ISSN: 2710-0170

Research Progress on the Intervention Effects and Mechanisms of Various Exercise Modalities in Patients with Drug Addiction

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Abstract

Drug addiction seriously endangers human physical and mental health. Recent studies have shown that exercise therapy, as a non-pharmaceutical intervention, has a significant effect on patients addicted to drugs. This article systematically analyzes the intervention effects of different types of exercise (aerobic exercise, resistance training, and combined exercise). The results show that exercise can effectively suppress drug craving, improve emotional state, enhance physical fitness, and alleviate withdrawal symptoms and the risk of relapse. However, the intervention effects vary with different exercise intensities. At present, the research on the mechanism of exercise intervention is still in the development stage. This article focuses on exploring the regulatory effects of exercise on neurotransmitters (dopamine, glutamic acid, endogenous opioid peptides), brain-derived neurotrophic factor (BDNF), and the immune system, revealing that it improves addiction symptoms through pathways such as dopaminergic reward pathway remodeling, BDNF-mediated neural plasticity repair, and inflammation inhibition. Future research should focus on the design of personalized exercise programs, deepen the empirical study of the dose-effect of exercise intensity, and deeply explore the interaction mechanisms of multiple systems to optimize the application of exercise therapy in the treatment of drug addiction.

Keywords

Drug addiction; Exercise intervention; Intervention effect; Mechanism.

1. Introduction

Drug addiction is a chronic brain disorder caused by the repeated use of psychoactive substances, characterized by the uncontrolled behavior of forced drug seeking and use. Its pathological mechanism mainly involves the physiological and psychological dependence resulting from the dysfunction of the brain's reward system and neurotransmitters [1]. The global situation of drug abuse is severe. According to the United Nations Office on Drugs and Crime's "World Drug Report 2025", approximately 316 million people worldwide used drugs (excluding alcohol and tobacco) in 2023, accounting for 6% of the 15-64 age group, a significant increase from 2013 (5.2%). According to the "2023 China Drug Situation Report", by the end of 2023, there were 896,000 drug users in China, accounting for 6.4% of the country's total population. Therefore, how to curb the abuse of drugs has become a common global issue [3].

Although the current mainstream drug addiction intervention methods (such as drug therapy, psychotherapy and physical therapy) have certain therapeutic effects, they still face limitations such as long treatment cycles, heavy economic burdens, significant drug side effects and high relapse rates. Recent studies have found that exercise intervention, as a low-cost, low-risk and highly accessible non-pharmaceutical therapy, can significantly improve withdrawal symptoms (such as anxiety and depression), reduce drug craving, and increase the success rate of long-term withdrawal [4-7]. However, traditional sports intervention models tend to be

ISSN: 2710-0170

monotonous and lack targeted research on different types, intensities and mechanisms of sports. This article systematically retrieved relevant literatures from 2000 to 2025 in databases such as Web of Science, PubMed, and China National Knowledge Infrastructure (CNKI), aiming to: (1) analyze the differentiated intervention effects of aerobic exercise, resistance training, and combined exercise on drug addiction; (2) Clarify the mechanism by which exercise regulates through neurotransmitters, activates neurotrophic factors and reestablishes immune balance; (3) Provide a theoretical basis for the formulation of personalized exercise prescriptions in clinical practice and promote a new paradigm in exercise-based drug rehabilitation research..

2. The intervention effect of aerobic exercise on drug - addicted patients

2.1. The impact on drug craving, executive function, and emotional improvement

Aerobic exercise helps to suppress craving levels. The beneficial effects of exercise intervention on methamphetamine addiction have been confirmed in both acute and long-term cases. Wang et al. [8] demonstrated through event-related potential (ERP) research that acute aerobic exercise (such as 30-minute moderate-intensity cycling) improves inhibitory control ability and reduces immediate craving by enhancing prefrontal cortex activation (manifested as an increase in the N2/P3 amplitude of ERP), and this effect is universal for multisubstance dependent individuals. Its mechanism is related to the release of endorphins and the regulation of emotions. Ellingsen et al. [9] further confirmed that acute exercise has cross-substance universality for individuals with polysubstance dependence. The reduction in desire after a single intervention is closely related to endorphin release and emotional regulation, such as alleviating anxiety and enhancing self-esteem. Zhao Qi et al. [10] found in their research that long-term intervention (such as 12-week regular training) continuously inhibits neural excitation induced by drug cues by regulating alpha neural oscillations and optimizing the synergy between the default mode network and the executive control network. Overall, acute exercise alleviates craving through rapid neurophysiological responses and psychological state improvements, while long-term regular exercise continuously supports withdrawal through neural oscillation remodeling and network function integration, providing a dynamic solution for addiction intervention.

In terms of executive function, acute high-intensity aerobic exercise has a more significant effect on the recovery of inhibitory control. ERP analysis revealed that the amplitudes of N2 and P3 components in the electroencephalogram of those who had withdrawn significantly decreased, indicating that after the intervention, the conflict between excessive focus on drug cues and cognitive control in those who had withdrawn decreased, thereby reducing their attention to drug-related cues [11]. In addition, Rong Hao et al. [12] found that the improvement in executive control ability after 30 minutes of high-intensity cycling was greater than that after moderate-intensity cycling. Chen Yifan et al. [13] further discovered that 35 minutes of high-intensity exercise can simultaneously reduce craving and enhance working memory, suggesting that this might be achieved by increasing the activation levels of related brain regions. However, the duration must be strictly controlled to avoid the risk of overtraining. Therefore, high-intensity aerobic exercise has a more significant effect on improving executive function and seems to be more conducive to enhancing the activation levels of related brain regions. However, during the intervention process, it is essential to scientifically control the duration of high-intensity aerobic exercise; otherwise, it may cause brain damage.

Long-term and excessive use of addictive drugs can cause abnormal psychological and physiological changes, which can have adverse effects on physical and mental health, such as causing symptoms like anxiety and depression. Currently, a large number of studies have

ISSN: 2710-0170

confirmed that aerobic exercise helps improve the emotional state of drug-dependent individuals and is closely related to neurobiochemical regulation. Xiawen Li et al. [14] found that acute moderate-intensity aerobic exercise can enable addicts to generate positive emotions and also enhance their ability to regulate negative emotions. Similar effects have also been observed in animal experiments. Regular swimming exercise can improve the anxiety and depression of methamphetamine withdrawal rats [15]. In addition, the positive emotions that aerobic exercise generates in addicts are also related to neurotransmitters in the brain [6]. The mechanism involves that aerobic exercise can prompt the peripheral and central nervous systems to release endogenous opioid peptides [16], and endogenous opioid peptides can enable addicts to experience positive emotional states [17]. Exercise enhances self-efficacy through various means, breaking the vicious cycle of desire and negative emotions.

2.2. The Impact of Aerobic Exercise on Physical Fitness and Quality of Life

Aerobic exercise can significantly enhance the muscle endurance and cardiopulmonary function of drug addicts and improve body composition. These physiological adaptations work in synergy with the recovery of neurological functions, jointly enhancing the overall health of patients and improving their ability to maintain withdrawal. In terms of muscle endurance, after 12 weeks of aerobic exercise, the push-ups of the experimental group (35.57±10.63) were significantly improved compared with those of the control group (24.77±15.77), and it was also found that the single-leg standing time of the lower limbs was significantly increased [18]. In the research of Geng Jingjing et al. [19], it was also confirmed that after three months of intervention with Tai Chi rehabilitation exercises, the subjects' time of standing on one leg with eyes closed was significantly improved. In addition, aerobic exercise can also promote the recovery of cardiovascular function in patients addicted to drugs. For instance, after 12 weeks of progressive aerobic exercise, the patient's cardiopulmonary function was significantly improved. The average lung capacity increased by 9.34%, the average step index rose by 11.70%, and the average 12-minute run performance improved by 21.48%[20]. After 12 weeks of moderate-intensity aerobic exercise intervention, the cardiopulmonary function of the subjects still showed significant improvement three months after the end of treatment. In addition, the subjects were able to reach 85% of their maximum heart rate at a relatively high metabolic equivalent level [21].

3. The intervention effect of resistance exercise on drug - addicted patients

3.1. The impact on drug cravings, emotional states, and relapse rates

At present, some studies have confirmed that resistance training can improve the emotional state of drug-addicted patients, reduce their psychological craving for drugs, and thereby lower the risk of relapse. Liu Xudong et al. [22] found that 16 weeks of neuromuscular training could reduce the subjects' desire for drugs, and compared with aerobic exercise, it could better increase the brain activity level of the subjects in response to positive emotional stimuli, thereby improving their emotional state. In addition, a study on acute moderate-intensity resistance training found that moderate-intensity resistance training immediately after exercise could significantly improve the emotional state of methamphetamine-dependent individuals, and was more effective in reducing their psychological cravings than low-intensity and high-intensity exercise. The reason for this is that moderate-intensity resistance training can better enhance the happiness and excitement of addicts. And by influencing their executive functions, the ability of attentional bias is re-regulated and redistributed, thereby reducing the drug craving level of addicts [5]. Li Kefeng et al. [23] also found similar results. After 12 weeks of moderate resistance training, they discovered that the anxiety levels of the subjects were

ISSN: 2710-0170

significantly improved both in the middle of the intervention and after the intervention. Moreover, after the intervention, the subjects' craving level for methamphetamine was significantly reduced. It was also confirmed that the mechanism for reducing craving is related to the remodeling and inhibitory functions of brain regions. Maintaining a high blood oxygen content in brain regions, keeping them highly active, and enhancing inhibitory capabilities are the keys to reducing craving. The research by Lu Zehui et al. [4] indicates that compared with low-intensity and moderate-intensity resistance exercises, high-intensity resistance exercises have the most significant improvement in the craving degree of heroin addicts, and there is a significant linear relationship between exercise intensity and craving degree. Some scholars believe that it might be due to the varying degrees of impact of different addictive drugs on the human body, which leads to different effects of exercise intensity on improving the body. Compared with other drugs, heroin may cause more harm and dependence on the human body, so high-intensity training can more effectively improve the craving of addicts [24]. In conclusion, resistance training has played a positive role in improving the craving and emotional state of drug addicts. However, resistance exercises of different intensities have shown different effects, and further exploration of the reasons for this is needed.

3.2. Impact on physical fitness and quality of life

Resistance training significantly enhances muscle and bone health, which is of great significance for addiction survivors whose physical functions have been impaired due to long-term drug use. This kind of training helps to enhance their physical fitness. A randomized controlled study showed that after 8 weeks of endurance and resistance training, the maximum oxygen uptake of the subjects increased by 0.63±0.22 liters per minute, approximately 21%, the leg bending strength increased by 20.6±5.7 kilograms, approximately 49%, and the body weight decreased significantly by 1.7±2.4 kilograms, approximately 2%. The body fat percentage decreased by 2.8±1.3%, approximately 15%, and the fat weight decreased by 2.8±1.8 kilograms, approximately 18%[25] (Brett A). Hansen Li et al. [26] found through an 8-week randomized controlled trial that resistance training reduced the diastolic and systolic blood pressure of the subjects, and also improved lung capacity, grip strength, balance and vertical jumping ability.

4. The Intervention Effect of Aerobic Combined with Resistance Exercise on Drug Addiction Patients

The combination of aerobic and resistance exercises can effectively control drug intake. Research has found that 30 minutes of aerobic training combined with 15 minutes of strength training over 8 weeks can inhibit the intake of methamphetamine [21]. In addition, Qinghua He et al. [27] compared the intervention effects of aerobic combined resistance exercise and aerobic exercise. The results showed that both aerobic exercise and aerobic combined resistance exercise could improve the mental health status, craving level and immune capacity of drug addicts, but the intervention effect of aerobic combined resistance exercise was better. Lu Chunxia et al. [28] adopted a 12-week moderate-intensity aerobic combined with resistance exercise intervention. The results showed that moderate-intensity aerobic combined with resistance exercise could increase the expression levels of dopamine, serotonin, and norepinephrine in the subjects' bodies, thereby reducing their negative emotions, improving their mental health, lowering their desire for medication, and increasing the success rate of the stage. Similar results were also found in an 8-week randomized controlled trial. Aerobic combined with resistance training could better alleviate anxiety, especially trait anxiety, improve the quality of life of methamphetamine addicts, and significantly reduce craving [29] (Li Songyang). JingSong Wang et al. [30] confirmed through an 8-week experiment that aerobic

ISSN: 2710-0170

combined with resistance exercise could alleviate peripheral inflammation in methamphetamine addicts (significantly reducing the levels of IL-1β, TNF-α, and IL-6 in peripheral blood), and could significantly reduce their craving levels.

In conclusion, aerobic combined with resistance exercise integrates the advantages of both aerobic and resistance exercises. As a new form of exercise for drug rehabilitation intervention, it can have positive effects on the psychology, craving level, and physiology of addicts in many aspects, and shows superior effects compared to single aerobic and resistance exercises. It can be widely used in future empirical research.

5. Mechanisms of exercise intervention in drug addiction

5.1. Exercise and Neurotransmitters

Dopamine is an important catecholamine neurotransmitter in the central nervous system, and it is involved in physiological functions such as motor control, reward mechanisms, and emotion regulation. Long-term use of addictive drugs can reduce the release of DA in the body. As a result, addicts can only make up for the lost euphoria by continuing to use drugs. The dynamic changes in DA levels and the activity of their receptors are the core neurobiological mechanisms that regulate individual drug search behavior and drug craving, and are crucial for the occurrence and development of drug addiction-related behaviors. Exercise can improve the addiction symptoms of addicts by regulating the dopaminergic system, increasing the release, synthesis and secretion of DA, and correcting the abnormal activation of the reward circuit. Gong Dan et al. [31] confirmed in a study that short, moderate-intensity aerobic exercise can significantly increase the DA release of addicts, thereby promoting the generation of positive emotions. Similar results were also found in an animal experiment. Goekint et al. [32] discovered that after 60 minutes of high-intensity treadmill exercise, the release of hippocampal DA in rats significantly increased. Benjamin N et al. [33] found that six weeks of running wheel exercise increased the level of DA in rats and reduced the level of dopamine receptor-D2 mrna in the core area of the nucleus vaginae, altering the genes of the midbrain limbic reward neural circuit. In addition, long-term drug use can cause neuroadaptive changes in the DA system, such as up-regulating D1-type receptors and down-regulating D2-type receptors. However, exercise can improve such neuroadaptive changes. In animal models, Robison et al. [34] found that six weeks of treadmill exercise could reduce the binding level of D1 receptors in the nucleus accumbens and olfactory nodules of rats and increase the level of D2 receptors in the nucleus accumbens when studying the effect of exercise on dopamine receptors in rats. Similarly, Robertson et al. [35] found similar results in a human empirical study. Eight weeks of training could significantly increase the levels of D2 / D3 receptors in the striatum of methamphetamine users. The above research supports that exercise can increase dopamine concentration, regulate the levels of various receptors, and regulate psychological and physiological activities such as mood and craving levels by improving the midbrain limbic reward pathway, thereby playing a role in protecting drug addicts and preventing relapse.

In addition, long-term use of addictive drugs can lead to an increase in glutamic acid in the body. Glutamic acid is an important excitatory amino acid neurotransmitter in the central nervous system of the brain. Numerous studies have shown that long-term use of addictive drugs can cause an imbalance in glutamic acid homeostasis in the body, leading to a decrease in glutamic acid levels in glial cells and thereby increasing their sensitivity to drug-related stimuli [36]. The transmission of glutamate energy signaling systems plays a significant role in drug search behavior and relapse after long-term medication. Studies have shown that exercise can restore glutamate levels and protect against overstimulation of glutamate receptors due to long-term use of addictive drugs [37]. Shi Kaixuan et al. [38] found that after 4 weeks of treadmill exercise intervention in rats, the concentration of glutamic acid in their bodies was significantly reduced

ISSN: 2710-0170

compared with the control group. Han Yumei et al. [39] significantly reduced the glutamic acid level in rats after 4 weeks of high-intensity interval training intervention. Real et al. [40] discovered that moderate exercise can promote the plasticity changes of 2/3 of glutamate receptors in brain regions, inhibit the signaling hull of the glutamate energy system, and thereby reduce susceptibility to drugs. Yi He et al. [41] confirmed that long-term rotational exercise can activate a glutaminergic pathway from the macrocellular part of the red nucleus (RNm) to the ventral tegmental area (VTA), generating exercise rewards and reducing the intake of addictive drugs.

In addition, exercise also helps to increase the concentration of endogenous opioid peptides (EOP) in the plasma. Endogenous opioid peptides are a class of peptide substances synthesized by the human body itself, which are similar to opioid drugs. They are mainly divided into enkephalin family, endorphin family and dynorphin family. They are mainly involved in various physiological processes such as pain perception, emotion regulation and immune regulation, and are also related to drug reuptake and executive function. Studies have confirmed that exercise may reduce the use of addictive drugs through the release of endogenous opioid peptides [42]. Among them, endorphins (EP) can play a role in reward regulation, reducing craving and enhancing inhibition in the action of exercise intervention for addictive drugs [43]. The increase in the level of β-EP, which belongs to the endorphin family, can meet the demand for euphoria in drug-dependent individuals and reduce discomfort symptoms during withdrawal [44]. Moreover, the craving degree and anxiety level of abusers are negatively correlated with the β-EP level [45]. Currently, research has confirmed that exercise can increase the plasma β-EP concentration during and after exercise. Malinowski et al. [46] found that 12 weeks of treadmill training could significantly enhance the plasma β-EP concentration in horses. Similarly, Yu Dongzhen et al. [47] also found similar results: swimming training can significantly increase the concentration of β-EP in rats. However, some studies have found that the effects of different exercise intensities on plasma β-EP concentrations have shown inconsistent results. An early study suggested that the threshold of exercise intensity causing changes in β-EP concentration was 60%VO_2max, and it only increased with intensity within a certain range. Beyond a certain intensity, its concentration would instead decrease [48]. In addition, Hughes et al. [49] found through a resistance exercise involving blood flow restriction and different loading modes that both high-load resistance exercise and blood flow restriction could increase the plasma β-EP concentration, but low-load resistance exercise had no effect. Therefore, the relationship between exercise intensity and the release concentration of EOP still requires further in-depth research in the future.

5.2. Exercise and Neurotrophic Factors

In addition to exercise being able to regulate various neurotransmitters in the body, it is also closely related to neurotrophic factors in the brain. Brain-derived neurotrophic factor (BDNF) is an important nutritional molecule in the central nervous system, and its functions include neural development, brain plasticity, and pathological repair processes. BDNF can act on the endocrine levels of the hippocampus in the body, enabling exercise to replace the euphoria produced by addictive drugs in the brain by enhancing the gene transcription of endogenous opioid peptide neurotrophic factors [50]. Exercise can up-regulate BDNF levels and achieve multi-dimensional improvements in neurological function. Wang Xiaoge et al. [51] found that four-week treadmill exercise could increase the serum BDNF concentration in rats and improve the anxiety of rats by up-regulating the BDNF/TrkB-CREB pathway. Xiong,J.Y. et al. [52] also found in an animal experiment that five months of treadmill exercise could increase the BDNF level in mice and reduce the number of activated microglia, thereby significantly improving the spatial learning and memory deficits of mice. On the other hand, Morais et al. [53] demonstrated in a study on methamphetamine addiction that regular aerobic exercise continuously

ISSN: 2710-0170

upregulates BDNF expression, promotes the repair of synaptic plasticity in the prefrontal cortex, enhances inhibitory control ability, and thereby inhibits drug craving and relapse behavior. In addition, the high body temperature caused by exercise can enhance the permeability of the blood-brain barrier and blood flow rate, promote the transportation of biological factors in the brain and throughout the body, and thereby accelerate the efficiency of increasing BDNF content in the brain [54]. These studies collectively demonstrate that BDNF, as a core medium, can optimize cognition and emotion in the short term through exercise intervention and repair pathological neural circuits in the long term, providing important evidence for the application of exercise therapy in promoting brain health and intervening in neurological diseases.

5.3. Sports and the Immune System

Long-term drug use can cause damage to the body's immune system, leading to symptoms such as oxidative stress and inflammatory responses, and these symptoms are all important triggers for depressive moods. Research has found that opioid drugs may suppress immune responses and damage the functions of various immune cells [55]. Similarly, Mohamed et al. [56] found similar results in an animal experiment. By giving rats tramadol (an opioid) for 8 weeks, it led to an increase in the expression of pro-inflammatory cytokines (tumor necrosis factor -α and interleukin-6) as well as inducible nitric oxide synthase, tumor necrosis factor -α and interleukin-6. However, existing research has confirmed that exercise can enhance the body's immune capacity and protect the body from the risk of weakened immunity caused by long-term use of addictive drugs [57]. Lu Chunxia et al. [58] found that exercise can reduce the incidence of depression, anxiety and other conditions and improve the psychological state of drug addiction patients during the withdrawal period by activating the immune system and enhancing immune function. Moderate and regular exercise can promote an anti-inflammatory state and enhance the body's immune capacity. However, high-intensity exercise may also cause immunosuppression in the body [59]. Similarly, in a study using high-level rowers as experimental subjects, it was found that the main immune indicators of the athletes before winter training were significantly lower than those of ordinary people. After two months of winter training, there was a further decrease [60]. Therefore, it is particularly important to control the intensity of exercise and the state of the exerciser during the exercise.

6. Conclusion

Exercise intervention, as a non-pharmaceutical intervention method, has demonstrated multiple positive effects in the treatment of addictive drugs. Different types of exercise (aerobic exercise, resistance exercise, and combined aerobic and resistance exercise) have their own characteristics and advantages in the intervention effects on drug-addicted patients. Its mechanism of action involves multiple aspects such as neurotransmitter regulation, activation of neurotrophic factors, and improvement of neuroimmunity.

6.1. Intervention effects of different types of sports

Aerobic exercise: Acute aerobic exercise can immediately relieve drug craving and improve emotional state through rapid neurophysiological responses. Regular aerobic exercise over a long period of time can improve inhibitory function, continuously suppress drug-seeking behavior, and significantly enhance physical fitness such as heart and lung function and endurance.

Resistance exercise: It can effectively improve the emotional state of drug addicts, reduce their psychological craving for drugs, and at the same time enhance musculoskeletal health and improve body composition. It has also been found that the effects of resistance exercise of different intensities vary.

ISSN: 2710-0170

Aerobic combined resistance exercise: It integrates the advantages and characteristics of the first two types of exercise and is more effective in inhibiting drug intake, improving mood, reducing craving levels, enhancing neurotransmitter expression, and alleviating peripheral inflammation.

6.2. Mechanism of action

Neurotransmitter regulation: Exercise can increase the release of dopamine in the body and regulate the levels of dopamine receptors, correcting abnormal reward circuits. Restore glutamic acid homeostasis and inhibit excessive activation of the glutamic acid energy system; Promote the release of endogenous opioid peptides, meet the demand for euphoria, and reduce the discomfort symptoms of withdrawal.

Neurotrophic factor regulation: Exercise can upregulate BDNF levels, promote neural development and synaptic plasticity repair, thereby improving cognitive function, emotional regulation ability and inhibitory ability.

Immune system regulation: Moderate and regular exercise can enhance the body's immunity, suppress inflammatory responses, alleviate immune damage caused by long-term use of addictive drugs, as well as emotions such as depression and anxiety.

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