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Exploring the Effect of Exercise in Assisting the Treatment of Depression

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Abstract: Depression is a prevalent mood disorder that significantly impairs the quality of life for those affected. Studies have indicated that exercise offers significant benefits in the treatment of depression. Exercise not only ameliorates the emotional state, self-perception, and sleep quality of individuals with depression but also facilitates the production of neurotransmitters such as serotonin and dopamine, which play a regulatory role in mood and enhance the capacity of patients to combat depression, thereby assisting in treatment. Among these neurotransmitters, serotonin is considered the most critical. This study aims to investigate the effect of exercise in adjunctive therapy by examining the mechanism of serotonin in treating depression and the influence of exercise therapy on serotonin levels. Findings suggest that exercise therapy has a substantial effect on serotonin levels and can serve as an adjunctive treatment for depression. As an adjunctive treatment, exercise therapy can reduce treatment costs and provide a therapeutic option for patients who cannot undergo pharmacological treatment. Additionally, as a non-pharmacological treatment method, exercise holds significant meaning for the treatment of depression and warrants further promotion and application in clinical practice.

Keywords: Depression, Exercise Therapy, 5-HT, Serotonin

1. Introduction

With the rapid development of society, individuals increasingly face high levels of stress in their work and lives, coupled with a lack of physical exercise. This not only leads to a decline in physical immunity and susceptibility to illness but also poses significant risks to mental health, resulting in diseases such as depression and anxiety. Depression has become a common mental health issue in contemporary society. Statistics indicate that depression leads to millions of people worldwide seeking mental health services and treatment due to its severe impact on daily life. Depression not only affects the emotions of those suffering from it but can also impact their normal functioning, with severe cases potentially leading to suicidal behavior. Over the past few decades, researchers have explored various methods for treating depression, including pharmacotherapy, psychotherapy, and physical therapy. Among these, exercise as a non-pharmacological treatment has garnered considerable attention. Current research suggests that exercise can play a role in the prevention and adjunctive treatment of depression, although a direct causal relationship between depression and exercise has yet to be established. Exercise therapy, despite its low cost, requires a long-term commitment, which many patients find challenging to maintain [1]. This study aims to review the

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impact of exercise therapy on serotonin levels to explore its influence in the adjunctive treatment of depression. Exercise therapy, when integrated as an adjunctive treatment, can enhance the function of the heart and lungs, improve immune system capacity, and positively affect emotions [2]. As an adjunctive treatment for depression, exercise first provides an alternative for patients who are unwilling to accept pharmacological treatment. Furthermore, exercise therapy can effectively improve psychological health by alleviating negative emotions such as depression and anxiety, thus promoting a pleasant state of mind. While fostering psychological well-being, exercise also enhances overall physical health and reduces the risk of chronic diseases such as cardiovascular diseases and diabetes.

2. Introduction to Depression

2.1. Concept

Depression is a prevalent mental and psychological disorder characterized by a persistently low mood and a lack of interest in daily activities. Patients suffering from depression may experience insomnia, appetite changes, and in severe cases, suicidal tendencies. Depression is categorized into mild, moderate, and severe levels.

2.2. Etiology

The pathogenesis of depression is influenced by a multitude of factors, including genetic, social, and neurobiological elements. Despite extensive research, a definitive etiological mechanism has not been pinpointed. However, several significant hypotheses have been proposed from a biological perspective.

Neurotransmitter Hypothesis: Neurotransmitters play a crucial role in the pathophysiology of depression. These chemical substances facilitate the transmission of information between nerve cells and include serotonin, dopamine, and norepinephrine. This hypothesis suggests that individuals with depression exhibit abnormal levels of neurotransmitters, such as decreased serotonin levels or dopamine imbalances, which impair the normal functioning of the neurotransmitter system, leading to dysregulation of mood and depressive symptoms. The hypothesis supports the exploration of the efficacy of pharmacological and exercise therapies to modulate the neurotransmitter system, thereby improving symptoms and quality of life in patients with depression. Pharmacological treatments often involve selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants, which may alleviate depressive symptoms by modulating the neurotransmitter system. Exercise therapy can promote the release of neurotransmitters such as dopamine and serotonin in the brain, helping to elevate mood and reduce feelings of depression. Additionally, the hypothesis highlights the interaction between different neurotransmitter systems, as well as abnormalities in receptor density and function.

HPA Axis Hypothesis: The hypothalamic-pituitary-adrenal (HPA) axis holds a significant position in the pathogenesis of depression. When individuals face stress, stimuli in the hypothalamus trigger the release of corticotropin-releasing hormone (CRH), which activates the pituitary to release adrenocorticotropic hormone, stimulating the adrenal cortex to secrete cortisol. Excessive cortisol and an imbalanced negative feedback mechanism may lead to functional abnormalities and exacerbate depression. In summary, chronic stress can lead to overactivation of the HPA axis, contributing to depression [3].

Cytokine Hypothesis: Cytokines in the immune system play a vital role in the development of depression. This hypothesis posits that immune activation due to inflammatory responses may lead to the onset of depression. Specifically, chronic inflammatory states can lead to the release of a plethora of cytokines, which can affect the functionality of the nervous system, damage neuronal

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connections, and impact the production and transmission of neurotransmitters, resulting in depression [4]. Persistent inflammatory responses, such as those seen in infectious and immune-mediated diseases, can precipitate depressive symptoms. The cytokine hypothesis offers a novel perspective, suggesting that inflammation and abnormal immune system activation may be associated with the pathogenesis of depression, providing a new angle for studying the pathophysiological mechanisms and therapeutic approaches of depression. Given the multifactorial influences on the etiology of depression, treatment modalities can encompass pharmacological interventions as well as physical approaches such as exercise. Exercise can stimulate an increase in neurotransmitter levels and enhance the brain's stress response, allowing individuals to alleviate stress and regulate emotions [5].

3. Treatment Methods for Depression

The treatment of depression primarily consists of pharmacological and physical therapies. Physical therapies encompass psychotherapy, exercise therapy, Electroconvulsive Therapy (ECT), Transcranial Magnetic Stimulation (TMS), among others [6]. Pharmacological treatment most commonly employs Selective Serotonin Reuptake Inhibitors (SSRIs) and tricyclic antidepressants, which ameliorate depressive symptoms by modulating the neurotransmitter system. However, these medications can have significant side effects, including nausea, sleep disturbances, and sexual dysfunction, impacting normal life. Psychotherapy, particularly Cognitive Behavioral Therapy (CBT), is widely used and aims to alleviate depressive symptoms by helping patients identify and change negative thought patterns and behaviors. Yet, it requires a long treatment period and the cooperation of one or two individuals. Electroconvulsive Therapy (ECT) can be an option for patients who do not respond to other treatments, working by inducing a brief seizure in the brain to alleviate depressive symptoms, but it is costly and may cause memory issues. Exercise therapy is straightforward, side-effect free, and can enhance physical fitness while treating depression.

3.1. Introduction to 5-HT and Its Mechanism in Treating Depression

5-Hydroxytryptamine (5-HT), a derivative of indole and a monoamine neurotransmitter, is found in both the central nervous system and the peripheral system, with independent functions but the same synthetic pathway. Numerous 5-HT receptor subtypes have been identified in mammals, with 5-HT1AR being particularly well-studied and playing a significant role in the central nervous system, including in depression, sleep-wake cycles, eating behavior, and cognitive abilities [7], exerting a substantial influence on emotional stability.

In 1991, Healy D noted that the biochemical basis of depression is largely concentrated on 5-HT, norepinephrine (NE), dopamine (DA), and their receptors, with 5-HT and NE being particularly prominent. Studies suggest a relationship between depression and 5-HT, but the pathogenesis remains unclear. In terms of mood regulation, research indicates that 5-HT modulates the plasticity of the hippocampal structure for mood regulation, but the mechanism is not yet clear. Regarding the control of impulsive emotional responses, studies show neurotransmitter disorders in rats during anger or depression, but the mechanism is not yet clear [7]. In terms of emotional processing, research indicates that 5-HT plays an important role [8].

From the aforementioned studies, it is only proven that 5-HT is related to the regulation of mood by modulating brain areas responsible for emotional regulation, thereby modulating anxiety and depression, but many pathogenic mechanisms are still unclear [7].

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3.2. Physical Therapies

3.2.1. Psychotherapy

Psychotherapy is a treatment method that establishes a good therapeutic relationship with patients, helps them resolve psychological issues, and encourages positive changes. The most commonly used psychotherapy for depression is Cognitive Behavioral Therapy (CBT), which aims to help patients identify and change negative thinking patterns, thereby improving mood and behavior. During treatment, patients are guided to recognize how their thought patterns affect their behavior or emotions and to think about problems positively to alleviate depressive symptoms. Another therapy is insight-oriented therapy, which helps patients express and understand their inner feelings through conversation and interaction with a psychotherapist, discovering and resolving potential psychological issues. Psychotherapists often develop targeted treatment plans based on the patient's condition and needs, and continuously adjust these plans during treatment to achieve the best therapeutic effect.

3.2.2. Exercise Therapy

Exercise therapy refers to the treatment method that promotes mental and physical health through physical exercise such as aerobic exercise, group activities, strength training, and rhythmic movement. Physiologically, exercise promotes the release of neurotransmitters like 5-HT and dopamine in the brain, helping patients alleviate anxiety and depression. Psychologically, it increases self-esteem and reduces stress, thereby alleviating depressive symptoms, and studies have shown [9] that exercise has certain advantages as a first-line treatment for mild to moderate depression compared to medication and psychotherapy. Even in 2016, Canadian guidelines recommended exercise as a first-line treatment for mild depression. Literature also indicates that many patients are unwilling to accept drug treatment or are unable to undergo drug treatment due to physical reasons, and exercise therapy as an adjunctive treatment may be effective for patients [9]. In exercise therapy, therapists also provide personalized treatment based on the patient's physical condition and mental health.

3.2.3. Transcranial Magnetic Stimulation (TMS)

TMS is a relatively safe, non-invasive neuromodulation technique that does not require craniotomy and is a non-invasive treatment method. By placing a coil on a specific scalp location and providing stimulation to modulate neuronal activity, it alleviates depression. TMS can stimulate neuronal activity in the cerebral cortex, regulate nerve conduction and neurotransmitter release, and help patients improve their mood, sleep, and reduce anxiety and depressive emotions, thereby alleviating the symptoms of patients with depression. TMS is suitable for patients who are ineffective in treating depression with medication or cannot tolerate it and can be used to treat depression, anxiety, and occupational diseases. However, TMS is not suitable for all mental illnesses, so a comprehensive assessment of the patient should be conducted before TMS treatment, and personalized treatment should be provided to help patients recover better. TMS has many side effects, such as headaches, scalp discomfort, slight muscle twitching in the target muscles, tinnitus, and even brief memory loss. Therefore, TMS treatment should be carried out in a professional medical institution, and any discomfort should be reported promptly to ensure the safety and effectiveness of the treatment. However, these side effects are not long-term and can be reduced or disappear after the end of the side effects.

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4. The Effect of Exercise Therapy on Depression

4.1. The Effect of Exercise Therapy on 5-HT Levels

Numerous scientists have conducted experiments on animals and humans to determine the influence of exercise on 5-HT. Figure 1 illustrates the experimental procedure for animals, showing that rats were divided into four groups, each consisting of 10 rats, namely the control group, the exercise group, the stress-induced group, and the combination of exercise and stress-induced groups. The control group rats underwent forced swimming tests to confirm the depressive state, followed by euthanasia, brain tissue sectioning, and protein blotting to detect the expression of 5-HT1A in the dorsal raphe. The exercise group rats ran on a treadmill for 30 minutes daily for four weeks. The stress-induced group received inescapable 0.2 mA foot electric stimulation three times a day for seven days [10].

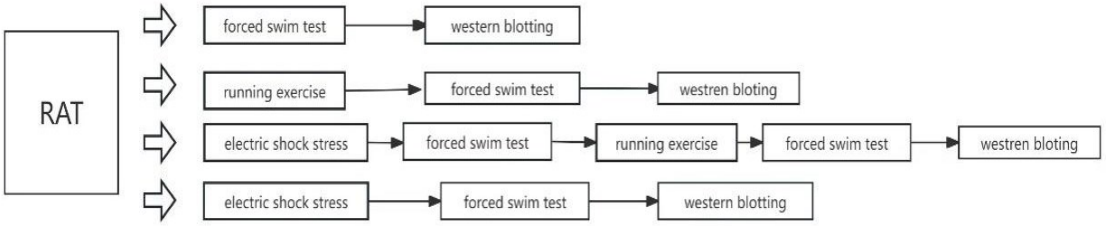

Figure 1: Flowchart of the Animal Experiment Procedure

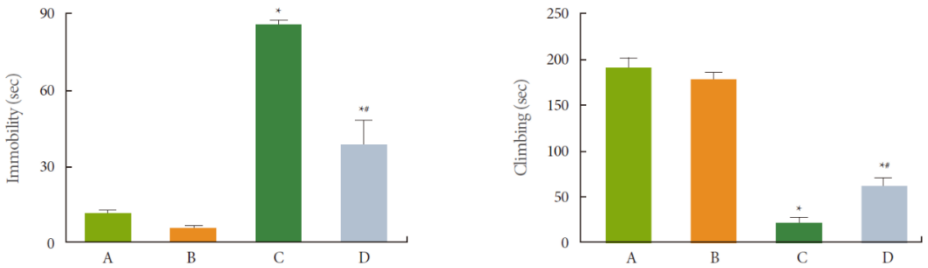

Figure 2: The Effect of Treadmill Exercise on Depressive-Like Behavior in the Forced Swimming Test. (A) Control Group, (B) Control and Exercise Groups, (C) Stress-Induced Group, (D) Stress-Induced and Exercise Groups [10].

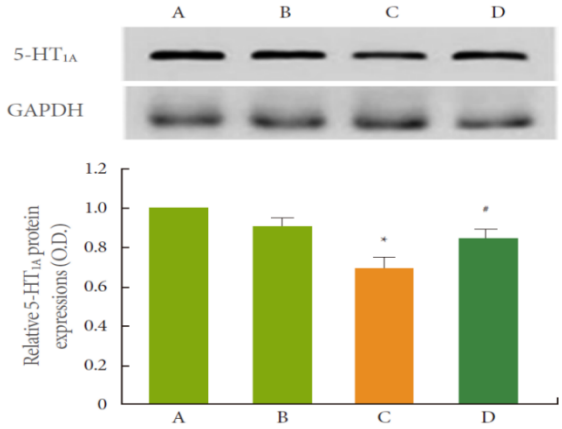

Figure 3: The Effect of Treadmill Exercise on the Expression of 5-Hydroxytryptamine 1A (5-HT1A) Receptors in the Dorsal Raphe. (A) Control Group, (B) Control and Exercise Groups, (C) Stress-Induced Group, (D) Stress-Induced and Exercise Groups [10].

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It can be observed from Figure 2 and Figure 3 that exercise effectively alleviates anxiety and depressive symptoms in stressed rats. The immobility time caused by electric shock was reduced, while the climbing time was increased as a result of exercise.

4.2. Different Exercise Modalities Have Different Effects on the Treatment of Depression

Different types of exercise can have certain therapeutic effects on depressive mood, but they require specific conditions. Studies have shown that aerobic exercises, such as jogging, swimming, and jumping rope, can increase the levels of monoamine neurotransmitters in the brain, such as serotonin and dopamine, enhance neuronal plasticity, and thus reduce the occurrence of negative emotions. Resistance exercises improve depressive and anxious moods by regulating the gut microbiota. High-intensity interval training stimulates the body's stress response, affecting the structure of multiple brain tissues and the synthesis and release of neurotransmitters, thereby improving depressive mood [11]. Social exercises, such as team sports and cooperative games, can increase communication with others, enhance social relationships, reduce feelings of social isolation, and thus improve depressive symptoms. Nature-based exercises, such as mountain climbing, hiking, and cycling, place individuals in natural environments, providing healing and relaxation effects. These activities contribute to promoting mental health and alleviating depressive symptoms.

5. Conclusion

From these studies, it is understood that exercise can influence the treatment of depression by promoting the synthesis of serotonin. Exercise can increase the activity of the tryptophan transporter (TRYPT) in the brain, facilitating the conversion of tryptophan to serotonin, thereby increasing serotonin levels in the brain. This increase helps to stabilize mood swings and alleviate depressive symptoms. Additionally, appropriate exercise can improve the metabolic process of serotonin, promoting its normal synthesis, reuptake, and maintaining a balance of neurotransmitters, which is crucial for individuals with depression. Therefore, exercise can serve as an effective adjunctive treatment to help alleviate depressive symptoms. Moderate exercise can improve the emotional state, self-perception, and cognitive function of individuals with depression, contributing to enhanced psychological well-being.

However, many mechanisms are not yet clear, such as how exercise therapy affects the neurological mechanisms of depression, and more research is needed to address these issues. Exercise therapy, as a cost-effective treatment with minimal side effects, holds great promise for the future treatment of depression. The efficacy of exercise as an adjunctive therapy for depression may be influenced by factors such as the type, frequency, and intensity of exercise. Therefore, personalized exercise prescriptions and ongoing monitoring are significant for maximizing therapeutic outcomes, and in the future, personalized services can be developed to better treat depression. In the experiments mentioned in this paper that measure serotonin levels before and after exercise in rats, the exercise was singular, without comparison of exercise intensity. Furthermore, during the literature search, it was found that there are few clinical trials on exercise therapy, with most being animal experiments, lacking clinical trials to provide more feasibility for exercise therapy as an adjunctive treatment for depression.

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