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Physical Activity and Mental Health: Systematic Review of Neurobiological Mechanisms and Clinical Effects

Katarzyna Miemczyk

ORCID <https://orcid.org/0009-0008-2675-3373>

katmiem27@gmail.com

Independent Researcher, Wrocław, Poland

Karolina Natalia Mularczyk

ORCID <https://orcid.org/0009-0006-7756-0809>

mkarola1999@gmail.com

Independent Researcher, Wrocław, Poland

Igor Mszyca

ORCID <https://orcid.org/0009-0002-5121-0131>

mszycaigor99@gmail.com

Independent Researcher, Wrocław, Poland

Katarzyna Superson

ORCID <https://orcid.org/0009-0003-2307-5873>

kasiasuperson@gmail.com

Independent Researcher, Wrocław, Poland

Emilia Browarska

ORCID <https://orcid.org/0009-0009-8090-5523>

ebrowarska00@gmail.com

Independent Researcher, Wrocław, Poland

Mateusz Łyko

ORCID <https://orcid.org/0009-0009-2530-2789>

matlyk@wp.pl

Independent Researcher, Wrocław, Poland

Filip Kasperczak

ORCID <https://orcid.org/0009-0000-9758-0889>

fkasperczak98@gmail.com

Independent Researcher, Opole, Poland

Filip Tadeusz Wolek

ORCID <https://orcid.org/0009-0003-6139-0233>

filipwolek99@gmail.com

Independent Researcher, Wrocław, Poland

Łukasz Michalski

ORCID <https://orcid.org/0009-0005-5511-5475>

lukasz.michalski.98@gmail.com

Independent Researcher, Wrocław, Poland

Nicole Gajewska

ORCID <https://orcid.org/0009-0006-0231-0135>

gajewska.nicole1@gmail.com

Independent Researcher, Wrocław, Poland

Kacper Kucharski

ORCID <https://orcid.org/0009-0004-5709-8974>

kacper.kucharski1129@gmail.com

Independent Researcher, Wrocław, Poland

Anna Aksamit

ORCID <https://orcid.org/0009-0002-7929-5966>

ania.aksamit@interia.pl

Independent Researcher, Wrocław, Poland

Corresponding Author

email: katmiem27@gmail.com

Abstract

Introduction: Depressive and anxiety disorders represent a global health and economic problem, drastically reducing the quality of life for the population. The search for effective, low-cost methods to complement traditional psychiatric treatment, ones that are free of serious side effects, has led to a resurgence in research on lifestyle medicine.

Research Objective: The objective of this article is to provide a critical synthesis and integration of the latest scientific evidence regarding the effectiveness of regular physical activity in reducing symptoms of depression and anxiety, to identify optimal dosage parameters: type, intensity, volume, and to analyze the neurobiological mechanisms underlying these changes.

Methodology: This review draws on a structured search of the PubMed and Scopus databases conducted through June 2026. Keywords included: „physical activity”, „mental health”, „depressive disorders”, „anxiety”, „exercise neurobiology”, „resistance training”, „aerobic training”. This review prioritized the latest network meta-analyses, umbrella reviews, and prospective cohort studies (published from 2021 to 2026). It synthesizes data from clinical and non-clinical populations across the entire ontogenetic spectrum.

Results: Regular physical activity has a strong therapeutic effect, often comparable to pharmacotherapy and psychotherapy in mild to moderate depression. The combination of aerobic and resistance training achieves the best results.

Conclusions: Therapeutic strategies must systematically incorporate physical activity as an integral part. Physical activity effectively prevents and treats depression and anxiety across

diverse populations. These benefits stem from complex brain mechanisms: stimulating the BDNF axis, regulating neurotransmitters, suppressing inflammation, and stabilizing the HPA axis.

Keywords: physical activity, mental health, depressive disorders, anxiety, exercise neurobiology, resistance training, aerobic training

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1. Introduction

Modern societies are facing an unprecedented mental health crisis. According to data from the World Health Organization, depression and anxiety disorders severely diminish global productivity and constitute a leading cause of disability worldwide. Although pharmacotherapy and psychotherapy remain the pillars of psychiatry, they are fraught with challenges such as delayed response to medication, several side effects, high treatment costs, and limited availability of specialists.

In this context, physical culture studies and lifestyle medicine provide strong evidence that physical activity is among the most effective non-pharmacological methods for the prevention and treatment of mood disorders. The traditional understanding of quality, which

focuses on motor performance, infrastructure, or biomechanical optimization, is expanded to include the ability of sports systems to generate mental health capital. This paper aims to provide a detailed discussion of the mechanisms, effectiveness across different age groups, and the optimal amount of physical activity that leads to benefits in reducing depressive and anxiety symptoms.

2. Epidemiology and epidemiological evidence: Physical activity as a protective factor

Understanding the relationship between physical activity and mental health requires examining long-term prospective studies. Meta-analyses of multicenter cohort studies clearly demonstrate a negative correlation between levels of physical activity and the risk of developing depression in the future. Individuals with the highest levels of physical activity in their daily lives have up to a 20–30% lower risk of developing depression compared to those with a sedentary lifestyle [1].

Additionally, multinational cross-sectional studies conducted in the post-pandemic era clearly indicate that maintaining an exercise routine served as a key buffer against increased anxiety during periods of social crisis [2]. Crucially, from a public health perspective, a dose-response analysis conducted by Pearce and colleagues (2022) showed that the greatest transition from complete inactivity to moderate activity provides relative protective benefits.[3]. Even meeting just half of the commonly recommended standards (1.25 hours of brisk walking per week) is associated with an 18% reduction in the risk of developing depression [3].

Exercise interventions lead to a significant and immediate reduction in symptoms in populations already experiencing psychopathological symptoms. Umbrella reviews, combining data from hundreds of randomized controlled trials (RCTs), rank physical activity as an intervention with a high effect size (Cohen's d often greater than 0.7) in reducing rates of depression, anxiety, and chronic distress [4,5]. In many cohorts, this effectiveness exceeds or matches that achieved with psychotherapy and standard pharmacotherapy [4].

3. Advanced neurobiological mechanisms

The benefits of exercise on mental health extend beyond psychosocial factors, as measurable neurobiological changes in the central nervous system also play a key role.

In chronic depression, neuronal atrophy occurs in regions involved in memory and emotional regulation, particularly the hippocampus and prefrontal cortex. Physical exercise, especially aerobic exercise, effectively increases the expression of brain-derived neurotrophic

factor (BDNF) and vascular endothelial growth factor (VEGF) [6]. BDNF acts as fertilizer for the brain, stimulating neurogenesis in the dentate gyrus of the hippocampus and improving synaptic plasticity [6].

Physical exercise modifies neurotransmitter metabolism in a manner analogous to the action of SSRI or SNRI medications [7]. There is an increase in the synthesis and release of serotonin, dopamine, and norepinephrine in the synaptic clefts [7]. Additionally, exercise of appropriate intensity activates the endocannabinoid system and induces the release of beta-endorphins, which are responsible for the runner's high and the immediate suppression of anxiety [7,8].

Individuals with anxiety disorders and depression frequently experience ongoing hyperactivity of the HPA axis, which results in consistently elevated cortisol levels and potential damage to brain structures. While exercise is considered an acute stressor, regular exercise fosters adaptation by lowering resting HPA axis reactivity, reducing pulsatile cortisol secretion, and improving biological tolerance to psychological stressors [9].

Contemporary psychiatry strongly links depression to chronic low-grade inflammation (the so-called inflammatory theory of depression). Proinflammatory cytokines (IL-6, TNF- α) activate the enzyme indoleamine dioxygenase (IDO), which redirects tryptophan (a serotonin precursor) into the neurotoxic quinolinic acid pathway. Regular physical exercise has a strong anti-inflammatory effect; it stimulates skeletal muscles to secrete myokines (e.g., IL-6, which acts anti-inflammatorily in this metabolic context, and IL-10). It increases the expression of kynurenine aminotransferases in muscles [12].

A review by Heissel et al. (2023) confirms that the reduction in inflammatory biomarkers following exercise correlates directly with a decrease in depressive symptom severity [11]. As a result, this process converts neurotoxic kynurenine into kynurenic acid, which cannot cross the blood-brain barrier, thereby protecting neural tissue from excitotoxicity [12].

Meta-analyses also show that systematic neurobiological suppression of inflammation can be achieved through targeted yoga and meditation programs that reduce oxidative stress in people with mental disorders [13]. Additionally, recent reports suggest that incorporating polyphenols (compounds with strong antioxidant potential) into the diet synergizes with physical activity, accelerating the regeneration of brain structures and optimizing cognitive function [10].

4. Analysis of effectiveness across ontogenetic and clinical dimensions

Adolescence is a critical phase for the development of the nervous system. Network meta-analyses indicate that in children and adolescents, interventions based on structured physical activity (both team sports and individual aerobic strategies) result in a significant reduction in anxiety and depressive symptoms [14,15,16]. A particularly interesting phenomenon is the effect of acute exercise. Research shows that a single 20–30 minute session of moderate-intensity exercise produces an immediate anxiolytic effect in young adults and adolescents [8]. It can serve as an immediate tool for coping with panic attacks or test anxiety. In the long term, regular physical activity in adolescents prevents the entrenchment of avoidance behaviors and strengthens self-esteem [14,15,16].

In the case of major depressive disorder (MDD) in adults, physical activity has therapeutic effects. A groundbreaking network meta-analysis published in the BMJ (Noetel et al., 2024) demonstrated that certain forms of exercise are as effective as cognitive-behavioral therapy (CBT) and new-generation antidepressants [17]. Research also shows that physical exercise is highly effective in cases of severe mental illness (SMI). High-intensity protocols, such as HIIT, provide significant benefits for both mental health and physical health outcomes in this patient group [18].

Exercise should no longer be treated solely as an adjunct to treatment, but as an equivalent first-line therapeutic method in mild and moderate episodes of MDD, as well as a key adjunctive therapy in severe forms [17,18,19,20]. It also applies to structured group exercises, which recent research supports as clinically effective [20]. Furthermore, umbrella reviews of resistance training provide precise guidelines confirming its effectiveness as a standalone tool for reducing anxiety in clinical populations [21]. Equally strong evidence applies to clinical forms of anxiety disorders, such as generalized anxiety disorder (GAD) or panic disorder [9,22].

In older adults, depression very often overlaps with cognitive deficits, dementia, and a sense of social alienation. Physical activity interventions in this group significantly alleviate depressive symptoms while simultaneously stimulating working memory and slowing cortical atrophy [23,24,25]. As Marconcin et al. (2022) point out, any positive change in physical activity habits among older Europeans brings measurable benefits to their mental health [25].

Additionally, advanced network meta-analyses demonstrate that tailored exercise programs for older adults with comorbid chronic somatic conditions effectively break the cycle of helplessness and reduce chronic low mood [26]. Physical activity in this group dramatically

improves subjective quality of life, reduces fear of falling, and enables maintenance of functional autonomy [23,24].

The impact of exercise on mental health is crucial in patients with chronic diseases. In Chronic Obstructive Pulmonary Disease (COPD), the fear of shortness of breath leads to a vicious cycle of exercise avoidance and secondary, severe depression. Studies show that COPD patients who maintain regular physical activity exhibit significantly lower levels of anxiety and depression [27].

5. Characteristics of the intervention: optimization of training variables, physical activity recommendations for different age groups

Recommendations for physical activity vary depending on the age and health status of the target group. For children and adolescents, aerobic exercises such as team sports, swimming, and cycling are highly recommended. The optimal intensity for this group should be moderate to high, ranging from 60% to 80% of maximum heart rate. For the training to yield the expected results, it should be performed 3 to 4 times a week for 40 to 60 minutes per session [28, 15].

For adults struggling with major depressive disorder (MDD) or anxiety, the best choice is a combined training program that includes both aerobic and resistance exercises. In this case, high-intensity exercise is key. The minimum exercise plan involves working out 3 times a week for 45 to 60 minutes, for at least 10 to 12 weeks [17, 22].

For older adults, on the other hand, resistance exercises, walking, and yoga are most appropriate. The intensity should be low to moderate, defined as levels 4 to 6 on the Borg (RPE) scale. The minimum recommended frequency is 2 to 3 times per week, with each session lasting from 30 to 45 minutes [23, 24].

For decades, researchers believed that only aerobic exercise had psychotherapeutic properties. Modern research has fully vindicated resistance training. Research shows that progressive strength training has significant anxiolytic potential [21,29]. It forces full concentration on the body, improves body image, and induces the release of anabolic hormones, which, in turn, help reduce anxiety [29]. A review by Ye et al. (2024) also sheds new light on mind-body exercises (e.g., yoga), which offer an excellent alternative that combines physical benefits with mental calmness [30]. However, the latest data indicate that mixed protocols, combining elements of aerobic exercise with resistance training, demonstrate the highest clinical effectiveness [22].

Although any activity is better than none, research on dose optimization indicates the existence of tipping points [31]. For students and young adults, this relationship follows a strict

dose-response pattern, where an optimal training volume protects against academic burnout and test anxiety [32]. In the case of major depression in adults, higher exercise intensity often correlates with faster and deeper symptom remission [17,31]. In contrast, in children and adolescents, this relationship follows a U-shaped curve: too little volume does not induce adaptive changes in the brain, while extreme volumes (often associated with competitive sports and performance pressure) may aggravate psychological distress and have negative effects [14].

A significant barrier to treating depression is a lack of motivation (abulia). Modern approaches include online exercise interventions, which enhance accessibility. Research shows that structured training programs delivered via mobile apps or digital platforms, including those with remote monitoring by a trainer, are highly effective in reducing anxiety and depression [33]. Recent reports confirm that digital aerobic interventions are a fully valid form of therapeutic support for adult patients with MDD [34]. Analyses conducted by Liu et al. (2025) among a group of students demonstrate that e-health apps are as effective as in-person programs, making them an excellent first-line tool [35]. The removal of logistical obstacles, the anxiety of social judgment at a conventional gym, and the stigma linked to attending treatment centers are significant advantages of this solution.

6. Discussion and implications

Today, mental health in society is closely linked to quality management in sports and recreation. The quality of sports services, facilities, and staff competence should be evaluated based on their ability to adapt offerings for individuals facing mental health challenges.

Implementation remains the main challenge. A person in a severe mental crisis is unlikely to undertake intensive training on their own. It requires creating a new profile for a specialist, coach, or instructor trained in the basics of psychopathology and motivational techniques. True quality in sports is not about the cult of the perfect body or the pressure that harms mental well-being.

It is important to create a space where everyone feels safe and exercises at their own pace, adapted to their current mental and physical condition.

7. Conclusions

Based on the findings of this study, the following conclusions can be drawn:

- Physical activity has strong, scientifically proven preventive and therapeutic effects that lead to a significant reduction in depressive and anxiety symptoms across age and clinically diverse populations.
- Multidirectional biochemical and structural cascades in the brain underlie these changes, including stimulation of the BDNF axis, regulation of neurotransmission, suppression of inflammation, and stabilization of the HPA axis.
- The most comprehensive and recommended protocol for adult populations is combining aerobic exercise with resistance training, while maintaining individually tailored doses and intensities.
- Digital forms of sport constitute a highly effective and promising method for overcoming barriers to access to physical activity interventions.

Disclosure

Author Contributions:

Conceptualization: Katarzyna Miemczyk, Karolina Natalia Mularczyk, Kacper Kucharski

Methodology: Katarzyna Miemczyk, Katarzyna Superson, Emilia Browarska

Formal analysis: Kacper Kucharski, Filip Tadeusz Wołek, Igor Mszyca, Łukasz Michalski

Data curation: Karolina Natalia Mularczyk, Anna Aksamit, Filip Kaspercak, Filip Tadeusz Wołek

Writing - rough preparation: Emilia Browarska, Anna Aksamit, Nicole Gajewska

Writing - review and editing: Igor Mszyca, Katarzyna Superson, Filip Kaspercak

Visualization: Filip Kaspercak, Katarzyna Miemczyk, Mateusz Łyko, Anna Aksamit

Supervision: Mateusz Łyko, Igor Mszyca, Karolina Natalia Mularczyk, Łukasz Michalski

Project administration: Katarzyna Miemczyk

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