

# Hemispheric dominance during the mental rotation task in patients with schizophrenia

Jiu CHEN, Laiqi YANG\*, Jin ZHAO, Lanlan LI, Guangxiong LIU, Wentao MA, Yan ZHANG, Xingqu WU, Zihe DENG, Ran TUO

**Background:** Mental rotation is a spatial representation conversion capability using an imagined object and either object or self-rotation. This capability is impaired in schizophrenia.

**Objective:** To provide a more detailed assessment of impaired cognitive functioning in schizophrenia by comparing the electrophysiological profiles of patients with schizophrenia and controls while completing a mental rotation task using both normally-oriented images and mirror images.

**Methods:** This electroencephalographic study compared error rates, reaction times and the topographic map of event-related potentials in 32 participants with schizophrenia and 29 healthy controls during mental rotation tasks involving both normal images and mirror images.

**Results:** Among controls the mean error rate and the mean reaction time for normal images and mirror images were not significantly different but in the patient group the mean (sd) error rate was higher for mirror images than for normal images (42% [6%] vs. 32% [9%],  $t=2.64$ ,  $p=0.031$ ) and the mean reaction time was longer for mirror images than for normal images (587 [11] ms vs. 571 [18] ms,  $t=2.83$ ,  $p=0.028$ ). The amplitude of the P500 component at Pz (parietal area), Cz (central area), P3 (left parietal area) and P4 (right parietal area) were significantly lower in the patient group than in the control group for both normal images and mirror images. In both groups the P500 for both the normal and mirror images was significantly higher in the right parietal area (P4) compared with left parietal area (P3).

**Conclusion:** The mental rotation abilities of patients with schizophrenia for both normally-oriented images and mirror images are impaired. Patients with schizophrenia show a diminished left cerebral contribution to the mental rotation task, a more rapid response time, and a differential response to normal images versus mirror images not seen in healthy controls. Specific topographic characteristics of the EEG during mental rotation tasks are potential biomarkers for schizophrenia.

## 1. Introduction

Mental rotation (MR) is the ability to rotate mental representations of two dimensional and three dimensional objects. This usually involves creating a mental image of an object (or self), and then rotating the object mentally. Initially proposed by Shepard and his colleagues in the early 1970s,<sup>[1]</sup> most authors report that the cognitive activity for performing MR tasks predominantly occurs in the right cerebral hemisphere.<sup>[2]</sup> Patients with schizophrenia usually have impaired performance on MR tasks.<sup>[3]</sup> Most of these conclusions, however, were based on behavioral indicators. The current study aims to use event-related brain potential (ERP) topographic mapping techniques to compare the location and intensity of cognitive activity during MR tasks in patients with schizophrenia versus those in healthy

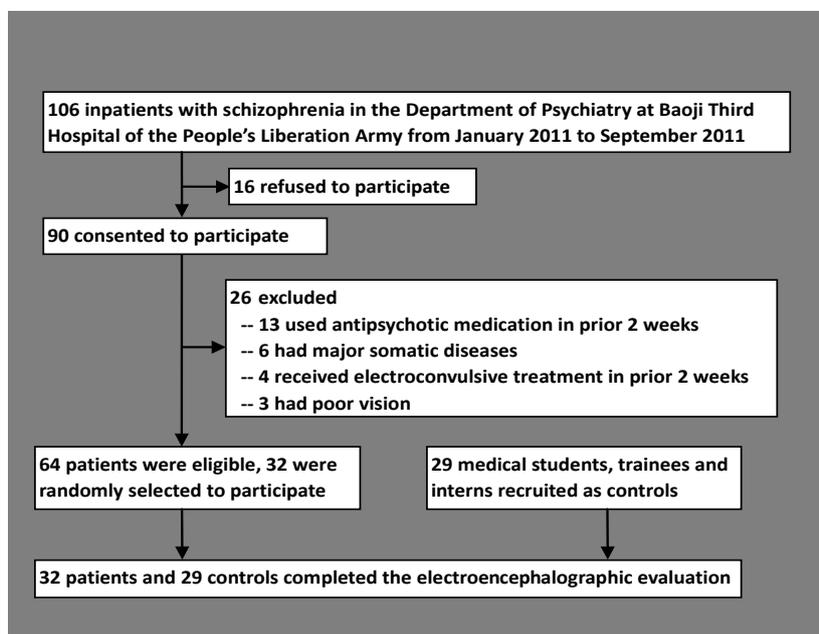
controls and, thus, more precisely define the cognitive deficits in schizophrenia.

## 2. Participants and methods

### 2.1 Subjects

The enrollment of participants is shown in Figure 1. Inpatients at the Department of Psychiatry of the Third Hospital of the People's Liberation Army in Baoji, Shaanxi from January 2011 to September 2011 with a diagnosis of schizophrenia based on the criteria in the third edition of the Chinese Classification of Mental Disorders<sup>[4]</sup> (which only requires a one-month duration of psychotic symptoms) were screened for participation. Among the 106 patients screened 42 were excluded because they had taken antipsychotic

Figure 1. Flowchart of subject enrollment



or other psychotropic medications or received electroconvulsive treatment in the prior 2 weeks, had a history of major neurological or medical illness, were unable to adhere to the research protocol (i.e., 40 minutes of testing with ongoing electroencephalogram), were left-handed, had poor vision, or refused to provide written informed consent. There were 64 eligible individuals; 32 participants were randomly selected for participation in the study. They included 16 men and 16 women aged 17-42 years; their mean (sd) age was 28.1 (6.3) years; their mean years of schooling was 12.8 (4.1) years; their mean duration of illness was 13 (6) weeks; and their mean score on the Brief Psychiatric Rating Scale<sup>[5]</sup> (conducted immediately before the encephalographic examination) was 38.5 (3.4) (range 35 to 57). Only 12 of the patients had a duration of illness greater than six months and, thus, met DSM-IV<sup>[6]</sup> criteria of schizophrenia; the remaining 20 patients met DSM-IV criteria of schizophreniform disorder. This army hospital serves both the military and the surrounding community; 18 of the 32 participants were active members of the military and the remaining 14 were community members.

A convenience control group of 29 medical students, trainees and interns at the Baiji Hospital who responded to a recruitment notice and who had no personal or family history of mental illness was identified. They included 15 men and 14 women aged 18-37 years; their mean (sd) age was 24.2 (5.2) years; and their mean years of schooling was 14.3 (2.1) years. There were no significant differences between cases and controls by gender ( $\chi^2=0.12$ ,  $p=0.105$ ), age ( $t=0.31$ ,  $p=0.127$ ), or years of education ( $t=0.25$ ,  $p=0.121$ ).

This study was approved by the Medical Ethics Commission of the Baoji Third Hospital of the People's Liberation Army.

## 2.2 Research Methods

### 2.2.1 Electrophysiological measurement

Using a BrainAmp MR 32 portable ERP system (Brain Products GmbH, Munich, Germany), two blinded investigators conducted the electrophysiological measurements for all participants in the morning. Both investigators had received training in the use of the apparatus and had good inter-rater reliability when independently assessing the wave amplitudes of ten patients ( $r=0.85-0.90$ ). Participants were asked to wear a BrainCAP-MR 32-electrode cap to record EEG signals. The electrodes were located according to the International 10-20 system,<sup>[7]</sup> two ear electrodes served as reference electrodes, and the AFz electrode was used for grounding. The apparatus used a sampling rate of 500Hz, scalp impedance of  $<5k\Omega$ , stimulation duration of 1200ms, sensitivity of  $5\mu V$ , and a band-pass of 0.1-30Hz. The EEG epochs were folded over 60 times. With a pre-stimulus baseline of 200ms, the analysis process lasted until 1000ms after stimulus presentation. Artifacts such as blinking were corrected offline. EEG signals with an amplitude greater than  $\pm 70\mu V$  were interpreted as artifacts and rejected. P500 was measured in two completely independent analytic time windows via the triggering and recording systems; the response time and error count were automatically recorded.

### 2.2.2 Test procedures

The tests were performed with E-Prime 2.0 software (Psychology Software Tools). The participant was seated in a soft chair about 60cm away from the monitor (a 17-inch color monitor, with a refresh rate of 75Hz) in a quiet, dimly lit environment (relatively sound-proofed, with a temperature of about 24 °C). The participant was instructed to focus on the center of the screen throughout the test and trained in the test procedures until the rate of correct responses reached at least 60% prior to starting the formal testing period (all participants were able to achieve the 60% correct rate). During the test two stimulus pictures ('R' and 'F') were randomly presented. The pictures included normal and mirror images, each of which had 12 rotation angles: 0°, 30°, 60°, 90°, 120°, 150°, 180°, 210°, 240°, 270°, 300°, and 330°. The area of these pictures was no larger than 1.58 cm × 1.58 cm, with a visual angle of about 1.1° × 1.0°. During the procedures, a fixation point (the '+' symbol) appeared at the center of the screen for about 500ms followed by the stimulus pictures. The participant was asked to indicate whether the pictures 'R' or 'F' were normally oriented or mirror images by clicking the right or left mouse.

During the formal test, each picture appeared 720 times (i.e., random presentation 30 times at each of the 12 angles). The participant was asked to make 1440 judgments on the rotations. Each task was divided in two sessions; 360 pictures were presented during each session. There was an interval between the two sessions, the duration of which was determined by the participant. The whole test lasted about 40 minutes. Electrophysiological measurements were performed simultaneously.

### 2.3 Statistical Analysis

The data were processed and analyzed using SPSS 17.0 software. Based on the literature,<sup>[4,5,7]</sup> P500 was chosen as the indicator for analyzing MR. Thirty-two observations with extreme reaction times (greater than three standard deviations beyond the mean) were excluded from the analysis. Differences between the groups in the mean error rate, mean reaction time, and the mean P500 at the Pz, Cz, P3 and P4 sites for both normally-oriented images and mirror images were compared using unpaired t-tests. Comparisons of specific measures for normally-orientated versus mirror images within each group were made using paired t-tests. All tests used a two-sided alpha of 0.05.

## 3. Results

### 3.1 Comparison of behavioral data

In the control group the error rates for normal images and mirror images were similar (29.1% v. 32.0%;

paired-t=1.61, p=0.053) and the reaction times were also similar (602 ms v. 606 ms, paired-t=0.72, p=0.128). But in the patient group the error rate for mirror images was significantly higher than that for normally-oriented images (42.4% v. 32.2%, paired-t=3.46, p=0.029) and the reaction time was significantly longer (587ms v. 571 ms, paired-t=4.01, p=0.023).

As shown in Table 1 the error rate for normal images was not significantly different between groups but the error rate for mirror images was significantly higher in the patient group than in the control group. The reaction time for both normal images and mirror images was significantly shorter in the patient group.

### 3.2 Comparison of ERP data

As shown in Table 2 the amplitudes of P500 at Pz, Cz, P3, and P4 were all significantly lower in the patient group than in the control group for both the normal images and the mirror images. In the control group the amplitudes of P500 at all four sites were significantly higher for normal images than for mirror images (Pz: paired-t=3.62, p=0.028; Cz: paired-t=3.81, p=0.024; P3: paired-t=3.41, p=0.034; P4: paired-t=4.26, p=0.019). However, in the patient group the difference between the P500 amplitude for normal images and mirror images was only statistically significant at the P4 electrode (Pz: paired-t=0.75, p=0.172; Cz: paired-t=1.02, p=0.163; P3: paired-t=0.62, p=0.201; P4: paired-t=2.31, p=0.043). The P500 amplitude at electrode P4 was significantly higher than that at P3 for all four assessments: normal images in the patient group (t=2.16, p=0.041), normal images in the control group (t=3.62, p=0.031), mirror images in the patient group (t=2.01, p=0.046), and mirror images in the control group (t=2.13, p=0.045).

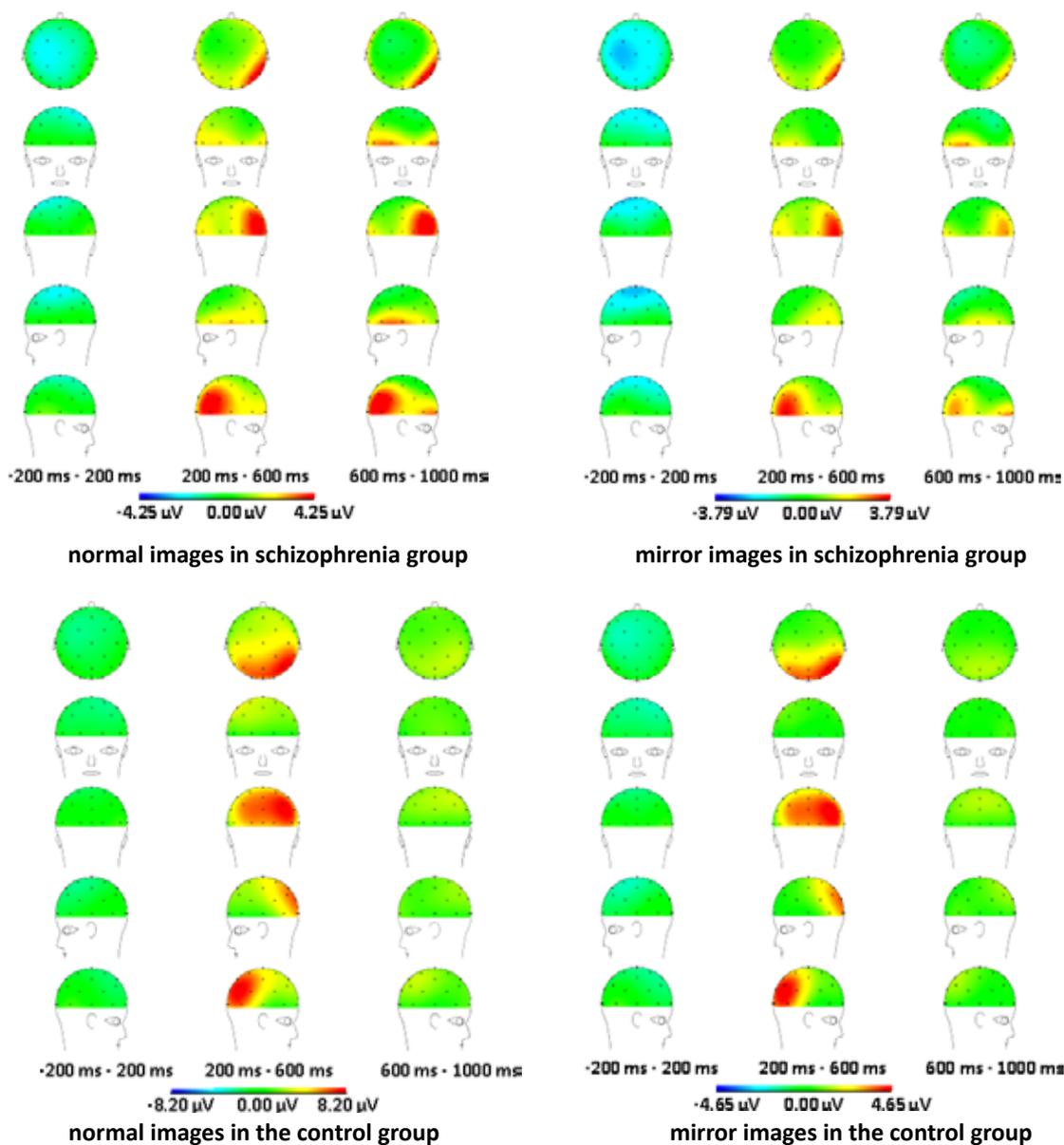
### 3.3 Comparison of ERP topographic mapping results

The ERP topographic mapping results (Figure 2) of the normal and mirror images show differences at certain time ranges between the patient group and the control group. Strong positive components from 200ms to 600ms were observed at the parietal lobe, the occipital lobe, and between these two lobes in the control group and at the right parietal-occipital lobe in the patient group; but the activity was lower in the patient group than in the control group. In the patient group there was very little activity in the left parietal lobe or in the region between the left parietal lobe and the left occipital lobe; and there was a delay in the activation in these regions for the normally oriented image. In the control group the activation for the normal-orientation image and the mirror image was quite similar but in the patient group the activity was much stronger with the normal image than with the mirror image. When comparing the left hemisphere with the right hemisphere, the activation resulting from

**Table 1. Comparison of the mean (sd) error rate and the mean (sd) reaction time for the normal images and mirror images in the patient and control groups**

Indicators	Stimuli	Schizophrenia group (n=32)	Control group (n=29)	t-value	p-value
Error rate (%)	Normal images	32.2 (8.3)	29.1 (10.2)	1.32	0.218
	Mirror images	42.4 (6.2)	32.0 (9.3)	5.18	0.032
Reaction time (ms)	Normal images	571 (18)	602 (25)	4.31	0.043
	Mirror images	587 (11)	606 (14)	4.75	0.040

**Figure 2. Comparison of ERP topographic mapping results between the two groups**



**Table 2. Comparison of the mean (sd) amplitudes ( $\mu\text{V}$ ) of P500 at electrodes Pz, Cz, P3, and P4 between the patient and control groups**

Stimuli	Electrode placement	Schizophrenia group (n=32)	Control group (n=29)	t-value	p-value
<b>Normal images</b>	Pz	3.13(1.01)	7.77(3.03)	5.17	0.032
	Cz	3.05(1.02)	8.20(3.10)	5.24	0.026
	P3	3.21(0.30)	7.00(3.11)	5.08	0.041
	P4	4.45(1.02)	8.58(4.12)	5.30	0.021
<b>Mirror images</b>	Pz	3.10(1.01)	4.59(2.04)	2.26	0.041
	Cz	2.99(2.03)	4.12(2.06)	2.64	0.038
	P3	3.37(1.01)	4.00(2.13)	2.14	0.044
	P4	3.79(1.12)	4.62(2.04)	2.05	0.048

Pz= parietal area ; Cz= central area ; P3= left parietal area ; P4= right parietal area

the normal and mirror images in both patients and controls were greater in the right parietal-occipital lobe than in the left parietal-occipital lobe. In the patient group, at the -200 ms to 200 ms interval there was a prominent negative component for both normal and mirror images that was not seen in the control group.

#### 4. Discussion

##### 4.1 Main findings

The mental rotation (MR) task is an important tool for measuring spatial ability—one of the core cognitive capabilities of humans—and the P500 component of the ERP is a useful electrophysiological indicator of MR functionally.<sup>[8-11]</sup> Using this methodology we confirmed the findings of other studies<sup>[12-14]</sup> which report that the cortical regions activated during the MR task include the parietal lobe, parietal-occipital lobe, occipital lobe, and frontal lobe. We also identified several important differences in the electrophysiological responses to the MR task between patients with schizophrenia and control participants.

Consistent with several previous studies<sup>[2,15-17]</sup> in healthy controls we found strong evidence for right hemisphere dominance during the MR task but there was also activity in the left hemisphere indicating that both hemispheres participate during the task. Patients with schizophrenia also demonstrate right hemisphere dominance during the MR task, but the activity in the left hemisphere almost disappears and the amplitude of the P500 in the right hemisphere when presented both normal and mirror images is much lower than that seen in healthy controls. This suggests that MR abilities for both normal images and mirror images are impaired in patients with schizophrenia.

The MR ability of patients with schizophrenia is characterized by a significantly increased mirror image-related error rate and a significantly decreased reaction

time for both normal and mirror images. These findings are consistent with the results of Vignemont and colleagues<sup>[3]</sup> who suggest that patients' MR deficits may be related to their tendency to forfeit accuracy for speed or to increased impulsivity when selecting responses. Our results suggest that the processing mechanisms for normal and mirror images during the MR task are different in patients than in controls, a conclusion that is supported by the findings of other researchers.<sup>[15,18]</sup>

As previously described by Band and colleagues<sup>[19]</sup> we found that a negative readiness potential precedes the actual execution of MR tasks. Patients with schizophrenia have higher negative readiness potentials than controls, suggesting that they consume more mental resources when preparing for their response to the stimuli. This may reflect a higher expectation that could result in a greater emphasis on the speed of response rather than on the accuracy of response.

##### 4.2 Limitations

Our analysis of hemispheric dominance during the MR task was limited to a time-based analysis. We did not analyze changes in the ERP topographic mapping related to the angles of presenting the images and did not assess potential confounding factors such as age, gender and duration of illness. All the patients had a very short duration of illness (only 12 of the 32 patients met the 6-month duration of illness criteria used in the DSM-IV diagnostic system). This ensured that long term use of antipsychotic medication did not influence the results, but results may be different among patients with longer durations of illness. Further study with larger samples that include participants with varying lengths of illness, that follow changes in these parameters over time, and that assess these markers in first-degree family members of patients are needed to address these issues.

### 4.3 Implications

Our study confirms previous findings that there is a right hemisphere advantage or dominance for the MR task for both patients with schizophrenia and for controls and that the left hemisphere participation in the MR task is much weaker in patients with schizophrenia than in controls. We also found that the reaction times to stimuli in the MR task were faster in patients than in controls and that patients had a differential response to normally oriented versus mirror images that was not seen in controls. Further research is needed to confirm these findings and to determine whether or not the electrophysiological differences identified between patients and controls during the MR task can be used as biological markers for identifying individuals at high risk for schizophrenia.

### Conflict of interest

The authors report no conflict of interest.

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• 论著 •

# 精神分裂症患者心理旋转的优势半球效应

陈玖 杨来启\* 赵瑾 李兰兰 刘光雄 马文涛 张彦 吴兴曲 邓自和 拓冉

中国人民解放军第三医院全军精神疾病防治中心, 陕西宝鸡

\*通信作者: ericst@yahoo.cn

## 摘要

**背景** 心理旋转(mental rotation)是一种想象客体或自我旋转的空间表征转换能力。精神分裂症患者的心理旋转能力受损。

**目的** 记录精神分裂症患者和健康对照者完成正像和镜像心理旋转任务时的脑电生理指标, 比较这些指标的差异, 深入评估精神分裂症患者的认知损害情况。

**方法** 对来自解放军第三医院精神科32例精神分裂症患者和29例健康对照者在完成正像和镜像的心理旋转任务时的事件相关电位测定, 比较两组错误发生比例、反应时以及事件相关电位的脑地形图。

**结果** 对照组正像与镜像的错误率比较无明显差异, 正像与镜像的反应时间亦无明显差异。而患者组镜像的平均(标准差)错误率比正像高 [42% (6%) 比32% (9%),  $t=2.64$ ,  $p=0.031$ ], 患者组镜像的反应时比正像长 [587 (11) ms比571 (18) ms,  $t=2.83$ ,  $p=0.028$ ]。无论是镜像还是正像, 患者组Pz(顶区)、Cz(中央区)、P3(左侧顶区)和P4(右侧顶区)的P500波幅均低于对照组。与P3极点相比, 两组正像和镜像P4点波幅都偏高。

**结论** 精神分裂症患者正像和镜像心理旋转能力都受损。患者大脑左半球心理旋转能力减弱, 反应时缩短, 对正像与镜像反应存在差异, 这些都与对照组不同。研究提示完成心理旋转任务时特定的脑地形图可作为诊断精神分裂症的一个辅助参考指标。