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Study on Neurobiological Mechanism of Exercise Antidepressant

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Abstract: As a new strategy to prevent and treat depression, exercise has a good therapeutic effect on depressive symptoms associated with major diseases such as cardiovascular and cerebrovascular diseases and tumors; However, whether exercise can be used as an independent factor in the prevention and treatment of depression still lacks sufficient theoretical basis. Based on neural plasticity and the neurobiological changes related to neurons and glial cells, this topic will explore the occurrence of depression and the antidepressant effect of exercise from multiple angles and levels, so as to provide a more reliable theoretical basis for exercise as an independent factor in the prevention and treatment of depression.

1. Introduction

Exercise has a positive effect on depression, which can be compared with psychological intervention or medication[1]. Even more exercise is effective. It can reduce the incidence rate of cardiovascular disease and diabetes[2]. Although exercise as an antidepressant intervention has attracted extensive attention, its internal mechanism is not clear[3-4]. Based on the existing hypotheses of the pathogenesis of depression, combined with the empirical research of exercise antidepressant, we pay attention to the analysis of the neurobiological mechanism of exercise antidepressant, which may involve the changes of central monoamine neurotransmitters and neurotrophic substances, as well as the morphological structure of the central nervous system. Exercise and antidepressants may act through a common neuromolecular mechanism. Based on these experimental evidences and corresponding inferences, a series of neurobiological hypotheses have been formed, such as monoamine neurotransmitter hypothesis, endorphin hypothesis, neurotrophic factor hypothesis and so on[5-6]. Based on these hypotheses, the researchers compared the depression and neurobiological indexes before and after exercise by establishing an animal model of depression or based on human experiments, so as to analyze the role of the changes of these indexes in the relationship between exercise and depression. At present, many molecular biology hypotheses have been supported by some empirical research evidence, and a large number of experimental studies continue to explore in depth, making this field continue to become a research hotspot [1-2].

2. Exercise and Changes of Monoamine Neurotransmitters and Corresponding Receptors

The dysfunction of central monoamine neurotransmitter system is the most important hypothesis in the biological mechanism of depression, which has been accepted by most people. The earlier monoamine hypothesis holds that depression is due to the insufficient function of monoamine transmitters norepinephrine (NE) and serotonin (5 ~ HT) in the brain, and most antidepressants play an antidepressant role by increasing the level of monoamine transmitters at synapses. Studies by Hou Gang and others have shown that the concentrations of 5-HTT and NE in cerebrospinal fluid of patients with depression are significantly lower than those of normal patients, but the monoamine hypothesis is difficult to explain the action mechanism of some antidepressants and the contradiction between slow onset of antidepressants and rapid change of neurotransmitters. For example, antidepressants can increase the concentration of neurotransmitters in synaptic space several hours after administration, However, the antidepressant effect began to appear after 2 ~ 4 weeks of continuous treatment; This has caused relevant experts and scholars to put forward the receptor hypothesis since the 1970s, and believe that depression is due to the changes in the number and sensitivity of Ne / 5-HTT receptors in the brain. Whale et al. Found that the sensitivity of postsynaptic 5-httd receptor decreased significantly in patients with depression, which may be an adaptive response to the increase of postsynaptic 5-HT level after treatment with SRIS. Thus, the pathogenesis of depression involves not only the reduction of monoamine neurotransmitter content, but the change of the function of the whole neurotransmitter system. Recent studies have shown that the deficiencies of some other monoamine neurotransmitters, such as dopamine (DA), acetylcholine (ACh), R aminobutyric acid (GABA), are also closely related to the pathogenesis of depression. DA receptor antagonists have antidepressant effects.

In general, the role of several monoamine transmitters in the pathogenesis of depression and exercise antidepressant mechanism has attracted more attention, but it is difficult to put forward and explore the systematic changes of neurotransmitters caused by depression and other neurobiological hypotheses, which has been challenged. However, it needs to be clear that monoamine neurotransmitters play a role in the pathogenesis and remission of depression, and are closely related to other neurobiological hypotheses. 5-HTT and its receptors have important effects on nerve regeneration in hippocampus and other parts. During exercise, how these monoamines interact and act together with antidepressant pathways such as nerve regeneration to alleviate depression is a problem worthy of in-depth discussion.

3. Motor and Neurotrophic Factor Changes and Neurogenesis

After the 1980s, it was clearly concluded that some different types of growth factors can regulate the growth and survival of human nerve cells, and these neurotrophic substances are collectively referred to as neurotrophic factors (NTFS). Stress or depression can lead to neuronal atrophy and cell loss in hippocampus, prefrontal lobe and amygdala, and reduce the expression of neurotrophic factors; On the contrary, the use of antidepressants can promote adult hippocampal neurogenesis and increase the expression of neurotrophic factors. Based on this, a neurotrophic hypothesis of depression is proposed. Neurotrophic factors play an important role in neural development and neural plasticity, among which the role of brain-derived neurotrophic factors in depression has attracted much attention. Stress reduces the expression, and antidepressants effectively reverse this effect. A variety of stress can reduce the activity of BDNF pathway in hippocampus, and antidepressants can enhance the activity of this pathway. Other studies show that the division of progenitor cells in the sublayer of granular cells in dentate gyrus of hippocampus in depression model rats is reduced, and the level of BP NF is low, all of which show the loss of positive brown granules, The content of nerve growth factor (NGF) and RNA expression in hippocampal and

parietal cortical neurons decreased. BDNF affects neuronal neurogenesis by promoting cell proliferation, differentiation and survival. Adverse factors such as stress and depression can inhibit adult hippocampal neurogenesis, while antidepressants can induce the continuous production of new neurons in hippocampal dentate gyrus (DG), resulting in the emergence of adult hippocampal neurogenesis. Exercise can increase the expression of neurotrophic factors and induce adult hippocampal neurogenesis, which also belongs to another mechanism of exercise antidepressant effect. Among all neurotrophic factors, BDNF may be the most sensitive to the regulation of movement. Relevant studies show that exercise can increase the expression of BDNF mRNA and increase the protein content of BDNF. Exercise can be used as an effective means to prevent depressive behavior caused by chronic stress (cums). Exercise can reverse the depressive behavior caused by CUMS by increasing the level of individual BDNF. BDNF plays an important regulatory role in the process of motor changes in neurotransmitter activity. In addition to BDNF, other neurotrophic factors are also related to the mechanism of exercise antidepressant [3-4].

The change of endogenous cannabinoid signal pathway is an important factor in exercise-induced neurogenesis. Exercise can promote hippocampal neurogenesis through the signal pathway of vascular endothelial growth factor (vi 1gf), so as to play an antidepressant role. Insulin like growth factor-1 (IGF-1) plays a role in exercise antidepressant. Although the effects of BDNF, VEGF and other neurotrophic factors are different, qigong can complement or even overlap, which plays an important role in exercise antidepressant. Exercise can fully induce neurogenesis and increase the expression of neurotrophic factors in adult hippocampus, which may be the main mechanism of exercise's antidepressant effect, which is similar to the therapeutic effect of antidepressants. In addition, neurotrophic factor signaling pathway shows the opposite regulatory effect on depressive behavior in hippocampus, prefrontal cortex and midbrain limbic system, which suggests that neurotrophic factors will appear the necessary regulatory phenomenon by affecting the emotional regulation neural network rather than the activity of a single brain region. For the changes of neurotrophic factors involved in the process of exercise antidepressant, Future research should shift from a single brain region to the role of the whole neural network.

4. Changes of Motor and Neuroendocrine System Function

The dysfunction of neuroendocrine system plays a very important role in the occurrence of depression, and the hypothalamus pituitary adrenal axis (HPA) is an important endocrine axis. Glucocorticoid (GC) and corticotropin releasing hormone (CRF) are two key basic substances of the system. In recent years, the role of neuroimmune mechanism in the process of exercise antidepressant has received special attention, because neuroimmune factors not only directly affect depression, but also may affect depression through other mechanisms (nerve regeneration, HPA axis function regulation, etc.). The outstanding performance is: acute exercise can bring about a temporary increase in the level of immune factors, while long-term regular exercise can promote the body to produce immune adaptation to specific stimuli, and exercise also promotes the immune system to release more anti-inflammatory cytokines. From this perspective, depression can be regarded as a series of pro-inflammatory cytokines and anti-inflammatory cytokines interacting under the specific influence of innate and acquired immune regulation mechanisms. Depression brings about the release of pro-inflammatory cytokines and activates HPA axis, resulting in the release of ACTH and cortisol, which is easy to lead to long-term depression. Exercise has a positive effect on regulating the balance of pro-inflammatory cytokines and anti-inflammatory cytokines, and can fully reverse the occurrence and development trend of depression.

5. Exercise and Changes of Individual Immune System Function

Depression can be regarded as a mental neuroimmune disorder, and its pathogenesis is closely related to the activation of inflammatory response system. The body can release inflammatory cytokines to activate peripheral immune cells, thus causing neuroendocrine and immune system dysfunction, leading to the occurrence of mental neurologic diseases, thus forming the "inflammatory response (IRS) model of depression, The plasma CK concentration of patients with depression is increased, so the increased CK can be used as a state index of depression. Depressive symptoms most often occurred in IFN-a and IL-2 cytokine treatment, occasionally in ifn-b treatment, but not in ifn-7 treatment. Comprehensive preclinical and clinical studies can find that exercise can reduce inflammatory response and oxidative stress through many cellular and humoral immune changes. Inflammatory response and oxidative stress are important inducements of depression. Exercise may reduce stress-induced depression by reducing interleukin (IL-6 and IL-18) and tumor necrosis factor (TNF-a). Recent studies have shown that exercise up regulates IGF in prefrontal cortex and hippocampus_ 1, so as to improve the depressive behavior induced by chronic stress. The hormone mechanism regulated by nficb is used for stress-induced depression in female animals, and then represents a mechanism of gender difference in depression. In fact, the effect of CK on depression through NFkB is an optional mechanism of depression. The functions of neuroendocrine system and neuroimmune system are not completely separated, but form the regulation of neuroendocrine immune network. In the future, the research on the mechanism of exercise antidepressant should not be limited to the respective functions of neuroendocrine or neuroimmune system, but should be integrated into the nerve.

6. Movement and Morphological Changes of Individual Central Nervous System

Depression is closely related to abnormal brain histomorphology and structure. Depressed people are more prone to atrophy and loss of integrity in bilateral hippocampus, prefrontal cortex and amygdala. Taking hippocampus as an example, most studies have found that the volume of hippocampus in depressed people is smaller than that in the control group. At the same time, exercise also has a positive effect on the volume and plasticity of these brain regions. The cross-sectional study at the initial stage shows that CRF has a positive correlation with the volume of prefrontal lobe and anterior cingulate cortex. Six months of aerobic exercise can further improve the volume of prefrontal lobe and anterior cingulate cortex, and CRF and physical activity have a positive correlation with the microstructure integrity of white matter. Exercise can enhance the effect of human physical activity behavior, improve aerobic fitness, and offset the damage caused by depression to the volume and plasticity of many brain regions, which is also an important way of anti depression played by exercise.

7. Conclusion

The changes of monoamine neurotransmitters, neurotrophic substances, the functions of neuroendocrine system and neuroimmune system, and the structure of central nervous system do not occur independently. They affect each other in the process of exercise antidepressant. The changes of central nervous system in depression are not only the decline of functional neurotransmitter transmission function, but also the changes of nerve cell morphology. Future research should focus on their own leading research directions and take into account the overall function of the central nervous system, which may be more meaningful [5-7].

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