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Schizophrenia Research xxx (2013) xxx-xxx

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 xxxx

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 electro-physiological 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.

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#### 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

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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 facespecific 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.

Please cite this article as: Komlósi, S., et al., Fearful face recognition in schizophrenia: An electrophysiological study, Schizophr. Res. (2013), http:// dx.doi.org/10.1016/j.schres.2013.06.044

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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; Chlorpromazineequivalent 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.<sup>a</sup>

	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

<sup>a</sup> 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 electrooculogram (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

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