Basic and Clinical
NEUROSCIENCE
March & April 2026, Vol 17, No. 2

Research Paper

Structural and Functional Brain Connectivity in Patients With Borderline Personality Disorder Compared to Healthy Controls: A Magnetic Resonance Imaging Study

Morteza Afshani[1], **Alireza Mohammadi**[2*]

1. Student Research Committee, Baqiyatallah University of Medical Sciences, Tehran, Iran.
2. Neuroscience Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran.

Use your device to scan and read the article online

Citation Afshani, M., & Mohammadi, A. (2026). Structural and Functional Brain Connectivity in Patients With Borderline Personality Disorder Compared to Healthy Controls: A Magnetic Resonance Imaging Study. *Basic and Clinical Neuroscience, 17*(2), 243-260.

http://dx.doi.org/10.32598/bcn.17.2.2572.2

Article info:
Received: 15 Dec 2025
First Revision: 28 Dec 2025
Accepted: 19 Feb 2026
Available Online: 01 Mar 2026

Keywords:
Borderline personality disorder (BPD), Functional neuroimaging, Emotion regulation, Emotional abuse, Gray matter

ABSTRACT

Introduction: Borderline personality disorder (BPD) is a syndrome that significantly impacts a person's capacity to cope with his/her emotions. Here, we aimed to demonstrate whether emotionally unstable personality traits are associated with alterations in brain structural and functional connectivity in individuals with BPD.

Methods: Twenty BPD participants and 16 healthy controls (HCs) underwent structural and functional magnetic resonance imaging (fMRI) during the Cyberball task. Functional connectivity multivariate pattern analyses (fc-MVPA), cortical thickness (CT), and gray matter volume (GMV) measures were extracted. Functional analyses were conducted using the CONN and SPM12 toolboxes. To ensure the reliability and accuracy of our fMRI analysis, we implemented rigorous automated quality control measures. Group-level analyses were performed using a general linear model (GLM).

Results: We did not identify any overall structural or functional differences between BPD patients and HCs. In patients with BPD, higher scores on the Hamilton depression rating scale (HAM-D) were associated with reduced GMV in several brain regions, including the left cerebellum VI, left caudate, right temporal pole, and right cerebellum V and VI. CT analyses further revealed significant inverse correlations between physical neglect and CT in the left superior frontal gyrus, right middle frontal gyrus, and right postcentral gyrus. The fc-MVPA demonstrated that emotional neglect scores were inversely correlated with connectivity in the right temporal pole. Additional fc-MVPA findings indicated inverse associations between HAM-D scores and both the left precentral and postcentral gyri, as well as between sexual abuse scores and connectivity in the left and right cerebellum IX.

Conclusion: This study localizes the emotionally unstable personality networks associated with abnormal brain connectivity in BPD, guiding future interventions for early diagnosis and treatment.

*** Corresponding Author:**
Alireza Mohammadi, Associate Professor.
Address: *Neuroscience Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran.*
Tel: *+98 (21) 87554490*
E-mail: *ar.mohammadi@bmsu.ac.ir*

Highlights

- HAM-D scores were associated with lower GMV in the left cerebellar lobule VI, left caudate, right temporal pole, and right cerebellar lobules V and VI.

- CT analyses revealed significant inverse associations between physical neglect scores and CT in the left superior frontal gyrus, right middle frontal gyrus, and right postcentral gyrus.

- Emotional neglect scores were inversely associated with functional connectivity involving the right temporal pole.

- fc-MVPA revealed inverse associations between HAM-D scores and functional connectivity involving the left precentral and postcentral gyri.

- Sexual abuse scores were inversely associated with functional connectivity involving bilateral cerebellar lobule IX.

Plain Language Summary

Borderline personality disorder (BPD) is characterized by marked emotion dysregulation that affects emotional processing and interpersonal functioning. This study investigated whether clinical symptoms and childhood trauma were associated with alterations in brain structure and functional connectivity in individuals with BPD. Twenty patients with BPD and 16 healthy controls underwent structural MRI and task-based functional MRI during the Cyberball task. Gray matter volume (GMV), cortical thickness (CT), and functional connectivity multivariate pattern analysis (fc-MVPA) were examined using the CONN and SPM12 toolboxes, with rigorous automated quality-control procedures. Group-level analyses were performed using a general linear model. No significant between-group differences in brain structure or functional connectivity were detected. However, within the BPD group, greater depression severity, as measured by HAM-D scores, was associated with lower GMV in the left cerebellar lobule VI, left caudate, right temporal pole, and right cerebellar lobules V and VI. Higher physical neglect scores were associated with lower CT in the left superior frontal gyrus, right middle frontal gyrus, and right postcentral gyrus. Functional connectivity analyses showed that emotional neglect was associated with reduced connectivity involving the right temporal pole. Greater depression severity and higher sexual abuse scores were associated with altered connectivity involving the left sensorimotor cortex and bilateral cerebellar lobule IX, respectively. These findings suggest potential neural correlates of depression severity and childhood trauma in BPD and may inform future research aimed at improving clinical assessment and developing targeted therapeutic interventions.

Introduction

People with borderline personality disorder (BPD) experience persistent emotional difficulties, including intense and unstable emotions, impulsivity, difficulties in maintaining relationships, and an unstable sense of self (APA, 2013). Individuals with BPD often struggle with emotion regulation, feeling easily overwhelmed and requiring longer periods to return to baseline (Cattane et al., 2017). Affecting approximately 3% of the Western population, BPD is associated with significant distress and functional impairment (Trull et al., 2010). Common clinical features include impulsivity, dissociation, aggression, self-harm, and chronic suicidal ideation (Leichsenring et al., 2011), leading to greater social and psychological impairment compared to other mood and personality disorders (Ansell et al., 2007). As a result, individuals with BPD frequently use mental health services and are overrepresented in both outpatient and inpatient settings (Ansell et al., 2007; Korzekwa et al., 2008). Although BPD was previously considered chronic and difficult to treat, recent evidence on its longitudinal course and the effectiveness of specialized interventions has challenged this view (Bateman & Fonagy, 2008). However, its underlying biological mechanisms remain poorly understood.

Emotional dysregulation, defined as difficulty managing intense emotional responses, is a core feature of BPD. It involves rapid mood shifts, heightened emotional reactivity, and slow recovery to emotional baseline (Chapman et al., 2026; Gratz et al., 2010). This instability is reflected in diagnostic criteria, such as affec-

tive instability and inappropriate anger, and is thought to underlie many other BPD symptoms (Beauchaine & Crowell, 2020). For example, identity disturbance, feelings of emptiness, and fear of abandonment are linked to emotional instability (Gratz et al., 2016), while interpersonal difficulties often arise from heightened emotional sensitivity and impulsivity. Emotional dysregulation is also associated with cognitive distortions, including dissociation and paranoia, as well as self-harm and risky behaviors (Donges et al., 2016; Maffei & Fusi, 2016). Beyond clinical symptoms, it can impair functioning across life domains, including work, education, and relationships, contributing to difficulties in maintaining employment, social connections, and effective stress coping (Reichenberger et al., 2017; Salsman & Linehan, 2012; Scheiderer et al., 2016; Schulze et al., 2011).

A number of previous studies on brain structure in BPD have used manual tracing techniques, which are particularly effective for identifying subtle variations in volume within specific brain regions. However, more recent research has incorporated automated methods, allowing for more comprehensive and reliable assessments of brain structure. Much of this research has focused on the limbic system, revealing significant reductions in gray matter volume (GMV) in regions, such as the amygdala and hippocampus (Mulert & Shenton, 2014). However, some studies have not detected any differences in amygdala volume (Mulert & Shenton, 2014). These inconsistencies in findings related to the limbic system may be partly attributed to the varying co-occurring conditions present in the BPD samples studied. In addition to the limbic system, researchers have also investigated structural abnormalities in the frontal lobe of patients with BPD (Sala et al., 2011). Notably, the advent of voxel-based morphometry (VBM) has facilitated unbiased quantification of structural properties across the whole brain, rather than limiting the analysis to a few selected areas (Mechelli et al., 2005; Nemoto, 2017). Overall, the results of prior VBM studies predominantly indicate abnormalities in the prefrontal regions in individuals with BPD, including the anterior cingulate cortex (ACC), dorsolateral prefrontal cortex (DLPFC), and orbitofrontal cortex (OFC) (Enzi et al., 2013; Ludäscher et al., 2009; Niedtfeld et al., 2012). The structural characteristics of these regions may serve as potential biomarkers for distinguishing individuals with BPD from healthy controls (HCs) (Sato et al., 2012).

Studies utilizing functional neuroimaging techniques indicate abnormalities in the limbic and frontal lobe regions of patients with BPD during various tasks. For instance, emotionally charged stimuli processing elicited more amygdala activation than in HCs (Kober et al., 2008). BPD patients demonstrated reduced effectiveness in managing their emotional states through cognitive control strategies, likely due to impaired functioning in prefrontal areas, particularly the DLPFC and the medial and lateral regions of the OFC (Enzi et al., 2013; Michel et al., 2024). Given the intense emotional lability and difficulty modulating affect that characterize BPD, individuals may, unfortunately, resort to self-harming or dissociative behaviors as maladaptive attempts to regulate overwhelming emotional states. These behaviors, while seemingly counterproductive, may serve a temporary function in reducing acute distress. Investigating the neural underpinnings of these coping mechanisms has revealed an intriguing and somewhat paradoxical association in neuroimaging studies. Specifically, one study found that self-harming or dissociative behaviors were associated with increased activity in the prefrontal areas (Aguilar-Ortiz et al., 2018; Enzi et al., 2013). This suggests that the perceived calming effects of self-harm on intense emotions could be related to a temporary upregulation of 'top-down' control exerted by the medial and DLPFC over the limbic system (Nenadić et al., 2020), potentially interrupting the cascade of intense emotional processing. Further research is needed to fully elucidate this complex interplay between self-harm and prefrontal regulation in individuals with BPD.

Furthermore, research has examined the neural processes underlying BPD patients' difficulties in interpersonal relationships, particularly their ability to comprehend others' mental and emotional states (Mulert & Shenton, 2014). Dziobek et al. provided evidence indicating that individuals diagnosed with BPD exhibit reduced activation in both the left superior temporal sulcus (STS) and the superior temporal gyrus (STG) within the context of cognitive empathy (Dziobek et al., 2011). Additionally, the STS and STG are involved in the capacity to interpret the mental states of others, as noted by Saxe & Wexler (2005) and further corroborated by Dodell-Feder et al. (2011). Furthermore, the bilateral STS and the temporoparietal junction are essential components of the fundamental neural network associated with mentalizing (Dodell-Feder et al., 2011; Dziobek et al., 2011; O'Neill et al., 2015; Saxe & Wexler, 2005). These studies found abnormal activity in the superior temporal sulcus، a region known to be involved in processing social cues. This finding suggests that the intense and poorly regulated emotional states experienced by individuals with BPD may create a neural environment that disrupts the efficient processing of social information within the superior temporal sulcus, thereby contributing to difficulties in social cognition.

Childhood trauma is known to affect brain structure and function in individuals with BPD, including reduced GMV in regions, such as the hippocampus and amygdala (Dannlowski et al., 2012; Schmahl et al., 2003; Teicher et al., 2012; Zhang et al., 2022), as well as disrupted frontolimbic connectivity involved in emotion regulation and social cognition. These alterations are thought to contribute to core symptoms, such as emotional dysregulation and interpersonal difficulties. However, despite this evidence, it remains unclear how structural and functional brain alterations jointly relate to key clinical features of BPD, particularly comorbid depressive symptoms and specific dimensions of childhood maltreatment. Moreover, few studies have directly examined these associations using multimodal neuroimaging approaches or compared these relationships between BPD and healthy populations. To address this gap, the present study employed a multimodal neuroimaging approach to investigate whether brain structure (CT and GMV) and functional connectivity multivariate pattern analyses (fc-MVPA) are associated with depressive symptom severity (Hamilton depression rating scale [HAM-D]) and different forms of childhood maltreatment. Importantly, we examined these relationships in both individuals with BPD and HCs. By linking distributed connectivity patterns and regional brain structure to clinically relevant variables, this study aimed to clarify the neurobiological mechanisms underlying the interaction between early adversity, depression, and BPD, and to identify potential biomarkers that may inform more targeted interventions.

Materials and Methods

Dataset and participants

Twenty individuals with BPD were recruited from local outpatient and support facilities in Edinburgh, Scotland. The structured clinical interview for DSM (SCID) and the HAM-D were used to verify symptoms. The childhood trauma questionnaire (CTQ) was utilized to evaluate negative childhood experiences. Twelve BPD individuals were taking antipsychotic medication, while fifteen participants were receiving antidepressant medications. Twenty community members were selected as an age- and sex-matched control group; four were eliminated due to technical difficulties during the imaging process, leaving 16 control subjects. Exclusion criteria for all participants included pregnancy, MRI contraindications, a diagnosis of psychotic disorders, a history of head trauma, or current illicit drug abuse. Ethical approval was granted by the Lothian National Health Service Research Ethics Committee, and written informed consent was obtained from each participant prior to participation. All methods were conducted in accordance with the relevant guidelines and regulations outlined in the study protocol approved by the Research Ethics Committee of Baqiyatallah University of Medical Sciences.

Cyberball task

Participants completed the Cyberball social exclusion task (Williams et al., 2000), a virtual ball-toss game during functional magnetic resonance imaging (fMRI), which was adapted from an earlier version (Kumar et al., 2009). In the experiment, two computer-automated participants played a game of catching a virtual ball while the player could be systematically included or excluded from the game. Suddenly, the computer-controlled players completely excluded the participant, tossing the ball only to each other. This task was chosen because it measures neural reactions to social exclusion, can be modeled using reinforcement learning techniques, and is known to stimulate different social brain areas. The task was then redesigned to vary exclusion dynamically across three levels: 33%, 66%, and 100%. This was accomplished by breaking the work into nine-throw blocks, each involving one, two, or three tosses to the participant. The introduction of the cartoon figures after a period of rest signaled the start of each block, which lasted for 24 seconds and was partially based on reaction times. The end of the final throwing animation marked the conclusion of this phase. Random blocks were interspersed during 13-second rest intervals. Within these discrete blocks, the timing of throwing events was randomized to enhance event differentiation for the purpose of examining reinforcement learning.

Image preprocessing

In summary, the parameters for fMRI data acquisition were as follows: repetition time (TR)=1560 ms, number of volumes=347, voxel size=3.4×3.4×5 mm, and field strength=3 T. We implemented rigorous quality control (QC) measures to ensure the accuracy and reliability of our sMRI analyses. Each image was meticulously inspected for distortions or artifacts that could compromise data integrity. Once the images were deemed suitable for analysis, we employed the CAT12 (Gaser et al., 2024) automatic pipeline to extract fundamental structural metrics. This pipeline is widely used and well validated for processing sMRI data. It automatically performs several critical steps, including normalization (voxel size: 1.5 mm), which aligns the brain images to a standard template (MNI152NLin2009cAsym space) to facilitate comparisons across individuals; bias field correction

(performed by an adaptive non-local mean filter), which eliminates intensity variations caused by magnetic field inhomogeneities; brain extraction, isolating the brain tissue from surrounding non-brain regions using a default tissue probability map that includes six probability classes; segmentation, dividing the brain into distinct tissue types, such as gray matter, white matter, and cerebrospinal fluid; and surface reconstruction, creating a surface model of the cortex to measure cortical thickness (CT). Using this pipeline, we efficiently and accurately calculated GMV and CT.

Functional analyses were performed using the CONN toolbox (version 22) (Morfini et al., 2023; Whitfield-Gabrieli & Nieto-Castanon, 2012) and the SPM12 (Ashburner & Friston, 2005) toolbox. Three patients were excluded from the study due to leakage of structural or functional images. Functional data were preprocessed using a flexible preprocessing pipeline, including realignment with correction for susceptibility distortion interactions, slice timing correction, outlier detection, direct segmentation, MNI space normalization, and smoothing. The functional data were realigned using the SPM realign and unwarp procedure, where all scans were co-registered to a reference image (the first scan of the first session) using the least squares method and a 6-parameter transformation (rigid body) and resampling using B-spline interpolation to correct for interactions between motion and magnetic susceptibility. Temporal misalignment between the different slices of functional data (acquired in interleaved bottom-up order) was corrected using SPM slice-timing correction (STC), where synchronous sync temporal interpolation was used to resample each slice of the BOLD time series to a common mid-acquisition time point. Potential outlier scans were identified using ART as acquisitions with framewise displacement above 0.9 mm or global BOLD signal changes of more than 5 standard deviations, and a reference BOLD image was calculated for each subject by averaging all scans excluding outliers. The functional and anatomical data were normalized into standard MNI space and segmented into gray matter, white matter, and CSF tissue classes. They were resampled with 3 mm isotropic voxels using a direct normalization procedure based on the SPM unified segmentation and normalization algorithm with the default IXI-549 tissue probability map template. Finally, the functional data were smoothed by spatial convolution with a Gaussian kernel of 6 mm full width at half maximum (FWHM). To ensure the accuracy of the preprocessing, the final results were visually assessed in the QC phase.

The functional data were denoised using a standard denoising pipeline that included the regression of potential confounding effects represented by white matter time series (5 CompCor noise components), CSF time series (5 CompCor noise components), motion parameters and their first order derivatives (12 factors), outlier scans (below 29 factors), session and task effects and their first-order derivatives (16 factors), and linear trends (2 factors) within each functional run. This was followed by bandpass frequency filtering of the BOLD time series between 0.008 Hz and 0.09 Hz. CompCor noise components in white matter and CSF were estimated by calculating the average BOLD signal, the largest principal components orthogonal to the BOLD average, the motion parameters, and the outlier scans within each subject's eroded segmentation masks. Based on the number of noise terms included in this denoising strategy, the effective degrees of freedom of the BOLD signal after denoising were estimated to range from 69.6 to 77, with an average of 75.4 across all subjects.

Functional connectivity analysis

fc-MVPA was used to characterize subject- and condition-specific patterns of whole-brain connectivity (Morfini et al., 2023). Functional connectivity between pairs of voxels was first estimated using Pearson' correlation coefficients between their BOLD time series, defined as, where and denote the time series of voxels and. Prior to this step, BOLD signals were Z-score normalized, and dimensionality reduction was performed at the subject level using singular value decomposition (SVD), retaining 64 components for each subject and condition to improve computational efficiency and reduce noise.

For each seed voxel, a connectivity matrix was then constructed, with rows representing target voxels and columns representing subject-condition pairs. Group-level SVD was applied to this matrix, such that, where contains the spatial eigenpatterns (i.e. principal connectivity modes across the brain) and contains the corresponding eigenpattern scores for each subject and condition. These eigenpatterns and their associated scores were computed separately for each seed voxel, representing the principal axes of variability in functional connectivity across subjects.

The first ten eigenpatterns were retained, capturing the dominant sources of inter-subject and inter-condition heterogeneity in connectivity. For each subject and condition, the corresponding eigenpattern score images provide a compact representation of the whole-brain functional connectome, reflecting the degree to which each

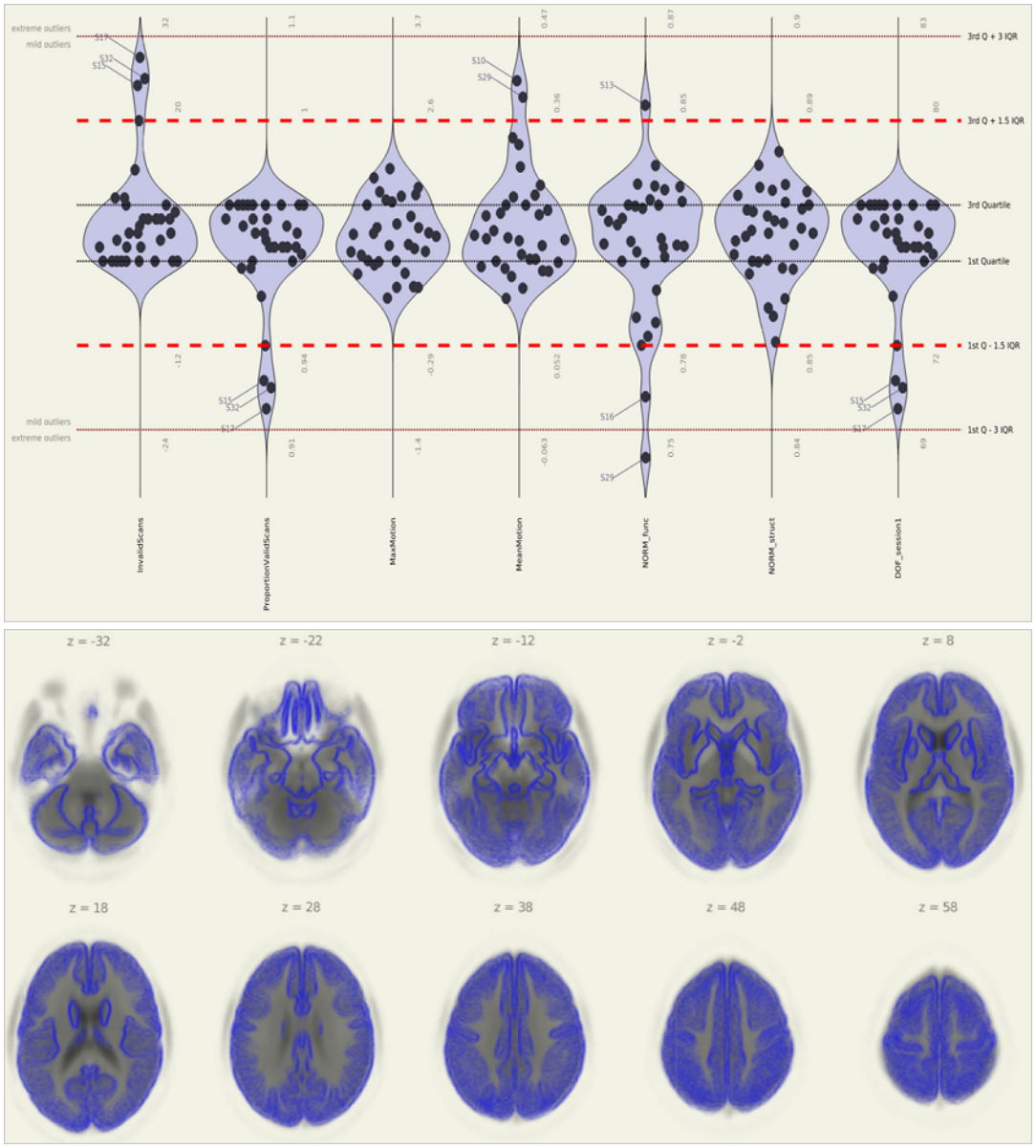


Figure 1. Automated QC measures of preprocessed and denoised data

QC: Quality control; IQR: Interquartile range.

Note: The distributions of automated QC measures extracted from the full fMRI-open-QC dataset. QC measures were calculated from preprocessed functional, anatomical, and denoised functional data. Extreme outliers were identified as values 3 IQR below the 1st quartile or above the 3rd quartile (red dotted lines). Mild outliers were defined as values 1.5 IQR below the 1st quartile or above the 3rd quartile (red dashed lines). All figures were generated using the CONN toolbox by MA.

connectivity pattern is expressed. This approach enables the identification of distributed connectivity profiles and their associations with clinical variables.

Quality control

To ensure the reliability and accuracy of our fMRI analysis, we implemented rigorous automated QC measures. The registration of functional data in MNI space was visually inspected to exclude unwanted artifacts. Furthermore, both the preprocessed and denoised data were examined to identify potential issues that could affect the integrity of our results. For the preprocessed functional data, we calculated several QC metrics: InvalidScans (number of invalid scans), MeanMotion (mean head motion), NORMfunc (normalized functional signal), Pro-

Table 1. Relationship between emotionally unstable personality traits and demographic variables

Variables	Mean±SD		P
	Patients with BPD (n=20)	Healthy Controls (n=16)	
Age (y)	35.8±8.6	34.8±9.6	0.97
Sex (F: M)	17:3	13:3	0.76
Handedness (R: L)	19:1	15:1	0.87
IQ	114.8±7.9	114.5±6	0.58
HAM-D	15.65±8.34	0±0	<0.001
Physical abuse	2.51±1.45	1.09±0.24	0.002
Physical neglect	2.14±1.11	1.28±0.32	0.010
Emotional abuse	3.79±1.1	1.25±0.41	<0.001
Emotional neglect	3.35±1.36	1.54±0.77	<0.001
Sexual abuse	3.14±1.74	1.28±0.32	<0.001

NEUROSCIENCE

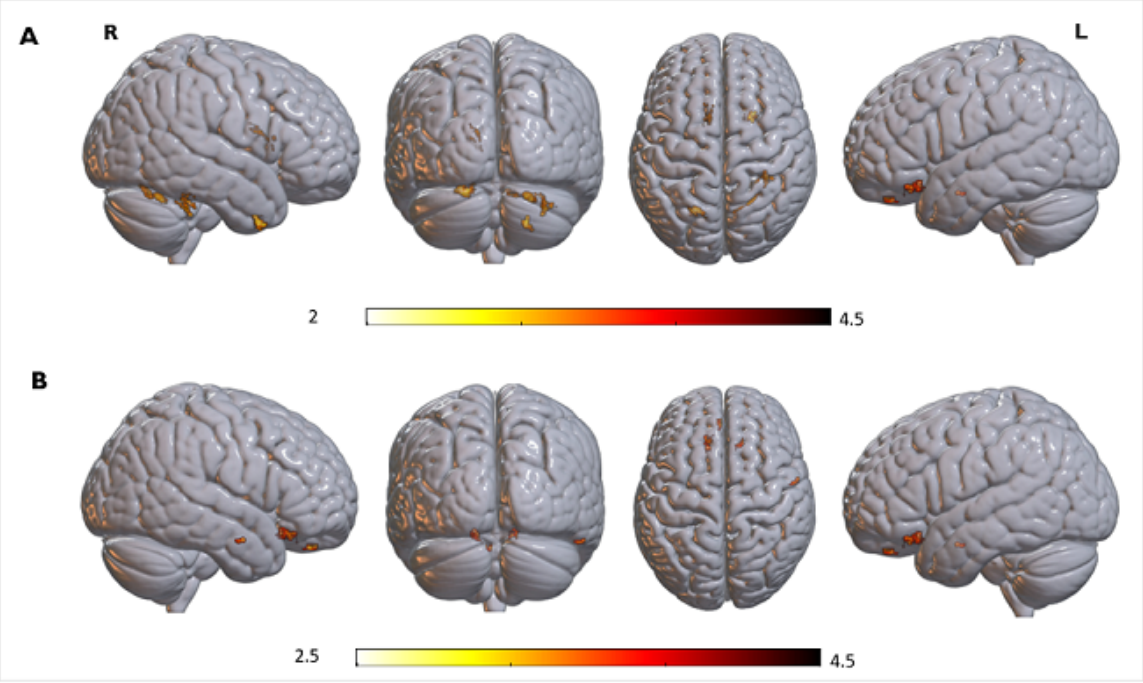
portionValidScan (percentage of valid scans), and Max-Motion (maximum head motion). For the preprocessed anatomical data, we computed NORManat (normalized anatomical signal) (Morfini et al., 2023). Finally, we calculated DOF (degrees of freedom) for the denoised functional data. To identify outliers in these QC measures, we used a robust statistical method based on interquartile ranges (IQR) (Morfini et al., 2023). Extreme outliers were defined as values that were more than 3 IQR below the first quartile or above the third quartile. Mild outliers were defined as scores between 1.5 and 3 IQR below the first quartile or above the third quartile. These thresholds were chosen to achieve a balance between sensitivity and specificity in detecting anomalies that could indicate data quality issues (Figure 1).

Table 2. Relationship between emotionally unstable personality traits and GMV variations

Phenotype	Cluster	PFDR	T-value	X Y Z	Region	L/R
HAM-D	210	<0.001	4.79	-17 -63 -28	Cerebellum VI	L
	195	<0.001	4.80	+26 +09 -49	Temporal pole	R
	138	<0.001	5.84	+25 -53 -31	Cerebellum VI	R
	123	<0.001	4.32	-07 +18 +04	Caudate	L
	122	<0.001	5.14	+31 -37 -40	Cerebellum VI	R
	111	<0.001	6.03	+31 -34 -35	Cerebellum V	R
Physical neglect	177	<0.001	5.94	-9 +34 -25	Frontal medial cortex	L
	90	0.004	4.98	+08 +26 -22	Subcallosal cortex	R
	71	0.016	5.13	-04 +38 -29	Frontal medial cortex	L
	65	0.021	5.23	+55 -04 -25	Middle temporal gyrus	R

L: Left hemisphere; R: Right hemisphere.

NEUROSCIENCE



NEUROSCIENCE

Figure 2. Relationship between emotionally unstable personality traits and GMV variations

A) HAM-D scores in patients with BPD were associated with reduced GMV compared to HCs in the left cerebellum VI, left caudate, right temporal pole, and right cerebellum V and VI; B) Similarly, increased physical neglect scores in patients with BPD were linked to reduced GMV in the left frontal medial cortex (in two compartments), right subcallosal cortex, and right middle temporal gyrus

Note: All figures were generated using the CONN toolbox by MA.

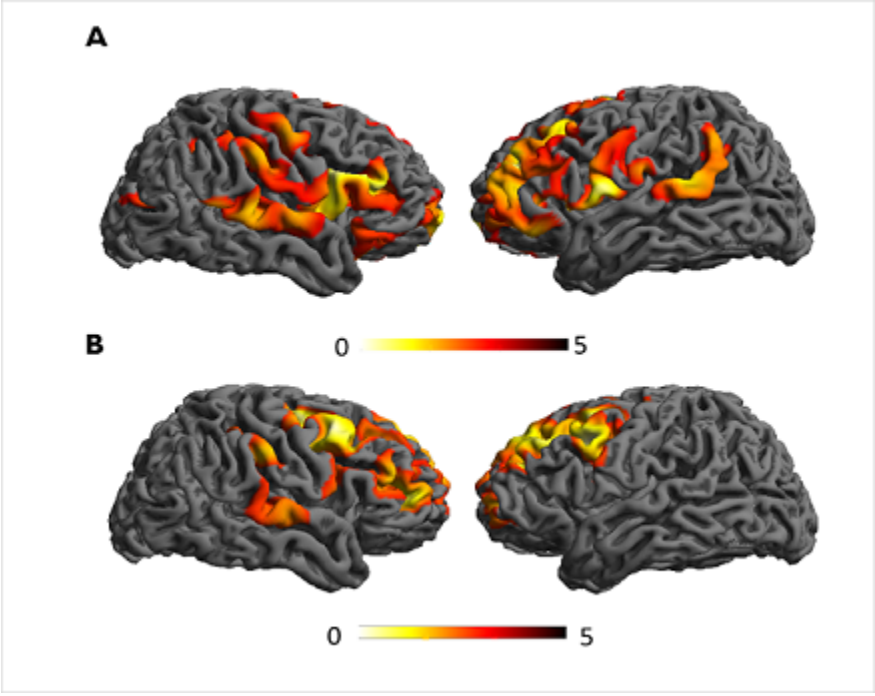
Statistical analysis

Group-level analyses were performed using a general linear model (GLM). A separate GLM was estimated for each voxel, with the first-level connectivity measurements at that voxel as dependent variables (one independent sample per subject and one measurement per task or experimental condition, if applicable) and the groups or other subject-level identifiers as independent variables. Voxel-level hypotheses were assessed using multivariate parametric statistics with random effects between subjects and covariance estimation across multiple measurements. Inferences were made at the individual cluster level (groups of contiguous voxels). Group status, age, and sex were included as covariate factors in our statistical models to account for any potential group-related differences. Cluster-level inferences were based on parametric statistics derived from Gaussian random field theory. Results were determined using a combination of a cluster-forming threshold of P<0.001 at the voxel level and a family-wise corrected threshold of p-FDR <0.05 for cluster size.

Results

Relationship between emotionally unstable personality traits and demographic variables

We found that patients with BPD had significantly higher scores on the HAM-D (15.65±8.34 vs 0±0) than HCs (P<0.001). Moreover, physical, emotional, and sexual abuse scores in patients with BPD were significantly higher (2.51±1.45 vs 1.09±0.24, 3.79±1.1 vs 1.25±0.41, 3.14±1.74 vs 1.28±0.32) than those of HCs (P=0.002, P<0.001, and P<0.001; respectively). Furthermore, physical (2.14±1.11 vs 1.28±0.32) and emotional (3.35±1.36 vs 1.54±0.77) neglect scores in patients with BPD were significantly higher than those of HCs (P=0.010 and P<0.001; respectively). There were no significant differences between groups in terms of age (35.8±8.6 vs 34.8±9.6), sex (F:M; 17:3 vs 13:3), IQ (114.8±7.9 vs 114.5±6.0), or handedness (R:L; 19:1 vs 15:1) (Table 1).



NEUROSCIENCE

Figure 3. Relationship between emotionally unstable personality traits and CT variations

A) Higher HAM-D scores in patients with BPD were associated with lower CT compared to HCs in the right and left precentral-middle frontal gyrus, right lateral occipital cortex, right supramarginal/angular gyrus, right superior frontal gyrus, right frontal pole, and left postcentral gyrus; B) Similar to the effects of physical neglect on GMV, a significant inverse correlation between CT and physical neglect was observed in the left superior frontal gyrus, right middle frontal gyrus, and right postcentral gyrus

Note: All figures were generated using the CONN toolbox by MA.

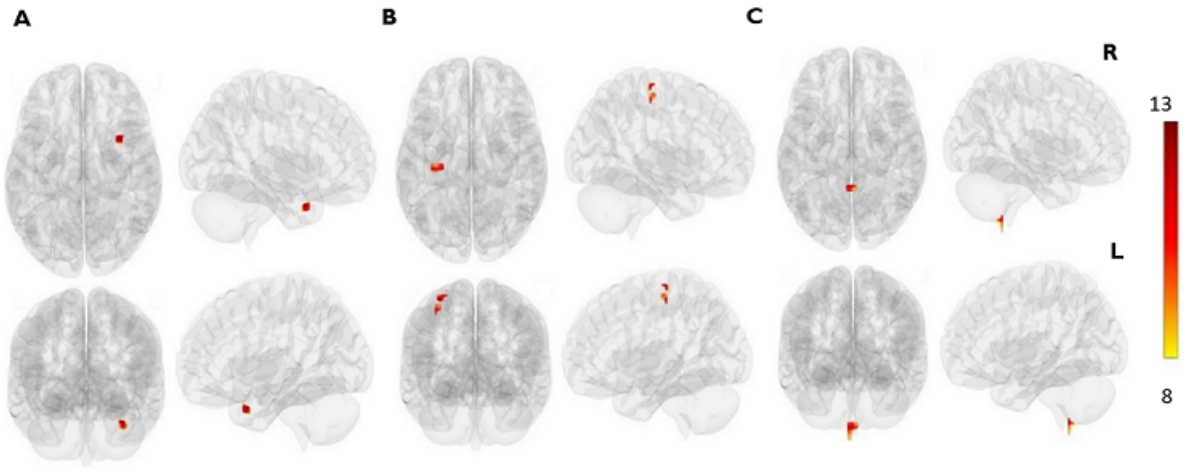


Figure 4. Relationship between emotionally unstable personality traits and fc-MVPA variations

NEUROSCIENCE

A) The fc-MVPA analysis revealed a significant inverse correlation between emotional neglect and the right temporal pole in patients with BPD compared to HCs; B) This trend was also observed in the HAM-D scores for the left precentral and postcentral gyrus regions; C) This variation in connectivity correlated with scores of sexual abuses for both the left and right cerebellum IX

Note: All figures were generated using the CONN toolbox by MA.

Table 3. Relationship between emotionally unstable personality traits and CT variations

Phenotype	Cluster	PFDR	T-value	X Y Z	Region	L/R
HAM-D	2756	<0.001	4.21	+50 +26 +66	Precentral-middle frontal gyrus	R
	2214	<0.001	4.37	-23 +50 +67	Precentral-middle frontal gyrus	L
	947	0.009	4.40	+38 -60 +65	Lateral occipital cortex	R
	933	0.009	3.50	+57 -41 +54	Supramarginal/angular gyrus	R
	906	0.009	2.77	+12 +42 +56	Superior frontal gyrus	R
	823	0.014	3.62	+03 +64 +39	Frontal pole	R
	796	0.016	3.22	-53 -32 +62	Postcentral gyrus	L
Physical neglect	3369	<0.001	4.02	-02 +37 +77	Superior frontal gyrus	L
	3011	0.001	3.79	+43 +13 +89	Middle frontal gyrus	R
	865	0.021	2.81	+58 -21 +74	Postcentral gyrus	R

L: Left hemisphere; R: Right hemisphere.

NEUROSCIENCE

Relationship between emotionally unstable personality traits and GMV variations

The overall results of the HAM-D indicated a significant inverse correlation between depressive symptoms and brain volume. Specifically, higher HAM-D scores in patients with BPD were associated with reduced GMV compared to HCs in the left cerebellum VI, left caudate, right temporal pole, and right cerebellum V and VI (P<0.001).

Likewise, this inverse correlation holds for physical neglect scores. Our results demonstrated that higher physical neglect scores in patients with BPD were related to reduced GMV compared to HCs in the left frontal medial cortex (in two compartments) (P<0.001 and P=0.016), right subcallosal cortex (P=0.004), and right middle temporal gyrus (P=0.021) (Table 2 and Figure 2).

Relationship between emotionally unstable personality traits and CT variations

There was also a significant inverse correlation between HAM-D depressive scales and CT variations. Higher HAM-D scores in patients with BPD were associated with lower CT compared to HCs in the right and left precentral-middle frontal gyrus (P<0.001), right lateral occipital cortex (P=0.009), right supramarginal/angular gyrus (P=0.009), right superior frontal gyrus (P=0.009), right frontal pole (P=0.014), and left postcentral gyrus (P=0.016). In addition, similar to the effects of physical neglect on GMV, a significant inverse correlation between CT and physical neglect was observed in the left superior frontal gyrus (P<0.001), right middle frontal gyrus (P=0.001), and right postcentral gyrus (P=0.021) (Table 3 and Figure 3).

Table 4. Relationship between emotionally unstable personality traits and fc-MVPA variations

Phenotype	Cluster	PFDR	F-value	X Y Z	Region	L/R
Emotional neglect	39	<0.001	13.57	+34 +08 -30	Temporal pole	R
HAM-D	25	<0.001	8.85	-36 -24 +54	Precentral gyrus	L
	25	<0.001	11.57	-32 -24 +62	Postcentral gyrus	L
Sexual abuse	44	0.007	12.83	+00 -48 -60	Cerebellum IX	R/L

L: Left hemisphere; R: Right hemisphere.

NEUROSCIENCE

Relationship between emotionally unstable personality traits and functional connectivity variations

After applying the false discovery rate (FDR) correction, we conducted a functional connectivity analysis using fc-MVPA. Simultaneously, the exclusion level in the Cyberball task decreased from 100% to 33%. The fc-MVPA analysis revealed a significant inverse correlation between emotional neglect and activity in the right temporal pole in patients with BPD compared to HCs (P<0.001). Furthermore, this trend was also observed for HAM-D scores in both the left precentral and postcentral gyrus regions (P<0.001) and sexual abuse scores in both the left and right cerebellum IX (P=0.007) (Table 4 and Figure 4).

Discussion

Patients with BPD have significant difficulties in emotion regulation, impulsivity, and decision-making. This study aimed to enhance our understanding of how the size and activity of specific brain regions change in individuals with BPD. We sought to determine whether emotionally unstable personality traits are associated with abnormal structural and functional brain connectivity in BPD.

We identified no direct structural or functional differences between BPD patients and HCs. While the absence of significant structural and functional differences between the BPD and HC groups in our study is consistent with a subset of the literature, it contrasts with other studies that report alterations in GMV, CT, and connectivity patterns in BPD. Several factors may contribute to this discrepancy. First, the relatively small sample size may have limited the statistical power to detect subtle group differences. Second, BPD is a highly heterogeneous disorder, and the neurobiological alterations may be more closely linked to specific symptom dimensions or trauma subtypes rather than the diagnostic label alone. This is supported by our correlation analyses, which revealed meaningful associations between clinical measures and neuroimaging metrics within the BPD group. Finally, differences in methodology—including imaging parameters, preprocessing pipelines, and analytic strategies—may account for inconsistencies across studies. Our findings suggest that within-group variability, particularly concerning clinical severity and trauma history, may provide more informative insights than categorical group comparisons alone.

However, we observed numerous inverse correlations between the scores for HAM-D, physical and emotional neglect, sexual abuse, and measures of GMV, CT, and fc-MVPA. Our results indicated that patients with BPD reported significantly higher scores for physical, emotional, and sexual abuse, as well as physical and emotional neglect, compared to HCs. Additionally, these patients exhibited higher scores on the HAM-D than HCs. These findings align with previous research suggesting that individuals with BPD have a markedly higher prevalence of physical and sexual abuse and an increased subjective experience of depression (Goldman et al., 1992; McLean & Gallop, 2003; Stanley & Wilson, 2006).

Several sMRI volumetric analyses have presented conflicting results that vary significantly and lack consistency (Aguilar-Ortiz et al., 2018; Brambilla et al., 2004; Brunner et al., 2010; Chanen et al., 2008; Driessen et al., 2000; Goodman et al., 2011; Irle et al., 2005; Jin et al., 2016; Kuhlmann et al., 2013; Labudda et al., 2013; Lyoo et al., 1998; Mechelli et al., 2005; Minzenberg et al., 2008; Mulert & Shenton, 2014; Nunes et al., 2009; Rodrigues et al., 2011; Rüsch et al., 2003; Sala et al., 2011; Sato et al., 2012; Schmahl et al., 2003; Soloff et al., 2008; Tebartz van Elst et al., 2003; Völlm et al., 2009; Weniger et al., 2009; Zetzsche et al., 2006; Zetzsche et al., 2007). These discrepancies may be attributed to uncontrolled rates of comorbidities, small sample sizes, or heterogeneous patient populations, including variations in age and gender. Conversely, consistent with the findings of Labudda et al. (2013) and Kreisel et al. (2015), some studies do not support any differences between patients with BPD and HCs. We identified several inverse correlations between HAM-D scores, physical and emotional neglect, sexual abuse, and measures of GMV, CT, and fc-MVPA. Specifically, higher HAM-D scores in BPD patients were linked to reduced GMV in regions, such as the left cerebellum VI, left caudate, right temporal pole, and right cerebellum V and VI compared to HCs (Table 2 and Figure 2). These findings may indicate that heightened depressive symptoms in BPD are associated with structural alterations in brain areas implicated in emotion regulation and motor coordination. Moreover, higher HAM-D scores in BPD patients were associated with decreased CT in regions, including the right and left precentral-middle frontal gyrus, right lateral occipital cortex, right supramarginal/angular gyrus, right superior frontal gyrus, right frontal pole, and left postcentral gyrus (Table 3 and Figure 3). These areas are involved in executive function, sensory processing, and motor control, suggesting that depressive symptoms in BPD may reflect widespread cortical involvement, particularly in regions related to cognitive and affective processing. These patterns highlight the potential role of structural brain alterations in the manifestation of de-

pressive symptoms in BPD, supporting the notion that emotional dysregulation in this disorder may be partly rooted in specific neuroanatomical changes.

Some authors have reported severe volume losses of the amygdala and hippocampus in patients with BPD (Driessen et al., 2000; Goodman et al., 2011; Nunes et al., 2009; Rodrigues et al., 2011; Schmahl et al., 2003; Tebartz van Elst et al., 2003). Weniger et al. (2009) suggested that patients with BPD displayed significantly reduced amygdala (22%) and hippocampus (11%) than HCs. Nonetheless, Schmahl et al. (2009) demonstrated that the volume of the hippocampus does not exhibit a reduction in individuals diagnosed with BPD unless they concurrently present with post-traumatic stress disorder (PTSD). Kuhlmann et al. (2013) reported that female patients with BPD exhibited reductions in left-sided hippocampal volume and increases in hypothalamic volume compared with HCs. However, no significant alterations were observed in the amygdala or the ACC. Unlike other authors who did not find volume reductions in the amygdala and hippocampus (Brambilla et al., 2004; Chanen et al., 2008), Minzenberg et al. (2008) reported an increase in amygdala volume. Driessen et al. (2000) stated that individuals diagnosed with BPD exhibit approximately 16% and 8% smaller hippocampus and amygdala volumes than the HCs, respectively. In addition, Teicher et al. (2012) and Dannlowski et al. (2012) demonstrated that individuals who experienced childhood maltreatment exhibit a significant reduction in both hippocampal and extra-hippocampal volumes. Nonetheless, other studies have not identified any direct cerebral abnormalities associated with maltreatment (Driessen et al., 2000; Kreisel et al., 2015; Kuhlmann et al., 2013; Labudda et al., 2013; Schmahl et al., 2009; Schmahl et al., 2003). These studies along with our current research, suggest a lack of a direct association between childhood traumatic experiences and neural morphology in individuals diagnosed with BPD. Previous meta-analyses (Nunes et al., 2009; Rodrigues et al., 2011; Ruocco et al., 2012) suggest that adult patients with BPD have bilaterally smaller amygdala and hippocampal volumes compared to HCs.

On the other hand, studies have found volume losses within frontal brain regions, such as the OFC, DLPFC, and ACC in BPD patients (Aguilar-Ortiz et al., 2018; Brunner et al., 2010; Chanen et al., 2008; Goodman et al., 2011; Soloff et al., 2008; Tebartz van Elst et al., 2003). In this context, Aguilar-Ortiz et al. (2018) demonstrated that individuals with BPD exhibit clusters of volume reduction in the DLPFC and the pregenual/subgenual medial frontal cortex. Additionally, there is evidence of right-sided enlargement of the hippocampus or the amygdala. However, they found no significant structural differences between BPD patients with and without major depression (MD) (Aguilar-Ortiz et al., 2018). Tebartz et al. revealed a significant reduction in volume in the left OFC, right ACC, amygdala, and hippocampus in patients with BPD (Tebartz van Elst et al., 2003). In contrast, Rüsch et al. (2003), Brambilla et al. (2004), and New et al. (2007), did not corroborate these findings in a larger sample. Moreover, Brunner et al. (2010) proposed that the reductions in ACC volume are not exclusive to BPD, as individuals diagnosed with BPD exhibited no significant variation in ACC volumes compared to a heterogeneous psychiatric cohort. Consequently, the presence of MD comorbidity may have influenced the relationship between ACC volumes and the severity of BPD (Brunner et al., 2010; Goodman et al., 2011). Furthermore, it was observed that reduced volumes of the ACC correlated with heightened severity of BPD symptoms in individuals with comorbid MD (Brunner et al., 2010; Goodman et al., 2011). Nonetheless, their analysis of the association between structural brain changes and symptom severity was limited to the mesiofrontal brain region (Goodman et al., 2011). Moreover, Völlm et al. (2009) stated that patients with BPD exhibit reduced GMV in the frontal, parietal, and temporal cortices, which may be associated with impulsivity. Similarly, Soloff et al. (2008) identified GMV decreases in the frontal and mesiotemporal volume in individuals with BPD compared to HCs. Nevertheless, these differences diminished when impulsivity was used as a covariate.

In our study, increased physical neglect scores in patients with BPD were linked to reduced GMV in the left frontal medial cortex (in two compartments), right subcallosal cortex, and right middle temporal gyrus. Furthermore, we observed a significant inverse correlation between CT and physical neglect in the left superior frontal gyrus, right middle frontal gyrus, and right postcentral gyrus. In contrast to the findings of Teicher et al. (2012) and Dannlowski et al. (2012), which reported reductions in hippocampal and extra-hippocampal volumes among children who have experienced childhood maltreatment, our study aligns with the study by Labudda et al. (2013) and Kreisel et al. (2015), who did not identify a direct association or significant abnormalities related to maltreatment in patients with BPD and HCs. Our findings are consistent with those of Labudda et al. (2013), Driessen et al. (2000), Schmahl et al. (2003), Kuhlmann et al. (2013), Schmahl et al. (2009) and Kreisel et al. (2015), all of whom similarly found no direct correlation between childhood maltreatment and manually assessed volumes of the ACC, amygdala, and hippocampus.

From another perspective, similar to structural outcomes, numerous fMRI studies have reported conflicting, markedly different, and inconsistent results (Baczkowski et al., 2017; Cullen et al., 2011; Krause-Utz et al., 2014; Nenadić et al., 2020; Noor et al., 2024; Schulze et al., 2019; Shafie et al., 2023; Stopyra et al., 2023; Visintin et al., 2016; Westlund Schreiner et al., 2017; Westlund Schreiner et al., 2019; Xiao et al., 2023; Xu et al., 2016; Zhang et al., 2022). In a meta-analysis, Schulze et al. (2016) found that individuals with BPD exhibited hyperactivity in the left amygdala and posterior cingulate cortex (PCC), while showing reduced activity in the bilateral DLPFC compared to HCs. In another study, Schulze et al. (2019) reported that individuals with BPD and PTSD displayed increased limbic activation relative to HCs. In contrast, patients with MDD demonstrated reduced amygdala activation compared to HCs. Despite these differences, there was a significant overlap of neural abnormalities in response to negative stimuli among patients with BPD, MDD, and PTSD, characterized by hyperactivation of the right median cingulate gyri and hypoactivation of the right middle frontal gyrus and right middle occipital gyrus (Schulze et al., 2019).

Our fc-MVPA analysis identified a significant inverse correlation between emotional neglect and the right temporal pole in patients with BPD compared to HCs. Additionally, this pattern was observed for HAM-D scores in both the left precentral and postcentral gyrus regions, as well as for sexual abuse scores in both the left and right cerebellum IX.

While this study provides important insights into the relationship between clinical symptoms and neuroimaging measures in individuals with BPD, several limitations must be acknowledged. First, the relatively small sample size may limit the statistical power and generalizability of our findings. A larger cohort would increase the robustness of the results and enhance the external validity of the study. Second, the use of medications, including antipsychotics and antidepressants, by a significant proportion of participants could potentially confound the neuroimaging results. These medications may influence brain structure and function, and their effects were not controlled for in the current analysis. Future research should consider accounting for medication use to better isolate the impact of BPD-related neural changes from pharmacological effects.

Furthermore, the cross-sectional design of this study restricts our ability to establish causal relationships between clinical symptoms, trauma history, and neuroimaging measures. Longitudinal studies are needed to examine how neural alterations may evolve in response to changes in symptomatology or treatment. Lastly, while we focused on specific clinical variables, such as the HAM-D and trauma history, other potential mediators, including comorbid psychiatric conditions and environmental factors, were not considered in the analysis. These additional variables may contribute to the observed neural alterations and warrant further investigation in future studies.

Conclusion

In conclusion, this study provides preliminary evidence of the relationship between clinical symptoms in BPD and alterations in brain structure and function, as measured by neuroimaging techniques. We found significant correlations between clinical variables, such as depression severity and trauma history and GMV, CT, and functional connectivity. These findings suggest that BPD symptoms, particularly those related to emotional regulation and trauma exposure, may be linked to underlying neural changes. The observed correlations offer valuable insights into the potential neural mechanisms associated with the disorder. Further studies with larger sample sizes and longitudinal designs are needed to confirm these findings and explore the role of medications and comorbidities in shaping these neural alterations.

Ethical Considerations

Compliance with ethical guidelines

All methods were conducted in accordance with the relevant guidelines and regulations outlined in the study protocol, which was approved by the Research Ethics Committee of Baqiyatallah University of Medical Sciences, Tehran, Iran (Code: IR.BMSU.REC.1402.050).

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

Data analysis and writing the original draft: All authors; Conceptualization, supervision, review and editing: Alireza Mohammadi.

Conflict of interest

The authors declared no conflict of interest.

Acknowledgments

We wish to convey our sincere appreciation to the Neuroscience Research Center at Baqiyatallah University of Medical Sciences for valuable support and resources, which were instrumental in the successful completion of this study. We also acknowledge OpenfMRI and OpenNeuro for their contribution in sharing the data. Additionally, we extend our gratitude to Professor Jeremy Hall and Liana Romaniuk for sharing the data.

References

Aguilar-Ortiz, S., Salgado-Pineda, P., Marco-Pallarés, J., Pascual, J. C., Vega, D., & Soler, J., et al. (2018). Abnormalities in gray matter volume in patients with borderline personality disorder and their relation to lifetime depression: A VBM study. *Plos One, 13*(2), e0191946. [DOI:10.1371/journal.pone.0191946] [PMID]

Ansell, E. B., Sanislow, C. A., McGlashan, T. H., & Grilo, C. M. (2007). Psychosocial impairment and treatment utilization by patients with borderline personality disorder, other personality disorders, mood and anxiety disorders, and a healthy comparison group. *Comprehensive Psychiatry, 48*(4), 329-336. [DOI:10.1016/j.comppsych.2007.02.001] [PMID]

Ashburner, J., & Friston, K. J. (2005). Unified segmentation. *Neuroimage, 26*(3), 839-851. [DOI:10.1016/j.neuroimage.2005.02.018] [PMID]

Baczkowski, B. M., van Zutphen, L., Siep, N., Jacob, G. A., Domes, G., & Maier, S., et al. (2017). Deficient amygdala-prefrontal intrinsic connectivity after effortful emotion regulation in borderline personality disorder. *European Archives of Psychiatry and Clinical Neuroscience, 267*(6), 551–565. [DOI:10.1007/s00406-016-0760-z] [PMID]

Bateman, A., & Fonagy, P. (2008). 8-year follow-up of patients treated for borderline personality disorder: Mentalization-based treatment versus treatment as usual. *The American Journal of Psychiatry, 165*(5), 631–638. [DOI:10.1176/appi.ajp.2007.07040636] [PMID]

Beauchaine, T. P., & Crowell, S. E. (2020). *The Oxford handbook of emotion dysregulation*. Oxford: Oxford University Press. [DOI:10.1093/oxfordhb/9780190689285.001.0001]

Brambilla, P., Soloff, P. H., Sala, M., Nicoletti, M. A., Keshavan, M. S., & Soares, J. C. (2004). Anatomical MRI study of borderline personality disorder patients. *Psychiatry Research, 131*(2), 125–133. [DOI:10.1016/j.pscychresns.2004.04.003] [PMID]

Brunner, R., Henze, R., Parzer, P., Kramer, J., Feigl, N., & Lutz, K., et al. (2010). Reduced prefrontal and orbitofrontal gray matter in female adolescents with borderline personality disorder: is it disorder specific? *Neuroimage, 49*(1), 114-120. [DOI:10.1016/j.neuroimage.2009.07.070] [PMID]

Cattane, N., Rossi, R., Lanfredi, M., & Cattaneo, A. (2017). Borderline personality disorder and childhood trauma: Exploring the affected biological systems and mechanisms. *BMC Psychiatry, 17*(1), 221. [DOI:10.1186/s12888-017-1383-2] [PMID]

Chanen, A. M., Velakoulis, D., Carison, K., Gaunson, K., Wood, S. J., & Yuen, H. P., et al. (2008). Orbitofrontal, amygdala and hippocampal volumes in teenagers with first-presentation borderline personality disorder. *Psychiatry Research, 163*(2), 116–125. [DOI:10.1016/j.pscychresns.2007.08.007] [PMID]

Chapman, J., Jamil, R. T., Fleisher, C., Torrico, T. J. Borderline personality disorder. [Updated 2024 Apr 20]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-. Available from: [Link]

Cullen, K. R., Vizueta, N., Thomas, K. M., Han, G. J., Lim, K. O., & Camchong, J., et al. (2011). Amygdala functional connectivity in young women with borderline personality disorder. *Brain Connectivity, 1*(1), 61–71. [DOI:10.1089/brain.2010.0001] [PMID]

Dannlowski, U., Stuhrmann, A., Beutelmann, V., Zwanzger, P., Lenzen, T., & Grotegerd, D., et al. (2012). Limbic scars: Long-term consequences of childhood maltreatment revealed by functional and structural magnetic resonance imaging. Biological Psychiatry, 71(4), 286-293. [DOI:10.1016/j.biopsych.2011.10.021] [PMID]

Dodell-Feder, D., Koster-Hale, J., Bedny, M., & Saxe, R. (2011). fMRI item analysis in a theory of mind task. *Neuroimage, 55*(2), 705-712. [DOI:10.1016/j.neuroimage.2010.12.040] [PMID]

Donges, U. S., Dukalski, B., & Suslow, T. (2016). Borderline personality disorder and automatic processing of valence and self-other relevance information. *Psychopathology, 49*(2), 116-123. [DOI:10.1159/000445804] [PMID]

Driessen, M., Herrmann, J., Stahl, K., Zwaan, M., Meier, S., & Hill, A., et al. (2000). Magnetic resonance imaging volumes of the hippocampus and the amygdala in women with borderline personality disorder and early traumatization. *Archives of General Psychiatry, 57*(12), 1115–1122. [DOI:10.1001/archpsyc.57.12.1115] [PMID]

Dziobek, I., Preißler, S., Grozdanovic, Z., Heuser, I., Heekeren, H. R., & Roepke, S. (2011). Neuronal correlates of altered empathy and social cognition in borderline personality disorder. *Neuroimage, 57*(2), 539-548. [DOI:10.1016/j.neuroimage.2011.05.005] [PMID]

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders. Washington, D.C: American Psychiatric Association. [Link]

Enzi, B., Doering, S., Faber, C., Hinrichs, J., Bahmer, J., & Northoff, G. (2013). Reduced deactivation in reward circuitry and midline structures during emotion processing in borderline personality disorder. *The World Journal of Biological Psychiatry, 14*(1), 45-56. [DOI:10.3109/15622975.2011.579162] [PMID]

Gaser, C., Dahnke, R., Thompson, P. M., Kurth, F., Luders, E., & The Alzheimer's disease neuroimaging initiative (2024). CAT: A computational anatomy toolbox for the analysis of structural MRI data. *GigaScience, 13,* giae049. [DOI:10.1093/gigascience/giae049] [PMID]

Goldman, S. J., D'Angelo, E. J., DeMaso, D. R., & Mezzacappa, E. (1992). Physical and sexual abuse histories among children with borderline personality disorder. *The American Journal of Psychiatry, 149*(12), 1723–1726. [DOI:10.1176/ajp.149.12.1723] [PMID]

Goodman, M., Hazlett, E. A., Avedon, J. B., Siever, D. R., Chu, K. W., & New, A. S. (2011). Anterior cingulate volume reduction in adolescents with borderline personality disorder and co-morbid major depression. *Journal of Psychiatric Research, 45*(6), 803–807. [DOI:10.1016/j.jpsychires.2010.11.011] [PMID]

Gratz, K. L., Moore, K. E., & Tull, M. T. (2016). The role of emotion dysregulation in the presence, associated difficulties, and treatment of borderline personality disorder. *Personality Disorders, 7*(4), 344-353. [DOI:10.1037/per0000198] [PMID]

Gratz, K. L., Rosenthal, M. Z., Tull, M. T., Lejuez, C., & Gunderson, J. G. (2010). An experimental investigation of emotional reactivity and delayed emotional recovery in borderline personality disorder: The role of shame. *Comprehensive Psychiatry, 51*(3), 275-285. [DOI:10.1016/j.comppsych.2009.08.005] [PMID]

Irle, E., Lange, C., & Sachsse, U. (2005). Reduced size and abnormal asymmetry of parietal cortex in women with borderline personality disorder. *Biological Psychiatry, 57*(2), 173–182. [DOI:10.1016/j.biopsych.2004.10.004] [PMID]

Jin, X., Zhong, M., Yao, S., Cao, X., Tan, C., & Gan, J., et al. (2016). A Voxel-Based Morphometric MRI Study in Young Adults with Borderline Personality Disorder. *Plos One, 11*(1), e0147938. [DOI:10.1371/journal.pone.0147938] [PMID]

Kober, H., Barrett, L. F., Joseph, J., Bliss-Moreau, E., Lindquist, K., & Wager, T. D. (2008). Functional grouping and cortical-subcortical interactions in emotion: A meta-analysis of neuroimaging studies. *Neuroimage, 42*(2), 998-1031. [DOI:10.1016/j.neuroimage.2008.03.059] [PMID]

Korzekwa, M. I., Dell, P. F., Links, P. S., Thabane, L., & Webb, S. P. (2008). Estimating the prevalence of borderline personality disorder in psychiatric outpatients using a two-phase procedure. *Comprehensive Psychiatry, 49*(4), 380-386. [DOI:10.1016/j.comppsych.2008.01.007] [PMID]

Krause-Utz, A., Veer, I. M., Rombouts, S. A., Bohus, M., Schmahl, C., & Elzinga, B. M. (2014). Amygdala and anterior cingulate resting-state functional connectivity in borderline personality disorder patients with a history of interpersonal trauma. *Psychological Medicine, 44*(13), 2889–2901. [DOI:10.1017/s0033291714000324] [PMID]

Kreisel, S. H., Labudda, K., Kurlandchikov, O., Beblo, T., Mertens, M., & Thomas, C., et al. (2015). Volume of hippocampal substructures in borderline personality disorder. *Psychiatry Research, 231*(3), 218–226. [DOI:10.1016/j.pscychresns.2014.11.010] [PMID]

Kuhlmann, A., Bertsch, K., Schmidinger, I., Thomann, P. A., & Herpertz, S. C. (2013). Morphometric differences in central stress-regulating structures between women with and without borderline personality disorder. *Journal of Psychiatry & Neuroscience: JPN, 38*(2), 129–137. [DOI:10.1503/jpn.120039] [PMID]

Kumar, P., Waiter, G., Ahearn, T., Milders, M., Reid, I., & Steele, J. D. (2009). Frontal operculum temporal difference signals and social motor response learning. *Human Brain Mapping, 30*(5), 1421-1430. [DOI:10.1002/hbm.20611] [PMID]

Labudda, K., Kreisel, S., Beblo, T., Mertens, M., Kurlandchikov, O., & Bien, C. G., et al. (2013). Mesiotemporal volume loss associated with disorder severity: A VBM study in borderline personality disorder. *Plos One, 8*(12), e83677. [DOI:10.1371/journal.pone.0083677] [PMID]

Leichsenring, F., Leibing, E., Kruse, J., New, A. S., & Leweke, F. (2011). Borderline personality disorder. *The Lancet, 377*(9759), 74-84. [DOI:10.1016/S0140-6736(10)61422-5] [PMID]

Ludäscher, P., Greffrath, W., Schmahl, C., Kleindienst, N., Kraus, A., & Baumgärtner, U., et al. (2009). A cross-sectional investigation of discontinuation of self-injury and normalizing pain perception in patients with borderline personality disorder. *Acta Psychiatrica Scandinavica, 120*(1), 62-70. [DOI:10.1111/j.1600-0447.2008.01335.x] [PMID]

Lyoo, I. K., Han, M. H., & Cho, D. Y. (1998). A brain MRI study in subjects with borderline personality disorder. *Journal of Affective Disorders, 50*(2-3), 235–243. [DOI:10.1016/s0165-0327(98)00104-9] [PMID]

Maffei, C., & Fusi, V. (2016). Emotion dysregulation in borderline personality disorder: A literature review. *Phenomenology and Mind, (11),* 210-220. [DOI:10.13128/Phe_Mi-20120]

McLean, L. M., & Gallop, R. (2003). Implications of childhood sexual abuse for adult borderline personality disorder and complex posttraumatic stress disorder. *The American Journal of Psychiatry, 160*(2), 369–371. [DOI:10.1176/appi.ajp.160.2.369] [PMID]

Mechelli, A., Price, C. J., Friston, K. J., & Ashburner, J. (2005). Voxel-based morphometry of the human brain: Methods and applications. *Current Medical Imaging, 1*(2), 105-113. [DOI:10.2174/1573405054038726]

Michel, C. A., Schneck, N., Mann, J. J., Ochsner, K. N., Brodsky, B. S., & Stanley, B. (2024). Prefrontal cortex engagement during an fMRI task of emotion regulation as a potential predictor of treatment response in borderline personality disorder. *Journal of Affective Disorders, 364,* 240-248. [DOI:10.1016/j.jad.2024.08.041] [PMID]

Minzenberg, M. J., Fan, J., New, A. S., Tang, C. Y., & Siever, L. J. (2008). Frontolimbic structural changes in borderline personality disorder. *Journal of Psychiatric Research, 42*(9), 727–733. [DOI:10.1016/j.jpsychires.2007.07.015] [PMID]

Morfini, F., Whitfield-Gabrieli, S., & Nieto-Castañón, A. (2023). Functional connectivity MRI quality control procedures in CONN. *Frontiers in Neuroscience, 17,* 1092125. [DOI:10.3389/fnins.2023.1092125] [PMID]

Mulert, C., & Shenton, M. E. (2014). *MRI in Psychiatry*. Berlin: Springer. [DOI:10.1007/978-3-642-54542-9]

Nemoto, K. (2017). [Understanding voxel-based morphometry (Japanese)]. *Brain and Nerve= Shinkei kenkyu no shinpo, 69*(5), 505-511. [PMID]

Nenadić, I., Voss, A., Besteher, B., Langbein, K., & Gaser, C. (2020). Brain structure and symptom dimensions in borderline personality disorder. *European Psychiatry, 63*(1), e9. [DOI:10.1192/j.eurpsy.2019.16] [PMID]

New, A. S., Hazlett, E. A., Buchsbaum, M. S., Goodman, M., Mitelman, S. A., & Newmark, R., et al. (2007). Amygdala-prefrontal disconnection in borderline personality disorder. *Neuropsychopharmacology, 32*(7), 1629-1640. [DOI:10.1038/sj.npp.1301283] [PMID]

Niedtfeld, I., Kirsch, P., Schulze, L., Herpertz, S. C., Bohus, M., & Schmahl, C. (2012). Functional connectivity of pain-mediated affect regulation in borderline personality disorder. *Plos One, 7*(3), e33293. [DOI:10.1371/journal.pone.0033293] [PMID]

Noor, L., Hoffmann, J., Meller, T., Gaser, C., & Nenadić, I. (2024). Amygdala functional connectivity in borderline personality disorder. *Psychiatry Research. Neuroimaging, 340,* 111808. [DOI:10.1016/j.pscychresns.2024.111808] [PMID]

Nunes, P. M., Wenzel, A., Borges, K. T., Porto, C. R., Caminha, R. M., & de Oliveira, I. R. (2009). Volumes of the hippocampus and amygdala in patients with borderline personality disorder: A meta-analysis. *Journal of Personality Disorders, 23*(4), 333–345. [DOI:10.1521/pedi.2009.23.4.333] [PMID]

O'Neill, A., D'Souza, A., Samson, A. C., Carballedo, A., Kerskens, C., & Frodl, T. (2015). Dysregulation between emotion and theory of mind networks in borderline personality disorder. *Psychiatry Research, 231*(1), 25-32. [DOI:10.1016/j.pscychresns.2014.11.002] [PMID]

Reichenberger, J., Eibl, J. J., Pfaltz, M., Wilhelm, F. H., Voderholzer, U., & Hillert, A., et al. (2017). Don't praise me, don't chase me: Emotional reactivity to positive and negative social-evaluative videos in patients with borderline personality disorder. *Journal of Personality Disorders, 31*(1), 75-89. [DOI:10.1521/pedi_2016_30_238] [PMID]

Rodrigues, E., Wenzel, A., Ribeiro, M. P., Quarantini, L. C., Miranda-Scippa, A., & de Sena, E. P., et al. (2011). Hippocampal volume in borderline personality disorder with and without comorbid posttraumatic stress disorder: A meta-analysis. *European Psychiatry, 26*(7), 452-456. [DOI:10.1016/j.eurpsy.2010.07.005] [PMID]

Ruocco, A. C., Amirthavasagam, S., & Zakzanis, K. K. (2012). Amygdala and hippocampal volume reductions as candidate endophenotypes for borderline personality disorder: A meta-analysis of magnetic resonance imaging studies. *Psychiatry Research, 201*(3), 245–252. [DOI:10.1016/j.pscychresns.2012.02.012] [PMID]

Rüsch, N., van Elst, L. T., Ludaescher, P., Wilke, M., Huppertz, H. J., & Thiel, T., et al. (2003). A voxel-based morphometric MRI study in female patients with borderline personality disorder. *Neuroimage, 20*(1), 385-392. [DOI:10.1016/s1053-8119(03)00297-0] [PMID]

Sala, M., Caverzasi, E., Lazzaretti, M., Morandotti, N., De Vidovich, G., & Marraffini, E., et al. (2011). Dorsolateral prefrontal cortex and hippocampus sustain impulsivity and aggressiveness in borderline personality disorder. *Journal of Affective Disorders, 131*(1-3), 417-421. [DOI:10.1016/j.jad.2010.11.036] [PMID]

Salsman, N. L., & Linehan, M. M. (2012). An investigation of the relationships among negative affect, difficulties in emotion regulation, and features of borderline personality disorder. *Journal of Psychopathology and Behavioral Assessment, 34*(2), 260-267. [DOI:10.1007/s10862-012-9275-8]

Sato, J. R., de Araujo Filho, G. M., de Araujo, T. B., Bressan, R. A., de Oliveira, P. P., & Jackowski, A. P. (2012). Can neuroimaging be used as a support to diagnosis of borderline personality disorder? An approach based on computational neuroanatomy and machine learning. *Journal of Psychiatric Research, 46*(9), 1126-1132. [DOI:10.1016/j.jpsychires.2012.05.008] [PMID]

Saxe, R., & Wexler, A. (2005). Making sense of another mind: The role of the right temporo-parietal junction. *Neuropsychologia, 43*(10), 1391-1399. [DOI:10.1016/j.neuropsychologia.2005.02.013] [PMID]

Scheiderer, E. M., Wang, T., Tomko, R. L., Wood, P. K., & Trull, T. J. (2016). Negative affect instability among individuals with comorbid borderline personality disorder and posttraumatic stress disorder. *Clinical Psychological Science, 4*(1), 67-81. [DOI:10.1177/2167702615573214] [PMID]

Schmahl, C., Berne, K., Krause, A., Kleindienst, N., Valerius, G., Vermetten, E., & Bohus, M. (2009). Hippocampus and amygdala volumes in patients with borderline personality disorder with or without posttraumatic stress disorder. *Journal of Psychiatry & Neuroscience: JPN, 34*(4), 289–295. [DOI:10.1139/jpn.0938] [PMID]

Schmahl, C. G., Vermetten, E., Elzinga, B. M., & Bremner, J. (2003). Magnetic resonance imaging of hippocampal and amygdala volume in women with childhood abuse and borderline personality disorder. *Psychiatry Research, 122*(3), 193-198. [DOI:10.1016/S0925-4927(03)00023-4] [PMID]

Schulze, L., Domes, G., Krüger, A., Berger, C., & Fleischer, M., Prehn, K., et al. (2011). Neuronal correlates of cognitive reappraisal in borderline patients with affective instability. *Biological Psychiatry, 69*(6), 564-573. [DOI:10.1016/j.biopsych.2010.10.025] [PMID]

Schulze, L., Schmahl, C., & Niedtfeld, I. (2016). Neural correlates of disturbed emotion processing in borderline personality disorder: A multimodal meta-analysis. *Biological Psychiatry, 79*(2), 97–106. [DOI:10.1016/j.biopsych.2015.03.027] [PMID]

Schulze, L., Schulze, A., Renneberg, B., Schmahl, C., & Niedtfeld, I. (2019). Neural correlates of affective disturbances: a comparative meta-analysis of negative affect processing in borderline personality disorder, major depressive disorder, and posttraumatic stress disorder. *Biological Psychiatry. Cognitive Neuroscience and Neuroimaging, 4*(3), 220–232. [DOI:10.1016/j.bpsc.2018.11.004] [PMID]

Shafie, M., Shahmohamadi, E., Cattarinussi, G., Sanjari Moghaddam, H., Akhondzadeh, S., & Sambataro, F., et al. (2023). Resting-state functional magnetic resonance imaging alterations in borderline personality disorder: A systematic review. *Journal of Affective Disorders, 341,* 335–345. [DOI:10.1016/j.jad.2023.09.001] [PMID]

Soloff, P., Nutche, J., Goradia, D., & Diwadkar, V. (2008). Structural brain abnormalities in borderline personality disorder: A voxel-based morphometry study. *Psychiatry Research, 164*(3), 223–236. [DOI:10.1016/j.pscychresns.2008.02.003] [PMID]

Stanley, B., & Wilson, S. T. (2006). Heightened subjective experience of depression in borderline personality disorder. *Journal of Personality Disorders, 20*(4), 307–318. [DOI:10.1521/pedi.2006.20.4.307] [PMID]

Stopyra, M. A., Simon, J. J., Rheude, C., & Nikendei, C. (2022). Pathophysiological aspects of complex PTSD - a neurobiological account in comparison to classic posttraumatic stress disorder and borderline personality disorder. *Reviews in The Neurosciences, 34*(1), 103–128. [DOI:10.1515/revneuro-2022-0014] [PMID]

Tebartz van Elst, L., Hesslinger, B., Thiel, T., Geiger, E., Haegele, K., & Lemieux, L., et al. (2003). Frontolimbic brain abnormalities in patients with borderline personality disorder: A volumetric magnetic resonance imaging study. *Biological Psychiatry, 54*(2), 163–171. [DOI:10.1016/s0006-3223(02)01743-2] [PMID]

Teicher, M. H., Anderson, C. M., & Polcari, A. (2012). Childhood maltreatment is associated with reduced volume in the hippocampal subfields CA3, dentate gyrus, and subiculum. *Proceedings of the National Academy of Sciences of the United States of America, 109*(9), E563–E572. [DOI:10.1073/pnas.1115396109] [PMID]

Trull, T. J., Jahng, S., Tomko, R. L., Wood, P. K., & Sher, K. J. (2010). Revised NESARC personality disorder diagnoses: Gender, prevalence, and comorbidity with substance dependence disorders. *Journal of Personality Disorders, 24*(4), 412-426. [DOI:10.1521/pedi.2010.24.4.412] [PMID]

Visintin, E., De Panfilis, C., Amore, M., Balestrieri, M., Wolf, R. C., & Sambataro, F. (2016). Mapping the brain correlates of borderline personality disorder: A functional neuroimaging meta-analysis of resting state studies. *Journal of Affective Disorders, 204,* 262–269. [DOI:10.1016/j.jad.2016.07.025] [PMID]

Völlm, B. A., Zhao, L., Richardson, P., Clark, L., Deakin, J. F., & Williams, S., et al. (2009). A voxel-based morphometric MRI study in men with borderline personality disorder: Preliminary findings. *Criminal Behaviour and Mental Health: CBMH, 19*(1), 64–72. [DOI:10.1002/cbm.716] [PMID]

Weniger, G., Lange, C., Sachsse, U., & Irle, E. (2009). Reduced amygdala and hippocampus size in trauma-exposed women with borderline personality disorder and without posttraumatic stress disorder. *Journal of Psychiatry & Neuroscience: JPN, 34*(5), 383–388. [DOI:10.1139/jpn.0950] [PMID]

Westlund Schreiner, M., Klimes-Dougan, B., Mueller, B. A., Eberly, L. E., Reigstad, K. M., & Carstedt, P. A., et al. (2017). Multi-modal neuroimaging of adolescents with non-suicidal self-injury: Amygdala functional connectivity. *Journal of Affective Disorders, 221,* 47–55. [DOI:10.1016/j.jad.2017.06.004] [PMID]

Westlund Schreiner, M., Klimes-Dougan, B., Mueller, B. A., Nelson, K. J., Lim, K. O., & Cullen, K. R. (2019). Neurocircuitry associated with symptom dimensions at baseline and with change in borderline personality disorder. *Psychiatry Research. Neuroimaging, 290,* 58–65. [DOI:10.1016/j.pscychresns.2019.07.001] [PMID]

Whitfield-Gabrieli, S., & Nieto-Castanon, A. (2012). Conn: A functional connectivity toolbox for correlated and anticorrelated brain networks. *Brain connectivity, 2*(3), 125-141. [DOI:10.1089/brain.2012.0073] [PMID]

Williams, K. D., Cheung, C. K., & Choi, W. (2000). Cyberostracism: effects of being ignored over the Internet. *Journal of Personality and Social Psychology, 79*(5), 748-762. [DOI:10.1037/0022-3514.79.5.748] [PMID]

Xiao, Q., Fu, Y., Yi, X., Ding, J., Han, Z., & Zhang, Z., et al. (2023). Altered cortical thickness and emotional dysregulation in adolescents with borderline personality disorder. *European Journal of Psychotraumatology, 14*(1), 2163768. [DOI:10.1080/20008066.2022.2163768] [PMID]

Xu, T., Cullen, K. R., Mueller, B., Schreiner, M. W., Lim, K. O., & Schulz, S. C., et al. (2016). Network analysis of functional brain connectivity in borderline personality disorder using resting-state fMRI. *NeuroImage. Clinical, 11,* 302–315. [DOI:10.1016/j.nicl.2016.02.006] [PMID]

Zetzsche, T., Frodl, T., Preuss, U. W., Schmitt, G., Seifert, D., & Leinsinger, G., et al. (2006). Amygdala volume and depressive symptoms in patients with borderline personality disorder. *Biological Psychiatry, 60*(3), 302–310. [DOI:10.1016/j.biopsych.2005.11.020] [PMID]

Zetzsche, T., Preuss, U. W., Frodl, T., Schmitt, G., Seifert, D., & Münchhausen, E., et al. (2007). Hippocampal volume reduction and history of aggressive behaviour in patients with borderline personality disorder. *Psychiatry Research, 154*(2), 157–170. [DOI:10.1016/j.pscychresns.2006.05.010] [PMID]

Zhang, J., Zhao, T., Zhang, J., Zhang, Z., Li, H., & Cheng, B., et al. (2022). Prediction of childhood maltreatment and subtypes with personalized functional connectome of large-scale brain networks. *Human Brain Mapping, 43*(15), 4710-4721. [DOI:10.1002/hbm.25985] [PMID]

This Page Intentionally Left Blank