

The Brain Structure of Patients with Borderline Personality Disorder: A Review of Positron Emission Tomography and Structural Magnetic Resonance Imaging

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Abstract: Borderline personality disorder (BPD) is a severe mental disorder characterized by a consistent pattern of emotional inconsistency, poor impulse management, unstable personal relationships, and a constantly fluctuating self-image. Researchers have lately made significant progress in grasping the potential neurobiological underpinnings of BPD, and neuroimaging has emerged as a pivotal instrument in examining differences between BPD patients and healthy controls. This article will explore past studies on neuroimaging of patients with bipolar disorder, including PET and sMRI. BPD patients are likely to display hypometabolism in prefrontal regions and metabolic changes in temporal and parietal lobes. There are also studies pointing to the significance of anterior cingulate cortex (ACC) and structural volume. However, the results are mainly inconsistent. The limiting sample sizes may be one of the reasons for such a high level of variance. Therefore, studies with larger and more inclusive sample sizes are needed to reach firm conclusions. Moreover, the relationship between medication/therapy and the changes in BPD patients' brain activities also needed to be explored.

Keywords: Borderline personality disorder, positron emission tomography, functional magnetic resonance imaging, neuroimaging

1. Introduction

A persistent and detrimental way of thinking characterizes a personality disorder. Such conditions are common in the general public and even more so among clinical groups. All personality disorders can be identified in the pediatric group except for antisocial personality disorder, provided the problematic behavior has persisted for at least a year. The Diagnostic and Statistical Manual of Mental Disorders 5th edition(DSM-5) categorizes a total of ten personality disorders into three different groups. Borderline personality disorder (BPD), is one of the four disorders in group B, alongside antisocial, narcissistic, and histrionic personality disorders [1].

A borderline personality disorder is usually defined by a consistent pattern of emotional inconsistency, poor impulse management, unstable personal relationships, and a constantly fluctuating self-image. Symptoms of this disorder involve difficulty in controlling emotions, impulsive behavior, recurring self-harm, and persistent suicidal thoughts [2]. Patients with BPD frequently have coexisting mental disorders that require simultaneous evaluation. A national

epidemiological study from the US indicates that BPD patients show lifetime rates of 78.2% for substance use disorders, 84.5% for anxiety disorders, and 82.7% for mood disorders. Notably, there are also elevated rates of co-occurring post-traumatic stress disorder (PTSD), attention deficit hyperactivity disorder (ADHD), bipolar disorder I, and bipolar disorder II [3].

BPD is a chronic form of psychopathology that involves severe psychosocial impairment and a notably high suicide rate: 10% of patients with this condition would commit suicide, which is almost 50 times higher than the average population. On average, BPD patients attempt suicide three times in their lifetime, with overdosing being the most common method. As a result, patients with BPD often need more resources than those who have other psychiatric disorders [4][5], and it would be critical to explore more about BPD.

Over recent decades, people's knowledge of the neurobiological foundations of BPD has expanded greatly. As a result, neuroimaging has become one of the most significant tools for identifying discrepancies in individuals diagnosed with BPD in comparison to those without the disorder. For example, positron emission tomography (PET) has been employed to examine neurotransmitter systems within the brain, functional magnetic resonance imaging (fMRI) has been utilized to investigate brain activities through variations in cerebral blood flow, and structural magnetic resonance imaging (sMRI) has been used to characterize the human brain's structure without invasive methods. Given the strong correlation between early life traumatic events and the development of BPD, the disorder is frequently categorized within a range of mental disorders associated to trauma, with PTSD being central to this classification [6]. Neuroimaging studies investigating the neurobiological deviations in PTSD have laid the foundation for analogous research in BPD. The techniques employed in PTSD neuroimaging, like the volumetric analysis of various brain areas, are often adapted for BPD research. For the past several years, an increasing amount of research on neuroimaging have employed structural and functional connectivity methods to explore the dynamic interplay between brain regions during experimental scenarios and rest periods in BPD.

This article will provide an overview of the up-to-date research on neuroimaging in BPD, focusing on PET scans and sMRI.

2. Epidemiology

Extensive epidemiological studies from 2007 and 2008 have shown that BPD occurs in approximately 1.6% of the whole population., and the lifetime occurrence is about 5.9%. Although the reported gender is 3 females to 1 male in the clinical settings, the prevalence of this disorder was observed to be similar for both men and women [1].

On the other hand, from a group selected from the overall population of children and adolescents, the occurrence of borderline personality disorder was around 11% for ages 9-19 and 7.8% for ages 11-21. The disorder was found to be more prevalent in girls than in boys. However, it is uncertain whether it appears more frequently in children compared to adults due to the study's less-than-ideal method of symptom assessment [3].

3. Diagnosis and Treatments

In the past decade, significant transformations have taken place in the categorization of personality disorders, particularly BPD. Currently, BPD can be classified using four distinct systems: the conventional criteria found in section II of the DSM-5, an optional framework in section III of the same manual, and the models outlined in the ICD-10 and ICD-11 [3].

Following the psychiatric categorization outlined in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), BPD is defined by a widespread fluctuating pattern in personal relationships, self-perception, impulsiveness, and mood. For a diagnosis of

borderline personality disorder, individuals need to fulfill a minimum of five out of the nine criteria. While tendencies toward self-harm or suicide stand out as the most pivotal indicators for a precise diagnosis, these tendencies, coupled with volatile relationships, are the most foretelling characteristics observed in subsequent studies [3].

Psychotherapy has often been noted as least effective for individuals with BPD since 1980, the post of DSM. However, the continuous development of specific treatment approaches has made huge contributions towards therapeutic optimism, and psychotherapy has become the most recommended treatment for BPD patients [7]. There are several treatments that have shown efficacy, including dialectical behavior therapy (DBT) and mentalization-based therapy (MBT); they are mostly derived from the cognitive behavior approach and the psychodynamic approach [8]. A study conducted in 2022 shows that psychotherapies show positive impacts on various key aspects, including the main results related to BPD severity, psychosocial functioning, self-harm, and outcomes related to suicidal behaviors, as well as the secondary outcomes involving particular BPD diagnostic criteria and depression. Nonetheless, it is critical to note that the quality and certainty of the evidence were generally assessed as being of low or deficient quality in most instances [7].

Past research indicates that many patients find it difficult to achieve recovery from BPD, encompassing both effective psychosocial functioning and symptomatic remission. However, research also suggests that it is still possible for patients with BPD to attain recovery, which tends to be stable over time [9].

4. Current Neurobiological Findings

4.1. PET Scan

Initial studies on BPD employed PET to discern differences in brain activity at the initial assessment and during particular circumstances. These studies evaluated either the regional cerebral blood flow (rCBF) or cerebral metabolic rate of glucose to detect irregularities in BPD brain functions. Early imaging revealed decreased glucose metabolism in BPD patients' prefrontal and premotor areas during rest, linking metabolic brain activity alterations to BPD traits like impulsivity and affect dysregulation. Although some findings were inconsistent, these studies have still provided valuable insights into BPD's neurobiological bases. One of the most consistent findings is hypometabolism in prefrontal regions, especially linked to impulsiveness. Research also found correlations between prefrontal glucose metabolism and traits like hostility [10].

BPD patients' responses to aggression triggers highlighted abnormal frontolimbic connections. In contrast to healthy individuals, BPD patients show heightened metabolism in areas associated with aggression upon provocation. A re-analysis of this data revealed gender-based metabolic variations in BPD [10].

The ACC also appeared significant in BPD pathology. Because of its associations with prefrontal and limbic regions of the brain, ACC is believed to influence cognitive control, affect regulation, and pain perception. However, the findings were inconsistent and could be attributed to diverse study factors [10].

Other studies using PET identified metabolic changes in temporal and parietal lobes, focusing on the hippocampus and hypothalamus. These changes correlated with altered stress reactions, memory lapses, and dissociative symptoms in BPD patients [10].

Early studies employed PET to examine differences in brain activities. All had an overly high concentration on brain metabolic activity or blood flow, and these aspects can now be more affordably and readily evaluated using MRI. Moreover, these initial studies were unable to shed light on the neurochemical foundations of particular brain regions potentially associated with the disorder or its underlying pathological processes. With more advanced technologies, later studies done with PET

have been mainly focusing on neurochemical abnormalities of BPD, which mainly indicate changes in the monoaminergic systems, enhanced activation of the opioid system when inducing depressing feelings such as sadness, and irregularities in the brain's endocannabinoid system related to BPD [10].

4.2. Structural MRI

Many early studies show that BPD is linked to a decrease in size in regions like the hippocampus and amygdala, which are crucial for emotion regulation and memory. Recent investigations have employed voxel-based morphometry (VBM) to get more accurate results. Key findings include decreased volumes in the amygdala, hippocampus, and other related areas in individuals with BPD in contrast to those without the condition [11]. BPD patients consistently exhibited a reduction in hippocampal volume. Alterations in amygdala volume were also observed in a significant number of studies, although less consistently. In contrast to adolescent patients with normal hippocampal and amygdala volumes, reduced volumes of the orbitofrontal cortex (OFC) and the ACC appear to serve as early indicators of the disorder [12].

In addition to volume reductions, other structural brain abnormalities in BPD patients were also studied, showing relationships with psychological metrics, including suicidal tendencies. Cortical changes have also been explored in BPD patients. Several studies highlighted alterations in the frontal-limbic regions, with some providing insights into cortical thickness, curvature, and folding patterns, suggesting early neurodevelopmental issues in BPD. Other studies investigated areas of reduced or increased gray matter density in BPD, emphasizing the cortical areas responsible for functions that are often deregulated in these patients [11].

Many studies have conducted research on several characteristics of BPD, including impulsivity, trauma, depression, and aggression. Therefore, this review would focus on the neuroimaging findings in these four aspects to investigate BPD.

4.2.1. Relationship between impulsivity and brain structure

Impulsivity was evaluated in several studies using different scales. According to one study, impulsivity ratings distinguished between individuals who had attempted suicide in the past and those who had not. The study found a negative link between impulsivity and several brain regions in the group with a lower level of lethality. These regions included the amygdala, fusiform gyrus, lingual gyrus, insula, middle-superior temporal cortex, and OFC. Positive relationships were observed in the parahippocampus, fusiform gyrus, and middle-superior temporal cortex in the high lethality group. However, a slight negative correlation was discovered between impulsivity and the insula in the high-lethality group [13].

Other studies had mixed results. No significant correlations between impulsivity and various brain regions were found within several studies, while One investigation indicated a notable negative association with the caudate, while no such correlation was observed in the frontal or hippocampal regions. Another study reported negative correlations with the middle frontal gyrus, OFC, pre and postcentral gyri, the temporal pole, and the inferior and superior parietal cortex. A 2009 study discovered a positive association between gray matter volume (GMV) and the hippocampus, with no observed correlation with the amygdala. On the other hand, another research discovered negative correlations between impulsivity and the anterior and posterior cingulate gyri, and prefrontal regions, and a positive correlation with the OFC. Dorsolateral regions showed no significant relationship with impulsivity [13].

Overall, impulsivity was most consistently associated with frontal brain regions and had fewer correlations with limbic structures. It is important to note that some of the relationships found could not be replicated in more robust whole-brain analyses.

4.2.2. Relationship between trauma and brain structure

The evidence regarding the relationship between trauma and GMV in individuals with BPD was mixed. Some studies did not find any significant relationship between trauma and GMV. However, one research conducted in 2013 identified a positive correlation between trauma severity and the hypothalamus (but not the anterior cingulate cortex, hippocampus, or amygdala). In contrast, another study done in 2005 discovered a negative correlation between hippocampal GMV and trauma severity. It is important to note that the varying findings might be attributed to differences in the measures of trauma used in these studies [13].

Additionally, the relationships found in these studies could not be consistently replicated in other robust whole-brain analyses, and interpretations were limited. Nevertheless, there is some evidence suggesting a potential link between trauma and both hypothalamic and hippocampal structures in individuals with BPD [13].

4.2.3. Relationship between depression and brain structure

The relationship between depression and GMV in individuals with BPD was examined in several studies using measures such as the Beck Depression Inventory (BDI) and the Hamilton Rating Scale for Depression (HAM-D). Among the studies, only one reported a positive correlation between depression and GMV, specifically in the right amygdala. It is worth noting that this study received a lower quality assessment score [13].

On the other hand, many other studies did not find any significant correlations between depression and GMV in their research [13].

A study done in 2014 did not directly incorporate depression into its model but instead compared groups based on baseline differences, and their results did not indicate a clear correlation exists between GMV and depression in BPD patients. [13].

4.2.4. Relationship between aggression and brain structure

A review conducted in 2022 reported that no significant relationship was found between aggression and specific brain regions, such as the amygdala, hippocampus, or cingulate cortex. However, a positive correlation exists between aggression and the right amygdala's GMV within a unique BPD subgroup distinguished by decreased suicide lethality. Male patients, in particular, displayed a noticeable positive trend in the connection between aggression and the volume of the right amygdala. Furthermore, a significant positive correlation was observed between aggression and the forms of the left superficial and laterobasal amygdala. [14].

The hippocampus displayed mixed results, with some studies indicating a notable negative association between aggression and the volume of the hippocampal, while others found no correlation. However, a subsequent study revealed a positive correlation between aggression and the right hippocampus and parahippocampus among individuals with BPD. [14].

The cingulate cortex (CC) also yielded mixed findings. In a particular study, a negative correlation was observed between aggression and the white matter volume (WMV) in the posterior cingulate gyrus. while other investigations did not observe a significant link between aggression and GMV in the ACC. However, among a subset of BPD patients with elevated suicidal lethality, a positive correlation was identified between aggression and GMV in the ACC. [14].

Studies on frontal regions, including the OFC, dorsolateral prefrontal cortex (dlPFC), and ventrolateral prefrontal cortex (vlPFC), revealed various relationships with aggression. Aggression was positively related to the white matter volume in the left OFC, but no correlation was found with the GMV in the right OFC. The bilateral dlPFC exhibited a positive correlation with hostility and irritability-assaultiveness, while the GMV in dlPFC showed a negative relationship with impulsivity,

but not with aggression itself. One study involving vIPFC reported reduced GMV in the right vIPFC, which was negatively correlated with aggression [14].

Additionally, specific brain regions, such as the caudal superior temporal gyrus and the somatosensory cortex, were linked to aggression in adolescent individuals diagnosed with BPD who have a background of aggressive incidents. In some BPD subgroups, various brain regions, including the fusiform gyrus, middle-superior temporal cortex, and lingual gyrus, showed a positive correlation between their volumes and aggression [14].

These findings demonstrate a complex and multifaceted relationship between aggression and brain structures in individuals with BPD, with potential moderating factors like suicidality influencing these relationships.

5. Discussion

Lately, there has been a notable surge in the number of neuroimaging studies focusing on borderline personality disorder. This increase highlights the growing interest and commitment within the scientific community to understand the intricacies of this disorder. However, the results are highly conflicting.

Potential methodological problems may be one of the factors. The methodologies adopted across different studies need to be more uniform. This lack of standardization in approaches, ranging from the techniques used to the instruments employed, can lead to varied results even when studying similar aspects of the disorder.

Another crucial factor that cannot be overlooked is the differing gender compositions across studies. As gender can potentially play a crucial role in the manifestation and neurobiology of BPD, studies that focus predominantly on one gender might yield results that are not universally applicable. This is compounded by the variability in sample sizes across different studies. While some studies may involve a large and diverse group of participants, others may be limited to a smaller cohort, which can influence the generalizability of the findings.

Furthermore, the presence of comorbidities among research participants adds another layer of complexity. When individuals with borderline personality disorder also suffer from other disorders or are on specific medications, it can introduce confounding variables that might skew the results. This makes it challenging to discern whether the observed neuroimaging patterns are attributable to borderline personality disorder or other overlapping conditions.

Therefore, future studies must be more inclusive, encompassing a broader range of participants. This would not only enhance the reliability of the findings but also reduce the variance observed within groups.

A significant area of concern that emerged from the review of existing literature is the reliability of the quality assessment tools, especially those used for MRI analyses. The current tools need rigorous validation to ensure they are accurately gauging the quality of the research.

The varied nature of existing research and the inconsistencies in their reporting methodologies make the task of meta-analysis highly challenging. This limitation is a significant setback as it hinders the drawing of comprehensive conclusions from available data. As the field progresses and researchers adopt standardized methodologies, it is hopeful that future reviews will be able to delve deeper, providing more coherent and insightful analyses of borderline personality disorder through neuroimaging.

Moreover, future research can also explore the impacts of treatments on BPD patients' neuroimaging findings. Limited research has delved into the influence of medications on brain function in individuals with BPD. A review conducted in 2021 shows that while antidepressants (AD), antipsychotics (AP), and mood stabilizers (MS) may not have a substantial impact on brain activation and connectivity during emotional tasks in individuals with BPD, a vast amount of literature and

clinical practice evidence suggests that psychiatric medications can effectively mitigate BPD symptoms. This raises the possibility that the therapeutic effects of frequently prescribed medications for BPD may not directly correlate with brain function but could be associated with alternative pathways, such as neurochemical or neuroendocrine processes. Preliminary findings from PET and MRS studies suggest that pharmacological treatments in BPD directly influence brain metabolism, which correlates with clinical outcomes. To gain deeper insights, future research should focus on larger and more consistent participant groups, adopt longitudinal study models, and implement strict treatment protocols. This would not only enhance the understanding of the potential effects of therapies on brain functions in BPD patients but also shed light on their influence on brain metabolism [15].

6. Conclusion

In recent times, there has been a heightened focus on borderline personality disorder (BPD). Research has provided insights into potential reasons and provocations for the disorder. With the increase in the number of studies, researchers are starting to go beyond external influences like environmental and psychosocial stressors; many studies are now employing neuroimaging techniques to investigate borderline personality disorder. However, most of the results are conflicting and how treatments influence neuroimaging results in individuals with BPD remains largely unknown. As a result, further research is still needed since there are not enough studies to draw definitive conclusions.

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