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Research Progress on the Gut-Muscle Axis in Sarcopenia

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Abstract: In recent years, the gut muscle axis has become an important direction for studying skeletal muscle atrophy. With a deeper understanding of the gut microbiota, an increasing number of studies have shown a close relationship between gut health and skeletal muscle function. Skeletal muscle atrophy is an important issue affecting the health of the elderly population, and its pathogenesis is complex, involving multiple aspects such as metabolic factors, inflammatory reactions, and nutritional status. However, despite the increasing number of related studies, the specific mechanisms by which gut microbiota affects skeletal muscle health are still not clear enough. This review aims to explore the relationship between gut microbiota and skeletal muscle health, analyze its potential mechanisms and clinical significance. The article first introduces the basic concept of the gut muscle axis and recent research progress, then delves into its influencing factors in skeletal muscle atrophy, summarizes the latest research results, and finally proposes future research directions and possible clinical applications, in order to provide reference for further research in this field.

Keywords: gut microbiota; skeletal muscle atrophy; gut muscle axis; metabolic factors; nutritional interventions

1. Introduction

Sarcopenia is a common health problem among the elderly, characterized by a decline in muscle mass and function, which seriously affects the patient's quality of life [1]. In recent years, studies have found that the gut microbiota plays an important role in the metabolism and health status of hosts, especially in its interaction with skeletal muscle, forming the so-called "gut muscle axis". This concept provides a new perspective for understanding the mechanism of skeletal muscle atrophy. This article aims to summarize the latest research progress on the gut muscle axis in skeletal muscle atrophy, and explore its mechanism and clinical significance.

Firstly, the composition and function of the gut microbiota play an important role in the muscle health of elderly individuals. Research has shown that the diversity of the gut microbiota is positively correlated with muscle mass, and dysbiosis of the gut microbiota is often associated with a decline in muscle mass. For example, certain beneficial microorganisms such as Bifidobacterium and short chain fatty acid (SCFA) producing bacteria play a critical role in the metabolism of skeletal muscle, promoting muscle synthesis and growth by improving insulin sensitivity and regulating inflammatory responses [2,3]. On the contrary, the imbalance of gut microbiota may lead to an increase in chronic inflammation, which is considered an important pathological mechanism of skeletal muscle atrophy [4].

Secondly, the mechanism of the gut muscle axis involves multiple physiological processes, including energy metabolism, endocrine regulation, and immune response. The gut microbiota can affect the host's metabolic status by producing metabolites such as SCFAs, which not only provide energy for skeletal muscles but also affect muscle mass by regulating muscle protein synthesis and breakdown. In addition, the composition of the gut microbiota can also affect the level of inflammation throughout the body, thereby affecting muscle function and quality. For example, the decrease in diversity of gut microbiota is closely related to the decline in muscle strength [5].

In terms of clinical significance, interventions targeting the gut muscle axis are considered a new strategy for preventing and treating skeletal muscle atrophy. Research has shown that dietary adjustments, probiotic supplementation, and appropriate exercise interventions can effectively improve muscle mass and function in elderly people [6,7]. For example, some animal experiments have shown that supplementation with probiotics can improve muscle function and enhance physical performance in elderly mice [8]. These research results suggest that the regulation of gut microbiota may become a potential target for the treatment of skeletal muscle atrophy.

In summary, the gut muscle axis plays an important role in the occurrence of skeletal muscle atrophy. By delving into the mechanism of this axis, we can not only better understand the pathological process of skeletal muscle atrophy, but also provide new ideas and strategies for its clinical management. Future research should focus on changes in the composition of gut microbiota and their impact on muscle health, in order to explore more effective intervention measures.

2. Intestinal Muscle Axis

2.1. Concept and Mechanism of Gut Muscle Axis

The gut muscle axis refers to the mechanism of interaction between the gut microbiota and skeletal muscle, and this concept has gradually gained attention in recent research. The gut microbiota affects muscle health through various pathways, including the production of metabolites, regulation of immune responses, and absorption of nutrients. Research has shown that changes in the composition and function of the gut microbiota may be closely related to the occurrence of sarcopenia, especially in the elderly population. Dysbiosis of the gut microbiota may lead to chronic inflammation, malnutrition, and other issues, thereby affecting muscle mass and function [1,9].

2.1.1. Composition and Function of Gut Microbiota

The gut microbiota is a complex microbial ecosystem primarily composed of bacteria, fungi, viruses, and protozoa. Its composition is influenced by various factors, including genetics, diet, environment, and lifestyle. A healthy gut microbiota typically has high diversity and can effectively participate in the host's metabolic processes, synthesizing important metabolites such as vitamins and short chain fatty acids (SCFAs). These substances are not only crucial for gut health, but can also affect the body's metabolism and immune function through blood circulation. For example, SCFAs such as acetic acid, propionic acid, and butyric acid can regulate the host's energy metabolism, inflammatory response, and immune function, thereby affecting muscle growth and repair [8,10].

2.1.2. Effects of Microbial Metabolites on Muscle Health

The gut microbiota has a significant impact on skeletal muscle health through its metabolites. Research has shown that SCFAs can not only be utilized by muscle cells as an energy source, but also promote muscle protein synthesis by activating specific signaling pathways. For example, butyric acid can enhance the insulin signaling pathway, promote the absorption and utilization of amino acids by muscle cells, thereby supporting muscle growth and repair [5,8]. In addition, microbial metabolites can also affect muscle health by regulating inflammatory responses, and chronic inflammation is considered one of the important factors leading to muscle atrophy [4,11].

2.1.3. The Role of the Immune System in the Gut Muscle Axis

The immune system plays an important regulatory role in the gut muscle axis. The gut microbiota regulates the inflammatory state of the body by affecting the function and distribution of immune cells. Research has found that dysbiosis of the gut microbiota can lead to abnormal immune system responses, increasing levels of inflammatory markers, which may accelerate muscle decline and decrease [4,7]. For example, specific bacterial species can stimulate the production of regulatory T cells (Tregs), which play a key role in maintaining immune tolerance and suppressing inflammatory responses. Through these mechanisms, the gut microbiota may play an important role in muscle health and reducing the occurrence of diseases [8,12].

In summary, the study of the gut muscle axis provides a new perspective for understanding the mechanism of skeletal muscle atrophy and emphasizes the important role of gut microbiota in regulating muscle health. Future research should further explore how to improve muscle health, especially in the elderly population, by regulating the gut microbiota.

2.2. The Role of Gut Muscle Axis in Skeletal Muscle Atrophy

2.2.1. Pathological and Physiological Mechanisms of Skeletal Muscle Atrophy

Skeletal muscle atrophy is an age-related syndrome characterized by a gradual decline in skeletal muscle mass and function. Its pathological and physiological mechanisms are complex and involve multiple factors, including malnutrition, chronic inflammation, endocrine disorders, and insufficient physical activity. As age increases, the rate of muscle synthesis decreases, and the balance between muscle protein synthesis and degradation is disrupted, leading to muscle atrophy. In addition, chronic low-grade inflammation is considered an important promoting factor for skeletal muscle atrophy, and inflammatory factors such as tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6) play a key role in muscle atrophy [4]. These inflammatory factors activate muscle degradation pathways, such as the ubiquitin proteasome pathway, further accelerating muscle degradation and leading to a decrease in muscle mass [13].

2.2.2. Relationship between Gut Microbiota Dysbiosis and Muscle Mass Decline

The gut microbiota plays an important role in maintaining host health, and recent studies have shown that dysbiosis of the gut microbiota is closely related to sarcopenia. The reduced diversity of gut microbiota may lead to poor nutrient absorption, thereby affecting muscle synthesis and function [6]. For example, short chain fatty acids (SCFAs) are products of gut microbiota metabolism that can promote muscle synthesis and inhibit muscle degradation. Research has found that the composition of the gut microbiota changes in the elderly population, with specific beneficial bacteria (such as bifidobacteria) significantly reduced in patients with skeletal muscle atrophy, which is closely related to the decline in muscle mass [4]. Therefore, regulating the composition of the gut microbiota may become a new strategy for preventing and treating skeletal muscle atrophy.

2.2.3. Interactive Effects of Inflammation and Muscle Atrophy

There is a complex interaction between inflammation and muscle atrophy. Chronic low-grade inflammation is not only an important pathological feature of skeletal muscle atrophy, but also a promoting factor in its development [14]. Under inflammatory conditions, metabolic pathways in muscle cells undergo changes, leading to reduced synthesis and increased degradation of muscle proteins [5]. For example, inflammatory factors can promote muscle degradation pathways by activating the NF-κ B signaling pathway, leading to muscle atrophy [15]. In addition, dysbiosis of the gut microbiota may exacerbate inflammatory reactions, forming a vicious cycle and further exacerbating muscle loss [10]. Therefore, interventions targeting inflammation, such as using anti-inflammatory drugs or regulating gut microbiota, may have a positive effect on improving symptoms of skeletal muscle atrophy [16].

2.3. The Regulatory Effect of Nutritional Intervention on the Gut Muscle Axis

2.3.1. Protein Intake for Maintaining Skeletal Muscle

Protein is a key nutrient for maintaining skeletal muscle quality and function, especially in the elderly population. Adequate protein intake is considered an important strategy for preventing and treating sarcopenia. Research has shown that as age increases, the muscle's response to protein synthesis gradually weakens, a phenomenon known as "anabolic resistance" [17]. Therefore, elderly people need to increase their protein intake to stimulate muscle synthesis and combat muscle atrophy.

Multiple studies have shown that increasing protein intake can effectively improve muscle mass and strength in older adults. For example, a study found that consuming protein above the Recommended Dietary Intake (RDA) can significantly improve muscle mass and function in older adults [18]. Specifically, it is recommended that elderly people consume 1.2–1.5 g of protein per kilogram of body weight per day to maximize the effectiveness of muscle synthesis [19]. In addition, the distribution of protein in daily diet is particularly important. Studies have shown that sufficient protein intake for breakfast helps with muscle growth and maintenance [20].

Among different types of proteins, whey protein has received widespread attention due to its rapid digestion and high biological value. Research has found that supplementing whey protein can significantly increase muscle synthesis rate and improve muscle strength in elderly people [8]. In addition, animal protein hydrolysate has been shown to have a positive effect on improving muscle mass and function in elderly mice [7]. Therefore, nutritional interventions for the elderly should pay attention to the types and intake of proteins to promote muscle health.

2.3.2. Clinical Application Prospects of Probiotics and Prebiotics

In recent years, the potential of probiotics and prebiotics in improving intestinal health and enhancing muscle function has attracted widespread attention. The gut microbiota plays an important role in host metabolism and immune function through the gut muscle axis. Studies have shown that the composition and function of gut microbiota are closely related to skeletal muscle health. Supplementation with probiotics and prebiotics can help improve the diversity of gut microbiota, which may have a positive impact on muscle mass and function.

Clinical studies have shown that specific probiotics, such as Bifidobacterium adolescentis, can improve muscle mass and function by regulating metabolites [21]. In addition, prebiotics such as oligofructose and inulin can promote the growth of beneficial bacteria and enhance muscle synthesis and inhibit inflammatory responses by producing short chain fatty acids (SCFAs). This mechanism, which regulates the gut microbiota, provides a new approach for the treatment of skeletal muscle atrophy.

However, despite the promising prospects of probiotics and prebiotics in the prevention and treatment of skeletal muscle atrophy, more randomized controlled trials are still needed to validate their clinical efficacy and safety [8]. Future research should focus on determining the optimal types, dosages, and combined effects of probiotics and prebiotics, in order to provide more effective nutritional intervention strategies for the elderly population [10].

In summary, nutritional intervention plays an important role in regulating the gut muscle axis, especially with moderate protein intake and the application of probiotics and prebiotics, which may become effective means of preventing and treating skeletal muscle atrophy. With the deepening of relevant research, these intervention measures are expected to be more widely applied in clinical practice.

2.4. The Impact of Exercise on Gut Microbiota and Muscle Health

Exercise plays an important role in promoting muscle health and maintaining the balance of the gut microbiota. As research on the gut muscle axis deepens, more and more evidence suggests that exercise not only helps improve muscle mass and strength, but also affects overall health by regulating the composition and function of the gut microbiota.

2.4.1. The Relationship between Aerobic Exercise and Muscle Mass

Aerobic exercise is widely recognized as an important means of improving cardiovascular health and promoting weight management. Recent studies have also shown that aerobic exercise has a significant impact on muscle mass. Research has shown that regular aerobic exercise can help older adults maintain or increase muscle mass and slow down the process of muscle atrophy. For example, a study targeting older adults found that individuals participating in aerobic exercise exhibited significant improvements in muscle mass and function, particularly in enhancing muscle strength and endurance. In addition, aerobic exercise can indirectly support muscle synthesis by improving insulin sensitivity and promoting fat metabolism, which is crucial for preventing age-related muscle wasting (i.e., sarcopenia).

The benefits of aerobic exercise are also reflected in its impact on the gut microbiota. Research has found that aerobic exercise can increase the diversity of gut microbiota and promote the growth of beneficial bacteria such as bifidobacteria and lactobacilli, which are closely related to muscle health [6]. Through this method, aerobic exercise not only directly enhances the physiological function of muscles, but also promotes overall health by improving the composition of the gut microbiota.

2.4.2. The Regulatory Effect of Strength Training on the Gut Muscle Axis

Strength training is considered an effective method for maintaining and enhancing muscle mass. Recent studies have shown that strength training not only directly improves muscle mass and strength, but may also affect muscle health by regulating the composition of the gut microbiota. Participants in strength training typically exhibit higher rates of muscle synthesis and lower rates of muscle breakdown, which is closely related to the health status of the gut microbiota [22].

Strength training affects the gut muscle axis through multiple mechanisms. Firstly, strength training can promote the secretion of growth factors (such as IGF-1) in muscle cells, which not only promote muscle synthesis but may also improve intestinal health by affecting the metabolic activity of the gut microbiota. Secondly, strength training can also promote the growth of beneficial microorganisms and inhibit the proliferation of harmful microorganisms by reducing systemic inflammatory responses and improving intestinal barrier function.

In addition, the interaction between strength training and gut microbiota is also manifested in the recovery phase after exercise. Research has found that after strength training, the composition of the gut microbiota changes, manifested as an increase in beneficial bacteria and a decrease in harmful bacteria. This change is closely related to muscle recovery and growth. Therefore, strength training is not only an effective means of improving muscle mass, but also an important way to regulate the gut muscle axis, providing new ideas for preventing and treating muscle wasting.

In summary, the impact of exercise on gut microbiota and muscle health is multifaceted. Aerobic exercise and strength training interact through different mechanisms to promote muscle mass improvement and balance of gut microbiota, providing effective intervention strategies for the elderly and patients with muscle atrophy. Future research should further explore the specific mechanisms between exercise and gut microbiota in order to provide stronger support for clinical practice.

2.5. Future Research Directions

As the understanding of the gut muscle axis deepens, future research directions will focus more on the relationship between personalized nutrition and microbiota, as well as exploring clinical intervention strategies for the gut muscle axis. These studies will provide new ideas and methods for the prevention and treatment of skeletal muscle atrophy.

2.5.1. Relationship between Personalized Nutrition and Microbial Community

Personalized nutrition has been a hot research topic in recent years, especially under the influence of gut microbiota. Research has shown that there are significant differences in the metabolic responses of individuals to the same food, which are not only related to their genetic background, but also closely related to the composition of their gut microbiota. The gut microbiota plays an important role in the occurrence and development of skeletal muscle atrophy by regulating the host's metabolism, immune function, and inflammatory response, affecting muscle mass and function.

An important aspect of personalized nutrition is to develop a dietary plan based on an individual's gut microbiota characteristics. For example, certain specific microbial communities are associated with maintaining muscle mass, such as *Akkermansia muciniphila* and *Bacteroides dorei*, which can promote muscle health by metabolizing bioactive substances such as short chain fatty acids [23]. Therefore, future research can explore how to optimize gut microbiota through personalized dietary interventions to improve muscle health, prevent and treat sarcopenia.

In addition, personalized nutrition should also consider the impact of dietary components on the gut microbiota. Research has found that dietary fiber, prebiotics, and probiotics can effectively improve the diversity and function of the gut microbiota, thereby having a positive impact on the host's metabolism and immune status [24]. Therefore, future research should focus on how to regulate gut microbiota through dietary interventions to achieve personalized nutrition goals.

2.5.2. Exploration of Clinical Intervention Strategies for Gut Muscle Axis

The study of the gut muscle axis provides new ideas for the intervention of skeletal muscle atrophy. Current research suggests that the composition and function of the gut microbiota are closely related to muscle mass and strength. Therefore, interventions targeting the gut microbiota may become a new strategy for treating sarcopenia [5].

Clinical intervention strategies can include dietary intervention, exercise intervention, and medication treatment. In terms of dietary intervention, increasing the intake of foods rich in dietary fiber and prebiotics can promote the growth of beneficial microorganisms, improve the diversity of gut microbiota, and thus have a positive impact on muscle health [25]. Exercise intervention is equally important. Studies have shown that regular strength training and aerobic exercise can improve muscle mass and may enhance its effectiveness by improving the composition of the gut microbiota [26].

In addition, drug intervention is also worth paying attention to. In recent years, research on drugs targeting the gut microbiota, such as probiotics, prebiotics, and antibiotics, has gradually increased. These drugs can improve muscle mass and function by regulating the gut microbiota, reducing chronic inflammation levels. Future research should explore the efficacy of these drugs in patients with skeletal muscle atrophy and evaluate their impact on the gut muscle axis.

In summary, future research directions should focus on the relationship between personalized nutrition and microbiota, as well as exploring clinical intervention strategies for the gut muscle axis. These studies not only deepen our understanding of the pathogenesis of skeletal muscle atrophy, but also provide new ideas and methods for clinical treatment.

3. Conclusions

When exploring the relationship between the gut muscle axis and skeletal muscle atrophy, we noticed that research in this field is rapidly developing and demonstrating significant potential. In recent years, increasing evidence suggests that the gut microbiota has a profound impact on host metabolism, immunity, and muscle health. The decline in muscle mass is not only related to aging, but also closely related to various chronic diseases, malnutrition, and lifestyle. Therefore, understanding how gut microbiota affects the physiological function of skeletal muscle is crucial for developing new intervention strategies.

Existing research shows that the composition and metabolites of the gut microbiota can directly or indirectly affect the quality and function of skeletal muscle. For example, certain specific microbial communities may promote muscle protein synthesis or inhibit muscle protein breakdown, providing a new perspective for our understanding of the pathogenesis of sarcopenia. In addition, short chain fatty acids (SCFAs) produced by gut microbiota play a key role in regulating muscle metabolism and inflammatory response, providing new targets for future treatment plans.

However, despite numerous studies pointing to the importance of the gut muscle axis in muscle wasting, there are still some controversies and challenges in this field. On the one hand, there are significant differences in the gut microbiota of different individuals, which limits the generalizability of research results. On the other hand, there is insufficient clinical evidence regarding whether microbiota intervention can effectively reverse or improve muscle atrophy. Therefore, when designing future research, individual differences, types and timing of interventions need to be considered to better evaluate the impact of gut microbiota on skeletal muscle.

When balancing different research perspectives, it is important to emphasize the importance of interdisciplinary collaboration. Experts in the fields of intestinal microbiology, exercise physiology, nutrition, and clinical medicine should work together to integrate their respective research results and form a more comprehensive understanding. This not only helps clarify the specific mechanism of the gut muscle axis, but also contributes to the development of personalized intervention strategies to address the issue of muscle mass decline.

Future research should focus on establishing a causal chain between gut microbiota and skeletal muscle, and verifying the impact of microbial interventions on muscle health through large-scale clinical trials. In addition, exploring other factors that interact with the gut microbiota, such as diet, exercise, and genetic background, will also provide us with a deeper understanding. These research findings are expected to provide new ideas for the prevention and treatment of muscle atrophy, ultimately promoting the quality of life and health level of the elderly population.

In summary, the study of the gut muscle axis has shown significant application prospects in the field of skeletal muscle atrophy. By delving into the mechanism of action of the microbiota, we hope to provide patients with more effective treatment plans, improve muscle health, and enhance their quality of life.

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The authors declare no conflict of interest.

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