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Neurocognitive impairment on motor imagery associated with positive symptoms in patients with first-episode schizophrenia: Evidence from event-related brain potentials

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A B S T R A C T

Motor imagery provides direct insight into an anatomically interconnected system involved in the integration of sensory information with motor actions, a process that is associated with positive symptoms in schizophrenia (SCZ). However, very little is known about the electrophysiological processing of motor imagery in first episode SCZ. In the current study, we used a visual hand mental rotation (MR) paradigm to manipulate the processing of motor imagery while event-related brain potentials (ERPs) were recorded in 42 SCZ participants and 40 healthy controls (HC). The 400–600 ms window was measured and analyzed for peak latencies and amplitudes. Participants with SCZ had slower reaction time (RT) and made more errors than did HC participants. Moreover, SCZ participants had lower amplitudes in the 400–600 ms window and the typical MR function for amplitudes of MR was lacking. Interestingly, the scalp activity maps for MR in SCZ exhibited an absence of activation in the left parietal site as shown in HC. Furthermore, deficits of amplitude for MR were positively correlated with positive symptom scores in SCZ. These results provide novel evidence for relationships between the electrophysiological processing of motor imagery and positive symptoms in SCZ. They further suggest that the impaired information processing of motor imagery indexed by amplitudes and specific topographic characteristics of the EEG during MR tasks may be a potentially useful and early defining biomarker for SCZ.

1. Introduction

Mental rotation (MR) is thought to be a cognitive ability that alters mental representations of two- and three-dimensional objects or body parts, and usually involves the creation of a mental image of an object and its subsequent rotation (Shepard and Metzler, 1971). It is often considered as a prototypical form of higher level cognitive processing of motor imagery, which is involved with the integrity of specific cortical–subcortical motor structures (motor and premotor areas and basal ganglia) and sensory systems (somatosensory and visual) (de Lange et al., 2006). The mental simulation of real perceptual-motor behaviors can be regarded as a sort of internal or cognitive analogue of actual movements, useful for motor planning and prediction (Duncombe et al., 1994). Numerous authors (e.g., Parsons, 1987; Wraga et al., 2005; Lenggenhager et al., 2008) have studied tasks involving body parts in different postures and rotated angles, in which subjects are required to judge whether the body part belongs to the right or left side of the body. These studies have indicated that subjects appear to mentally simulate the kinematic properties of the physical action of their body part moving from its resting posture to that of the stimulus during that procedure.

Numerous studies have demonstrated that the amplitude of an event-related brain potential (ERP) component increases linearly with the angle of rotation in a hand MR task, indicating the presence of the expected MR function. This ERP component, known as "rotation-related negativity", was first reported in a study conducted by Stuss et al. (1983), which suggested that ERP negativity should be considered as a direct electrophysiological correlate of the MR

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process itself. The ERP component consists of a negative-going waveform, maximum over parietal regions, whose amplitude is modulated by the angle of rotation: the greater the angle of misorientation, the larger the rotation-related negativity (Wijers et al., 1989). The rotation-related negativity has been repeatedly demonstrated in studies with alphanumeric characters (Heil and Rolke, 2002; Núñez-Peña and Aznar, 2009), letter-like shapes (Hamm et al., 2004; Núñez-Peña et al., 2005), paper-folding stimuli (Milivojevic et al., 2003), left-right hands (Thayer and Johnson, 2006), and geometric objects (Muthukumaraswamy et al., 2003). Previous studies have demonstrated that the ERP negative-going waveform of MR appears in parietal negativity approximately between 350 and 800 ms (Wijers et al., 1989; Heil and Rolke, 2002), 400–600 ms (Harris and Miniussi, 2003), around 400–550 ms over the right hemisphere and ~610 ms over the left hemisphere (Milivojevic et al., 2009), and 400–500 ms (Núñez-Peña and Aznar, 2009) post-stimulus onset. Corresponding evidence suggests that the amplitude modulation can be used as a neurophysiological indicator of the high-level cognitive process of MR. It further suggests that the onset of the ERP effect can be used as a chronopsychophysiological marker for the onset of the process.

Several studies have indicated that the main underlying cognitive deficits in SCZ patients involve a severe degree of impairment on the 'general executive function' factor (Polgár et al., 2010), a difficulty in differentiating between imagination and reality (Brebion et al., 2000), and an inability to anticipate the sensory consequences of their own movements (Wolpert et al., 1995). Given the similarities between motor imagery and physical actions (Jeannerod and Decety, 1995), previous studies have found that SCZ patients have an impaired ability of MR due to problems in imagining the performance of a movement (Potvin et al., 2013). The disruption of motor imagery might be expected to lead to endopathic experiences, in which patients with SCZ can no longer compare the performed movement with the anticipated outcome of these movements and thus feel alienated from their own actions (Frith et al., 2000; de Vignemont et al., 2006). Furthermore, patients with motor impairments such as parietal damage (Sirigu and Duhamel, 2001) or impairment of the right basal ganglia (Harris et al., 2002) also suffer from difficulties in motor imagery. Motor imagery thus provides direct insight into action representations (de Vignemont et al., 2006). However, while the disrupted information processing of motor imagery has been addressed in numerous studies of patients with motor impairments, very little is known about the processing of motor imagery in SCZ, particularly in first episode patients.

The objective of the present study was thus to evaluate whether any impairments would be specific to the brain visuomotor electrophysiological processing mechanism in SCZ. Based on previous studies (de Vignemont et al., 2006; Potvin et al., 2013), we hypothesized that if SCZ patients were impaired in motor imagery, the onset of the amplitude modulation of the rotation-related negativity would be delayed and the mean peak amplitudes would be reduced over parietal regions. Moreover, we predicted that the patterns of reaction times (RTs) and the amplitudes of the rotation-related negativity would lead to the absence of a typical MR function. The impaired electrophysiological processing of motor imagery is particularly relevant to positive symptom in SCZ. Such an impairment, if confirmed, might be a potential biomarker of SCZ.

2. Methods

2.1. Participants

We recruited 42 first episode SCZ patients (22 males and 20 females, age range 22–55 years, mean age 36.62 ± 8.71 years; see Table 1). All of them were inpatients (Chinese Han and right-handed) at the Center for Mental disease Control and Prevention of Baoji Third Hospital of the People's Liberation Army in China. Psychiatric diagnoses were made using a structured clinical interview (SCID). At least two psychiatrists agreed on a diagnosis based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision, American Psychiatric Association (DSM-IV).

Table 1
Demographics and clinical measures of patients with SCZ and HC subjects.

Items	HC $n=40$	SCZ $n=42$	t Values (χ^2)	p Values
Age (years)	33.1 (10.8)	36.62 (8.71)	1.246	0.214
Gender (male/female)	20/20	22/20	0.041	0.689
Education level (years)	12.65 (3.22)	12.88 (3.60)	0.804	0.363
PANSS scores	4.83(2.11)	82.33 (12.22)	18.829	0.000*
PSS	1.66(0.12)	24.61(15.06)	8.201	0.000*
NSS	1.80(1.01)	25.36(11.82)	8.862	0.000*
GPS	1.43(2.11)	33.63 (16.08)	10.526	0.000*
Years worked	15.62 (3.64)	8.69 (6.38)	5.720	0.002*
Employment status				
Unemployed	72.2%	10.6%	4.811	0.006*
Duration of illness (months)	–	19.92 ± 4.63	–	–
Age of illness onset	–	19.74 (6.45)	–	–

Notes: Values are expressed as mean (standard deviation). Abbreviation: HC: health controls; SCZ: schizophrenic patients. PANSS: positive and negative syndrome scale; PSS: positive symptom subscale; NSS: negative symptom subscale; GPS: general psychopathology subscale.

* Significant differences were found between SCZ and HC. p Values were obtained by t test except for gender (χ^2 test).

Duration of illness ranged from 6 months to 25 years (mean illness duration: 19.92 ± 4.63 months). Years of education ranged from 8 years to 20 years (mean schooling 12.88 ± 3.60 years). Clinical symptoms of SCZ were evaluated with the Positive and Negative Syndrome Scale (PANSS, Kay et al., 1986). Patients were in their first episodes and had normal or corrected-to-normal vision. All patients received at least one atypical antipsychotic (28 patients received one, 11 received two, 3 received three; clozapine: $n=28$, mean dosage = 431.03 ± 58.41 mg; olanzapine: $n=16$, mean dosage = 14 ± 3.8 mg; risperidone: $n=5$ mean dosage = 4.00 ± 1.32 mg; quetiapine: $n=8$, mean dosage = 545.00 ± 312.34 mg) (chlorpromazine-equivalent dosage was calculated). Patients were clinically stable at the time of testing.

For comparison, 40 healthy control (HC) subjects (20 males and 20 females), without any history of psychiatric illness, were matched to the SCZ patients on age, gender, and education (HC subjects were aged 22–50 years; mean age: 33.1 ± 10.8 years). Exclusion criteria for the patients and the control subjects were a history of substantial head injury, seizures, neurological diseases, dementia, impaired thyroid function, corticoid use, or alcohol or substance abuse or dependence.

Table 1 presents demographic information for the experimental subjects. Both patients and control subjects gave their written informed consent after a full description of the experimental procedure. The Human Participants Ethics Committee of Baoji Third Hospital of the People's Liberation Army approved all procedures.

2.2. Apparatus

The hand MR task was selected at random from the set {back in picture plane, palm in picture plane, side from little finger, and side from thumb} (Fig. 1a), and it was presented in a left- or right-hand form, rotated by 0°, 60°, 120°, or 180° clockwise and counterclockwise from an upright position (Fig. 1b). Each combination of hand form and rotation angle occurred with equal probability (Parsons, 1987; Ionta and Blanke, 2009).

2.3. Procedures

The experiment was performed with E-Prime 2.0 software. Each stimulus was presented in a separate block, including 160 trials in random order. All subjects completed a total of 640 trials, with a short break between each block.

Subjects sat in front of a 17-in computer screen (refresh rate 75 Hz) placed at a distance of 70 cm from their eyes in a quiet, dimly lit, sound-proofed room, with an ambient temperature of approximately 24 °C. Following task instructions, subjects performed 14 practice trials pertaining to the relevant stimulus with practice continued until the participants achieved an accuracy of at least 75%. Subjects were instructed to avoid tilting their head and to keep their gaze on the fixation point