Oscillatory responses to reward processing in borderline personality disorder

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Abstract
Objectives. Previous electrophysiological studies have confirmed impaired reward processing in patients with BPD. However, it is not clear which aspects of reward processing are affected and which brain regions are involved. The present study investigated both evoked and induced event-related oscillations (EROs) to feedback events (thought to represent different aspects of feedback processing), and used source localization (sLORETA) to assess activity in two areas known to contribute to reward processing, the dorsomedial prefrontal/anterior cingulate cortex (dmPFC/ACC) and the orbitofrontal cortex (OFC).

Methods. Eighteen patients with BPD and 22 healthy controls performed a gambling task, while 64-channel electroencephalographic activity was recorded. Evoked and induced theta and high-beta band EROs as well as activity in the two regions of interest were investigated depending on the valence and magnitude of feedback events.

Results. Theta-band responses to negative feedback were reduced in BPD, an effect that involved only evoked responses and the dmPFC/ACC region, and was associated with trait impulsivity in patients. sLORETA analyses revealed disturbed evoked responses depending on feedback magnitude in the theta (OFC) and high-beta (dmPFC/ACC and OFC) frequency range.

Conclusions. The results indicate multiple dysfunctions of feedback processing in patients with BPD, implicating several distinct subsets of reward-processing mechanisms.

Key words: feedback-related negativity, event related potentials, impulsivity, anterior cingulate cortex, orbitofrontal cortex

Introduction
Borderline personality disorder (BPD) is a chronic disorder characterized by three major symptom clusters: impulsivity, affective dysregulation and disturbed interpersonal relatedness (Sanislow et al. 2002; Skodol et al. 2005). The former of these three dimensions has been suggested to represent a very early trait of predisposed individuals (Crowell et al. 2009) and constitutes a critical factor for the prognosis of BPD, through a higher risk of suicide attempts (Zouk et al. 2006; McGirr et al. 2007; Yen et al. 2009) and through its associations with impairment across multiple areas of functioning (Bagge et al. 2004; Sio et al. 2011; Samuel et al. 2012). Understanding the factors that underlie impulsivity is therefore important for improving treatment in this disorder characterized by severe and sustained functional impairment (Gunderson et al. 2011).

Early neuropsychological studies postulated a frontal (especially orbitofrontal) lobe dysfunction at the origin of impulsivity and other problem behaviours in BPD (Bazanis et al. 2002). Indeed, patients with BPD demonstrate impaired performance on tests of frontal lobe functions such as decision-making and planning (Bazanis et al. 2002; Ruocco 2005; LeGris and van Reekum 2006). In this context, impulsivity in BPD was viewed as an expression of behavioural disinhibition (Hochhausen et al. 2002; Rentrop et al. 2008). However, more recent conceptualizations place greater emphasis on learning mechanisms, in particular on the influence of reward processing on decision-making. For example, patients with BPD tend to devalue delayed rewards (Lawrence et al. 2010), and display a typical “high-gain, high-risk” performance profile in gambling tasks (Haaland and Landro 2007; Kirkpatrick et al. 2011).
2007) that correlates with trait impulsivity scores (Schuermann et al. 2011). Based on these observations, it has been suggested that patients with BPD display a specific deficit in using feedback information to inform future behaviour (Kirkpatrick et al. 2007; Schuermann et al. 2011).

Several electrophysiological responses have been identified as markers of feedback information processing. In the event-related potential (ERP) domain, one such established marker is the feedback-related negativity (FRN). This negative ERP belongs to the N200 family (Hajihosseini and Holroyd 2013) and appears in response to stimuli that indicate loss in gambling tasks with a peak around 250–300 ms post-stimulus. In the time-frequency domain, negative feedback is associated with a frontally distributed increase in theta-band oscillatory power (Cohen et al. 2007; Marco-Pallares et al. 2008; Leicht et al. 2013). In contrast, positive events are accompanied by an increase of power in the high-beta (Cohen et al. 2007; Marco-Pallares et al. 2008; Leicht et al. 2013) and/or low-gamma frequency band (Hajihosseini et al. 2012). Importantly, trait impulsivity has been associated with reduced amplitude of the FRN and theta event-related oscillatory responses (EROs; Kamarajan et al. 2009; Kamarajan et al. 2010; De Pascalis et al. 2012; Leicht et al. 2013).

In patients with borderline personality disorder, two previous studies have shown reduced FRN (Schuermann et al. 2011) and theta EROs (Vega et al. 2013) in response to loss feedback during gambling tasks compared to healthy controls; in one of these studies (Schuermann et al. 2011), this reduction correlated with trait impulsivity scores. However, it is not clear what these results imply in terms of reward processing. Given that the FRN and theta EROs have been suggested to code unpredicted outcomes (Hajihosseini and Holroyd 2013), it has been suggested that reduction of these responses in patients with BPD might reflect a greater expectancy of receiving punishment (Vega et al. 2013). However, a study (Schuermann et al. 2011) that additionally assessed the P300 potential as a marker of feedback salience drew exactly the opposite conclusion, i.e., that negative feedback was unexpected for patients with BPD. Another unclear point is whether observed deficits in patients with BPD apply to the processing of loss events only (Vega et al. 2013), or also to positive (i.e., gain) feedback (Vollm et al. 2007) – a relevant question, in light of the fact that these two functions might represent distinct sub-processes subserved by different regions of the reward network (Yacubian et al. 2006; Haber and Knutson 2010).

The present study aimed to provide a more detailed account of feedback processing and its associations with impulsivity in BPD. We used a gambling paradigm that has been shown to reliably produce robust electrophysiological responses to the valence (i.e., positive vs. negative) and magnitude of outcome feedback in previous studies of our own and other groups (Gehring and Willoughby 2002; Marco-Pallares et al. 2008; Leicht et al. 2013; Vega et al. 2013). Theta and high-beta EROs were assessed as indices of negative (loss) and positive (gain) feedback, respectively. A critical consideration for analyses was that oscillatory responses to an event can be divided into two types of activity: oscillations that are stimulus-locked, i.e., consistent in phase across trials (“evoked”), and oscillations that are inconsistent in phase across trials (“induced”). The present study investigated these two types of activity separately, in light of the assumption that evoked and induced theta EROs represent different aspects of feedback processing – with evoked EROs marking reinforcement signals, whereas induced EROs reflect cognitive responses to unexpected events (Hajihosseini and Holroyd 2013).

In order to provide further insights into the affected processes, EEG source localization was applied to assess frequency-specific activity in response to feedback. The focus was on two regions of interest: The dorsomedial prefrontal/anterior cingulate cortex (dmPFC/ACC), presumed to constitute the origin of the FRN and theta EROs (Cohen et al. 2011; Hajihosseini and Holroyd 2013), and the orbitofrontal cortex (OFC), which is consistently implicated in the processing of rewarding stimuli (Haber and Knutson 2010), and has been suggested to contribute both to high-beta oscillations associated with positive feedback (Marco-Pallares et al. 2008; Cohen et al. 2011) and impulsivity (Wolf et al. 2012) in patients with BPD.

**Material and methods**

**Participants**

For the present study, 20 patients with BPD and 23 healthy controls were recruited; for reasons explained below, the final sample included in analyses consisted of 18 patients and 22 control subjects, which were matched regarding age, gender, education and parental education (see Table I). Patients were recruited from the in- and outpatient clinics of the Department for Psychiatry and Psychotherapy, University Hospital Hamburg-Eppendorf; healthy controls were recruited through advertisements and word-of-mouth. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committee; all participants provided their written informed consent prior to inclusion in the study.
Patients were required to fulfill criteria of BPD according to DSM-IV. The Mini International Neuropsychiatric Interview (Sheehan et al. 1998) and the Structured Clinical Interview for DSM-IV Axis II (Wittchen et al. 1997) were used to establish the diagnosis of BPD and assess Axis I comorbidities in patients. In order to minimize the effects of comorbid disorders associated with reward system dysfunction, patients were excluded from the study if they presented a current depressive episode or a score higher than 12 on the Montgomery–Asberg Depression Rating Scale (MADRS; Montgomery and Asberg 1979); alcohol or drug dependence, or alcohol or drug abuse, in the past year; or a lifetime diagnosis of psychotic or bipolar disorder. Further exclusion criteria for all subjects were neurological and developmental disorders, and the presence of uncorrected visual problems or hearing loss. In healthy controls, additional exclusion criteria were a family history of psychotic disorders or a personal history of any psychiatric disorder or treatment.

Symptom severity in patients was assessed with the Borderline Symptom List – Short Form (BSL-23; Bohus et al. 2009). The Barratt Impulsiveness Scale (BIS-11; Patton et al. 1995) was used as a measure of trait impulsivity. The scale consists of a 30-item Likert-type self-report questionnaire with good reliability and validity, yielding scores for attentional, motor and non-planning impulsivity.

**Gambling task**

Participants performed a computerized two-choice gambling task (adapted from Gehring and Willoughby 2002) used in previous studies by our group and others (Marco-Pallares et al. 2008; Leicht et al. 2013; Vega et al. 2013). Each trial began with the presentation of two numbers (5 and 25) on a computer screen (randomized left-right order) for 1 s. Within this time, participants were required to select one of the two numbers per mouse-click. After a delay of 700 ms, one of the two numbers randomly turned green and the other red (feedback stimulus). If the selected number turned green, the participant gained the corresponding amount of points; a color change to red indicated a respective loss of points. Thus, the feedback stimulus varied along two dimensions, valence (positive vs. negative feedback) and magnitude (5 vs. 25 points). The feedback stimulus was displayed on the screen for 700 ms followed by a display of the current account status for 2000 ms. A 3-s fixation square preceded the next trial.

The Presentation software v14.4 was used for stimulus presentation. Participants were instructed in a standardized way to freely choose one of the two presented numbers (5 or 25) in every trial and to gain as many points as possible during each block. Thus, participants were not required to choose 5 and 25 in an equal ratio (relevant for statistical analyses, see below). The instruction stated that participants would receive €10 for study participation, plus an additional amount of money depending on the total points won. The paradigm comprised a short practice block and four experimental blocks of 108 trials each. Participants started each block with 1000 points on their account. The occurrence of loss and gain events was maintained at equal probability (50% each).

### Table I. Sociodemographic characteristics and impulsivity scores of the two participant groups, and clinical characteristics of patients with borderline personality disorder (BPD).

|                         | Healthy controls (N = 22) | BPD (N = 18) | \( \chi^2/t \) | P       |
|-------------------------|---------------------------|--------------|---------------|---------|
| Gender (m/f)            | 4/18                      | 1/17         | 1.44          | 0.35    |
| Age                     | Mean 26.27, SD 4.9         | Mean 28.28, SD 5.8 | 1.18          | 0.25    |
| Education (years)       | Mean 12.18, SD 1.4         | Mean 11.44, SD 1.6 | 1.56          | 0.13    |
| Parental education (years) |                         |              |               |         |
| Father                  | Mean 11.67, SD 1.7         | Mean 11.00, SD 1.9 | 0.88          | 0.38    |
| Mother                  | Mean 10.82, SD 1.7         | Mean 10.53, SD 1.8 | 0.46          | 0.65    |
| BIS-11 total score      | Mean 61.45, SD 6.6         | Mean 71.72, SD 8.6 | 4.27          | <0.001  |
| MADRS score             | Mean 8.56, SD 4.0          | Mean 27.61, SD 15.7 |             |         |
| BSL-23 total score      | Mean 15/3                 |              |               |         |
| Medication (y/n)        |                           |              |               |         |
| Antidepressants         | 13                        |              |               |         |
| Atypical antipsychotics | 8                         |              |               |         |
| Antiepileptics          | 4                         |              |               |         |

BIS-11, Barratt Impulsiveness Scale; MADRS, Montgomery–Asberg Depression Rating Scale; BSL-23, Borderline Symptom List, short form.
EEG recording and pre-processing

Recordings took place in a sound-attenuated and electrically shielded room. Participants were seated in a slightly reclined chair with a head rest, at a distance of 1 m from a 19 computer screen. Electroencephalographic activity was recorded at a sampling rate of 1000 Hz with 64 Ag/AgCl electrodes mounted on an elastic cap (ActiCaps, Brain Products, Munich, Germany), using the Brain Vision Recorder software version 1.10 (Brain Products, Munich, Germany). Electrodes were arranged according to a modified 10/10 system without electrodes at positions FPz, F9, F10, T9, T10, CP3, CP4, P9, P10, PO7, PO8, and with two additional electrodes at positions PO9 and PO10. Eye movements were recorded with four EOG channels (positioned at the outer canthi bilaterally and infra- and supraorbitally on the right). An electrode at the FCz position was used as the reference, while the electrode at position AFz served as ground.

Offline preprocessing was performed with Analyzer 2.0 (Brain Products GmbH). After band-pass filtering (0.1–100 Hz, Butterworth zero-phase filter 24 dB/octave), prominent non-stereotyped artefacts such as movement artefacts and channel drifts were removed by visual inspection. Independent component analysis (ICA) was applied to remove blink and eye movement artefacts. A restricted Infomax algorithm was used for ICA; components representing ocular artefacts were identified and removed based on their topography, power spectrum and time course. Subsequently, the continuous EEG was segmented into 3-s epochs starting 1800 ms prior to the feedback stimulus. Segments including amplitudes exceeding ±95 μV, voltage steps higher than 50 μV between sampling points, a difference higher than 200 μV between the highest and lowest value within a segment or activity below 0.5 μV were automatically rejected. After re-referencing to the common average reference, baseline correction (using the 200 ms pre-stimulus interval) was applied. Only subjects with a minimum number of 20 artefact-free trials per condition were considered in further analyses; one female patient had to be excluded based on this criterion. Two further subjects (one female patient and one male control subject) did not complete all blocks of the paradigm. Thus, the final sample consisted of 18 patients and 22 healthy controls.

FRN

FRN amplitude was measured at electrode Fz. “Base-to-peak” amplitude was measured, i.e., the distance between the negative local maximum value within the timeframe 220–330 ms following the feedback stimulus (±40 ms from the observed peak in the grand average, 260 ms post-stimulus, see Figure 2) and the preceding positivity defined as the most positive value within the timeframe 140–220 ms post-stimulus (±40 ms from the observed latency of this peak around 180 ms post-stimulus, see Figure 2).

Time-frequency analysis

Time-frequency information was extracted for EEG activity at electrode Fz using complex Morlet wavelet convolution for the frequencies from 2 to 50 Hz (formula: \( w(t) = A \exp(-t^2/2) \exp(i2\pi\nu t) \), 15 frequency steps distributed on a logarithmic scale, Morlet parameter \( \nu = 5 \), Gabor Normalization). Evoked (i.e., stimulus-locked) power was determined by applying wavelet transformation directly to the averaged ERPs. For induced power, the ERP was subtracted from the single-trial series and wavelet transformation was applied at the single-trial level prior to averaging (cf. Witzel et al. 2011). In order to assess theta and high-beta activity across conditions, we extracted wavelet layers with central frequencies of 5 Hz (theta) and 25 Hz (high-beta), similar to a previous study by our group (Leicht et al. 2013). Based on visual inspection of maximal differences between gain and loss conditions, peak amplitudes of activity in these frequencies of interest were defined as the highest values within the timeframes 100–700 and 200–600 ms post-stimulus for theta and high-beta, respectively.

sLORETA analysis

Intracortical sources of brain electrical activity were localized using standardized low-resolution electromagnetic tomography (sLORETA; Pascual-Marqui 2002). sLORETA belongs to a group of three-dimensional, distributed, linear minimum-norm inverse solutions that have been extensively used and cross-validated (Mulert et al. 2004; Mobascher et al. 2009; Olbrich et al. 2009). The sLORETA software (http://www.uzh.ch/keyinst/sloreta.htm) was used to calculate time-varying cross-spectra from the average ERPs (evoked activity) and from single trials after subtracting the average ERP (induced activity). This transformation applied a sliding Gaussian Window function with a centre frequency of 5 Hz (window length 1 s) and 25 Hz (window length 0.25 s) for the theta and high-beta frequency range, respectively. sLORETA computations were made in a realistic head model (Fuchs et al. 2002), using the MNI152 template (Mazziotta et al. 2001). The source space (6239 voxels at a spatial resolution of
5 mm) was restricted to cortical gray matter and hippocampi, as determined by the probabilistic Talairach atlas (Lancaster et al. 2000).

The time frame for current source density computations was defined at 300–500 ms following the feedback stimulus, based on the grand average of oscillatory power at electrode Fz in patients and controls. Whole-brain (voxel-wise) comparisons of the two extreme conditions (gain 25 points, loss 25 points), conducted separately for each group, are reported in the Supplemental material (available online at http://informahealthcare.com/doi/abs/10.3109/15622975.2015.1054880) in order to provide a general overview of activity patterns depending on valence. However, because the experimental design included two factors (valence and magnitude) resulting in four conditions, non-parametric voxel-wise comparisons across groups and conditions (as implemented in the sLORETA software) were not applicable. Therefore, we adopted a region-of-interest (ROI) approach. ROIs were constructed for the dorsomedial prefrontal/anterior cingulate cortex (Brodmann areas 32, 24, 25 and medial part of 8) and the orbitofrontal cortex (medial part of Brodmann area 10, as well as Brodmann areas 11 and 47) by including all voxels with coordinates corresponding to the respective Brodmann areas (see Figure 1 for a visualization of ROIs). Subsequently, mean source density power values at each ROI for each participant and condition were computed and used in statistical analyses.

**Statistical analyses**

Statistical analyses were performed using SPSS 21.0. The pattern of “high-gain, high-risk” behaviour during the gambling task, i.e., the percentage of trials, in which participants selected the higher number, was contrasted between groups with an independent t-test. Differences between groups in the number of artefact-free trials were assessed with a 2 (magnitdue) × 2 (valence) × 2 (group) repeated-measures ANOVA.

The above analyses revealed significant differences between groups regarding the mean number of trials included in the averages for each condition, due to the fact that patients with BPD chose the higher number (25) much more often than healthy controls (see below). It was calculated that an attempt to match the number of trials between the two groups by randomly selecting only a subset of trials (equal across conditions and comparable between groups) would result in removal of 41% of trials in patients with BPD and 55% in healthy controls, leading to an unacceptable increase of noise in the data. Therefore, we followed an alternative

![Figure 1. Graphic depiction of ROIs used in analyses. (A) Dorsal medial prefrontal cortex/ACC; (B) orbitofrontal cortex.](image-url)
approach that allowed us to use all available data while adjusting for any confounding effects of this variable: All further analyses were conducted with linear mixed models, including the number of valid trials in each condition as a covariate. Linear mixed models have been successfully implemented in the past for analysis of EEG data (Bachman et al. 2008; Kamarajan et al. 2010). Apart from the possibility to include condition-specific covariates, linear mixed models carry additional advantages compared to traditional repeated-measures designs, as they can accommodate departures from the assumptions of homogeneity of regression slopes and independence, and thus are better suited to model interindividual variability (Gueorguieva and Krystal 2004; Field 2013). For ERP and ERO analyses, dependent variables were peak amplitude and power (respectively) within the predetermined time windows; group variables were peak amplitude and power (respectively) in all minimal magnitude conditions. All further analyses were conducted with artefact-free trials, the main effect of group was not significant \( F(1,39) = 0.961, P = 0.33 \). However, there was a significant group \( \times \) magnitude interaction \( F(1,39) = 10.423, P = 0.003 \); there were significantly more trials in the high-stake than in the low-stake condition in patients \( F(1,18) = 22.995, P < 0.001 \), whereas controls had an equal number of trials in the two conditions \( F(1,21) = 0.488, P = 0.49 \).

**Results**

Patients with BPD placed significantly more often a “higher bet”, i.e., selected significantly more often 25 compared to healthy controls [55.2 vs. 45.9%, \( r(38) = 2.220, P = 0.03 \)]. Regarding the number of artefact-free trials, the main effect of group was not significant \( F(1,39) = 0.961, P = 0.33 \). However, there was a significant group \( \times \) magnitude interaction \( F(1,39) = 10.423, P = 0.003 \); there were significantly more trials in the high-stake than in the low-stake condition in patients \( F(1,18) = 22.995, P < 0.001 \), whereas controls had an equal number of trials in the two conditions \( F(1,21) = 0.488, P = 0.49 \).

**Evoked event-related responses**

Significant group \( \times \) valence interactions were noted at electrode Oz for both the FRN \( F(1,112.09) = 8.708, P = 0.004 \) and theta-band evoked power \( F(1,68.67) = 4.878, P = 0.03 \), which increased more in controls than in patients following loss compared to gain trials (Figures 2 and 3). There were no significant main effects or interactions involving group regarding high-beta evoked power (all \( P > 0.2 \)).

In the ACC/mPFC ROI, there was a significant group \( \times \) magnitude interaction \( F(1,62.47) = 4.122, P < 0.05 \) with respect to evoked theta power; as can be seen on Figure 3, the increase of activity in this ROI following negative compared to positive feedback was significantly greater in controls than in patients with BPD. In contrast, in the OFC we observed a significant group \( \times \) magnitude interaction \( F(1,73.729) = 5.848, P = 0.02 \). Evoked theta activity was higher in controls following feedback with regard to high stakes, whereas in patients it was higher for low stakes (Figure 4).

In the high-beta frequency range, significant group \( \times \) magnitude interactions emerged both in the ACC/mPFC \( F(1,65.72) = 4.752, P = 0.03 \) and in the OFC ROI \( F(1,60.576) = 4.511, P = 0.04 \). In both ROIs, high-beta evoked activity was higher following feedback concerning low bets in patients, but not in controls (Figure 4). However, inspection of the data indicated one patient with extreme outlier values (i.e., exceeding 3 standard deviations from the group mean) in all minimal magnitude conditions. After removal of this patient from analyses, the group \( \times \) magnitude interaction only achieved a trend level
for the evoked theta ERO and BIS total score (rho = 0.611, P = 0.01), i.e., the smaller the evoked theta response to loss compared to gain feedback, the greater the BIS total score. Exploratory analyses using the three subscores of the BIS in place of the total score showed that all correlations of the evoked theta valence difference score with BIS subscores were negative (rho = 0.154, 0.418 and 0.581 for attentional, motor and non-planning impulsivity, respectively), but achieved significance only in the case of non-planning impulsivity (P = 0.01) – although a trend could be also observed in the case of motor impulsivity (P = 0.10).

No associations of electrophysiological responses with trait impulsivity were noted in healthy controls. However, in this group, the percentage of “high bets” negatively correlated with the magnitude difference scores for both evoked theta (rho = 0.671, P = 0.001) and high-beta responses (rho = 0.449, P = 0.01) in the OFC, and for evoked high-beta activity in the ACC/mPFC (rho = 0.508, P = 0.02). Trait impulsivity did not correlate with “high-risk, high-gain” behavior in neither group (both P > 0.65).

**Discussion**

In the present study, patients with borderline personality disorder exhibited impaired feedback processing compared to healthy controls in the context
of a gambling task. This impairment concerned multiple aspects of feedback processing, only some of which were associated with trait impulsivity in patients. Both dorsal mediofrontal and orbitofrontal areas were involved in impaired feedback processing in patients.

As expected based on previous studies (Haaland and Landro 2007; Kirkpatrick et al. 2007), patients with BPD displayed abnormal performance profiles, with a bias towards “high-gain, high-risk” options. The observed electrophysiological responses in patients are also consistent with previous findings of reduced FRN (Schurmann et al. 2001; Vega et al. 2013) and theta EROs (Vega et al. 2013) in response to negative feedback in BPD. On the other hand, evoked high-beta activity in response to positive feedback was not altered in patients. This finding is in accordance with evidence supporting the existence of two distinct systems for the processing of positive and negative feedback, which might be differentially affected in BPD (see the Introduction). Reduced evoked theta oscillatory responses to loss were associated with higher trait impulsivity in patients with BPD, in line with previous findings in healthy individuals and patients with alcohol dependence (Kamarajan et al. 2009; Kamarajan et al. 2010; Leicht et al. 2013). These findings are in accordance with the hypothesis of a “reward deficiency syndrome” (Comings and Blum 2000) in impulsive individuals – at least in what regards low-frequency EROs to loss, as such an association could not be confirmed for high-beta responses to gain (Leicht et al. 2013).
Impaired processing of negative feedback in patients was associated with reduced activity in the dorsomedial prefrontal cortex and ACC compared to healthy controls, consistent with the assumption that the FRN and theta-band responses to feedback originate within this region (Cohen et al. 2011; Hajihosseini and Holroyd 2013), as well as with studies reporting structural and functional ACC abnormalities in patients with BPD (Mak and Lam 2013; Krause-Utz et al. 2014). Reductions of oscillatory activity and sLORETA current source density in the dmPFC/ACC applied only to evoked theta-band responses, while induced responses were not affected in patients. This finding is interesting in view of the different roles suggested for these two types of theta-band response in the context of feedback processing. More specifically, it has been proposed that the FRN and evoked theta-band responses to feedback represent the relaying of dopamine-mediated reinforcement signals from the midbrain to the ACC (Holroyd and Coles 2002), whereas induced theta EROs correspond to cognitive processing of unexpected events in general (Hajihosseini and Holroyd 2013). If this assumption holds, our finding of impaired evoked theta-band response is consistent with a genuine deficit in the processing of feedback valence (cf. Schurmann et al. 2001), rather than with increased expectations of punishment (Vega et al. 2013) in patients with BPD. Moreover if, as suggested (Holroyd and Coles 2002; Holroyd et al. 2008), gain and loss events reduce and increase FRN amplitude through respective increases and decreases in phasic dopamine activity, then the pattern of electrophysiological responses in patients suggests a dopaminergic dysregulation that results in increased dopamine activity irrespective of feedback valence. This suggestion is in line with some accounts postulating aberrant dopaminergic functioning in patients with BPD (Friedel 2004; Joyce et al. 2014) and in disorders of impulse control (Dalley and Roiser 2012) – although the relation between dopamine and impulsive behaviour is complex (Dalley and Roiser 2012). It is also in accordance with studies reporting a beneficial effect of dopamine antagonists in treat-
ing impulsivity symptoms in BPD (Rosenbluth and Sinyor 2012). However, it should be noted that empirical support for the proposed dopaminergic model of the FRN is still lacking (Cohen et al. 2011). Thus, the above conclusion is only tentative; other neurotransmitter abnormalities suggested to contribute to BPD might be responsible for the observed pattern of results. For example, the relationship between dopamine and impulsivity might be modulated by serotonergic activity (Dalley and Roiser 2012). Moreover, the glutamatergic system has also been implicated in reward processing (Gleich et al. 2012) and in impulsive behaviours in patients with personality disorders and healthy controls (Hoerst et al. 2010; Coccaro et al. 2013).

Processing not only of feedback valence, but also of feedback magnitude, was impaired in patients with BPD in the present study. This is a novel finding and emerged only in source-level analyses, with patients showing increased theta activity in the OFC, and (less prominently so) increased high-beta activity in both ROIs, following feedback that related to low-risk bets. The prominent involvement of the OFC in this effect is consistent with previous reports of OFC abnormalities in BPD (Mak and Lam 2013; Krause-Utz et al. 2014), and with a resting-state study that revealed a link between disturbed OFC connectivity and trait impulsivity in patients (Wolf et al. 2012). The physiological significance of this finding is not clear, but a possible clue might be derived from previous neuroimaging studies implicating the orbitofrontal cortex in the dysregulation of emotion and behaviour in BPD (Silbersweig et al. 2007; New et al. 2009; Schulze et al. 2011; Diaz-Marsa et al. 2011). State impulsivity and behavioural inhibition increase in the context of negative emotion (Brown et al. 2012; Cackowski et al. 2014). As feedback magnitude processing was associated with “high-risk” behaviour (albeit only in healthy controls) in the present study, it might be that abnormalities observed in patients reflected disturbed emotional processing of feedback magnitude.

A strength of the present study lies in the application of strict criteria for the exclusion of common comorbidities of patients with BPD such as major depression or substance dependence disorders, which are also linked to reward system dysfunction and might have confounded findings in patients. Nevertheless, it also suffers from certain limitations: first, although EEG has several advantages when it comes to assessing the precise timing of neural oscillations at different frequencies, it is limited both in its spatial resolution and in its capacity to detect activity in deep-located structures such as the ventral striatum or the midbrain, which constitute important nodes of the reward system. The fact that most patients included in the present study were medicated constitutes another possible limitation, given that both serotonergic (Abler et al. 2012; Macoveanu et al. 2014) and dopaminergic agents (McCabe et al. 2011; Oei et al. 2012) have an effect on the reward system. However, total medication load did not have a significant effect as a covariate in subsidiary analyses conducted in the BPD group. It is also in theory rather unlikely that the specific pattern of deficit observed in patients with BPD in the present study can be attributed to medication effects. Serotonergic agents have been reported to affect OFC activation during the anticipation of outcome (Macoveanu et al. 2014), and to reduce primary striatal/midbrain responses to positive feedback (Abler et al. 2012; Macoveanu et al. 2014). Although not directly estimable in the current context, such effects would have at most influenced the magnitude of electrophysiological responses to positive feedback in patients, which was not observed in the present study. On the other hand, dopaminergic agents are also known to reduce striatal and/or ACC responses to rewarding stimuli (McCabe et al. 2011; Oei et al. 2012), of which there was no evidence in the present study.

In summary, the results of the present study indicate specific dysfunctions in the way valence and magnitude of reward-related feedback are processed in patients with BPD. These dysfunctions possibly implicate several distinct subsets of reward-processing mechanisms, and were partly associated with trait impulsivity in patients. These findings provide further insights into reward processing in general, and in the neurophysiological underpinnings of impulsivity in BPD in particular.

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Statement of Interest

None to declare.

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Supplementary material available online
sLORETA whole-brain analyses
Supplementary Figure 1–3
Calculation of total medication load