DOI: https://doi.org/10.17816/nb677346 EDN: VYZUFR

Borderline Personality Disorder: Identification, Comorbidity, and Emerging Treatment Opportunities

Mikhail L. Zobin

Centre of transformational therapy of addictions, Dobrota, Montenegro

ABSTRACT

This article analyses the diagnostic criteria for borderline personality disorder as defined in the 5th edition of Diagnostic and Statistical Manual of Mental Disorders and the 11th revision of International Classification of Diseases. The combination of categorical and dimensional diagnostic models improves its validity, which meets the needs of clinical practice. At the same time, the heterogeneity and persistent conceptual ambiguity of borderline personality disorder are emphasized. The phenomenology of comorbidity between borderline and addictive disorders is considered as overlapping symptoms that exacerbate overall clinical presentation. Challenges in diagnosing borderline personality disorder are noted when constitutional symptoms are masked by the consequences of psychoactive substance use. The article offers a brief overview of current approaches to the treatment of borderline personality disorder, highlighting the potential of ketamine therapy. The results of our own retrospective open study of 18 patients with dual (borderline personality disorder + alcohol/cocaine use disorder) and triple (borderline personality disorder + alcohol/cocaine use disorder + depression) diagnosis who received ketamine treatment are discussed. Patients received three ketamine infusions over one week (0.5–0.75 mg/kg over 40 minutes), followed by a booster session one month later. Preliminary results of treatment are discussed, which are quite comparable with the effectiveness of specialized psychotherapy. These findings suggest that ketamine therapy may offer a novel perspective on the traditionally pessimistic therapeutic outlook for borderline personality disorder.

Keywords: borderline personality disorder; alcohol and cocaine related disorders; ketamine therapy.

To cite this article:
Zobin ML. Borderline Personality Disorder: Identification, Comorbidity, and Emerging Treatment Opportunities. *Neurology Bulletin.* 2025;57(2):150–159. DOI: 10.17816/nb677346 EDN: VYZUFR

Submitted: 19.03.2025 **Accepted:** 24.03.2025 **Published online:** 28.05.2025

DOI: https://doi.org/10.17816/nb677346 EDN: VYZUFR

Пограничное расстройство личности: идентификация, коморбидность и новые возможности лечения

М.Л. Зобин

Центр трансформационной терапии аддикций, Доброта, Черногория

АННОТАЦИЯ

В статье анализируются диагностические критерии пограничного расстройства личности в рамках DSM-5 и МКБ-11. Сочетание категориальной и размерной диагностической модели повышает её валидность, что соответствует потребностям клинической практики. Одновременно подчёркивается неоднородность и сохраняющаяся концептуальная неопределённость пограничного расстройства. Феноменология коморбидности пограничного и аддиктивного расстройства рассматривается как взаимопроникающая симптоматика, усугубляющая совокупную динамику. Отмечаются сложности диагностики пограничного расстройства личности, когда конституциональная симптоматика маскируется последствиями употребления психоактивных веществ. Приводится краткий обзор современных подходов к лечению пограничного расстройства с акцентом на потенциальных возможностях кетаминовой терапии. Обсуждаются результаты собственного ретроспективного открытого исследования 18 пациентов с двойным (пограничное расстройство личности + расстройство вследствие употребления алкоголя/кокаина) и тройным (пограничное расстройство личности + расстройство вследствие употребления алкоголя/кокаина + депрессия) диагнозом, получавших лечение кетамином. Приводится недельный протокол трёх инфузий кетамина в дозе 0,5–0,75 мг/кг в течение 40 мин с последующей бустерной процедурой через месяц. Обсуждаются предварительные результаты лечения, вполне сопоставимые с эффективностью специализированной психотерапии. Делается вывод о том, что применение кетаминовой терапии позволяет пересмотреть традиционный терапевтический нигилизм в отношении пограничного расстройства личности.

Ключевые слова: пограничное расстройство личности; расстройство вследствие употребления алкоголя и кокаина; кетаминовая терапия.

Как цитировать:
Зобин М.Л. Пограничное расстройство личности: идентификация, коморбидность и новые возможности лечения // Неврологический вестник. 2025. Т. 57, № 2. С. 150–159. DOI: 10.17816/nb677346 EDN: VYZUFR

Рукопись получена: 19.03.2025 **Рукопись одобрена:** 24.03.2025 **Опубликована online:** 28.05.2025

DOI: https://doi.org/10.17816/nb677346 EDN: VYZUFR

Шәхеснең чик тайпылышлары: идентификация, коморбидлык һәм дәвалауның яңа мөмкинлекләре

М.Л. Зобин

Аддикцияләрне трансформация юлы белән дәвалау үзәге, Доброта (Изгелек), Черногория

АННОТАЦИЯ

Мәкаләдә DSM-5 һәм МКБ-11 кысаларында шәхеснең чик тайпылышларын диагностикалау критерийлары анализлана. Категориаль һәм үлчәмле диагностика модельләренең үзара ярашуы аның валидлыгын арттыра, бу клиник практика ихтыяҗларына туры килеп тора. Бер үк вакытта чик тайпылышларының бертөрле булмавы һәм саклана торган концептуаль билгесезлеге ассызыклана. Чик һәм аддиктив тайпылыш коморбидлыгы феноменологиясе гомуми динамиканы катлауландыручы, бер-берсенә үтеп керә торган симптоматика буларак карала. Шәхеснең чик тайпылышларын диагностикалауның катлаулылыгы билгеләнә, конституцион симптоматика психоактив матдәләр куллану нәтиҗәләре белән маскировкалана. Кетамин терапиясенең потенциаль мөмкинлекләренә басым ясап, чик буе тайпылышын дәвалауга заманча алымнарга кыскача күзәтү ясала. Кетамин белән дәвалау алган икеләтә (шәхеснең чик тайпылышы + алкоголь/кокаин куллану нәтиҗәсендәге тайпылыш) һәм өчләтә (шәхеснең буе тайпылышы + алкоголь/кокаин куллану нәтиҗәсендәге тайпылыш + депрессия) диагнозлы 18 пациент белән уздырылган шәхси ретроспектив ачык тикшеренү нәтиҗәләре тасвирлана. 40 минут дәвамында 0,5–0,75 мг/кг дозада өч кетамин инфузиясенең атналык протоколы мисал итеп китерелә, аннан соң бер айдан соң бустер процедурасы үткәрелә. Дәвалауның махсуслаштырылган психотерапия нәтиҗәлелеге белән чагыштырырлык башлангыч нәтиҗәләре турында фикер алышалар. Кетамин терапиясен куллану шәхеснең чик тайпылышын дәвалаудагы традицион терапия нигилизмны яңадан карарга мөмкинлек бирә дигән нәтиҗә ясала.

Төп төшенчәләр: шәхеснең чик тайпылышы; алкоголь һәм кокаин куллану нәтиҗәсендәге тайпылыш; кетамин терапиясе.

Өземтәләр ясау өчен:
Зобин М.Л. Шәхеснең чик тайпылышлары: идентификация, коморбидлык һәм дәвалауның яңа мөмкинлекләре // Неврология хәбәрләре. 2025. Т. 57, № 2. 150–159 б. DOI: 10.17816/nb677346 EDN: VYZUFR

Кулъязма алынган: 19.03.2025 **Кулъязма хупланган:** 24.03.2025 **Бастырылган online:** 28.05.2025

INTRODUCTION

In the 5th edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-5), borderline personality disorder (BPD) is defined by a pervasive pattern of instability in self-image, interpersonal relationships, and affectivity. It is included among a broader group of specific personality disorders. However, BPD is not a fully homogeneous construct, as the diagnosis requires meeting only five out of nine possible criteria. In addition to the categorical model, a dimensional diagnostic approach is concurrently applied. This model assumes varying levels of functional impairment in at least two of four domains (identity, self-direction, empathy, and intimacy) and the presence of at least four of seven personality traits: emotional lability, anxiousness, separation insecurity, depressivity, impulsivity, risk-taking, and hostility. These functional impairments and pathological traits must be pervasive and relatively stable [1].

One important aspect not included in the DSM-5 criteria for BPD is the tendency toward regression, defined as the manifestation of emotions or behavioral responses that are inappropriate for the individual's developmental age in unstructured situations. This characterological feature is poorly responsive to psychotherapy and is associated with reduced treatment efficacy [2].

The adoption of the 11th revision of International Classification of Diseases (ICD-11) marked a paradigmatic shift in the diagnosis and classification of personality disorders. To establish the diagnosis, it has become necessary to determine the severity (mild, moderate, or severe) of general impairments in self and interpersonal functioning. The earlier categorical scheme, although not entirely eliminated, has been replaced by five personality trait domains (negative affectivity, detachment, dissociality, disinhibition, and anankastia) and an optional BPD specifier. These five trait domains, which function as subdiagnostic specifiers comparable to personality trait accentuations, are not regarded as pathological entities. Instead, they serve to identify clinically relevant factors that may influence behavior rather than to be the primary targets of therapeutic intervention [3, 4].

Coherent BPD syndrome typically manifests in adolescence and develops in parallel with symptoms of internalizing disorders (depression and anxiety) and/or externalizing disorders (behavioral problems, hyperactivity, and psychoactive substance (PAS) use) [5]. Although an integrated etiological model has not been established, substantial evidence indicates that the interaction between genetic vulnerability and adverse childhood experiences plays a central role in the etiology of BPD. Phenotypic factors are believed to influence gene expression through modulation mechanisms [6].

Core symptoms of instability in self-perception, interpersonal relationships, and affect are typically accompanied by impulsivity, intense anger, chronic feelings of emptiness, fear of abandonment, suicidal ideation, and/or self-injurious behavior. During periods of distress, transient paranoid ideation or dissociative symptoms may also occur.

Most individuals with BPD present with relatively stable comorbid psychiatric conditions: depressive disorders, 32%–83%; dysthymia, up to 30%; anxiety disorders, approximately 60%; posttraumatic stress disorder (PTSD), 25%–55%; and eating disorders, in more than 33% of cases [7].

Among maladaptive coping mechanisms, one of the most common impulsive responses to stress is PAS use. The link between addictive and personality disorders has long been considered so close that PAS dependence was previously conceptualized as a manifestation of personality pathology rather than a distinct disorder. Although personality and addictive disorders are now recognized as separate nosological entities, their high rate of comorbidity, driven by shared psychopathological spectra and neurophysiological dysfunctions, remains a frequent clinical phenomenon [8–10]. This overlap is so prevalent that some experts have proposed abandoning the classification of addictive comorbidity as a separate diagnosis in favor of viewing it as part of a unified dual disorder construct [11, 12].

Whereas the prevalence of BPD in the general population is estimated at 0.7%–2.7% [13], this figure ranges 34%–73% among individuals with alcohol or drug dependence [14, 15], and the rate of substance use disorders among individuals with BPD reaches 75% [5] and even 84% in some studies [7].

The primary reason is thought to be the impulsivity and need for immediate gratification characteristic of BPD. This limited capacity to delay reward reinforces a persistent pattern of PAS use [7].

Overall, BPD is more strongly associated with drug dependence than with alcohol dependence, and this association tends to diminish with age. However, in all cases, the severity of BPD positively correlates with the severity of substance use disorder, complicating treatment and worsening clinical outcomes [16, 17]. Importantly, substance use may obscure BPD symptomatology, which becomes more evident during periods of abstinence yet is still misattributed to the effects of substance abuse. This underrecognition of BPD can result in inappropriate pharmacological treatment, which is typically of limited efficacy [6].

It is still unclear whether BPD should be conceptualized as a specific disorder or as a broader disturbance of mental functioning [18, 19]. A substantial overlap has been observed between BPD and the general psychopathology factor (the *p* factor), which reflects a liability to a broad spectrum of mental disorders [20–22]. From this perspective, comorbid psychopathology in BPD reflects a more global set of vulnerabilities, with the *p* factor helping to explain the challenges in identifying specific etiological factors, biomarkers, and effective targeted treatments for individual psychiatric syndromes. This has contributed to the growing prominence of dimensional and transdiagnostic models of psychopathology.

DOI: https://doi.org/10.17816/nb677346

TREATMENT

Caring for patients with BPD has always been a challenging therapeutic task, as pathological behavioral patterns combined with constitutional traits of functioning tend to be highly resistant to change. In a 20-year prospective study, remission reaching the level of recovery, defined as symptom reduction along with restoration of social and occupational functioning, was observed in 39% of patients with BPD, compared with 73% of those with other personality disorders [23]. Patients with BPD often have difficulty achieving full recovery, even over extended periods. Moreover, most of the 290 inpatients included in that study received pharmacological and/or psychotherapeutic treatment, so the findings do not reflect the natural course of BPD in the absence of therapeutic interventions.

In both Russian and international clinical guidelines on personality disorders, BPD receives the most attention, whereas other personality disorders are typically addressed only in general terms, without further specification. At the same time, disagreements persist among different schools of thought regarding both the diagnostic boundaries of BPD and the recommended treatment strategies [24–26]. A unifying point is the recommendation to use psychotherapy as the first-line intervention, with a minimum duration of 3 months [27]. Among the specialized approaches developed for treating BPD are dialectical behavior therapy (a form of cognitive-behavioral therapy); mentalization-based therapy (a structured approach targeting unstable self-identity and interpersonal functioning); transference-focused psychotherapy (a psychoanalytic modality centered on the disintegration of object relations); and schema therapy (an integrative approach combining cognitive-behavioral, psychodynamic, and experiential methods to address maladaptive communication and thinking patterns) [2].

Evidence suggests that specialized psychotherapeutic techniques are more effective than standard treatment approaches, particularly in complex patients [28]. However, none of the specialized modalities has demonstrated clear superiority over the others [29]. Whereas the effect sizes of specialized interventions for core BPD symptom severity are estimated at 0.5–0.65 [2] nearly half of patients remain unresponsive to talk therapy, underscoring the need for continued efforts to identify more effective therapeutic interventions [30].

In the absence of specific pharmacologic treatments for BPD, certain medications have been effective as symptomatic therapy. Notably, second-generation antipsychotics, mood stabilizers, and omega-3 fatty acid supplements have demonstrated some beneficial effects [31]. Antidepressants may also be helpful in cases with comorbid depressive states [5]. Thus, pharmacologic interventions are not recommended as primary treatment for BPD *per se* but are used as adjunctive therapy to target discrete and severe comorbid conditions (e.g., major depressive episodes, persistent anxiety, transient psychotic symptoms) during acute crisis situations [25, 32]. None of the currently available medications has shown a significant effect on the core symptoms of BPD, such as chronic feelings of emptiness, disturbances in identity, or pervasive alienation [32, 33]. For this reason, psychedelic-assisted therapies, which may act on the fundamental aspects of subjective experience, are being considered as potentially effective.

It is well established that subanesthetic doses of the glutamatergic modulator ketamine[1] demonstrate rapid antidepressant and antisuicidal effects [34], assist in overcoming substance use disorders [35, 36], and exert beneficial effects in a range of other pathological conditions [37, 38]. A short ketamine therapy protocol (4 infusions of 0.5–0.75 mg/kg over two weeks) in patients with treatment-resistant depression and comorbid BPD has been shown to improve symptoms, with a positive correlation between outcomes for both disorders [39]. Ketamine may be effective in mixed states in which depressive symptoms coexist with generalized anxiety, irritability, and agitation [40]. The reduction in suicidal ideation following ketamine therapy may occur independently of improvements in depressive symptoms [41], which is particularly relevant for patients prone to stress-induced suicidal responses, as is often the case in BPD [42, 43].

In the vast majority of ketamine trials for depression, patients with comorbid BPD were not excluded; however, they were not analyzed as a distinct subgroup either. Therefore, the efficacy and safety of ketamine treatment specifically for these patients have rarely been evaluated. In the few studies targeting BPD populations, ketamine administration was not accompanied by psychotherapy or psychedelic integration [43–45].

We find no justification for the view that patients with severe manifestations of BPD should be disqualified from receiving ketamine treatment [46]. Such concerns are based on the conceptualization of BPD as a prepsychotic level of personality organization, associated with impaired psychological defenses, identity disintegration, and poor impulse control [47]. Isolated reports suggesting that ketamine may trigger undesirable symptoms, such as impulsive behavior or emotional dysregulation [48], stand in contrast to data from systematic reviews, which describe adverse effects as minimal and limited to transient psychosensory dissociation during therapeutic sessions [34, 35, 37]. No significant risks have been identified when ketamine is administered under controlled medical conditions [36, 49–51]. Many participants have described ketamine therapy as transformative: both in reducing alcohol dependence and in addressing problems related to identity and self-definition [52].

[1] The use of narcotic substances for the treatment of psychiatric and substance use disorders is prohibited under the Russian law.

RESEARCH SECTION

This open retrospective study included a sample of 18 patients (14 men and 4 women), aged 22 to 48 years (mean age, 30.0 ± 7.2 years), all of whom were receiving outpatient treatment for addictive and/or depressive disorders with comorbid BPD. The diagnosis of BPD was established according to DSM-5 criteria. Eleven patients had a dual diagnosis (BPD + addictive disorder), three had BPD + dysthymia, and four had a triple diagnosis (BPD + addiction + depressive disorder). Additional comorbid diagnoses were as follows: panic disorder in 3 patients; attention-deficit/hyperactivity disorder (ADHD) in 2; posttraumatic stress disorder (PTSD) combined with an eating disorder in 1; and bipolar II disorder in 1. Disorder severity was evaluated using ICD-11 criteria. Ten patients met the criteria for mild BPD (6D10.0), and eight for moderate BPD (6D10.1).

Only 1 patient sought treatment primarily for core BPD symptoms. Three patients presented with depressive or anxiety-spectrum disorders, whereas 14 sought medical advice for addictive disorders. In 6 cases, the addiction was alcohol-related; in 4, a combination of cocaine/crack and alcohol; and in another 4, cocaine use alone. In 5 patients, a history of benzodiazepine misuse was also reported. In 3 cases, pathological gambling was noted alongside substance use. It is recognized that specific treatment for BPD should take precedence over the management of comorbid conditions, except for severe substance use [33].

Half of the patients in our sample had prior experience with pharmacologic treatment; however, their depressive symptoms remained fairly resistant, and none had undergone psychotherapy. Among these nine patients, only four had been diagnosed with emotionally unstable personality disorder (borderline and impulsive types). In the other five patients, no personality disorder had been identified.

Meanwhile, BPD symptoms were traceable from late adolescence in 8 out of 18 patients and preceded the onset of substance use disorders. In four cases, substance abuse was preceded by other psychiatric conditions, ADHD, PTSD with anorexia, and bipolar disorder. A common feature among the analyzed cases was that BPD symptoms were masked by substance use. Impairments in social functioning and emotional instability were frequently interpreted as consequences of substance abuse.

All patients underwent a standardized short-protocol treatment at a medical center: three ketamine infusions (0.5–0.75 mg/kg over 40 minutes) over the course of one week following motivational interviewing, with a subsequent fourth booster session 4 to 6 weeks later. Psychedelic integration (the therapeutic processing of insights from peak experiences) was provided to varying degrees during the sessions. Psychopharmacologic agents were prescribed for the treatment of comorbid conditions, alongside counseling support for the patients and their immediate social environment. No specialized psychotherapy was conducted. Counseling was provided without delay, both in-office and remotely. In cases of relapse related to the addictive component, as well as in other crisis situations, the protocol was resumed, often with adjustments to the therapeutic regimen. Documented psychometric monitoring during and after treatment was not conducted, as the efficacy of ketamine for the treatment of addiction or depression with comorbid BPD had not initially been the focus of investigation.

In the retrospective assessment of the identified cohort, positive changes of varying degrees were observed in 14 patients, based on self-reports and feedback from relatives. The effect size appears at least comparable to the outcomes reported for specialized psychotherapeutic approaches to BPD [2]. According to visual analog scale estimates, patients reported improvements in their condition ranging 20%–80%. In addition to sustained abstinence from PAS use, ketamine-assisted interventions had a beneficial impact on core features of BPD, including emotional and behavioral dysregulation, impulsivity, and interpersonal hypersensitivity. A phenomenological analysis of the responses from patients who responded positively to the ketamine intervention suggests that changes in self-identity were associated with the most salient aspects of the subjective experience encountered during the dissociative state [53].

Four patients were unresponsive to the ketamine treatment protocol. These individuals exhibited no significant reduction in BPD symptoms within 1 month after the three infusions and subsequent booster session, and no stable remission from addictive disorders was achieved. All of them met the ICD-11 criteria for moderate borderline personality disorder (6D10.1).

DISCUSSION

The presented data are only for reference. As the study was not initially focused on BPD, the target group was identified post hoc. The result reliability is limited by the retrospective open-label design, the absence of a control group, and the lack of dimensional measures of change. Standardized assessment tools such as the Level of Personality Functioning Scale [54], the Borderline Symptom List [55], or the Inventory of Personality Organization [56] were not employed.

Nevertheless, a positive response to ketamine-assisted transformation was observed in three-fourths of patients with BPD, compared with approximately half in specialized psychotherapy settings [30]. Moreover, the proposed approach appears to be more cost-effective and feasible, as access to specialized psychotherapy is often quite limited.

Given the importance of traumatic experiences in the development of BPD, the potential of psychedelic integration should not be overlooked as a means of improving outcomes, especially when peak experiences during sessions

are associated with painful memories and current symptoms. Integration involves clarifying and supporting the meanings of the experienced insights and, ideally, should facilitate the incorporation of new self-awareness into daily life [57].

Abstinence from PAS use is a significant indicator of positive changes in BPD and concurrently exerts a beneficial effect on interpersonal relationships, self-esteem, and comorbid depressive symptoms.

Encouraging results regarding the use of ketamine in BPD therapy are largely attributable to its direct and rapid antidepressant and anxiolytic effects [39, 43, 44]. This property promotes better adherence to treatment and facilitates the establishment of a therapeutic alliance [38]. Given the frequent treatment discontinuation among patients with BPD [30, 58, 59], interventions that enhance compliance offer additional advantages.

The weak response to previously prescribed antidepressants observed in our patients may reflect the nature of BPD symptoms, which are often resistant to pharmacologic interventions. In contrast, the antidepressant effects of ketamine contribute to reducing impulsivity, affective lability, irritability, and somatic manifestations. Patients with stress-induced suicidal ideation, a common feature of BPD, tend to respond better to ketamine, with improvements noted in emotional instability and self-injurious behavior [39, 43, 46].

At the neurobiological level, ketamine-induced changes may foster a more stable sense of identity, along with improved top-down cognitive control and bottom-up emotional regulation [60]. This is particularly relevant given that patients with BPD typically exhibit reduced activation in frontal executive regions and hyperactivation of emotion-related limbic areas. Enhanced neuroplasticity between limbic structures and neural circuits responsible for emotional and behavioral regulation is likely to be a critical factor in the treatment of BPD [46].

An alternative perspective suggests that the subjective intensity of the psychedelic experience, rather than neuroplastic activation, serves as the primary predictor of therapeutic response regardless of diagnosis [61].

Such a dichotomy between neurobiological and mental content appears artificial, as the "brain vs mind" contradiction is addressed both in the nondualistic philosophy of enactivism, which views the brain and consciousness as inseparable, mutually influencing aspects of a unified whole [62], and in the concept of supervenience, which refers to the dependency of one system's parameters on the state of another [63].

An analysis of four cases with no expected response to ketamine revealed consistently impaired functioning among treatment-resistant patients, characterized by the predominance of primitive defense mechanisms in conflict situations, poor differentiation between intrapsychic and external stimuli, and cognitive and affective immaturity. Their addictive behaviors often appeared as typical stress responses or as a consequence of lacking a productive behavioral strategy in ambiguous situations. These manifestations of behavioral regression may require more prolonged intervention. Some researchers point to the therapeutic benefit of higher doses of ketamine followed by integration of deep psychedelic experiences [36].

CONCLUSION

The ICD-11 approach, which moves beyond a purely categorical framework, helps clarify that individuals with more severe disorders do not necessarily exhibit more pronounced manifestations of a specific typological trait, as it is often assumed. They are more likely to display broader and more disharmonious personality features affecting multiple domains of functioning. In other words, the severity of personality disorder is determined by the pervasiveness and diversity of behavioral disturbances rather than by the specificity of the personality type [64].

The high comorbidity of BPD with a wide range of mental and behavioral disorders is a key factor driving pharmacologic intervention and polypharmacy in these patients. Pharmacotherapy may be appropriate in severe cases or when psychotherapy proves ineffective. Conversely, patients undergoing BPD-specific psychotherapy typically require fewer medications.

Because PAS use is a common manifestation of behavioral dysregulation in individuals with BPD, addictive behaviors are often the primary reason for seeking medical care. In such cases, effective treatment of addiction becomes an essential component of comprehensive care for BPD. Ketamine-based therapeutic interventions may not only support abstinence and alleviate depressive symptoms but also offer a novel avenue for addressing core features of BPD. In treatment-resistant cases, combined therapeutic strategies or prolonged protocols employing repeated dosing may be considered. Further research is needed to evaluate the clinical efficacy, optimal dosing strategies, and safety profile of ketamine in the treatment of BPD. However, the emerging progress in understanding therapeutic options already invites a re-evaluation of the traditional therapeutic nihilism surrounding BPD.

ADDITIONAL INFORMATION

Author contributions: M.L. Zobin — conceptualization, methodology, clinical examination, literature analysis, writing—original draft, writing—review & editing. The author confirms confirm that his authorship meets the ICMJE criteria (the author made a substantial contribution to the conceptualization, investigation, and manuscript preparation, and reviewed and approved the final version prior to publication).

Consent for publication: Written informed consent was obtained from all patients and/or their legal representatives for the publication of personal data in a scientific journal and its online version. The scope of published data was approved by the patients.

Funding sources: No funding.

Disclosure of interests: The authors have no relationships, activities, or interests for the last three years related to for-profit or not-for-profit third parties whose interests may be affected by the content of the article.

Statement of originality: No previously published material (text, images, or data) was used in this work.

Data availability statement: The editorial policy regarding data sharing does not apply to this work.

Generative AI: No generative artificial intelligence technologies were used to prepare this paper.

Provenance and peer review: This work was submitted unsolicited and reviewed following the standard procedure. The review process involved members of the editorial board, and the in-house scientific editor.

REFERENCES | СПИСОК ЛИТЕРАТУРЫ

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-5. Arlington: American Psychiatric Association; 2013. ISBN: 978-0-89042-554-1

2. Leichsenring F, Fonagy P, Heim N, et al. Borderline personality disorder: a comprehensive review of diagnosis and clinical presentation, etiology, treatment, and current controversies. *World Psychiatry.* 2024;23(1):4–25. doi: 10.1002/wps.21156

3. WHO. ICD-11 Clinical descriptions and diagnostic guidelines for mental and behavioural disorders. Geneva: World Health Organisation; 2022. ISBN: 978-92-4-007726-3

4. Bach B, Kramer U, Doering S, et al. The ICD-11 classification of personality disorders: a European perspective on challenges and opportunities. *Bord Personal Disord Emot Dysregul.* 2022;9(1):12. doi: 10.1186/s40479-022-00182-0

5. Bohus M, Stoffers-Winterling J, Sharp C, et al. Borderline personality disorder. *Lancet.* 2021;398(10310):1528–1540. doi: 10.1016/S0140-6736(21)00476-1

6. Gunderson JG, Herpertz SC, Skodol AE, et al. Borderline personality disorder. *Nat Rev Dis Primers.* 2018;4:18029. doi: 10.1038/nrdp.2018.29

7. Shah R, Zanarini MC. Comorbidity of borderline personality disorder: current status and future directions. *Psychiatr Clin N Am.* 2018;41(4):583–593. doi: 10.1016/j.psc.2018.07.009

8. Szerman N, Peris L. Personality disorders and addiction disorders. In: el-Guebaly N, Carrà G, Galanter M, editors. *Textbook of Addiction Treatment: International Perspectives.* Springer, Milano; 2015. P. 2063–2083. doi: 10.1007/978-88-470-5322-9_120

9. Trull TJ, Freeman LK, Vebares TJ, et al. Borderline personality disorder and substance use disorders: an updated review. *Borderline Personal Disord Emot Dysregul.* 2018;5:15. doi: 10.1186/s40479-018-0093-9

10. Stetsiv K, McNamara IA, Nance M, Carpenter RW. The co-occurrence of personality disorders and substance use disorders. *Curr Psychiatry Rep.* 2023;25(11):545–554. doi: 10.1007/s11920-023-01452-6

11. Szerman N, Torrens M, Maldonado R, et al. World association on dual disorders (WADD). addictive and other mental disorders: a call for a standardized definition of dual disorders. *Transl Psychiatry.* 2022;12(1):446. doi: 10.1038/s41398-022-02212-5

12. Maremmani A, Maremmani I. It's time to admit the existence of a psychopathology specific to addiction. *Neurology Bulletin.* 2025;57(1):5–11. doi: 10.17816/nb637368

13. Chapman J, Jamil RT, Fleisher C, Torrico TJ. Borderline personality disorder. In: *StatPearls.* Treasure Island (FL): StatPearls Publishing; 2024.

14. Trull TJ, Jahng S, Tomko RL, et al. Revised NESARC personality disorder diagnoses: gender, prevalence, and comorbidity with substance dependence disorders. *J Pers Disord.* 2010;24(4):412–426. doi: 10.1521/pedi.2010.24.4.412

15. Parmar A, Kaloiya G. Comorbidity of personality disorder among substance use disorder patients: a narrative review. *Indian J Psychol Med.* 2018;40(6):517–527. doi: 10.4103/IJPSYM.IJPSYM_164_18

16. Jahng S, Trull TJ, Wood PK, et al. Distinguishing general and specific personality disorder features and implications for substance dependence comorbidity. *J Abnorm Psychol.* 2011;120(3):656–669. doi: 10.1037/a0023539

17. Fraser R, Isaif L, Teles D, Laporte L. Personality disorders and addiction disorders. In: el-Guebaly N, Carrà G, Galanter M, Baldacchino AM, editors. *Textbook of Addiction Treatment.* Springer, Cham; 2021. doi: 10.1007/978-3-030-36391-8_96

18. Mulder RT, Horwood LJ, Tyrer P. The borderline pattern descriptor in the International Classification of Diseases, 11th Revision: A redundant addition to classification. *Aust N Z J Psychiatry.* 2020;54(11):1095–1100. doi: 10.1177/0004867420951608

19. Gutiérrez F, Aluja A, Ruiz Rodríguez J, et al. Borderline, where are you? A psychometric approach to the personality domains in the International Classification of Diseases, 11th Revision (ICD-11). *Personal Disord.* 2023;14(3):355–359. doi: 10.1037/per0000592

20. Caspi A, Houts RM, Belsky DW, et al. The p factor: one general psychopathology factor in the structure of psychiatric disorders? *Clin Psychol Sci.* 2014;2(2):119–137. doi: 10.1177/2167702613497473

21. Gluschkoff K, Jokela M, Rosenström T. General psychopathology factor and borderline personality disorder: Evidence for substantial overlap from two nationally representative surveys of U.S. adults. *Personal Disord.* 2021;12(1):86–92. doi: 10.1037/per0000405

22. Sharp C, Wall K. DSM-5 level of personality functioning: refocusing personality disorder on what it means to be human. *Annu Rev Clin Psychol.* 2021;17:313-337. doi: 10.1146/annurev-clinpsy-081219-105402

23. Zanarini MC, Temes CM, Frankenburg FR, et al. Description and prediction of time-to-attainment of excellent recovery for borderline patients followed prospectively for 20 years. *Psychiatry Res.* 2018;262:40–45. doi: 10.1016/j.psychres.2018.01.034

24. Clinical guidelines: Specific personality disorders. 2024–2025–2026 (23.08.24). Approved by the Ministry of Health of the Russian Federation. (In Russ.) URL: http://disuria.ru/_ld/14/1459_kr24F60F61MZ.pdf

25. National Institute for Health and Care Excellence. Borderline personality disorder: recognition and management. Clinical guideline. London: National Institute for Health and Care Excellence; 2009. URL: https://www.nice.org.uk/guidance/cg78

26. Simonsen S, Bateman A, Bohus M, et al. European guidelines for personality disorders: past, present and future. *Borderline Personal Disord Emot Dysregul.* 2019;6:9. doi: 10.1186/s40479-019-0106-3

27. Cristea IA, Gentili C, Cotet CD, et al. Efficacy of psychotherapies for borderline personality disorder: a systematic review and meta-analysis. *JAMA Psychiatry.* 2017;74(4):319–328. doi: 10.1001/jamapsychiatry.2016.4287

28. Smits ML, Luyten P, Feenstra DJ, et al. Trauma and outcomes of mentalization-based therapy for individuals with borderline personality disorder. *Am J Psychother.* 2022;75(1):12–20. doi: 10.1176/appi.psychotherapy.20210027

29. Setkowski K, Palantza C, van Ballegooijen W, et al. Which psychotherapy is most effective and acceptable in the treatment of adults with a (sub)clinical borderline personality disorder? A systematic review and network meta-analysis. *Psychol Med.* 2023;53(8):3261–3280. doi: 10.1017/S0033291723000685

30. Woodbridge J, Townsend M, Reis S, et al. Non-response to psychotherapy for borderline personality disorder: A systematic review. *Aust N Z J Psychiatry.* 2022;56(7):771–787. doi: 10.1177/00048674211046893

31. Gartlehner G, Crotty K, Kennedy S, et al. Pharmacological treatments for borderline personality disorder: A systematic review and meta-analysis. *CNS Drugs.* 2021;35(10):1053–1067. doi: 10.1007/s40263-021-00855-4

32. Stoffers J, Völlm BA, Rücker G, et al. Pharmacological interventions for borderline personality disorder. *Cochrane Database Syst Rev.* 2010;(6):CD005653. doi: 10.1002/14651858.CD005653.pub2

33. Pascual JC, Arias L, Soler J. Pharmacological management of borderline personality disorder and common comorbidities. *CNS Drugs.* 2023;37(6):489–497. doi: 10.1007/s40263-023-01015-6

34. Yavi M, Lee H, Henter ID, et al. Ketamine treatment for depression: a review. *Discov Ment Health.* 2022;2(1):9. doi: 10.1007/s44192-022-00012-3

35. Jones JL, Mateus CF, Malcolm RJ, et al. Efficacy of ketamine in the treatment of substance use disorders: a systematic review. *Front Psychiatry.* 2018;9:277. doi: 10.3389/fpsyt.2018.00277

36. Dakwar E, Nunes EV, Hart CL, et al. A sub-set of psychoactive effects may be critical to the behavioral impact of ketamine on cocaine use disorder: Results from a randomized, controlled laboratory study. *Neuropharmacology.* 2018;142:270–276. doi: 10.1016/j.neuropharm.2018.01.005
37. Walsh Z, Mollaahmetoglu OM, Rootman J, et al. Ketamine for the treatment of mental health and substance use disorders: comprehensive systematic review. *BJPsych Open.* 2021;8(1):e19. doi: 10.1192/bjo.2021.1061
38. Drozdz SJ, Goel A, McGarr MW, et al. Ketamine assisted psychotherapy: A systematic narrative review of the literature. *J Pain Res.* 2022;15:1691–1706. doi: 10.2147/JPR.S360733
39. Danayan K, Chisamore N, Rodrigues NB, et al. Real world effectiveness of repeated ketamine infusions for treatment-resistant depression with comorbid borderline personality disorder. *Psychiatry Res.* 2023;323:115133. doi: 10.1016/j.psychres.2023.115133
40. McIntyre RS, Lipsitz O, Rodrigues NB, et al. The effectiveness of ketamine on anxiety, irritability, and agitation: Implications for treating mixed features in adults with major depressive or bipolar disorder. *Bipolar Disord.* 2020;22(8):831–840. doi: 10.1111/bdi.12941
41. Grunebaum MF, Galfalvy HC, Choo TH, et al. Ketamine for rapid reduction of suicidal thoughts in major depression: A midazolam controlled randomized clinical trial. *Am J Psychiatry.* 2018;175(4):327–335. doi: 10.1176/ appi.ajp.2017.17060647
42. Lengvenyte A, Olie E, Courtet P. Suicide has many faces, so does ketamine: a narrative review on Ketamine's antisuicidal actions. *Curr Psychiatry Rep.* 2019;21(12):132. doi: 10.1007/s11920-019-1108-y
43. Nandan NK, Soni PK, Parsaik A, Hashmi A. "Esketamine" in borderline personality disorder: a look beyond suicidality. *Cureus.* 2022;14(4):e24632. doi: 10.7759/cureus.24632
44. Rogg H, Avram M, Müller F, et al. Ketamine as a treatment option for severe borderline personality disorder: a case report. *J Clin Psychopharmacol.* 2023;43(1):64–65. doi: 10.1097/JCP.0000000000001642
45. Fineberg SK, Choi EY, Shapiro-Thompson R, et al. A pilot randomized controlled trial of ketamine in borderline personality disorder. *Neuropsychopharmacology.* 2023;48(7):991–999. doi: 10.1038/s41386-023-01540-4
46. Więdłocha M, Marcinowicz P, Komarnicki J, et al. Depression with comorbid borderline personality disorder — could ketamine be a treatment catalyst? *Front Psychiatry.* 2024;15:1398859. doi: 10.3389/fpsyt.2024.1398859
47. Wöller W, Huppertz BJ. Borderline — eine diagnostische Einheit? [Borderline — a diagnostic entity?]. *Fortschr Neurol Psychiatr.* 1984;52(10):338–345. doi: 10.1055/s-2007-1002031
48. Vanicek T, Unterholzner J, Lanzenberger R, et al. Intravenous esketamine leads to an increase in impulsive and suicidal behaviour in a patient with recurrent major depression and borderline personality disorder. *World J Biol Psychiatry.* 2022;23(9):715–718. doi: 10.1080/15622975.2022.2031287
49. Krupitsky E, Burakov A, Romanova T, et al. Ketamine psychotherapy for heroin addiction: immediate effects and two-year followup. *J Subst Abuse Treat.* 2002;23(4):273–283. doi: 10.1016/S0740-5472(02)00275-1
50. Rothberg RL, Azhari N, Haug NA, Dakwar E. Mystical-type experiences occasioned by ketamine mediate its impact on at-risk drinking: Results from a randomized, controlled trial. *J Psychopharmacol.* 2021;35(2):150–158. doi: 10.1177/0269881120970879
51. Chiappini S, d'Andrea G, De Filippis S, et al. Esketamine in treatment-resistant depression patients comorbid with substance-use disorder: A viewpoint on its safety and effectiveness in a subsample of patients from the REAL-ESK study. *Eur Neuropsychopharmacol.* 2023;74:15–21. doi: 10.1016/j.euroneuro.2023.04.01 145
52. Mollaahmetoglu OM, Keeler J, Ashbullby KJ, et al. "This is something that changed my life": A qualitative study of patients' experiences in a clinical trial of ketamine treatment for alcohol use disorders. *Front Psychiatry.* 2021;12:695335. doi: 10.3389/fpsyt.2021.695335
53. Nielson EM, May DG, Forcehimes AA, Bogenschutz MP. The psychedelic debriefing in alcohol dependence treatment: illustrating key change phenomena through qualitative content analysis of clinical sessions. *Front Pharmacol.* 2018;9:132. doi: 10.3389/fphar.2018.00132
54. Hutsebaut J, Bender DS. The clinical utility of the level of personality functioning scale: a treatment perspective. *J Psychiatr Pract.* 2024;30(6):411–420. doi: 10.1097/PRA.0000000000000822
55. Kleindienst N, Jungkunz M, Bohus M. A proposed severity classification of borderline symptoms using the borderline symptom list (BSL-23). *Borderline Personal Disord Emot Dysregul.* 2020;7(1):11. doi: 10.1186/s40479-020-00126-6
56. Unoka Z, Csáky-Pallavicini K, Horváth Z, et al. The Inventory of personality organization: A valid instrument to detect the severity of personality dysfunction. *Front Psychiatry.* 2022;13:995726. doi: 10.3389/fpsyt.2022.995726
57. Gren J, Gorman I, Ruban A, et al. Call for evidence-based psychedelic integration. *Exp Clin Psychopharmacol.* 2024;32(2):129–135. doi: 10.1037/pha0000684
58. Iliakis EA, Ilagan GS, Choi-Kain LW. Dropout rates from psychotherapy trials for borderline personality disorder: a meta-analysis. *Personal Disord.* 2021;12(3):193–206. doi: 10.1037/per0000453
59. Leichsenring F, Sarrar L, Steinert C. Drop-outs in psychotherapy: a change of perspective. *World Psychiatry.* 2019;18(1):32–33. doi: 10.1002/wps.20588
60. Sicorello M, Schmahl C. Emotion dysregulation in borderline personality disorder: A fronto-limbic imbalance? *Curr Opin Psychol.* 2021;37:114–120. doi: 10.1016/j.copsyc.2020.12.002
61. Romeo B, Hermand M, Pétillion A, et al. Clinical and biological predictors of psychedelic response in the treatment of psychiatric and addictive disorders: A systematic review. *J Psychiatr Res.* 2021;137:273–282. doi: 10.1016/j.jpsychires.2021.03.002
62. Varela FJ, Thompson ET, Rosch E. *The embodied mind: cognitive science and human experience.* MIT press; 1993. 308 p.
63. Davidson D. *The material mind. Essays on actions and events.* New York: Oxford University Press; 2001. 346 p.
64. Tyrer P, Mulder R, Kim YR, Crawford MJ. The development of the ICD-11 classification of personality disorders: an amalgam of science, pragmatism, and politics. *Annu Rev Clin Psychol.* 2019;15:481–502. doi: 10.1146/annurev-clinpsy-050718-095736

AUTHOR'S INFO

Mikhail L. Zobin, MD, Cand. Sci. (Medicine);
address: Centre of transformational therapy of addictions, Krivaja st, Dobrota, Montenegro, 85331;
ORCID: 0000-0002-8239-3770;
eLibrary SPIN: 2440-1383;
e-mail: dr.zobin@gmail.com

ОБ АВТОРЕ

Зобин Михаил Леонидович, канд. мед. наук;
адрес: Черногория, 85331, Доброта, ул. Кривая, Центр трансформационной терапии аддикций;
ORCID: 0000-0002-8239-3770;
eLibrary SPIN: 2440-1383;
e-mail: dr.zobin@gmail.com