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Movement in the Shadow of Sadness: How Physical Activity Supports the Fight Against Depression

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Abstract

Physical activity plays a critical role in promoting physical and mental health, positively influencing the prevention of non-communicable diseases (NCDs) and enhancing brain function. Research indicates that regular physical exercise, such as aerobic or strength training, aids in the prevention and treatment of mental disorders such as depression, schizophrenia, and Alzheimer's disease. The biological mechanisms associated with physical activity include improved cerebral blood flow, modulation of neurotransmitter systems, and increased levels of neurotrophic factors like BDNF. Exercise also affects the balance of neurotransmitters, such as serotonin, dopamine, and GABA, contributing to improved mood, cognitive abilities, and quality of life. Additionally, physical effort reduces inflammation and oxidative stress, supporting brain health and countering neurodegenerative processes. Regular moderate exercise is an effective method to prevent central fatigue and enhance the adaptability of the central nervous system. This paper explores the complex impact of physical activity on mental health and cognitive function, emphasizing its vital role in supporting the therapy of neurological and psychiatric disorders.

Keywords: Depression, exercise, physical activity

INTRODUCTION

Physical activity is most simply defined as “any bodily movement produced by skeletal muscles that requires energy expenditure” [1]. It significantly impacts the health of both men and women. The benefits of physical activity largely depend on fitness level, the characteristics of specific groups, age, and exercise intensity [2]. General recommendations in many countries suggest at least 150 minutes of moderate aerobic activity per week (or 75 minutes of high-intensity activity). As countries develop economically, inactivity levels increase, potentially reaching 70%, due to changing transportation patterns, increased use of technology for work and recreation, cultural values, and sedentary lifestyles. Sedentary behavior refers to periods of low energy expenditure, such as sitting and watching television. Both a sedentary lifestyle and insufficient physical activity negatively affect healthcare systems, the environment, economic development, community well-being, and individual quality of life [3].

Physical activity takes various forms, including strength training, cardio, dancing, gymnastics, martial arts, walking, or even household chores. Everyone can choose a sport that suits them best. It has been proven that regular physical activity helps prevent non-communicable diseases (NCDs) such as heart disease, hypertension, stroke, diabetes, and many cancers. It also helps maintain a healthy weight and improves mental health, quality of life, and overall well-being [4,5]. Physical exercise plays a significant role in improving mental health, particularly in individuals with severe conditions like schizophrenia, depression, or Alzheimer’s disease. Clinical studies confirm its efficacy as an adjunct therapy [6,7].

The mechanisms by which physical activity exerts its effects are complex and include both physiological and molecular aspects. Diseases like schizophrenia and depression belong to a group of chronic mental disorders that are among the most common causes of mental disability [8]. Physical activity shows particularly promising effects in supporting neuropsychiatric disorders' therapy and improving cognitive function in older adults. Regular effort can also delay neurodegenerative processes characteristic of diseases like Alzheimer’s. Although physical exercise can stress the body, moderate intensity brings benefits, mitigating the negative effects of other stress factors.

These benefits arise from mechanisms such as increased neurotransmitter release (serotonin and dopamine), elevated levels of neurotrophic factors like BDNF, which supports neuron regeneration and stimulates neurogenesis, and improved cerebral blood flow. These processes translate into better functioning of brain structures responsible for memory and learning. All these biological mechanisms explain why regular physical activity benefits both the prevention and treatment of mental health disorders and supports cognitive abilities in the aging brain [9].

The Impact of Physical Activity on Brain Functions

The positive impact of physical activity on brain functions has been documented in animal studies and a growing number of clinical trials in humans. Numerous mechanisms contribute to these beneficial effects, including processes related to neuroinflammation, improved vascularization, antioxidant activity, energy adaptation, and the regulation of neurotrophic and neurotransmitter factors. Among the neurotransmitters modulated by exercise, dopamine (DA), norepinephrine (NE), and serotonin (5-HT) play a central role.

Physical activity is extensively analyzed for its positive effects, attributed to increased brain metabolic reserves and enhanced antioxidant mechanisms [10,11]. Furthermore, physical exercise regulates the secretion of critical neurotrophic factors, vasculotropic agents, inflammatory mediators, and neurotransmitters, significantly influencing the brain's cognitive and adaptive capabilities [12-15]. The release of neurotransmitters, especially monoamines, is particularly crucial in neuroadaptation associated with physical exertion.

Initial research into the interaction between physical activity and monoamines stemmed from the "central fatigue hypothesis," which suggested that increased serotonin (5-HT) secretion in the brain could lead to central fatigue due to its impact on sleep processes, energy reduction, and motivation decrease [16]. Subsequent studies revealed that central fatigue is a more complex process influenced by factors such as exercise intensity and duration. Excessive effort leading to overtraining can result in hyperactivation of monoaminergic systems, contributing to fatigue and limiting the brain's adaptive efficiency [17-19].

In contrast, regular moderate exercise stimulates monoaminergic systems without causing central fatigue. Moreover, this activity is considered one of the most effective ways to support central nervous system (CNS) adaptation and plasticity [22]. Clinical evidence also suggests that monoamines play a vital role in regenerative processes and building CNS resilience, particularly in mental illnesses and Parkinson's disease (PD) [23].

Depression

Depression is a severe mental disorder characterized by a prolonged low mood, loss of interest and pleasure, and impaired daily functioning. According to the American Psychiatric Association's DSM-5 criteria, a depressive episode occurs when symptoms like sadness, low energy, sleep problems, concentration difficulties, feelings of worthlessness, or suicidal thoughts persist for at least two weeks. Symptoms can range from mild to severe, potentially requiring hospitalization.

Depression affects approximately 3.8% of the global population, translating to an estimated 280 million people worldwide. Among adults, the prevalence is 5%, with women being more affected (6%) than men (4%). This disparity arises from a combination of biological, hormonal, and social factors. For instance, women are particularly vulnerable during pregnancy and postpartum, with over 10% experiencing postpartum depression.

A key aspect of depression is its varied occurrence by age. People over 60 are among the most vulnerable, with a prevalence rate of 5.7%. In contrast, suicide, a tragic outcome of depression, is the fourth leading cause of death among individuals aged 15–29. Annually, more than 700,000 deaths occur due to suicide.

While effective treatments like pharmacotherapy, psychotherapy, and behavioral therapy exist, a significant treatment gap persists, especially in low- and middle-income countries, where over 75% of individuals with depression lack adequate support. Barriers include insufficient qualified personnel, limited healthcare funding, and the social stigma surrounding mental illnesses.

Interestingly, studies demonstrate that physical activity can play a crucial role in depression prevention and treatment. Regular exercise helps regulate stress hormones such as cortisol and increases endorphin production—natural mood enhancers. The WHO recommends at least 150 minutes of moderate physical activity weekly, significantly reducing the risk of depressive symptoms.

Depression is not only an individual issue but also a significant challenge for societies and healthcare systems worldwide. Its increasing prevalence calls for both preventive measures and social education to more effectively combat stigma and provide support to those in need.

Recent studies indicate that exercises such as walking, running, yoga, or strength training are effective and well-tolerated in treating depression. Their efficacy has been compared to psychotherapy, pharmacotherapy, and other active control methods. Physical exercise proves to be an effective treatment for depression, with activities like walking or jogging, yoga, and strength training being particularly impactful, especially when performed at high intensity. Exercise has shown comparable effectiveness in individuals with and without comorbidities and across various levels of baseline depression. The effects of activities such as walking/running or yoga were found to be comparable to or even greater than traditional therapies like pharmacotherapy (e.g., SSRIs) or cognitive-behavioral therapy (CBT). Combining exercise with SSRIs or therapy also yielded good results. Exercise should be considered a key component of depression treatment due to its positive impact on both mental and physical health. [26]

Depression and anxiety disorders are associated with abnormalities in the catecholaminergic and monoaminergic systems, involving neurotransmitters such as dopamine, norepinephrine, and serotonin. Brain-derived neurotrophic factor (BDNF) also plays a significant role in the pathophysiology of depression. Dysfunctions in glutamate signaling in the hippocampus and prefrontal cortex are linked to stress and depression, as are abnormalities in the orexinergic and neuropeptide Y (NPY) systems. Current treatments for depression often suffer from delayed response and limited efficacy, necessitating novel therapeutic approaches. Research suggests that physical activity can modulate neurotransmitter systems, positively influencing depression. Exercise, through the release of irisin and improved cerebral blood flow, increases levels of serotonin, dopamine, and norepinephrine, alleviating depressive symptoms. Additionally, it stimulates neurogenesis and enhances mood. Physical activity appears to be a promising natural method for supporting depression treatment, particularly in mild to moderate cases. Regular exercise has a substantial impact on improving mood and mental health, primarily by boosting serotonin levels in the brain. Serotonin, released during activity, exerts antidepressant effects by supporting hippocampal neurogenesis, which enhances memory, mood, and cognitive abilities. Activities like running or swimming increase the activity of serotonin receptors (e.g., 5-HT1A and 5-HT3) and improve brain signaling pathways, counteracting the effects of chronic stress. Studies show that aerobic training and Pilates effectively reduce depression symptoms while improving muscle strength, flexibility, and endurance, with noticeable benefits after just a few weeks of regular practice. [27,28]

Endogenous opioids such as endorphins, enkephalins, and dynorphins are peptides with properties similar to exogenous opioids like morphine. They bind to opioid receptors (μ, κ, δ) in the brain, spinal cord, and nervous system, influencing pain, mood, appetite, and memory. [29] Endorphins, released during physical activity, act as natural pain relievers and mood enhancers. High-intensity exercise increases β-endorphin levels, providing antidepressant effects and reducing anxiety. Dopamine, a neurotransmitter that regulates reward, motivation, and mood, also rises during exercise. Training strengthens D1 and D2 receptors in the brain, enhancing cognitive function, memory, and reducing depressive symptoms. Animal studies show that activities like running or swimming increase dopamine and serotonin levels, counteracting stress effects. [30] Regular physical activity, both strength and aerobic training, boosts the production of opioids and dopamine, improving mood, quality of life, and cognitive abilities. It also supports the treatment of depression, anxiety, and neurological disorders, serving as an effective therapeutic strategy.

Irisin, a hormone released by muscles during physical activity, connects muscles to the brain, benefiting brain health. It stimulates dopamine levels and reduces norepinephrine in stress-related brain areas, providing antidepressant effects. In mice treated with irisin, increased levels of BDNF and IGF-1—key for nervous system development—resulted in reduced depression symptoms. [31] In humans, low irisin levels are associated with post-stroke depression, highlighting its diagnostic and therapeutic potential. Aerobic exercises like swimming enhance the PGC-1α/FNDC5/Irisin pathway, supporting neurogenesis, serotonergic functions, and reducing oxidative stress. [32] Regular training also improves metabolic parameters such as cholesterol and reduces inflammation through irisin's anti-inflammatory and antioxidant effects.

Orexin-A and -B, hypothalamic neuropeptides, influence mood, motivation, and cognitive functions. Exercise increases their levels in cerebrospinal fluid, supporting neurogenesis and hippocampal functions. [33] Regular physical activity strengthens orexin activity, enhancing memory, cognitive abilities, and mood while countering depression and obesity. In summary, irisin and orexin play crucial roles in depression therapy, and regular training fosters their beneficial effects.

GABA (gamma-aminobutyric acid) is the main inhibitory neurotransmitter, responsible for relaxation, synaptic transmission modulation, improved mood, and reduced insomnia and depression. In depressed patients, GABA levels are reduced by up to 52% compared to healthy individuals. GABA dysfunction is linked to excess glutamate—a stimulating neurotransmitter that, in excess, leads to neurotoxicity, neuronal damage, and worsened mood. Physical exercise plays a vital role in restoring the balance between GABA and glutamate. [34] Regular activities like running or yoga stimulate GABA synthesis by increasing GAD67 enzyme activity and GABA receptor expression (e.g., GABAA α1, α2, γ2). [35] Additionally, exercise reduces inflammation and glutamate neurotoxicity, improving synaptic plasticity and the function of the hippocampus and prefrontal cortex.

High-intensity training, such as running or cycling, enhances cerebral blood flow, promoting neurogenesis and neuron survival. Post-exercise, a 19% increase in glutamate and glutamine levels in the visual cortex has been observed, which may explain its antidepressant effects. [36,37] Physical activity acts as a natural antidepressant, alleviating depression symptoms, improving mood, and brain function, making it an effective method for supporting the treatment of mental disorders.

Acetylcholine (ACh), as a neurotransmitter, plays a pivotal role in the central and peripheral nervous systems. Nicotinic (nAChR) and muscarinic (mAChR) receptors have demonstrated antidepressant properties. For instance, activation of nAChR receptors reduces depression symptoms, while inhibitors of these receptors can reverse increased acetylcholinesterase (AChE) activity, leading to mood improvement. [38] Depression in patients with Parkinson's disease is associated with a decrease in α4β2 nicotinic receptors in the brain. [39,40] Therapies targeting these receptors may be effective in treating depression in older adults. Interestingly, nicotine, as an agonist of nAChR receptors, shows antidepressant potential in both animal and human studies.

Physical exercise plays a critical role in restoring balance between GABA and glutamate. Regular activities such as running or yoga stimulate GABA synthesis by increasing GAD67 enzyme activity and GABA receptor expression. [41] For example, a 4-week exercise program increases GABA levels by 18%, and a 60-minute yoga session boosts them by as much as 27%. Additionally, exercise reduces inflammation and glutamate neurotoxicity, enhancing synaptic plasticity and the function of the hippocampus and prefrontal cortex.

Physical activity also improves cholinergic system function. Studies on rats with depression induced by Alzheimer's disease show that exercise significantly enhances spatial memory, increases dopamine and acetylcholine levels in the brain, and reduces the number of dead cells. Furthermore, exercise in rats with Parkinson's disease elevated BDNF and dopamine levels in the nucleus accumbens, independent of acetylcholine levels, contributing to alleviating depressive symptoms. [42,43]

These findings indicate that physical activity supports depression treatment by influencing various neurotransmitter pathways, including serotonin, dopamine, and acetylcholine. However, further research is needed to better understand the complex mechanisms of these processes.

CONCLUSION

Physical activity plays a crucial role in improving mental and physical health, positively impacting overall functioning and preventing various conditions, including mental disorders. Regular exercises, such as aerobic and strength training, or activities like yoga and walking, aid in treating depression, schizophrenia, and neurodegenerative diseases. The underlying biological mechanisms include improved cerebral blood flow, regulation of neurotransmitters such as serotonin, dopamine, and norepinephrine, and increased levels of brain-derived neurotrophic factor (BDNF). These processes support neuron regeneration, stimulate neurogenesis, and enhance cognitive functions, resulting in better mood, resilience, and quality of life.

Exercise acts as an anti-inflammatory agent and counters oxidative stress, protecting the nervous system from neurodegenerative processes. Research shows that regular moderate exercise is an effective method for supporting depression treatment, comparable in efficacy to pharmacotherapy and psychotherapy. Exercise restores neurotransmitter balance, including serotonin and dopamine, whose dysfunction is a key factor in depression. Physical activity also boosts endorphin levels, serving as a natural mood enhancer and stress reducer.

Depression, one of the most common mental disorders, affects a significant portion of the population and leads to severe consequences, such as loss of functionality or increased suicide risk. Regular physical activity plays a vital role in alleviating depression symptoms, especially in mild and moderate cases. During exercise, neuropeptides like irisin are released, which protect the brain, promote its regeneration, and improve mood.

Stress hormones like cortisol are better regulated during physical activity, limiting their adverse effects on the body. Exercises such as running, swimming, or strength training not only improve mental health but also strengthen cognitive functions and the brain's adaptive capabilities. Scientific evidence indicates that physical activity reduces the risk of central fatigue, enhances energy balance, and boosts nervous system resilience.

Research findings unequivocally confirm that physical activity is a key element in the prevention and treatment of depression and other mental disorders. Through regular exercise, individuals struggling with these issues can improve their mood, cognitive abilities, and quality of life. Incorporating physical activity into therapy produces synergistic effects, enhancing the efficacy of medications and psychotherapy. Given the increasing prevalence of depression, promoting physical activity should become an essential part of preventive and therapeutic measures.

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