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Neural bases for impaired social cognition in schizophrenia and autism spectrum disorders

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Abstract

Schizophrenia and autism both feature significant impairments in social cognition and social functioning, but the specificity and mechanisms of these deficits remain unknown. Recent research suggests that social cognitive deficits in both disorders may arise from dysfunctions in the neural systems that underlie social cognition. We explored the neural activation of discrete brain regions implicated in social cognitive and face processing in schizophrenia subgroups and autism spectrum disorders during complex social judgments of faces. Twelve individuals with autism spectrum disorders (ASD), 12 paranoid individuals with schizophrenia (P-SCZ), 12 non-paranoid individuals with schizophrenia (NP-SCZ), and 12 non-clinical healthy controls participated in this cross sectional study. Neural activation, as indexed by blood oxygenation level dependent (BOLD) contrast, was measured in *a priori* regions of interest while individuals rated faces for trustworthiness. All groups showed significant activation of a social cognitive network including the amygdala, fusiform face area (FFA), superior temporal sulcus (STS), and ventrolateral prefrontal cortex (VLPFC) while completing a task of complex social cognition (i.e. trustworthiness judgments). ASD and P-SCZ individuals showed significantly reduced neural activation in the right amygdala, FFA, and left VLPFC as compared to controls and in the left VLPFC as compared to NP-SCZ individuals during this task. These findings lend support to models hypothesizing well-defined neural substrates of social cognition and suggest a specific neural mechanism that may underlie social cognitive impairments in both autism and paranoid schizophrenia.

Keywords: Amygdala; Fusiform face area; Paranoia; fMRI; Schizophrenia; High-functioning autism

1. Introduction

Social cognition is defined as "the mental operations underlying social interactions, which include the human ability to perceive the intentions and dispositions of others" (Brothers, 1990, p. 28). Neurobiological models

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of social cognition posit that a network of neural structures is critically involved in processing social stimuli (Adolphs, 2001; Brothers, 1990; Phillips et al., 2003). These models focus on regions of the occipital and temporal cortices such as the Fusiform Gyrus (FG) and Superior Temporal Sulcus (STS) which underlie face processing (Haxby, Hoffmann and Gobbini, 2000; Winston, Henson, Fine-Goulden, and Dolan, 2004) and the amygdala which plays a critical role in detecting threat, recognizing emotions, and making complex social judgments (Adolphs et al., 1994; Adolphs et al., 1998; Amaral et al., 2003; Winston et al., 2002). Such models provide a foundation for understanding the neural mechanisms underlying social deficits in several clinical disorders, particularly schizophrenia and autism.

Although schizophrenia and autism have different symptom presentations, ages of onset, and developmental courses, impaired social functioning is a hallmark characteristic of both disorders (DSM-IV-TR), and these social deficits are related to impairments in social cognition (Couture et al., 2006; Hughes et al., 1997; Klin et al., 2002; Pinkham et al., 2003). Behavioral data suggest both disorders show comparable social cognitive deficits, particularly on tasks requiring higher levels of social cognitive skill (i.e. complex social judgments; Craig et al., 2004; Pilowsky et al., 2000); however, our understanding of these deficits, and the potential similarities between disorders, remains incomplete. Specifically, behavioral findings are complicated by heterogeneity within disorders, particularly in schizophrenia, as individuals with persecutory delusions perform differently both at behavioral and neural levels on social cognitive tasks relative to individuals without persecutory delusions (Bentall et al., 2001; Davis and Gibson, 2000; Phillips et al., 1999; Ueno et al., 2004; Williams et al., 2004). Additionally, despite evidence of abnormal activation in the neural systems of social cognition in schizophrenia and autism (Pinkham et al., 2003; Pelphrey et al., 2004), no studies have used fMRI to directly compare the neural substrates underlying social cognitive performance in both disorders. Thus, comparing these two disorders may illuminate the general mechanisms underlying social cognitive deficits and inform the etiologies of social dysfunction seen in these disparate disorders.

We used event-related functional magnetic resonance imaging (fMRI) to measure neural activation during complex social judgments (i.e. trustworthiness) of faces in four groups: high-functioning individuals with autism spectrum disorders (ASD), paranoid individuals with schizophrenia (P-SCZ), non-paranoid individuals with schizophrenia (NP-SCZ), and non-clinical healthy controls. As previous research has demonstrated significantly greater amygdala activation in non-paranoid, relative to paranoid individuals with schizophrenia (Phillips et al., 1999; Williams et al., 2004), two separate groups of patients with schizophrenia were recruited in order to provide the most comprehensive comparison with ASD and to account for known differences between schizophrenia subgroups. Further, decisions of trustworthiness were employed due to previous work demonstrating that these judgments fully engage the neural regions implicated in social cognition in healthy individuals (Winston et al., 2002) and to the likelihood that these judgments would be particularly salient in assessing differences between paranoid and non-paranoid individuals.

Based on neurobiological models of social cognition and face processing, and previous behavioral and imaging work utilizing trustworthiness judgments (Adolphs et al., 1998; Winston et al., 2002), comparisons of neural activation were limited *a priori* to discrete brain regions comprising a face processing/social cognitive neural circuit, which included the amygdala, fusiform face area of the FG, STS, and ventrolateral prefrontal cortex (VLPFC; BA 47). Although the VLPFC has not been included in all previous studies of face processing, recent evidence implicates this region in making evaluative judgments (Cunningham et al., 2003), and it has been found to modulate activation of the amygdala while viewing faces and labeling facial expressions (Cunningham et al., 2004; Hariri et al., 2003). As such, this region may play an important role in top-down processing of social stimuli.

We predicted healthy controls would show greater neural activity than all clinical groups in the amygdala, FFA, STS, and VLPFC when making complex social judgments. For the direct comparison between schizophrenia and ASD, one would expect the ASD group to differ from both the NP-SCZ and P-SCZ groups due to clinical distinctions between the disorders; however, careful examination of the social cognition literature actually suggests that ASD should be most similar to the P-SCZ group. Specifically, increased rates of paranoia are often seen clinically in individuals with Asperger's syndrome (Hare, 1997; Wing, 1996), and two studies have found increased rates of paranoia in ASD as compared to healthy controls (Blackshaw et al., 2001; Craig et al., 2004). Further, only minimal differences in social cognition have been observed between individuals with autism and those with schizophrenia when the latter group was higher in paranoid symptoms (Craig et al., 2004; Pilowsky et al., 2000). Thus, based on this evidence and in conjunction with work suggesting greater