



Similar patterns of brain activation abnormalities during emotional and non-emotional judgments of faces in a schizophrenia family study

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ABSTRACT

Schizophrenia patients have impaired performance and abnormal brain activation during facial emotion recognition, which may represent a marker of genetic liability to schizophrenia. However, it remains unclear whether the impairment is specific to recognizing emotion from faces or is instead attributable to more generalized dysfunction. The current study aimed to distinguish between specific and generalized neural dysfunction underlying impaired facial emotion recognition in schizophrenia and examine associations with genetic liability. Twenty-eight schizophrenia patients, 27 nonpsychotic first-degree relatives, and 27 community controls underwent functional magnetic resonance imaging while making judgments about either the emotion or age of emotional faces. Patients had performance deficits during the emotion and age discrimination conditions compared to relatives and controls, while relatives had intact performance. Patients had hypoactivation compared to controls across conditions, mainly in medial prefrontal cortex. Unlike controls, patients demonstrated a failure to recruit the dorsomedial prefrontal cortex, a region involved in social cognition and decision-making, and relatives had a pattern of recruitment intermediate between patients and controls. Compared to controls, relatives had greater deactivation of regions associated with the default mode network, and patients had similar findings during age discrimination. The common patterns of performance deficits and activation abnormalities during emotion and age discrimination in schizophrenia suggest that generalized cognitive impairment, notably in social cognition and decision-making, contributes to impaired facial emotion recognition. Similar functional activation patterns in relatives, despite intact performance, suggest that brain activation may represent a more sensitive marker of genetic liability than behaviour. Hyperdeactivation of default mode network regions in relatives may represent cognitive inefficiency, or compensatory mechanisms that help maintain intact performance.

1. Introduction

Schizophrenia patients are consistently found to have deficits in perceiving and recognizing facial emotions (Kohler et al., 2010). These deficits are of particular significance because they have been directly linked to functional outcome in schizophrenia (Couture et al., 2006; Flett et al., 2011). Furthermore, facial emotion recognition deficits have been documented in nonpsychotic relatives of schizophrenia patients (Lavoie et al., 2013) and appear to be stable across phases of illness (prodromal, first-episode, chronic) (Green et al., 2012), suggesting an association with the genetic liability to schizophrenia.

An important area of debate in the literature is whether these deficits in schizophrenia are specific to recognizing emotions from faces, or rather part of more generalized cognitive or perceptual dysfunction. Behavioural studies addressing this question have com-

pared performance during facial emotion recognition to performance on non-emotional tasks of face processing (e.g., age, gender, or identity discrimination). A meta-analysis (Chan et al., 2010) of these studies in schizophrenia patients compared to controls reported a larger deficit for facial emotion recognition ($d = -.85$) than general face processing ($d = -.70$), suggesting that a specific deficit for facial emotion recognition may be present in the context of a more generalized deficit. The two previous similar studies with nonpsychotic relatives yielded inconclusive results. One study reported no deficits in relatives for either facial emotion or age discrimination (Goghari et al., 2011). The other reported an intermediate deficit in relatives that was between schizophrenia patients and controls for facial emotion recognition, but no group differences in performance on the gender discrimination control task (Bediou et al., 2007).

Functional magnetic resonance imaging (fMRI) has also been used

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to study the neural dysfunction associated with impaired facial emotion recognition in schizophrenia. A meta-analysis (Taylor et al., 2012) of fMRI studies of facial emotion perception found brain activation differences between schizophrenia patients and controls, with primarily hypoactivation in limbic (amygdala/hippocampus), frontal (medial and ventrolateral prefrontal cortex, anterior cingulate), and occipito-temporal (occipital pole, fusiform, superior temporal gyrus) regions, which are thought to comprise the distributed network for processing social information such as faces (Adolphs, 2009; Gobbini and Haxby, 2007). The few similar studies conducted with nonpsychotic relatives have yielded mixed results, including hypoactivation (Barbour et al., 2010; Habel et al., 2004), hyperactivation (Li et al., 2012), or no activation differences compared to controls (Rasetti et al., 2009).

fMRI studies typically use either explicit facial emotion recognition tasks (i.e., making an emotional judgment about emotional faces) or implicit tasks where the emotional aspects of faces are not relevant to making a response, similar to the non-emotional comparison tasks described above (i.e., making a non-emotional judgment about emotional faces). When the Taylor et al. (2012) meta-analysis synthesized the results separately for the two task types, the pattern of group activation differences was much more widespread for explicit tasks, with only mediofrontal/cingulate and amygdala/hippocampal clusters emerging as significant for implicit contrasts. These findings converge with behavioural evidence in suggesting that both generalized cognitive dysfunction and dysfunction specific to evaluating the emotional content of faces may account for impaired facial emotion recognition in schizophrenia.

However, in contrast to behavioural studies, very few individual neuroimaging studies of facial emotion recognition in schizophrenia have included a comparison task of non-emotional judgments, which helps to account for other associated cognitive processes to refine inferences about the nature of impairment. The first neuroimaging study of facial emotion recognition in schizophrenia to incorporate both emotion and age discrimination conditions did not report the group comparisons for the age discrimination condition (R.E. Gur et al., 2002). In a more recent study, comparable hypoactivation in schizophrenia patients was found across emotion and gender face discrimination tasks, suggesting common mechanisms of impairment (Johnston et al., 2005). Moreover, neither study included nonpsychotic relatives, which can help to distinguish genetic from disease-process related abnormalities.

Further motivation for investigating the specific vs. generalized mechanisms underlying facial emotion recognition deficits in schizophrenia includes the existence of deficits and associated neural dysfunction in social cognitive abilities that overlap with facial emotion recognition (e.g., theory of mind, social perception) (Green et al., 2015), and in neurocognitive processes commonly recruited by facial emotion recognition tasks (e.g., cognitive control, working memory) (Reichenberg and Harvey, 2007). Evidence also suggests that schizophrenia patients have dysfunction in the brain's 'default mode' network, which has been implicated both in the performance of social cognitive tasks, and in optimizing task-related cognitive engagement through the suppression of this network (Li et al., 2014; Pettersson-Yeo et al., 2011; Whitfield-Gabrieli and Ford, 2012). Finally, much of the previous research into the neural basis of facial emotion recognition in schizophrenia has emphasized the perceptual/sensory aspects of dysfunction (e.g., examining the brain's response to emotional vs. neutral faces or positive vs. negative emotions; judging the similarity between emotional face images using emotional face matching paradigms; restricting analyses to limbic regions such as the amygdala) while relatively few fMRI studies have focused specifically on top-down evaluative processes involved in facial emotion recognition schizophrenia.

Therefore, in the current study, we investigated functional activation patterns during emotional and non-emotional (age) judgments of emotional faces in schizophrenia patients, nonpsychotic relatives, and

community controls. This design aimed to clarify the nature and specificity of activation abnormalities underlying facial emotion recognition deficits in schizophrenia, and to examine associations with the genetic liability to the disorder. We used a response format and face stimuli that have successfully been used in previous studies to reveal functional activation abnormalities in schizophrenia (R.E. Gur et al., 2002, 2007): participants were required to make a forced choice about whether the face in the trial matches the target category (e.g., "Happy" or "Not Happy"; "Over 30" or "Under 30"). We hypothesized that schizophrenia patients and nonpsychotic relatives would display similar patterns of abnormalities (primarily hypoactivation) compared to controls, in previously reported occipito-temporal, limbic, and prefrontal regions involved in face perception, social cognition, and decision-making. Furthermore, we hypothesized that functional activation abnormalities would be present in patients and relatives for both facial emotion and age judgments, but to a greater extent during explicit facial emotion recognition.

2. Methods

2.1. Participants

Participants included 21 patients with schizophrenia and 7 patients with schizoaffective disorder (combined into one group; hereafter referred to as schizophrenia patients), 27 first-degree nonpsychotic relatives, and 27 community controls. Patients were recruited through outpatient clinics and community support programs in Calgary, Canada. Researchers identified first-degree biological relatives by completing a pedigree with the patients and obtaining permission to contact. Controls were recruited through advertisements posted in the community and online. Participant informed consent was obtained prior to participation and the study protocol was approved by the University of Calgary Conjoint Health Research Ethics Board.

Participant inclusion criteria were: age between 18 and 65 years and estimated intelligence quotient (IQ) above 70, and exclusion criteria were: current diagnosis of alcohol or drug dependence or abuse, history of head injury leading to hospitalization or unconsciousness over 20 min, history of neurological condition, history of electroconvulsive therapy, and MRI contraindications. Further exclusion criteria for relatives and controls were: personal history of psychotic or bipolar disorders, current major depressive episode, Axis II Cluster A personality disorder, and use of antipsychotic medication. An additional exclusion criterion for controls was a family history of psychotic or bipolar disorders.

Diagnoses were confirmed using the Structured Clinical Interview for DSM-IV (First et al., 2002) and the Structured Clinical Interview for Schizotypy (Kendler et al., 1989) with supplemental questions. The Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999) provided an estimate of IQ. Symptomatology and functioning were assessed with the Positive and Negative Syndrome Scale (Kay et al., 1987), the Social Functioning Scale (Birchwood et al., 1990), and the Global Assessment of Functioning (GAF) Scale (American Psychiatric Association, 2000).

2.2. fMRI task

Participants completed four runs of facial emotion discrimination under a particular target emotion condition (either Anger, Fear, Happy, or Sad) and one run of Age discrimination, with run order randomized for each participant. During the facial emotion discrimination conditions, participants made a key-press to indicate whether the face presented was target or non-target, depending on the emotion condition (for example, during the Fear condition, participants had to indicate whether or not the face presented depicted a fearful emotion). During the Age condition, similar emotional faces were presented and participants indicated whether the face was above or below the age of

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