
**eAppendix.** Methods and statistics

**eTable.** Main and interaction effects of the repeated measures analysis of covariance

**eReferences**

This supplementary material has been provided by the authors to give readers additional information about their work.
Methods and Statistics

Sample characteristics.

Patients with BPD and patients with BPD in remission were recruited via internet (www.kfo-256.de and social media), newspaper adds, flyers, and via referral from psychotherapists and other psychiatric hospitals. In addition, (former) study patients as well as in- and out patients of the Central Institute for Mental Health, Mannheim and the Department of General Psychiatry, Heidelberg were invited to take part in the study. This way, over 500 patients with BPD and more than 100 patients with BPD in remission could be recruited and were screened (see below); about 40% of both groups met the general inclusion criteria of the Clinical Research Group and were thus invited to take part in some of the studies. The current sample consists of a subsample of this general sample due to more restrict inclusion criteria (right handedness, no neurological and cardiac disorders, no psychotropic medication) and organizational reasons.

Healthy volunteers, who had never received a psychiatric diagnosis or undergone any psychological or psychiatric treatment, were also recruited via internet (www.kfo-256.de and social media), flyers, and newspaper adds, and matched to the sample of patients with BPD with regard to sex, age, and intelligence.

The general exclusion criterion current alcohol/drug abuse or dependence in the last 12 months was validated by urine toxicology screening and interview.
All participants took part in the same two step diagnostic process consisting of a two-hour telephone screening interview (including BPD criteria) and an onsite face-to-face interview (with trained diagnosticians with at least M.Sc. in psychology or MD and extensive diagnostic training by a senior clinician). Telephone interviewers’ were blind to the potential group status of participants.

Initially, our sample consisted of 39 patients with BPD and 36 healthy volunteers as well as 18 patients with BPD in remission. Data of five patients with BPD, five healthy volunteers, and one patient with BPD in remission had to be discarded due to technical problems causing severe artifact in the EEG and/or ECG measurements.

The diagnosis of BPD according to the Diagnostic and Statistical Manual for Mental Disorder IV\textsuperscript{1} was assessed with the International Personality Disorder Examination (IPDE)\textsuperscript{2}. For the current BPD group, the patients had to currently fulfill five or more criteria, whereas patients were included into the remitted group when they fulfilled three or less criteria at the time of the investigation, but had fulfilled full BPD diagnostic criteria (i.e., at least five criteria) at an earlier time-point for at least five years. The inclusion criterion for remission time was at least two years.

We intended to recruit all patients with BPD in remission by re-contacting former in-, out- and study patients from who an initial BPD diagnosis with structured diagnostic interviews from trained diagnosticians was available. This way, we were able to recruit eight patients with BPD in remission, while the additional nine patients of this group were recruited via flyers (N=4), internet (N=3), and others (N=2). None of the current as
well as the patients with BPD in remission had known cardiac or neurological consequences of past suicide attempts.

Current comorbid psychiatric diagnoses of patients with BPD included affective (N=10), anxiety (N=13), and eating disorders (N=9), PTSD (N=8), avoidant (N=6) and antisocial (N=2) personality disorders; in the remitted BPD group, they included anxiety (N=1) and eating disorders (N=1), and avoidant personality disorder (N=2).

Lifetime psychiatric disorders of patients with BPD were: affective disorders (N=27, 79%), anxiety disorders (N=18, 53%), eating disorders (N=16, 47%), PTSD (N=10, 29%), substance abuse (N=4, 12%) as well as avoidant (N=6, 18%) and antisocial (N=3, 9%) personality disorders. Lifetime psychiatric disorders of patients with BPD in remission were: affective disorders (N=16, 94%), eating disorders (N=9, 26%), anxiety disorders (N=6, 25%), PTSD (N=1, 6%), substance abuse (N=4, 24%), and avoidant personality disorder (N=3, 18%).

ECG data

Data processing. Heart rates were calculated with ARTiiFACT\(^3\) for semiautomatic detection of R peaks in filtered (bandpass: 0.1-35 Hz) ECG data.

Structural MRI data.

Data processing. The VBM8 standard workflow consisted of the following steps: First, images were segmented into gray matter, white matter, and cerebrospinal fluid partitions using the tissue prior free segmentation routine of the VBM8 toolbox (isotropic voxel size of 1.5 mm\(^3\)). The gray and white matter partitions of each subject were then
high-dimensionally registered to a crisp template of average anatomy in MNI space (IXI template) using the DARTEL algorithm. Flow fields resulting from the DARTEL registration to the IXI template were used to warp the gray matter segments, and voxel values were modulated for volumetric changes introduced by the high-dimensional normalization, such that the total amount of gray matter volume present before warping was preserved. For statistical analyses, normalized gray matter maps were smoothed with a Gaussian smoothing kernel of 8mm full width at half maximum.

Source analysis.

The artifact-corrected, averaged EEG data were subjected to an adapted form of spatio-temporal source analysis\textsuperscript{4-6}, as implemented in the BESA 5.1 software package (BESA GmbH, Germany) with a spherical head model and a homogeneous volume conductor. In BESA, equivalent current dipoles are modeled to represent the intracortical generators of the EEG activity measured at the scalp; the dipole model includes the spatial position of each source as well as its electrophysiological activity across time (source waveform).

For the present study, we built a dipole model with four regional sources: left anterior insular cortex, right anterior cingulate cortex, left and right frontal opercula. The spatial coordinates of these regional sources were set according to the peak voxels derived from the structural MRI analysis (correlation between mean HEP amplitudes and gray matter volume, see above). For the left anterior insula and the right anterior cingulate cortices, peak voxels of the hypothesis-driven region of interest analyses were used, while peak voxels for the bilateral opercula were derived from the unbiased whole
brain VBM. Source positions were kept fixed across all participants, in an effort to form a spatial filter for the derivation of each participant’s individual source waveforms. For each individual data set, we also included a principal component (PC) that caught activity within the time range of the R-wave; within this time interval, the PC explained 93.4% of the variance in the grand average data. For each individual data set, the three spatial orientations of each regional source were rotated such that the first orientation of a given source caught maximum activity within the interval of 455 to 595ms after the R-wave; then, the waveforms corresponding to each regional source were manually checked for correct polarity and exported to MATLAB (The MathWorks, USA) and SPSS 21 (IBM, USA) for further processing. Within the 455 to 595ms interval, the source model explained a mean of 74.4% of the variance of the scalp EEG data ($SD=9.13\%$), and 67.5% ($SD=12.1\%$) when the PC was excluded from the model (the importance of this PC component was reflected by a significant difference between the models with and without the PC component, $P\leq.001$; importantly, groups did not differ with respect to explained variance, $P=.477$).

The statistical evaluation of the source model including the PC was based on the mean amplitude in the 455 to 595ms interval of the waveform corresponding to the first spatial orientation of each regional source. The baseline was set to the mean activity in the interval from 150 to 50ms before the R-wave for all statistical analyses. In a repeated measures analysis of covariance (ANCOVA), we controlled for age and sex and additionally used the dipole amplitude at $t=0$ms (R-wave maximum) in each participant as a covariate, in order to control for possible residual influences of R-wave related activity.
eTable. Main and interaction effects of the repeated measures analysis of covariance including the between-subject effect group (patients with BPD vs. healthy volunteers), the within-subject effect electrode site (Fz, Cz, Pz, Oz), and the control factors age and sex. Post hoc tests revealed significantly reduced HEP amplitudes in patients with BPD compared with healthy volunteers at Pz and Oz (P<.01), while amplitudes were increased in patients with BPD compared with healthy volunteers at Fz (P<.05) and did not significantly differ between groups at Cz (P>.05).

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eReferences


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