DOI: 10.66069/ojspub.27450816

Bidirectional Regulatory Mechanism of Acupuncture in Treating Post-stroke Dysphagia Based on the Brain-Pharynx-Gut Axis

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Abstract: ***Post-stroke dysphagia (PSD) is a common and debilitating complication of stroke that severely affects patient outcomes. Acupuncture has demonstrated clear therapeutic efficacy for PSD, yet its underlying mechanisms remain incompletely elucidated. This paper proposes the "Brain-Pharynx-Gut Axis" as an integrative theoretical framework to systematically articulate the bidirectional regulatory mechanisms of acupuncture in treating PSD. At the cerebral level, acupuncture reinstates the central drive for swallowing via three convergent routes: activation of the cortical-brainstem network, modulation of rhythmic generation within brainstem central pattern generator (CPG) nuclei, and suppression of neuroinflammation. At the pharyngeal level, acupuncture facilitates descending CPG commands to pharyngeal muscles, directly coordinates muscle contractions, and transmits pharyngeal afferent signals via the nucleus tractus solitarius (NTS) to the sensory cortex, establishing a closed loop of "peripheral stimulation → central activation → real-time feedback." At the gastrointestinal level, acupuncture engages the vagus nerve to restore intestinal barrier integrity, remodel gut microbiota, and attenuate central neuroinflammation through the gut-brain axis, while also improving gastrointestinal motility to indirectly optimize the pharyngeal execution milieu. These three tiers operate synergistically to form a dynamic closed-loop system encompassing "descending drive – peripheral execution – ascending feedback – gastrointestinal synergy," thereby providing a comprehensive theoretical reference for clinical optimization and mechanistic investigation of acupuncture in PSD.***

Keywords: Post-Stroke Dysphagia, Acupuncture, Brain-Pharynx-Gut Axis, Bidirectional Regulation, Closed-Loop Regulation.

1. Introduction

Post-stroke dysphagia (PSD) is a frequent and serious complication of stroke, with an estimated incidence of 37%–78% [1]. It predisposes patients to aspiration pneumonia, malnutrition, dehydration, and even death, severely impairing prognosis and quality of life while imposing substantial healthcare burdens [2]. Current therapeutic options include behavioral interventions, dietary modifications, neuromuscular electrical stimulation, pharyngeal electrical stimulation, balloon dilatation, and surgical procedures. Although these modalities can improve swallowing function to varying degrees, they are limited by considerable inter-individual variability in response, prolonged treatment courses, poor patient adherence, and operational complexity [3]. Acupuncture, a distinctive therapy of Traditional Chinese Medicine (TCM), is widely employed in the management of PSD. Multiple systematic reviews and meta-analyses have confirmed that acupuncture effectively improves swallowing function [4] [5], yet its mechanisms have not been systematically elucidated. Existing studies predominantly focus on single targets and lack an overarching integrative framework. Drawing upon the "central–peripheral–central" closed-loop rehabilitation theory and the "brain–gut axis" concept, this paper proposes the "Brain-Pharynx-Gut Axis" as an integrative framework, and elaborates the bidirectional regulatory mechanism of acupuncture from four interlinked dimensions—descending drive, peripheral execution, ascending feedback, and gastrointestinal synergy—to provide a theoretical foundation for clinical optimization and mechanistic research.

2. Theoretical Connotation of the "Brain-Pharynx-Gut Axis" and Post-stroke Dysphagia

2.1 Conceptual Connotation and Theoretical Basis

The "Brain-Pharynx-Gut Axis" is an integrative functional concept that emphasizes swallowing as the synergistic outcome of the central nervous system, pharyngeal effector organs, and the gastrointestinal system. This concept is grounded in two major theoretical pillars. First, the "central–peripheral–central" closed-loop theory is progressively being incorporated into rehabilitation medicine [6]. This theory advocates the synergistic integration of central and peripheral interventions: central-directed approaches accelerate the activation of functional brain regions, while peripheral interventions correct aberrant sensory and motor control patterns. Functional improvements at the peripheral level can, in turn, provide positive feedback to central brain regions, establishing a virtuous cycle [7]. This theoretical framework directly supports the application of peripheral acupuncture interventions in swallowing rehabilitation. Second, the "brain–gut axis" theory describes a bidirectional regulatory network between the central nervous system and the gastrointestinal tract. The descending arm modulates gastrointestinal function through the autonomic nervous system (particularly the vagus nerve) and the hypothalamic-pituitary-adrenal (HPA) axis, whereas the ascending arm conveys signals to the brain via the enteric nervous system, vagal afferents, immune factors, and gut microbial metabolites [8]. Notably, vagal afferent fibers

project pharyngeal and gastrointestinal sensory signals directly to the NTS, a critical nexus for triggering the swallowing reflex [9]. The "Brain-Pharynx-Gut Axis" unifies central regulation, pharyngeal execution, and gastrointestinal synergy within a single conceptual framework, offering an integrative theoretical lens for mechanistic research and acupuncture intervention in PSD.

2.2 Relevance to Traditional Chinese Medicine Theory

In TCM, the brain is regarded as the "House of the Original Spirit" (Yuan Shen Zhi Fu), governing complex motor functions including swallowing. Stroke impairs the brain's governing capacity, leading to pharyngeal dysfunction and dysphagia. The Ling Shu · Jing Mai states: "The Stomach Meridian of Foot-Yangming … runs along the throat and enters the supraclavicular fossa" [10]. The pharynx is considered the gateway to the stomach; unobstructed stomach qi ensures smooth pharyngeal function, whereas ascending stomach qi may cause pharyngeal discomfort and reflux. After stroke, the stomach fails to harmonize and descend, disrupting qi movement and exacerbating pharyngeal dysfunction. Furthermore, the Ling Shu · Ping Ren Jue Gu states: "The spirit is the essence of water and grain" [11], indicating that the brain depends on the nutritive essence derived from the spleen and stomach's transformation of food. Stroke impairs the spleen and stomach's transport and transformation functions, reducing the production of qi and blood, depriving the brain of nourishment, and aggravating neurological deficits. Thus, TCM posits a functional linkage among the brain, pharynx, and gastrointestinal tract through meridian connections, qi and blood distribution, and ascending–descending qi movement, which is intrinsically consistent with the closed-loop regulation concept of the modern "Brain-Pharynx-Gut Axis."

2.3 Physiological Basis and Post-stroke Pathological Features

Under physiological conditions, the "Brain-Pharynx-Gut Axis" maintains swallowing integrity through bidirectional interactions. In the descending direction, the corticobulbar tract activates the medullary swallowing central pattern generator (CPG); the NTS integrates sensory afferents, while the nucleus ambiguus (NA) innervates pharyngeal muscles via the vagus nerve to produce timed sequential contractions; concurrently, the dorsal motor nucleus of the vagus (DMV) regulates the lower esophageal sphincter and gastric fundus function [12] [13]. In the ascending direction, pharyngeal sensation is transmitted to the NTS via the glossopharyngeal and vagus nerves, while gastrointestinal signals ascend to influence the brain through vagal afferents and hormonal mediators [14]. After stroke, this network descends into a vicious cycle: diminished central drive leads to delayed pharyngeal reflex and inadequate laryngeal elevation; autonomic imbalance disrupts intestinal barrier integrity and gut microbiota; concurrently, impaired pharyngeal clearance and gastroesophageal reflux mutually exacerbate each other, while abdominal distension may further restrict laryngeal elevation. Microbial metabolites and pro-inflammatory cytokines enter the bloodstream and cross the blood–brain barrier, intensifying neuroinflammation [15] and further impeding the plastic repair of the swallowing network. This systemic disruption provides the pathological substrate for the multi-targeted intervention of acupuncture.

3. Acupuncture Regulation of the Central Drive Layer of the Brain-Pharynx-Gut Axis

3.1 Neural Regulation of the Cortical-Brainstem Swallowing Network by Acupuncture

Acupuncture at scalp points directly modulates swallowing-related cortices. Jin et al. [16] employed bilateral scalp electroacupuncture combined with body acupuncture in patients with cortical-type PSD. Compared with body acupuncture alone, the combined approach significantly improved oral onset delay time (ODT) and oral transit time (OTT) ($P < 0.05$), and increased approximate entropy (ApEn) values in bilateral central, parietal, and posterior temporal regions on electroencephalography ($P < 0.05$); however, no significant effects were observed on pharyngeal delay time (PDT), pharyngeal transit time (PTT), or Rosenbek Penetration-Aspiration Scale scores ($P > 0.05$). These findings suggest that the improvement in oral-phase swallowing function by scalp acupuncture may be related to enhanced cortical excitability. Clinical studies have further demonstrated that clustered scalp acupuncture significantly upregulates serum levels of brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) in PSD patients ($P < 0.05$), indicating that acupuncture promotes neural network repair and reorganization through neurotrophic factor-mediated mechanisms [17]. In addition to direct scalp stimulation, pharyngeal acupoints can indirectly activate the cortical-brainstem network via peripheral afferent signals. Xu et al. [18] employed chemogenetics to first verify that modulation of M1 excitatory neurons effectively controlled the activity of the mylohyoid muscle, a key swallowing muscle. Subsequent chemogenetic inhibition of the NTS markedly attenuated the swallowing electromyographic (EMG) signals evoked by M1 activation, whereas electroacupuncture restored these signals, confirming that the NTS is a critical downstream effector node of M1. Based on this evidence, the team elucidated for the first time the mechanism by which electroacupuncture at CV23 (Lianquan) improves swallowing function through activation of layer V excitatory neurons in M1, thereby modulating the "M1 → PBN → NTS" cortical-brainstem neural circuit. At the clinical network level, the "Three Needles for the Tongue" (She San Zhen) can instantaneously reorganize the functional brain network in patients with infratentorial post-stroke dysphagia, enhancing functional connectivity between the frontal lobe and temporoparietal cortex on one hand, and strengthening interhemispheric connectivity between bilateral sensorimotor cortices on the other [19].

3.2 Central Integration: Acupuncture Regulates Rhythmic Generation of Brainstem CPG Nuclei

The brainstem central pattern generator (CPG) comprises the NTS, nucleus ambiguus (NA), and ventrolateral medulla (VLM), and serves as the core hub that receives descending cortical commands and autonomously generates rhythmic swallowing motor patterns. At the NTS level, electroacupuncture at GV16 (Fengfu) and CV23 (Lianquan) significantly increased the positive expression of 5-HT1A

receptors in the rat NTS; microinjection of the 5-HT1A receptor antagonist WAY100635 into the NTS markedly attenuated electroacupuncture-induced EMG discharges, indicating that this receptor mediates the swallowing-promoting effect of acupuncture [20]. At the NA level, electroacupuncture at CV23 and GV16 excited 66.67% and 71.11% of NA swallowing-related motor neurons, respectively, significantly higher than that of PC6 (Neiguan) and ST36 (Zusanli) ($P < 0.01$); chemical lesioning of bilateral NA abolished the acupuncture effect, confirming that the NA is a critical node for acupuncture action [21]. At the VLM level, in vivo electrophysiological recordings revealed that electroacupuncture at CV23 induced a firing response rate of 78.3% in VLM interneurons, with a significant increase in c-Fos-positive cells compared with controls, and a shift from irregular firing to rhythmic burst discharge patterns [22]. Collectively, these studies demonstrate that acupuncture directly modulates neuronal activity within CPG nuclei, enhancing the generation and output of swallowing rhythm.

3.3 Microenvironment Optimization: Acupuncture Inhibits Neuroinflammation

Acupuncture mitigates neuroinflammation through multiple targets, thereby creating a favorable microenvironment for repair of the swallowing network. Animal studies have shown that electroacupuncture at GV20 (Baihui) modulates the TLR4/NF-κB/TXNIP/NLRP3 signaling pathway, shifting microglial polarization from the M1 toward the M2 phenotype, and thereby alleviating cerebral ischemia-reperfusion injury [23]. Other investigations have demonstrated that electroacupuncture downregulates IL-1β expression and upregulates IL-10 levels in the infarcted region of permanent cerebral ischemia rats, modulating microglial polarization balance [24]. Notably, acupuncture at ST36 (Zusanli) and other gastrointestinal acupoints alone significantly reduces pro-inflammatory cytokine levels (IL-1β, TNF-α, IL-6, IL-8) in key brain regions, exerting potent anti-neuroinflammatory effects [25]. This suggests that the optimization of the central microenvironment by acupuncture may be partially mediated by ascending anti-inflammatory signals originating from the gastrointestinal tract.

4. Acupuncture Regulation of the Peripheral Execution and Feedback Layers of the Brain-Pharynx-Gut Axis

4.1 Ascending Feedback: Acupuncture Enhances Pharyngeal Sensory Afferents to Activate CPG

Post-stroke impairment of pharyngeal sensory afferent pathways attenuates CPG drive and delays the pharyngeal reflex. Dai et al. [26] demonstrated in a PSD mouse model that electroacupuncture at CV23 significantly improved swallowing function: compared with the untreated group, PTT was shortened by 32% ($P < 0.05$), and blood perfusion in the CV23 region and S1 area was enhanced. Using transsynaptic viral retrograde tracing, they verified the existence of a three-tiered "NTS → VPM → S1" sensory afferent pathway. Furthermore, chemogenetic inhibition of VPM significantly attenuated the acupuncture-induced improvement in swallowing, confirming that local pharyngeal acupuncture enhances ascending sensory feedback to achieve an "peripheral stimulation → central activation" ascending effect. Clinical studies further support this mechanism. Gao et al. [27] randomized 120 PSD patients with absent pharyngeal reflexes, and demonstrated that acupuncture at the adjacent CV23 points combined with acupressure significantly improved pharyngeal reflex function, with superior Penetration-Aspiration Scale (PAS), Videofluoroscopic Dysphagia Scale (VDS), and Standardized Swallowing Assessment (SSA) scores compared with the control group ($P < 0.05$), confirming that targeted local intervention at the "pharyngeal node" alone can produce tangible therapeutic effects.

4.2 Descending Command: Acupuncture Enhances CPG Conduction to Pharyngeal Muscles

The vagal pharyngeal branches originating from the NA directly innervate pharyngeal constrictor muscles, constituting the critical conduit through which CPG rhythmic signals are transmitted to the periphery. Meng et al. [28] found that electroacupuncture at CV23 significantly shortened the first swallowing latency in rats ($P < 0.01$), increased the number of swallows, and elevated the amplitude and frequency of mylohyoid EMG signals ($P < 0.01$), whereas electroacupuncture at PC6 produced no such changes. Immunofluorescence revealed a significant increase in c-Fos-positive cells in the NA region after electroacupuncture at CV23 ($P < 0.01$), confirming its specific activation of NA neurons. This mechanism provides experimental support for the clinical efficacy of the "Three Needles for the Pharynx" (Yan San Zhen: CV23 Lianquan, Zhiqiang, and Tunyan), which directly stimulate the glossopharyngeal, hypoglossal, recurrent laryngeal, and superior laryngeal nerves to promote reconstruction of the pharyngeal swallow reflex efferent pathway [29]. Song et al. [30] observed that breathing training combined with Yan San Zhen significantly increased the maximum and mean amplitudes of the submental muscle group in early-stage PSD patients ($P < 0.05$), shortened swallowing duration, and reduced SSA scores ($P < 0.05$).

4.3 Pharyngeal Execution: Acupuncture Coordinates Pharyngeal Muscle Contraction

Acupuncture at cervical acupoints directly coordinates the contraction velocity, strength, and amplitude of pharyngeal muscles. Gao et al. [31] employed surface electromyography (sEMG) to evaluate the immediate effect of acupuncture at GB20 (Fengchi), and found that it immediately shortened the swallowing duration of the submental and infrahyoid muscle groups ($P < 0.05$) and increased their amplitudes ($P < 0.05$). In a subsequent randomized controlled trial, the same team confirmed that acupuncture at GB20 immediately reduced the movement time of the geniohyoid muscle and increased its movement displacement ($P < 0.05$) [32]. Huang et al. [33] reported that acupressure at Yan San Zhen combined with feeding–swallowing training significantly increased the vertical and horizontal displacement distances of the thyroid cartilage and hyoid bone in PSD patients ($P < 0.05$), shortened swallowing time ($P < 0.05$), and increased the maximum EMG amplitude ($P < 0.05$).

5. Ascending Regulation and Metabolic Support of the Brain-Pharynx-Gut Axis by Acupuncture

5.1 Intestinal Barrier Repair and Microbiota Remodeling: Acupuncture Regulates the Gut-Brain Axis via the Vagus Nerve

Post-stroke cerebral ischemia activates the HPA axis and sympathetic nervous system, disrupting the intestinal mucosal barrier (reduced tight junction proteins, increased permeability, ultrastructural damage to intestinal mucosa) and causing gut microbiota dysbiosis [34] [35]. Dysbiosis has been shown to exacerbate central neuroinflammation by influencing glial cell function [36]. Because intestinal barrier disruption is a primary event that triggers dysbiosis, restoring barrier integrity is critical for breaking the "brain–gut–brain" vicious cycle. Zhao et al. [37] demonstrated in MCAO rats that electroacupuncture activates vagal efferent fibers, upregulates Fut2 expression and α1,2-fucosylation, increases Muc2+ goblet cell density and tight junction proteins, and repairs the intestinal barrier. Further experiments revealed that (i) subdiaphragmatic vagotomy completely abolished these effects, and (ii) fecal microbiota transplantation (FMT) from electroacupuncture-treated rats to germ-free recipient rats reproduced the neuroprotective effects—infarct volume was reduced by 33% and survival rate increased by 30% ($P = 0.012$)—solely through microbiota transfer. Thus, electroacupuncture at ST36 modulates central neuroinflammation via the "vagus nerve → gut → microbiota" axis.

5.2 Nutritional Metabolic Support: Acupuncture Enhances Pharyngeal Muscles and Neural Repair by Improving Nutritional Status

Patients with PSD frequently develop malnutrition due to feeding difficulties. Malnutrition and dysphagia form a vicious cycle: inadequate protein intake accelerates catabolism of pharyngeal muscles, leading to sarcopenic dysphagia characterized by reduced laryngeal elevation and prolonged pharyngeal transit [38]; simultaneously, the scarcity of amino acids and fatty acids required for neural repair delays the remodeling of swallowing centers [39]. Electroacupuncture at ST36 elevates serum gastrin and motilin levels, accelerates bowel sound recovery, and increases gastric antral contraction frequency and motility index on ultrasonography, indicating effective promotion of gastric motility and gastric emptying to provide a kinetic foundation for nutrient absorption [40]. Li et al. [41] selected ST36 and CV12 (Zhongwan), and found that 30-minute needle retention significantly elevated serum albumin, total protein, and hemoglobin levels, improved intestinal barrier markers (D-lactate, lipopolysaccharide, and diamine oxidase) in PSD patients, with a total effective rate of 93.33%. Mechanistic studies indicate that acupuncture may protect intestinal mucosal barrier function by inhibiting the p38MAPK signaling pathway and reducing intestinal epithelial cell apoptosis, thereby providing structural support for nutrient absorption [42].

6. Integration and Prospects

6.1 Bidirectional Closed-loop Regulatory Mechanism of the Brain-Pharynx-Gut Axis

The mechanisms by which acupuncture treats PSD can be synthesized into a bidirectional closed-loop model of the "Brain-Pharynx-Gut Axis," encompassing three synergistic tiers: central regulation, peripheral feedback, and gastrointestinal modulation. At the central level, scalp acupuncture directly activates swallowing-related cortices and enhances rhythmic output from the brainstem CPG; the CPG drives pharyngeal muscles via the NA to execute swallowing, while simultaneously modulating gastrointestinal motility and barrier function through the DMV. Concurrently, cervical acupoints (e.g., CV23) send peripheral afferent signals that ascend to activate the cortical-brainstem network (M1 → PBN → NTS), providing positive feedback to the CPG. At the peripheral level, pharyngeal sensation is relayed via the "NTS → VPM → S1" pathway to the sensory cortex, forming a positive feedback loop to the CPG; acupuncture also directly augments pharyngeal muscle contraction and improves gastrointestinal motility, thereby optimizing the pharyngeal execution environment. At the gastrointestinal level, acupuncture engages the vagus nerve to repair the intestinal barrier and remodel the microbiota, which attenuates central neuroinflammation through the gut-brain axis, creating a favorable microenvironment for repair of the swallowing network. These three tiers mutually reinforce one another, establishing a positive feedback regulatory circuit through which the local effects of acupuncture are amplified into global functional improvement.

6.2 Research Limitations and Future Directions

Several limitations currently constrain the field. First, acupuncture parameters lack standardization; considerable heterogeneity exists across studies in electroacupuncture frequency, intensity, waveform, and needle retention time, and the "dose–response" relationships among these parameters remain unclear. Second, causal chains have not been fully delineated; particularly, the causative link between gut microbiota, neuroinflammation, and swallowing improvement, though suggested by FMT experiments, requires validation in dysphagia-specific models. Third, clinical translational evidence is sparse; many mechanistic findings from basic research have yet to be validated in humans using functional neuroimaging or electrophysiological approaches. Future directions may include: Parameter optimization: using meta-analyses or factorial designs to systematically screen optimal parameter combinations targeting specific nodes of the Brain-Pharynx-Gut Axis (scalp points, Yan San Zhen, ST36); Causal validation: employing chemogenetics, optogenetics, and FMT in PSD animal models to clarify the sufficiency and necessity of each pathway and the causal role of gut microbiota; Multi-omics integration: combining metagenomics, metabolomics, and functional brain imaging (fMRI/fNIRS) to construct a multidimensional regulatory network; and Clinical translation: conducting large-sample

randomized controlled trials with objective outcomes such as videofluoroscopic swallowing study (VFSS) and sEMG to verify the superiority of integrated "central + peripheral" acupuncture protocols.

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