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Key Words
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ABSTRACT

In psychiatrically-well subjects the modulation of event related potentials (ERPs) by emotional facial expressions is found in several ERPs from ~100 ms and later. A face-related EPR, the N170, is abnormally reduced in schizophrenia to faces relative to other complex objects and research suggests emotional modulation of N170 may be reduced as well. To further examine facial emotion modulation of N170, subjects detected neutral facial expressions from among five emotional expressions (happy, sad, fearful, angry, and disgusted). Over occipitotemporal sites, psychiatrically-well subjects showed bilateral differences in N170 amplitude among expressions ($P=0.014$). Schizophrenia subjects failed to show this modulation ($P=0.551$). Accuracy on the task did not differ between groups, nor did the pattern of errors. However, in patients, greater positive and negative symptom ratings were associated with increased failure to button press to neutral faces, suggesting misattribution of emotion to neutral expressions in the more ill patients. Because the N170 is largely specific to faces, these results suggest that an impairment specific to the visual processing of facial expressions contributes to the well-known behavioral abnormalities in facial emotion tasks in schizophrenia.

INTRODUCTION

A history of behavioral studies documents biased facial emotion recognition in schizophrenia, particularly involving expressions of negative or intense affect.[1] For example, patients with persecutory delusions are slower than normal controls to identify angry faces,[2] and patients misattribute disgust and fear to neutral faces at higher rates than controls.[3] In addition to behavioral abnormalities, individuals with schizophrenia also exhibit neurophysiological impairments associated with face and facial expression processing. Modulation of neurophysiological processes by facial expression is found in several event related-potentials (ERPs) in psychiatrically-well subjects. Here we focus on the N170, thought to reflect a predominantly face-specific process modulated by emotional expression.

THE FACE-RELATED POTENTIAL

In control subjects, pictures of faces elicit a particularly large ERP relative to pictures of non-face objects, such as buildings or flowers[4]. Peaking at approximately 170 ms, when recorded from occipitotemporal electrodes the negative-going ERP is known as the N170.5 At Cz, a voltage inversion is known as the Vertex Positive Potential (VPP[6]). Here we will use the term "face related potential" (FRP) to refer to N170, VPP, and their magnetoencephalographic counterparts. Though it shows sensitivity to category-independent perceptual stimulus qualities such as interstimulus perceptual variation[7] the FRP is considered to reflect neural encoding of perceptual details,[8] particularly of faces, in the service of cognitive processing, e.g., individual identification.[9,10]

Effects of emotional expression on the FRP have not been consistently reported. However, growing evidence suggests that the FRP can be modulated by facial emotion. Among such studies, neutral expressions uniformly elicit small amplitudes relative to emotional faces.[11-14] Happy faces have been found to elicit smaller amplitude than other emotions (disgusted>happy[14]; fear = happy faces at N170 but fear>happy at VPP[13,15]; fear>happy and sad at N170[16]).

In schizophrenia, the FRP is reduced to all faces relative to psychiatrically-well subjects.[16-21] This impairment appears to be specific to faces; the FRP is not significantly reduced to non-face objects. Regarding emotional modulation, Campanella et al.[16] did not find the fearful>happy and sad pattern in patients that their controls exhibited. Turetsky et al.[21] found that neutral faces elicited lower N170 global field power than happy and sad faces, particularly evident among controls, suggestive of attenuated modulation of N170 in schizophrenia.

METHODS

Subjects

Twenty-four chronically-ill schizophrenia subjects (9 female) and 8 control subjects (3 female) participated. Informed consent was obtained after complete description of the study. All subjects were right-handed. Recruitment, criteria for enrollment, and diagnostic procedures are described elsewhere.[20] Groups were matched on age, Wechsler Adult Intelligence Scales-II (WAIS) Information scaled score, parental socioeconomic status, years of education, handedness, and gender proportion (Table 1). The schizophrenia sample comprised 12 paranoid and 6 disorganized subtype patients; and 6 schizoaffective disorder patients (5 depressed subtype, 1 bipolar subtype). Patient symptom ratings were obtained using the Scale for the Assessment of Negative Symptoms (SANS, mean = 9.0 ± 5.46 [SD]) and the Scale for the Assessment of Positive Symptoms (SAPS, mean = 6.6 ± 3.68). Chlorpromazine-equivalent antipsychotic medication dose[22] was mean = 409.0 ± 376.66.

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Table 1
Demographic measures and classification performance on emotional faces

Measure	Control Mean	Control (SD)	Schizophrenia Mean	Schizophrenia (SD)	P
Age (years)	41.0	(7.86)	35.5	(9.42)	0.15
Education (years)	15.8	(2.19)	14.8	(2.43)	0.33
Parental SES	1.8	(0.89)	1.9	(1.14)	0.71
WAIS Information (scaled)	13.0	(1.93)	12.4	(2.19)	0.51
Handedness	0.8	(0.12)	0.8	(0.19)	0.90
#Errors Neutral	5.3	(3.92)	7.6	(5.8)	0.35
#Errors Angry	5.5	(2.78)	4.8	(2.92)	0.22
#Errors Disgusted	0.4	(0.52)	0.9	(1.47)	0.32
#Errors Fearful	1.3	(1.58)	2.2	(2.19)	0.49
#Errors Happy	0.6	(1.06)	1.5	(1.96)	0.55
#Errors Sad	5.9	(2.90)	6.5	(4.94)	0.79
Accuracy	0.4	(0.19)	0.3	(0.27)	0.32

Stimuli and Experimental Design

Two experiments were run: Emotional Faces and Structural Faces. For both experiments subjects viewed the images serially on a computer screen from 1.3 m distant and stimuli subtended approximately 6° visual angle. Stimulus presentation and button press responding were accomplished with SuperLab Pro 2 (Cedrus Corp.). Stimuli were preceded by a 200 ms fixation cross at the center of the screen followed by a 200 ms blank screen. Stimuli were shown in the center of the screen for 500 ms.

In Emotional Faces, stimuli comprised 16 examples each of neutral, sad, angry, happy, fearful, and disgusted expressions.[23] Each image was shown twice, in random order within repetition block. Subjects were instructed to button-press with their right index finger when they saw “a face with a neutral or blank expression.” Stimuli were followed by an 800, 933, 1066, or 1200 ms blank screen, with the variable durations balanced across expression and gender. All subjects passed, on first try, a pretest in which they were asked to indicate which one of six simultaneously presented faces from a different stimulus set (Japanese and Caucasian Facial Expressions [JaCFE], Paul Ekman Group, LLC) showed a neutral expression.

In Structural Faces, stimuli were images of faces, cars, and butterflies.[20] Face stimuli comprised 32 faces (16 male, 16 female JaCFE faces, half Asian, half Caucasian). Thirty-two images showed cars from a 3/4-profile view, and 10 images were of butterflies shown in a “pinned” perspective. Subjects button pressed when they saw a butterfly. Stimuli were followed by a 1000 ms blank screen.

Electrophysiological Recording and Processing

EEG activity was recorded with a 64-channel system. During recording, the right mastoid served as the reference. Recordings were rereferenced to the average reference as computed from all scalp electrodes. Epochs were 1100 ms duration, including a 100 ms pre-stimulus baseline. Additional recording and processing details are described elsewhere.[20] Averages were computed separately for each emotional category. Amplitude and latency of the N170 ERP were measured for each subject using automated peak detection, searched separately on each channel, with subsequent manual confirmation.

Statistical Analyses

The N170 ERP was examined at four bilateral posterior electrode sites (T5/T6, P9/P10, PO7/PO8, PO9/PO10; odd# denotes left hemisphere, even denotes right). ERP amplitude and latency were analyzed with mixed design ANOVAs using diagnosis as a between-subjects factor and stimulus type (six levels for Emotional Faces, two for Structural Faces), hemisphere (left, right), and electrode site (four in each hemisphere) as within-subject factors. Degrees of freedom were adjusted with the Huynh-Feldt epsilon for factors with greater than two levels. T-tests and Pearson correlations were two-tailed.

RESULTS

Accuracy in the Emotional Faces experiment [(correct detections–false alarms)/(number of neutral face presentations)] did not differ between groups (t_{30}=1.3, P=0.2, Table 1). The number of false alarms delivered to the different expressions differed among expressions ($F_{4,120}$=30.8, P<0.0001). However, the pattern of false alarm responses to different expressions did not differ between groups ($F_{4,120}$=0.5, P>0.58). Higher symptom ratings were associated with a larger number of missed detections of neutral faces (SAPS: r=0.47, P=0.039; SANS: r=0.57, P=0.009). Symptom ratings were not correlated with the number of false alarm responses, false alarm distribution across facial expressions, or medication.

For the Emotional Faces experiment, we examined ERPs only from trials on which subjects correctly button-pressed to neutral faces or withheld response to other expressions. N170 amplitude was reduced in schizophrenia subjects relative to controls ($F_{1,30}$=9.1, P=0.005). A main effect of emotion was also present ($F_{5,150}$=2.3, P=0.048), interacting with group ($F_{5,150}$=3.2, P=0.009; Figure 1). Follow-up ANOVAs within group indicated that controls modulated N170 ($F_{5,35}$=3.6, P=0.014) while patients did not ($F_{5,115}$=0.8, P=0.551). Controls showed significant differences in N170 amplitude to facial expressions at all four bilateral sites ($F_{5,35}$>2.7, P<0.034), whereas patients showed no effect of emotion at any site ($F_{5,115}$<1.0, P>0.45).

Among controls, we conducted paired t-tests of N170 amplitude between each emotional condition at P9/P10, the site of greatest amplitude modulation. At P9, controls showed significantly greater amplitude to sad faces than to neutral (t_7=5.4, P=0.001), fearful (t_7=3.5, P=0.010), or happy faces (t_7=2.4, P=0.050). N170 to happy faces was marginally larger than to fearful faces (t_7=3.2, P=0.068). Results were similar at P10; sad faces elicited significantly greater amplitude than neutral (t_7=3.4, P=0.012), fearful (t_7=2.6, P=0.033), and happy (t_7=3.3, P=0.013) faces, with marginally greater amplitude than disgusted faces (t_7=2.3, P=0.056). Angry faces were marginally larger than neutral (t_7=2.1, P=0.071) and fearful (t_7=2.1, P=0.074) faces, and disgusted faces were marginally larger than neutral faces (t_7=2.3, P=0.057).

N170 amplitudes to particular emotional conditions did not correlate with task performance in either group, and patients showed no correlations between N170 amplitude and medication. An ANOVA at P9/P10 comparing N170 latencies among emotions and groups found no differences.

In the structural Faces experiment, patients showed reduced amplitude to both faces and cars relative to controls (main effect of group: $F_{1,28}$=7.2, P=0.012; EEG data of 2 patients were lost due to technical malfunction) but, overall, exhibited relatively unimpaired augmentation of faces relative to cars (group x stimulus interaction: $F_{1,28}$=0.3, P=0.868).

As indices of N170 modulation we constructed emotional and structural N170 peak amplitude differences. In patients, but not

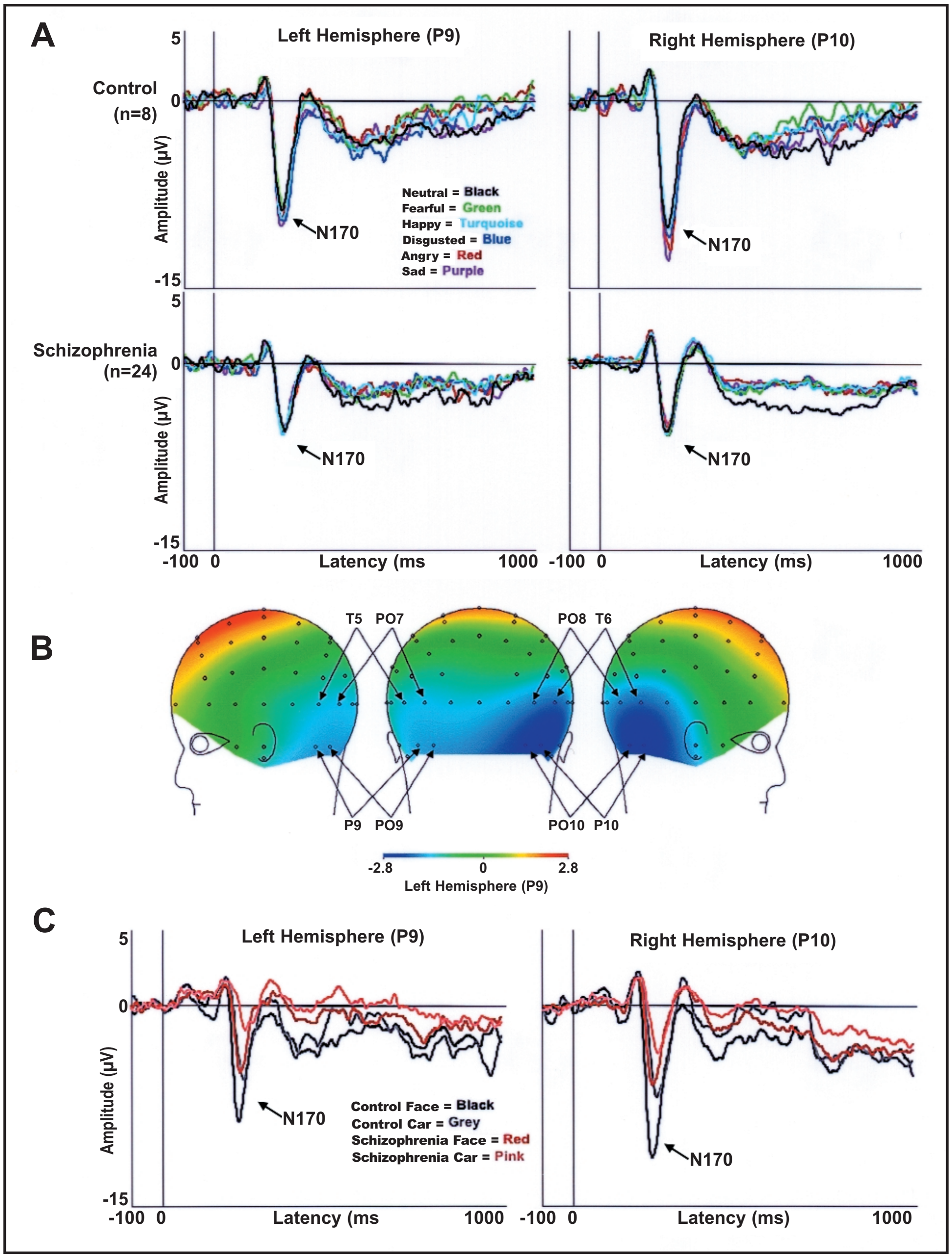

Figure 1.
The N170 ERP in schizophrenia and control subjects. (A) Grand average ERPs elicited by six facial expressions from control and schizophrenia subjects. (B) Topography of N170 emotional modulation (sad–neutral) in controls. (C) Augmentation of N170 to faces relative to cars.

controls, smaller emotional modulation of N170 amplitude (neutral–sad difference) was associated with smaller face-specific augmentation of N170 (face–car difference) at electrodes T6 (r=0.44, P=0.017), P10 (r=0.53, P=0.005), and, marginally, at P09 (r=0.34, P=0.063) and PO10 (r=0.35, P=0.055).

DISCUSSION

Control subjects showed significant differences in N170 amplitude elicited by facial expressions. The right hemisphere tended to show greater differentiation than the left. Schizophrenia patients failed to exhibit these modulations. We found that greater positive and negative symptom ratings were associated with failure to button press to neutral faces. This pattern is suggestive of a tendency toward misattribution of emotion to neutral expressions in more symptomatic patients and congruent with poorer classification performance in patients given unlimited time to view this stimulus set.[3]

Individuals with schizophrenia are impaired in their ability to recognize faces, and discriminate among and respond to emotional facial expressions.[1] Within the behavioral schizophrenia facial expression literature, a question persists about the extent to which emotional deficits revealed with the use of face stimuli arise from an impairment specific to face processing rather than from a more general affective deficit. Studies using non-face stimuli[24,25] document a general emotional deficit in schizophrenia that could clearly influence processes operating on emotional faces. However, because the N170 is largely specific to faces, our results suggest that an impairment specific to the visual processing of facial expressions contributes to the well known behavioral abnormalities in facial expression tasks. Furthermore, the correlation in patients between emotional modulation and structural augmentation impairments suggests that this "emotional" deficit occurs at N170 generators rather than arising from impaired modulation of N170 by another source.

The special nature of faces as biologically prepotent stimuli, combined with the established deficits in early visual processing of faces, makes faces unparalleled stimuli for investigation of the social deficits of schizophrenia and the mechanisms of how neurocognitive impairments scale up to positive and negative clinical symptoms and behavioral impairments. Understanding and treating the emotional and social abnormalities of schizophrenia will require measuring the different contributions of affective, social, and more traditionally sensory and cognitive deficits on any one experimental task. Further research should address the hypothesis that N170 deficits cascade down the face processing stream,[18,21] and, as well, quantify the contribution of non-face-specific emotion processing deficits to behavioral and neurocognitive impairments in emotional expression evaluation.

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