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Perception of social stimuli in mania: An fMRI study

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ABSTRACT

Patients with mania show alterations of social behaviour. Neuropsychological studies in euthymic bipolar disorder (BD) have revealed deficits in cognitive, but not emotional aspects of social cognition (SC). Here, we studied the neural signature of social stimulus processing in mania. We expected alterations in regions associated with cognitive SC (dorsal-medial prefrontal cortex, dMPFC). Participants comprised 14 manic patients and 14 matched healthy controls who viewed standardized pictures with social and non-social content during functional magnetic resonance imaging (fMRI). Region-of-interest-analyses focused on areas related to SC (dorsal/ventral medial prefrontal cortex; temporo–parietal junction), determined by a quantitative meta-analysis. Between-group comparisons ('social > non-social') revealed reduced BOLD responses in the right dMPFC in manic patients, but no significant group difference in the ventral MPFC. In addition, manic patients showed elevated BOLD activation in the right temporo–parietal junction during perception of social stimuli, which was correlated with increased delusional ideation. Patients with mania show diminished BOLD responses to social stimuli in the right dMPFC, associated with cognitive SC and this may be related to reported deficits in understanding others' mental states. At the same time, manic patients show hyperactivation of the right temporo–parietal junction, likely related to exaggerated attribution of meaning to social stimuli.

1. Introduction

Clinical observation suggests altered social behavior in manic patients with bipolar disorder (BD), characterized by excessive involvement in pleasurable social activities and inappropriate social communication and interaction. These psychopathological symptoms and deficits in social competence in mania may in part be caused by underlying impairments in social cognitive functions, such as the cognitive ability to mentalize about other people's mental states ('theory of mind', ToM) or to empathize with others, mostly regarding their emotional experiences (Cusi et al., 2010).

Recently, behavioral studies investigating these capacities in BD have found impairments in various ToM paradigms (Cusi et al., 2012), although in general this still remains an under-researched topic. Bipolar patients show deficits in social cognitive tests even in the euthymic state (Samamé et al., 2012). To specify these deficits in BD, several studies have distinguished cognitive and affective aspects of social cognition, based on findings in healthy participants and individuals with brain lesions (Hynes et al., 2006; Shamay-Tsoory et al., 2009) that suggest two separable aspects of social cognition. Concordantly, these behavioral findings indicated that individuals with BD were only impaired when they had to cognitively ascribe mental states to others or adopt someone else's point of view, but were not affected when identifying or empathizing with the emotional state of another person (Shamay-Tsoory et al., 2009; Cusi et al., 2010; Montag et al., 2010; Seidel et al., 2012; Barrera et al., 2013).

In BD, this dissociation between cognitive and affective aspects of social processes has only been investigated at the behavioral level, but not yet with neuroimaging methods that would allow the identification of underlying brain regions. To date only two functional magnetic resonance (fMRI) studies have examined the neural correlates of social cognition in BD. These studies examined euthymic bipolar patients and did not distinguish between cognitive and affective social cognitive processes (Malhi et al., 2008; Kim et al., 2009). Both studies found diminished activation within the mirror system in BD patients, related to lower level action perception processing, but no differences in comparison with controls in regions of the well-established 'ToM network'.

Extensive neuroimaging work in healthy subjects has very consistently found involvement of the medial prefrontal cortex

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(MPFC) and the temporo–parietal junction (TPJ) during ToM tasks (Amodio and Frith, 2006; Van Overwalle, 2009). Furthermore, it has been proposed that a dorsal–ventral distinction within the MPFC during social cognition might exist. On the basis of previous meta-analyses (Koski and Paus, 2000; Steele and Lawrie, 2004), it has been suggested that the MPFC, including the anterior cingulate cortex (ACC), might be functionally subdivided into a posterior cognitive zone and an anterior emotional region (including autonomic and visceral aspects) (Koski and Paus, 2000; Ochsner et al., 2004; Amodio and Frith, 2006). Similarly, emotional cognition, in contrast to cognitive social cognition, activated ventral vs. dorsal MPFC, respectively (Hynes et al., 2006; Keysers and Gazzola, 2007). Thus, considering the well-reported selective behavioral deficit in BD for cognitive, but not affective, social processes, the question arises whether fMRI will reveal corresponding alterations in the dorsal MPFC, but not the ventral MPFC, during social processing.

Previous neuroimaging studies in healthy individuals mostly used social tasks, which predominantly necessitated explicit social processing. However, social processing may also occur implicitly without an explicit instruction. Social processing is automatically triggered, for example, when perceiving humans or moving stimuli that signify animacy and intentionality (Heider and Simmel, 1944; Castelli et al., 2000). Findings of fMRI have indicated that tasks involving implicit mentalizing activate the same network involved during explicit processing (Mitchell et al., 2002; German et al., 2004). In the present study in manic patients, we thus chose a task involving implicit processing of social scenes, a task that is especially suited for the investigation of this patient population, as it is easy to understand and perform and is largely independent of additional cognitive processes.

In this study, we used fMRI to compare social stimulus processing in manic patients with processing in age- and IQ-matched healthy controls. The present study investigating social processing in symptomatic BD patients extends the existing neuroimaging studies on social cognition conducted in the euthymic state. During fMRI, participants viewed stimuli with social content, i.e., involving one or more humans. Scenes without humans (e.g., nature scenes, objects) served as a control condition. We hypothesized that regions implicated in social cognition, namely the MPFC and the TPJ, would be differentially activated in the mania group compared with the control group. This hypothesis was based on clinical observations and previous behavioral findings of social deficits in mania. We furthermore wanted to specifically investigate whether group differences would particularly involve the dorsal (i.e., cognitive), but not the ventral (i.e., affective), part of the MPFC. It may be possible that patients with mania especially show deficits only in the more cognitive, dorsal part of the MPFC, in line with previous behavioral reports (Montag et al., 2010). Furthermore, patients with mania often show an enhanced responsivity to social cues and, in extreme cases, delusions of reference. Therefore, questionnaire data on delusional ideation (including ideas of reference) were correlated with brain activation in the regions of interest to identify areas showing higher activation when enhanced delusional ideation is present.

2. Methods

2.1. Participants

Fourteen right-handed (assessed with the Edinburgh Handedness Inventory) patients with bipolar I disorder, who satisfied the DSM-IV (American Psychiatric Association, 1994) criteria for a manic episode, participated in the experiment. Patients were assessed using the Structured Clinical Interview for DSM-IV Part I (SCID-I; First et al., 2002) to exclude the possibility of any other axis I psychiatric disorder. The patients included in the study did not have any comorbid psychiatric or neurological disorders. We used the Young Mania Rating Scale (YMRS) (Young et al., 1978) to quantify manic symptoms. In addition, we used the Hamilton Rating Scale for Depression (HAM-D) (Hamilton, 1960) to rule out the possibility that participants were in a mixed episode. An HAM-D score <7 was considered normal. The patients could use antimanic (e.g. antipsychotics, mood stabilizers) medication, but no benzodiazepines. The medication on the day of examination was taken after the scanning session early in the morning upon previous agreement with the patient's psychiatrist. Out of 33 manic patients who were screened for the study, 14 were finally included. Common exclusion criteria for fMRI studies were considered (pregnancy, metal implants, tattoos and permanent make-up, unremovable piercing).

The 14 mentally healthy right-handed control subjects were matched to the patients for age, gender, verbal IQ, and duration of education. Patients and healthy controls did not differ significantly with regard to tobacco smoking status (Table 1). Healthy controls were also interviewed with the SCID I to ensure that they had no current or previous axis I psychiatric disorder. They were medication free.

The study was conducted in compliance with the Declaration of Helsinki and was authorized by the local ethics committee of Charité – Universitätsmedizin Berlin. Written informed consent was obtained from all participants. The study was conducted in accordance with current safety guidelines and no known risks were associated with participation.

2.2. Stimuli and design

The fMRI paradigm employed here has been used earlier to study healthy individuals (Sajonz et al., 2010). Experimental stimuli comprised 160 standardized non-erotic pictures selected from the IAPS (International Affective Picture System

Table 1
Clinical and demographic characteristics of study populations.

Characteristic	Manic ($n=14$)	Controls ($n=14$)	P
Sex, F/M, n	4/10	4/10	1.000
Age, mean ± S.D., years	33.4 ± 10.4	38.1 ± 5.8	0.192
Smokers, n	10	6	0.127
Verbal IQ (WST), mean ± S.D.[a]	107.2 ± 12.1	114.1 ± 13.1	0.168
Duration of education in years, mean ± S.D.[a]	15.2 ± 2.0	17.2 ± 3.6	0.085
Duration of illness in years, mean ± S.D.[b]	8.8 ± 9.7	–	–
Manic episodes, mean ± S.D.[b]	3.6 ± 2.4	–	–
Depressive episodes, mean ± S.D.[c]	2.8 ± 2.8	–	–
Psychotropic medication, n			–
Lithium	6	–	
Valproaic acid	7	–	
Carbamazepine	1	–	
Clozapine	1	–	
Quetiapine	4	–	
Olanzapine	5	–	
Risperidone	4	–	
Biperiden	2	–	
Flupentixol	1	–	

[a] Data were missing for 1 manic subject.
[b] Data were missing for 4 subjects.
[c] Data were missing for 3 subjects.