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Self-reported empathy and neural activity during action imitation and observation in schizophrenia

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ABSTRACT

Introduction: Although social cognitive impairments are key determinants of functional outcome in schizophrenia their neural bases are poorly understood. This study investigated neural activity during imitation and observation of finger movements and facial expressions in schizophrenia, and their correlates with self-reported empathy.
Methods: 23 schizophrenia outpatients and 23 healthy controls were studied with functional magnetic resonance imaging (fMRI) while they imitated, executed, or simply observed finger movements and facial emotional expressions. Between-group activation differences, as well as relationships between activation and self-reported empathy, were evaluated.
Results: Both patients and controls similarly activated neural systems previously associated with these tasks. We found no significant between-group differences in task-related activations. There were, however, between-group differences in the correlation between self-reported empathy and right inferior frontal (pars opercularis) activity during observation of facial emotional expressions. As in previous studies, controls demonstrated a positive association between brain activity and empathy scores. In contrast, the pattern in the patient group reflected a negative association between brain activity and empathy.
Conclusions: Although patients with schizophrenia demonstrated largely normal patterns of neural activation across the finger movement and facial expression tasks, they reported decreased self perceived empathy and failed to show the typical relationship between neural activity and self-reported empathy seen in controls. These findings suggest that patients show a disjunction between automatic neural responses to low level social cues and higher level, integrative social cognitive processes involved in self-perceived empathy.

1. Introduction

Social dysfunction is among the most debilitating and treatment refractory features of schizophrenia. Rapidly growing evidence indicates that deficits in the domain of social cognition are among the most important determinants of poor functioning. Schizophrenia is characterized by impaired emotion processing, social perception, attributional style, and mentalizing, which account for unique variance in functional outcome above and beyond non-social neurocognitive deficits and clinical symptoms (Green and Horan, 2010). Although these findings demonstrate the unique functional significance of social cognition deficits in schizophrenia, our understanding of their scope (e.g., whether relatively automatic social cognitive processes are also impaired) and neural correlates is limited (Brunet-Gouet et al., 2011).

Social neuroscience research indicates that imitative behavior is a basic prerequisite for the development of social cognition. It has been proposed that a mirror neuron system (MNS) provides the neurophysiological basis for imitation, which facilitates understanding the actions and even emotions of others through a "simulation" mechanism. First described in the ventral premotor and inferior parietal cortices of monkeys (Rizzolatti and Craighero, 2004), neurons with mirroring properties fire both when performing and merely observing actions performed by another agent. More recent electrophysiological studies in monkeys provide evidence of neurons with mirroring properties in the lateral intraparietal area (Shepherd et al., 2009) and ventral intraparietal area (Ishida et al., 2010) in the intraparietal sulcus, the dorsal premotor and primary motor cortices (Cisek and Kalaska, 2004; Dushanova and Donoghue, 2010; Tkach et al., 2007), the supplementary

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motor area, and the medial temporal cortex (Mukamel et al., 2010). These findings demonstrate that mirroring is a neuronal property present in many neural systems in the primate brain. Brain imaging studies in humans have also shown that multiple areas in the frontal and parietal cortices are active during action observation, execution and imitation (Caspers et al., 2010; Iacoboni, 2005, 2009; Iacoboni et al., 1999). This common coding of motor perception and motor action is believed to enable us to represent and understand the actions of others in terms of our own actions.

The MNS also appears to be involved in higher-level socio-emotional processes, such as decoding and empathizing with the emotional states of others. Several fMRI studies have examined MNS activity during observation and imitation of facial emotional expressions (Carr et al., 2003; Dapretto et al., 2006; Leslie et al., 2004; Schulte-Ruther et al., 2007). Both imitation and observation of facial expressions activate a neural network that includes mirroring areas, the insula and the limbic system (i.e., the amygdala). Consequently, it has been proposed that one way of empathizing is through the embodiment of the facial emotional expressions displayed by others, enabling the translation of an observed expression into its internally felt emotional significance. Consistent with this notion, MNS activation has been linked to individual differences in self-reported empathy (e.g., Gazzola et al., 2006; Kaplan and Iacoboni, 2006; Schulte-Ruther et al., 2007). Furthermore, diminished MNS activation has been documented in autism spectrum disorders, which are characterized by imitative and empathic disturbances in response to simple hand movements and facial expressions (Dapretto et al., 2006; Iacoboni and Dapretto, 2006; Williams et al., 2006).

Although disturbances in the MNS and the "social brain" have been theoretically linked to schizophrenia (e.g., Burns, 2006; Iacoboni, 2009), very little work has directly evaluated this area. While behavioral studies show impaired imitation of complex hand movements and facial emotional expressions in schizophrenia (e.g., Kohler et al., 2008; Lee et al., 2014; Matthews et al., 2013; Park et al., 2008; Varcin et al., 2010), the few studies of MNS activity have been inconsistent. Three electrophysiological studies examined Mu suppression, a hypothesized biomarker of MNS activity. The first reported normal Mu suppression in schizophrenia during observation of hand movements and social interaction stimuli, but diminished Mu suppression during observation of basic biological motion (point light animation) (Singh et al., 2011). The second focused on hand movement stimuli and found normal or, in one task condition, enhanced Mu suppression in schizophrenia, which correlated with higher levels of psychotic symptoms (McCormick et al., 2012). The third reported that a small sample of drug-free patients showed diminished Mu suppression during a video depicting a handshake (only hands shown), and that this disturbance did not improve with four weeks of treatment with antipsychotic medications (Mitra et al., 2014). Thus, EEG studies appear to be intact under at least some experimental conditions.

A few studies have used transcranial magnetic stimulation (TMS) paradigms to study MNS activity in schizophrenia. One found that patients demonstrated reduced motor evoked potential facilitation during hand action observation (Enticott et al., 2008). A series of studies by Mehta et al. found that unmedicated, though not medicated, patients had reduced motor evoked potentials during action observation, and that individual differences among patients correlated with scores on performance measures of facial affect perception and theory of mind (Mehta et al., 2012, 2013). Thus, TMS studies provide more consistent evidence of impaired MNS activation in schizophrenia.

Although fMRI paradigms have been extensively used to examine MNS activity in healthy and clinical samples, to our knowledge such paradigms have only been applied in one prior study of schizophrenia. Thakkar et al. (2014) used a finger movement observation–imitation task and found that individuals with schizophrenia ($n = 16$) showed lower activation than healthy controls ($n = 16$) in one MNS region, the right inferior parietal lobe, during observation of finger movements, but higher activation than controls in this region during imitation of finger movements. Neither neural responses to faces nor self-perceived empathy was examined. The current study applied an observation–imitation–execution paradigm to individuals with schizophrenia that included both finger movement and facial emotional expression conditions. The goals of the study were to (1) compare MNS activity in patients and controls on these two types of stimuli, and (2) examine whether individual differences in self-reported empathy differentially relate to neural activation in patients and controls.

2. Methods

2.1. Participants

Twenty-three outpatients with schizophrenia and 23 healthy controls participated in the study. Schizophrenia patients were 18–60 years of age and recruited from outpatient clinics at the VA Greater Los Angeles Healthcare System and through local board and care facilities. Patients were clinically stable and received the Structural Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Axis I Disorders (SCID; First et al., 1996) to confirm diagnosis of schizophrenia. Patients were medicated at clinically determined dosages with 17 receiving atypical antipsychotics, one receiving typical antipsychotics, and five receiving both types of antipsychotic medication. The mean dose of antipsychotic medication was equivalent to 282.51 mg/day of chlorpromazine ($SD = 162.49$) (Andreasen et al., 2010). Exclusion criteria for patients included (1) substance abuse or dependence in the last 6 months, (2) $IQ < 70$, (3) history of loss of consciousness > 1 h, (4) identifiable neurological disorder, and (5) not sufficiently fluent in English.

Healthy control participants were recruited through flyers posted in the local community, newspaper advertisements, and website postings. Exclusion criteria for control participants included (1) history of schizophrenia or other psychotic disorder, bipolar disorder (no history of a manic or hypomanic episode), recurrent depression (no subjects were experiencing a depressive episode at the time of testing), dysthymia, history of substance dependence, or any substance abuse in the last 6 months based on the SCID, (2) avoidant, paranoid, schizoid, and schizotypal disorders based on the SCID for Axis II (First et al., 1994), (3) history of loss of consciousness > 1 h, (4) schizophrenia or other psychotic disorder in a first-degree relative, (5) significant neurological disorder, and (5) not sufficiently fluent in English. All participants were evaluated for their capacity to give informed consent and provided written informed consent after all procedures were fully explained, according to procedures approved by the institutional review boards at the University of California, Los Angeles (UCLA) and the Greater Los Angeles VA Health Care System.

2.2. Clinical and empathy measures

For patients, we assessed clinical symptoms using the expanded Brief Psychiatric Rating Scale (BPRS; Kopelowicz et al., 2008; Lukoff et al., 1986; Overall and Gorham, 1962) and examined the BPRS total score as well as the BPRS mean subscales for positive symptoms, negative symptoms, and depression/anxiety. All interviewers were trained through the Treatment Unit of the VA Desert Pacific Mental Illness Research, Education, and Clinical Center. SCID interviewers were trained to a minimum kappa of 0.75 for key psychotic and mood items, and BPRS raters were trained to a minimum intraclass correlation of .80 (Ventura et al., 1993). In addition, all participants filled out the Interpersonal Reactivity Inventory (IRI; Davis, 1983), indicating to what extent 28 short phrases described them on a 5-point scale (from "does not describe me at all" to "describes me very well"). This measure was chosen because it taps a variety of aspects of empathy, although it does not directly address motoric aspects like mimicry.