REVIEW PAPER Curr Probl Psychiatry, Vol. 24(2023):192-198

DOI:10.12923/2353-8627/2023-0018

Czasopismo indeksowane na liście MNiSW - 70 pkt.

The meaning of lithium and naltrexone pharmacotherapy in the treatment of borderline personality disorder – a narrative review

Zuzanna Joanna Wingralek[1] ABDEFG, https://orcid.org/0000-0003-3253-9345,
Aleksandra Marczak[1] ABDEFG, https://orcid.org/0000-0001-5950-3567,
Justyna Tomasik[1] ABDEFG, https://orcid.org/0000-0001-6114-6992,
Adrian Giermasiński[1] ABDEFG,
Michał Dzikowski[2] ABDEFG, https://orcid.org/0000-0002-4252-7308,

[1]Student Research Group at the I Department of Psychiatry, Psychotherapy, and Early Intervention, Medical University of Lublin, Poland
[2] I Department of Psychiatry, Psychotherapy, and Early Intervention, Medical University of Lublin, Poland

Abstract

Introduction: Borderline personality disorder (BPD) affects approximately 1%-3% of the population. As the most common personality disorder, BPD features behavioural, emotional and social dysfunctions. It often co-occurs with self-harm, suicidal tendencies and substance abuse. To date, pharmacological treatment does not provide sufficient therapeutic effects. The aim of our study is to analyse the neurobiological, genetic and environmental components in the aetiopathogenesis of BPD and to collect data on the innovative use of lithium and naltrexone in the therapy of BPD.

Methods: Basing on PubMed and Google Scholar databases using the following keywords: borderline, lithium, naltrexone for papers published from 1979 to 2022.

Results: Difficult childhood, and emotional, sexual and physical abuse are the strongest predictors of BPD development. The core symptoms of BPD may be related to dysfunction of the serotonin, dopaminergic, endogenous system and opioid systems. Variation in 5-HTT, COMT, FKBP5 and oxytocin receptor genes may influence the course of BPD. Imaging studies have shown structural and functional abnormalities in the prefrontal cortex, amygdala and hippocampus. Lithium reduces impulsivity, aggression, suicidal tendencies and self-harm in BPD. Naltrexone may effectively reduce self-harm without suicidal tendencies, impulsivity, substance abuse and suicidality.

Conclusions: No unified model has been developed to account for environmental, genetic and neurobiological components in the pathogenesis of BPD. Understanding the mechanisms is a crucial step towards personalising treatment. The use of lithium and naltrexone may have positive therapeutic effects. Randomised clinical trials are required to establish the efficacy and safety of both drugs in long-term treatment.

Keywords: borderline, lithium, naltrexone

Streszczenie

Wstęp: Zaburzenie osobowości typu borderline (BPD) występuje u około 1%-3% populacji. Jednocześnie jest najczęstszym zaburzeniem osobowości. BPD charakteryzuje się dysfunkcjami behawioralnymi, emocjonalnymi i społecznymi. Często współwystępuje z samookaleczaniem, tendencjami samobójczymi oraz nadużywaniem substancji psychoaktywnych. Dotychczasowe leczenie farmakologiczne nie przynosi wystarczających efektów terapeutycznych. Dlatego celem naszej pracy jest przeanalizowanie komponentów neurobiologicznych, genetycznych i środowiskowych w etiopatogenezie BPD oraz zebranie danych na temat innowacyjnego zastosowania litu i naltreksonu w leczeniu BPD.

Metody: Dokonano przeglądu narracyjnego dostępnej literatury, przeszukując bazy PubMed oraz Google Scholar przy użyciu następujących słów-kluczy: borderline, lit, naltrekson dla prac opublikowanych od roku 1979 do roku 2022.

Wyniki: Czynniki środowiskowe m.in. trudne dzieciństwo, przemoc emocjonalna, seksualna i fizyczna są najsilniejszym predyktorem rozwoju BPD. Podstawowe objawy BPD mogą mieć związek z dysfunkcją układu serotoninowego,

dopaminergicznego, endogennego układu opioidowego. Zmienność w genach 5-HTT, COMT, FKBP5 i receptora oksytoniny może mieć wpływ na przebieg BPD. W badaniach obrazowych wykazano zaburzenia strukturalne i funkcjonalne w korze przedczołowej, ciele migdałowatym i hipokampie. Lit wpływa na redukcję impulsowości, agresji, tendencji samobójczych i samookaleczeń w przebiegu BPD. Naltrekson jest szczególnie skuteczny w zmniejszaniu liczby samookaleczeń bez tendencji samobójczych, ale także impulsowości, nadużywania substancji psychoaktywnych i samobójstw.

Wnioski: Pomimo szerokiego rozpowszechnienia BPD w społeczeństwie nie opracowano jednolitego modelu, który uwzględniałby komponenty środowiskowe, genetyczne i neurobiologiczne w patogenezie BPD. Poznanie mechanizmów jest kluczowym krokiem w kierunku personalizacji leczenia. Doniesienia literatury sugerują, że zastosowanie litu i naltreksonu może przynieść pozytywne efekty terapeutyczne. Konieczne jest przeprowadzenie randomizowanych badań klinicznych w celu określenia skuteczności i bezpieczeństwa obydwu leków w długoterminowym leczeniu.

Słowa kluczowe: borderline, lit, naltrekson

Introduction

Borderline personality disorder is the most common personality disorder. It is estimated to affect between 1% and 3% of the population. Psychiatric patients account for 10% of those treated on an outpatient basis and up to 20% in an inpatient setting [1]. Concerning the practice of a family physician working in primary care, up to 6.4% of patients may suffer from BP. Therefore, it is an underdiagnosed personality disorder [2]. It is characterised by behavioural and emotional dysfunctions that manifest as unstable, intense and sudden mood changes, instability in affect regulation, impulsivity, violent outbursts of anger and self-harm [1–3]. Social maladjustment is characterized by fear of abandonment, a permanent need to be accepted by peers, avoiding loneliness, building superficial relationships and making reckless social decisions. At the same time, there is a fluctuating and unstable self-image, with features of paranoia or dissociative elements. This is associated with co-occurring, uncharacteristic symptoms such as vague somatic problems, risky sexual behavior, substance abuse and eating disorders [2]. BPD sufferers definitely have an increased risk of self-harm and suicidal tendencies [1–3]. According to literature reports, functional and structural changes in neuronal networks can significantly affect the development of borderline personality. Among other things, dysregulated self-image may be associated with abnormalities in the structures of the midline (temporoparietal junction, medial prefrontal cortex). Meanwhile, abnormalities in the limbic system and prefrontal control determine emotional and social distress [3].

In the literature on the subject, one can also find attempts to integrate genotypic, phenotypic and endophenotypic traits affecting the development of BPD [1].

In borderline personality disorder, there may be disturbances in the cholinergic and adrenergic systems that affect the development of affective vacillation. Therefore, lithium and carbamazepine may be potentially effective in supporting treatment of BPD [4].

The first references to the usage of lithium in lithium treatment date back to the 19th century. However, the drug was later forgotten for a long time. In 1949, John Cade revived the use of lithium in the treatment of mania [5]. Today, lithium is used as a mood-stabilizing drug. Depending on the severity of particular features of borderline personality disorder, it can also be used to treat it [6]. The high efficacy and widespread use of lithium are not fully explained. It acts on several neurotransmitter pathways. Under the influence of the drug, there is stimulation of the NMDA receptor and inhibition of glutamate reuptake, which increases the availability of glutamate at the postsynaptic neuron. Therefore, positive effects are observed in the treatment of depressive disorders, in which there is a reduced level of the aforementioned neurotransmitter. In contrast, chronic use of lithium counteracts the development of mania by down-regulating the NMDA receptor and increasing glutamate reuptake. The drug inhibits the release and postsynaptic transmission of dopamine, acting as an antimanic. At the same time, it reduces the level of γ-aminobutyric acid (GABA), reducing excessive nervous excitation. Lithium has neuroprotective effects, increasing synaptic plasticity and cellular immunoreactivity through its action on glycogen synthase kinase-3 (GSK-3). Lithium reduces the availability of inositol in areas of the brain where there is too much of it. Inositol affects the amount of myoinositol, which regulates the amount of phospholipids in neuronal cell membranes. Therefore, it has an important effect on cell signaling. However, in both mania and depression, there is an increase in the level of myoinositol in certain areas of the brain. It means that lithium has antidepressant and antimanic effects [7]. Also, according to literature reports, lithium may potentially show a positive effect in treating behavioural and interpersonal disorders in BPD [6].

Over the past decade, the role of the endogenous opioid system (EOS) and dopaminergic system in the pathogenesis of BPD has begun to be investigated. According to reports from experimental and preclinical studies, dysfunction of the endogenous opioid system may impair bonding and social relationships, reduce affect, emotion control and constructive adaptive coping methods. Therefore, it may be related to the pathomechanism of the development of the core symptoms of BPD [8].

Naltrexone as an opioid receptor antagonist may upregulate EOS, while chronic therapy leads to an increase in μ-opioid receptor sensitivity [8].

Taking into account the above, we assume that treatment with lithium and naltrexone may have a positive effect on the treatment of BPD, especially after taking into account genetic and neurobiological aspects.

Therefore, the aim of the present study is :

1. To analyze the neurobiological, genetic and environmental factors present in borderline personality disorder, taking into account the ICD-11 and DSM-5 classifications.
2. To collect data on the use of lithium and naltrexone in the treatment of BPD.

Methods

Basing on PubMed and Google Scholar databases using the following keywords: borderline, lithium, naltrexone for papers published from 1979 to 2022.

Results

1. An analysis of the neurobiological, genetic and phenotypic factors present in borderline personality disorder, considering the ICD-11 and DSM-5 classifications.

The DSM-5 classification suggests three diagnostic steps for BPD. The first is to 'identify the type' along with its severity. The next step is to describe the intensity of the traits prevalent in the course of BPD. A total of ten traits are categorised into four groups: negative emotionality (self-injury, isolation insecurity, anxiety, emotional vacillation, lowered self-esteem, depression), antagonism (aggression and hostility), schizotypal disorder (dissociative disorder traits) and disinhibition (impulsivity). The final stage consists of an assessment of the patient's self- and interpersonal functioning. A coherent self-image, integral identity and self-orientation form the first aspect of the assessment. Social skills, on the other hand, are assessed in terms of the expression of empathy, the need for intimacy, the willingness to cooperate in a group and the integration of other social qualities [1].

In the case of the ICD-11 classification, the strict division of personality disorders has been replaced by a multidimensional model. The basis for making a diagnosis is determining whether the personality disorder is mild, moderate or severe. The "dominant personality traits and patterns" are then established. “The borderline pattern” (6D11.5 according to the ICD-11 classification) characterizes people who are more impulsive, with superficial relationships, distorted self-image and labile affect [9–12]. Dysregulation of one's self-image affects disturbed identity construction, the presence of dissociative traits and paranoid ideas. It leads to emotional distress, resulting in self-harm or extended suicidal tendencies. In parallel, there is the building of unstable relationships with other people, experiencing fear of social rejection and provoking risky sexual behaviour [3].

The ICD-10 classification classifies BPD as an emotionally unstable personality disorder, and studies have identified both neurobiological, genetic and environmental factors that contribute to the development and persistence of the disorder. Studies have shown that people with BPD have reduced levels of serotonin and abnormalities in the serotonin system, which plays a key role in regulating mood, behavior and impulse control [13]. Chronic dysphoria, reduced effect and anhedonia may be underlain by a compensatory increase in μ-opioid and κ-opioid receptors with reduced basal EOS activity. Endogenous endorphins specifically affect the hypothalamus, basolateral amygdala, semi-lateral nucleus accumbens, thalamus and ventral striatum via μ-opioid receptors. It indicates a reciprocal influence of the dopaminergic system and EOS. Reduced levels of β-endorphin and met-enkephalin in the cerebrospinal fluid may influence self-destructive behaviour, e.g.: self-harm without suicidal tendencies, as compensation for reduced stimulation of the EOS and the dopaminergic system [8]. Abnormalities in brain structure and function may also be another contributing factor. In the study of S.C. Herpertz et al. participated six women with BPD and six patients from the control group. Brain imaging techniques have shown structural and functional differences in the brains of people with BPD, particularly in the prefrontal cortex, amygdala and hippocampus. These differences are associated with emotional dysregulation, impulsivity and memory impairment [13]. Although environmental factors, such as childhood trauma and stress, are known to contribute to the development of BPD, there is also evidence to suggest that genetic factors may play a role.

A study published by S. Torgersen et al. has shown that BPD tends to run in families. People with a first-degree relative with BPD are five times more likely to develop the disorder compared to the general population. In addition, twins are more likely to share a diagnosis of BPD, suggesting a genetic influence [14]. Several genes

potentially playing a role in the development of BPD have been identified. One such gene is the serotonin transporter gene (5-HTT). Among other things, this gene regulates serotonin neurotransmission, which is involved in mood regulation. People with a variation in this gene, called the short allele, may be more susceptible to developing BPD, especially in the presence of stress early in life [15]. Another gene linked to BPD may be the catechol-O-methyltransferase (COMT) gene, which plays a role in the metabolism of the neurotransmitters dopamine and norepinephrine, involved in emotional regulation. A study published by Arqam Qayyum et al. implies that people with a variant of this gene, called the Val/Val genotype, may be more susceptible to developing BPD [16]. Other genes that may play a role in the pathogenesis of BPD include those involved in regulating the stress response, such as the FKBP5 gene and social behavior, such as the oxytocin receptor gene. However, it should be noted that the genetics of BPD are complex and no single gene has been identified as the definitive cause of the disorder [17]. It should also be noted that while genetics may have a significant impact on the development of BPD, environmental factors may be a major amplifying factor. Childhood trauma, such as physical, emotional or sexual abuse, is a known risk factor for BPD. In addition, stress and other life events can trigger BPD symptoms [18]. People with BPD experience intense and rapidly changing emotions that may be triggered by minor events or rejection by peers. This dysregulation is a hallmark of the disorder and can lead to impulsive and self-destructive behavior. People with BPD often engage in compulsive behavior, such as substance abuse and overeating, as a way of coping with emotional distress [19,20].

2. Lithium treatment in borderline personality disorder.

Lithium belongs to a group of drugs called mood stabilizers. Lithium reduces sudden fluctuations of emotions and mood, which stabilizes the patient's mental state [7]. Referring to the American Psychiatric Association (APA) guidelines, lithium therapy is crucial in preventing acute manic and mixed episodes, particularly in bipolar affective disorder (ChAD). Lithium may also be used to treat BPD. The two disorders may share common diagnostic features and mood swings, types of impulsivity and progressiveness of the disorder must be carefully analyzed to distinguish them from each other [6]. Suggesting these links between BPD and ChAD, several researchers have shown that the use of lithium therapy also in the treatment of BPD may have benefits over standard antidepressants in treating emotional disturbances and in reducing patients' aggression levels, among other things [6,21]. Despite the reported positive therapeutic effect in the treatment of BPD in numerous studies, its use has declined in recent years due to the availability of newer antipsychotic drugs and concerns about its toxicity [6,22–24].

The first reports on lithium treatment in BPD were published in 1990, where the efficacy of lithium therapy was tested against a group receiving a placebo or desipramine. Results indicated that suicidal symptoms and impulsivity decreased among 8/11 patients taking lithium, which was not observed in those taking placebo. In contrast, in the desipramine group, symptoms were reduced in only 4 patients [22]. Also available meta-analyses have shown that long-term use of lithium is associated with a reduction in suicide attempts, with greater efficacy compared with other mood-stabilising drugs or antidepressants [25,26]. This effect may be related to the effect of lithium in reducing aggression and impulsivity [23]. Most likely lithium has also neuroprotective effects, which may help prevent neurodegeneration associated with depression, which coexist with BPD [27]. An article written by Hasan Belli et al. showed that lithium therapy affected reducing the frequency and intensity of self-harming behaviour in people with BPD. Self-harming behaviour is a common symptom in people with BPD. Reducing the frequency and intensity of these behaviours is an important treatment goal [6]. A randomised trial in 2000 tested the effectiveness of lithium therapy in treating aggression, which is a common symptom in PDB. Lithium carbonate was used in a group of children and adolescents with conduct disorder characterised by persistent aggression. It was shown that 16 out of 20 subjects in the lithium therapy group achieved a reduction in aggression compared to the placebo group, where only 6 out of 20 responded. Assessment of the aggression scale showed a significantly better effect among the lithium treatment group compared to the placebo group. Of the side effects noted, vomiting and increased urinary frequency were noted in more than half of the patients [28]. Referring to the above study, it can be concluded that short-term lithium therapy for the treatment of aggression has very good effects, but will not be well tolerated by every patient. The case of each patient should be considered individually to achieve the best therapeutic results [27,28].

3. Naltrexone treatment in borderline personality disorder.

As early as the 1990s, the effect of naltrexone therapy among patients with BPD began to be studied. Schmal et al. from the University Clinic for Psychiatry and Psychotherapy in Freiburg conducted a study involving three patients with PDB. They were given 50 mg of naltrexone daily for several weeks, which eventually

resulted in a reduction of dissociative symptoms in all subjects. This study, due to the small number of patients, was not reliable, but it created the basis for further research [29]. In the early 2000s, Joel R. Saper of the Michigan Head Pain & Neurological Institute, while treating chronic headaches with opioids, noticed that patients with the disorder became less withdrawn and more aggressive than they had been before the use of drugs in this group. This allowed him to conclude that the increased activity of the opioid system exacerbates dissociative symptoms [30]. It has been hypothesised that dysfunction of the endogenous opioid system is one of the main neurobiological causes of the onset of borderline personality disorder [31].

The use of naltrexone in the treatment of BPD has increased over the years. A 2019 study, showed that the drug was used more frequently between 2008 and 2012 compared to the 1996-2004 interval [32]. It is therefore crucial to understand the effect of naltrexone in reducing BPD symptoms. The literature suggests that the effect of naltrexone is biphasic. First, the treatment affects the reduction of self-destructive behaviours, e.g.: self-harm, substance abuse or eating disorders, by regulating EOS. In contrast, chronic use of naltrexone improves neural transmission by increasing opioid receptor sensitivity [8]. Successful treatment with opioid μ antagonists of symptoms associated with BPD supports this theory. They reduce symptoms such as substance abuse, self-harm, anorexia and compulsive sexual behaviour [31]. Charles Timäus from the Department of Psychiatry and Psychotherapy at the University of Göttingen, Germany and others performed a retrospective analysis of patients hospitalised between 2010 and 2013. The effectiveness of naltrexone and other pharmacotherapies in BPD was assessed. The most important aim of the analysis was to assess the relative contribution of the opioid antagonist naltrexone and other psychotropic drugs to the improvement of BPD patients. Patients were treated with the following groups of medications: mood stabilisers, antidepressants, low- and high-potency antipsychotics, sleeping aids, psychostimulants, maintenance medication, medications used in drug treatment and the opioid antagonist naltrexone. Patients' clinical improvement during their hospital stay was monitored based on BPD symptom analysis. During hospital admission and discharge, the following symptoms were assessed: mood disorders, suicidal thoughts or behaviour, self-injurious behaviour, impulsivity and insufficient adherence to treatment. Individuals who showed significant improvement in at least four of the above symptoms were considered to be responders to treatment. The statistical analysis performed showed that among BPD patients treated with naltrexone, treatment response was significantly higher than among patients not treated with the drug. A high daily dose of naltrexone was associated with a higher response rate compared to BPD patients without naltrexone. Taking low doses of naltrexone was significantly associated with symptom improvement, compared with other drugs. Low-potency antipsychotics showed some positive effects without reaching significance levels. Naltrexone was the only drug that significantly contributed to symptom relief during the treatment period, so the study confirmed the pathogenetic role of the endogenous opioid and reward system in BPD [8].

Conclusions

Recently, more and more research is being produced on aspects of BPD development due to its increasing prevalence in society [1,2]. According to literature reports, many environmental, genetic and neurobiological factors may influence the development of BPD8 [1,3,4,8,13,14,18].

Understanding these mechanisms will help in the prevention and early intervention of BPD, which should become a public health priority. There are a number of theories of BPD development that identify how certain factors interfere with the development of emotion regulation, disrupt self-presentation, increase aggression or lead to self-destructive behavior. These factors include harsh parenting, emotional neglect, sexual abuse or physical violence, among others [18]. Despite the strongest impact of environmental factors on the development of BPD, we should not forget about the relationship between individual genes, neurotransmitters, functional and structural disorders of the brain in the severity of BPD features [8,13,15–17]. It is assumed that dysfunctions in the serotonergic, dopaminergic and endogenous opioid systems may have an impact [8,13]. Among the genetic component, the variability in the 5-HTT, COMT, FKBP5 genes stands out [14–17]. However, an analysis of the available literature shows that no unified model has yet been developed that incorporates the impact of individual factors on the development of PBD [17]. It is worth highlighting the fact that this is a key step toward personalizing treatment. This will make it possible to tailor effective therapy individually to each patient [1,33].

The most common method of treating personality disorders is cognitive-behavioral and psychodynamic psychotherapy, while pharmacotherapy is used only supportively and symptomatically [34,35]. The lack of fully effective therapy of BPD forces the search for new ways of treating this disorder [35]. The inclusion of lithium and naltrexone in the treatment seems to be a promising direction of therapy. Lithium may show positive effects in the treatment of behavioural and interpersonal disorders and reduces aggressiveness in BPD sufferers. Lithium

also reduces suicide rates and reduces self-destructive behaviour, e.g.: self-harm [6,21–23,25–28]. Individual studies emphasize the strong effect of naltrexone on reducing impulsivity, the frequency of self-destructive behavior, e.g. self-mutilation without suicidal tendencies and substance abuse [8,31,36]. Therefore, according to literature reports, both drugs reduce the basic symptoms of BPD, contributing to the reduction in the number of committed suicides and improving the quality of life of patients [8,22,25,26]. However, lack of widespread use of these drugs and not fully explained mechanism of their action cause distrust of its use among clinicians and patients [8,25]. An important step towards starting new pharmacological methods in inhibiting the development of BPD is to conduct extensive randomized clinical trials that will confirm the efficacy and safety of lithium and naltrexone in the long-term treatment of BPD [8,21,26,37].

Conflict of interest

The authors have declared no conflict of interest.

References

1. Trull TJ, Distel MA, Carpenter RW. DSM-5 Borderline Personality Disorder: At the Border Between a Dimensional and a Categorical View. Curr Psychiatry Rep. 1 luty 2011;13(1):43–9.
2. Mendez-Miller M, Naccarato J, Radico JA. Borderline Personality Disorder. Am Fam Physician. luty 2022;105(2):156–61.
3. Bertsch K, Herpertz SC. Neurobiologische Grundlagen der Borderline-Störung: eine Integration in das ICD-11-Modell der Persönlichkeitsstörungen. Nervenarzt. 1 lipiec 2021;92(7):653–9.
4. Coccaro EF, Kavoussi RJ. Biological and pharmacological aspects of borderline personality disorder. Hosp Community Psychiatry. październik 1991;42(10):1029–33.
5. Shorter E. The history of lithium therapy. Bipolar Disord. 2009;11(s2):4–9.
6. Belli H, Ural C, Akbudak M. Borderline personality disorder: bipolarity, mood stabilizers and atypical antipsychotics in treatment. J Clin Med Res. październik 2012;4(5):301–8.
7. The science and practice of lithium therapy - Gin S Malhi, Michelle Tanious, Pritha Das, Michael Berk, 2012 [Internet]. [cytowane 5 czerwiec 2023]. Dostępne na: https://journals.sagepub.com/doi/10.1177/0004867412437346?fbclid=IwAR09bR247b5uPglScNNOYDQdNmyTU4zz7jnGhMX7MzpyUaMylT9Aq19u2C0&
8. Timäus C, Meiser M, Wiltfang J, Bandelow B, Wedekind D. Efficacy of naltrexone in borderline personality disorder, a retrospective analysis in inpatients. Hum Psychopharmacol Clin Exp. 2021;36(6):e2800.
9. Bach B, Kramer U, Doering S, di Giacomo E, Hutsebaut J, Kaera A, i in. The ICD-11 classification of personality disorders: a European perspective on challenges and opportunities. Borderline Personal Disord Emot Dysregulation. 1 kwiecień 2022;9:12.
10. Akademia Ignatianum w Krakowie, Kraków, Polska, Krzysztof-Świderska A, Małek D, Akademia Ignatianum w Krakowie, Kraków, Polska. Borderline personality disorder in ICD-11 and DSM-5 – the relational nature of the criteria for the disorder. Psychiatr Psychol Klin. 30 grudzień 2022;22(3):175–9.
11. Bach B, First MB. Application of the ICD-11 classification of personality disorders. BMC Psychiatry. 29 październik 2018;18:351.
12. Bach B, Mulder R. Clinical Implications of ICD-11 for Diagnosing and Treating Personality Disorders. Curr Psychiatry Rep. 1 październik 2022;24(10):553–63.
13. Herpertz SC, Dietrich TM, Wenning B, Krings T, Erberich SG, Willmes K, i in. Evidence of abnormal amygdala functioning in borderline personality disorder: a functional MRI study. Biol Psychiatry. 15 sierpień 2001;50(4):292–8.
14. Torgersen S, Lygren S, Oien PA, Skre I, Onstad S, Edvardsen J, i in. A twin study of personality disorders. Compr Psychiatry. 2000;41(6):416–25.
15. Margoob MA, Mushtaq D. Serotonin transporter gene polymorphism and psychiatric disorders: Is there a link? Indian J Psychiatry. 2011;53(4):289–99.
16. Qayyum A, Zai CC, Hirata Y, Tiwari AK, Cheema S, Nowrouzi B, i in. The Role of the Catechol-o-methyltransferase (COMT) Gene Val158Met in Aggressive Behavior, A Review of Genetic Studies. Curr Neuropharmacol. grudzień 2015;13(6):802–14.
17. Bakermans-Kranenburg MJ, van IJzendoorn MH. Oxytocin receptor (OXTR) and serotonin transporter (5-HTT) genes associated with observed parenting. Soc Cogn Affect Neurosci. czerwiec 2008;3(2):128–34.
18. Chan JC. Acid-base, calcium, potassium and aldosterone metabolism in renal tubular acidosis. Nephron. 1979;23(2–3):152–8.
19. Bohus M, Stoffers-Winterling J, Sharp C, Krause-Utz A, Schmahl C, Lieb K. Borderline personality disorder. The Lancet. 23 październik 2021;398(10310):1528–40.
20. Trull TJ, Solhan MB, Tragesser SL, Jahng S, Wood PK, Piasecki TM, i in. Affective instability: measuring a core feature of borderline personality disorder with ecological momentary assessment. J Abnorm Psychol. sierpień 2008;117(3):647–61.
21. Stone MH. Borderline Personality Disorder: Clinical Guidelines for Treatment. Psychodyn Psychiatry. marzec 2019;47(1):5–26.
22. Links PS, Steiner M, Boiago I, Irwin D. Lithium Therapy for Borderline Patients: Preliminary Findings. J Personal Disord. czerwiec 1990;4(2):173–81.
23. Cipriani A, Hawton K, Stockton S, Geddes JR. Lithium in the prevention of suicide in mood disorders: updated systematic review and meta-analysis. BMJ. 27 czerwiec 2013;346:f3646.
24. Luu B, Rodway G. Lithium Therapy for Bipolar Disorder. J Nurse Pract. 1 luty 2018;14(2):93–9.
25. Smith KA, Cipriani A. Lithium and suicide in mood disorders: Updated meta-review of the scientific literature. Bipolar Disord. 2017;19(7):575–86.
26. Ripoll LH. Psychopharmacologic treatment of borderline personality disorder. Dialogues Clin Neurosci. czerwiec 2013;15(2):213–24.
27. Rybakowski JK. Antiviral, immunomodulatory, and neuroprotective effect of lithium. J Integr Neurosci. 23 marzec 2022;21(2):68.
28. Malone RP, Delaney MA, Luebbert JF, Cater J, Campbell M. A Double-Blind Placebo-Controlled Study of Lithium in Hospitalized Aggressive Children and Adolescents With Conduct Disorder. Arch Gen Psychiatry. 1 lipiec 2000;57(7):649–54.
29. Schmahl C, Stiglmayr C, Böhme R, Bohus M. Behandlung von dissoziativen Symptomen bei Borderline-Persönlichkeitsstörungen mit Naltrexon. Nervenarzt. 1 marzec 1999;70(3):262–4.
30. Borderline Personality, Opioids, and Naltroxone - Saper - 2000 - Headache: The Journal of Head and Face Pain - Wiley Online Library [Internet]. [cytowane 5 czerwiec 2023]. Dostępne

na: https://headachejournal.onlinelibrary.wiley.com/doi/abs/10.1046/j.1526-4610.2000.00137-1.x?sid=nlm%3Apubmed
31. Bandelow B, Wedekind D. Possible role of a dysregulation of the endogenous opioid system in antisocial personality disorder. Hum Psychopharmacol Clin Exp. 2015;30(6):393–415.
32. Timäus C, Meiser M, Bandelow B, Engel KR, Paschke AM, Wiltfang J, i in. Pharmacotherapy of borderline personality disorder: what has changed over two decades? A retrospective evaluation of clinical practice. BMC Psychiatry. 12 grudzień 2019;19:393.
33. Gartlehner G, Crotty K, Kennedy S, Edlund MJ, Ali R, Siddiqui M, i in. Pharmacological Treatments for Borderline Personality Disorder: A Systematic Review and Meta-Analysis. CNS Drugs. 1 październik 2021;35(10):1053–67.
34. Bozzatello P, Bellino S. Combined therapy with interpersonal psychotherapy adapted for borderline personality disorder: A two-years follow-up. Psychiatry Res. 30 czerwiec 2016;240:151–6.
35. Zanarini MC. Psychotherapy of Borderline Personality Disorder. Acta Psychiatr Scand. listopad 2009;120(5):10.1111/j.1600-0447.2009.01448.x.
36. Moghaddas A, Dianatkhah M, Ghaffari S, Ghaeli P. The Potential Role of Naltrexone in Borderline Personality Disorder. Iran J Psychiatry. kwiecień 2017;12(2):142–6.
37. Palmer BA, Pahwa M, Geske JR, Kung S, Nassan M, Schak KM, i in. Self-report screening instruments differentiate bipolar disorder and borderline personality disorder. Brain Behav. 2021;11(7):e02201.

Corresponding author

Zuzanna Wingralek
e-mail: z.wingralek@gmail.com
Student Research Group at the I Department of Psychiatry, Psychotherapy, and Early Intervention, Medical University of Lublin, Poland

Otrzymano: 06.06.2023
Zrecenzowano: 14.06.2023, 21.06.2023
Przyjęto do publikacji: 08.09.2023