on the Matlab platform, and the task was presented to the subjects on a laptop. The present study employed the colour-recall paradigm which was developed by Zhang and Luck at UC Davis in 2008.[8] At the beginning of every trial, a cross-hair point appeared in the centre of the screen, and the presentation duration ranged from 300 to 500 ms. After the cross-hair point disappeared, three square blocks with different colours were presented for 500 ms. The following was a 900 ms long blank delay period without any information presented. At last, the selection reaction stage was presented. Three black blocks were presented on the screen (the locations were corresponding to the previous three coloured blocks), and there was a coloured ring with 180 colours around the black block. The subjects were asked to click on the colour of the targeted block (the black block was bold) on the coloured ring using the mouse. Provided that subjects with schizophrenia could not concentrate for a long period of time, the subjects were allowed to control the duration of breaks themselves after every trial. They entered the next trial by pressing the space button. Every subject was required to complete 80 trials in the present study.

The memory targets used in the present study were three square blocks with different colours presented on a grey background (the side length was a viewing angle of 1.5°). The 180 colours used in the coloured blocks were from a gradient coloured ring (the radius was 8.2° and the width was 1.5°). The whole coloured ring was divided into 180 equal parts and every part represented a colour with all colours' brightness being the same.[2] In each trial, the coloured ring's direction rotated randomly, but the location did not change. In each trial, the three coloured blocks were presented in three spots out of eight established spots, and these eight spots were on an invisible ring with a 4.5° radius.

Baseline was tested before the official test in the present study. During the baseline, the memory targets and the coloured ring were presented on the screen together for the subjects to select, which was to serve as the instruction before the tests and the baseline survey. In addition, it was able to distinguish the subjects with unreported colour weakness and other colour visual disorders from the rest.

The present study focused on the difference between the colours selected by the subjects and the correct colours. Based on the difference of the angles, CircStat software package in Matlab was used to obtain the variance S0 of the reaction difference distribution,[9] which was used to present the accuracy of subjects' visual working memory. The bigger the S0 value is, the worse the accuracy of the visual working memory is; in contrast, the smaller the S0 value is, the better the accuracy of the visual working memory is.

Clinical evaluation

Scale for the Assessment of Positive Sympto

SAPS was mainly used to evaluate the positive symptoms of subjects with schizophrenia, including hallucinations, delusions, disorganised behaviour and positive thinking disorder. There are 18 items in total in four subscales. The total score of the scale represents the severity of positive symptoms, ranging from 0 to 170. The individual scores of subscales reflect the severity of four specific positive symptoms, ranging from 0 to 5. Evaluations were conducted by two trained psychiatric doctors, and it took about 45–60 min. This scale's reliability and validity are good; according to Zhang and colleagues' data,[10] the joint inspection intraclass correlation coefficient (ICC) is 0.94 and the test–retest reliability is 0.80.

Scale for the Assessment of Negative Symptoms

This scale was mainly used to assess the negative symptoms of subjects with schizophrenia, including diminished emotion expressiveness, lack of thinking, avolition, lack of interests and social activities and attention disorder.[10] There are 24 items in total in five subscales. The total score of the scale represents the severity of negative symptoms, ranging from 0 to 120. The individual score of each subscale reflects the severity of each of five specific negative symptoms, ranging from 0 to 5. Evaluations were conducted by two trained psychiatric doctors, and it took about 45–60 min. This scale's validity and reliability are good; according to Zhang and colleagues' data, the joint inspection ICC is 0.94 and the test–retest reliability is 0.80.

Statistics

The independent variable of the present study was S0 which represented the accuracy of visual working memory, and the dependent variable was the group. Whether there was a significant difference between the two groups' S0 values or not could they be tested through independent sample t-test, thereby exploring whether the patients with schizophrenia suffered significant impairments in the accuracy of visual working memory compared with the healthy controls. In order to discuss the influcing factors of the accuracy of visual working memory of patients with schizophrenia, a series of Spearman correlation analyses between S0 values and demographic information and scores of clinical evaluation scales, respectively. Moreover, the present study compared the accuracy of visual working memory of the patients with single drug use and the ones with combined drug use by using the independent sample t-tests to explore whether this aspect would affect the accuracy of visual working memory or not.

RESULTS

The comparison on the accuracy of visual working memory between 61 patients with schizophrenia and 61 healthy controls

In the baseline testing, there was no significant difference in completion status between the patients with schizophrenia and healthy controls (t=1.954, p=0.053). In the official testing, the S0 value of the patients with schizophrenia was 1.284 (0.474) and the S0 value of the healthy controls was 1.036 (0.404); the patient group's S0 value was significantly larger than that of healthy controls (t=3.062, p=0.003).

Correlation analyses' results

The correlation between the accuracy of visual working memory and demographic information of patients with schizophrenia

As shown in table 1, the S0 value of patients with schizophrenia was not correlated with age (r=0.023, p=0.860), the age of onset (r=−0.003, p=0.979), the duration of illness (r=−0.038, p=0.769), years of education (r=−0.181, p=0.162) and continuous working time before illness (r=−0.107, p=0.413); however, it was positively correlated with the number of hospitalisations (r=0.471, p<0.001).

Table 1 Correlation coefficients (r) between the accuracy of visual working memory of patients with schizophrenia and their demographic information

	r	P values
Age	0.023	0.860
Age of onset	−0.003	0.979
Duration of illness	−0.038	0.769
Education level	−0.181	0.162
Continuous working time before illness	−0.107	0.413
The number of hospitalisations	0.471	0.000**

**P<0.01.

Table 2 Correlation coefficients (r) between the accuracy of visual working memory of patients with schizophrenia and clinical symptoms

	r	P values
The total score of SAPS	−0.388	0.002**
The total score of SANS	0.416	0.001**
The total score of diminished emotion expressiveness	0.352	0.005**
The total score of language disorder	0.118	0.366
The total score of avolition	0.200	0.123
The total score of lack in interests and social activities	−0.023	0.863
The total score of attention disorder	0.310	0.015*

*p<0.05; **p<0.01.
SANS, Scale for the Assessment of Negative Symptoms; SAPS, Scale for the Assessment of Positive Symptoms.

The correlation between the accuracy of visual working memory and clinical symptoms of patients with schizophrenia

As shown in table 2, the total SAPS score of patients with schizophrenia was negatively correlated with their S0 values (r=−0.388, p=0.002).

The S0 values of patients with schizophrenia were positively correlated with their total SANS scores (r=0.416, p=0.001), the total scores of diminished emotion expressiveness (r=0.352, p=0.005) and the total scores of attention disorder (r=0.310, p=0.015).

The correlation between the accuracy of visual working memory and drug treatments of patients with schizophrenia

As shown in table 3, patients' daily dose of antipsychotics was not correlated with their S0 values (r=0.062, p=0.635). The results of comparisons between the single drug use group and the combined drug use group indicated that there were no significant differences in age (t=0.010, p=0.992), the number of hospitalisations (t=0.656, p=0.514), the duration of illness (t=0.701, p=0.486), the total SANS score (t=0.078, p=0.938), the total SAPS score (t=1.815, p=0.079) and the daily dose of antipsychotics (t=1.794, p=0.078); however, there was significant difference in S0 values (t=2.515, p=0.015).

DISCUSSION

Main findings

The present study's results indicated that patients with schizophrenia showed significantly worse accuracy of visual working memory than healthy controls did. This is in accordance with the results of other research on the visual working memory capacity of patients with schizophrenia,[11–13] which indicates that patients with schizophrenia do suffer from significant visual working memory impairments.

In the present study, the number of hospitalisations and the degree of working memory impairments were positively correlated. The more times patients have been hospitalised, the worse their working memory impairments are.

Table 3 Comparisons on the accuracy of visual working memory between patients with schizophrenia with a single use of drug and those with a combined use of drugs

	Patients with a single use of drug (n=35)	Patients with a combined use of drugs (n=26)	t	P values
Age	35.829 (6.900)	35.846 (6.577)	0.010	0.992
The number of hospitalisation	3.657 (2.960)	3.192 (2.400)	0.656	0.514
Duration of illness	12.657 (6.254)	13.769 (5.948)	0.701	0.486
The total score of SANS	24.229 (12.197)	24.462 (10.674)	0.078	0.938
The total score of SAPS	4.143 (4.117)	7.731 (9.434)	1.815	0.079
Daily dose of antipsychotics	1.46 (0.805)	1.855 (0.904)	1.794	0.078
S0	1.377 (0.497)	1.159 (0.422)	2.515	0.015*

Data were presented as mean (SD).
*$p<0.05$
SANS, Scale for the Assessment of Negative Symptoms; SAPS, Scale for the Assessment of Positive Symptoms.

The frequent hospitalisation suggests the reoccurrence of the illness; and this result also suggests that if the reoccurrence rate of schizophrenia increases, the prognosis will get worse and worse.[14] It was not found in the present study that age, the age of onset, the duration of illness, education level, the continuous working time before illness and the dose of antipsychotics were not significantly correlated with working memory impairments, which is similar to the findings of other scholars.[15] The previous longitudinal research and horizontal comparisons between patients with first episode and chronic patients indicate that the cognitive impairments of patients with schizophrenia stay stable for a relatively long period of time, unlike positive symptoms with obvious fluctuation.[16 17]

Many studies indicate that the negative symptoms of patients with schizophrenia are significantly correlated with their cognitive functions; the more severe negative symptoms are, the worse cognitive functions are.[18 19] The present study's results are in accordance with this. Moreover, the diminished emotional expressiveness and attention disorder have higher correlation rates; the more severe the diminished emotion expressiveness and attention disorder are, the more obvious the working memory impairments are. The negative symptoms and cognitive disorders in schizophrenia are also considered to be correlated with abnormalities in the functions of the dopamine system. Dopamine D1 receptors' dysfunction in the prefrontal cortex leads to the appearance of negative symptoms. Some scholars have conducted research on the short-term memory of patients with schizophrenia and found that the dysfunction of dopamine functions in the prefrontal cortex in patients with schizophrenia might cause them to fail to maintain short-term memory.[20 21]

According to the results of the present study, the more severe positive symptoms are, the less severe visual working memory impairments are, which is not in accordance with other studies' results that cognitive impairments are not significantly correlated with clinical symptoms, especially positive symptoms.[19] One of the possible reasons for this is that the patients with schizophrenia in the present study have scored relatively low on SAPS scales and the degree of their positive symptoms is different from that in other research.

Currently, the use of atypical antipsychotics is more common clinically. Some scholars have found that atypical antipsychotics can improve patients' working memory.[22 23] In the present study, 96.7% of the patients with schizophrenia were taking atypical antipsychotics, and the results showed that the accuracy of visual working memory of patients with a combined drug use was better than that of patients with a single drug use after the effects of age, the number of hospitalisations, the duration of illness, clinical symptoms and the dose of antipsychotics were excluded. The action mechanism of atypical antipsychotics is not limited to the blockade of dopamine D2 receptors, but also regulates serotonin (5-HT) and glutamatergic systems. In many neurobiological studies on schizophrenia, the dysfunction of many different receptors can affect patients' cognitive functions. Some scholars state that the interaction between 5-HT1A receptors and glutamatergic energy might be the mechanism of the cognitive impairments in schizophrenia; and other scholars state that new antipsychotic drugs should have D2/5-HT1A dual receptor mechanism, that is, both the antagonistic mechanism of D2 receptors and the agonistic effect of 5-HT1A receptors can improve the prognosis of schizophrenia comprehensively.[24 25] Further more comprehensive research on whether a combined use of antipsychotics, especially different atypical antipsychotics which affect different receptors, will improve cognitive functions or not is needed.

Limitations

The sample size of the present study is small, which shows the limitation of the present study. Furthermore, the present study is a horizontal study without follow-ups.

Implications

The present study employed the colour-recall paradigm to measure the visual working memory of young adult patients with schizophrenia. This paradigm is easy to administrate and applies to subjects with different

educational levels. The present study indicates that the accuracy of visual working memory of patients with schizophrenia is significantly correlated with high numbers of hospitalisations and severe negative symptoms; and the accuracy of visual working memory of patients with a combined use of drugs is better than that of patients with a single use of drug, which provides new directions for clinical treatments.

Contributors LZ was responsible for performing working memory evaluations, scale evaluations and data collections on participants, and writing and revising this paper. XR was responsible for performing working memory evaluations on participants, analysing the data and revising this paper. TL was responsible for evaluating participants with scales. YK was responsible for providing guidance for the present study and paper. LL, TH and WY recruited the participants and performed the working memory evaluations and scale evaluations.

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Competing interests None declared.

Patient consent for publication Obtained.

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