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Borderline Personality Disorder: Emerging Symptoms, Evolving Therapies, and the Role of Physical Activity in Treatment

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Abstract
Background:
Borderline Personality Disorder (BPD) is a complex and heterogeneous mental health condition, traditionally characterized by emotional dysregulation, impulsivity, unstable interpersonal relationships, and a distorted self-image. In recent years, clinical research has increasingly identified atypical symptom presentations and highlighted challenges related to diagnosis, treatment responsiveness, role of physical activity and long-term prognosis.
Aim:
This review aims to provide a comprehensive overview of emerging symptoms associated with BPD, assess the development of novel and evolving therapeutic approaches, and discuss key prognostic factors that influence clinical outcomes.
Material and Methods:
A systematic literature review was conducted using PubMed as a primary database. Peer-reviewed articles published between 2000 and 2024 were included, with a focus on empirical studies, meta-analyses, and recent clinical guidelines related to BPD symptomatology, treatment, and prognosis.
Conclusions:
Understanding the broader spectrum of BPD symptoms and the dynamic nature of treatment response is essential for accurate diagnosis and effective intervention. An individualized, trauma-informed approach combined with ongoing research into prognostic markers holds promise for improving long-term outcomes in individuals with BPD.
Key words: Borderline Personality Disorder, Physical Activity, Emerging Symptoms, Atypical Presentations, Psychotherapy, Mentalization-Based Treatment, Personality Disorders

Content

1. Introduction

Borderline Personality Disorder (BPD) is a complex psychiatric condition characterized by significant emotional instability, difficulties in maintaining interpersonal relationships, and disturbances in self-image. Traditionally recognized symptoms of BPD include impulsivity, a chronic sense of emptiness, intense fear of abandonment, and a tendency toward self-destructive behaviors. Increasingly, research highlights the existence of less typical manifestations of this disorder, which may complicate diagnosis and influence treatment outcomes. The aim of this review paper is to discuss the atypical symptoms of Borderline Personality Disorder, their impact on prognosis, and current therapeutic strategies. Understanding the full spectrum of BPD symptoms is crucial not only for accurate diagnosis but also for tailoring effective treatment approaches and improving patients' long-term health outcomes.

2. Neurobiological Foundations of BPD

BPD has long been recognized as one of the most complex and difficult-to-treat mental disorders. Contemporary neurobiological research is increasingly providing data that help elucidate its underlying mechanisms. Mounting evidence from brain imaging studies suggests that dysfunction within fronto-limbic circuits, which are responsible for emotion regulation, affective information processing, and impulse control, plays a key role in the pathophysiology of BPD. Resting-state functional magnetic resonance imaging (rs-fMRI) studies consistently reveal disruptions within and between three major brain networks: the default mode network (DMN), associated with self-referential processing and introspection; the salience network (SN), involved in detecting and processing emotional stimuli and shifting attention; and the central executive network (CEN), which is crucial for cognitive control and decision-making. Connectivity disturbances within these networks may account for clinical symptoms of BPD, such as severe mood fluctuations, impulsivity, chronic feelings of emptiness, and difficulties in interpersonal relationships (Shafie et al., 2023).

Furthermore, research points to selective alterations in the activity and structure of specific regions such as the amygdala, hippocampus, cingulate gyrus, and prefrontal cortex. Notably, although such changes were once considered characteristic of BPD, recent large-scale studies ($N > 1000$) have not confirmed the existence of distinct, disorder-specific structural brain markers. Neither structural MRI studies nor task-based functional fMRI studies have revealed clear, replicable differences between individuals with BPD and healthy controls (Degasperi et al., 2021; Baranger et al., 2020).

As a result, a transdiagnostic model is increasingly being adopted, positing that disruptions in fronto-limbic networks are not unique to BPD but are shared across various psychiatric conditions, including depression, bipolar disorder, and post-traumatic stress disorder (PTSD). These disorders may share a common neurobiological foundation, with clinical differences arising from varying symptom intensities or their interactions. This perspective also supports the hybrid model, which integrates dimensional approaches (focusing on symptom spectra and severity) with traditional categorical classification. Future research should therefore prioritize the investigation of shared mechanisms underlying symptoms such as emotion dysregulation, impulsivity, and deficits in social cognition, regardless of diagnostic labels (Choi-Kain et al., 2022).

3. Typical Clinical Presentation of BPD

Borderline Personality Disorder is most frequently characterized by pronounced instability in

emotions, self-image, impulsive behaviors, and interpersonal relationships. Individuals with BPD often begin experiencing intense and rapidly shifting emotions during adolescence, with emotional reactions that are disproportionate to the triggering events indicating deeply rooted difficulties in emotional regulation (Skabeikyte et al. 2021; Bohus et al., 2021). This is frequently accompanied by a chronic sense of emptiness and a heightened fear of abandonment, which may lead to desperate attempts to maintain interpersonal connections, often resulting in the destabilization of those very relationships (Leichsenring et al., 2024; Miller et al., 2022, Waloch et al. 2024).

Interpersonal relationships in BPD are typically tumultuous and emotionally charged, marked by extremes of idealization and devaluation. This dynamic results in cycles of intense involvement followed by abrupt rejection (Paris, 2018). Additionally, patients frequently display an unstable sense of identity, struggling to define long-term goals and personal values (Oumaya et al., 2008; Rao et al. 2019). A hallmark feature of BPD is impulsivity, which may manifest through substance abuse, compulsive sexual behavior, uncontrolled spending, or engaging in risky behaviors such as reckless driving (Liakopoulou et al., 2023; Chanen et al., 2020).

There is also a significantly elevated risk of suicidal behaviors and self-injury (e.g., cutting), which poses a serious threat to the health and lives of individuals with BPD and remains one of the primary reasons for psychiatric hospitalization in this population (Francis et al., 2024). Self-harm may also take other forms, such as non-adherence to medical recommendations or misuse of prescribed medications. Despite the heterogeneity of symptoms, a core feature of BPD remains a severely impaired capacity to regulate emotions in response to both interpersonal and internal stressors, which substantially impacts daily functioning.

4. Other Atypical Symptoms of BPD

Based on a review of the literature, a range of atypical clinical symptoms can be identified in patients with BPD that extend beyond the classical diagnostic criteria.

4.1 Psychotic Symptoms and Hallucinations

Psychotic symptoms represent a frequently overlooked component of the clinical presentation of Borderline Personality Disorder. Patients often experience transient psychotic features, most commonly paranoid ideation and auditory hallucinations, particularly in the context of heightened emotional stress (Glaser et al., 2010; Cavelti et al., 2021). Earlier theoretical models referred to such phenomena as “pseudopsychotic,” but recent findings suggest that these symptoms do not significantly differ in quality or clinical impact from psychotic manifestations observed in classic psychotic disorders (Cavelti et al., 2021). Evidence indicates that individuals with BPD exhibit significantly higher stress sensitivity in relation to psychotic symptom onset compared to other clinical groups, which may point to a distinct vulnerability mechanism for altered reality perception (Glaser et al., 2010).

Psychotic symptoms in BPD are also closely associated with dissociative experiences and overall emotional dysregulation, further complicating diagnostic and therapeutic approaches (D'Agostino et al., 2019). Moreover, the presence of psychotic features is linked to poorer prognostic outcomes, increased risk of self-injury and suicidal behaviors, thus necessitating their routine consideration in clinical assessment and therapeutic planning.

4.2 Self-Injurious Behavior

Self-injurious behaviors, encompassing both non-suicidal self-injury (NSSI) and suicidal behaviors (SB), are core features of BPD. NSSI, defined as the repeated infliction of superficial injuries without suicidal intent, is particularly common among adolescents and often precedes the full manifestation of BPD. Studies suggest that in individuals with BPD, NSSI emerges earlier, persists longer, and may serve as an early indicator of the disorder. The primary function of NSSI is believed to involve emotional regulation either as an escape from negative affect or an attempt to induce a transient positive state consistent with conceptualizing BPD as a disorder

rooted in profound emotional dysregulation (Reichl et al, 2021).
While suicidal behaviors are also prevalent in BPD, they carry a higher risk of lethality, particularly among young adults. The literature identifies BPD as one of the strongest predictors of repeated suicide attempts, even after controlling for other psychiatric disorders. Individuals with BPD may also exhibit less common and harder-to-detect forms of self-injury, such as self-embedding behavior (SEB), which involves inserting sharp objects into soft tissues and is rarely reported to healthcare providers, necessitating heightened diagnostic vigilance (Mannarino et al. 2017).
Longitudinal and ecological momentary assessment (EMA) studies have shown dynamic interactions between affective fluctuations and self-injurious behaviors - negative affect often precedes NSSI episodes, followed by further emotional deterioration and interpersonal dysfunction. Thus, symptoms such as emotional and relational instability not only predispose individuals to self-harm but also reinforce its persistence over time. A significant proportion of BPD-related hospitalizations is due to recurrent self-injury episodes, often involving high-risk behaviors such as foreign body ingestion, posing substantial burdens on the healthcare system (Kaazan et al., 2023).
Given the scale of the issue, early identification of self-injurious behaviors as clinical warning signs of BPD is crucial. Research shows that targeted therapeutic interventions, particularly Dialectical Behavior Therapy (DBT) and Mentalization-Based Treatment (MBT) can effectively reduce self-injury frequency and improve emotional regulation and interpersonal functioning in patients with BPD.

5. Treatment

5.1 Psychotherapy

One of the fundamental approaches to treating borderline personality disorder involves the use of psychotherapy. The following section presents various therapeutic models employed in the treatment of this disorder, along with a comparison of their effectiveness.
Interpersonal Psychotherapy (IPT) was initially developed for major depression, treating BPD as a mood-related disorder with anger outbursts. Like IPT for depression, it focuses on interpersonal issues, with therapists using a nondirective approach to help patients resolve them. Treatment duration is longer, and it includes telephone support to prevent crises and strengthen the therapeutic alliance, along with psychoeducation for the patient's family (Setkowski et al., 2023).
Cognitive Behaviour Therapy (CBT) focuses on identifying and addressing maladaptive thoughts and beliefs, and their impact on behavior. The goal is to challenge and reframe dysfunctional beliefs. Behavioral interventions, like teaching adaptive coping strategies, are also used to modify harmful behaviors. CBT often includes tasks to be completed between sessions as part of the treatment (Setkowski et al., 2023).
Dialectical behaviour therapy (DBT) is a comprehensive treatment that blends elements of CBT with mindfulness and systemic approaches. Its primary aim is to foster behavioural change and emotional regulation through skill-building in areas such as distress tolerance, emotion management, interpersonal effectiveness, and mindfulness (Stoffers et al., 2012).
Mentalisation-based therapy (MBT) is a sophisticated therapy rooted in psychoanalytic principles. It seeks to enhance the individual's ability to reflect on and understand both their own emotional experiences and the emotions they elicit in others (Stoffers et al., 2012).
Psychodynamic Psychotherapy (PDP) focuses on improving patients' understanding and awareness of unconscious intrapsychic conflicts and their impact on interpersonal relationships. Therapists examine childhood experiences and historical relationships, aiming to strengthen the self-image, promote self-reflection, and mature maladaptive defense and coping strategies. The therapy also includes emotion regulation, identifying dysfunctional impulses, and reflecting on behavior. Different forms of PDP vary in approach, from neutral therapists focusing on

increasing awareness to more supportive forms that encourage mature defense mechanisms. All forms involve clarification, confrontation, and interpretation (Setkowski et al., 2023).

Schema-focused therapy (SFT) integrates behavioural and psychoanalytic concepts. It supports individuals with borderline personality disorder (BPD) in identifying harmful core beliefs that originate from unmet emotional needs during childhood and manifest as unhelpful coping mechanisms in adulthood. The primary goal of SFT is to help patients fulfill their emotional needs more effectively (Stoffers et al., 2012).

Transference-focused psychotherapy (TFP), aims to help patients develop a cohesive sense of self and others by addressing immature defense mechanisms and resolving fragmented identity structures. This is achieved through detailed examination of the therapeutic relationship, with the intention of evolving basic, polarized relational patterns into more mature and integrated forms (Stoffers et al., 2012).

Current research on psychotherapy for BPD is limited, and more studies are needed to confirm existing findings. The strongest evidence supports DBT, while other therapies rely on single studies. Psychotherapy shows promise for treating both core BPD symptoms and related issues, even in patients with additional conditions like PTSD or addiction.

Disorder-specific treatments appear more effective than general approaches such as CBT, IPT, or client-centered therapy (CCT). Short-term interventions may be helpful, especially as additions to longer therapies, though their impact on previously treated patients is unclear. Group therapies are often combined with individual treatment, making it hard to isolate their effects. Overall, a 12-18 month treatment duration is suggested, though the ideal length remains unknown (Stoffers et al., 2012).

Patients with borderline personality disorder receiving DBT or MBT in routine community services can achieve improvements in BPD traits, self-harm, emotional dysregulation, dissociation and interpersonal relationships. There may be differences in the extent and speed of reductions in self harm and emotional dysregulation among those offered DBT and MBT, but experimental studies examining treatment fidelity, mechanisms and longer-term outcomes are needed to fully examine potential differences in the clinical and cost effectiveness of these treatments (Barnicot et al. 2019).

Comparing DBT and Schema Therapy (ST) for individuals with borderline personality disorder. Both treatment groups demonstrated substantial clinical improvement, suggesting that even severely affected patients with multiple comorbidities can benefit from either approach. No significant differences were observed between treatments overall, with the exception of greater reductions in anger and lower treatment retention in the DBT group. These findings support the need for a formal equivalence trial to determine whether DBT and ST offer comparable effectiveness in treating BPD (Assmann et al., 2024).

Findings from a multisite randomized controlled trial examining the prevalence and influence of childhood trauma on treatment outcomes in individuals diagnosed with borderline personality disorder were assessed across two modalities of MBT: a day hospital format (MBT-DH) and an intensive outpatient format (MBT-IOP), over a 36-month follow-up period beginning at treatment initiation. The results indicate that, overall, childhood trauma does not exert a significant influence on MBT outcomes in individuals with BPD. However, individuals with a history of severe trauma exhibited slightly more favorable outcomes when treated in the MBT-DH setting compared to the MBT-IOP format. These findings suggest the potential value of further investigation into the benefits of incorporating a more explicit focus on trauma during the initial stages of MBT, particularly with regard to optimizing outcomes in MBT-IOP (Smits et al., 2022).

5.2 Pharmacology

The combination of pharmacotherapy and psychotherapy yields clinically significant improvements in mood and behavioral symptoms among individuals diagnosed with borderline personality disorder (BPD)

Below, we present several classes of medications that have demonstrated efficacy in the treatment of various symptoms associated with borderline personality disorder (BPD).

5.2.1 Antipsychotics

Antipsychotic medications are primarily prescribed for the management of schizophrenia and the psychotic features associated with mood disorders. In the context of long-term treatment, these agents may also support mood stabilization in individuals diagnosed with major depressive disorder and bipolar disorder. Furthermore, antipsychotics are frequently utilized in the clinical management of a range of symptoms observed in patients with borderline personality disorder (BPD) (Del Casale et al., 2021).

Olanzapine

Substantial evidence supports the efficacy of olanzapine in alleviating a wide range of symptoms associated with borderline personality disorder (BPD). Even at lower doses, the medication has been shown to significantly improve symptoms such as intense anger, affective instability, chronic feelings of emptiness, identity disturbance, impulsivity, frantic efforts to avoid abandonment, and unstable interpersonal relationships (Schulz et al., 2008; Zanarini et al., 2001; Linehan et al., 2008). At higher doses, olanzapine has been found to contribute to a reduction in paranoid ideation, dissociation, irritability, and suicidal behaviors (Zanarini et al. 2011). Subsequent research has indicated that the combination of olanzapine with fluoxetine may offer greater efficacy than olanzapine monotherapy in addressing depressive symptoms in individuals with borderline personality disorder (BPD) (Zanarini et al., 2004). Additional data revealed a significant reduction in both depressive symptoms and clinical anxiety. Furthermore, the integration of dialectical behavior therapy was associated with a markedly greater improvement in the frequency of impulsive and aggressive episodes (Soler et al., 2008). Olanzapine has also demonstrated effectiveness in treating anxiety symptoms and episodes of distress in women diagnosed with BPD (Zanarini et al., 2001).

Quetiapine

Quetiapine has demonstrated efficacy in the treatment of several core symptoms of borderline personality disorder (BPD), including intense anger, affective instability, chronic feelings of emptiness, identity disturbance, frantic efforts to avoid abandonment, and unstable interpersonal relationships (Del Casale et al., 2021). High-dose treatment has been associated with a reduction in hypomanic and manic symptoms. However, quetiapine has not consistently shown effectiveness in managing impulsivity (Black et al., 2014). Evidence supports its use in alleviating depressive and anxiety symptoms, as well as in reducing emotional instability and psychological distress in individuals with BPD (Villeneuve et al., 2005; Van den Eynde et al., 2008; Bellino et al., 2006; Lee et al., 2016; Perrella et al., 2007), though findings regarding its impact on depressive symptoms remain somewhat inconsistent (Bellino et al., 2006). Some studies have also reported the effectiveness of quetiapine in managing psychotic symptoms in BPD patients, particularly at higher dosages (Bellino et al., 2006; Lee et al., 2016; Perrella et al., 2007; Gruettert et al., 2005). Additional findings suggest potential benefits in improving cognitive symptoms (Van den Eynde et al., 2009) and enhancing overall social and occupational functioning (Bellino et al., 2006; Lee et al., 2016; Perrella et al., 2007; Gruettert et al., 2005). Nevertheless, current evidence remains insufficient to support the efficacy of quetiapine in reducing suicidality and self-injurious behaviors among individuals with BPD (Del Casale et al., 2021).

Asenapine

Asenapine has been shown to improve overall functioning, as well as reduce anxiety, aggression, and impulsivity in individuals with borderline personality disorder (BPD). Similar to olanzapine, it has demonstrated efficacy in alleviating emotional lability, dissociative symptoms, and paranoid ideation. However, there is currently insufficient evidence to support its effectiveness in addressing depressive symptoms, suicidal or self-injurious behaviors, and identity disturbance in patients with BPD (Bozzatello et al., 2017; Del Casale et al., 2021).

Haloperidol

Haloperidol has demonstrated effectiveness in the treatment of various symptoms in individuals with borderline personality disorder (BPD), including depression, anger, hostility, and impulsivity. It has also shown particular benefit in addressing schizotypal features such as paranoid ideation, illusions, and ideas of reference (Soloff et al., 1993). Additional evidence suggests that the combination of haloperidol and phenelzine may lead to modest short-term improvements in irritability and depressive symptoms (Cornelius et al., 1993). However, the long-term efficacy of neuroleptics and monoamine oxidase inhibitor (MAOI) antidepressants in the treatment of BPD remains limited (Cornelius et al., 1993).

Clozapine

Clozapine has been reserved for the treatment of severe cases of borderline personality disorder (BPD), primarily due to its limited indication and notable tolerability concerns, including the risk of agranulocytosis, cholinergic side effects, and eosinophilic myocarditis (Del Casale et al., 2021). Its administration has been associated with improvements in thought disturbances, perceptual alterations, suspiciousness, illusions, dissociative symptoms, and bizarre beliefs among individuals with severe BPD (Benedetti et al., 1998). However, clozapine has not demonstrated efficacy in addressing symptoms such as psychomotor retardation, depressed mood, feelings of guilt, emotional blunting, or grandiose ideation in this population (Frankenburg et al., 1993).

Aripiprazole

In patients with borderline personality disorder (BPD), aripiprazole has demonstrated efficacy in treating a range of symptoms, including obsessive-compulsive tendencies, insecurity in social relationships, depression, anxiety, aggression/hostility, phobic symptoms, paranoid thinking, and other psychotic manifestations (Nickel et al., 2007; Nickel et al. 2006). In long-term treatment, aripiprazole has been shown to improve depressive and anxious symptoms, as well as reduce anger in individuals with BPD (Nickel et al., 2007). Additionally, the augmentation of aripiprazole for three months in sertraline-resistant BPD patients resulted in improvements in global clinical impression and was effective in addressing impulsivity, dissociation, and paranoid ideation. However, this add-on treatment did not produce significant changes in anxiety or depression, nor did it improve feelings of abandonment, interpersonal relationships, identity disturbances, parasuicidal behavior, affective instability, emptiness, or outbursts of anger (Bellino et al., 2008).

5.2.2 Antidepressants

Several studies have examined the potential efficacy of antidepressant medications, including selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), in the treatment of borderline personality disorder (BPD) symptoms, both as monotherapy and as adjunctive treatment to psychotherapy (Del Casale et al., 2021).

Duloxetine

Duloxetine has proven effective not only in the treatment of mood disorders and panic disorder but also in addressing several symptom clusters of borderline personality disorder (BPD) (Knadler et al., 2011). Studies have shown that patients treated with duloxetine exhibited statistically significant improvements in clinical status, overall psychopathology, and

depressive symptoms. Duloxetine appeared to be particularly effective in reducing impulsivity and affective dysregulation, including outbursts of anger and emotional instability. Additionally, it may serve as an effective treatment for BPD patients presenting with somatic symptoms (Bellino et al., 2010).

Fluoxetine

Fluoxetine has demonstrated effectiveness in the pharmacological treatment of borderline personality disorder (BPD), particularly in reducing impulsive behaviors, self-injurious tendencies, and sensitivity to rejection (Salzman et al., 1995). Evidence suggests that its impact on aggressive behavior may be more pronounced in male patients compared to females (New et al. 2004). The symptoms most responsive to fluoxetine include rejection sensitivity, anger, depressed mood, mood instability, irritability, anxiety, obsessive-compulsive symptoms, and various forms of impulsivity, such as substance use and overeating (Norden et al., 1989). An eight-week course of fluoxetine has been associated with significant improvements in overall psychopathological severity, emotional distress, and psychotic symptoms, including paranoid ideation. Reductions in impulsivity have also been reported (Cornelius et al., 1990). When administered at doses up to 60 mg, fluoxetine has proven effective in improving the general symptom profile of BPD, with particularly notable effects on mood symptoms and aggressiveness, including substantial reductions in anger and depression. Compared to placebo, patients receiving fluoxetine have shown marked decreases in both anger and depressive symptoms (Salzman et al., 1995). Overall, fluoxetine appears to be beneficial for the management of anger, aggression, emotional distress, paranoid ideation, mood instability, and overall functioning in individuals with BPD. Its efficacy in mitigating aggression may be linked to the tendency of BPD patients to exhibit aggressive behavior during periods of mood dysregulation (Del Casale et al., 2021).

Flupentixol

The dual dopaminergic and noradrenergic mechanism of action appears to be particularly effective in alleviating depressed mood, fatigue, low energy, and other core symptoms associated with major depressive disorder (Del Casale et al., 2021).

Fluvoxamine

The overall antidepressant efficacy of fluvoxamine has been shown to be comparable to that of various tricyclic antidepressants, including imipramine, clomipramine, and desipramine (Wilde et al., 1993). Its effectiveness has been demonstrated in the treatment of depression in individuals with comorbid conditions such as obesity, obsessive-compulsive disorder, and bulimia nervosa-conditions that may also co-occur with borderline personality disorder (BPD) (Burton et al., 1991). Consequently, fluvoxamine has been proposed as a potential treatment for BPD symptoms (Schatzberg et al., 2000). While it has proven effective in managing rapid mood fluctuations in BPD, it has not demonstrated significant efficacy in addressing impulsivity or aggressive behaviors (Rinne et al., 2002).

Venlafaxine

Given its potential efficacy in addressing various aspects of borderline personality disorder (BPD), venlafaxine has been evaluated in patients exhibiting somatic symptoms and self-injurious behavior. Studies have demonstrated a significant reduction in both symptom domains following treatment (Markovitz et al., 1995).

5.2.3 Antiepileptics

Valproate

Several studies have investigated the use of valproate in the treatment of borderline personality disorder (BPD). An open-label trial indicated that valproate could be an effective treatment for impulsive and aggressive symptoms in patients who did not respond to other pharmacological agents, including serotonergic antidepressants (Kavoussi et al., 1998). Additionally, other studies demonstrated reductions in impulsive aggression and irritability in

BPD patients (Hollander et al., 2005; Simeon et al., 2007). One study comparing the efficacy of omega-3 fatty acids added to valproic acid versus valproic acid monotherapy found that the combination therapy had positive effects, particularly on characteristic BPD symptoms such as impulsive behavioral dyscontrol, anger outbursts, and self-harm. Long-term combined therapy proved significantly effective in managing outbursts of anger. This suggests that the combination of omega-3 fatty acids and valproic acid could be a justified long-term therapeutic approach, particularly when anger behaviors are the predominant feature of the disorder (Bozzatello et al., 2018). However, valproate treatment, when added to dialectical behavior therapy (DBT), did not show greater efficacy than DBT alone, underscoring the critical role of psychological interventions in BPD (Moen et al., 2012). In conclusion, valproic acid has demonstrated effectiveness in managing irritability and aggression in BPD patients.

Lamotrigine

Several studies have explored the use of lamotrigine as a mood stabilizer in borderline personality disorder (BPD). One study demonstrated significant improvements in symptoms of anger and anger traits (Tritt et al., 2005). Additionally, lamotrigine was found to be effective in treating affective instability and general impulsivity (Reich et al., 2009). Another study revealed that lamotrigine was more effective than a placebo in addressing aggression, specifically in terms of the intensity and threshold of the perceived feeling of anger (Leiberich e al., 2008). In summary, while multiple studies have provided evidence of lamotrigine's efficacy in reducing aggressive symptoms, affective lability, and impulsivity in BPD, the largest study failed to observe any significant effects (Crawford et al., 2018).

Topiramate

Topiramate has shown efficacy primarily in the treatment of anger in individuals with borderline personality disorder (BPD) (Nickel et al., 2005). One study demonstrated significant improvements in somatization symptoms, interpersonal sensitivity, anxiety, hostility, phobic anxiety, and the overall severity of symptoms. However, it lacked effectiveness in addressing obsessive-compulsive symptoms, depression, paranoid ideation, and psychoticism. Regarding interpersonal issues, improvements were noted in traits such as being overly autocratic, competitive, introverted, and expressive. Additionally, weight loss was observed as a side effect (Loew et al., 2006).

Gabapentin

This drug has demonstrated efficacy in treating anxiety, affective instability, and depressive symptoms in patients with borderline personality disorder (BPD), although it was frequently used in conjunction with other concurrent treatments, including anxiolytics (47%), antidepressants (27%), and antipsychotics (13%) (Peris et al., 2007).

5.2.4 Other Drugs

Oxytocin

Oxytocin plays a role in the pathophysiology of anxiety disorders through its involvement in social attention, positive social evaluation, prosocial behaviors, and its anxiolytic effects (Rhodes et al., 1981; Viero et al., 2010; Jones et al., 2017). Given that anxiety and social functioning difficulties are key symptoms of borderline personality disorder (BPD), oxytocin has been explored as a potential treatment. A pilot study demonstrated its effects on dysphoric emotional responses to stress, with a tendency toward a more attenuated cortisol response to stress (Simeon et al., 2011). Another recent study found that intranasal oxytocin, when compared to placebo, significantly improved affective empathy and approach motivation in BPD patients, indicating a positive effect of a single dose on social functioning in women with BPD, aligning their behavior more closely with that of healthy controls (Domes et al., 2019). A noteworthy perspective is that dysfunction in social interactions may be a major issue in BPD, and treatment with oxytocin could improve this aspect, subsequently benefiting other

BPD symptoms. However, there remains a paucity of evidence regarding its efficacy, and further studies with larger sample sizes are necessary.

Omega-3 fatty acids

Treatment with omega-3 has been correlated with significant benefits in patients experiencing depressive episodes, including those with major depressive disorder and bipolar disorder (Freeman 2007). Omega-3 polyunsaturated fatty acids, when combined with valproate, have been shown to be effective in treating impulsivity and hostility in patients with borderline personality disorder (BPD) (Bellino et al., 2014). Additionally, ethyl-EPA has proven to be both safe and effective as an 8-week monotherapy in women with moderately severe BPD. Patients treated with ethyl-EPA, compared to those receiving placebo, demonstrated a significant improvement in overall aggressive and depressive symptoms (Zanarini et al., 2003).

Ketamine

A randomized controlled trial provides the first prospective evidence supporting the safety and tolerability of ketamine in individuals with borderline personality disorder (BPD). No serious adverse events were observed, and dissociative symptoms resolved rapidly following infusion, even among participants with a history of dissociation. Although ketamine was associated with greater numerical reductions in depressive symptoms and suicidal ideation compared to midazolam, these differences did not reach statistical significance, likely due to the small sample size and considerable individual symptom variability. Both groups showed improvements in BPD symptoms and anxiety, which may reflect either non-specific therapeutic effects or the natural fluctuation of symptoms in BPD. Notably, social and occupational functioning improved to a greater extent in the ketamine group, correlating with reductions in depression (Fineberg et al., 2023).

5.3 Physical Activity

A growing body of clinical research indicates that physical activity (PA) may play a supportive role in the treatment of BPD, with several studies demonstrating improvements in emotional regulation, stress reduction, and overall well-being (Buric et al., 2023; Riegler et al., 2023; Harty, 2024; Veenstra-Spruit et al., 2024; de Girolamo, 2024). Interventions included a wide range of PA types, such as dance movement therapy (Harty, 2024; Manford, 2014), yoga (Romero, 2022), ergometer cycling (Mehren, 2024; St-Amour et al., 2022; Taylor et al., 2019), and structured or home-based exercise programs (St-Amour, Brunet, et al., 2024). While most interventions were group-based, recent data suggest that individual formats may be preferable for many patients (St-Amour, Cailhol, et al., 2024), supporting the need for tailored approaches. Despite heterogeneity in PA type and intensity, many studies reported beneficial effects on emotion regulation, which was the most frequently targeted outcome across interventions. However, variation in measurement tools, such as the use of seven different scales to assess emotional states across six studies complicates comparisons and meta-analyses. Furthermore, although somatic comorbidities are common in BPD, only a few studies acknowledged physical health outcomes (Kern and Becker, 2012; St-Amour et al., 2022; St-Amour, Brunet, et al., 2024; Manford, 2014). Most interventions were short-term, typically lasting less than three months, which may be insufficient given the complexity of BPD. Moreover, limited reporting on long-term follow-up, adherence, and motivational factors highlights the need for more robust, theory-driven research to determine the sustained impact of PA in this population.

6. Prognostication

A longitudinal study was undertaken to assess the psychopathological and functional outcomes of individuals five years after receiving a diagnosis of BPD during adolescence. Of the initial cohort of 111 participants, 97 (87%) were successfully followed up at ages 19 to 23. The most commonly diagnosed conditions at follow-up included Attention-Deficit/Hyperactivity Disorder (ADHD; 59%), any personality disorder (47%), with 24% continuing to meet diagnostic criteria for BPD, anxiety disorders (37%), depressive disorders

(32%), post-traumatic stress disorder (PTSD) or complex PTSD (20%), schizophrenia-spectrum disorders (16%), and eating disorders (13%). Notably, only 16% of the sample did not fulfill the diagnostic criteria for any mental disorder at the time of follow-up. Approximately 50% of participants were engaged in ongoing psychological and/or pharmacological treatment. Functional impairments persisted, as evidenced by 36% of individuals being classified as not in education, employment, or training (NEET), a rate nearly four times higher than that observed in the general population of the same age group (Jørgensen et al., 2024).

Another study examining non-response to psychotherapy in individuals with BPD indicates that approximately 50% of patients do not exhibit significant improvement, regardless of the type or duration of treatment. The underlying factors contributing to this lack of therapeutic response remain insufficiently understood. To address this gap, both quantitative and qualitative investigations, along with more systematic reporting of a broader array of potential influencing variables, are warranted. Furthermore, it is recommended that future research efforts actively engage both clinicians and service users to gain deeper insight into the reasons why some individuals with BPD may fail to benefit from psychotherapeutic interventions (Woodbridge et al., 2022).

7. Conclusions

Borderline Personality Disorder remains one of the most complex and clinically challenging psychiatric conditions, characterized by profound emotional dysregulation, unstable interpersonal relationships, and high rates of self-injurious behaviors. This review highlights that, beyond the traditional diagnostic criteria, patients with BPD may exhibit a range of emerging and atypical symptoms including transient psychotic features, somatic disturbances, and autonomic dysregulation, which complicate both diagnosis and treatment. Advances in neurobiological and psychophysiological research have contributed to a deeper understanding of the disorder’s underlying mechanisms, supporting a shift toward transdiagnostic and dimensional models of psychopathology. Despite promising developments in therapeutic approaches, particularly DBT and MBT, long-term outcomes remain variable and are often hindered by the disorder's chronicity and comorbidity profile. Pharmacological interventions for BPD are primarily adjunctive, targeting specific symptom domains such as affective instability, impulsivity, and transient psychotic symptoms, rather than the core pathology of the disorder. While no medication is approved specifically for BPD, selective serotonin reuptake inhibitors and other antidepressants are frequently utilized to address comorbid depressive and anxiety symptoms, mood stabilizers such as lamotrigine and valproic acid may attenuate affective dysregulation and impulsivity, and atypical antipsychotics -including olanzapine, aripiprazole, and quetiapine - have demonstrated efficacy in reducing anger, cognitive-perceptual disturbances, and behavioral dyscontrol in some patients. Evidence for these pharmacotherapies remains heterogeneous, with meta-analyses and randomized controlled trials often yielding modest or inconsistent results, underscoring the necessity of individualized treatment planning and the primacy of psychotherapeutic modalities, particularly dialectical behavior therapy, as the foundation of BPD management. Physical activity shows promise as a complementary intervention for individuals with BPD, particularly in enhancing emotional regulation and well-being, though its effectiveness is influenced by the type, format, and duration of the intervention. Future research should address gaps related to somatic health outcomes, long-term adherence, and motivational mechanisms, using standardized measures and theory-based frameworks to strengthen the evidence base. Early identification of atypical manifestations and implementation of tailored, multidisciplinary interventions are essential for improving prognostic trajectories and enhancing quality of life in individuals affected by BPD.

Disclosure

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