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Research Progress and Mechanism Analysis of Different Acupuncture Methods in the Treatment of Cognitive Dysfunction after Stroke

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Abstract: ***Post-stroke cognitive impairment (PSCI) is one of the common sequelae of stroke patients. At present, a large number of studies have been devoted to discovering and improving the treatment methods of cognitive dysfunction after stroke, among which acupuncture treatment as a traditional Chinese medicine therapy has attracted much attention. Acupuncture can obtain therapeutic effects by stimulating specific acupoints, which can adjust the physiological functions of the body and promote the recovery of patients. This article will review the research progress of different acupuncture methods in the treatment of cognitive dysfunction after stroke, aiming to provide guidance and reference for clinical practice.***

Keywords: Cerebral stroke, Cognitive dysfunction, Acupuncture method, Research progress**.**

1. Introduction

Post-stroke cognitive impairment (PSCI) is one of the common complications after stroke. Its symptoms are mainly persistent or progressive problems such as inattention, memory loss, delayed thinking, decreased logical reasoning ability, difficulty in language comprehension and impaired executive function. The development of PSCI may have a significant impact on patients' quality of life and daily functions. Acupuncture therapy, as a non-drug intervention, has attracted much attention in the treatment of cognitive dysfunction after stroke. By sorting out the references in recent ten years, the author found that acupuncture has significant curative effect on PSCI, and can improve the self-care ability and social participation of PSCI patients. Therefore, this article will analyze the efficacy and possible regulation mechanism of acupuncture in the treatment of PSCI patients from the perspectives of different acupuncture methods such as scalp acupuncture, body acupuncture, electroacupuncture, combination of acupuncture and medicine, and characteristic acupuncture, so as to provide scientific theoretical basis and clinical significance for clinical and scientific researchers, which are summarized as follows.

2. Scalp Acupuncture Improves Post-stroke Cognitive Impairment

Scalp acupuncture therapy, as a special acupuncture technique based on the traditional theory of zang-fu organs, and meridians and combined with modern cerebral cortex function localization research, aims to regulate the brain function state by accurately stimulating specific reflex areas or acupoints on the head. It has shown significant potential in the intervention of PSCI, and its efficacy and mechanism of action are increasingly attracting the attention of neuroscience research. Existing clinical studies have confirmed [1] that scalp acupuncture can effectively improve the cognitive function score and daily living ability scale (ADL) score of PSCI patients. In-depth exploration of its neuroprotective mechanism revealed that, this therapy may inhibit the decline of NeuN (neuronal nuclear antigen) expression in the ischemic lateral brain tissue after stroke, and significantly down-regulate the expression levels of key pro-inflammatory factors, such as interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α) and interleukin-6 messenger ribonucleic acid (IL-6 mRNA), thereby effectively suppressing the neuroinflammatory cascade and reducing ischemic brain injury. It is worth noting that the combined application of scalp acupuncture (especially scalp acupuncture in the motor area) and cognitive function training, compared with monotherapy, shows synergistic effects in improving clinical symptoms, improving cognitive function, enhancing activities of daily living and optimizing event-related potential P300 index of PSCI patients [2]. This synergistic effect suggests that its mechanism of action may involve regulation of functional connectivity of distributed brain networks, enhancement of neuronal activity and optimization of neurotransmitter homeostasis. At the cellular and molecular levels, scalp acupuncture shows clear neuroprotective properties. Studies have revealed [3] that it can regulate the NLRP3/Caspase-1 inflammasome signaling pathway, inhibit the over-activation of microglia (manifested as the reduction of processes), improve the morphological abnormalities of damaged neurons, and significantly reduce the rate of neuronal apoptosis. In addition, scalp acupuncture treatment for the selection of specific acupoints (such as Baihui, Du Meridian, Sishencong and Benshen, and Fengchi, the intersection point of Foot Shaoyang Gallbladder Meridian and Yangwei Meridian) can effectively improve the hemodynamic state of brain microcirculation in PSCI patients, and promote blood perfusion in ischemic areas [4]. This not only helps to stimulate the potential compensatory function of cerebral cortex, but also provides an important hemodynamic basis for cognitive function recovery. Further mechanism studies have shown [5] that scalp acupuncture therapy may enhance neuroplasticity, by promoting the expression of synapse-related proteins in the affected hippocampus (a key brain region closely related to learning and memory), and upregulating protein functions involved in cognitive processes. At the same time, this therapy can improve the blood supply status in the ischemic penumbra area, and reduce

NOS-mediated oxidative stress damage and reduce the production of oxygen free radicals by inhibiting the overexpression of nitric oxide synthase (NOS). Multi-target and multi-level protect nerve tissue and promote functional repair.

3. Body Acupuncture Therapy Improves Cognitive Impairment after Stroke

Body acupuncture therapy is rooted in the theory of meridians and acupoints in traditional Chinese medicine. By selecting specific acupoints on the meridians system of the whole body for acupuncture stimulation, it can regulate qi and blood, balance yin and yang, and then promote the recovery of body function. It has shown clear clinical value in the field of PSCI intervention, and its mechanism of action involves multi-level neurobiological regulation. Available evidence suggests that body acupuncture therapy is effective in improving core dimensions of cognitive function in PSCI patients, including memory encoding and retrieval, attention concentration and allocation, and flexibility in executive function [6,7]. Its neuroprotective effect is partly due to the regulation of oxidative stress and neuroinflammatory state in the brain. Specifically, body acupuncture intervention was confirmed [6] to significantly inhibit the excessive oxidative stress response and pro-inflammatory factor cascade, while inhibiting the pathological activation of astrocytes, thereby alleviating the neuroinflammatory microenvironment, reducing neuronal apoptosis, and ultimately playing a role in protecting the structural and functional integrity of brain tissue and improving cognition. At the level of clinical practice, the synergistic application of body acupuncture therapy and conventional rehabilitation training of specific acupoint combinations (such as Baihui, Shenting and other key points of Governor Meridian) has been proved to significantly improve the overall cognitive function score of PSCI patients [7]. This synergistic effect suggests that, body acupuncture may provide a neurobiological basis for the recovery of cognitive function, by promoting the remodeling and functional reorganization of damaged cognitive neural circuits. It is worth noting that, the characteristic acupuncture method based on the theory of “Tongdu Tiaoshen” in traditional Chinese medicine- “Tongdu Jieyu” acupuncture method shows unique advantages in the treatment of PSCI. A comparative study found [8], that both “Tongdu Jieyu” acupuncture and conventional western medicine donepezil hydrochloride tablets, can effectively improve the Montreal Cognitive Assessment Scale (MoCA) and Mini Mental State Examination (MMSE) scores of PSCI patients. However, the study further revealed that the “Tongdu Jieyu” acupuncture method was significantly better than the drug control group, in improving the speed of MMSE and MoCA scores and the final improvement range, suggesting that it may have better clinical efficacy in improving PSCI cognitive function. There are many potential mechanisms for the overall efficacy of “Tongdu Jieyu” acupuncture and body acupuncture therapy. It is believed that it may include: (1) directly or indirectly regulating the release and balance of excitatory and inhibitory neurotransmitters (such as glutamate, GABA, acetylcholine, etc.) in the central nervous system; (2) improving local hemodynamic parameters of brain tissue, increasing cerebral blood flow (CBF) and oxygenation levels in ischemic or hypoperfused areas; (3) alleviating secondary neurological damage; (4) activating endogenous neuroprotection and repair pathways and promoting changes in neuroplasticity. These comprehensive effects together constitute the biological basis of body acupuncture therapy to improve cognitive impairment in PSCI.

4. Electroacupuncture Therapy Improves Cognitive Impairment after Stroke

Electroacupuncture therapy (EA), as a fusion of traditional acupuncture and modern bioelectrical stimulation technology, realizes systematic regulation of nerve-vascular-immune network, by applying a micro pulse current similar to human bioelectricity at Deqi acupoint. It shows the advantages of multi-target intervention in PSCI treatment, which can simultaneously improve cognitive domain function (including memory coding, executive control and information processing speed) and emotional disorders. The core neuroprotective mechanism is embodied in dual regulation of hippocampus. Electroacupuncture can significantly reduce neuronal structural damage and mitochondrial dysfunction, block free radical chain reaction by activating endogenous antioxidant system (enhancing superoxide dismutase SOD and glutathione peroxidase GSH-Px activity), and inhibit abnormal apoptotic pathway to reduce neuronal loss [9]. Further studies found [10] that electroacupuncture can increase the phosphorylation level of PI3K/Akt signaling pathway, enhance hippocampal synaptic plasticity and postsynaptic receptor activity, and drive up-regulation of synaptophysin (SYN) and postsynaptic dense protein 95 (PSD-95) expression, laying a cytological foundation for cognitive remodeling. At the hemodynamic level, electroacupuncture antagonizes serotonin (5-HT)-mediated vasospasm and ATPase depletion by inhibiting the pathological secretion of vascular endothelial cells and glial cells [11], and promotes endothelin release to improve local microcirculation. The therapy can also reduce glutamatergic excitotoxicity, and alleviate metabolic damage caused by calcium overload [12], thereby optimizing cerebral perfusion and alleviating neurovascular unit damage. Clinical studies have confirmed that electroacupuncture stimulation of key acupoints, such as Baihui and Zusanli can significantly improve MoCA score, MMSE score and ADL index of PSCI patients [13], and its efficacy is closely related to regulating the expression of serotonin transporter (5-HTT), and balancing monoaminergic neurotransmission. It is worth noting that, the synergistic program of electroacupuncture combined with routine rehabilitation training, can improve cognitive function and quality of life significantly better than single intervention, highlighting the integrated therapeutic value of its multi-channel regulation.

5. Combined Acupuncture and Medicine Therapy Improves Post-stroke Cognitive Impairment

Acupuncture-drug combination therapy (API) integrates the neuromodulatory advantages of acupuncture with the molecular targeting characteristics of drugs, through the mechanism of temporal synergy and spatial complementarity, and constructs a multi-dimensional intervention network for PSCI. Clinical studies have confirmed [14] that the effect size

of API in improving MMSE score and MoCA score is significantly better than that of monotherapy. Its synergistic effect stems from the systematic remodeling of the neurovascular unit (NVU): the active ingredients of the drug scavenge free radicals and inhibit platelet aggregation by activating superoxide dismutase (SOD), thereby stabilizing arterial plaque and reducing cerebral infarction volume; Simultaneously, acupuncture can inhibit the expression of adhesion molecules (VCAM-1/ICAM-1), reduce inflammatory cell infiltration and blood-brain barrier leakage, and dilate cerebral blood vessels to increase capillary blood flow velocity and oxygen delivery efficiency. At the level of neuroprotection, Tongdu Yijing Decoction combined with acupuncture can significantly increase plasma neuroglobulin (Ngb) levels [15] and reduce oxidative stress injury by binding free hemoglobin; Scalp acupuncture combined with nimodipine antagonizes cerebrovascular smooth muscle L-type calcium channels and central neuron NMDA receptors through dual targeting [16], blocks excitotoxicity caused by calcium overload, and activates PI3K/Akt/CREB pathway to drive brain-derived neurotrophic factor (BDNF) synthesis, thereby enhancing hippocampal synaptic plasticity [17]. API also optimizes neuronal energy metabolism by regulating the immune metabolic microenvironment (such as reducing hippocampal lactate accumulation and upregulating SIRT1 deacetylase activity), and accelerates damaged brain tissue repair and neurological function reorganization [18]. This integrated strategy, not only achieves the simultaneous improvement of cognitive function and quality of life, but also provides an efficient and low-toxicity treatment paradigm for PSCI, through the three-level synergistic model of "pharmacological intervention-electrical nerve stimulation-metabolic reprogramming".

6. Characteristic Acupuncture Improves Post-stroke Cognitive Impairment

Characteristic acupuncture, as a precise intervention paradigm based on individualized syndrome differentiation, uses specific acupuncture parameters (depth/angle/stimulation amount), to reconstruct the neuro-immune-vascular network of PSCI patients by integrating classical meridian theory with modern neuroanatomical positioning. The core mechanism is embodied in triple regulatory effects [19, 20]: (1) regulating cerebral hemodynamic parameters and optimizing microcirculation perfusion; (2) Inhibit microglia TLR4/NF-κB inflammatory pathway and reduce serum IL-6 levels; (3) Improve hemorheological indexes and reverse hypercoagulable state. Clinical studies have confirmed [21] that the "Tongdu Tiaoshen" acupuncture method can significantly improve the MoCA score by enhancing the blood perfusion of temporal lobe-prefrontal cortex, and its cognitive improvement effect is closely related to the inhibition of IL-6-mediated blood-brain barrier destruction and neuronal apoptosis. Simultaneously, "Tiaoshen Tongqiao" acupuncture combined with neuromuscular electrical stimulation, can synergistically improve the functional connection of hippocampus-default mode network, and increase MMSE score and MoCA score [22]. This effect is due to the activation of hypoxia-inducible factor-1α (HIF-1α)/vascular endothelial growth factor (VEGF) axis by acupuncture [23], which promotes angiogenesis and synaptic remodeling in the injured area. This multi-target intervention model, by reconstructing the homeostasis of neurovascular units, ultimately achieves the recovery of cognitive function and the overall improvement of quality of life in PSCI patients.

7. Other Therapies Improve Post-stroke Cognitive Dysfunction

In addition to acupuncture therapy, the intervention system of PSCI is expanding to a multi-modal combined therapy paradigm, the core of which is to rebuild the nerve remodeling microenvironment through neuromodulation technology, metabolic optimization and microbial-gut-brain axis regulation. Transcranial direct current stimulation (tDCS), as a non-invasive neuromodulation technology, regulates cortical excitation/inhibition balance through polarity-dependent regulation, enhances regional cerebral blood flow and default mode network functional connection strength [24], thus improving working memory and information processing speed. Clinical studies have shown [25] that tDCS combined with Baduanjin training can produce synergy. Baduanjin activates the cholinergic pathway increases the α-wave power spectral density of the cerebral cortex, and synchronously regulates the sympathetic-vagal nerve balance. The combined regimen significantly improves the MoCA score and MMSE score of PSCI patients, and significantly optimizes the event-related potential P300 parameters and daily living ability. The mechanism involves the induction of long-term synaptic potentiation (LTP) by tDCS, and the promotion of neurotrophic factor BDNF synthesis by Baduanjin. At the level of microbial intervention, specific probiotic strains (such as Bifidobacterium BB-12 and Lactobacillus GG) competitively inhibit pathogen colonization, enhance intestinal mucosal barrier integrity, and reduce circulating lipopolysaccharide (LPS) levels, thereby reducing systemic inflammation; At the same time, brain-gut peptides (such as GLP-1 and Ghrelin) are transported to the hippocampus through the vagal nerve pathway, activating the CREB/BDNF signaling axis [26]. Innovative combined strategies, such as probiotics-tDCS synergistic therapy [27], regulate the efficiency of glutamatergic synaptic transmission through tDCS, optimize the α diversity of intestinal flora with probiotics, and further improve the MoCA score. This effect confirms that the two-way regulation of neurotransmitter homeostasis and metabolic internal environment balance plays a key role in PSCI rehabilitation.

8. Summary

As a non-drug treatment method, acupuncture treatment has fewer side effects and dependence, and has gradually attracted the attention of PSCI patients. Scalp acupuncture, body acupuncture, electroacupuncture, combination of acupuncture and medicine, characteristic acupuncture, etc. all show certain therapeutic effects. In addition, different acupuncture methods can also be combined with other treatment methods to form a comprehensive treatment plan and improve the treatment effect. A comprehensive analysis of the application and efficacy of different acupuncture methods in the treatment of cognitive dysfunction after stroke shows that acupuncture methods have certain potential in improving patients' cognitive function and quality of life. Overall, different acupuncture methods provide a potential option for the

treatment of post-stroke cognitive dysfunction and show broad application prospects in clinical practice. Future research needs to further clarify the efficacy and mechanism of action of different acupuncture methods, establish standardized acupoint selection and stimulation methods, carry out larger-scale and longer-term clinical trials, explore the combined application of different acupuncture methods and other treatment methods, and optimize clinical treatment methods.

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