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Bipolar disorder - analysis of the impact of selected factors on treatment and course - review

1. Ewelina Justyna Janicka– corresponding author [EJJ]

COPERNICUS Medical Entity Sp. z o. o. Nowe Ogrody 1-6, 80-803 Gdańsk, Poland

https://orcid.org/0009-0006-5139-1728

e-mail: ewelina.janicka97@gmail.com

2.Kamila Rosińska- [KR]

Voivodeship Integrated Hospital of Jędrzej Śniadecki in Bialystok,

Marii Skłodowskiej-Curie 26, 15-278 Bialystok, Poland

https://orcid.org/0009-0001-8158-2051

e-mail:kamrosinska98@gmail.com

3. Julia Natalia Skibicka- [JNS]

Grochowski Hospital, Grenadierów 51/59, 04-073 Warsaw, Poland

https://orcid.org/0009-0000-1832-2938

e-mail:julia.lojewska@gmail.com

4. Monika Niedźwiedzka [MN]

Medical University of Bialystok, Jana Kilińskiego 1, 15-089 Białystok, Poland

https://orcid.org/0009-0004-9952-3414

e-mail:mon.niedzwiedzka@gmail.com

5. Mateusz Rosiński [MR]

Medical University of Bialystok, Jana Kilińskiego 1, 15-089 Białystok, Poland

https://orcid.org/0009-0009-6193-8282

e-mail: mattt03300@gmail.com

Abstract

Introduction: Bipolar Disorder (BD) affects millions worldwide, impacting emotional, social, and cognitive functioning. This disorder, characterized by alternating episodes of mania and depression, carries high risks including suicide. Pharmacological treatment is the cornerstone of management, but its effectiveness can be limited, prompting the exploration of adjunctive treatment methods. This paper discusses the potential of interventions such as physical activity, sleep regulation, psychotherapy, and research on inflammation and gut microbiota as supplementary elements to standard BD treatment.

Objective: This review aims to evaluate the role of adjunctive therapies, including physical activity, sleep regulation, inflammation, gut microbiota interventions, and psychotherapy, in improving outcomes for patients with BD.

Materials and Methods: A literature review covering research on various forms of treatment for bipolar disorder, the impact of physical activity, inflammation, microbiota, sleep and psychotherapy in the treatment of this disease, published on the PubMed and Google Scholar platforms.

Conclusions: Emerging evidence suggests that non-pharmacological interventions can complement standard treatments for BD. Physical activity helps alleviate depressive symptoms and improve psychosocial functioning, while regulating sleep patterns can reduce mood disturbances and suicidality. Managing systemic inflammation and optimizing gut microbiota may address neuropsychiatric symptoms and enhance cognitive performance. Psychotherapeutic approaches like CBT and MBCT lower relapse rates and improve quality of life. Integrating these strategies into routine care could enhance long-term management of BD.

Keywords: bipolar disorder, physical activity, inflammation, microbiota, psychotherapy, sleep regulation, sleep

Introduction:

In 2019, bipolar disorder affected approximately 1 in 150 adults worldwide, accounting for 40 million people. The disorder primarily occurs in individuals of working age, although it can also be observed among adolescents. [1] An increasing number of elderly individuals live with symptoms of this condition, and this percentage is expected to rise steadily. [2]

People with bipolar disorder experience mood swings, cycling between extreme emotional states such as mania (impulsivity, reduced need for sleep, increased energy and hyperactivity, decreased anxiety and depression) and depression (helplessness, anhedonia, reduced energy and activity). [3]

Bipolar disorder (BD) is divided into two subtypes: type I (BD-I) and type II (BD-II). BD-I is characterized by the occurrence of at least one fully symptomatic manic episode, whereas BD-II involves alternating episodes of depression and hypomania. The disorder is associated with a high risk of premature death, significant disability, psychosocial functioning difficulties [4], and cognitive impairments. [5] Among BD patients, approximately 10% will die by suicide. [6]

Bipolar disorder is a highly heterogeneous and multifactorial disease, marked by a significant individual and societal burden. [7]

Recent large-scale genetic studies in humans have confirmed that the risk of developing bipolar disorder has a complex polygenic nature and shares common features with other major neuropsychiatric disorders. [8]

Its development, course, and outcomes may be influenced by various factors, including biological (e.g., genetic), psychological, social, and structural factors. Adverse life events or challenging circumstances, such as bereavement, violence, or the breakdown of relationships, may trigger or exacerbate symptoms of the disorder. Additionally, alcohol and drug use can affect the development and progression of bipolar disorder. [1]

The cornerstone of treatment for bipolar disorder is pharmacological therapy, which includes the prophylactic use of lithium salts or sodium valproate, an antiepileptic drug. Mood episodes are treated with antipsychotics, antidepressants, and anticonvulsants. Psychoeducation and

various forms of psychological therapy are essential support in treatment. However, currently available treatment methods have limited efficacy, and the medications used may cause significant side effects. [6]

BIPOLAR DISORDER AND PHYSICAL ACTIVITY

Physical activity (PA) is recommended as part of lifestyle intervention in the treatment of various mental disorders and has shown specific therapeutic benefits for unipolar depression. Due to the similarity of depressive symptoms in individuals with bipolar disorder (BD) and unipolar depression, it can be assumed that physical exercise may also offer benefits in the treatment of bipolar depression. A study included fifteen patients diagnosed with BD type I or type II who were experiencing a depressive episode. After physical and functional assessments, the patients participated in supervised training sessions, including aerobic exercises followed by strength training, three times a week for 12 weeks (36 training sessions). Nine patients (82%) showed an antidepressant response, defined as a reduction of more than 50% in depressive symptoms by the 12th week, with five of these patients (45%) meeting the criteria for full remission. This study provides significant data supporting the use of physical activity to alleviate depressive symptoms in BD and suggests its potential adjunctive antidepressant effects. Additionally, physical exercise had a positive impact on muscle strength and body composition. [9]

Programs that include low-intensity activities, such as walking, optional elements of social and healthy lifestyle engagement, and guidance from an instructor who can provide support in motivation and overcoming physical and mental health barriers experienced by adults with BD, may be best suited to the preferences of this group regarding physical activity. Individuals with poor mental health may require greater support to overcome these barriers. [10]

Strong evidence indicates that physical activity (PA) has a beneficial effect on the treatment of mild and moderate depression in children, adolescents, and adults, as well as severe depression, anxiety disorders, and psychotic disorders in adults. It reduces the risk of developing depression, anxiety, and, to a lesser extent, psychosis. Additionally, it improves cardiorespiratory fitness and sleep quality in individuals with mental health disorders. [11]

BIPOLAR DISORDER AND INFLAMMATION

Knowledge about the immune response in mental disorders highlights the correlation between inflammation and various aspects of bipolar disorder (BD). [12] Inflammatory processes may play a role in increasing morbidity and mortality risks in individuals with bipolar disorder, indicating a mutual interaction between inflammation and the course of the disease. The aim of a pilot study was to analyze the relationship between C-reactive protein (CRP) levels and the severity of BD symptoms. In a retrospective observational study, data from 61 hospitalized patients were analyzed, measuring CRP levels at admission (T0) and after seven days of hospital treatment (T1). After one week, a statistically significant decrease in CRP levels ($p < 0.001$) was observed, along with a positive correlation between CRP levels and CGI scores both at the beginning and after one week of treatment. Patients exhibited reduced CRP levels during the first week of therapy, suggesting a potential link between inflammation reduction and improvement in BD symptoms. [13]

Individuals exposed to higher levels of inflammation over a prolonged period experienced more manic symptoms, suggesting that inflammatory processes may have a cumulative impact on the course of the disorder, particularly in the context of manic episodes. [14] Additionally, individuals with BD exhibit deficits in cognitive-affective processing, which may persist despite the remission of acute symptoms. One possible biological mechanism for these deficits is chronic low-grade inflammation, which is associated with impairments in executive functions and memory. A study involving 119 adult patients with BD I and II confirmed that inflammation, as measured by CRP levels, may influence the integration of cognitive-affective processes. This study highlights the connection between inflammation and cognitive abilities in BD, increasing the likelihood that inflammation also impacts the integration of cognitive-behavioral processing. [15]

The pro-inflammatory hypothesis in BD is supported by evidence showing that both antipsychotic medications and lithium reduce the expression of inflammatory genes in monocytes in individuals suffering from the disorder. Key mechanisms linking immuno-inflammatory signaling with mood disorders include altered serotonin metabolism in the central nervous system and dysregulation of the hypothalamic-pituitary-adrenal axis. [16]

GUT MICROBIOTA AND BIPOLAR DISORDER

Growing evidence supports a bidirectional relationship between the brain and gut microbiota, known as the "gut-brain axis," which may influence behavior and the pathology of mental illnesses. [17]
Gastrointestinal pathologies, considered common comorbidities in BD and other mental disorders, suggest a connection between gastrointestinal dysfunctions and mental health. Irritable bowel syndrome (IBS), with a prevalence of approximately 11% in the general population, is one such example. [18]

Fecal microbiome analyses revealed that patients with BD have a reduced abundance of Firmicutes and *Faecalibacterium spp.* compared to healthy controls. Moreover, this difference correlated with the severity of reported symptoms. [19]
Studies on probiotic interventions yielded the following results: administering probiotics containing strains of *Lactobacillus spp.* and *Bifidobacterium lactis* significantly reduced the frequency of psychiatric rehospitalizations in patients recently discharged after a manic episode. This effect was particularly pronounced in individuals with initially elevated levels of systemic inflammation. [20]

The impact of probiotic treatment was also examined regarding gastrointestinal symptoms in patients with the euthymic form of BD, with such symptoms observed in over half of the participants. Approximately one-third of the patients reported improvement, including reduced bloating and more frequent bowel movements. Additionally, reduced cognitive reactivity to a sad mood and significant alleviation of manic symptoms were noted. [21]

The future of research into the connections between gut microbiota and neurocognitive aspects in BD patients appears promising. Current studies have provided solid evidence that microbiota-derived metabolites, neurotransmitters, and gut-related hormones play a crucial role in cognitive processes. [22]

BIPOLAR DISORDER AND SLEEP

Sleep disturbances are common in the psychiatric population and significantly affect the course and effectiveness of treatment for mental disorders. Abnormal sleep is also a key symptom of bipolar disorder (BD), with 23% to 78% of patients reporting symptoms of hypersomnia. [23] Insomnia is associated with an increased risk of suicidal ideation and manic episodes. Sleep disturbances frequently occur in BD patients during various phases of the illness, including euthymia [24] and remission. These disturbances include not only insomnia but also disruptions in sleep-wake rhythms, such as delayed sleep phase disorder. The patterns of these disturbances vary depending on the mood phase. During manic episodes, most patients (66–99%) experience a reduced need for sleep, prolonged sleep onset latency, and difficulty maintaining sleep. Sleep deprivation can act as a trigger for manic episodes. In depressive states, sleep disturbances may include both insomnia (40–100%) and excessive sleepiness (23–78%).

Studies have shown that circadian rhythm disturbances in sleep-wake cycles occur in 32.4% of patients with BD type I or II. An early onset of the disorder and a family history of suicide were significantly associated with these disturbances. [23] Patients in remission exhibited prolonged total sleep time, increased wakefulness after sleep onset, greater variability in sleep-wake rhythms, and reduced sleep efficiency. [25]

A two-year study examined the relationship between sleep quality and mood symptoms in adolescents with bipolar disorder, focusing on how sleep quality affected emerging mood symptoms. Adolescents with bipolar disorder showed poor sleep quality, which initially improved but later stabilized. After six months, poorer sleep quality was associated with increased depression, hypomania, and suicidal ideation in the following month. Adolescents who attempted suicide during the study had worse sleep quality compared to those who did not. Similarly, in the months preceding a suicide attempt, sleep quality was worse than in months without such attempts. Furthermore, higher depression severity predicted decreased sleep quality at the beginning of the study and during the third and eighteenth months. In contrast, the severity of suicidal ideation influenced worsening sleep quality at the start of the study and during the twelfth and eighteenth months. [26]

BIPOLAR DISORDER AND PSYCHOTHERAPY

It is increasingly emphasized that pharmacotherapy alone is insufficient to prevent relapses in bipolar disorder or to completely alleviate post-episode symptoms and functional impairments. [27] Psychotherapy can be considered a supportive method. [28]

Outpatients with bipolar disorder may benefit from psychosocial skill-based interventions combined with pharmacotherapy. [29] Psychotherapeutic interventions have been shown to be effective in reducing depressive symptoms. Both psychoeducation and cognitive-behavioral therapy (CBT) are associated with prolonging the time to relapse or the next mood episode. Mindfulness-based cognitive therapy (MBCT) has shown particular effectiveness in alleviating symptoms of depression and anxiety. There is substantial evidence supporting the effectiveness of psychotherapeutic interventions in treating bipolar disorder. [30]

Patients significantly improved their psychosocial functioning, with effects observed from baseline to the end of treatment. During the intervention period, patients' quality of life improved significantly in terms of physical health. [31] Psychoeducation combined with CBT significantly reduced manic symptoms. [32]

Summary

Bipolar affective disorder (ChAD) is a complex mental disorder characterized by alternating episodes of mania and depression, significantly impacting cognitive, social, and physical functioning. While pharmacological treatment is effective, it often requires supplementation with non-pharmacological therapies such as physical activity, psychotherapy, or sleep regulation. New research directions highlight the significant role of inflammation and gut microbiota in the course of ChAD, suggesting opportunities for the development of more individualized therapies. An integrated treatment approach that combines various interventions improves the effectiveness of therapy and quality of life for patients.

Author's contribution

Conceptualization, EJJ; methodology, KR; software, EJJ, KR, JNS, MN; check, MN, MR; formal analysis EJJ, KR; investigation, JNS, MN; resources, EJJ, MR; data curation, KR; writing– rough preparation MN, MR ; writing-review and editing, EJJ, ; visualization, JNS, KR,; supervision, MN, EJJ, JNS ; project administration, MR

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