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Exercise Intervention for Depression from the Perspective of Gut Microbiota Dysbiosis: A Review

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Abstract: Depression is a mental disorder with a complex pathogenesis. In recent years, the "gut-brain axis" theory has revealed the key role of gut microbiota dysbiosis in its development. Studies have shown that exercise can effectively improve gut microbiota dysbiosis and alleviate depressive symptoms. From the perspective of gut microbiota dysbiosis, this paper systematically explores the potential mechanisms of exercise in preventing and treating depression. The paper reviews how exercise intervenes in neurotransmitter pathways and HPA axis function through multiple dimensions, such as regulating microbial structure, inhibiting the proliferation of pro-inflammatory bacteria, and promoting the synthesis of short-chain fatty acids. Combined with the traditional Chinese medicine (TCM) theory of "Yu syndrome", the article proposes an integrated prevention and treatment approach of "exercise—gut microbiota—brain function." Finally, it looks forward to future research directions.

Keywords: Gut microbiota; Depression; Exercise therapy; Gut-brain axis; Yu syndrome

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1. Gut microbiota dysbiosis and depression

Gut microbiota plays an important role in regulating the function of the central nervous system. The mechanisms by which microbiota dysbiosis leads to depression mainly include the following aspects.

1.1. Decreased microbiota diversity

Gut microbiota diversity is an important indicator of intestinal health. There are significant differences in gut microbial diversity between patients with depression and healthy individuals. Kelly JR et al. confirmed through 16S RNA sequencing of fecal samples that depression is associated with reduced richness and diversity of the gut microbiota [1]. Exercise can significantly increase gut microbiota diversity. A recent study by Clarke et al. showed that the gut microbiota of rugby players is more diverse compared to healthy non-

athlete professional men; the α-diversity of the microbiota of elite athletes is higher than that of the general population in the two control groups [2].

1.2. Proliferation of pro-inflammatory bacteria

Pro-inflammatory bacteria proliferate under stress. Lipopolysaccharide, a component of their cell walls, can activate immune responses, trigger low-grade inflammation in the intestines and even the whole body, thereby affecting the central nervous system and ultimately leading to depressive behaviors. Liu Lanxiang et al. found that the abundance of pro-inflammatory bacteria, such as Proteobacteria, in the feces of inactive people is increased, which is highly consistent with the microbial characteristics of patients with depression [3]. Regular exercise can reduce the relative abundance of pro-inflammatory bacteria. A systematic review by Mailing et al. pointed out that aerobic exercise can significantly reduce the relative abundance of Proteobacteria and Enterobacteriaceae, reduce LPS translocation, and thus improve the state of systemic low-grade inflammation [4].

1.3. Impaired synthesis of short-chain fatty acids (SCFAs)

Short-chain fatty acids (SCFAs) have anti-inflammatory, intestinal barrier-protecting, and neuroprotective effects. A sedentary lifestyle may lead to a significant decrease in the overall level of intestinal SCFAs, while regular exercise can promote the proliferation of butyrate-producing bacteria, thereby increasing SCFAs levels. The promoting effect of exercise on SCFAs has been directly verified by experimental studies. J M Allen et al. found that after transplanting the gut microbiota of exercise-trained mice to recipient mice, the ratio of propionic acid to butyric acid in the intestines of the recipient mice was significantly increased [5].

2. Connection between gut microbiota dysbiosis and pathological mechanism hypotheses of depression

2.1. Gut microbiota and monoamine neurotransmitter hypothesis

Monoamine neurotransmitters have significant biological activities in regulating mood, cognitive function, and stress response, and are closely related to the occurrence and development of depression. Liu Lanxiang et al. found that the expression levels of genes related to the monoamine neurotransmitter pathway in germ-free mice are significantly reduced, and depressive behaviors are increased [3]. After gut microbial re-colonization, depressive behaviors can be significantly improved.

Exercise can reshape the gut microbiota. Its metabolites, such as acetic acid (a type of SCFA), can cross the blood-brain barrier and regulate the balance of neurotransmitters such as dopamine. Some microbiota can directly synthesize neurotransmitters such as GABA; at the same time, SCFAs can also provide precursors for the synthesis of 5-HT by regulating pathways such as tryptophan metabolism, thereby systematically improving the function of monoamine neurotransmitters. This indicates that regulating the gut microbiota through exercise and its metabolites is an important link for exercise to exert antidepressant effects.

2.2. Gut microbiota and HPA axis dysregulation hypothesis

Stress activates the HPA axis, leading to increased levels of hormones such as cortisol. Long-term hyperactivity can damage nerve cells and produce depressive behaviors. Exercise can improve HPA axis function. Chen Xuemei et al. found that when the gut microbiota of rats that exercised was transplanted

into ASD rats, the activation of the HPA axis in the transplanted ASD rats was lower than that in the control group [6]. Thus, it can be initially concluded that exercise balances HPA axis activation by improving the gut microbiota, thereby regulating depression.

3. Treatment of depression from the perspective of exercise

Exercise therapy is an important treatment method for depression, including aerobic exercise such as jogging and swimming, strength training, and flexibility training. A large number of empirical studies have strongly shown that exercise therapy can improve the composition of gut microbiota. Therefore, this article believes that exercise can indirectly target depression to achieve therapeutic effects.

3.1. Aerobic exercise

A randomized controlled trial on adults with mild depression found that moderate-intensity running training (3 times a week for 12 weeks) significantly increased the relative abundance of *Akkermansia muciniphila* and *Faecalibacterium prausnitzii* in feces. Both types of bacteria are closely related to anti-inflammatory effects and enhanced intestinal barrier function [7]. In addition, the gut microbiota shaped by running itself has anti-inflammatory properties. Transplanting the microbiota of exercisers to germ-free mice can reduce the inflammation level of the latter.

3.2. Mind-body exercise

Mind-body exercises, such as meditation and Tai Chi, have been widely used in the auxiliary intervention of emotional disorders in recent years, and their potential to regulate gut microbiota has also attracted attention. Raman M et al. found that beta diversity showed significant changes in the microbial composition of meditators (P=0.001) [8]. At the same time, meditators had higher levels of branched-chain short-chain fatty acids (SCFAs). The above studies suggest that mind-body exercise may improve microbial structure, enhance SCFAs synthesis, and reduce neuroinflammation through bidirectional regulation of the “gut-brain axis”, thereby alleviating depressive symptoms.

4. Conclusion and prospect

The pathogenesis of depression involves interactions between multiple systems, and the “gut-brain axis” provides a new perspective for understanding its mechanism. Gut microbiota dysbiosis is involved in the occurrence of depression by affecting inflammation, neurotransmitters, the HPA axis, and synaptic plasticity.

As a holistic intervention, exercise can improve depressive symptoms through multiple pathways, such as reshaping gut microbiota structure, inhibiting pro-inflammatory bacteria, and promoting SCFAs synthesis. Integrating TCM “Yu syndrome” theory, this article proposes an integrated prevention and treatment approach of “exercise—gut microbiota—brain function.”

In the future, more in-depth research is needed to explore the optimal exercise intensity, duration, and type for regulating gut microbiota and exerting antidepressant effects; clarify the key microbial species and their metabolites involved in the antidepressant effect of exercise; and further verify the clinical application value of the “exercise—gut microbiota—brain function” intervention model, so as to provide more personalized and effective treatment options for patients with depression.

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Disclosure statement

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