Reduced motor facilitation during action observation in schizophrenia: A mirror neuron deficit?

Peter G. Enticott a,⁎, Kate E. Hoy a, Sally E. Herring a, Patrick J. Johnston b, Zafiris J. Daskalakis c, Paul B. Fitzgerald a

a Alfred Psychiatry Research Centre, School of Psychology, Psychiatry and Psychological Medicine, Monash University and the Alfred, Australia
b Brain Sciences Institute, Swinburne University of Technology, Australia
c Centre for Addiction and Mental Health, University of Toronto, Canada

Received 20 February 2008; received in revised form 18 March 2008; accepted 2 April 2008
Available online 15 May 2008

Abstract

Impairments in social cognitive functioning are well documented in schizophrenia, however the neural basis of these deficits is unclear. A recent explanatory model of social cognition centers upon the activity of mirror neurons, which are cortical brain cells that become active during both the performance and observation of behavior. Here, we test for the first time whether mirror neuron functioning is reduced in schizophrenia. Fifteen individuals with schizophrenia or schizoaffective disorder and fifteen healthy controls completed a transcranial magnetic stimulation (TMS) experiment designed to assess mirror neuron activation. While patients demonstrated no abnormalities in cortical excitability, motor facilitation during action observation, putatively reflecting mirror neuron activity, was reduced in schizophrenia. Dysfunction within the mirror neuron system may contribute to the pathophysiology of schizophrenia.

© 2008 Elsevier B.V. All rights reserved.

Keywords: Schizophrenia; Social cognition; Mirror neurons; Transcranial magnetic stimulation; Primary motor cortex; Premotor cortex

1. Introduction

Individuals with schizophrenia often experience difficulties when processing social information. These social cognitive deficits, including impaired theory of mind and facial emotion processing (Harrington et al., 2005; Shamay-Tsoory et al., 2007), have been linked to functional outcome in schizophrenia (Couture et al., 2006). Despite this, the neural basis of impaired social cognition in schizophrenia is not well understood.

Recent theoretical accounts propose a central role for the mirror neuron system (MNS) in social cognition (Rizzolatti and Craighero, 2004). Mirror neurons are cortical neurons that become active during both the action and observation of a particular motor activity. Comprising a neural network including the superior temporal sulcus, inferior parietal lobe, and inferior frontal gyrus, the MNS was initially thought important for imitation and action understanding. The mirror neuron system, however, also appears to code for the intention of behavior (Iacoboni et al., 2005), and is now...
thought to provide the basis for understanding the behavior of a conspecific through an internal “embodied” simulation of their behavior. Accordingly, theoretical perspectives implicate mirror neurons in higher-order social cognitive processes that allow effective social interactions, including empathy, theory of mind, and facial emotion processing (Rizzolatti and Craighero, 2004).

It is therefore reasonable to speculate that schizophrenia could also involve impairment in the MNS; specifically, reduced mirror neuron activation during behavioral observation. Initial imaging evidence indicates that individuals with schizophrenia demonstrate abnormal activation of mirror neuron-related cortical regions whilst viewing emotional stimuli (Quintana et al., 2001), although a recent MEG study reported impaired motor cortical reactivity in schizophrenia (rather than a specific mirror neuron abnormality) (Schurmann et al., 2007).

The current study investigated whether individuals with schizophrenia or schizoaffective disorder demonstrate specific impairment in mirror neuron activation. This was achieved by combining emotionally neutral visual stimuli (demonstrating motor activity) with transcranial magnetic stimulation (TMS) of the primary motor cortex (M1) using a hand-held, 70 mm figure-of-eight coil that was positioned over the scalp. Motor-evoked potentials (MEP) were recorded from the right abductor pollicis brevis (APB) muscle. Resting motor threshold was defined as the minimum stimulation intensity required to evoke a peak-to-peak MEP of > 50 μV in at least 3/5 consecutive trials.

Participants were first administered 14 pulses (at 120% RMT) while at rest (baseline MEP). Consistent with Maeda et al. (2002), TMS was then administered during the quasi-random presentation of 10 s video clips that showed right-hand APB activity that was either meaningless (lateral thumb movement to and from index finger), goal-directed (pen grasp), or continuing (handwriting). Participants were positioned 1.2 m from a 17″ CRT monitor that displayed the visual stimuli. Each of the three videos was presented 14 times, and the TMS pulse was delivered 6 s into each 10 s video clip.

During observation of the movement of the muscle under study, mirror neuron activity is increased in the premotor cortices. Premotor input to the primary motor cortices increases primary motor cortical excitability and results in enhanced MEP amplitude when the corresponding cortical region is stimulated. Accordingly, any increase during action observation (compared with baseline stimulation) represents mirror neuron activation, with goal-directed and meaningful actions often eliciting a further enhanced mirror neuron response.

2.2. Procedure

Participants completed a transcranial magnetic stimulation (TMS) experiment designed to measure mirror neuron activation. Single pulse TMS (Magstim-200 stimulator; Magstim Company Ltd, UK) was administered to the left primary motor cortex (M1) using a hand-held, 70 mm figure-of-eight coil that was positioned over the scalp. Motor-evoked potentials (MEP) were recorded from the right abductor pollicis brevis (APB) muscle. Resting motor threshold was defined as the minimum stimulation intensity required to evoke a peak-to-peak MEP of > 50 μV in at least 3/5 consecutive trials.

Participants were first administered 14 pulses (at 120% RMT) while at rest (baseline MEP). Consistent with Maeda et al. (2002), TMS was then administered during the quasi-random presentation of 10 s video clips that showed right-hand APB activity that was either meaningless (lateral thumb movement to and from index finger), goal-directed (pen grasp), or continuing (handwriting). Participants were positioned 1.2 m from a 17″ CRT monitor that displayed the visual stimuli. Each of the three videos was presented 14 times, and the TMS pulse was delivered 6 s into each 10 s video clip.

2.3. Data analyses

TMS trials in which tonic activity (as measured via EMG) was evident were discarded prior to data analysis.
Tonic activity was evident in very few trials, and there was no difference in the mean number of trials discarded per group (schizophrenia: 1.13; controls: 1.47), $t(28) = -0.20$, $p = .844$. Mean peak-to-peak MEP amplitude was then calculated for each of the four conditions (baseline, and lateral, goal-directed, and continuing APB activity). Of primary interest was each group’s level of mirror neuron activation, which was indexed by the MEP amplitude for each of the movement observation conditions relative to the baseline condition:

$$\left(\frac{\text{[APB observation mV - baseline mV]}}{\text{baseline mV}}\right) \times 100$$

A greater increase reflects enhanced mirror neuron activation. $T$-tests were used to compare groups on mirror neuron activation. Repeated-measures ANOVA (with simple contrasts) was then used to compare the four TMS conditions (baseline, lateral, goal-directed, and continuing) for each group.

### 3. Results

There was no difference between the two groups in MEP amplitude for the baseline condition, $t(28) = -1.04$, $p = .305$, indicating comparable cortical excitability when at rest. The MEP percentage increase of each observation condition (relative to the baseline condition) is displayed in Fig. 1. Compared with the schizophrenia group, healthy controls obtained a significantly greater percentage increase for the lateral, $t(28) = -2.56$, $p = .018$, goal-directed, $t(28) = -2.34$, $p = .027$, and continuing, $t(28) = -2.42$, $p = .027$, conditions. This difference is further illustrated by MEP amplitudes following TMS for each of the four conditions (as shown in Fig. 2). Among controls, MEP amplitude was significantly increased (compared with baseline) for the lateral, $F(1,14) = 11.06$, $p = .005$, goal-directed, $F(1,14) = 15.81$, $p = .001$, and continuing, $F(1,14) = 8.90$, $p = .010$, conditions. This facilitatory effect, however, was absent in the schizophrenia group, with no difference in MEP amplitude for the four conditions, $F(3,42) = 1.54$, $p = .236$.

### 4. Discussion

Individuals with schizophrenia or schizoaffective disorder show reduced MEP facilitation during the observation of action within the stimulated muscle. Action observation is thought to invoke premotor mirror neuron activity and, by consequence, to increase motor cortical excitability. Thus, these results appear to
indicate reduced mirror neuron activity in the premotor cortices of patients with schizophrenia. This is the first demonstration of reduced mirror neuron activation in schizophrenia, although other studies of this population have noted deficits in various aspects of social cognitive processing. Importantly, there was no difference in MEP amplitude for the baseline condition, signaling that this result does not reflect a general dysfunction in cortical excitability. These novel findings, however, should be interpreted with caution. All patients were medicated, and although the overwhelming majority of research suggests no effect of neuroleptic medication on cortical excitability (e.g., Boroojerdi et al., 1999; Daskalakis et al., 2003; Davey et al., 1997; Fitzgerald et al., 2002, 2003, 2004; Oxley et al., 2004; Ziemann et al., 1997; see Haraldsson et al., 2004 and Stanford et al., in press for reviews), a minority of studies have found that medication is associated with either lower RMT (e.g., Daskalakis et al., 2002) or higher RMT (e.g., Pascual-Leone et al., 2002). If there is a possible effect of medication on cortical excitability, it was not seen in our patients, as there were no differences in our baseline measure of motor cortical excitability. While it could be argued that these findings simply reflect reduced attention to the visual stimuli during TMS, this seems unlikely; an experimenter monitored each participant throughout to ensure that visual attention to the stimuli was maintained (i.e., that their gaze was directed toward the screen), and mirror neuron activation has been shown to be a relatively automatic process that is not susceptible to the influence of top-down processes (Iacoboni et al., 2005). Thus, simply watching the visual presentation should be sufficient to induce mirror neuron activation. Despite this, some of the medications taken by the clinical group could affect attention to stimuli, and this possibility should be formally tested in future studies, as should potential visual processing abnormalities in schizophrenia. Given the limitations of the study design, the current findings could also be interpreted as reflecting a more general dysfunction of neural (functional) connectivity (including premotor and primary motor cortex connectivity), which appears common to autism and schizophrenia (Murias et al., 2007; Okugawa et al., 2006), rather than specific dysfunction within mirror neurons. However, even if this were the case, it does not necessarily follow that a mirror neuron explanation of aspects of schizophrenia is irrelevant, but rather that reduced mirror neuron activation in this study is indicative of broader neural deficits. Notwithstanding, reduced mirror neuron activity is likely to have behavioral consequences regardless of whether or not it is the primary deficit. A
connectivity account may go a long way toward explaining the social cognitive similarities in autism and schizophrenia, and a functional imaging study to determine the extent of putative mirror neuron disruption is now warranted. The MNS in schizophrenia should also be examined in the context of aspects of social cognition that might benefit from internal simulation, including theory of mind and facial emotion processing, for which there is substantial evidence of dysfunction in schizophrenia.

Role of Funding Source
Funding for this study was provided by Monash University’s Faculty of Medicine, Nursing and Health Sciences. PF was supported by an NHMRC Practitioner Fellowship. PJ was supported by an NHMRC Clinical Training Fellowship. These organisations had no further role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

Contributors
Authors Enticott, Hoy, Herring, and Fitzgerald designed the study, conducted the experiments, undertook statistical analyses and wrote the manuscript. Authors Johnston and Daskalakis contributed to data interpretation of the writing of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of Interest
All authors declare that they have no conflicts of interest.

Acknowledgment
The authors wish to thank Ms. Frances Biffin, Ms. Kate Filia, and Ms. Sacha Filia for their assistance with participant recruitment.

References


