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Increased medial temporal lobe activation during the passive viewing of emotional and neutral facial expressions in schizophrenia

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Abstract

Introduction: Patients with schizophrenia show deficits in facial affect and facial identity recognition and exhibit structural and neurophysiological abnormalities in brain regions known to mediate these processes. Functional neuroimaging studies of neural responses to emotional facial expressions in schizophrenia have reported both increases and decreases in medial temporal lobe (MTL) activity in schizophrenia. Some of this variability may be related to the tasks performed and the baseline conditions used. Here we tested whether MTL responses to human faces in schizophrenia are abnormal when unconstrained by a cognitive task and measured relative to a low-level baseline (fixation) condition.
Methods: 15 patients with schizophrenia and 16 healthy control subjects underwent functional magnetic resonance imaging (fMRI) while passively viewing human faces displaying fearful, happy, and neutral emotional expressions.
Results: Relative to control subjects, the patients demonstrated (1) significantly greater activation of the left hippocampus while viewing all three facial expressions and (2) increased right amygdala activation during the initial presentation of fearful and neutral facial expressions.
Conclusions: In schizophrenia, hippocampal and amygdala activity is elevated during the passive viewing of human faces.

Keywords: Schizophrenia; Functional magnetic resonance imaging; Amygdala; Hippocampus; Emotion; Face

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1. Introduction

Over the past several decades, there has been increasing interest in understanding the role of affect processing abnormalities in the acute symptoms and the functional impairment observed in schizophrenia. Severity of emotional perception deficits (Kee et al., 2003) and negative symptoms, which include affective flattening, apathy and anhedonia (Milev et al., 2005), predict poor psychosocial outcome in schizophrenia. Also, it has been hypothesized that positive symptoms (delusions and hallucinations) arise from fundamental abnormalities in emotional perception and social cognition (Bentall et al., 2001; Phillips et al., 2003). One basic component of social cognitive functioning is facial affect recognition; recognizing and discriminating among distinct facial emotional expressions allows one to infer the state of mind of others. Both positive (Hall et al., 2004) and negative (Kohler et al., 2000; Martin et al., 2005; Sachs et al., 2004) symptoms have been correlated with poor facial affect recognition in schizophrenia. However, there is also evidence that these facial affect recognition deficits may be at least partially attributable to a number of factors unrelated to affect processing including a primary deficit in face perception (Onitsuka et al., 2003; Quintana et al., 2003), the overall neurocognitive impairments associated with the disorder (Addington and Addington, 1998; Bozikas et al., 2004; Kohler et al., 2000; Sachs et al., 2004; Whittaker et al., 2001), illness chronicity (Mueser et al., 1997; Penn et al., 2000) and medication effects (Whittaker et al., 2001).

Impaired facial affect processing in schizophrenia may be related to dysfunction of the amygdala and hippocampus. The amygdala is known to be crucial for the accurate recognition of facial expressions, particularly fear (Adolphs et al., 1994). Recently, it has become clear that the hippocampus, primarily known for its role in declarative memory, is also involved in the formation of emotional memories and associations (Buchel et al., 1999; Phelps, 2004; Sanders et al., 2003). During affect processing, the hippocampus and amygdala may influence one another via bi-directional projections (Krettek and Price, 1977; Pitkanen et al., 2000) and projections to common efferent targets (Canteras and Swanson, 1992; Nauta, 1986; Ragsdale and Graybiel, 1988). Evidence for amygdala–hippocampal interactions during affect processing has been provided by human neuroimaging studies which have shown concurrent, and in some cases correlated (Dolcos et al., 2004; Kensinger and Corkin, 2004), activation of the amygdala and hippocampus during the successful encoding of emotional information (Dolcos et al., 2004; Maratos et al., 2001; Smith et al., 2004), viewing of emotional facial expressions (Gur et al., 2002a; Williams et al., 2001), and acquisition of conditioned responses to aversive stimuli (Buchel et al., 1999). Because of these studies and evidence from post-mortem and morphometric MRI studies for structural changes in the hippocampus and amygdala (Heckers and Konradi, 2002; Nelson et al., 1998; Wright et al., 2000), we hypothesized that facial affect processing in schizophrenia is associated with hippocampal and amygdala dysfunction.

Previous functional neuroimaging studies of neural responses to emotional facial expressions in schizophrenia have demonstrated decreases in the amygdala (Gur et al., 2002b; Hempel et al., 2003; Phillips et al., 1999a; Schneider et al., 1998; Williams et al., 2004) and hippocampus (Gur et al., 2002b; Hempel et al., 2003). However, one functional magnetic resonance imaging (fMRI) study showed an increased response of the right amygdala to happy faces (Kosaka et al., 2002), and another demonstrated a sustained response of the right anterior hippocampus to fearful faces (Holt et al., 2005) in patients with schizophrenia. Differences among these studies in the baseline condition used or in the cognitive task performed by the subjects may account for some of the discrepancies among these results. In contrast to the studies which found increases (Holt et al., 2005; Kosaka et al., 2002), several studies which found abnormally reduced amygdala and/or hippocampal activation in schizophrenia used neutral (Phillips et al., 1999; Williams et al., 2004) or inverted neutral (Hempel et al., 2003) faces as the baseline condition. Amygdala activation occurs in response to neutral faces (Schwartz et al., 2003; Somerville et al., 2004) and patients with schizophrenia frequently respond to neutral stimuli–faces and words rated as "neutral" by healthy volunteers–as if they were emotional or arousing (Holt et al., submitted for publication; Kohler et al., 2003; Williams et al., 2004). Thus, studies which measure neural responses to emotional facial expressions relative to responses to neutral