Schizophrenia Research 149 (2013) 135–140

Contents lists available at SciVerse ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Fearful face recognition in schizophrenia: An electrophysiological study

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ARTICLE INFO

Article history:
Received 17 February 2013
Received in revised form 1 June 2013
Accepted 30 June 2013
Available online 18 July 2013

Keywords:
Schizophrenia
Social cognition
Facial emotion processing
EEG
Event-related potentials
Global field power

ABSTRACT

Background: Emotional expressions are important acts of communication, and impairment in facial emotion recognition has been shown to be related to impairments in social cognition in schizophrenia. We used an event-related potential (ERP) paradigm to identify and delineate the temporal characteristics in the electrophysiological cascade related to fearful facial affect processing in patients with schizophrenia as compared to healthy controls.

Methods: Twenty-four subjects with schizophrenia and 24 individually matched healthy controls participated in an emotion recognition task. Ekman faces displaying neutral and fearful facial expressions were used as stimuli. ERPs were recorded using a 128-channel EEG system.

Results: Based on the analysis of Global Field Power (GFP) in the 150–190 ms time window both groups differentiated between fearful and neutral faces. Schizophrenia patients showed an additional differential processing of fearful vs. neutral faces in the 330–450 ms time window, and this ERP effect correlated with psychopathology.

Conclusions: Both patients and healthy controls differentiate fearful and neutral faces in early phases of emotion processing. Our results also indicate that schizophrenia patients show increased responsivity to fearful faces at a later processing stage. This could be related to the overrating of negative emotions, and the symptomatology associated with fear processing in patients with schizophrenia.

1. Introduction

The emotional states of others as conveyed by facial emotional expressions constitute a key cue in social interactions. The ability to read faces is essential for social cognition, and it has gained considerable interest over the past decades in schizophrenia research. It has been shown to be closely related to psychosocial functioning and quality of life in schizophrenia (Kee et al., 2003; Brekke et al., 2005). Extensive research has accumulated suggesting a robust impairment in emotion perception in schizophrenia, especially in the recognition of negative emotions (Gur et al., 2002; Kohler et al., 2003; Morris et al., 2009).

Use of event-related potential (ERP) paradigms to measure neural activity during emotion processing has become a major approach in cognitive affective neuroscience, since this method captures the exact time course of the emotional information-processing cascade from early to later processing stages with a millisecond-resolution (Luck et al., 2011). ERP studies of emotion recognition paradigms with schizophrenia patients have yielded divergent and often controversial results as to where and when abnormal activation patterns occur in the course of emotion processing as compared to healthy controls. Deficits in both early and late ERP components of facial emotion processing have been found, such as the P100 (Wolwer et al., 2011), suggesting a deficit in early visual processing; the face-specific N170 (Turetsky et al., 2007; Wynn et al., 2008), suggesting a dysfunction in face-selective visual processing capacities; the N250 (Wynn et al., 2008), suggesting a disturbance in evaluative affect-recognition processes; and in the P300 (Turetsky et al., 2007), indicating disturbed higher-order cognitive processes associating the structural representation of a face with its affective and contextual information. Results of impaired activation patterns at different processing stages have led to the question where in the time course of emotional information processing the effect of emotions enters and modifies the information processing cascade. The variability of findings has given room for interpreting results as supporting both a bottom–up, initial sensory-encoding-deficit-view (Turetsky et al., 2007), and also a later, top–down contextual-attention deficit view (Horan et al., 2010). Accordingly, these diverse results in the schizophrenia population and their interpretations necessitate further research into the neurobiological basis of emotion processing.

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http://dx.doi.org/10.1016/j.schres.2013.06.044

In our study, we specifically aimed to investigate the neurobiological basis of fearful face processing. Although patients with schizophrenia show impairment in overall emotion recognition, they appear particularly impaired in recognizing negative emotions (Strauss et al., 2011), especially fear (Morris et al., 2009). This study aimed to address facial emotion processing in schizophrenia by investigating the difference in the temporal sequence of face processing as elicited by fearful and neutral faces in individually matched groups of schizophrenia patients and healthy controls. Based on a growing body of literature indicating that the effect of emotions appears at initial stages of information processing (Wolwer et al., 2011; De Sanctis et al., in press) we expected emotion effects to fearful faces to develop at time ranges between 100 and 200 ms after stimulus presentation. Furthermore, based on prior literature on reductions of ERP components in relation to attentional processing in schizophrenia (Turetsky et al., 2007; Hajcak and Olvet, 2008) in the schizophrenia group we expected that a disruption would occur primarily at later latencies (after 300 ms), reflecting the involvement of higher levels of processing, which require the correct allocation of attentional resources to the facial emotional stimuli. Furthermore, in patients with schizophrenia, the amplitude of specific ERP components (e.g. for MMN, see Naatanen et al., 2011, for P300, see Jeon and Polich, 2003) has been shown to correlate with clinical measures, including symptom severity. We tested the hypothesis that the differential activity, evoked by processing of fearful as compared to neutral faces, would correlate with scores of psychopathology as measured by the PANSS.

2. Methods and materials

2.1. Subjects

Twenty-four patients meeting the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) criteria for schizophrenia (13 men and 11 women, mean age: 34 yr, SD = 10.2) and twenty-four healthy controls (13 men and 11 women, mean age: 33.1 yr, SD = 9.9) were enrolled in the study. Healthy controls were individually matched to the patients by gender, age (+/−5 years), and years of education (+/−3 years), thus resulting in 24 matched pairs. With the exception of three left-handed patients and two left-handed healthy controls all participants were right-handed and had normal or corrected-to-normal vision. Participants did not receive payment for their participation, and provided written informed consent after all procedures were fully explained according to procedures approved by the Institutional Review Board of the Semmelweis University, Budapest, Hungary.

Patients were recruited from both the inpatient and outpatient units of the Department of Psychiatry and Psychotherapy of the Semmelweis University, Budapest (inpatient: outpatient ratio = 9:15). All patients were assessed on the Positive and Negative Syndrome Scale (PANSS, Kay et al., 1987) by a trained psychiatrist or psychologist. All patients were taking antipsychotic medication at the time of testing (mean CPZ equivalent dose of 601 mg/day, SD = 445.5; Chlorpromazine-equivalent doses for antipsychotics were computed according to Woods (2003) and Janssen et al. (2004)). Twenty three patients were taking second generation antipsychotics, and one patient was taking first generation antipsychotic medication. The ratio of schizophrenia subtypes among patients was as follows: 13 paranoid, 2 catatonic, 6 disorganized, and 3 undifferentiated. The exclusion criteria for patients with schizophrenia were any other DSM-IV Axis I disorder, any other central nervous system disease, mental retardation, history of head injury with loss of consciousness for more than 1 h, and alcohol or drug abuse.

Exclusion criteria for healthy controls included history of any psychiatric or neurological disease, mental retardation, history of head injury with loss of consciousness for more than 1 h, and alcohol or drug abuse. Demographic information for both groups and clinical characteristics of the schizophrenia group are presented in Table 1.

Table 1
Basic demographic and descriptive characteristics of the two study groups.[a]

	Patients (n = 24)	Controls (n = 24)
Gender (male/female)	13/11	13/11
Age (years)	34.2 (10.3)	33.2 (9.8)
Education (years)	13.9 (10.1)	15.0 (2.6)
Handedness (right/left)	21/3	22/2
Duration of illness (years)	9.7 (7)	N/A
CPZ equivalent (mg)	601.9 (445.5)	N/A
Antipsychotic medication (atypical/typical)	23/1	N/A
PANSS total	59.4 (21.6)	N/A
PANSS positive	14.5 (6.0)	N/A
PANSS negative	15.1 (7.5)	N/A
Schizophrenia subtypes: Paranoid/catatonic/disorganized/undifferentiated	13/2/6/3	N/A
Inpatients/outpatients	9/15	N/A

[a] Continuous variables are characterized by mean (SD); categorical variables are represented by frequencies (n).

As a clinical screening measure, the Symptom Checklist-90 (SCL-90; Derogatis, 1977), a 90-item Symptom Checklist assessing general dimensions of psychopathology was administered for each participant. According to the Derogatis criteria for 'caseness' (i.e.: high risk for a psychiatric disorder), a global severity index of >114 on the SCL-90 was an additional exclusion criteria for healthy controls (Derogatis, 1994; Unoka et al., 2004). No subjects were excluded from the control group based on these criteria.

2.2. Stimuli and procedures

Subjects were seated in a dimly lit, sound-attenuated room. A computer screen was placed at a viewing distance of approximately 50 cm. The experiment was programmed and presented with the Presentation 13.0 software (Neurobehavioral Systems, Inc.). The facial stimuli used in the experiment were chosen from Ekman and Friesen's Face stimuli (Ekman and Friesen, 1976) with hair removed from the stimuli to avoid gender cues other than facial structure and features. Five female and five male faces were used, each displaying a neutral and a fearful expression, yielding altogether 20 stimuli. Stimuli were presented for 200 ms, followed by a blank screen with a fixation cross until the participant's behavioral response. The interval between the response and presentation of subsequent stimulus varied between 600 ms and 700 ms. As non-face control stimuli, phase-randomized patches were generated from the Ekman-faces that were presented with a 1:4 ratio to facial stimuli, also for 200 ms. Occasionally (with a 1:10 ratio to stimuli) a schematic picture of an eye was presented to the participants for 1000 ms followed by a 1000 ms interval of a blank screen, giving them the chance to blink and thus to achieve reduction in blink-related artifacts during facial stimulus presentation.

Participants were instructed to respond as quickly and accurately as possible by pressing one of two buttons whenever they perceived the facial expression displayed as neutral, and the other button whenever they perceived the facial expression displayed as fearful. No response was asked to be given to the non-face patches and to the schematic eye. Fig. 1 gives an overview of representative experimental trials.

2.3. Recordings

EEG was recorded from DC with a low-pass filter at 100 Hz using a high-density 128-channel BioSemi ActiveTwo amplifier (Metting van Rijn et al., 1990). The electrode cap covered the whole head with an equidistant-layout. Eye movements were monitored by two electro-oculogram (EOG) electrodes placed below the left and above the right external canthi. Data were digitized at 24 bit resolution and a sampling rate of 512 Hz. Subsequent data analyses were carried out

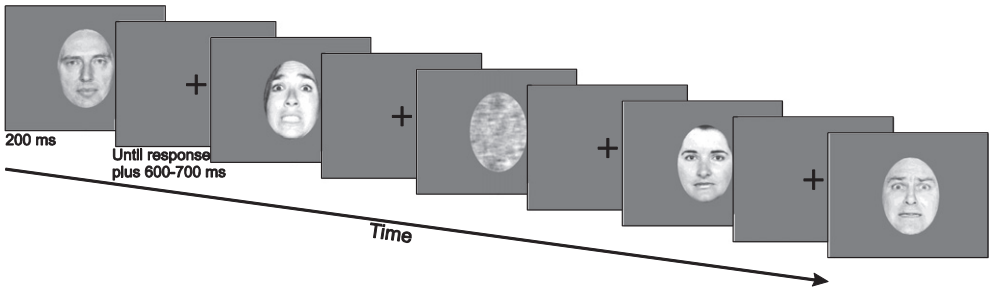

Fig. 1. Overview of representative experimental trials.

off-line using built-in and self-developed functions as well as the EEGLAB toolbox (Delorme and Makeig, 2004) in Matlab (MathWorks, Natick, MA). Further statistical analyses were carried out using the SAS ® 9.2 software (SAS Institute Inc., Cary, NC). EEG was re-referenced to the common average potential and filtered off-line between 0.1 and 30 Hz using zero-phase shift Butterworth filter. Epochs of 100 ms prestimulus to 600 ms poststimulus were extracted from the continuous EEG for further analysis and corrected for prestimulus baseline. To avoid potential artifacts, epochs with a voltage exceeding ±120 μV on any EEG or EOG channel were rejected from the analysis. Total trial number per each picture type (fearful and neutral) was 192. After artifact rejection, for the controls an average of 167 trials (SD = 20.6) and 168 trials (SD = 17.2) remained in the fearful and neutral conditions, respectively. For patients with schizophrenia the analogous numbers were the following: 155 trials (SD = 26.7) for the fearful condition and 156 trials (SD = 26.3) for the neutral condition.

2.4. Data analysis

As a preliminary analysis and "quality check", we investigated whether a face-specific response (N170 component) was detectable in our neutral facial stimuli as compared to the non-face patches. To this end, we used the General Linear Model (GLM) analysis.

In our principal analyses, first we aimed to identify the time periods during which any of the two groups showed a statistically significant discrimination in the ERPs for the fearful vs. neutral stimuli. Second, we aimed to test whether in the identified time periods there was a significant difference between the ERP waveforms between the two groups.

In particular, affect-related modulations for each of the ERP time intervals were tested by computing the difference wave for the fear vs. the neutral stimuli using the Global Field Power (GFP). Specifically, the principal statistical analysis investigated the effect of valence in each group and compared the valence effects between the two groups in time windows with >10 consecutive time points significantly differing from zero in any of the two study groups.

Random regression hierarchical linear modeling (HLM) (Gibbons et al., 1988; Brik and Raudenbush, 1992) was the primary statistical approach; this method (in contrast to the traditional ANCOVA analysis) makes allowance for heterogeneity among treatment groups and takes into account the time-dependent correlation structure of the sampling points. In the HLM model, repeated assessments of the difference wave within each specified time window served as the dependent variable. The two independent variables were "study group" and "time" (sampling point relative to stimulus onset). Study group served as the between-subject factor, and time (ms) as the within-subject, random effect factor. Interaction between study group and time was included in the model and was tested by F-statistics. Significance of the Least Squares Mean (LSM) effects was tested by the t-statistics and indicated whether there was a statistically significant valence effect in a given group. In order to compare the valence effect between groups, we formulated a pairwise group contrast for the two groups. Analogous HLM analyses were conducted for the reaction time and error data as well as for the ERP amplitudes in exploratory analyses in each of 5 brain regions of interest: frontal, central, parietal, temporal, and occipital areas (see Fig. 3, top left map for channel layout and regions of interest).

3. Results

3.1. Behavioral results

3.1.1. Hit rates in the two study groups

In the emotion recognition task during the EEG experiment, the difference between the hit rates of controls and schizophrenia patients was significant ($F(1,46) = 9.4$, $p = 0.004$), with controls showing a slightly higher hit rate than patients. In particular, both groups showed a relatively high recognition rate of emotions: controls correctly recognized emotions with a median value of 95%, schizophrenia patients with a median value of 91%. The effect of emotion on hit rates ($p = 0.4$) and the interaction between study group and emotion were not significant ($p = 0.7$).

3.1.2. Reaction times in the two study groups

Controls had a significantly ($F(1,48) = 33.2$, $p < 0.0001$) shorter reaction time (Mean = 639 ms, SD = 196 ms) during the emotion recognition task than patients with schizophrenia (Mean = 747 ms, SD = 270 ms). The main effect of emotion and the emotion by study group interaction were not significant ($p > 0.5$).

3.2. Electrophysiological results

3.2.1. Preliminary analysis of the N170 for face vs non-face stimuli

To test whether a face-specific N170 response was detectable in our neutral facial stimuli as compared to the non-face patches, the effects of stimulus condition (face vs. non-face), study group (control vs. schizophrenia) and the interaction of these effects on the N170 component were analyzed by General Linear Model (GLM) analysis. According to our expectations, we found a significantly larger N170 component in both groups to neutral faces as compared to non-face patches in the occipital region, where the N170 component reached its maximum ($F = 31.1$, $p < 0.0001$, non-face: −1.6 (SD = 4.6) and face: −6.5 (SD = 5.0) for the control group; non-face: −1.1 (SD = 3.9) and face: −6.1 (SD = 3.6) for the schizophrenia group). There was no significant group difference regarding the N170 component (effect of study group: $F = 0.2$, $p = 0.66$), nor was there a significant interaction effect ($F = 0$, $p = 0.98$).

3.2.2. Analysis of the difference GFP waveforms

GFP is a robust measure of the spatiotemporal characteristics of brain activity, corresponding to the spatial standard deviation of the electrical potentials recorded at each time point across all electrodes (Lehmann and Skrandies, 1980). GFP difference waveforms were determined separately in the two study groups by subtracting the GFP to fearful stimuli from the GFP to neutral stimuli. Then we analyzed the GFP difference waveforms in order to identify emotion effects,

i.e., to identify the time intervals where they significantly differed from zero (i.e., an effect of emotion on the ERPs was detectable). Based on this approach the time windows in the mid-latency (150–170 ms) and late latency (330–450 ms) range were selected for further analysis (Fig. 2). Fig. 3 provides topographical maps of ERP amplitudes for Neutral and Fearful faces, and Neutral minus Fearful difference waves for both time intervals for both groups.

3.2.2.1. Comparison of the GFP difference waveforms in the two study groups in the mid-latency range. GFP difference waveforms in the 150–170 ms time window for both groups showed a significant difference from zero, i.e. $p < 0.05$ for all time points in this time window, indicating that in this time period both groups exhibited a differential processing of fearful vs. neutral faces.

3.2.2.2. Comparison of GFP difference in the two study groups in the late latency range. In the 330–450 ms time window GFP difference waveforms showed a significant difference from zero in the schizophrenia group ($p < 0.05$ for all time points in this time window), but not in the healthy control group ($p > 0.24$ for all time points in this time window). To test whether the emotion effect in the difference GFP waveform between the study groups in this time range was significant, the GFP difference waveform was analyzed with a repeated measures HLM analysis, using study group, time, and the interaction of these two factors as independent variables. The analysis yielded a significant main effect of study group ($F(1;46) = 77.2$, $p < 0.0001$), while the main effect of time ($F(50;2300) = 0.04$, $p = 0.999$) and the interaction of time and group ($F(50;2300) = 0.03$, $p = 0.999$) were non-significant.

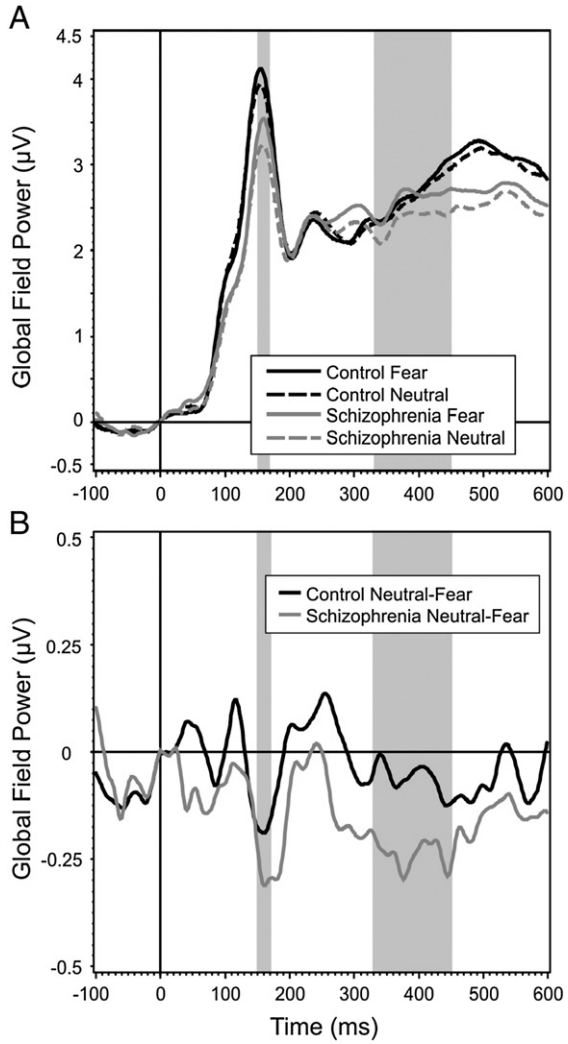

Fig. 2. A. Grand Average GFP (Global Field Power) of the control and schizophrenia groups in the two conditions, fear and neutral. **B.** GFP difference waves in the two groups, derived by subtracting the GFP to fearful stimuli from the GFP to neutral stimuli in each group. Gray-colored time intervals refer to the two intervals (150–170 ms and 330–450 ms) in which any of the two groups' GFP difference waves significantly differed from zero, showing an emotion effect, i.e. discrimination in the processing of fearful vs neutral faces. Only in the earlier time window (150–170 ms) did both groups' GFP difference waves show a significant difference from zero. In the later time window (330–450 ms) only the schizophrenia group's GFP difference wave significantly differed from zero.

3.3. Correlation between psychopathological, behavioral, and electrophysiological results in the schizophrenia group

Association between potentially important covariates, such as behavioral indices, clinical symptoms of schizophrenia, and medication as a confounder with the GFP difference values was investigated by HLM analyses. In these analyses the response variable was the GFP difference and the explanatory variables included the covariate of interest, time, and the interaction. A separate analysis was performed for each covariate. In the earlier, 150–170 ms time window, after Hochberg correction for multiple comparisons, there were no significant correlations between psychopathology, behavioral results, medication, and EEG data (for all values $p > 0.05$). For the later, 330–450 ms time window, however, with regard to ratings of psychopathology, the main effect of symptom severity was highly statistically significant for both positive and negative symptoms. The effect of time and the interaction did not reach significance in any of the analyses ($p > 0.1$). The results are summarized in Table 2, where the estimated changes are shown for one standard deviation (SD) unit increase in the independent variables (PANSS scores and the behavioral results including emotion recognition and reaction time, respectively, and CPZ-equivalent). As shown in the table, increase in the PANSS positive scale was associated with a significant increase in the GFP difference values (resulting in more negativity for the GFP difference, as shown by the negative sign of the regression estimate), while one SD unit increase in the PANSS negative scale was associated with a decrease in the GFP difference (yielding a more positive value for the GFP difference). Thus, more positive symptoms were associated with a larger difference between emotion-related GFP (with a greater emotional response to fearful faces, deviating from the response to neutral faces), while negative symptoms were associated with a smaller difference between emotion-related GFP (with a smaller emotional response to fearful faces, becoming more similar to the response to neutral faces).

The correlation of GFP difference values with hit rates or reaction times did not obtain significance.

With regard to medication as a potential confounder, the correlation of GFP difference values with the CPZ-equivalent showed significance, with a direction similar to that of the PANSS positive subscales: larger doses of antipsychotic medication were associated with a larger difference between emotion-related GFP (with a greater emotional response to fearful faces, deviating from the response to neutral faces).

4. Discussion

In our study we investigated the electrophysiological response to fearful faces in schizophrenia, as of all other basic emotions fear seems to have the most prominent role in attention allocation and emotional processing. To our knowledge, this is the first electrophysiological study with dense-array 128-channel electrode distribution to investigate the time course of fearful facial emotion processing in patients with schizophrenia as compared to individually matched healthy controls.

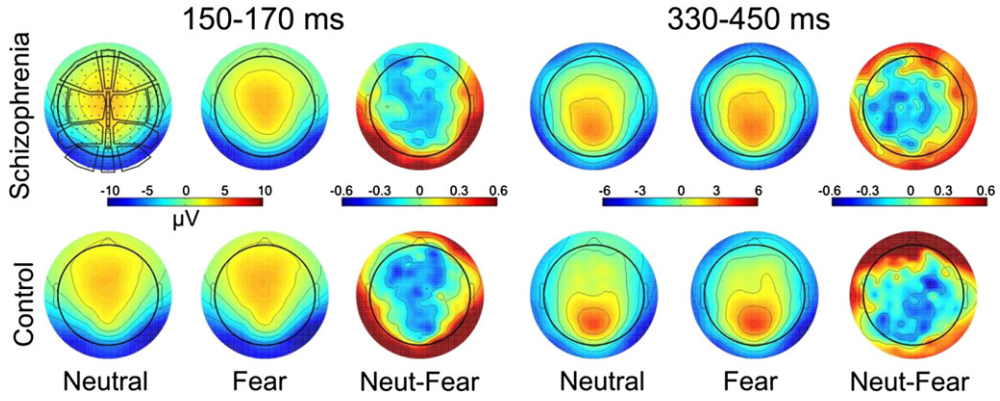

Fig. 3. Topographical maps of ERP amplitudes for Neutral and Fearful faces, and Neutral minus Fearful difference waves. The left panel shows data from the 150–170 ms, the right panel from the 330–450 ms interval. Upper row: schizophrenia group, lower row: control group. Plots show mean amplitude within the selected intervals. Top left map shows channel layout, and Regions of Interests used for statistical analysis.

Regarding behavioral data, although reaction times in schizophrenia patients were significantly longer, and emotion recognition performance was significantly worse than in healthy controls, both groups showed a relatively high hit rate (>90%) in correctly identifying fearful and neutral faces. Emotion showed no effect on hit rates or reaction times, suggesting there was no overt behavioral differentiation between fearful vs. neutral faces in either of the study groups.

Although fear-provoking faces seemed to elicit no differential response on a behavioral level in either study group, differentiation between fearful and neutral faces on an electrophysiological level was detectable in the time interval of 150–170 ms in both groups, confirming previous results (Pourtois et al., 2005; Blau et al., 2007) and suggesting an early, consistently reported electrocortical response to emotional faces. Patients also displayed an additional electrophysiological differentiation of fearful compared to neutral faces at a later, 330–450 ms time interval, showing a deviation from zero in their emotion-related GFP, indexing greater processing effort for fearful face stimuli. Consequently, our results call attention to a later stage of facial emotion processing, which proved to be distinguishing between the patient and control groups. The finding of additional activity in schizophrenia patients to fearful stimuli in the later processing stage might reflect a hyperresponsivity to fearful stimuli, i.e. an additional cognitive-contextual processing component that was absent in healthy controls. Furthermore, earlier evidence has shown that schizophrenia patients might be oversensitive to emotional facial expressions in general, as they might find the emotions evoked by faces anxiogenic and thus avoid making eye contact or paying attention to these stimuli (Mandal et al., 1998).

Table 2
Relationship between GFP difference (neutral minus fear) and psychopathological and behavioral indices and medication in the schizophrenia group[a] (N = 24).

Relationship of GFP difference with	Regression slope estimate[b]	StdErr	tValue	p[c]
PANSS total score	−0.021	0.012	−1.800	0.087
Positive symptoms subscale	−0.088	0.011	−7.660	**0.00001**
Negative symptoms subscale	0.044	0.012	3.744	**0.001**
General psychopathology subscale	−0.024	0.012	−2.007	0.058
CPZ-equivalent	−0.046	0.012	−3.93	**0.00009**
Hit rate	0.016	0.010	1.538	0.138
Reaction time	0.001	0.009	0.061	0.952

[a] Relationship was investigated by random regression hierarchical linear modeling (HLM) analysis of variance using GFP difference as dependent variable and psychopathological and behavioral indices and CPZ-equivalent as explanatory variables (in separate analyses).
[b] Regression slope estimates represent regression coefficients from the HLM analysis, and indicate GFP difference in microvolts between neutral and fear stimuli associated with a unit increase in the independent variable.
[c] $p < 0.05$.

Contextualizing our findings, recent research has corroborated that emotions have a primary effect on information processing, appearing within the first 100 ms of face processing within a distributed brain network (e.g. Liu and Ioannides, 2010). This brain network exhibits dysfunctions in many areas that play a role in facial affect recognition in schizophrenia, involving brain structures active in early and in later processing stages (Li et al., 2010). These findings suggest that the interpretation of reduced early or late ERP components such as the P100, N170, N250, P300, as manifestations of either pure structural or attentional encoding deficits in schizophrenia, represents an oversimplified view. Emotional and attentional processes that underlie facial emotion processing are not discrete or separable, and the available data indicate that the entire social brain network seems to be dysfunctional in schizophrenia.

The fact that more attention is allocated to the processing of fearful as compared to neutral faces at a later emotion processing stage might be further elucidated if we interpret the electrophysiological findings in the context of clinical symptomatology. Correlation analyses in this later time interval in the schizophrenia group revealed that more severe positive symptoms were associated with a greater difference in the GFP between the two conditions, suggesting a more accentuated processing difference of fearful vs. neutral faces in the schizophrenia group with more pronounced positive symptoms. By contrast, more severe negative symptoms correlated with a diminishing difference in the GFP, which suggests that schizophrenia patients with more negative symptoms show a smaller distinction at the electrophysiological level between fearful vs. neutral faces. This reciprocal relationship suggests that the above finding is modulated by an underlying clinical symptomatology of fear processing in schizophrenia. Positive symptoms, such as paranoid delusions, seem to enhance neural hyperresponsivity to fear, while negative symptoms, such as blunted affect, seem to attenuate the neural response to fear.

Interpreting our findings in the context of previous research, the association between P3 reduction and clinical symptomatology has been less intensely studied and the results have been variable, partly due to inconsistent methodologies among emotion recognition studies and to P3's sensitivity to task-specific factors. In particular, while a P3 reduction (in either visual or auditory modalities) has been found to be related to positive (Kutas et al., 1997) or negative symptoms (Strik et al, 1993; Mori et al., 2012), some of the recent studies exploring this relationship in emotion processing paradigms reported no or only weak correlations (Wolwer et al., 2011). Our results indicate that positive symptoms correlate with a prolonged, long-latency activation to fearful faces. Whereas alternative explanations are possible, this might be interpreted as a reflection of behavioral adjustment (e.g., a withdrawal to negative emotional stimuli with these symptoms) to an enhanced response detectable at the electrophysiological

level—perhaps through deficits in attention allocation, as suggested by previous studies (Nuechterlein and Dawson, 1984; Corrigan et al., 1990). However, due to the small number of studies and their methodological inconsistencies, more research is clearly needed for further insights into the nature of associations between ratings of clinical symptoms and electrophysiological measures of facial emotion processing.

Certain limitations regarding methodological issues and medication should be considered, as noted earlier. A limitation of our experimental design might be that in this study we only used fearful faces as emotional faces compared to neutral faces. Thus, we cannot draw general conclusions about emotion processing in schizophrenia, only about fearful facial processing. Future experiments are planned to include positive, happy facial stimuli in order to be able to draw broader conclusions on emotion processing patterns in schizophrenia. In our study stimuli were presented for 200 ms and intertrial interval randomly varied between 600 and 700 ms after button press. Thus, a carry-over effect, i.e. effects that might persist from one stimulus presentation to the next between individual trials, as in most ERP studies, is conceivable; however, due to the random sequences that we used these effects were likely to be canceled out and were therefore unlikely to confound the findings. Nonetheless, future research should consider to use longer intertrial intervals in order to further minimize the possibility of carry-over effects. In addition, focusing on longer time windows after 500 ms post-stimulus needs to be considered in order to investigate even later phases of emotion processing. With regard to medication, similar to other facial emotion recognition studies, the patients participating in our study were taking antipsychotic medication. As stated by Horan et al. (2010), our current knowledge about the effect of antipsychotic medication on emotional processing is by far not as comprehensive as to be able to determine its extent, but evidence suggests that such effects are minimal (Berenbaum and Oltmanns, 1992; Horan et al., 2010).

Taken together, our results indicate that while there is no overt behavioral differentiation between fearful vs. neutral faces in either of the study groups, there is evidence for differential processing of fearful vs. neutral faces between schizophrenia patients and matched healthy controls in terms of evoked brain responses which was manifested in the later stages of emotion processing. These results might reflect a compensatory strategy of the schizophrenia patients for achieving similarly good results on a behavioral level through a greater processing effort of fearful faces as indexed by a greater difference in the GFP difference wave in the later time range on an electrophysiological level.

Role of funding source

The study was supported by the National Research Fund of Hungary (OTKA, 71600).

Contributors

S.K., G.C., G.S., and I.C. designed research; S.K. and G.C. performed research; G.C., G.S., S.K., and P.C. analyzed data; S.K., G.C., G.S., P.C. and I.B. wrote the paper.

Conflict of interest

All authors report no biomedical financial interests or potential conflicts of interest.

Acknowledgments

We thank all participants for their willingness to participate in the study.

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