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Social appraisal in chronic psychosis: Role of medial frontal and occipital networks☆

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ABSTRACT

Persons with schizophrenia often appraise other individuals as threatening or persecutory. To evaluate social appraisal in schizophrenia, we probed brain networks with a task in which subjects judged whether or not they liked face stimuli with emotional expressions. We predicted that appraising negative expressions would engage patients, more than controls, and negative faces would be related to higher levels of negative affect and produce increased activity in the medial frontal cortex, an area involved in social appraisal. Twenty-one stable outpatients with chronic non-affective psychosis (16 schizophrenic, 5 schizoaffective) and 21 healthy subjects underwent functional magnetic resonance imaging. Compared with the control subjects, patients were slower to respond, but particularly slow when they judged negatively-valenced faces, a slowness correlated with negative affect in the psychosis patients. Appraisal activated the medial prefrontal cortex (mPFC) across all face valences. For negative expressions, patients exhibited greater activation of the dorsal anterior cingulate cortex (dACC). A psychophysiological interaction analysis of the dACC revealed co-modulation of the mPFC in controls, significantly less in patients, and a trend for co-modulation of occipital cortex in the patients. Activity in occipital cortex correlated with poor social adjustment and impaired social cognition, and co-modulation of the occipital gyrus by the dACC was correlated with poorer social cognition. The findings link appraisal of negative affect with aberrant activation of the medial frontal cortex, while early sensory processing of this social cognitive task was linked with poor social function, reflecting either top-down or bottom-up influences.

Appraisal refers to processes that establish value and significance according to personal goals and needs (Ellsworth and Scherer, 2003; Frijda, 1986; Smith and Ellsworth, 1985), and one form of appraisal, relevant for schizophrenia, is *social appraisal*. As eminently social animals, humans have evolved critical processes for appraising others. First impressions form quickly, often automatically, to guide our behavior (Schiller et al., 2009; Willis and Todorov, 2006). Psychosis is often marked by aberrant appraisals of others, as in persecutory and referential delusions, or in social anxiety, a common co-morbid symptom in schizophrenia (Pallanti et al., 2004; Voges and Addington, 2005). The evaluation of social stimuli by schizophrenia patients has been approached through social cognition, generally using relatively objective tasks, such as the identification of facial emotion. Patients with schizophrenia, as well as relatives, have difficulty identifying emotional expressions (Gur et al., 2007), but important aspects of appraisal that demand the exercise of subjective preference have not been examined in schizophrenia.

Recent work has begun to identify some of the neural systems involved in social appraisal. Appraising a stimulus for personal preference reliably activates the medial prefrontal cortex (mPFC) and anterior cingulate cortex (ACC; Elliott and Dolan, 1998; Killgore et al., 2003; Zysset et al., 2002), and social appraisal in particular has been linked to the dorsal aspect of the mPFC (Mitchell et al., 2002). The mPFC is also involved in appraisals of other types of emotional stimuli (Ochsner et al., 2004; Phan et al., 2002) and personal associations with stimuli (Phan et al., 2004), as well as self-related judgments and judgments about the mental state of other individuals (Amodio and Frith, 2006; Frith and Frith, 1999; Northoff and Bermpohl, 2004). Put more generally, it may be said

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that in social appraisal, the mPFC engages stimuli in a socio-emotional context, which includes an individual's preferences, representations of the social world, and emotional valences elicited by that social stimulus. Posterior regions, such as the fusiform face area (FFA; Mitchell et al., 2002) and the superior temporal sulcus (Allison et al., 2000), are thought to carry out perceptual categorization of social stimuli, whereas the amygdala, which has long been implicated in assessing value (Baxter and Murray, 2002; Costafreda et al., 2008; Sander et al., 2003), appears to detect the relative salience of face stimuli (Gerber et al., 2008; Gobbini and Haxby, 2007; Sander et al., 2003). The posterior cingulate cortex has recently been implicated in the formation of first impressions of individuals (Schiller et al., 2009). Lastly, the network of regions described here exhibits complex interactivity, e.g. the amygdala has been suggested to up-regulate FFA activity when a salient stimulus appears (Vuilleumier and Pourtois, 2007). As with most complex processes, functionality likely emerges through distributed interactions, which probably involve other regions, not as well characterized. Nevertheless, identification of candidate regions that carry out social appraisal has enabled the not only a preliminary mapping of these functions, but an analysis of the dysfunction found in psychiatric conditions.

Many of the nodes involved in social appraisal have also been implicated in schizophrenia. Reduced activation in patients during emotional challenges has been reported in the mPFC (Lee et al., 2006; Taylor et al., 2002; Williams et al., 2004), the ACC (Hempel et al., 2003; Reske et al., 2007) and the amygdala (Gur et al., 2002; Rasetti et al., 2009; Schneider et al., 1998; Taylor et al., 2005, 2007), although other groups have found increased activation (Holt et al., 2006a; Kosaka et al., 2002) or tonically elevated activity in the amygdala (Taylor et al., 2005). When viewing faces, schizophrenia patients have exhibited less focused BOLD signal in visual cortex (Pinkham et al., 2008; Seiferth et al., 2009), and electrophysiological studies of face processing have shown reduced amplitude of the N170, an early event-related potential localized to the occipito–temporal junction (Bediou et al., 2007; Turetsky et al., 2007). Abnormal early processing of visual stimuli has been tied to later, higher level processing (Butler and Javitt, 2005; Turetsky et al., 2007), highlighting the importance of interactions between these networks. Since some investigators have shown evidence for reduced connectivity in schizophrenia (Das et al., 2007; Fletcher et al., 1999; Foucher et al., 2005; Friston and Frith, 1995), abnormal network interactions may be an important feature of aberrant appraisal in the brain of a person with schizophrenia.

The present study sought to evaluate neural correlates of social appraisal in schizophrenia to identify dysfunctional circuitry related to social processing deficits. In a social preference task, never before studied in schizophrenia patients, subjects viewed face stimuli, with negative, neutral or positive expressions, judging whether or not they liked each face. The preference judgment was contrasted with judging the gender of faces, controlling for basic perception and motor responses.

We had three objectives. The first objective focused on mPFC activity, since this node has been suggested to provide socio-emotional context for appraisals, as reviewed above. Although hypoactivation of the mPFC (Lee et al., 2006; Taylor et al., 2002; Williams et al., 2004) to neutral socio-emotional stimuli has been reported, emotionally negative stimuli have caused increased activity (Crespo-Facorro et al., 2001a; Fakra et al., 2008; Paradiso et al., 2003; Rajarethinam et al., 2005; Taylor et al., 2002, 2007). Following up on this previous work, we predicted that patients with chronic psychosis would exhibit a hyperactive response in the mPFC when appraising negatively-valenced faces. Negative affect is a significant feature of schizophrenia. For example, behavioral studies show that schizophrenia patients engage more negative affective states, exhibited in higher levels of trait negative affect (Blanchard et al., 1998; Horan et al., 2008), experience mildly stressful situations as particularly aversive (Docherty, 1996; Horan et al., 2005; Jones and Fernyhough, 2007) and appraise neutral and positive stimuli as more aversive in laboratory tests (Cohen and Minor, 2010). Since the mPFC is engaged both by social and emotional stimuli (Ochsner, 2008; Phan et al., 2002), a greater mPFC signal in patients may represent greater 'resonance' with negative stimuli, possibly connected with a tendency to misconstrue social situations, a compensatory response for impairments in other symptoms, or inefficient regulation of negative emotions.

Additional objectives explored behavioral correlations and network relationships of the mPFC. As not all groups have found that aversive content induces a hyperactive signal in the mPFC (Takahashi et al., 2004), it has been suggested that the presence of high positive symptoms might account for differences between studies, such that patients with more delusional interpretations of the environment may be more engaged by negative stimuli (Taylor et al., 2007). Thus, a second objective was to explore symptom correlations with appraisal-related activation and test the prediction that mPFC activity would correlate with positive symptoms of reality distortion when appraising negative faces. We also explored correlations with performance measures of social cognition and social adjustment, searching for relationships between appraisal-related regions and poor social function. Our third objective was to evaluate connectivity patterns during appraisal, predicting that patients would have less connectivity in medial frontal regions during appraisal and evaluating connectivity with posterior areas involved in early sensory processing. As will be shown, the findings revealed dysfunction of the mPFC during social appraisal, as well as the association of impaired social cognition with early sensory processing.

1. Methods

1.1. Subjects

From a university-staffed community mental health center, 22 stable, medicated outpatients were recruited with DSM-IV schizophrenia (17) or schizoaffective (5) disorder (American Psychiatric Association, 1994) established by a Structured Clinical Interview for Diagnosis (First et al., 1995). All patients were without active depression, alcohol/substance abuse/dependence (>6 months without abuse/dependence), and significant medical illness that could affect cerebral function (e.g. diabetes mellitus, hypertension). Because one schizophrenic subject failed to follow instructions during scanning, he was excluded from the analysis, leaving 21 subjects for analysis (Table 1). Subject assessment included clinical ratings by an experienced clinician (SFT) on the Brief Psychiatric Rating Scale (Overall and Gorham, 1962), Hamilton Scale for Depression, 17 items (HAM-D; Hamilton, 1960), and the Scale for the Assessment of Negative Symptoms (Andreasen, 1983).

Twenty-one healthy comparison subjects were recruited from community advertisements, selected to match the age range, gender distribution and family education level of the patients. They were without Axis I psychiatric disorders (Structured Clinical Interview for Diagnosis, non-patient version (First et al., 1996)), without first-degree relatives with psychosis, and not taking medication.

As a measure of educational achievement, subjects took the Wide Range Achievement Test, revised, Reading subtest (WRAT-R; Jastak and Wilkinson, 1984). For assessment of socio-emotional function, they completed the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT), Managing Emotions branch (Mayer