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Neural processing of facial expressions of emotion in first onset psychosis

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ABSTRACT

Schizophrenia is characterized by deficits in face and facial emotion processing. This is the first study using event-related potentials (ERPs) to investigate the corresponding neural activation in first onset psychosis. ERPs for 108 first onset psychosis participants and 108 matched healthy controls were recorded while they viewed facial expressions. Group differences on general (neutral) face processing and emotional valence were examined under both unmasked (conscious) and backward-masked (nonconscious implicit) conditions over frontal and temporo-occipital regions. Clinical significance was assessed by comparing diagnoses and correlating ERPs with symptoms. During general face processing, patients showed reduced activation within 70 ms and exaggerated later processing from 160 ms over the frontal region, with a negative shift in voltage over left temporal and occipital regions across the time course. In addition, from 70 ms onwards, patients showed a positive shift in voltage for disgust whereas controls showed a negative shift in voltage for fear and anger (both compared to happy) over temporo-occipital regions. Effects were related to disorganization and depression symptoms and (preliminarily) were apparent across psychotic diagnoses. These results suggest that first onset psychosis is characterized by general as well as emotion-specific face processing impairments from the earliest, automatic processing period.

1. Introduction

A hallmark of schizophrenia is a deficit in processing faces and facial emotion (Morris et al., 2009). Our aim is to identify the neural correlates of impaired face and facial emotion processing present at the first onset of psychosis, and determine whether these impairments occur early or late in the neural processing time course.

Deficits in facial emotion processing have been proposed as a potential endophenotype for schizophrenia (Gur et al., 2007), given they are also present in high risk groups (Edwards et al., 2001; Pinkham et al., 2007; Bediou et al., 2007a; Addington et al., 2008). They are also likely to contribute to the substantial burden of illness in schizophrenia given their association with negative symptoms, poor interpersonal and social functioning and functional outcome (Hooker and Park, 2002; Kohler et al., 2000).

Most studies of facial emotion processing in schizophrenia and related psychotic disorders have used behavioral measures. There remains debate over whether the observed behavioral impairments are emotion-specific (and in particular, *negative*-emotion-specific) or reflect a general problem with face processing (Bryson et al., 1997; Johnston et al., 2006; Schneider et al., 2006). Because behavioral measures reflect the output of processing, it is also not known where in the processing time course specific or general face processing impairments occur in schizophrenia. In line with theories of sensory gating problems (McGhie and Chapman, 1961) and abnormal salience detection (Kapur, 2003) in schizophrenia, abnormalities in facial emotion processing may occur very early in processing, perhaps due to the inability to 'gate in' the salient emotions that signal threat (fear and anger) and 'gate out' the less salient emotions for immediate survival (such as happy).

Event-related potentials (ERPs) provide a high temporal resolution measure of neural activity independent of behavior. There is little in the ERP literature that examines the question of whether there are specific or general impairments in face processing in schizophrenia, and where in the time course of neural processing they may occur. This is mostly due to the majority of studies only considering limited emotions and relatively few ERP time points. Of the few previous ERP studies which have considered multiple emotions (at least one positive and one negative, in addition to neutral), results are mixed for each emotion and processing

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window, including several null results (see Fig. S1 for a summary; Bediou et al., 2007b; Caharel et al., 2007; Herrmann et al., 2006; Jetha et al., 2013; Johnston et al., 2005; Lee et al., 2007, 2010;Lynn and Salisbury, 2008; Wynn et al., 2008). It is difficult to make comparisons of patterns across these studies, since their ERP component time periods are often not aligned, and for those that are, the emotions included are not similar. Thus more work is required to give a comprehensive analysis of several emotions across multiple time points. Furthermore, these studies have focused on chronic schizophrenia patients. ERPs have also not previously been used to examine the timing of emotion processing neural impairments during nonconscious processing. We know from imaging work, however, that facial emotion impairments at the first onset of schizophrenia occur for both nonconscious and conscious processing of facial emotions (Das, et al., 2007).

In this study, we draw on the previous work to examine the time course of neural processing in response to general (neutral) and emotional face processing in first onset psychosis. We include multiple psychotic diagnoses to account for the difficulty in diagnosing psychotic disorders at first presentation, and to focus on psychosis symptoms rather than diagnostic categories, which aligns with current key psychiatric research strategies of examining cognitive systems, neural circuits, and behaviour across diagnostic boundaries (Insel et al., 2010; Morris and Cuthbert, 2012). Behavioral (Addington and Addington, 1998; Vaskinn et al., 2007) and ERP (see Fig. S1) results rarely compare across diagnostic boundaries and are unclear as to whether there are differences in facial emotion processing among different psychotic disorders. Our primary aims are to examine: i) whether general face processing impairments are early (within 200 ms) or late (>200 ms), ii) whether there are specific effects of facial *emotion* processing, over and above those of general face processing (as measured by difference scores between neutral and each emotion), iii) whether specific emotion processing impairments are also present during the non-conscious (backward masked) condition. As second-level aims, we also considered iv) whether there are differences in neural impairments among different diagnoses, and v) whether there is a relationship between neural impairments and symptoms in face and facial emotion processing. All aims were addressed in patients experiencing the first onset of a psychotic disorder, thereby limiting potential confounds from duration of illness and treatment. We hypothesize that impairments in general and emotional face processing will appear early during sensory processing, in line with sensory gating hypotheses of schizophrenia (McGhie and Chapman, 1961), and some observations in previous ERP studies (see Fig. S1). Emotional face processing impairments will be present during both controlled (conscious) and automatic (nonconscious) processing, given that early sensory processing for salient stimuli can occur without consciousness (Das et al., 2007). We also suspect that these effects will be common across psychotic diagnoses, but more impaired in schizophrenia, and will be associated with increased symptoms.

2. Methods

2.1. Participants

Analyses were conducted on data accessed from the Brain Resource International Database. This database is made available for free and transparent scientific use by BRAINnet – an independent, not-for-profit organization (www.brainnet.net). The first onset psychosis (FOP) group comprised of 108 of the 134 FOP participants in the database (26 participants did not have ERP data for the task of interest). All participants were recruited and tested by members of the BRAINnet Early Psychosis Collaborative Group (which includes the authors) from the early intervention services of both the Western Sydney and the South Western Sydney Local Health Districts, as well as a regional public mental health service in the northern suburbs of Adelaide. Participants were recruited if they met criteria for any psychotic disorder (including schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, bipolar disorder with psychotic features, major depression with psychotic features, substance induced psychotic disorder, and psychosis not otherwise specified) according to the Structured Clinical Interview for DSM-IV (First et al., 2002). First onset status was defined as within 12 months of first contact with a mental health service for psychotic symptoms. Prior mental health contact for non-psychotic symptoms did not disqualify them for inclusion in the study. Symptom severity was assessed (on the same day as the EEG recording) by the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) and the Calgary Depression Scale for Schizophrenia (CDSS; Addington et al., 1990). Reports on a subset of this cohort (approximately the first 50% of the Sydney sample) have been previously published on general and social cognition (Williams et al., 2008), gamma synchrony (with an emotion task: Williams et al., 2009; with a selective attention task: Flynn et al., 2008) and brain imaging (Das et al., 2007). This is the first paper to report on ERP outcomes.

Healthy controls ($n=108$) age- and sex-matched to each FOP patient were also provided via BRAINnet. These controls had no history of a psychiatric disorder. Demographic and clinical details are outlined in Table 1.

For both groups, exclusion criteria were i) an inability to speak English, ii) current drug dependence, iii) history of neurological disorder, physical brain injury or significant head injury (loss of consciousness for ≥ 10 minutes), and iv) any other serious medical conditions. All participants had normal or corrected-to-normal vision (with their vision checked prior to the testing procedure) and were asked to refrain from smoking or consuming caffeine 2 h prior to testing.

Written informed consent was provided by all participants contributing to the database, in accordance with Australian National Health and Medical Research Council guidelines. Ethical approval was provided by the Human Research Ethics Committees of the Western Sydney Local Health District, the South Western Sydney Local Health District, and the Queen Elizabeth Hospital, Adelaide.

2.2. Facial emotion task and ERP recording

The emotion task and ERP recording followed a previously reported design (Williams et al., 2007). Standardized face stimuli, equated for size, luminance and location of the eyes in the horizontal plane were presented on a computer monitor with a refresh cycle resolution of 100 Hz. There were a total of 192 stimuli, representing eight different individuals, each depicting neutral and evoked expressions of happiness, fear, sadness, anger and disgust. Blocks of eight stimuli were presented with stimuli randomized within blocks.

Participants viewed the faces under both conscious and nonconscious conditions (Fig. 1). In the conscious condition, stimuli were each displayed for 500 ms, with an interstimulus interval of 700 ms for a total stimulus onset asynchrony of 1200 ms. In the nonconscious condition, backward masking was employed. Each stimulus was presented for 10 ms, immediately followed by a neutral face for 150 ms. This neutral face mask was superimposed over the first stimulus, spatially offset by 1° in one of four randomly selected diagonals. In this condition, the interstimulus interval was 1040 ms, such that the total stimulus onset asynchrony was equal to that in the conscious condition (1200 ms). Presentation of stimuli in this format for the nonconscious condition has been shown to effectively mask the emotional expressions such that participants are not consciously aware of the emotional expression, but still show physiological processing differences, suggesting that they are processing them nonconsciously (Williams, et al., 2004; Williams et al., 2007).

Conditions were presented in the order of nonconscious followed by conscious, in order to avoid the potentially confounding effects of suprathreshold perception on subsequent subthreshold perception (Bernat et al., 2001; Williams et al., 2004). No behavioral response was required in order to create a genuine masked condition, and to reduce any confound of brain activation related to a response. To ensure active attention to the stimuli participants were instructed to attend to the faces in preparation for further assessments relating to these faces at the conclusion of the tasks. We have previously demonstrated this task's sensitivity to emotion differences in brain activation between conscious and nonconscious processing in healthy participants, including corresponding changes in an independent measure of emotional response: skin conductance (Williams et al., 2004).

2.3. ERP data reduction and analysis

Electroencephalographic (EEG) data were acquired from participants as they completed the facial emotion perception task. Participants were seated in a sound- and light-attenuated room, with temperature controlled at 24 °C. A QuickCap and NuAmps DC system (Neuroscan) were used to record data at 500 Hz from 32 channels, comprising of 26 cephalic sites (placed according to the 10-10 international system), four electrooculogram (EOG) channels, orbicularis oculus and masseter. The focal sites of interest for this study were those implicated in face processing, and established in our previous study (Williams et al., 2006): temporal (left: T5, right: T6), occipital (left: O1, right: O2), and fronto-central (midline: Fz, Cz).

Skin resistance was maintained below 5 kΩ. The site Afz served as ground during recording, and data was referenced to the average of A1 and A2. Horizontal