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The face and its emotion: Right N170 deficits in structural processing and early emotional discrimination in schizophrenic patients and relatives

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ABSTRACT

Previous studies have reported facial emotion recognition impairments in schizophrenic patients, as well as abnormalities in the N170 component of the event-related potential. Current research on schizophrenia highlights the importance of complexly-inherited brain-based deficits. In order to examine the N170 markers of face structural and emotional processing, DSM-IV diagnosed schizophrenia probands ($n = 13$), unaffected first-degree relatives from multiplex families ($n = 13$), and control subjects ($n = 13$) matched by age, gender and educational level, performed a categorization task which involved words and faces with positive and negative valence. The N170 component, while present in relatives and control subjects, was reduced in patients, not only for faces, but also for face–word differences, suggesting a deficit in structural processing of stimuli. Control subjects showed N170 modulation according to the valence of facial stimuli. However, this discrimination effect was found to be reduced both in patients and relatives. This is the first report showing N170 valence deficits in relatives. Our results suggest a generalized deficit affecting the structural encoding of faces in patients, as well as the emotion discrimination both in patients and relatives. Finally, these findings lend support to the notion that cortical markers of facial discrimination can be validly considered as vulnerability markers.

1. Introduction

The symptomatic description of schizophrenia has been well established ever since classic early research. Scientific literature on schizophrenia has been largely devoted to understanding the underlying neurobiological mechanisms that account for both positive and negative symptoms of this disorder (Andreasen et al., 1995). Research scientists have only recently begun to look at these symptoms in more detail (e.g. Tamminga, 2006), trying to draw more profound relationships between clinical features and their potential neural substrates. Hence, there is considerable interest in a possible neurodevelopmental hypothesis of schizophrenia, which has specifically led to the hypothesis that cognitive and social cognition impairments, typical of the disorder, are actually pre-morbid traits rather than state-dependent deficits (Rapoport et al., 2005). Accordingly, such impairments are clinically identifiable upon 'disease onset' and tend to remain stable once acute episodes have remitted (Heydebrand, 2006). Moreover, genetic research on schizophrenia has offered consistent evidence regarding the hereditary factors which contribute to this disorder. All of the aforementioned findings have revealed that patients with schizophrenia — *and* unaffected relatives — exhibit cognitive and social cognition impairments. Findings of this caliber have led to a growing interest in studying multiplex families, that is, families in which there are two or more schizophrenic patients. Naturally, studying these families in detail can help identify cognitive and behavioral impairments associated with genetic vulnerability in schizophrenia (Holden, 2003).

1.1. Emotional impairments in schizophrenia families and the role of N170

Emotional disturbances in schizophrenia, including flattened affect, inappropriate affect, and depression, have become the focus of much research effort. Indeed, one of the most consistent findings is that patients with schizophrenia have deficits in recognizing and

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discriminating facial emotions (Kohler et al., 2003). Recognizing the expression of facial emotion is a complex social cognition ability, which involves several stages for successful processing, including initial visual processing, structural encoding of a face and later association of the representation with cognitive, semantic, and affective information for distinguishing between the emotions (Balconi and Lucchiari, 2005; Jacques and Rossion, 2009). Despite extensive research in schizophrenia, there is an ongoing and yet unresolved debate regarding whether emotion identification deficits reflect a specific or generalized form of cognitive impairment in this disorder (Kerr and Neale, 1993; Whittaker et al., 2001); nonetheless, studies have shown that emotion processing deficits are uniquely related to clinical symptoms (Sachs et al., 2004).

The N170 is an event-related potential (ERP) with a negative waveform, achieving a peak amplitude approximately 150–180 ms post-stimulus (commonly detected at the occipito-temporal sites). It is commonly thought to reflect early perceptual processes involving the structural encoding of faces (Eimer, 2000). The N170 component is hypothesized to arise primarily from the fusiform gyrus and superior temporal sulcus (STS); it can be readily distinguished from the ERP response to other classes of stimuli (Herrmann et al., 2005). In addition, the N170 component has been reported to be lateralized, suggesting right-lateralized topography for face stimuli, whereas N170 for words tends to be more left-lateralized or bilateral (Rossion et al., 2003). Larger N170 waves have been shown for faces compared to words in the right scalp (Rossion et al., 2000, 2003), especially when faces and words are presented in the same block in an alternating fashion (Maurer et al., 2008).

N170 has also been described as a component modulated by emotional faces and emotions (Pizzagalli et al., 2002; Batty and Taylor, 2003; Ashley et al., 2004; Blau et al., 2007; but see Eimer and Holmes, 2002 and Eimer et al., 2003 for an absent emotional modulation). Specifically, when face and word categorization tasks are used, the N170 component has been reported to present increased amplitude for positive stimuli relative to negative stimuli (Schacht and Sommer, 2009). Overall, N170 is thought to be a neural marker of early face-selective processing modulated by emotional clues, but not influenced by processing of other objects.

In schizophrenia, despite limited ERP data, recent studies have documented an N170 deficit for visual encoding of faces. The N170 Amplitude difference of stimulus type discrimination (e.g., faces vs. objects) is reduced in schizophrenic patients (Herrmann et al., 2004). Abnormalities in N170 of emotional faces in patients have been reported, with larger responses to faces expressing emotions relative to neutral faces (Caharel et al., 2007). Moreover, an enhanced N170 amplitude in response to fearful faces has been reported (Ramos-Loyo et al., 2009). Probably, these effects suggest difficulties in encoding the structure of a face and subsequent familiarity and emotion evaluation. As well, the amplitude of the N170 responses to sad faces has been associated with the severity of positive symptoms in schizophrenic patients (Johnston et al., 2005; Turetsky et al., 2007). N170 deficits have been found more pronounced over the right scalp (Herrmann et al., 2004). In order to explore other ways in which ERPs of emotional processing could also be altered or affected, DSM-IV diagnosed schizophrenia probands, their unaffected first-degree relatives, and control subjects matched by age, gender, and educational level performed a classification task that involved the categorization of pleasant and unpleasant words, along with faces of anger and happiness.

1.2. The goal of this study

In the present study we propose that the N170 component (modulated by valence and stimulus type) has the potential to be a marker of vulnerability both in patients and relatives. This vulnerability should be more accentuated in multiplex families (families in which there are two or more schizophrenic patients). A subclinical impairment of emotional inference and stimulus type discrimination may be the basis for further studies of underlying risk and stable trait markers, or endophenotypes (Gottesman and Gould, 2003; Braff et al., 2007). Several reasons support such speculations. First, social cognition performance has been extensively studied in schizophrenic patients and their relatives (Brüne, 2005; Harrington et al., 2005; Beer and Ochsner, 2006; Irani et al., 2006; Green and Leitman, 2008; Bora et al., 2009). Second, recent reports suggest that complex social skills depend on basic emotional facial processing and emotional inference (Grossmann, 2010). Faces (especially eyes and gaze; Itier and Batty, 2009) constitute multi-dimensional stimuli that are directly related to important social incentives (Ohman and Mineka, 2001). Facial emotional expression can provide an automatic and rapid shortcut to alarm signals, mentalizing, and inter-subjective communication. Third, recent experimental data suggest that the key elements that evoke the N170 effect are the eyes of a face stimulus (Itier et al., 2007), thus constituting the most important area of the face as regards the inference of affective social cognition. Finally, as briefly reviewed above, in schizophrenia research, impairments in both stimulus type and emotional valence as captured by the N170 component have already been reported. Nevertheless, no previous report assessing such N170 modulations in first-degree relatives had been assessed until now.

In sum, cortical markers of facial-semantic valance (N170) could be a shortcut to basic subclinical impairments in schizophrenia families. One theoretical implication of this would be that emotional, as well as social cognition impairments in schizophrenia families may be connected to the early brain process involved in basic cognitive discrimination of stimulus type (face and words) and valence. In order to test this hypothesis, we chose an N170 paradigm that has been previously found to be affected by stimulus type and emotional valence.

2. Methods

2.1. Subjects

Thirteen schizophrenic patients, thirteen first-degree relatives, and thirteen controls were enrolled in this study. The three groups had the same distribution for age, level of education, and proportion of males to female. In the Supplementary data section, specific age comparisons between controls vs. patients, as well as controls vs. relatives can be found. In addition, our behavioral as well as ERP results were reanalyzed considering age as a covariate. All reported significant differences remained after introduce age as covariate (see Supplementary data). No difference between groups was observed with regards to either intellectual capabilities or speed processing, as assessed by the Raven Test (Raven et al., 2003) and Trail Making Test — Part A, respectively. No significant difference was observed in executive function performance, either, as assessed by the Trail Making Test — Part B (Bowie and Harvey, 2006). The Positive and Negative Symptoms Scale (PANNS; Kay et al., 1987) was evaluated in the patient group. A summary of demographic and clinical characteristics of the groups is presented in Table 1. Inclusion criteria for patients were: (1) the diagnosis of paranoid schizophrenia according to DSM-IV-TR criteria (First et al., 1996) and confirmed with the Schedules of Clinical Assessment in Neuropsychiatry (SCAN) (World Health Organization, 1992) applied by a trained physician; and (2) the presence of one or more relatives with the diagnosis of schizophrenia (no greater than a third-degree relative), evidenced by the Family Interview for Genetic Studies (FIGS) applied to the relative (NIMH, 1992). All patients were under antipsychotic medication (all except one, atypical). Healthy relatives had to be first-degree relatives and to have never been diagnosed with schizotypical disorder or any psychiatric disease. All relatives were family members of the patients. Participants recruited were aged 20–55 years. Written informed consent was obtained from all subjects, and they were paid for their participation.

2.2. Procedure

The task involved a valence categorization of stimuli with a positive or negative dimension valence: happy ($n = 20$) and angry ($n = 20$) faces along with pleasant words ($n = 71$) and unpleasant words ($n = 72$). Stimuli were controlled for frequency, content, valence, type of word, moderate levels arousal (for words), as well as physical features, valence, gender, moderate levels of and arousal (for faces). All stimuli were selected from a previously reported dataset (e.g., Hurtado et al., 2009; Ibáñez et al., 2010a,b, 2011a; Guex et al., 2011). A greater number of word stimuli relative to faces were selected in order to reduce repetition effect of words (see discussion, Section 4.5, for more details). Each block started with a brief explanation of which keys were assigned to each word/face category. Subsequently, the trials were presented one by one with strict alternation between words and faces (in order to enhance the stimulus type differences between faces and words in the right scalp previously reported by Maurer et al. (2008). Previous reports using stimuli strict alternation have been proved useful for the expected behavioral and N170 modulation specific to the task and independent of the alternation (e.g., Krombholz et al., 2007; Maurer et al., 2008; Hurtado et al., 2009; Ibáñez et al., 2010a, 2011c). The practice blocks involved