

# An Analysis of the Role of Acupuncture in Different Types of Cognitive Impairment from the Perspective of “Brain-Gut Interaction”

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**Abstract:** *Modern medicine holds that the brain-gut interaction, mediated by the gut microbiota, establishes a dynamic connection between the central nervous system and the gastrointestinal tract through neural, immune, and endocrine pathways, and is closely associated with the onset and progression of various types of cognitive impairment. Acupuncture stimulation can influence the gut microbiome, neuroinflammation, and neurotransmitters by balancing the gut microbiota and acting through the brain-gut interaction, thereby improving the clinical symptoms of patients with various types of cognitive impairment. Based on the perspective of brain-gut interaction, this paper conducts an in-depth study of acupuncture therapies targeting the gut microbiota and explores the mechanisms of action of acupuncture in various types of cognitive impairment, with the aim of providing new insights and approaches for the clinical treatment of these conditions.*

**Keywords:** Brain-gut interaction, Acupuncture, Cognitive impairment, Gut microbiota, Brain-gut axis.

## 1. Introduction

Cognitive impairment is a syndrome characterized by persistent impairment of cognitive function, accompanied by reduced ability in daily living and work, behavioral changes, and other symptoms. Its types often include mild cognitive impairment, Alzheimer's disease, vascular dementia, Parkinson's disease, and post-stroke cognitive impairment. It has been reported that there are approximately 38.77 million patients with MCI among people aged 60 years and older in China [1], while the global number of PD patients is expected to increase to 10 million by 2030 [2]. It is estimated [3], that the global number of dementia patients will increase to 152 million by 2050, and the cost of dementia will reach 9.12 trillion US dollars. Cognitive impairment is an important health problem facing older adults, seriously affecting patients' quality of life and imposing a heavy burden on families and society. At present, the main treatments for cognitive impairment are pharmacotherapy, physical therapy, and exercise intervention, but there is no high-quality evidence supporting that the above methods can improve clinical symptoms and delay its progression [4]. At the same time, acupuncture has definite therapeutic efficacy for different types of cognitive impairment [5], especially in improving symptoms, delaying disease progression, and improving patients' quality of life. As an external treatment method based on the principles of traditional Chinese medicine, it can activate the body's inherent regulatory capacity and exert multi-pathway and multi-target regulatory effects [6].

Recent studies have shown that brain-gut interaction is closely related to brain cognition [7], and plays an important role in the occurrence and development of different types of cognitive impairment. Gut microbiota, as a key target through which acupuncture inhibits neuroinflammation and enhances cognitive function [8, 9], and acupuncture stimulation can regulate brain-gut interaction by affecting gut microbiota to modulate cognitive function [10]. However, the specific

mechanism of action remains to be further elucidated. Therefore, based on the perspective of brain-gut interaction, this paper explores the mechanisms of acupuncture in treating different types of cognitive impairment, aiming to provide a theoretical basis and practical guidance for the clinical treatment of chronic diseases such as different types of cognitive impairment.

## 2. Brain-gut Interaction Theory

### 2.1 The Brain-gut Axis is the Material Carrier of Brain-gut Interaction

The brain-gut axis refers to the complex bidirectional communication between the brain and the gastrointestinal tract via neural, immune, and endocrine pathways. As a bidirectional signal regulatory system, it regulates the normal operation of human psycho-neuro-gastrointestinal functions [11]. Brain-gut interaction refers to the relationship of mutual action and mutual influence between the brain and the gut [12]. It mainly includes two aspects: on the one hand, the descending pathway from the brain to the gut, which mainly acts through hormones secreted by the adrenal cortex and medulla and sympathetic and parasympathetic efferent neurons [13]; on the other hand, the ascending pathway from the gut to the brain, which mainly acts through molecular signals released by gut microbiota to the brain, cytokines carrying immune information, endocrine information released by intestinal cells, and neural information carried by afferent neurons [14]. The brain-gut axis connects the central nervous system and the gastrointestinal tract through the neuro-endocrine network, and brain-gut interaction regulates brain and gut functions through the bidirectional loops between the brain-gut axis [12]. The two are closely related in concept but not completely identical; their difference reflects a difference in research perspective. The brain-gut axis emphasizes complex network connections, while brain-gut interaction emphasizes mutual action. In practical application, they are often used interchangeably.

## 2.2 Gut Microorganisms are a Key Link in Brain-gut Interaction

As an important component of the intestinal microecology, gut microbiota is regarded as the human “second brain” and plays a core role in the bidirectional response between the intestine and the central nervous system [11]. It can establish connections with the brain through the immune system, endocrine system, neurotransmitters, etc. [15], thereby affecting the host’s cognitive function. Gut microorganisms can directly or indirectly regulate the dynamic balance of the host central nervous system through various chemical signals such as short-chain fatty acids, 5-hydroxytryptamine, and gamma-aminobutyric acid, via the blood-brain barrier or by affecting the vagus nerve and mucosal immune responses; at the same time, gut microbiota, as a regulator of intestinal, systemic, and CNS-resident immune cells, can communicate with the brain by regulating intestinal and peripheral immune cells, and communicate with the CNS via peripheral immune responses involving circulating cytokines, thereby affecting brain neural activity [11]. The key role of gut microorganisms in regulating host neural function and CNS-related behavior has also received widespread clinical attention: on the one hand, regulating the abundance and diversity of gut microbiota can affect brain development and function; on the other hand, the brain can also regulate gastrointestinal function and the survival state of gut microorganisms. Therefore, changing the structure or composition of gut microbiota can prevent and improve some brain diseases [16]. In summary, brain-gut interaction exchanges information in the forms of neural transmission, endocrine regulation, and immune networks. At the same time, the interaction between the two cannot occur without the participation of gut microbiota. The three together form an axis to maintain body homeostasis [17].

## 3. Brain-gut Interaction and Cognitive Impairment

### 3.1 Relationship Between Brain-gut Interaction and Cognitive Function

Brain-gut interaction uses gut microbiota as a medium and relies on various systems to regulate brain and intestinal functions, thereby affecting cognitive function. Gut microbiota dysbiosis can alter intestinal immune function and structural integrity, and further regulate gut-brain interaction, impairing cognitive function: (1) destroying the intestinal barrier, releasing pro-inflammatory factors; the secreted pro-inflammatory cytokines reach the brain through the bloodstream and maintain chronic subclinical inflammatory responses in the CNS. (2) altering the synthesis and release of neurotransmitters in the CNS [18]. GABA is an inhibitory neurotransmitter produced by gut microbiota metabolism. When gut microbiota dysbiosis occurs, especially when the abundance of *Bifidobacterium* and *Lactobacillus* decreases, the secretion of intestinal GABA is affected, which in turn reduces the GABA content in the brain, disrupting the balance between sympathetic and parasympathetic nerves, causing the brain to work overload; neurons may die due to overexcitation, ultimately affecting memory function [19]. (3) altering the expression of gut microbiota and metabolites such as SCFAs, indirectly affecting cognitive function. Gut microbiota

disorder can lead to a decrease in SCFAs [20]. Reduced SCFA levels can increase NF- $\kappa$ B activity and increase TNF- $\alpha$  and IL-8 levels, thereby triggering intestinal inflammation and systemic inflammation, and ultimately promoting the occurrence of related cognitive dysfunction [21]. The above shows that gut microbiota can play a messenger role, directly or indirectly affecting the expression of inflammatory responses, neurotransmitters, metabolites, etc., thereby affecting brain-gut interaction and impairing cognitive processes.

### 3.2 Brain-gut Interaction Imbalance in Cognitive Impairment

The occurrence and development of different types of cognitive impairment may be related to brain-gut interaction imbalance. A large number of studies have shown [22] that gut microbiota plays a key role in brain-gut interaction imbalance and can trigger cognitive disorders, AD, PSCI, and other diseases by inhibiting the function of the neuro-endocrine system in secreting related substances. Studies have found [23] that in the analysis of fecal samples from AD model mice, there are manifestations such as reduced gut microbiota diversity, markedly reduced *Lactobacillus* in bacterial composition, and significantly increased *Bacteroides*. Gut microbiota can also synthesize and release neurotransmitters and neuromodulators, such as 5-HT and GABA, and their reduced levels are closely associated with cognitive dysfunction [24]. The release of inflammatory factors such as IL-6 and TNF- $\alpha$  is affected by changes in gut microbiota structure, and their expression is proportional to the degree of dementia. It has been reported that IL-6 and TNF- $\alpha$  levels in VD patients are significantly higher than those in normal individuals [25]. In addition, in terms of gut microorganisms, PSCI patients mainly show relatively higher abundance of opportunistic pathogens and lower abundance of beneficial bacteria, and significantly reduced contents of intestinal metabolites such as butyrate and acetate; moreover, during disease development, there are manifestations such as higher intestinal inflammation levels and increased barrier permeability [26]. In summary, different types of cognitive impairment exhibit manifestations of brain-gut interaction imbalance, and the mechanisms mainly involve changes in neurotransmitters, neuroinflammatory responses, gut microbiota, and metabolite expression.

## 4. Mechanism Research on Acupuncture Regulating Gut Microbiota and Affecting Brain-gut Interaction to Treat Cognitive Impairment

### 4.1 Intestinal Microecology

Studies have shown [27] that after implantation of *Lactobacillus* and *Bifidobacterium*, the behavior and cognitive function of germ-free mice are significantly improved. The mechanism is that normal microbiota can produce glutamate through metabolism and improve the host’s cognitive ability, thereby improving the clinical symptoms of AD. A large number of studies have used acupuncture at different acupoints to improve the diversity of gut microbiota and the content of beneficial bacteria, thereby

regulating gut microbiota and improving cognitive impairment [28, 29]. He et al. [30] used electroacupuncture at “Baihui” and “Zusanli” to intervene in AD. The results showed that electroacupuncture can increase the DNA abundance of *Lactobacillus* and *Bifidobacterium*, reduce the DNA abundance of *Escherichia coli* and *Bifidobacterium*, and improve the learning and memory ability of rats by regulating gut microbiota. Therefore, acupuncture can maintain the dynamic balance of intestinal microorganisms by increasing the abundance of dominant bacteria and reducing the number of pathogenic bacteria, regulate brain-gut interaction, and then regulate corresponding metabolites, thereby improving cognitive function.

#### 4.2 Neuroinflammation

A study selected “Baihui”, “Shenshu”, “Hegu” and other acupoints to perform acupuncture intervention on 8-month-old APP/PS1 double transgenic male mice. The results showed that acupuncture therapy can increase the number of beneficial gut bacteria in AD mice, reduce the plasma inflammatory factor LPS content and hippocampal A $\beta$  deposition, and improve their spatial learning and memory abilities [31]. The mechanism may be by balancing the number of gut microbiota in APP/PS1 mice, regulating the expression of Tau and A $\beta$  proteins in the hippocampus, and regulating the expression of serum IL-10 and TNF- $\alpha$ , thereby improving cognitive impairment. In addition, acupuncture at “Baihui” and other acupoints can regulate the imbalance of gut microbiota, inhibit the production of peripheral inflammatory factors, and improve cognitive dysfunction in VD rats [32]. Another study selected Baihui, Zusanli, and other acupoints for electroacupuncture treatment of VD rats. The results showed that electroacupuncture can reduce inflammatory cell infiltration, increase the abundance of beneficial bacteria, and effectively improve the cognitive level of VD rats. The mechanism may be by promoting gut microbiota rebalancing, inhibiting the expression of inflammatory factors, and reducing inflammatory responses, thereby improving cognitive impairment [32]. In summary, acupuncture can regulate the dynamic balance of gut microbiota, regulate brain-gut interaction, and then control brain neuroinflammation, thereby protecting cognitive function.

#### 4.3 Neurotransmitters

Electroacupuncture pretreatment at Baihui and Zusanli in AD rats can significantly increase the relative abundance of *Bifidobacterium* and *Lactobacillus*, significantly reduce the relative abundance of harmful bacteria *Enterococcus* and *Streptococcus*, reduce intestinal 5-HT levels, increase hippocampal 5-HT content, and thereby improve the learning and memory abilities of AD rats [33]. When gut microbiota becomes disordered, especially when the numbers of *Bifidobacterium* and *Lactobacillus* decrease, intestinal GABA levels decrease, ultimately leading to a decrease in central GABA levels [34]. Acupuncture stimulation can increase the number of intestinal probiotics such as *Bifidobacterium* and *Lactobacillus*, both of which can convert glutamate to GABA and regulate the body's cognitive behavior [35]. Therefore, acupuncture can also regulate related neurotransmitters by balancing gut microbiota, achieving benign regulation of

brain-gut interaction, thereby affecting CNS neurotransmitter levels and thus affecting cognition.

### 5. Summary and Prospects

Based on the perspective of brain-gut interaction, under the close connection between the brain and gut, this paper more specifically and systematically elaborates the mutual influence between the central nervous system and the gastrointestinal tract, which helps establish the theory of “brain-gut interaction”. Acupuncture stimulation can improve the clinical symptoms of different types of cognitive impairment by regulating gut microbiota and brain-gut interaction, thereby modulating intestinal microecology, neuroinflammation, neurotransmitters, and other pathways. Gut microbiota, as an emerging field, remains to be further explored. Different types of cognitive impairment, as diseases affecting human health, urgently need to be addressed. Given various signs suggesting a possible correlation between the two, in-depth research targeting gut microbiota and exploring acupuncture treatment for different types of cognitive impairment can provide new ideas for elucidating its mechanisms.

Exploring acupuncture treatment for different types of cognitive impairment from the perspective of brain-gut interaction is the result of the integration of Chinese and Western medicine and will better adapt to changes in the clinical situation. However, current research still has shortcomings: (1) clinical research results are limited and sample sizes are small; (2) there is a lack of unified standards for the angle, entry point, clinical strategy, etc. of acupuncture intervention for different types of cognitive impairment; (3) current research results are mainly animal experiments, and there is also the problem of unclear causal relationship of treatment effects.

In response to these shortcomings, it is expected that in the future: (1) mechanism research can establish relatively unified standards according to the differences in brain-gut interaction among different types of cognitive impairment; (2) conduct multicenter, large-sample clinical trials to clarify the causal relationship of efficacy; (3) conduct comprehensive interdisciplinary exchanges, explore mechanisms from multiple perspectives, integrate various factors in the mechanism, and explore their interrelationships. Mechanism research on acupuncture treatment can also comprehensively use multiple technologies simultaneously.

With the continuous improvement of mechanisms, it will better help understand the complex interaction between the brain and gastrointestinal tract, actively explore the long-term significance of acupuncture in the clinical treatment of other diseases, and provide new ideas for their diagnosis, treatment, and prevention.

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