



## Processing of visual stimuli in borderline personality disorder: A combined behavioural and magnetoencephalographic study

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### ABSTRACT

**Background:** Behavioral studies on facial emotion recognition yielded heterogeneous results in patients with Borderline Personality Disorder (BPD). Extrastriate cortex hyperactivation has been demonstrated in imaging studies in patients with BPD during face recognition, but electrophysiological studies are lacking. The aim was to investigate temporal processes following face perception in patients with BPD.

**Methods:** Magnetoencephalography (MEG) was used in eleven non-medicated patients with BPD and nine age-matched healthy subjects. Behavioral responses to visual stimuli and an emotion discrimination task were evaluated. First, participants had to silently watch faces, houses and animals. Emotional expressive faces then had to be judged from two basic emotions in a two-alternative forced choice task. Regional field power (RFP) of MEG signals was obtained from two regions of interest: Temporal and occipital areas. Psychometric assessment was performed.

**Results:** Patients with BPD had significantly reduced RFP amplitudes in the right posterior occipital region of interest, for the time window between 150 and 160 ms, irrespective of the type of visual stimulus or the emotional face category. Patients with BPD had significantly higher error rates for recognition of emotional expressive faces compared to healthy controls though they showed a higher accuracy in detecting fearful faces. Controls improved during face recognition, whereas patients showed no learning effect.

**Conclusion:** This MEG study provides evidence for disturbances in cortical visual perception in BPD patients regardless of emotional salience of the stimulus. In line with previous studies subtle deficits in visual perception might be related to impairment in interpersonal communication in BPD.

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### 1. Introduction

Borderline Personality disorder (BPD) is a serious psychiatric disorder and the most prominent features are emotional instability, interpersonal disturbances, chronic emptiness and chronic suicidal tendencies (Linehan et al., 1993). BPD patients have a pattern of high psychiatric service use. The debate regarding the neurobiological mechanisms underlying BPD is still ongoing, and therefore identification of biomarkers would be a major step toward improving diagnostic accuracy and identifying therapeutic targets (Stanley and Siever, 2010). A common way to study the emotional instability of BPD is the measurement of responses after presentation of emotional stimuli. Faces convey information that is essential for interpersonal interactions and emotional expressions play a central role, since they

are crucial for inferring the observed person's feelings and intentions. A substantial number of behavioral studies have investigated emotional face recognition in patients with BPD, but they demonstrated heterogeneous results. So far, researchers used static images, i.e. Ekman faces and in these studies, BPD patients were able to correctly identify emotional expressions at times more accurately than healthy controls (Domes et al., 2008; Lynch et al., 2006; Wagner and Linehan, 1999). However, when facial emotion recognition tasks present more complex situations, by setting time limits for recognizing emotions in faces (Dyck et al., 2009), or with additional prosodic information (Minzenberg et al., 2006), patients with BPD showed increased error rates. The study by Lynch et al. (2006) used a morphing affect recognition paradigm with several emotion intensities and showed a "hyper-responsiveness" for patients with BPD especially towards fearful faces (Lynch et al., 2006). Imaging studies in BPD have shown fusiform gyrus, as well as amygdala, inferior and middle temporal cortical areas hyperactivity during emotional face expression tasks (Guitart-Masip et al., 2009; Herpertz et al., 2001).

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To date, the temporal dynamics of brain responses to emotional faces in BPD still remain unclear (Vuilleumier and Pourtois, 2007). Electrophysiological investigations in the primary visual or extrastriate cortex concerning the fundamental, visual-perceptive process of patients with BPD are sparse. An opportunity to measure the distinctive temporal electrophysiological responses towards face processing in vivo and non-invasively exists in the form of magnetoencephalography (MEG), a technique known for its excellent temporal resolution. A face-specific, event-related magnetic field (ERF) peaking at 170 ms (M170) post stimulus and recorded at posterior sensors corresponds to the right inferior occipito-temporal cortex (Deffke et al., 2007; Halgren et al., 2000). An even faster cortical response to the coarse recognition of faces in healthy subjects has been found as early as 100 ms (M100) (Liu et al., 2002). The “fusiform face area” (FFA) has been defined as an extrastriate module for face perception (Kanwisher et al., 1997). Posterior to the FFA, the “occipital face area” (OFA) (Gauthier et al., 2000), has been observed to respond preferably to faces than objects. The rOFA has been shown to be mandatory for recognition of face parts and emotional expressions after temporary lesions were produced in this area by applying repetitive transcranial magnetic stimulation (rTMS) (Pitcher et al., 2008).

Thus, the purpose of our study was to investigate if BPD patients, compared with healthy controls, show electrophysiological differences in the early visual processing pathways, represented as M170 in the occipito-temporal visual cortices areas while processing faces and other stimuli. The study is focused on the early visually evoked fields as they are known to yield stable MEG responses. The perception of facial expression implicates a large neural network (Adolphs et al., 2003) and the investigation of the ventral visual pathway in patients with BPD contributes to the understanding of an affect-sensitive network, which has not been assessed so far by MEG.

The current study implemented two visual processing tasks using different kinds of response formats. In the first task, subjects had to silently watch three stimulus categories: faces, houses and animals. With this simple task, we investigated electrophysiological responses to basic visual stimuli. The second task was an emotion-specific task in which subjects had to judge emotions within a distinct time limit. On the electrophysiological level, we expected differences between the two groups but had a non-directional differential hypothesis due to lacking prior MEG data with BPD patients. As BPD patients seem to have problems predominantly with the perception of the emotions fear and anger (Koenigsberg et al., 2002; Levine et al., 1997), we hypothesized differences in the perception of those negative emotions in patients with BPD compared to healthy controls in the behavioral task. Further, to address the issue of patients with BPD being a heterogeneous diagnostic group, we controlled for comorbid diagnoses, especially for comorbid post-traumatic stress disorder (PTSD) and major depression. Finally, we controlled for dissociation by implementing a dissociation rating during the MEG measures.

## 2. Materials and methods

### 2.1. Participants

Thirteen right-handed, female patients with BPD (range of age: 20 to 38 years) were recruited for the study from consecutively admitted inpatients to the Charité, Department of Psychiatry, Berlin University Medicine. Eleven right-handed, female healthy controls (range of age: 25 to 41 years) without any history of neurological or psychiatric disorders were carefully selected and age-matched (Oldfield, 1971). Healthy controls were interviewed by a brief, semi-structured psychiatric questionnaire to ensure that the subject had no former or current psychiatric history and were free of psychotropic medication. The healthy controls were recruited by newspaper advertisement and received compensation.

Patients fulfilled DSM-IV-TR criteria for BPD, assessed by the appropriate segment and German translation of the Structured Clinical Interview for DSM-IV-TR for Personality Disorders (SCID-II; Fydrich et al., 1997; Spitzer et al., 1992). At the department, the diagnosis of BPD was established by two independent clinicians using SCID-II (Spitzer et al., 1992), as well as a two week observation phase in the ward and an interview with a family member of the patient was completed. At the time of inclusion in the study, the patients were in the first week of a 12-week scheduled dialectic behavioural therapy (DBT) program (Bohus et al., 2004; Linehan et al., 1999). Axis I comorbidity was assessed by the Structured Clinical Interview for DSM-IV Axis I Disorders (MINI-SCID; (Ackenheil et al., 1999; Sheehan et al., 1998)). Exclusion criteria were schizophrenia, major depression (current not lifetime), substance abuse and neurological disorders in the previous 6 months and psychopharmacologic medication during the past two weeks. Patients had been free of psychotropic medication for a minimum of 2 weeks prior to MEG examination to ensure that medication was not a confounding effect on the electrophysiological and behavioral measures. Medication prior to study inclusion had been selective serotonin reuptake inhibitors (SSRIs) (30.8%, escitalopram), tricyclic antidepressants (15.4%, imipramine, 7.6%, doxepine) and atypical neuroleptics (15.4%, quetiapine). Four patients (30.8%) were drug naive. Five patients out of the 13 took a combination of SSRIs and atypical neuroleptics.

Patients and controls were thoroughly informed before the study and gave written consent assent before screening. The investigation was carried out in accordance with the latest version of the Declaration of Helsinki. The Local Ethics Committee of the Charité approved the study. MEG results of two patients and two controls were discarded due to head movements and artifacts in the MEG scanner leading to 11 patients and 9 controls included for further analysis.

### 2.2. Behavioral tasks

The study consisted of two experiments. In the first experiment, subjects had to silently watch a randomly presented sequence of single “pictures of facial affect”, selected from Ekman and Friesen’s standardized sets (Ekman, 1993). The faces presented were of basic emotions (happiness, anger, fear, disgust, surprise, and sadness) and of neutral faces. Emotional expressive faces were presented in equal numbers. The face pictures were randomly intermixed with single pictures of two control conditions (houses and animals), houses previously described in a study (Lueschow et al., 2004). All pictures were presented for 300 ms each with an inter-stimulus-interval (ISI) of 800 ms and a 800 ms cross-hair pattern at the beginning of each trial. For each of the three stimulus categories 65 images were presented leading to a total of 195 images. Task instruction was given prior to the experiment outside the MEG room and consisted of silently watching the pictures in the first experiment.

In the second experiment, a set of 112 faces comprising pictures of 16 male faces and 16 female faces with neutral or emotional expressions were presented. Each trial started with a cross-hair pattern, presented for 800 ms, followed by the face stimulus appearing for 300 ms, which was followed by an interval of 800 ms duration blank screen. Subjects were asked either to fixate the cross-hair or to watch the face. On the subsequent screen, two words were presented for 2000 ms and subjects were asked to decide between two words (one correct word and one distracter word, i.e. anger, fear, happiness, surprise, disgust, sadness, and neutral) which described best the emotional expression and press a button. In order to record the response and control for task compliance, we asked subjects to use a mouse button which was placed at each side next to the hips. Subjects were asked to indicate the valence of the facial expression within these two seconds by pressing one of two buttons with the index finger of the right or left hand. The side for the button press for a

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