

Research Progress on the Relationship between Post-Stroke Depression and Brain-Gut Axis and Chinese Medicine Intervention

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Abstract

With the increasing incidence of post-stroke depression, the theory of brain-gut axis intervention has gradually become the object of attention. The brain-gut axis is a two-way communication system that regulates the brain and the gut, which can facilitate the communication between the emotional and cognitive centers in the brain and the gut functions and mechanisms. The occurrence and development of post-stroke depression is closely related to the abnormal changes of the brain-gut axis. This article intends to explore its clinical guiding role through three aspects: the relationship between post-stroke depression and the brain-gut axis, the theory of traditional Chinese medicine, and clinical medication.

Keywords

Post-stroke Depression; Brain-gut Axis; Chinese Medicine; Brain-gut Peptide; Gut Flora.

1. Introduction

Post-stroke depression is the most common mental disorder after stroke, and one-third of stroke patients are affected by post-stroke depression (PSD), which has a certain degree of impact on patient survival, recovery, and quality of life. negative impact [1]. Post-stroke depression is often accompanied by apathy, fatigue, feelings of worthlessness, sleep disturbance, and anhedonia [2]. In fact, PSD is one of the main reasons for the poor prognosis of post-stroke patients, and it is closely related to disability, sleep disturbance, poor rehabilitation, cognitive impairment, social withdrawal and isolation, and increased mortality [3]. Modern medicine believes that the pathogenesis of PSD is mainly related to neurotransmitters, inflammatory factors, hypothalamic-pituitary-adrenal (HPA) axis, brain-derived neurotrophic factor (BDNF) and brain-gut axis. Among them, intestinal dysfunction and intestinal flora diseases caused by stroke can be involved in the pathogenesis of PSD through immune, endocrine, nervous system and other means [4]. At present, drug therapy is mostly used in clinical practice, and studies have confirmed that selective 5-hydroxytryptamine (5-HT) reuptake inhibitors (SSRIs) have certain effects in the prevention and treatment of PSD. However, western medicine treatment has shortcomings such as single medication, long treatment period, many side effects and high price [5]. Traditional Chinese medicine believes that PSD is a combination of "stroke" and "depression syndrome". After a stroke, the patient's desire is not fulfilled, the liver qi is stagnant, and the qi is stagnant and phlegm is blocked, resulting in low self-esteem, depression and other manifestations. It has many treatment methods, less side effects, It has obvious advantages such as outstanding clinical efficacy. Based on clinical practice and combined with ancient records such as "Neijing" and "Treatise on Febrile Diseases", modern physicians discovered that there is an important correlation

between the brain and intestines, and put forward the theory of "brain-gut interconnection". , "Spleen and Kidney Relation" expounds the interaction mechanism between "brain" and "intestine", laying a solid theoretical foundation for the treatment of PSD by traditional Chinese medicine [6, 7]. In recent years, studies have shown that the brain-gut axis is closely related to the occurrence and development of PSD, and Chinese medicine research on the regulation of brain-gut axis function in patients with post-stroke depression has gradually increased. Therefore, the author reviewed the related research on the relationship between post-stroke depression and the brain-gut axis and Chinese medicine intervention, in order to provide a reference for the clinical treatment of PSD.

2. Understanding of the Brain-Gut Axis in Traditional Chinese Medicine

There is no concept of the brain-gut axis in traditional Chinese medicine, and the understanding of the brain-gut axis by physicians and scholars in the past dynasties is also different. In traditional Chinese medicine, the regulation of the "brain" by the brain-gut axis can be understood as the regulation of cerebrovascular-related diseases and emotional disorders, and the regulation of the "gut" can be understood as the regulation of the functions of the viscera related to the digestive function. The understanding of the brain-gut axis in traditional Chinese medicine is not only the anatomical relationship between the brain and the intestine, but also the relationship between the brain and the spleen, the brain and the liver, and the brain and the kidney. Digestive function-related viscera to affect brain-related diseases and emotional and psychological disorders [4].

"Spiritual Pivot: Pingren's Ending Valley" says: "God is the essence of water and valley", pointing out that the spleen and stomach play an important role in people's spirit, thinking, and conscious activities. Professor Wei Wei[8] pointed out that most emotional diseases involve the liver and spleen, and disorder of qi mechanism is the main pathogenesis. Hou Wen[9] and others believed that the pathogenesis of PSD is closely related to spleen deficiency, the spleen is the foundation of acquired, the source of qi and blood biochemistry, and mainly transports and transforms the essence of water and grains, and distributes it everywhere, reaching up to the brain. The brain is the home of the primordial spirit, which is in charge of the activities of mental consciousness. The damaged brain of stroke patients will have disorders of consciousness and mental activity. The recovery of brain and spinal cord function depends on the transport and transformation function of the spleen.

"Plain Questions: Six Yuan Zheng Ji Da Lun" said: "Mu Yu reaches it", it is believed that the pathogenesis of depression syndrome is mainly "liver depression". Professor Huang Xinpei [10] believes that liver qi stagnation is the pathogenesis that runs through the whole process of post-stroke depression. Liver failure and qi stagnation can lead to abnormal emotional activity. Long-term abnormal emotional activity further aggravates liver qi stagnation, and the two interact with each other. influences. Professor Zhu Qingxia [11] proposed that stroke patients suffer from qi deficiency for a long time, and the blood circulation is weak, then the blood stasis blocks the arteries, the liver loses nourishment, the qi movement is not smooth, and the depression syndrome occurs for a long time.

"Plain Questions: Yin and Yang Yingxiang Great Theory": "The kidney governs the bone and generates the marrow", and the marrow is divided into the marrow, the spinal cord and the brain marrow, all of which are transformed by the kidney essence. "Lingshu·Sea Theory": "The brain is the sea of marrow", and the filling and development of the brain marrow is affected by the rise and fall of the essence and qi in the kidney. Cai Hanchao[12]

It is proposed that the pathogenesis of post-stroke depression is the loss of viscera and kidney essence, and then the brain and spinal cord are dystrophic and the brain is depleted. Professor Tang Qisheng[13] proposed that post-stroke depression is caused by kidney deficiency, while

liver-qi stagnation is caused by a combination of external factors on the basis of kidney deficiency, and the interaction of internal and external factors leads to post-stroke depression.

3. The Mechanism of Action of Western Medicine on the Brain-gut Axis

The brain-gut axis is a bidirectional regulatory axis that connects the nervous system between the gastrointestinal tract and the brain by the neuro-endocrine network and plays a role in mutual regulation. Research has shown that the emotional and cognitive centers of the brain and peripheral gut function can be linked through the brain-gut axis. The brain-gut axis can monitor and regulate gut function, facilitating communication between energy, mood, and cognitive centers in the brain and peripheral gut functions [14]. The interaction that transmits signals from the gastrointestinal tract to and is regulated by the central nervous system of the brain is called brain-gut interaction. The brain-gut interaction realizes the interaction between the gastrointestinal tract and the brain through the neuro-endocrine network system, brain-gut peptides, and intestinal flora. Brain-gut axis neuroendocrine cells are regulated by the central nervous system (CNS), autonomic nervous system (ANS), and enteric nervous system (ENS), and secrete related neurotransmitters, hormones To maintain the normal operation of the brain-gut axis [15].

3.1. Regulation of the Brain-gut Axis by the Central Nervous System

The central nervous system can integrate various information that is passed into the brain and then transmit the information to the ENS through the autonomic nervous system and the neuro-endocrine system or directly act on the gastrointestinal effector cells [16]. The gastrointestinal tract can also participate in the regulation of the nervous system by stimulating the vagus nerve to transmit brain-gut peptides to the central nervous system. The central nervous system mainly controls visceral movement in the limbic system. The limbic system can not only regulate the activities of gastrointestinal function, but also affect or produce emotions, which is the most important basis for regulating gastrointestinal activities and affecting emotional changes [17]. Regarding emotional and psychological activities, some studies have proposed that the mediating pathway between emotional psychology and gastrointestinal function is the emotional stress system, that is, the cortical structure, the limbic system, the nucleus locus coeruleus, the dorsal vagus nucleus, the autonomic nervous system, and the enteric nervous system [18].

3.2. Regulation of the Autonomic Nervous System on the Brain-gut Axis

The autonomic nervous system is the bridge between the nervous system and the digestive system, and can regulate the central nervous system and enteric nervous system [19]. Studies have shown that the ANS and the neuroendocrine system are involved in regulating the function of the gut, and the anatomical location of the ANS and the neuroendocrine system center is the same as the anatomical location of the subcortical integration center of the emotional center. ANS is inseparably related to emotion regulation [19]. Autonomic dysfunction is considered to be one of the important pathogenesis of digestive tract diseases. Psychological factors such as excessive vigilance, anxiety and depression can make the vagus nerve hyperreflexia, promote the increase of gastric acid secretion and gastrointestinal motility [21].

3.3. Regulation of the Enteric Nervous System on the Brain-gut Axis

The enteric nervous system is a broad system of reflex control of digestive function that functions in conjunction with the central nervous system and neural pathways through the sympathetic ganglia [22]. The enteric nervous system can not only connect the gastrointestinal tract with the central nervous system and the autonomic nervous system simultaneously

through the brain-gut axis network pathway, but also regulate gastrointestinal motility, local blood flow, intestinal epithelial material transport, and gastrointestinal immune responses and Inflammatory process, known as the "second brain" [23]. Studies have found that the enteric nervous system has a significant regulatory effect on intestinal muscle movement, and the expansion of the intestinal wall may be the initial stimulation of intestinal peristalsis, and the process is closely related to serotonin [24].

3.4. Brain-gut Peptide Regulation of Brain-gut Axis

Brain-gut peptide is a neurotransmitter produced by the neuro-endocrine system in the brain-gut axis. The brain-gut peptides related to post-stroke depression mainly include neuropeptide Y (neuropeptide Y, NPY), substance P (substance P, SP), γ - γ -aminobutyric acid (GABA), norepinephrine (NE), dopamine (DA), calcitonin gene related protein (CGRP), 5-HT, gastric Secretin (gastricn, GAS) and so on [25]. As a carrier of information transmission between CNS, ANS, ENS and gastrointestinal effector cells, brain-gut peptide plays an important regulatory function in each link of the brain-gut axis.

3.5. Regulation of Gut Microbiota on the Brain-gut Axis

The gut microbiota has undergone millions of years of evolution to form a complex symbiotic network. The brain can not only indirectly affect the gut microbiota by regulating gastrointestinal motility and secretion and altering intestinal permeability, but also through the intestinal Information released into the gut lumen by chromaffin cells, neurons, and immune cells directly affects the gut microbiota. Intestinal flora can synthesize neurotransmitters such as GABA, norepinephrine (NE), and dopamine (DA), which can pass through the intestinal mucosa and indirectly affect brain function [27]. In addition, disturbed gut microbiota and its bioactive metabolites, which affect brain function by modulating the immune system or afferent neurons, are closely related to neurological diseases. The bidirectional interaction between the brain and gut microbes plays an important role in regulating gut function and is involved in the regulation of mood [28].

4. Research Status of Traditional Chinese Medicine in the Treatment of Post-Stroke Depression based on the Brain-gut Axis

4.1. Traditional Chinese Medicine Compound Intervention

Zhang Zhuoran et al. [29] reported that Ditan Decoction has a significant therapeutic effect on PSD rats. They found that in the traditional Chinese medicine group treated with Ditan Decoction, the voluntary movement, sugar water consumption, and serum GAS and NPY contents of the rats were significantly increased. CGRP content decreased; while the model group was the opposite. The results of HE staining showed that compared with the model group, the Ditan Decoction group increased the number of neurons, reduced the degree of pyknosis and vacuolization, and the neuronal cell morphology in the modeling group was basically normal. , exert a neuroprotective effect, reduce neuronal damage, and improve post-stroke depression symptoms. Liu Haipeng[30] and others applied Yinao Jieyu Decoction to post-stroke stress model rats, and applied Illumina-MiSeq high-throughput sequencing technology to detect changes in the structure and composition of the fecal microbial community in rats. The results showed that Yinao Jieyu Decoction could make rats The content of Lactobacillus and Bacteroides in the gut was greatly increased, thereby effectively improving the depressive behavior of stressed rats. Zhang Hengjia et al[31] used Shunao Jieyu Decoction to treat 30 cases of post-stroke depression, and confirmed that Shunao Jieyu Decoction can significantly improve the depression in patients with PSD, increase neuropeptide Y, reduce the content of SP in serum, and increase the number of patients with PSD. The role of gut microbiota diversity. Ji Xuyan[32] and others also used Shunao Jieyu Decoction to clinically observe patients with post-stroke

depression. At the end of the treatment, the richness of intestinal flora in the Shunao Jieyu Decoction group and the paroxetine hydrochloride group decreased, and Bacteroides and lactobacilli decreased. The proportion of bacilli increased. It is confirmed that Shunao Jieyu Decoction can not only effectively improve the clinical symptoms of TCM in patients with post-stroke depression, but also change the diversity of patients' intestinal flora and their abundance at various taxonomic levels.

4.2. Traditional Chinese Medicine Combined with Acupuncture Intervention

Wang Duode[33] randomly divided 120 PSD patients into two groups, the control group was treated with amitriptyline hydrochloride tablets, and the research group was treated with modified Shugan Tongluo Decoction combined with Xingnao Kaiqiao acupuncture. The experimental results showed that the serum levels of BDNF and 5-HT in the study group were higher than those in the control group, while the HAMD score was lower than that in the control group. Modified Shugan Tongluo Decoction combined with Xingnao Kaiqiao acupuncture was more effective than Amitriptyline Hydrochloride Tablets in the treatment of PSD. . Zeng Xianjing[34] and others used Danzhi Xiaoyao Powder combined with acupuncture to treat 29 patients with PSD. The expression levels of serum BDNF and 5-HT in the study group were significantly increased; SDS, HAMD, and NIHSS scores were significantly lower than those before treatment.

4.3. Acupuncture Intervention

Studies have shown that acupuncture can regulate the gastrointestinal tract bidirectionally by stimulating acupoints, which can not only improve gastric motility in patients with gastrointestinal diseases, but also regulate brain-gut peptide secretion through neuroendocrine and immune mechanisms [35]. Electroacupuncture at Dachangshu and Tianshu points can significantly down-regulate the levels of 5-HT, SP, and CGRP in rats, and affect gastrointestinal motility [36]. Sun Caili[37] et al. used "Tongdu Tiaoshen" acupuncture to intervene in rats with post-stroke depression. Compared with the model group, the contents of NE, 5-HT and DA in the hippocampus of the rats in the Tongdu Tiaoshen group were significantly increased. increased, the damage of hippocampal neurons was reduced, and behavioral tests showed that their depression-like behaviors were significantly improved. Xiao Wei[38] et al. applied acupuncture to relieve depression and calm the nerves of PSD rats. Compared with the model group, the Zea Longa score of the acupuncture group decreased, and the hippocampal areas of 5-HT, NE, Ach, γ -GABA, Glu content increased significantly. Boliying[39] et al. used acupuncture for strengthening the spleen and soothing the liver to treat irritable bowel syndrome, which can significantly reduce the serum 5-HT, NPY, CGRP levels, SAS and SDS scores of the patients in the treatment group, and relieve the anxiety and depression of the patients. Chen Lujie [40] and others randomly divided 60 patients with PSD into two groups. The treatment group was treated with acupuncture for opening and closing the mind, and the control group was treated with oral duloxetine. The former high, the HAMD score decreased and the MBI index increased, and the difference was statistically significant. Su Dongmei[41] and other studies have shown that moxibustion at Shenque acupoint separated by ginger and herbs can significantly increase the content of beneficial bacteria-Bifidobacteria in the intestinal tract of patients. Mild moxibustion in Baihui, Neiguan, Taichong, Hegu, Qimen and Tanzhong in the treatment of PSD with liver-qi stagnation syndrome can effectively improve the degree of depression in patients. Moxibustion is located on the top of the head, which belongs to the projection area of the frontal and parietal lobes. The warmth of moxibustion can stimulate the frontal and parietal lobes of the brain, speed up blood flow in the brain, promote peripheral blood circulation, and stimulate the release of NE and 5-HT, thereby acting as anti-inflammatory effect of depression.

4.4. Other Therapies

Wu Zhimin[42] and others used sertraline hydrochloride combined with abdominal massage to treat PSD patients. After treatment, the HAMD and CSS scores of the experimental group were lower than those of the control group, and the serum 5-HT and GAS values were higher than those of the control group. The total effective rate of the experimental group was 91.43% and the control group was 77.78%, and the difference was statistically significant ($P < 0.05$). Some studies have found that aerobic exercise can increase intestinal bifidobacteria and lactobacilli, improve intestinal flora disturbance, and up-regulate BDNF levels, thereby exerting antidepressant effects [43]. Liu Li[44] and others used the "Five Tone Spirit Method" to treat 36 patients with post-stroke depression due to liver stagnation and spleen deficiency. Compared with the control group, the serum 5-HT level was higher than that of the control group, and the HAMD-17 score and GSRS score of the experimental group were lower than those of the control group.

5. Summary and Outlook

The pathogenesis of post-stroke depression is relatively complex. At present, the clinical treatment of post-stroke depression mainly targets 5-HT, among which SSRIs have been proven to have certain clinical efficacy. 5-HT is a brain-gut peptide with a variety of biological effects. It is widely present in the CNS and ENS. It not only regulates gastrointestinal motility, but also regulates the secretion of pepsin and gastric acid. cognition. Traditional Chinese medicine believes that the brain and the intestines are closely related. Although major physicians have different views on the etiology and pathogenesis of post-stroke depression, they can generally be classified as primary deficiency and excess. Deficiency, insufficient nourishment of the brain and fu-organs, mainly due to stagnation of liver qi, blood coagulation due to qi stagnation, and obstruction of the brain orifice and blood vessels, resulting in abnormal brain and fu-organ functions and emotional disorders. The brain-gut axis mainly regulates brain-gut peptides and gut microbiota through the neuroendocrine system to participate in the regulation of brain emotion and gastrointestinal activity.

In the current research on the treatment of post-stroke depression with prescriptions, it has been confirmed that traditional Chinese medicine can reduce serum SP levels, increase serum neuropeptide Y levels, increase serum GAS levels, reduce serum CGRP levels, increase 5-HT levels and Alteration of beneficial bacteria content and bacterial abundance in gut microbiota improves post-stroke depression symptoms. At present, the treatment of post-stroke depression in traditional Chinese medicine is mainly based on traditional Chinese medicine, which has the advantages of significant clinical efficacy, low price and few side effects. In addition, as a characteristic therapy of traditional medicine, acupuncture and moxibustion are often more effective in the treatment of post-stroke depression than simple western medicine treatment, and it has been confirmed that acupuncture can improve post-stroke depression by regulating the expression of 5-HT, and adverse reactions occur. Therefore, acupuncture should be actively used in the treatment of post-stroke depression.

In conclusion, the brain-gut axis plays an important role in post-stroke depression. The effectiveness and scientificity of traditional Chinese medicine in the treatment of post-stroke depression based on the brain-gut axis has been confirmed, providing a new idea for clinical treatment of post-stroke depression. However, there are relatively few studies on the relationship between PSD and the brain-gut axis. This article only summarizes the relevant research basis and theoretical basis, and more clinical studies are needed to explore this in the future.

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