

Structural Brain Alterations in Borderline Personality Disorder

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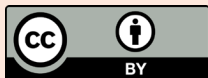
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ABSTRACT

Borderline personality disorder (BPD) is one of three clusters of personality disorders characterized by a pattern of difficulty regulating emotion, impulse control, interpersonal relationships, and self-image. Emotional dysregulation, impulsive aggression, repetitive self-injury, and chronic suicidal tendencies make these individuals frequent users of mental health services. BPD has a variety of causes and involves several factors which interact in various ways with each other. Emotional dysregulation and impulsivity can be caused by genetic factors and traumatic childhood experiences and lead to dysfunctional behaviors, psychosocial conflicts, and deficits that may exacerbate emotional dysregulation and impulsivity. BPD has been linked to anatomical alterations in brain areas in the prefrontal cortex, cingulate cortex, hippocampus, amygdala, hypothalamus, corpus callosum, and frontolimbic network. These brain changes can lead to the manifestation of the inability to control behavior, feelings, and interpersonal relationships, which often leads to violence. These symptoms may begin at a young age or in early adulthood and tend to continue as the individual ages. The goal of this article is to review how structural changes in the brain can cause BPD.

KEYWORDS Borderline personality disorder, MRI in BPD, BPD patients, personality disorders, structural imaging BPD, neurobiology BPD

OVERVIEW

Personality disorders (PD) are defined by persistent patterns of behavior and inner experiences that significantly deviate from what is expected of a person in their society. These recurring, inflexible behaviors start in adolescence or young adulthood and typically don't change over time. Characteristics of personality disorders include that they also cause distress or impairment. Based on descriptive similarities, the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5's classification of PD divides them into three clusters (A, B, and C). Cluster A: An individual with this kind behaves in a way that others consider unusual or eccentric. It includes paranoid, schizoid, and schizotypal

personality disorders. Cluster B: An individual with this characteristic has difficulties regulating their emotions and behavior. Borderline personality disorder (BPD) is one of four Cluster B disorders that also include borderline, antisocial, histrionic, and narcissistic personality disorders. Cluster C: An individual with this characteristic behaves in anxious or avoidant ways. Three disorders in this cluster are avoidant, dependent, and obsessive-compulsive personality disorders (1,2). BPD is a complex psychological condition characterized by instability in a wide variety of life domains due to neurological deficits as well as a variety of symptoms such as affective hyperreactivity, self-concept instability, emotional dysfunction, and social relationship

difficulties (3). Over the past few decades, structural and functional MRI investigations have been used to look for possible organic abnormalities supporting the emotionally intense behavioral manifestations of BPD (4). This article focused on the structural changes in neurological regions of BPD patients in order to learn more about the brain abnormalities that affect BPD patients.

BORDERLINE PERSONALITY DISORDER (BPD) SYMPTOMS

BPD is a psychiatric condition that causes emotional instability. The individual's mood is unpredictable and capricious, with a distinct predisposition to behave impulsively and without awareness of the consequences. There is a potential for outbursts of emotion and an incapacity to control behavioral explosions. There is a tendency for quarrelsome behavior and for conflicts with others, especially when impulsive acts are thwarted or censored. Two types may be distinguished: the impulsive type, characterized predominantly by emotional instability and lack of impulse control, and the borderline type, characterized in addition to the above by disturbances in self-image, aims, and internal preferences, by chronic feelings of emptiness, by intense and unstable interpersonal relationships, and by a tendency to self-destructive behavior, including suicide gestures and attempts, according to ICD-10, F-60.3, version 2019 (5). Intimate relationships easily elicit emotions of being misunderstood and even victimized, as well as increased fear of abandonment. BPD is generally linked to problems with emotion processing and control, as evidenced by rapidly changing, intense, unpredictable, and reactive emotions, such as anxiety, anger, or depression. Emotional hyperactivity is linked to various high-risk behaviors and deliberate acts, including substance abuse, self-harm, suicide attempts, and high suicide rates and affects 1–2 percent of the general population and 15–20 percent in psychiatric settings (6). This behavioral response is typically exhibited in situations where there has been a sense of distress, anger, dysphoria, and feelings of abandonment (7). It is frequently preceded by a life experienced in a harmful and traumatizing environment, such as a lack of

nurture, absence of parental affection, a high level of parental denial, repeated or chronic physical problems, and sexual and emotional abuse prior to adulthood (8). Adults with BPD frequently lack the skills required to figure out how to deal with daily emotionally stressful events, maintain stable relationships, and develop a strong self-concept and identity, leading to distress intolerance and a variety of problematic behaviors to escape or avoid emotions, such as self-harm (9). In a society of contingencies where social and intergenerational issues are on the increase, relationships have deteriorated, and family situations are becoming more unstable. As a consequence, the developmental psychobiological features of this condition must be considered in the context of pre-existing susceptibility, developmental impacts in childhood, society, lifestyle, and cultural behavior patterns (10).

Epidemiology

The most common personality disorder is BPD. It was estimated to have a point prevalence of 1.6 percent in the general population, with a lifetime prevalence of 5.9 percent (11,12). Clinical studies found that BPD was present in 6.4 percent of urban primary care patients, 9.3 percent of psychiatric outpatients, and approximately 20 percent of psychiatric inpatients (13–15). In clinical settings, the ratio of females to males with the disorder is higher than in the general population (3:1) (14). However, two epidemiological studies of the general population in the United States found no significant differences in the lifetime prevalence of BPD between men and women (11,12). This difference indicates that women with BPD are more likely than men to seek therapy. Men and women with BPD were found to have similar rates of childhood abuse history and levels of present psychosocial functioning (16). The National Alliance on Mental Illness (NAMI) estimated that 1.4 percent of the adult U.S. population experiences BPD. Nearly 75 percent of people diagnosed with BPD are women. Recent research suggests that men may be equally affected by BPD, but are commonly misdiagnosed with post-traumatic stress disorder (PTSD) or depression (17).

Etiology

BPD can be caused by a variety of factors. One factor is a genetic predisposition. Familial and twin studies have reported an estimated heritability of approximately 40 percent, strongly supporting the potential role of a genetic vulnerability at the root of BPD (18). According to two studies, the concordance rate for BPD was found to be higher in monozygotic twins compared with dizygotic twins (36 and 35 percent versus 19 and 7 percent) (19). In studies of Swedish individuals aged 20 years old, the hazard ratio was 11.5 (95% confidence interval (CI) = 1.6–83.8) for monozygotic twins and 7.4 (95% CI = 1.0–55.3) for dizygotic twins (20). Environmental variables linked to the development of BPD have been identified. Childhood maltreatment (physical, sexual, or neglect) affects up to 70 percent of people with BPD, as do maternal separation, insufficient maternal attachment, unsuitable family boundaries, parental substance abuse, and extensive parental psychopathology (21,22). Neuroimaging studies have identified that patients with BPD show abnormalities in the prefrontal cortex, amygdala, hippocampus, and medial temporal lobes, including frontolimbic network dysfunction as shown in Tables 1–3.

NEUROANATOMICAL FEATURES OF BPD

Brain structural abnormalities have been identified in areas associated with BPD symptoms and theoretical principles. As the amygdala is involved in emotion processing and fear responses, these findings are compatible with the neurologically-based theory of BPD. Patients with a history of childhood abuse had significantly reduced hippocampus volumes, emphasizing the heterogeneity of BPD and the importance of considering individual variances in the factors involved. Frontal area and amygdala defects have also been identified in BPD patients (23). The disorder's impairments in emotion regulation and impulse control may be connected to abnormalities in various portions of gray matter, white matter, and other brain areas in BPD patients as shown in Tables 1–3.

Gray matter and Frontolimbic Network

Alterations of gray matter areas of the brain are shown in Tables 1–2. The most consistent structural imaging finding in adults with BPD is a reduction in metabolic activation at the gray matter regions and volume in the anterior cingulate cortex (ACC), hippocampus, amygdala, and orbitofrontal cortex. This supports the theory that the limbic and prefrontal brain areas perform related functions (frontolimbic network) (24,25). The anterior cingulate cortex (ACC), the orbitofrontal cortex (OFC), the dorsolateral prefrontal cortex (DLPFC), the hippocampus, and the amygdala are all components of the frontolimbic network (26). In accordance with these anatomical changes, Ruocco et al. found that additional limbic areas such as the insula, the left temporal gyrus, and the dorsolateral prefrontal cortex had greater functional activity in BPD (27). Emotions (e.g., fear, anxiety, and anger) and behavioral impulse management are modulated and controlled by the frontolimbic network. According to Ninomiya et al. using tract-based spatial statistics (TBSS), the BPD group had three clusters that were significantly lower in axial diffusivity (AD) than the healthy control group (HC). One of these clusters was mainly in the cingulum, while the other two clusters were mainly in the inferior front-occipital and inferior longitudinal fasciculi. Regarding the AD values, one cluster was found in the cingulum and had a substantial negative correlation that was significantly associated with profile of mood states (POMS) (depression), while another cluster had a strong positive correlation with depression and anxiety cognitive scale (DACS) (future denial) and was situated in the inferior fronto-occipital fasciculus (IFOF) (3). Neuroimaging research has provided evidence of gray matter changes in the prefrontal-limbic network in BPD (10) (Table 1). The studies included 3 groups of females (age range 14–18 years): those with a diagnosis of BPD, a defined current psychiatric disorder, and healthy controls (HC). The study found that adolescent clinical control subjects displayed significantly decreased gray matter volume in the right DLPFC in comparison with the healthy control subjects. Between the BPD group and the clinical control group, no significant changes

Table 1. Studies of MRI-investigated brain alterations in BPD by year of publication (2016–2021)

Authors /year of publication	Brain areas	Alterations
Sampedro et al. (29), 2021	– Prefrontal cortex – Amygdala – Parahippocampal regions	Patients with BPD showed a reduced GM volume in the prefrontal areas but increased GM volume in the amygdala and parahippocampal regions
Lou et al. (30), 2021	– Orbitofrontal cortex – Anterior cingulate cortex – Posterior cingulate cortex (PCC)	GM volume reductions in the orbitofrontal gyrus and ACC but increases in the PCC and precuneus in BPD patients
Kelleher–Unger et al. (52), 2021	– Corpus callosum – Fornix	Reduced FA in the CC and fornix in BPD patients
Gosnell et al. (46), 2020	– Hippocampus – Amygdala	BPD patients had significant changes: smaller right hippocampus and amygdala than HC
Nenadić et al. (44), 2020	– Orbitofrontal cortex – Hippocampus	Group comparison between female BPD patients and healthy female controls showed bilateral orbitofrontal gray matter loss in BPD patients, but no significant changes in the hippocampus
Vandekerckhove et al. (10), 2020	– Corpus callosum – Inferior longitudinal fasciculus (ILF) – Superior longitudinal fasciculus (SLF)	– Lower FA values for both the left and the right cingulum, the genu, body, and splenium of the CC, left ILF, and right SLF were found in BPD compared to healthy individuals – MD values were higher for the genu and splenium of the CC in BPD
Lischke et al. (25), 2017	– Corpus callosum	Female BPD patients exhibiting suicidal behavior showed less FA and more MD in the splenium and genu of the CC than the HC group but non-suicidal BPD patients showed FA and MD in these regions similar to the HC group
Schulze et al. (23), 2016	– Amygdala	Left amygdala hyperactivity was found in unmedicated patients with acute BPD. This feature is consistent with negative environmental stimuli
Kimmel et al. (45), 2016	– Amygdala	Reductions in gray matter volume of the amygdala in older BPD patients

in gray matter were found. There were no differences between the groups in the limbic system or white matter structures. This study indicates that the early morphological changes in BPD are located in the prefrontal cortex (PFC). However, these changes may not be BPD-specific since similar changes were found in the clinical control group. Over the course of the disease, there may also be changes in limbic brain volumes and white matter structures (28) (Table 2). A recent study investigated structural brain abnormalities using voxel-based morphometry (VBM) and cortical thickness (Cth) analyses in a

large sample of patients with BPD: 61 individuals with BPD, and 19 HCs. Compared to controls, the BPD group showed a reduced gray matter volume (GMV)/Cth in prefrontal areas but an increased GMV in the limbic structures (amygdala and parahippocampal regions). Prefrontal anomalies were linked to greater baseline impulsivity and BPD severity scores. Several structural abnormalities (in, e.g., the middle and inferior prefrontal regions, the anterior insula, and the parahippocampal area) were shown to be associated with clinical severity and could be used as imaging biological correlate

biomarkers to predict psychotherapy response (29) (Table 1). A dual meta-analysis of common and distinct gray matter changes in BPD and PTSD revealed that both disorders had similar relative GM volume reductions in the orbitofrontal gyrus and anterior cingulate cortex; however, in BPD subjects, GM volume increased in the posterior cingulate gyrus and precuneus, while in PTSD subjects, GM volume decreased in the amygdala-hippocampal fear circuit and the fusiform gyrus. In BPD and PTSD, group comparisons and conjunction analyses revealed similar areas of GM volume decreases in the orbitofrontal gyrus and anterior cingulate cortex, which might give insight into the neurobiological underpinnings and clinical diagnosis of the two disorders (30) (Table 1).

Hippocampus and amygdala

The alterations of the hippocampus and amygdala are shown in Tables 1–3. Driessen et al. conducted the first investigation into the MRI-based volume of the hippocampus and amygdala, finding a bilateral decrease in the volume of both the hippocampus and the amygdala in women with BPD compared to HC (31). Other studies have confirmed that BPD patients have a decreased hippocampus volume compared to HC (32,33). A significant reduction of 11–17 percent in amygdala volumes was found in BPD patients (34). In addition, BPD patients had a significant 24 percent reduction in the left orbitofrontal cortex and a 26 percent reduction in the right ACC (35). Zetzsche et al. found that individuals with comorbid Major Depressive Disorder (MDD) had greater amygdala volumes than patients without comorbid MDD, suggesting that distinct subgroups of patients with BPD may differ in amygdala size (36). According to research comparing BPD patients to HC, BPD patients showed serotonergic dysfunction and smaller amygdala, hippocampus, and medial temporal lobe sizes (37). The amygdala and hippocampus volumes were found to be reduced in BPD patients with early trauma and PTSD (38) (Table 2). Amygdala hyperactivity is linked to BPD patients' intense and unpredictable emotions. The amygdala's function in interpreting negative environmental stimuli also reflects maladaptive top-down mechanisms

(39). Furthermore, some research suggests that people with BPD have defective amygdala habituation, which means the amygdala is unable to reduce neuronal responses when a negative stimulus is presented repeatedly (40). Those studies found that amygdala activation increased in response to repeated negatively valenced pictures, whereas in HC, amygdala activation decreased. Failure to habituate correlates clinically with higher levels of trait anxiety, aggression, and affective lability (41). The left amygdala showed increased coupling with the dorsolateral prefrontal cortex and ventral striatum in BPD patients compared to controls, suggesting a mechanism for abnormal top-down regulatory control (42). Findings from structural MRI studies suggest that individuals with BPD, compared with people with HC, have decreased volume in brain regions associated with emotion processing and regulation, which include the amygdala, hippocampus, orbitofrontal cortex, and ACC (34,35,43–45) as shown in Tables 1, 3. In recent research, hippocampus and amygdala volumes were compared across four groups based on diagnostic disorders: MDD ($n = 126$), bipolar disorder ($n = 111$), alcohol abuse or dependent disorder (AUD) ($n = 136$), and PTSD ($n = 67$). In addition to the diagnosis, participants in each of these categories had an average of two mental illnesses. A healthy control (HC) group of the same size was matched to each patient group based on demographic (sex, age and racial) factors. The results were that MDD patients had smaller left ($p = 8.79 \times 10^{-3}$) and right ($p = 3.13 \times 10^{-3}$) hippocampal volumes than the HC group, PTSD patients had smaller left ($p = 0.018$) and right ($p = 8.64 \times 10^{-3}$) hippocampal volumes, BPD patients had smaller right hippocampus ($p = 7.90 \times 10^{-3}$) and amygdala ($p = 1.49 \times 10^{-3}$) volumes, and AUD patients had smaller right hippocampus ($p = 0.034$) and amygdala ($p = 0.024$) volumes than HC. There were no differences between the four diagnostic categories and the psychiatric control group (46) (Table 1). Nenadic et al. used voxel-based morphometry on high-resolution magnetic imaging scans of 19 females with BPD and 50 matched female controls and found no significant changes in the hippocampus. The author's reason conclusion is limited primarily

Table 2. Studies of MRI investigated brain alterations in BPD by year of publication (2010–2015)

Authors of publication	Brain areas	Alterations
Lischke et al. (50), 2015	- Cingulum - Uncinate fasciculus	- Structural alterations in the uncinate fasciculus but not in the cingulum of BPD patients - Compared to the HC group, BPD patients showed lower FA and higher RD in the uncinate fasciculus
Kreisel et al. (38), 2015 Niedtfeld et al. (53), 2013	- Hypothalamus - HPA axis	An enlarged hypothalamus and dysregulated HPA axis, and a reduced volume of the amygdala and hippocampus were found in BPD patients with a history of early trauma and posttraumatic stress disorder (PTSD)
Kuhlmann et al. (54), 2013	- Hippocampus - Hypothalamus	The gray matter of patients with BPD was reduced in the hippocampus but increased in the hypothalamus compared with HC. Hypothalamic volume correlated positively with a history of traumatization in patients with BPD
Brunner et al. (28), 2010	- Dorsolateral prefrontal cortex - Orbitofrontal cortex	Adolescents with BPD showed reduced gray matter in the DLPFC bilaterally and in the left OFC compared to HC
Hall et al. (55), 2010	- Hippocampus - Amygdala	- A meta-analysis revealed significant bilateral decreases in hippocampal and amygdala volumes in patients with BPD compared with HC - Meta-regression demonstrated an association between increasing age and reduced hippocampal volumes in BPD

by the small sample size, which, although it is similar to several recent MR morphometry analyses, makes it prone to false positives, especially for correlation analysis in the exploratory section (44) (Table 1). In BPD, the hypothalamic-pituitary-gonadal, thyroid, and adrenal endocrine axes (hypothalamic-pituitary-gonadal, thyroid, and adrenal) have been reported to be dysregulated. There's also evidence of structural and functional alterations in the limbic system, particularly in the amygdala and hippocampus, as well as cortical areas within the corticolimbic system (47).

White matter

The alterations of white matter are shown in Table 1. Despite abundant research on gray matter correlates in BPD, only a few diffusion-tensor imaging (DTI) research studies have been conducted on the white matter neural pathways of BPD. Those studies found abnormalities in fractional anisotropy (FA) and mean diffusion (MD) in the DTI of BPD. The FA is a DTI scalar that represents axonal integrity and is strongly related to fiber integrity. The MD is a measure of the average molecular motion. The size and integrity of cells affect the MD, which

is known to be related to necrosis, edema, and cellularity (48). Some studies show decreased FA in both the uncinate fasciculus (UF) and the occipitofrontal fasciculus (OFF) (26,49,50). Higher traces and lower FA values in the inferior prefrontal and not in posterior prefrontal regions were found in individuals exhibiting BPD-self-injurious behavior. Higher degrees of dysfunctional affect regulation, anger-hostility, dissociative symptoms, and overall psychopathology have been linked to increased MD in the inferior prefrontal white matter (49). In a study of adolescent and adult BPD patients, decreased FA in the left inferior longitudinal fasciculus (ILF), the UF, and the OFF was shown in adolescents, but not in adults (26). In the cingulum and fornix, BPD patients had lower white matter integrity than controls. There were no significant links between FA and childhood trauma measures. However, there was a significant association between FA in the cingulum and clinical symptoms of anger and FA in the fornix with emotional instability and Zanarini rating scale measures of avoidance of abandonment (51). According to research by Lischke et al., structural changes in the CC, the major white matter tract linking functionally related

Table 3. Studies of MRI investigating brain alterations in BPD by year of publication (2007–2009)

Authors/year of publication	Brain areas	Alterations
Koenigsberg et al. (56), 2009	– Orbitofrontal cortex – Ventrolateral cortex – Dorsal anterior cingulate cortex	Hypoactivity in the orbitofrontal cortex, ventrolateral cortex, and dorsal anterior cingulate cortex in BPD patients compared with healthy individuals
Nunes et al. (43), 2009 Tebartz van Elst et al. (34), 2007	– Amygdala	A meta-analysis indicated that the amygdala volume in individuals with BPD was smaller than in HC
Soloff et al. (37), 2008	– Hippocampus – Amygdala – Medial temporal lobe	Serotonergic dysfunction and reductions in the amygdala, hippocampus, and medial temporal lobe volumes in BPD patients
Rüsch et al. (57), 2007	– Corpus callosum – Anterior cingulate cortex	A thinner isthmus of the CC was associated with decreased interhemispheric structural connectivity in both the ACC and fiber tracts that pass through the ACC and connect dorsal areas of the ACC in female patients with BPD
Minzenberg et al. (58), 2007	– Anterior cingulate cortex – Orbitofrontal cortex	Decrease in metabolic activation and volume in the ACC and volume reduction in the medial and orbitofrontal cortex in BPD patients
Zetsche et al. (59), 2007	– Hippocampus	Verified a smaller hippocampal volume in BPD patients compared to HC

brain areas in the two hemispheres, have been linked to emotional instability, impulsivity, and suicidality in various mental illnesses (25). Vandekerckhove et al. showed that BPD patients have lower FA values in the CC, inferior longitudinal fasciculus (ILF), and superior longitudinal fasciculus (SLF) compared to healthy individuals. In BPD, MD values were greater for the CC's genu and splenium. These findings indicate that a large-scale emotional brain network is affected in BPD with alterations in MD and FA of white matter prefrontal-limbic pathways that are involved in emotion processing and emotion regulation (10) (Table 1). In a recent meta-analysis by Kelleher-Unger et al., white-matter changes in BPD were found, with decreased white-matter integrity in the CC and fornix (52) (Table 1).

HYPOTHALAMIC PITUITARY ADRENAL (HPA) AXIS

Patients with BPD are more sensitive to stress, which may be connected to dysfunction of the HPA axis. Several BPD symptoms, including inappropriate and excessive anger, stress-related dissociation, and self-harm, have been linked to abnormalities in the HPA axis, one of the major endocrine stress systems (60). The HPA axis is a critical stress response system, and increasing

evidence shows it is dysfunctional in BPD patients. Maladaptive responses to trauma and stress have been observed in BPD patients, as have increasing levels of stress hormones such as basal cortisol and impaired feedback sensitivity (61,62). Stress sensitivity and reactivity are assumed to have a role in both the development and support of BPD symptomatology, with trauma exposure being a risk factor for development early in life and with acute stress modulating the symptom trajectory. HPA-axis dysfunction in BPD largely mirrors findings demonstrated in PTSD and may represent a valuable neuroendocrine target for diagnostic or treatment response biomarkers, or for which novel treatments can be investigated (62). The study by Drews E, et al. which included thirty-seven meta-analysis studies of BPD patients (n = 803) and controls (n = 1,092), found BPD patients displayed elevated continuous cortisol output and blunted cortisol response following psychosocial challenges (63).

From the many studies mentioned above (shown in Tables 1–3), it was found that structural and functional neuroimaging revealed a dysfunctional network of brain regions that seem to mediate important aspects of BPD symptomatology. MRI has shown reduced gray matter volume in the anterior cingulate cortex

as well as the orbitofrontal and the dorsolateral prefrontal cortex. The early morphological changes in BPD are located in the prefrontal cortex, which also has a smaller volume of the amygdala and hippocampus than HC but an increase in the hypothalamus compared with healthy participants. The enlarged hypothalamus was correlated positively in BPD with a history of traumatization in PTSD patients. In comparison to healthy individuals, lower FA values of the right and left cingulum, the genu, body, and splenium of the CC, left ILF, and right SLF were found in BPD. MD values were higher in the genu and splenium of the CC in BPD than in HC. Brain damage in those regions could cause a disturbance of impulse control, emotional and affective instability, specific cognitive dysfunctions, and a vulnerability to psychotic decompensation. The predisposing neuro-biological condition could depend on anatomical-functional damage, cognitive dysfunction, and limbic hyperactivity, with or without epileptic seizures, or monoamine neurochemical alterations involving the serotonergic and dopaminergic brain tone. The major causes of brain alteration are childhood neglect and abuse, as well as other forms of persistent severe stress and traumatic factors that alter the neurobiological abnormalities in BPD.

CONCLUSIONS

BPD is a psychiatric condition that affects the sufferer's emotions and thoughts about themselves and others. The patient may experience severe mood swings as well as intense emotions and impulsivity, which result in unpredictable thoughts and behaviors. As a consequence, it becomes difficult to establish relationships with others and to perform activities of everyday life. In clinical practice, the exact source of this disorder is still unknown. However, related factors such as genetics, environment, early stress, and brain abnormalities are predicted to be involved. The size of the brain areas responsible for emotion control, impulsiveness, and aggressive behavior has been found to decrease as a result of brain alterations. The disorder is also suspected of being caused by problems with mood-regulating neurotransmitters like serotonin and norep-

inephrine in the brain. Areas involved are the prefrontal, orbitofrontal, and anterior cingulate cortex, the amygdala, the hippocampus, and the corpus callosum as well as the functionality of the HPA axis. Changes in the brain have an impact on the patient's lifestyle and their relationships with those around them. Because patients tend to have impulsive emotions and behaviors, mood swings, and an inability to control their own emotions, this can lead to frequent job changes or quitting, inability to finish school, marriage problems, divorce, or risky behavior such as breaking the law, violence, self-harm, attempted suicide, using drugs or alcohol, injuring another person, having unprotected sex until pregnant, contracting a sexually transmitted disease, car accidents, or risking being physically harmed due to quarrels with others. Family, friends, and others close to the individual should be aware of and try to understand the symptoms of the illness. Improved understanding and having a good relationship with the individual may help promote good relationships and potentially make treatment more effective.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Personality Disorders. In: Diagnostic and statistical manual of mental disorders [Internet]. American Psychiatric Association; 2013 [cited 2021 Nov 12]. (DSM Library). Available from: <https://dsm.psychiatryonline.org/doi/full/10.1176/appi.books.9780890425596.dsm18>
2. Cluster B personality disorders: Types and symptoms [Internet]. 2020 [cited 2021 Nov 12]. Available from: <https://www.medicalnewstoday.com/articles/320508>
3. Ninomiya T, Oshita H, Kawano Y, Goto C, Matsushashi M, Masuda K, et al. Reduced white matter integrity in borderline personality disorder: A diffusion tensor imaging study. *J Affect Disord*. 2018; 225:723-32.

4. Krause-Utz A, Winter D, Niedtfeld I, Schmahl C. The latest neuroimaging findings in borderline personality disorder. *Curr Psychiatry Rep.* 2014; 16:438.
5. ICD-10 Version: 2019 [Internet]. [cited 2022 Mar 8]. Available from: <https://icd.who.int/browse10/2019/en#/>
6. Lis E, Greenfield B, Henry M, Guilé JM, Dougherty G. Neuroimaging and genetics of borderline personality disorder: a review. *J Psychiatry Neurosci JPN.* 2007; 32:162-73.
7. Samuel DB, Widiger TA, Pilkonis PA, Miller JD, Lynam DR, Ball SA. Conceptual changes to the definition of borderline personality disorder proposed for DSM-5. *J Abnorm Psychol.* 2012; 121:467-76.
8. McGowan A, King H, Frankenburg FF, Fitzmaurice G, Zanarini MC. The course of adult experiences of abuse in patients with borderline personality disorder and axis II comparison subjects: A 10-year follow-up study. *J Personal Disord.* 2012;26:192-202.
9. Chapman AL, Specht MW, Cellucci T. Borderline personality disorder and deliberate self-harm: Does experiential avoidance play a role? *Suicide Life Threat Behav.* 2005;35:388-99.
10. Vandekerckhove M, Berens A, Wang YL, Quirin M, De Mey J. Alterations in the fronto-limbic network and corpus callosum in borderline-personality disorder. *Brain Cogn.* 2020;138:103596.
11. Lenzenweger MF, Lane MC, Loranger AW, Kessler RC. DSM-IV personality disorders in the national comorbidity survey replication. *Biol Psychiatry.* 2007;62:553-64.
12. Grant BF, Chou SP, Goldstein RB, Huang B, Stinson FS, Saha TD, et al. Prevalence, correlates, disability, and comorbidity of DSM-IV borderline personality disorder: Results from the wave 2 national epidemiologic survey on alcohol and related conditions. *J Clin Psychiatry.* 2008;69:533-45.
13. Zimmerman M, Rothschild L, Chelminski I. The prevalence of DSM-IV personality disorders in psychiatric outpatients. *Am J Psychiatry.* 2005; 162: 1911-8.
14. American Psychiatric Association, American Psychiatric Association, editors. *Diagnostic and statistical manual of mental disorders: DSM-5.* 5th ed. Washington, DC: American Psychiatric Association; 2013. p. 947.
15. Perrotta G. Borderline personality disorder: Definition, differential diagnosis, clinical contexts, and therapeutic approaches. *Ann Psychiatry Treat.* 2020;4:043-056.
16. Johnson DM, Shea MT, Yen S, Battle CL, Zlotnick C, Sanislow CA, et al. Gender differences in borderline personality disorder: findings from the collaborative longitudinal personality disorders study. *Compr Psychiatry.* 2003;44:284-92.
17. Borderline personality disorder | NAMI: National Alliance on Mental Illness [Internet]. [cited 2022 Mar 8]. Available from: <https://www.nami.org/About-Mental-Illness/Mental-Health-Conditions/Borderline-Personality-Disorder>
18. Amad A, Ramoz N, Thomas P, Jardri R, Gorwood P. Genetics of borderline personality disorder: systematic review and proposal of an integrative model. *Neurosci Biobehav Rev.* 2014;40:6-19.
19. Kendler KS, Aggen SH, Czajkowski N, Røysamb E, Tambs K, Torgersen S, et al. The structure of genetic and environmental risk factors for DSM-IV personality disorders: a multivariate twin study. *Arch Gen Psychiatry.* 2008;65:1438-46.
20. Skoglund C, Tiger A, Rück C, Petrovic P, Asherson P, Hellner C, et al. Familial risk and heritability of diagnosed borderline personality disorder: a register study of the Swedish population. *Mol Psychiatry.* 2021;26:999-1008.
21. Chapman J, Jamil RT, Fleisher C. Borderline personality disorder. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing;2021 [cited 2021 Nov 12]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK430883/>
22. Dittrich K, Boedeker K, Klucznik D, Jaite C, Attar CH, Fuehrer D, et al. Child abuse potential in mothers with early life maltreatment, borderline personality disorder and depression. *Br J Psychiatry.* 2018;213:412-8.
23. Schulze L, Schmahl C, Niedtfeld I. Neural correlates of disturbed emotion processing in borderline personality disorder: A multimodal meta-analysis. *Biol Psychiatry.* 2016;79:97-106.
24. Krause-Utz A, Elzinga BM, Oei NYL, Paret C, Niedtfeld I, Spinhoven P, et al. Amygdala and dorsal anterior cingulate connectivity during an emotional working memory task in borderline personality disorder patients with interpersonal trauma history. *Front Hum Neurosci.* 2014;8:848.
25. Lischke A, Domin M, Freyberger HJ, Grabe HJ, Mentel R, Bernheim D, et al. Structural alterations in the corpus callosum are associated with suicidal behavior in women with borderline personality disorder. *Front Hum Neurosci.* 2017;11:196.
26. New AS, Carpenter DM, Perez-Rodriguez MM, Ripoll LH, Avedon J, Patil U, et al. Developmental differences in diffusion tensor imaging parameters in borderline personality disorder. *J Psychiatr Res.* 2013;47:1101-9.
27. Ruocco AC, Amirthavasagam S, Choi-Kain LW, McMain SF. Neural correlates of negative emotionality in borderline personality disorder: an activation-likelihood-estimation meta-analysis. *Biol Psychiatry.* 2013;73:153-60.
28. Brunner R, Henze R, Parzer P, Kramer J, Feigl N, Lutz K, et al. Reduced prefrontal and orbitofrontal gray matter in female adolescents with borderline personality disorder: is it disorder specific? *NeuroImage.* 2010;49:114-20.
29. Sampedro F, Farrés CC i, Soler J, Elices M, Schmidt C, Corripio I, et al. Structural brain abnormalities in borderline personality disorder correlate with

- clinical severity and predict psychotherapy response. *Brain Imaging Behav.* 2021;15:2502–12.
30. Lou J, Sun Y, Cui Z, Gong L. Common and distinct patterns of gray matter alterations in borderline personality disorder and posttraumatic stress disorder: A dual meta-analysis. *Neurosci Lett.* 2021;741:135376.
 31. Driessen M, Herrmann J, Stahl K, Zwaan M, Meier S, Hill A, et al. Magnetic resonance imaging volumes of the hippocampus and the amygdala in women with borderline personality disorder and early traumatization. *Arch Gen Psychiatry.* 2000;57:1115–22.
 32. Caetano SC, Hatch JP, Brambilla P, Sassi RB, Nicoletti M, Mallinger AG, et al. Anatomical MRI study of hippocampus and amygdala in patients with current and remitted major depression. *Psychiatry Res.* 2004;132:141–7.
 33. Schmahl CG, Vermetten E, Elzinga BM, Douglas Bremner J. Magnetic resonance imaging of hippocampal and amygdala volume in women with childhood abuse and borderline personality disorder. *Psychiatry Res.* 2003;122:193–8.
 34. Tebartz van Elst L, Ludaescher P, Thiel T, Büchert M, Hesslinger B, Bohus M, et al. Evidence of disturbed amygdalar energy metabolism in patients with borderline personality disorder. *Neurosci Lett.* 2007;417:36–41.
 35. Tebartz van Elst L, Hesslinger B, Thiel T, Geiger E, Haegele K, Lemieux L, et al. Frontolimbic brain abnormalities in patients with borderline personality disorder: a volumetric magnetic resonance imaging study. *Biol Psychiatry.* 2003;54:163–71.
 36. Zetzsche T, Frodl T, Preuss UW, Schmitt G, Seifert D, Leinsinger G, et al. Amygdala volume and depressive symptoms in patients with borderline personality disorder. *Biol Psychiatry.* 2006;60:302–10.
 37. Soloff P, Nutche J, Goradia D, Diwadkar V. Structural brain abnormalities in borderline personality disorder: a voxel-based morphometry study. *Psychiatry Res.* 2008;164:223–36.
 38. Kreisel SH, Labudda K, Kurlandchikov O, Beblo T, Mertens M, Thomas C, et al. Volume of hippocampal substructures in borderline personality disorder. *Psychiatry Res.* 2015;231:218–26.
 39. Dyck M, Kellermann T, Boers F, Gur R, Mathiak K. Dyck M, Loughhead J, Kellermann T, Boers F, Gur RC, Mathiak K. Cognitive versus automatic mechanisms of mood induction differentially activate left and right amygdala. *NeuroImage.* 2010;54:2503–13.
 40. Koenigsberg HW, Denny BT, Fan J, Liu X, Guerreri S, Mayson SJ, et al. The neural correlates of anomalous habituation to negative emotional pictures in borderline and avoidant personality disorder patients. *Am J Psychiatry.* 2014;171:82–90.
 41. Herpertz SC, Bertsch K. A new perspective on the pathophysiology of borderline personality disorder: A model of the role of oxytocin. *Am J Psychiatry.* 2015;172:840–51.
 42. New AS, Hazlett EA, Buchsbaum MS, Goodman M, Mitelman SA, Newmark R, et al. Amygdala-prefrontal disconnection in borderline personality disorder. *Neuropsychopharmacol Off Publ Am Coll Neuropsychopharmacol.* 2007;32:1629–40.
 43. Nunes PM, Wenzel A, Borges KT, Porto CR, Caminha RM, de Oliveira IR. Volumes of the hippocampus and amygdala in patients with borderline personality disorder: A meta-analysis. *J Personal Disord.* 2009;23:333–45.
 44. Nenadić I, Voss A, Besteher B, Langbein K, Gaser C. Brain structure and symptom dimensions in borderline personality disorder. *Eur Psychiatry J Assoc Eur Psychiatr.* 2020;63: e9.
 45. Kimmel CL, Alhassoon OM, Wollman SC, Stern MJ, Perez-Figueroa A, Hall MG, et al. Age-related parieto-occipital and other gray matter changes in borderline personality disorder: A meta-analysis of cortical and subcortical structures. *Psychiatry Res Neuroimaging.* 2016;251:15–25.
 46. Gosnell SN, Meyer MJ, Jennings C, Ramirez D, Schmidt J, Oldham J, et al. Hippocampal volume in psychiatric diagnoses: Should psychiatry biomarker research account for comorbidities? *Chronic stress.* 2020;4:2470547020906799.
 47. Ferber SG, Hazani R, Shoval G, Weller A. Targeting the endocannabinoid system in borderline personality disorder: Corticolimbic and hypothalamic perspectives. *Curr Neuropsychopharmacol.* 2021;19:360–71.
 48. Tae W-S, Ham B-J, Pyun S-B, Kang S-H, Kim B-J. Current clinical applications of diffusion-tensor imaging in neurological disorders. *J Clin Neurol.* 2018;14:129–40.
 49. Grant JE, Correia S, Brennan-Kohn T, Malloy PF, Laidlaw DH, Schulz SC. Frontal white matter integrity in borderline personality disorder with self-injurious behavior. *J Neuropsychiatry Clin Neurosci.* 2007;19:383–90.
 50. Lischke A, Domin M, Freyberger HJ, Grabe HJ, Mentel R, Bernheim D, et al. Structural alterations in white-matter tracts connecting (para-)limbic and prefrontal brain regions in borderline personality disorder. *Psychol Med.* 2015;45:3171–80.
 51. Whalley HC, Nickson T, Pope M, Nicol K, Romaniuk L, Bastin ME, et al. White matter integrity and its association with affective and interpersonal symptoms in borderline personality disorder. *NeuroImage Clin.* 2015;7:476–81.
 52. Kelleher-Unger I, Tajchman Z, Chittano G, Vilares I. Meta-analysis of white matter diffusion tensor imaging alterations in borderline personality disorder. *Psychiatry Res Neuroimaging.* 2021;307: 111205.
 53. Niedtfeld I I, Schulze L, Krause-Utz A, Demirakca T, Bohus M, Schmahl C. Voxel-based morphometry in women with borderline personality disorder

- with and without comorbid posttraumatic stress disorder. *PLoS ONE*. 2013;8: e65824.
54. Kuhlmann A, Bertsch K, Schmidinger I, Thomann PA, Herpertz SC. Morphometric differences in central stress-regulating structures between women with and without borderline personality disorder. *J Psychiatry Neurosci JPN*. 2013;38:129–37.
 55. Hall J, Olabi B, Lawrie SM, McIntosh AM. Hippocampal and amygdala volumes in borderline personality disorder: A meta-analysis of magnetic resonance imaging studies: Brain volumes in borderline personality. *Personal Ment Health*. 2010;4:172–9.
 56. Koenigsberg HW, Fan J, Ochsner KN, Liu X, Guise KG, Pizzarello S, et al. Neural correlates of the use of psychological distancing to regulate responses to negative social cues: a study of patients with borderline personality disorder. *Biol Psychiatry*. 2009;66:854–63.
 57. Rüsç N, Luders E, Lieb K, Zahn R, Ebert D, Thompson PM, et al. Corpus callosum abnormalities in women with borderline personality disorder and comorbid attention-deficit hyperactivity disorder. *J Psychiatry Neurosci JPN*. 2007;32:417–22.
 58. Minzenberg MJ, Fan J, New AS, Tang CY, Siever LJ. Fronto-limbic dysfunction in response to facial emotion in borderline personality disorder: an event-related fMRI study. *Psychiatry Res*. 2007;155:231–43.
 59. Zetzsche T, Preuss UW, Frodl T, Schmitt G, Seifert D, Münchhausen E, et al. Hippocampal volume reduction and history of aggressive behaviour in patients with borderline personality disorder. *Psychiatry Res*. 2007;154:157–70.
 60. Rausch J, Flach E, Panizza A, Brunner R, Herpertz SC, Kaess M, et al. Associations between age and cortisol awakening response in patients with borderline personality disorder. *J Neural Transm Vienna Austria*. 2021;128:1425–32.
 61. Rausch J, Gäbel A, Nagy K, Kleindienst N, Herpertz SC, Bertsch K. Increased testosterone levels and cortisol awakening responses in patients with borderline personality disorder: gender and trait aggressiveness matter. *Psychoneuroendocrinology*. 2015;55:116–27.
 62. Thomas N, Gurvich C, Kulkarni J. Borderline personality disorder, trauma, and the hypothalamus-pituitary-adrenal axis. *Neuropsychiatr Dis Treat*. 2019;15:2601–12.
 63. Drews E, Fertuck EA, Koenig J, Kaess M, Arntz A. Hypothalamic-pituitary-adrenal axis functioning in borderline personality disorder: A meta-analysis. *Neurosci Biobehav Rev*. 2019;96:316–34.