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Research Progress on Mechanisms of Acupuncture in the Treatment of Post-stroke Cognitive Impairment

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Abstract: ***Cognitive impairment is a common complication after stroke, which is easy to cause initiative, compliance and curative effect of rehabilitation treatment, and increase the lifetime disability rate and mortality rate. This paper reviews the mechanism of acupuncture treatment of post-stroke cognitive impairment in recent years, and reviews acupuncture from the aspects of improving cerebral microcirculation, promoting neural function recovery, regulating inflammatory response and apoptosis, improving synaptic plasticity, regulating intestinal flora, etc. so as to provide reference for acupuncture treatment of post-stroke cognitive impairment related research.***

Keywords: Acupuncture, Cognitive impairment after stroke, Mechanism research, Review.

1. Introduction

Cognitive impairment after stroke Post-stroke cognitive impairment (PSCI) refers to the clinical syndrome characterized by cognitive impairment that appears after stroke and persists for 6 months. The performance is mainly memory decline, the disease gradually worsens, and the understanding, memory and calculation ability are reduced, or the patient's temperament changes, and the patient cannot take care of himself [1]. According to the investigation, the prevalence rate of PSCI after stroke is about 66% [2], and relevant reports and clinical observations have found that the cognitive impairment of patients not only affects the daily life and social ability of patients, but also affects the initiative, compliance and efficacy of rehabilitation treatment, thus delaying the rehabilitation process of limbs and increasing their lifetime disability rate and mortality [3]. Clinical studies have shown that acupuncture treatment of PSCI has a significant effect, can improve the cognitive status of patients, improve quality of life, reduce the incidence of death, this article reviews the mechanism of acupuncture treatment of PSCI, to provide reference for related research.

2. TCM Understanding of Cognitive Impairment After Stroke

Cognitive disorder after stroke belongs to the concept of modern medicine. There is no relevant record of the name of this disease in ancient Chinese medicine. However, according to the clinical manifestations of patients 'stupidity, it can be classified into the categories of "stupid disease" and "forgetful" in Chinese medicine. The etiology and pathogenesis are also discussed from the perspective of "brain empty, mental machine loss". Ancient doctors believed that memory, cognition and thinking of human body were related to brain. If brain was healthy, mental machine was full, showing sharp thinking and strong memory. If the brain is damaged, the meridians are blocked, the brain is not nourished, and the performance is memory decline and cognitive function abnormality. The name of dementia is first found in the Secret Biography of Hua Tuo Divine Doctor. The theory of "mental stupor at the beginning of stroke" recorded in the Clinical Guide Medical Cases means that the disease is a change of stroke. The theory of "Su Wen·Tiaojing Lun" says: blood is in harmony with the lower part, qi is in harmony with the upper part, chaos and forgetfulness", that is, qi and blood are disordered, which goes up to the brain, leading to damage to the primordial spirit and forgetfulness. "Dialectical Strange News" mentioned that the pathogenesis of dementia and amnesia is liver depression by spleen, phlegm and dampness endogenous, accumulated in the chest, blocking the heart orifice, making the spirit unclear. Modern doctors believe that the brain is the sea of marrow, stroke for a long time, zang-fu dysfunction, deficiency of qi, blood and body fluid, marrow reduction and brain elimination, plus spleen deficiency, phlegm turbidity, blood stasis and other obstruction of brain orifices, resulting in unclear consciousness, abnormal spirit and emotion. To sum up, the disease is mainly caused by deficiency of origin and deficiency of essence and blood in kidney. Deficiency of origin refers to deficiency of qi and blood in nourishing brain orifices, deficiency of essence and blood in kidney, and deficiency of excess refers to pathological products such as "phlegm turbidity" and "blood stasis" blocking brain fu. The disease is located in brain and closely connected with kidney, heart, liver, spleen and other organs [4]. Treatment should regulate qi and blood yin of zang-fu organs and also awaken consciousness.

3. The Mechanism of Acupuncture in Treating Cognitive Impairment After Stroke

Modern medicine considers that the structural basis of PSCI formation is tissue atrophy and nerve function degeneration caused by chronic ischemia of brain tissue. The mechanism of acupuncture treatment of PSCI has not been fully revealed. Existing studies show that acupuncture mainly improves cognitive function of patients by improving brain microcirculation, promoting nerve function recovery, regulating inflammatory reaction and apoptosis, improving synaptic plasticity and regulating intestinal flora. At the same time, acupuncture can regulate biological processes such as

neurotransmitters, inflammatory factors and blood flow in the brain, thus improving brain function and preventing cognitive impairment.

3.1 Improve Brain Microcirculation

Most of the pathogenic factors causing PSCI are related to ischemia and hypoxia in specific areas of the brain. Studies have shown that acupuncture at specific acupoints can improve blood circulation in brain injury areas, increase cerebral oxygen levels, activate residual brain cell functions, and enhance functional connections between hippocampus and frontal lobe and parietal lobe, thus improving patients 'cognitive impairment and improving patients' ability of daily life.

Xi Ou et al. [5] divided 100 patients with PSCI into control group (rehabilitation training + conventional drug therapy) and observation group After 3 months of treatment, RI and serum ET-1 of bilateral VA, MCA and ACA in both groups were lower than those before treatment, and serum NO was higher than those before treatment, and the curative effect of observation group was better, which indicated that scalp acupuncture combined with rehabilitation training could improve cerebral circulation and vascular endothelial function, thus regulating hemodynamics. Wang Lina et al. [6] randomly divided 140 patients with PSCI and bilateral carotid atherosclerotic plaques into control group (oral atorvastatin + conventional therapy) and intervention group (oral atorvastatin + conventional therapy + acupuncture therapy), after treatment, bilateral arterial, vascular endothelial function and blood lipids of patients in both groups were improved compared with those before treatment, and the intervention group had better curative effect.

3.2 Promote the Recovery of Neurological Function

Cerebrovascular diseases often lead to neurological damage. Acupuncture therapy can stimulate neurons in cerebral cortex, improve their excitability and promote the recovery of neurological function.

Xiong Dan [7] found that on the basis of conventional rehabilitation treatment, scalp acupuncture combined with rTMS intervention for two weeks was beneficial to improve the overall cognitive function, neural function and attention of PSCI patients, and after treatment, the local nerve spontaneous activities of left precuneus lobe, right cerebellum, left fusiform gyrus and left superior parietal gyrus of PSCI patients changed significantly. Shang Yaxin et al. [8] randomly divided 60 patients with PSCI into control group (conventional therapy + transcranial magnetic stimulation) vs. treatment group After 4 weeks of treatment, MoCA score, serum BNDF level and mean blood flow velocity of middle cerebral artery (Vm) in both groups were significantly higher than those before treatment, and those in treatment group were significantly higher than those in control group. The results showed that scalp acupuncture combined with transcranial magnetic stimulation could effectively increase the serum BNDF level and cerebral blood perfusion in patients with cognitive impairment after stroke, thus improving their cognitive function.

3.3 Regulation of Inflammatory Response and Apoptosis

Inflammatory response is considered as a key factor in stroke pathophysiology, abnormal secretion of inflammatory cytokines can destroy extracellular matrix and blood-brain barrier, thus aggravating accidental damage of cerebral vessels, apoptosis is an important way of programmed cell death.

Yang Chao et al. [9] found that acupuncture Baihui, Sishencong and Dazhui of the affected rats could significantly reduce the TNF-α content in the serum of the affected rats and improve the nerve function of the affected rats, which may be related to the regulation of TNF-α-mediated inflammatory reaction and apoptosis. Wang Xiangfeng et al. [10] pre-stimulated the affected rats by Zhichan-san acupuncture. The study results showed that acupuncture could reduce the contents of IL-1β, IL-6 and TNF-α in plasma and hippocampus, and significantly reduce the percentage of apoptotic cells in hippocampus of the affected rats, thus alleviating the damage and apoptosis of hippocampus cells, and further improving cognitive function. This may be related to the inhibition of excessive expression of IL-1β, IL-6 and TNF-α in hippocampus of the affected rats by Zhichan-san acupuncture and the alleviation of inflammatory reaction in brain tissue. All the above studies indicate that acupuncture treatment mechanism of cognitive impairment may be related to acupuncture can regulate inflammatory response and apoptosis.

3.4 Increased Synaptic Plasticity

Within the brain, connections and communication between neurons depend on an intercellular structure called synapses. There are two main types of synapses: excitatory and inhibitory synapses, both of which are critical to the proper functioning of the brain. Synaptic plasticity refers to changes in the morphology and function of synaptic connections, including long-term changes in synaptic structure and number and short-term changes in the strength and potency of neurotransmitters. Some studies have shown that acupuncture treatment can improve synaptic numerical density and synaptic surface density, alleviate synaptic ultrastructure defect and promote synaptic plasticity to adapt to changes in external environment when it is intervened in early stage of PSCI.

Ou Mengning et al. [11] treated PSCI model mice with penetrating head acupuncture combined with body acupuncture. After 3 weeks of treatment, compared with the untreated group, the PI index of new object recognition of mice in this group increased, HE staining showed that the hippocampus cell structure of mice was more complete and arranged more orderly, Nissl staining showed that the nerve cell density of mice was larger, Nissl bodies were more, serum SOD content increased, MDA content decreased, SYN and PSD-95mRNA expression increased significantly, hippocampus IHC score increased, difference was statistically significant ($P<0.05$). It indicated that the combination of scalp penetration acupuncture and body acupuncture could promote the regeneration of hippocampal neurons, relieve oxidative stress reaction, increase the expression of synaptic protein SYN and PSD-95, and improve cognitive impairment of rats.

Xie et al. [12] treated the affected rats by acupuncture at Shenting and Baihui acupoints, and found that the number of synapses in the affected rats increased significantly after treatment, the synaptic vesicles were densely distributed, the synaptic gap was relatively small, and the behavioral test and neurological function defect score were improved. Feng Chuwen et al. [13] conducted visual analysis on a large number of literatures, and the results showed that acupuncture had an accurate effect on improving synaptic plasticity. The above research indicates that acupuncture can improve the neurological deficit symptoms by improving synaptic plasticity, promote the recovery of neural function, and thus improve the cognitive level of patients.

3.5 Regulate Intestinal Flora

Intestinal flora is a group of dynamic microflora, which is a large and complex symbiotic colony in mammalian intestine. Studies have shown that intestinal flora is related to the occurrence of cerebrovascular diseases. There is two-way communication between intestinal flora and brain. Stroke can cause changes in intestinal flora. The composition of intestinal flora can also affect the occurrence and development of stroke patients. It is called “brain-intestinal axis”. After stroke, the diversity and metabolite levels of intestinal flora are dynamically changed. Intestinal flora and its metabolites, especially short-chain fatty acids (SCFAs), can improve the prognosis of stroke patients by modulating GABA, brain-derived neurotrophic factor (BDNF), microglia and adaptive immune cells, thereby enhancing neural network plasticity and reducing neuroinflammation.

Xiao Yaping et al. [14] found through clinical observation that warm acupuncture can effectively improve the number of beneficial bacteria in intestinal tract of PSCI patients, increase GABA level, promote brain tissue repair and improve the cognitive level of patients. Jing Yali et al. [15] showed that acupuncture method for regulating Du and mind combined with cognitive function training can significantly improve the cognitive level, neurotransmitter level and intestinal flora of PSCI patients, and further improve the daily living ability of patients. Under the guidance of brain-gut axis theory, Han Qichen et al. [16] found that acupuncture can inhibit the relative hyperactivity of HPA axis, balance brain-gut peptides, regulate the diversity of intestinal flora and activate neuro-immune network, thus alleviating immune inflammatory reaction, realizing benign regulation of brain-gut axis and improving cognitive function of PSCI patients. The above research shows that acupuncture can improve the material changes in the brain by regulating the number and diversity of intestinal flora, and promote the recovery of neurological function of patients, thus improving their cognitive function.

4. Summary

PSCI has a high incidence and many complications, which seriously affects the quality of life of patients. Acupuncture has a significant clinical effect on PSCI, and the related mechanism has been widely studied, but there are still some problems: (1) Acupuncture treatment of PSCI mainly focuses on clinical efficacy research, and its mechanism research is not deep, and mainly focuses on improving ischemia, hypoxia injury and neural function recovery after stroke, while the specific contents of neurobiology and molecular biology involved in cognition are lack of systematic research, which still needs to be further deepened. For example, cognitive staging is not standardized and specific, clinical efficacy evaluation lacks objective quantitative indicators, mainly referring to cognitive impairment function evaluation scale, etc., hoping to standardize treatment schemes and evaluation indicators in the future, so as to provide more objective research evidence for the study of effect mechanism of acupuncture treatment of PSCI.

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