MEDS Clinical Medicine (2022)
Clausius Scientific Press, Canada

DOI: 10.23977/medsc.2022.030403
ISSN 2616-1907 Vol. 3 Num. 4

Effect of Interaction between Intestinal Flora and Brain-Gut Axis on Gastrointestinal Motility

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Keywords: Microorganism-brain-gut axis, Interaction, Gastrointestinal motil

Abstract: The normal operation of human function depends on the effective play of gastrointestinal motility. Gastrointestinal dysfunction leads to a series of related diseases, and its pathogenesis is not clear. In recent years, studies on microorganisms and brain-gut axis have found that intestinal flora and brain-gut axis interact and can influence each other. Gastrointestinal motility is affected by the bridge between central nervous system, intestinal nervous system, immune system and neuroendocrine system. This study briefly reviewed the mechanism of the interactio n between intestinal flora and brain-gut axis and its effect on gastrointestinal motility, in order to provide theoretical reference for in-depth understanding of the effect of brain-gut axis on gastrointestinal motility and related diseases.

1. Introduction

The normal operation of human body functions depends on the effective play of gastrointestinal motility, among which the factors affecting gastrointestinal motility are mainly intestinal flora and cerebrointestinal axis. The intestinal flora in the human body plays an important role in ensuring the normal peristalsis of the gastrointestinal tract, maintaining the homeostasis of the intestinal barrier, and regulating the immune response and nutrient absorption and metabolism, while the cerebrointestinal axis is affected by the central nervous system (CNS), the enteric nervous system (ENS), immunity and hypothalamus Regulation of the pituitary gland and epinephrine (HPA) axes is also critical for gastrointestinal motility, the body's stress response, and visceral sensitivity. According to relevant literature, the intestinal flora and the brain-intestine axis can not only affect gastrointestinal function, but also exist in a two-way relationship between them[1], and the microflora not only controls the release of various intestinal peptides, but also produces various neurotransmitters [2] Serotonin (5-HT), catecholamines (CA), and their metabolites, short-chain fatty acids (SCFA) and the like can act on the CNS, ENS, immune and endocrine systems to affect the cerebrointestinal axis, thereby affecting gastrointestinal motility; in turn, the cerebrointestinal axis It can also affect the homeostasis and variety of intestinal flora, thereby affecting gastrointestinal motility.

2. Regulation of Gastrointestinal Motility by Intestinal Flora

There is a diverse and balanced microbiota in the body, that is, the microbial flora, a large number of bacteria form a microbial barrier to provide energy and nutrition to the body, protect the intestinal structure, maintain the intestinal immune balance, resist the invasion of pathogenic bacteria [3], and the microflora affects various activities of the host physiological activities, including intestinal movement [4]. As a traditional Chinese medicine used for thousands of years, rhubarb has laxative, anti-inflammatory, adjuvant anti-tumor pharmacological effects, and the latest study shows that [5]rhubarb can maintain intestinal fatty acid levels, cause a decrease in helicobacterium mucus, increase the abundance of bacillus, and promote an increase in mucosal mucus secretion, the mechanism of which may be through mast cells and submucosal neural system changes Intestinal flora and SCFA to relieve constipation. Fecal microflora transplantation (FMT) is considered a way to treat functional gastrointestinal disorders by reconstructing the gut microenvironment, and a meta-analysis [6] systematically evaluated FMT for irritable bowel syndrome. With its efficacy and safety, FMT is expected to be an efficient and low-cost treatment for IBS. Patients with constipated IBS (IBS-C) have increased 5-HT release and significantly improved intestinal motility after probiotic treatment [7-8]. According to an experimental study of Xiaolong Ge et al. [9], mice transplanted from the fecal microflora of patients with slow transit (STC) were significantly slower in gastrointestinal transport. The long colonic transport test in mice, with significant symptoms of constipation and inhibition of smooth muscle movements, suggests that the fecal microbiota from the STC donor slows down the colonic propulsion in mice, resulting in insufficient gastrointestinal motility, possibly because the microbiota from the STC donor inhibits the contraction of the patient's colon smooth muscles. Mice in the aseptic state of the intestine have insufficient gastrointestinal motility, and the symptoms are relieved after transplantation of normal mice's intestinal flora, suggesting that the imbalance of intestinal flora can lead to a decrease in gastrointestinal motility. According to Bai Lu et al. [10], Bifidobacterium tetraline can effectively regulate the type and amount of intestinal flora, and proposed that the mechanism of gastrointestinal motility may be due to the increase in the number of bifidobacterium and lactobacillus in the intestine. The number of enterococcus and yeast decreases, resulting in shorter OCTT. Dimidi et al. [11] investigated the effects of probiotics on functional constipation in adults and found that probiotics in general shorten the passage time of the whole intestine and increase the frequency of stools, and this study also showed that the role of probiotics has a high heterogeneity, and different strains of Lactobacillus can improve the intestinal passage time, Stool frequency and consistency as well as bloating. In summary, the structural changes of the intestinal flora may enhance the sensitivity of internal organs, the imbalance of intestinal flora can lead to a decrease in gastrointestinal motility, FMC can rebuild the intestinal microenvironment, which is of great significance for restoring the number and type of intestinal flora, as well as functional constipation, IBS-C and other diseases.

3. Effect of the Brain-Intestinal Axis on Gastrointestinal Motility

The central nervous-sensory endocrine neural network that exists between the brain and the gastrointestinal tract closely links the brain and the gastrointestinal tract to each other, and is a two-way physiological regulation pivot axis that controls the interaction between the physiological functions of the human gastrointestinal tract and the central sensory nervous coordination system of the brain, so it is called the cerebrointestinal axis, also known as the “cerebrointestinal axis”. Second Brain” [12] The brain-gut axis is modulated by a variety of nervous systems, releasing a variety of cerebral intestinal peptides (BGP), such as actin (MTL), gastrin (GAS), leptin (Leptin), somatostatin (SS), vasoactive enteric peptide (VIP), 5-HT, gallbladder contractin (CCK), Ghrelin,

etc. to maintain its normal operation [13]. The cerebral intestinal axis can regulate gastrointestinal function is mainly completed by BGP, and its motilin, gastrin, gastric auxin and 5-HT can promote gastrointestinal motility, promote gastric emptying, and promote gastrointestinal motility; vasoactive peptides, leptin, gallbladder contractin, somatostatin, etc. can delay gastric emptying and reduce gastrointestinal hypersensitivity[14].Thus, cerebral enteropeptides play an important role in the microbial-gut-brain axis [15] and are the mediator of bidirectional regulation of the brain-intestinal axis, which is achieved Communication and contact between the brain and intestines.

4. Mechanism of Intestinal Microflora Interaction with the Brain-Intestinal Axis

Intestinal flora and brain-gut axis can not only affect gastrointestinal function separately, but also have a two-way connection between them, 5-HT, CA and SCFA can act on CNS, ENS Immunity and HPA affect the cerebrointestinal axis, thereby affecting gastrointestinal motility; in turn, the cerebrointestinal axis can also affect the homeostasis and variety of intestinal flora, thereby affecting gastrointestinal motility.

4.1 Intestinal Flora and Enteric Nervous System

The intestinal nerve is embedded in the intestinal wall, the intestinal epithelium acts as a barrier to isolate harmful substances in the intestine [16], and the intestinal flora changes the permeability of the intestinal mucosal barrier by regulating the expression of tightly linked proteins [17].It has been found that the intestinal flora can also regulate immunoglobulin production, mucin expression, prevent apoptosis of the intestinal epithelium, and inhibit the invasion of intestinal pathogens to maintain the stability of the intestinal epithelium [18]. In addition, microorganisms in the intestine can release 5-HT receptors acting on the sensory nerves of the gastrointestinal tract, alleviating pain directly caused by decreased gastrointestinal peristalsis caused by colon dilation [19], 5-HT Is a widely present neurotransmitter in ENS and CNS, plays a key role in regulating the movement of ENS, and can stimulate local intestinal nerve reflexes to initiate propulsive movements and regulate contractile activity [20-21]. Metabolites of various bacteria in the intestine, such as SCFA, can also inhibit or promote the rate of intestinal peristalsis by stimulating the gastrointestinal nervous system [22]; similarly, intestinal neurons, intestinal chromaffin cells, and immune cells can be secreted Substances such as CA and 5-HT can also enter the intestinal lumen under the regulation of the nerve center to affect the homeostasis of the intestinal microorganisms.

4.2 Intestinal Flora and Central Nervous System

Systems of vagus nerves, sympathetic nerves, and endogenous pathways that regulate pain can mediate the effects of emotions on body function, including gastrointestinal function. The vagus nerve (VN) is an integral part of the parasympathetic nervous system and is an important channel for neural communication between the central nervous system and the gut microflora [23].VN is actively involved in the gut microflora-brain bidirectional interaction to maintain the homeostasis of the brain and gut. Clinical studies have found that neurological disorders can lead to central nervous system dysfunction, such as mood disorders or neurodegenerative diseases, or gastrointestinal pathologies such as inflammatory bowel disease and irritable bowel syndrome [24]. Vagus nerve efferent fibers regulate the response of the gastrointestinal system to environmental or pathophysiological conditions by releasing neurotransmitters, and stimulate the vagus nerve by electro-needles, which can promote gastrointestinal movements of 30 to 120s, the mechanism of which may be electro-acupuncture through M2/3 and β1/2, respectively Receptor-mediated vagus

nerve reflexes and sympathetic reflexes regulate gastric motility [25]. In addition, electro-acupuncture stimulation of VN can effectively promote the expression and correct localization of tightly linked proteins, which can reduce intestinal permeability and protect the intestinal mucosal barrier function [26]. Blocking CA release from microbial depleted mice can rescue changes in their gastrointestinal motility, suggesting that increased sympathetic activity is part of the cause of gastrodynamic dysfunction in mice [27]. Neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease are often accompanied by abnormal gastrointestinal motility and intestinal dysbacteriosis[28], which may be due to intestinal flora disorders that lead to decreased expression of hippocampal and cerebral cortex brain-derived neuroactors (BDNF). This results in dysfunction and disorders of the central nervous system, and triggers behavioral abnormalities and cognitive dysfunction of the host [29-30].

4.3 Intestinal Flora and Immune System

The role of the microflora in a variety of physiological activities, including the immune system, has been well documented by many scholars [31]. In addition, the abnormal response expression and possibility of various microorganisms in the gut environment to key autoimmune response signals will also directly cause effects on the intestine and various other chronic immune diseases, such as various inflammatory gastrointestinal diseases, autoimmune reaction diseases and various chronic cancers. Dysregulation of microbial species may lead to the expression of atypical immune signals, cause homeostasis imbalances in the host, and even promote the development of diseases of the central nervous system [32]. In the sterile case, the expression of the intrinsic immune recognition receptor Nod2 at the end of the mouse ileum was significantly reduced, further suggesting that the intestinal flora is critical for immune function. SCFA acts as an energy source for intestinal epithelial cells[33], affects the expression of genes necessary for the intestinal epithelial barrier and defense function, and regulates native immune cells and specific immunity mediated by T cells and B cells [34]. Alterations in the composition of the gut microflora lead to various inflammatory diseases by modulating innate immunity, particularly NF-κB signaling. Campylobacter jejuni invasion caused by dysregulation of the gut microbiota also leads to activation of NF-κB, resulting in increased secretion of cytokines, thereby stimulating the expression of different immune cells. Multiple studies have shown that the interaction between microflora and NF-κB signaling is also responsible for inflammation of the central nervous system. For example, antibiotic treatment has led to disturbances in the type and number of gut microbiota, inhibition of the expression of brain-derived neurotrophic factors in the hippocampus, simultaneous activation of the NF-κB pathway, and a series of neuroinflammation and anxiety-like behaviors in animal models. Conversely, taking probiotics such as lactic acid bacteria can effectively reduce inflammation of the central nervous system and relieve anxiety and other related symptoms.

4.4 Intestinal Flora and Neuroendocrine System

The neuroendocrine system is classically defined as a group of organized cells with neural determination that produce hormones or neuropeptides. The hypothalamic-pituitary-adrenal (HPA) axis is thought to be the main neuroendocrine system that regulates various bodily processes, and the cerebrointestinal axis is subject to HPA Axis regulation, hpa axis is activated under pressure stimulation, releasing a variety of hormones, affecting the permeability of the intestine, motility and mucus production process, changing the intestinal environment, and then regulating the composition and activity of the intestinal microbiota, thereby counteracting the central nervous system, This eventually leads to behavioral and cognitive changes. In addition, it has been suggested that peptidoglycans derived from the gut microbiome can be transferred to the brain,

activating specific pattern recognition receptors of the innate immune system, thereby affecting brain development and behavior. In summary, the mechanism of interaction of the cerebral enterobacteria axis may be related to the neuroendocrine pathway, unlocking the exact mechanism of multidirectional communication between the intestinal microbiota and the neuroendocrine system, and can also bring new therapeutic possibilities for neuroendocrine system diseases.

5. Conclusion

A growing body of scientific research supports the interaction between the gut microbiota and the cerebrointestinal axis, i.e. the presence of a microbiome-brain-gut axis, which regulate gastrointestinal motility, brain development, and behavioral patterns through multisystem interactions. On the one hand, the intestinal flora and the cerebrointestinal axis affect the gastrointestinal motility respectively, that is, the structural changes of the intestinal flora may enhance the sensitivity of the internal organs, the gastrointestinal motility decreases, and the intestinal microenvironment can be reconstructed through FMC to restore the number and type of intestinal flora; the cerebrointestinal axis passes through the cerebral intestine Peptides, an intermediate medium, promote gastrointestinal peristalsis and reduce visceral sensitivity. On the other hand, ENS, CNS, the immune system, and the HPA axis are able to link the intestinal flora to the brain-gut axis Mutual influence of gastrointestinal motility, although the specific mechanism of the interaction of the microbial-brain-intestinal axis on gastrointestinal motility in the current literature has not been clarified, but for microorganisms - brain - In-depth study of the intestinal axis can provide us with new ideas and directions for the treatment of neurodegenerative diseases, inflammatory bowel diseases, functional gastrointestinal diseases and other diseases.

Acknowledgement

Shaanxi Province Natural Science basic Research Program Project Fund(2021JM-474);Clinical research of Qingfu Tongchang granule in the treatment of non-neoplastic intestinal obstruction based on the real world(2020ZJ003).

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