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Efficacy of identifying neural components in the face and emotion processing system in schizophrenia using a dynamic functional localizer

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ABSTRACT

Schizophrenia is associated with deficits in face perception and emotion recognition. Despite consistent behavioural results, the neural mechanisms underlying these cognitive abilities have been difficult to isolate, in part due to differences in neuroimaging methods used between studies for identifying regions in the face processing system. Given this problem, we aimed to validate a recently developed fMRI-based dynamic functional localizer task for use in studies of psychiatric populations and specifically schizophrenia. Previously, this functional localizer successfully identified each of the core face processing regions (i.e. fusiform face area, occipital face area, superior temporal sulcus), and regions within an extended system (e.g. amygdala) in healthy individuals. In this study, we tested the functional localizer success rate in 27 schizophrenia patients and in 24 community controls. Overall, the core face processing regions were localized equally between both the schizophrenia and control group. Additionally, the amygdala, a candidate brain region from the extended system, was identified in nearly half the participants from both groups. These results indicate the effectiveness of a dynamic functional localizer at identifying regions of interest associated with face perception and emotion recognition in schizophrenia. The use of dynamic functional localizers may help standardize the investigation of the facial and emotion processing system in this and other clinical populations.

1. Introduction

Schizophrenia is associated with a reduced capacity to recognize the emotional content of facial expressions (Kohler et al., 2000; Schneider et al., 2006). Behavioural deficits in facial emotion recognition are observed in schizophrenia patients across a wide array of experimental paradigms over the past three decades (Kohler et al., 2010) and are attributable to impairments in both emotion recognition and general face perception (Chan et al., 2010). These impairments in emotion recognition appear to be present across different stages of the disorder (Addington et al., 2006; Green et al., 2012) and are predictive of functional outcome in schizophrenia patients (Kucharska-Pietura et al., 2005; Addington et al., 2008; Amminger et al., 2012; Comparelli et al., 2013; Kohler et al., 2014). This suggests that facial emotion recognition may serve as an important biological marker for schizophrenia (Horan et al., 2012). However, there is not a standard means to identify face processing regions in the brain, making comparisons between studies difficult due to variability in methodological approaches. A more standardized means for localizing these regions would assist in the reliable interpretation of abnormal cortical activity associated with facial emotion recognition deficits that are observed in schizophrenia patients.

In the healthy population, one influential theory of face perception and emotion recognition proposes that these processes depend on the recruitment of a 'core' system that extends throughout the occipital and temporal lobes, and an "extended" system that extends from the middle superior temporal sulcus, through the amygdala and into the prefrontal cortex (Haxby et al., 2000a; Gobbini and Haxby, 2007; Fox et al., 2009). The core/extended model of facial perception has been generally supported across studies since first proposed by Haxby et al. (2000a), and has important implications for understanding impairments to facial emotion recognition in schizophrenia patients.

The core system comprises of three main regions. The first is located in the lateral portion of the fusiform gyrus, the second in

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the inferior occipital gyrus, and the third in the posterior section of the superior temporal sulcus. In terms of their functions, the occipital face area (OFA) has been associated with early visual processing of faces (Haxby et al., 2000b; Ishai et al., 2005), whereas the fusiform face area (FFA) has been associated with processing facial identity and invariant features of faces (Kanwisher et al., 1997; Haxby et al., 2000a; Ishai et al., 2005). The posterior superior temporal sulcus (pSTS) has been associated with processing facial expressions (Haxby et al., 2000a; Ishai et al., 2005), and is thought to process changeable aspects of face perception such as eye gaze direction and lip movement.

The putative extended system encompasses a broader set of brain regions that interact with the core system to process emotional, situational, and familiarity-based meaning derived from the visual features of a face (Haxby et al., 2000b; Gobbini and Haxby, 2007). Regions in the extended system include the anterior paracingulate cortex, posterior temporal parietal junction, and precuneus/posterior cingulate, which cooperatively combine beliefs about a familiar person – their personality, attitudes, and social roles – to their facial identity (Gobbini et al., 2004; Gobbini and Haxby, 2007). Also included in the extended system is the amygdala and anterior insula, regions which are believed to assist in understanding the emotional content of facial expressions.

With regards to schizophrenia, temporal lobe dysfunction is historically hypothesized as a key contributor to pathology, as well as a primary source of symptoms expressed by patients (Crow, 1985; Kraepelin, 1907), possibly due to reduced connectivity between regions in the temporal lobe and prefrontal cortex (Friston and Frith, 1995). This suggests that the observable deficits in facial emotion recognition could plausibly be related to abnormal structural and functional properties of components of the core/extended face processing system located across the temporal lobe. In support of this, previous studies using functional magnetic resonance imaging (fMRI) have shown that schizophrenia patients have reduced blood oxygen level dependent (BOLD) signal in the FFA while performing facial emotion discrimination and recognition tasks (Quintana et al., 2003; Johnston et al., 2005), and have more robust BOLD signal responses in the FFA when viewing neutral faces as compared to emotional faces (Surguladze et al., 2006). Similarly, reduced grey matter volume has been observed in the left FFA in schizophrenia patients, which was correlated with accuracy on a facial emotion recognition task (Goghari et al., 2011). The amygdala has also been shown to have abnormal functional responses in schizophrenia patients (Gur et al., 2002; Anticevic et al., 2012). However, findings from brain imaging studies on facial emotion recognition are not always consistent, with some studies reporting reduced (Gur et al., 2002; Das et al., 2007), increased (Kosaka et al., 2002; Holt et al., 2006) and intact (Seiferth et al., 2009) responses during facial emotion processing tasks. A meta-analysis of facial emotion processing concluded that schizophrenia patients show decreased BOLD signal responses in the amygdala and parahippocampal gyrus bilaterally, as well as in the right fusiform gyrus and the right superior frontal gyrus compared to controls (Li et al., 2010).

Despite increasing evidence for disruptions in functional responses within regions of the core and extended face processing system in schizophrenia, the precise nature of the neural mechanisms underlying facial emotion recognition remains inconclusive. This is in part due to different methodological approaches between studies that vary stimuli, duration, trial design, and response formats across both standardized and non-standardized assessments (Holt et al., 2006; Li et al., 2010; Taylor et al., 2012). Additionally, cross-study comparisons are limited by the inter-individual variability in the neuroanatomy of the core face perception system (Fox et al., 2009), which may be more pronounced in schizophrenia patients (Honea et al., 2005). Subject level functional localizers allow researchers to control for neuroanatomical differences by using perceptual tasks to identify regions of the cortex based on function, rather than relying on anatomical boundaries. These regions are then used in different experimental contexts to investigate hypothesized subject-level or group differences in affective and cognitive function resulting from experimental manipulations. In other words, a functional localizer is one way to independently generate ROIs to then use in another fMRI task to extract group differences. This helps to minimize between-subject variance (Duncan et al., 2009) by obtaining task-related parameter estimates at the single-subject level that can then be used for group comparisons. This is especially the case at higher statistical significance thresholds, because single-subject ROIs allow the experimenter to account for between-subject variance in location and size of BOLD signal changes, which is not controlled for in the group averaged approach (Gorgolewski et al., 2013). In this context, it is important to validate a face processing localizer task to limit the variability of results both between participants and studies that may be due to differences in experimental design rather than effects of interest. Defining a localizer task that is able to robustly identify the core face processing system, as well as regions in the extended system shown to be abnormally recruited in schizophrenia patients (i.e. amygdala), would assist in reliably interpreting functional neuroimaging findings of facial emotion recognition in schizophrenia. This is vital to building a more replicable and cumulative literature.

To facilitate the validation of a functional localizer task in schizophrenia patients, the current study investigated the robustness of a recently developed functional localizer task to identify brain regions comprising the face perception system in schizophrenia patients and controls. This task uses dynamic visual stimuli as opposed to traditional functional localizers that use static images to identify the putative regions of the core and extended face processing system. Static image localizers, such as those developed by Hariri et al. (2002), do not account for the dynamic nature of facial perception that is encountered in the real world, leading in some cases to lower levels of neural engagement (Kilts et al., 2003; Sato et al., 2004). In light of this, Fox et al. (2009) have shown that dynamic facial stimuli provide a more effective means for localizing the FFA, OFA, pSTS and portions of the 'extended' system in non-clinical samples.

We extend this research into the clinical domain by evaluating the success of the dynamic functional localizer in identifying the core system (i.e. FFA, OFA and pSTS), as well as the amygdala, and comparing the localization rates between schizophrenia patients and community controls. First, we hypothesized that the localizer task would allow for equal localization success rates between groups for our a priori ROIs. Second, due to past research identifying both functional (Quintana et al., 2003; Johnston et al., 2005; Surguladze et al., 2006) and structural (Goghari et al., 2011) abnormalities in schizophrenia associated with facial emotional recognition, we hypothesized that the patient group would show differences in the peak activity within each of the ROIs generated during the localizer task compared to controls.

2. Materials and methods

2.1. Participants

Inclusion criteria for all participants included: (1) age 18–65; (2) minimum IQ of 70; (3) no current diagnosis of drug or alcohol dependence or abuse; (4) no history of head injury or being unconscious for more than 20 min; (5) no history of electroconvulsive therapy; and (6) no history of stroke or other neurological condition. Further criteria for inclusion of community

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