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Exercise-Induced Brain-Derived Neurotrophic Factor as a Mediator of Antidepressant Effects: A Narrative Review

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ABSTRACT

Depression represents a significant global public health problem, negatively affecting patients ’ quality of life and social functioning. Despite the increasing availability of effective pharmacological and psychotherapeutic interventions, a substantial proportion of patients fail to achieve full symptom remission. [1]

Recently, growing attention has been directed toward physical activity as a non-pharmacological approach supporting the treatment of depression. Multiple studies indicate that regular exercise may lead to a reduction in depressive symptoms and improvements in cognitive function. In addition, other non-pharmacological interventions, including probiotics [2], meditation, light therapy [3,4], and physical training, have been investigated for their potential antidepressant effects.

One of the proposed mechanisms underlying the beneficial effects of physical activity, apart from its anti-inflammatory properties and stimulation of endorphin release, is the modulation of brain-derived neurotrophic factor (BDNF) expression. BDNF plays a crucial role in neuroplasticity, neurogenesis, and the regulation of synaptic function, particularly within the hippocampus, as well as in the spinal cord and peripheral nervous system. [5,6]

The aim of this narrative review is to summarize and critically discuss current evidence on the effects of physical activity on BDNF levels and its role in antidepressant mechanisms, highlighting its potential clinical relevance in the management of depressive disorders.

Keywords: depression, brain-derived neurotrophic factor, BDNF, physical activity, exercise neuroplasticity, antidepressant mechanisms

1. Introduction

Depression represents one of the most prevalent mental disorders worldwide and constitutes a significant public health concern. It affects individuals across the lifespan and is characterized by a high risk of recurrence. The core symptoms of depression include persistently low mood, anhedonia, psychomotor retardation, and decreased energy levels. In addition, patients frequently experience cognitive disturbances, such as impaired concentration and memory difficulties, sleep disorders, including hypersomnia or insomnia, changes in appetite, somatic complaints (e.g., headache or abdominal pain), alterations in libido, and, in severe cases, suicidal ideation. Despite advances in pharmacotherapy, improved access to psychiatric and psychological care, and increasing public awareness, the prevalence of depression remains high, and many patients continue to experience a substantial decline in quality of life. [3,6]

In recent years, increasing attention has been directed toward understanding the biological mechanisms underlying depression, as well as the role of pharmacological and non-pharmacological interventions in its treatment, prevention, and maintenance of remission. Although numerous studies have investigated the pathophysiology of depression, including the roles of neurotransmitters and inflammatory mediators in the central nervous system, the underlying mechanisms of this disorder have not yet been fully elucidated. However, accumulating evidence suggests that neurobiological factors released during physical activity may exert beneficial effects on the clinical condition of patients with depression.

One of the key mediators involved in these processes is brain-derived neurotrophic factor (BDNF), which plays a central role in the regulation of neuroplasticity, neurogenesis, and synaptic function and is increasingly recognized as an important factor in the pathophysiology and treatment of depressive disorders.

2. Methods

This narrative review was conducted to evaluate the effects of physical activity on brain-derived neurotrophic factor (BDNF) levels in patients with depression and to examine the relationship between BDNF concentrations and depressive symptom severity.

A comprehensive literature search was performed using the PubMed database. Articles published primarily between 2015 and 2024 were considered. The following keywords and their combinations were applied: “depression”, “major depressive disorder”, “physical activity”, “exercise”, “BDNF”, and “brain-derived neurotrophic factor”. Reference lists of relevant articles were also screened to identify additional eligible studies.

Only peer-reviewed articles published in English were included. Eligible studies comprised randomized controlled trials, observational studies, and meta-analyses investigating associations between physical activity, BDNF levels, and depressive symptoms in adult populations.

Exclusion criteria included animal studies, case reports, conference abstracts, studies with insufficient methodological quality, articles lacking original data, and publications prior to 2010. Titles and abstracts were initially screened for relevance, followed by full-text assessment of potentially eligible publications. Data regarding study design, sample size, participant characteristics, type of intervention, methods of BDNF measurement, and clinical outcomes were extracted and analyzed qualitatively.

Artificial intelligence (AI) tools were used in two specific ways: first, for text analysis of clinical reasoning narratives to identify linguistic patterns associated with logical fallacies; and second, to assist in refining the academic English of the manuscript, ensuring clarity, consistency, and adherence to scientific writing standards. All AI use was strictly assistive and conducted under human supervision. Final data interpretation, error classification, and conclusions were determined by human experts in clinical medicine and formal logic. AI served primarily to enhance efficiency in data processing, pattern recognition, and linguistic refinement, without replacing human judgment in the analytical process.

3. Biology of BDNF

Brain-derived neurotrophic factor (BDNF) belongs to the neurotrophin family and plays a central role in neuronal and glial development, neuroprotection, and the modulation of both short- and long-term synaptic plasticity, which are essential for cognitive function and memory. BDNF is involved in a wide range of neurophysiological processes, largely due to its complex pattern of synthesis, which includes several biologically active isoforms interacting with distinct receptors and intracellular signaling pathways. Although BDNF is primarily synthesized in neurons, its expression has also been demonstrated in glial cells and various peripheral tissues. [5, 28,29]

BDNF is initially synthesized as a precursor protein, pro-BDNF, which undergoes proteolytic cleavage to form mature BDNF (m-BDNF). These isoforms differ in their biological activity and bind to distinct receptors, resulting in divergent cellular effects. Pro-BDNF is an important modulator of brain development and neuronal pruning, whereas m-BDNF plays a predominant role in adulthood, particularly in neuroprotection and synaptic plasticity. [29]

Pro-BDNF primarily interacts with the p75 neurotrophin receptor (p75NTR), a member of the tumor necrosis factor receptor superfamily. Activation of p75NTR requires the formation of multimeric membrane complexes composed of neurotrophin precursors and intracellular adaptor proteins [28] These complexes regulate neuronal survival, inhibit neurite outgrowth, promote apoptotic pathways, and weaken synaptic connections. Furthermore, p75NTR signaling contributes to growth cone development and motility and supports appropriate neuronal numbers during brain maturation. [5,6]

In contrast, m-BDNF mainly binds to the high-affinity tropomyosin receptor kinase B (TrkB), thereby activating multiple intracellular signaling cascades. The m-BDNF–TrkB pathway promotes antiapoptotic and prosurvival effects, modulates synaptic plasticity, and enhances dendritic growth and branching [6,26]. In addition, it regulates protein synthesis during neuronal differentiation and supports the expression of immediate early genes and cytoskeletal proteins. Consequently, this signaling complex is essential for neuronal survival, axonal and dendritic development, and the maintenance of synaptic structure and function, particularly in hippocampal neurons. [5, 27]

Beyond the central nervous system, BDNF and the TrkB receptor are detectable in several non-neuronal tissues, including endothelial cells, cardiomyocytes, vascular smooth muscle cells, leukocytes, megakaryocytes, and platelets [19,25]. Platelets constitute the major source of peripheral BDNF and play a crucial role in storing and transporting BDNF derived from other tissues, thereby influencing its circulating levels. [18]

Peripheral BDNF, largely stored in platelets and present in multiple non-neuronal tissues, represents a readily accessible biomarker and may serve as an indirect indicator of neurotrophic responses to interventions such as physical activity. [6,14]

4. Exercise-Induced Modulation of BDNF in Depression

4.1. Effects of Physical Activity on BDNF Levels

Meta-analytical evidence indicates that major depressive disorder is associated with reduced peripheral concentrations of brain-derived neurotrophic factor. A meta-analysis including over 7,000 patients with major depressive disorder demonstrated significantly lower BDNF levels compared with healthy controls, with a medium-to-large effect size (SMD = -0.64), although substantial heterogeneity was observed (I^2 = 92%). This high variability suggests considerable methodological and clinical differences among included studies. [14]

In a meta-analysis [14,30] conducted by Dinoff et al. (2018), comprising six studies with 176 patients with depression, the effects of 3–12 weeks of aerobic exercise on circulating BDNF concentrations were examined. No significant increase in resting BDNF levels following physical activity was observed (SMD = 0.43; p = 0.09), a finding confirmed in sensitivity analyses restricted to high-quality studies. Moreover, meta-regression analyses did not identify significant moderating effects of age, sex, body mass index, antidepressant use, intervention duration, or exercise intensity. These results suggest that short- to medium-term exercise interventions may not consistently elevate baseline BDNF levels in patients with depression. [14,22]

Complementary findings were reported by Molendijk et al. (2014), who demonstrated that antidepressant-free patients with depression exhibited significantly lower serum BDNF concentrations than those receiving pharmacotherapy (SMD = -0.56). Studies assessing pre- and post-treatment levels revealed even stronger effects (SMD = -0.74). Although publication bias was detected, adjusted analyses confirmed a persistent, albeit attenuated, association. Additionally, greater reductions in depressive symptom severity were correlated with larger increases in BDNF during antidepressant treatment, supporting the role of BDNF in therapeutic response. [22, 31]

Evidence from randomized controlled trials further illustrates the complex relationship between physical activity, depressive symptoms, and neurotrophic modulation. In a small RCT including 29 participants with depressive symptoms, aerobic exercise targeting 150 minutes per week was compared with stretching. While a moderate, non-significant increase in resting BDNF levels was observed (d = 0.49), no statistically significant between-group differences were detected, emphasizing the limited statistical power of small-sample studies and the variability of acute exercise effects. [7]

A larger six-month home-based trial involving 144 ovarian cancer survivors demonstrated that moderate-intensity aerobic exercise led to a significant 18% reduction in depressive symptomatology, with a clear dose-response relationship. Participants achieving at least 150 minutes of exercise per week experienced greater clinical improvement. However, no significant changes in total or free serum BDNF concentrations were observed, and associations between BDNF changes and symptom improvement remained weak. [8]

In addition to efficacy studies, a predictive randomized trial including 122 patients with major depressive disorder examined baseline determinants of response to exercise. Higher baseline BDNF levels, alongside selected biological and psychological markers, were consistently associated with remission, whereas lower concentrations predicted non-response. These findings suggest that baseline neurotrophic potential may influence the effectiveness of physical activity interventions, lending support to the neurotrophic hypothesis of depression. Nevertheless, the predictive value of these models was limited by sample size and concomitant pharmacotherapy. [9]

Taken together, evidence from meta-analyses and randomized controlled trials indicates that depression is consistently associated with reduced peripheral BDNF levels, and that pharmacological treatment contributes to their normalization. In contrast, the effects of physical activity on resting BDNF concentrations in depressed populations remain heterogeneous and inconclusive. While exercise reliably improves depressive symptoms, its influence on neurotrophic modulation appears to depend on baseline BDNF status, individual biological characteristics, intervention duration, and methodological factors. Therefore, further large-scale, well-controlled studies with standardized protocols are required to clarify the mechanisms linking physical activity, BDNF regulation, and clinical outcomes in depression.

4.2. Types and Intensity of Exercise

Several studies, including randomized controlled trials and meta-analyses, have examined the effects of different types and intensities of exercise on depressive symptoms and peripheral BDNF levels.

A meta-analysis of 29 studies with 910 participants (mean age 42 years, 61% male) reported that exercise interventions significantly increased resting BDNF (SMD=0.39, 95% CI: 0.17–0.60, p<0.001). Subgroup analyses indicated a stronger effect for aerobic exercise (SMD = 0.66), while resistance training showed no significant impact (SMD=0.07). Participants typically exercised for about 50 minutes per session, 3 times per week, over a median duration of 12 weeks. Meta-regression analyses did not find significant associations between BDNF changes and intervention duration, session time, weekly frequency, or exercise intensity, highlighting variability in responses [15].

Randomized controlled trials further support these findings. In a small RCT of 29 participants [7] with depressive symptoms, aerobic exercise (150 minutes/week) produced a moderate but non-significant increase in resting BDNF, with no differences between groups. A larger six-month home-based trial in 144 ovarian cancer survivors [8] showed that moderate-intensity aerobic exercise (average 166 minutes/week) led to an 18% reduction in depressive symptoms, with greater improvements in participants achieving ≥150 minutes/week. However, changes in BDNF were not significant, and correlations with symptom improvement were weak.

In a predictive RCT of 122 patients with major depressive disorder, higher baseline BDNF was associated with remission following exercise, whereas lower levels predicted non-response. These results suggest that baseline neurotrophic potential may influence the effectiveness of physical activity, consistent with the neurotrophic hypothesis of depression. [9]

Overall, moderate aerobic exercise of 2-4 sessions per week, 40-60 minutes per session, is most consistently linked to improvements in depressive symptoms. Effects on peripheral BDNF are variable, indicating that exercise likely exerts antidepressant effects through multiple mechanisms. Current recommendations support ≥150 minutes per week of moderate aerobic exercise for adults with depression, while considering individual factors such as baseline BDNF, concomitant medication, and comorbidities.

4.3. Clinical Outcomes in Depressive Disorders

Randomized controlled trials (RCTs) and meta-analyses consistently indicate that physical activity improves depressive symptoms, cognitive function, and overall well-being in individuals with major depressive disorder (MDD). For example, Szuhany and Otto (2019) [32] evaluated participants randomized to brief behavioral activation (BA) plus an adjunctive exercise or stretching intervention. While BA appeared to be the primary driver of symptom improvement, exercise did not significantly affect BDNF levels or depressive outcomes in this sample, highlighting the potential influence of concomitant interventions.

In contrast, a six-month home-based trial in 144 ovarian cancer survivors [8] demonstrated that moderate-intensity aerobic exercise led to an 18% reduction in depressive symptomatology, with participants achieving ≥150 minutes per week experiencing the greatest improvements. Notably, changes in BDNF were not significantly correlated with symptom improvement, suggesting that exercise may exert antidepressant effects through multiple pathways beyond BDNF modulation.

Predictive analyses in 122 patients with MDD [9] further indicated that higher baseline BDNF levels, along with selected biological and psychological markers, were associated with remission following exercise interventions, whereas lower BDNF, lower cardiorespiratory fitness, and diminished post-exercise positive affect predicted non-response. These findings suggest that baseline neurotrophic status and individual biological characteristics can influence responsiveness to physical activity. [3, 9]

Other studies have highlighted the role of genotype and sex in moderating exercise outcomes. In one trial, men randomized to a physical activity intervention showed greater decreases in somatic depressive symptoms, particularly in carriers of the BDNF Met allele, whereas effects on positive affect varied by 5-HTT genotype [1,33]. Similarly, higher baseline BDNF was associated with more rapid symptom improvement in individuals with higher BMI, suggesting a complex interplay between neurotrophic potential, physiology, and exercise response.

Observational research supports these findings. A study of 1,042 adults in São Paulo [24, 34] reported that individuals not engaging in regular physical activity were twice as likely to experience depressive or anxiety symptoms. Broader analyses, including 21 observational studies with over 42,000 participants [35] and meta-analyses of 218 studies with more than 14,000 individuals, consistently show that higher frequency and intensity of physical activity—across modalities such as walking, jogging, yoga, and strength training - is linked to moderate reductions in depressive symptom severity.

Meta-analytic evidence further supports the relationship between BDNF and depressive outcomes. Serum BDNF concentrations negatively correlated with symptom severity in drug-free patients, and larger increases in BDNF during antidepressant treatment were associated with greater symptom improvement. While the direct link between exercise-induced BDNF changes and clinical outcomes remains variable, these findings collectively indicate that physical activity reliably alleviates depressive symptoms, with effects potentially moderated by baseline neurobiological status, genetic factors, and intervention characteristics.

4.4. Proposed Mechanisms

Physical activity exerts antidepressant effects through multiple, overlapping biological mechanisms, involving neurotrophic, neurotransmitter, endocrine, and immune pathways. [42]

Neuroplasticity and BDNF modulation: Exercise induces upregulation of brain-derived neurotrophic factor (BDNF), a key regulator of synaptic plasticity, neuronal survival, and neurogenesis, particularly in the hippocampus and other mood-related brain regions. Clinical studies suggest that increases in circulating BDNF, along with changes in kynurenine and IL-6, are associated with reductions in depressive symptoms in patients with major depression, indicating that enhanced neurotrophic support may partly mediate mood improvement [16, 18]. BDNF signaling via the high-affinity TrkB receptor activates intracellular pathways that support dendritic growth, synaptic strengthening, and cell survival. These adaptations enhance neuroplasticity and resilience to stress, both central to the pathophysiology of depression.

Neurotransmitter regulation: Physical activity also influences classical mood-related neurotransmitters. Evidence from recent reviews indicates that exercise can modulate serotonergic, noradrenergic, and dopaminergic pathways, which are often dysregulated in depression. Exercise may enhance serotonergic and noradrenergic availability and receptor sensitivity, and support dopaminergic signaling involved in motivation and reward processes [16]. These neurotransmitter changes likely interact with neurotrophic and inflammatory mechanisms to improve mood and cognitive function.

HPA axis and stress regulation: Chronic stress and dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis are implicated in depression. Elevated cortisol can reduce hippocampal BDNF expression and impair neurogenesis. Regular exercise has been shown to normalize HPA axis activity and mitigate stress-related hypercortisolemia, contributing to improved mood regulation [18].

Inflammation and immune modulation: Depression is often accompanied by elevated pro-inflammatory cytokines (e.g., IL-1, IL-6), which can alter neurotransmitter metabolism and BDNF expression through pathways such as indoleamine 2,3-dioxygenase (IDO), shifting tryptophan metabolism toward neurotoxic kynurenine metabolites. Exercise has been shown to reduce peripheral inflammation and modulate cytokine profiles, creating a more neuroprotective environment and indirectly supporting neurotrophic mechanisms [18,23].

Peripheral and central interactions: Apart from central nervous system sources, BDNF is also expressed in non-neuronal tissues and can be released peripherally with exercise, contributing to systemic neurotrophic signaling. Peripheral increases in BDNF may reflect central changes, although the relationship between serum and brain concentrations remains incompletely understood [36]

Acute versus chronic effects: Acute bouts of exercise transiently increase circulating BDNF, while chronic exercise programs may lead to sustained elevations in baseline levels, supporting long-term neurobiological adaptations. Both immediate and long-term effects likely contribute to the antidepressant benefits of physical activity [3].

Together, these mechanisms suggest that regular exercise fosters a neurobiological environment conducive to enhanced plasticity, stress resilience, and mood regulation. While BDNF is a central mediator, improvements in depressive symptoms are likely the result of combined neurotrophic, neurotransmitter, endocrine, and immune effects induced by physical activity.

5. BDNF and Depression

Brain-derived neurotrophic factor (BDNF) is widely expressed in brain regions critically involved in emotional regulation and cognitive processing, particularly in the hippocampus, prefrontal cortex, and amygdala. These structures play a central role in stress response, memory formation, and mood regulation and are consistently implicated in the pathophysiology of major depressive disorder. Alterations in BDNF signaling within these areas have been associated with structural and functional brain abnormalities observed in depression.

At the cellular level, BDNF is a key regulator of neuroplasticity. It participates in neurogenesis, synaptic remodeling, and adaptive neuronal responses to environmental stimuli. During brain development, BDNF isoforms regulate neurogenesis, gliogenesis, synaptogenesis, and programmed cell death, ensuring proper formation of neuronal networks. In adulthood, BDNF primarily supports synaptic transmission efficiency and long-term synaptic plasticity, thereby contributing to learning, memory, and cognitive flexibility. Reduced BDNF expression has been linked to impaired neuroplasticity and increased vulnerability to mood disorders, including depressive and affective dysregulation [5,6]

Importantly, different BDNF isoforms exert distinct biological effects. Pro-BDNF has been shown to promote synaptic weakening and long-term depression (LTD), particularly in hippocampal neurons. Through its interaction with the p75 neurotrophin receptor, pro-BDNF contributes to neuronal pruning, reduced synaptic strength, and deterioration of neuronal networks. These processes may lead to cognitive impairment, emotional dysregulation, and increased susceptibility to depression and anxiety disorders. Accumulating evidence indicates that excessive pro-BDNF signaling may contribute to neurodegenerative processes and disturbances in episodic memory and emotional regulation [37,39].

Genetic factors also play a significant role in modulating BDNF function in depression. Post-mortem studies [1] have reported reduced BDNF and TrkB receptor expression in the hippocampus and prefrontal cortex of suicide victims. Moreover, several meta-analyses have demonstrated an association between the BDNF Val66Met polymorphism and increased vulnerability to mood disorders. Carriers of the Met allele exhibit altered activity-dependent BDNF secretion and changes in brain structure and function, including variations in gray matter volume and prefrontal activation patterns. These genetic differences may partly explain individual variability in stress sensitivity and antidepressant response [38].

Epigenetic mechanisms further influence BDNF expression in depressive disorders. Changes in DNA methylation within the promoter IV region of the BDNF gene have been implicated in major depressive disorder. Hypomethylation of specific CpG sites in this region has been associated with reduced treatment response and altered emotional processing. Experimental studies indicate that disruption of promoter IV-derived BDNF transcripts impairs hippocampal-prefrontal plasticity and fear-related memory processing. These findings suggest that environmentally driven epigenetic modifications may contribute to long-term dysregulation of BDNF signaling in depression. [6,39]

From a clinical perspective, converging evidence supports a central role of BDNF in the neurobiology of depression. According to the neurotrophin hypothesis, depressive disorders result partly from impaired neuroplasticity within emotion- and memory-related brain circuits. Preclinical studies demonstrate that antidepressant treatments upregulate hippocampal BDNF expression, while clinical research consistently shows reduced peripheral BDNF levels in patients with major depressive disorder. These levels often increase during successful pharmacological and non-pharmacological treatment, including physical activity interventions. [5,38, 40]

Imaging genetics studies further suggest that interactions between BDNF polymorphisms and serotonergic genes influence white matter integrity, cortical activation patterns, and emotional regulation. Although current findings remain limited by small sample sizes and low statistical power, they highlight the potential of trans-diagnostic and biologically informed approaches in depression research.

Collectively, available evidence indicates that alterations in BDNF signaling at anatomical, molecular, genetic, and epigenetic levels contribute to impaired neuroplasticity and increased vulnerability to depressive disorders. These central disturbances provide a biological framework for understanding individual differences in disease susceptibility and treatment response. Furthermore, they support the relevance of BDNF as a key mediator linking physical activity, pharmacological interventions, and clinical improvement in depression.

6. Clinical Implications

From a clinical perspective, available evidence supports the inclusion of structured physical activity as an adjunctive strategy in the treatment of depressive disorders. Exercise may enhance treatment outcomes, particularly in patients with preserved neurotrophic capacity.

Baseline BDNF levels may serve as a potential biomarker for predicting response to exercise-based and pharmacological interventions, although further validation is required.

Regular physical activity may also contribute to relapse prevention and long-term functional recovery. However, substantial interindividual variability highlights the need for personalized treatment planning.

Moreover, long-term engagement in physical activity promotes brain neuroplasticity, which not only supports the treatment of depressive disorders but also facilitates a faster and more effective return to daily functioning through improvements in cognitive performance.

Importantly, the assessment of peripheral BDNF is relatively simple and minimally invasive, as it requires only a standard blood sample, with BDNF levels measurable in serum and platelet-rich fractions, enhancing its potential applicability in routine clinical practice.

7. Limitations

Several limitations should be considered when interpreting the findings of this review. Current evidence remains insufficient to conclusively determine the clinical significance of BDNF in the treatment of depression, partly due to the incomplete understanding of both depression pathophysiology and BDNF regulation.

The relationship between peripheral and central BDNF remains unclear, as serum and plasma levels may not accurately reflect brain concentrations. In addition, peripheral BDNF is largely derived from platelets, and variations in sample handling may influence measured values and limit comparability across studies.

Many studies assessed only total BDNF without distinguishing between pro-BDNF and mature BDNF, despite their distinct biological functions. Moreover, BDNF is synthesized in multiple tissues, further complicating precise assessment.

Substantial heterogeneity in study design, participant characteristics, intervention protocols, and outcome measures reduces reproducibility and generalizability. The frequent use of concomitant pharmacotherapy and relatively small sample sizes further limit causal inference.

Finally, publication bias and the predominance of short-term or observational studies may lead to overestimation of reported effects.

Taken together, these limitations indicate that current findings should be interpreted with caution. Further large-scale, longitudinal, and standardized studies are needed to clarify the clinical relevance of BDNF in depression and exercise-related neuroplasticity.

8. Conclusions

This narrative review highlights the complex relationship between physical activity, brain-derived neurotrophic factor (BDNF), and depressive disorders. Available evidence indicates that depression is consistently associated with reduced peripheral BDNF levels and impaired neuroplasticity, while regular physical activity reliably improves depressive symptoms and overall functioning. [41]

Although exercise may contribute to neurotrophic modulation, its effects on resting BDNF concentrations remain heterogeneous and appear to depend on individual biological characteristics, baseline neurotrophic status, and intervention parameters.

BDNF emerges as a promising, yet incompletely validated, biomarker linking neuroplastic mechanisms with clinical outcomes in depression. Its potential clinical utility requires further confirmation in large-scale, longitudinal, and methodologically standardized studies.

Overall, structured physical activity represents a valuable adjunctive strategy in the management of depressive disorders, acting through multiple neurobiological pathways that extend beyond BDNF alone. Integrating physical activity into personalized treatment approaches may enhance long-term recovery and functional outcomes in patients with depression.

Disclosure

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