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Mechanism of Acupuncture in Treating Stroke Patients with Foot-drop

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Abstract: ***Post-stroke foot drop leads to impaired walking ability and seriously affects the physical and mental health of patients and their families. This review discusses the effects of acupuncture on promoting the recovery of upper motor neurons, inhibiting the excitability of spinal motor neurons, regulating spasm-related transmitters, and regulating the balance of muscle tone between active and antagonist. This review discusses the effects of acupuncture on promoting the recovery of upper motor neurons, inhibiting the excitability of spinal motor neurons, regulating spasm-related transmitters, and regulating the balance of muscle tone between active and antagonistic muscles, with the aim of exploring the possible pathways of acupuncture in the treatment of post-stroke foot drop and providing a direction for the study of the mechanism of acupuncture in the treatment of post-stroke foot drop. It is important for the modernization of Chinese medicine treatment methods.***

Keywords: Stoke, Foot-drop, Acupuncture, Mechanism research**.**

1. Introduction

In recent years, the incidence of stroke has been increasing gradually, and it has become the first fatal disease in China, with the characteristics of acute onset, high disability rate and high mortality rate[1]. Spastic paralysis is the most common sequela of stroke. Spastic paralysis is one of the most common sequelae of stroke, and about 90% of the patients have different degrees of increased muscle tone, which seriously affects the functional recovery, quality of life, and prognosis of the patients, and also imposes a heavy economic burden on the family and society[2]. It also brings a heavy economic burden to the family and society. One of the main factors leading to gait abnormality in stroke patients is the foot drop symptom caused by spastic paralysis, and about 30% of stroke patients have foot drop symptom, which is clinically manifested as the affected side of the lower limb is in extensor mode, and often adopts postural compensation to show abnormal gait when walking, which not only seriously affects the motor function of the lower limbs and the ability of patients to walk, but also increases the risk of patients' secondary injuries, which is one of the key difficulties in the rehabilitation of stroke patients. It is one of the key difficulties in the rehabilitation of stroke patients. It is one of the key rehabilitation difficulties for stroke patients. To partially or completely restore the walking ability of stroke patients is the main rehabilitation goal, therefore, correcting foot drop is of great clinical value to restore the walking ability of post-stroke patients. In modern medicine, foot drop is treated with oral anti-spasticity drugs and local injection of botulinum toxin, which has poor therapeutic effect and adverse effects such as drowsiness, gastrointestinal reaction and liver injury. In recent years, more and more studies have shown that acupuncture has shown unique advantages in protecting the central nervous system, relieving muscle spasm and reducing the disability rate, and has become a routine rehabilitation treatment for foot drop after stroke. However, the intrinsic mechanism of acupuncture in the treatment of foot drop after stroke has not been systematically described, which deserves in-depth discussion. The present review discusses the mechanism of acupuncture in treating foot drop after stroke, aiming to provide a theoretical basis for clinical prevention and treatment of foot drop.

2. Promoting Upper Motor Neuron Recovery

The corresponding limbs are in a spastic state after central nerve injury, and the damaged upper motor neurons cannot effectively control the nerve impulse conduction of the lower motor neurons they innervate, thus releasing the originally inhibited reflexes. Therefore, we should focus on promoting the functional recovery of the damaged brain neurons, and promote the remodelling of the brain neurons by improving the efficiency of nerve signal conduction, in order to restore the normal spinal reflex pathway, and then to achieve the improvement of foot drop and the restoration of the motor function of the lower limbs. The main mechanism of neural pathway recovery after stroke is the plasticity of neural neural networks[3]. Plasticity changes in the brain occur at different times after stroke, so that there is still a recovery of the damaged function to varying degrees during the post-stroke treatment. Brain plasticity includes both structural plasticity in terms of synaptic and neuronal recommunication and functional plasticity in terms of functional improvement after different rehabilitation treatments. Acupuncture can stimulate the increase of nerve excitability, promote brain plasticity, achieve tissue and function reorganisation, and further restore normal motor function. It has been found that[4], electroacupuncture of Quchi and Yanglingquan points can elevate the content of synaptophysin and post-synaptic density protein-95 in the brain, indicating that acupuncture can promote the remodelling of synapses, improve the efficiency of synaptic transmission, and promote the recirculation of nerves, which in turn participates in the restoration of the motor function. And some studies have found[5] that electroacupuncture stimulation can regulate the level of brain-derived neurotrophic factor, thus promoting nerve cell and axon growth and further accelerating the recovery process of patients' motor function.

After stroke, brain tissue undergoes a series of pathological changes such as ischaemia and necrosis in the corresponding

areas due to bleeding or hemodynamic changes. Therefore, cerebrovascular microcirculation can be improved by improving blood rheology, reducing blood circulation resistance and other ways to correct cerebral tissue ischemia and hypoxia and then achieve the purpose of promoting cerebral neuron remodelling. In recent years, more and more studies have confirmed the efficacy of acupuncture in stroke[6], acupuncture treatment can improve cerebral blood circulation by lowering blood viscosity, improving cerebrovascular elasticity, and promoting the establishment of vascular collateral circulation in order to reduce cerebrovascular blood circulation resistance, thus improving cerebral blood circulation. Wang Ying et al. [7] found that acupuncture on rats with ischemic stroke by using the method of collateral stabbing at the points of "Fengfu" and "Mute Gate" not only has the effect of dredging meridians and activating collaterals, but also significantly increases the microcirculatory blood flow of the cerebral periaqueductum of the rats and significantly reduces blood viscosity, suggesting that collateral stabbing can reduce blood viscosity by improving the elasticity of the cerebral blood vessels and promoting the establishment of vascular collateral circulation, thus improving the blood circulation of the brain. This suggests that the method can improve the cerebral microcirculation and reduce the damage to the brain tissue caused by cerebral microcirculation due to stroke. Zhang Shengyu et al. [8] used a combination of acupuncture and hyperbaric oxygen in the treatment of patients with ischemic-hypoxic encephalopathy, and the results showed that the whole blood viscosity and erythrocyte aggregation index could be significantly reduced after the treatment to improve the cerebral blood rheology of the patients, which further confirmed the positive effect of acupuncture on neuronal recirculation.

Meanwhile, the degree of neuronal damage in the brain is closely related to the occurrence of cerebral oedema. After stroke, the blood brain barrier (BBB) is damaged and the BBB permeability is increased, which in turn leads to the occurrence of cerebral oedema. It has been found that[9], electroacupuncture at Shuigou acupoint can reduce the level of aquaporins (AQP4) in the brain tissue of rats with MCAO model, regulate BBB permeability, reduce cerebral oedema, and help to create a suitable environment for the remodelling and regeneration of synapses and neurons, protect and promote neuronal reorganization, and promote the recovery of the corresponding neurological functions.

3. The Inhibition of Spinal Motor Neuron Excitability

After stroke, upper motor neurons are damaged, and the inhibitory effect on spinal anterior horn motor neurons is completely or partially lost. An intact neural pathway is the basis for normal skeletal muscle tone expression, and spinal anterior horn motor neurons are the final guarantee that brain neuron impulses reach the skeletal muscle. Elevated excitability of spinal motoneurons is also closely related to enhanced detachment reflexes, including the dystonic and tendon reflexes. Muscle tone is maintained by the joint regulation of α and γ motor neurons. After stroke, γ motor neurons dominate, causing hyperactivity of the detachment reflex, which in turn increases muscle tone to a state of spasm, ultimately leading to the occurrence of foot drop. Acupuncture treatment can reduce the excitability of α-motor neurons and regulate the normal nerve impulse conduction in patients with foot drop after stroke, so as to achieve the purpose of lowering muscle tone and improving foot drop, thus gradually restoring the walking ability of patients. Studies have shown that[10], the use of acupuncture with rehabilitation training combined therapy for the treatment of post-stroke spastic hemiplegia, indicating that the reduction of muscle tone can significantly improve the abnormal gait, and improve the walking ability of patients.

With the development of medical technology, electromyography can be widely used in analysing and evaluating neuromuscular function. By recording and analysing neuromuscular electrical activity, EMG can objectively evaluate the degree of muscle spasm and provide a quantitative and objective basis for the spastic muscles associated with foot drop after stroke, and F wave, H-reflex, and MAS score are often used to evaluate the efficacy of the therapy. H-reflex can be used to determine the excitability of alpha motor neurons and the integrity of the neural pathway, which can indirectly reflect the degree of damage to the upper motor neurons[11]. The Hmax/Mmax The Hmax/Mmax ratio indicates spinal motor neuron excitability in spasticity, and Hmax/Mmax is significantly higher in the affected limb than in the healthy limb in stroke patients[12]. Sun Fan et al. [13] found that the combination of acupuncture and rehabilitation training at the pinched spine points could prolong the latency of the H-reflex and decrease the Hmax/Mmax ratio, suggesting that the combination of acupuncture and rehabilitation training could improve spasticity in post-stroke patients. Fan Liubo et al. [14] used ziwu liu jin and jiushun method of acupuncture to treat Hmax/Mmax significantly lower than the control group, indicating that ziwu liu jin and jiushun method is more conducive to stimulate the meridian qi and inhibit the abnormal excitation of α-motor neurons, thus relieving spasticity muscle muscle tone, and improving the ability of daily walking. Wang Fei et al. [15] observed the EMG changes before and after acupuncture treatment with different lengths of needling, and found that leaving the needle for 30 min was more advantageous than the two groups in prolonging the latency of H-reflex, and it could stimulate the active contraction of antagonist muscle against spasticity muscle, further regulate the abnormal nerve impulses, and improve the degree of foot prolapse. The above study not only confirmed the correlation between spinal motor neuron excitability and foot drop after stroke, but also proposed a more standardised acupuncture protocol from the perspectives of acupuncture technique and needle retention time.

4. The Modulation of Spasticity-related Transmitters

The dynamic balance of amino acid neurotransmitters in the central nervous system is essential for signal processing. Amino acid neurotransmitters can be classified into excitatory and inhibitory neurotransmitters, which are involved in the regulation of cerebral nerve injury and spasticity, respectively. Glutamic acid (Glu) is one of the important excitatory neurotransmitters in the central nervous system, and it is the amino acid with the highest concentration in the brain, which is mainly stored in axon terminals[16]. After stroke, the level

of Glu in the brain and spinal cord increases, and the level of Glu is positively correlated with the degree of nerve damage, and its excitotoxicity can cause the triceps muscle to be in a spastic state, which can lead to the occurrence of foot drop. γ-aminobutyrate (GABA) is an inhibitory neurotransmitter that is widely distributed in the CNS and is closely related to the increase of muscle tension caused by the injury of motor neurons. It is closely related to the elevated muscle tone resulting from motor neuron injury. After stroke, the levels of many neurotransmitters are altered, and the dynamic balance between inhibitory and excitatory neurotransmitters is disrupted, resulting in hyperexcitatory transmission, which is an important cause of limb spasms after stroke.

The transport of Glu in brain cells is mainly provided by Na+/K+-ATPase to provide a suitable electrochemical gradient environment, which enables EAATs to transport Glu to the outside of the cell. After stroke, the inability of Glu to be transported smoothly leads to an increase in the activation of Glu receptors, which puts the muscles in a state of spasm. Some studies have shown[17] that acupuncture can significantly increase the expression of Na+/K+-ATPase and EAATs analogues in hippocampal tissues on the focal side of cerebral ischemic rats and decrease the expression of Glu, while the muscle tone of rats is significantly reduced, indicating that acupuncture treatment regulates Na+/K+-ATPase and EAATs in the hippocampal area of the ischemic side is one of the keys to reduce the muscle tone, while at the same time protects the nerve cells. Foot drop after stroke is mainly due to the spasm of the triceps muscle, which belongs to the category of "tendon disease". According to the medical book "Bianjie Shenying Acupuncture and Moxibustion Yulongjing", "Yanglingquan is used to treat tendon disease, hemiplegia, waist, legs, knees and feet", indicating that Yanglingquan has a special efficacy in treating limb dysfunction after stroke. Modern research has found that[18], acupuncture Yanglingquan can improve the expression of inhibitory neurotransmitters by regulating the function of GABA receptors and the expression of related genes and proteins, and at the same time, promote the remodelling of neural synapses in the damaged brain tissues, which can in turn alleviate the spasticity of the triceps muscle of the calf. There is also a study[19], by observing the changes of Glu and GABA content in the cerebral cortex of rats in spasticity state of electroacupuncture stroke, it was found that electroacupuncture can reduce Glu and increase GABA, which indicates that acupuncture can play a synergistic effect by stimulating different receptors, thus regulating the dynamic balance of excitatory and inhibitory neurotransmitters, inhibiting abnormal impulse conduction, and thus lowering the muscle tension. The above study, centred on the expression of neurotransmitters, further reveals the mechanism of action of acupuncture in improving foot drop, indicating that acupuncture can reduce the expression of excitatory neurotransmitters, and at the same time increase the expression of inhibitory neurotransmitters, exerting the synergistic effect of acupuncture and facilitating the improvement of the symptoms of foot drop.

5. Regulation of Active and Antagonist Muscle Tone Balance

Stroke patients are often bedridden for a long time due to limb dysfunction, and their lower limbs are braked for a long time after being in the extensor mode, so there is a reduction of muscle volume and connective tissue adhesion on top of the increase in muscle tone, which further causes muscle wasting atrophy. Therefore, in stroke patients, while reducing muscle tone, attention should be paid to the stimulation of the antagonist muscles, so that the dorsiflexors and plantarflexors can reach a balance, and promote the production of detachment movements and the establishment of a normal movement pattern, in order to restore the ability of daily walking. Strengthening the stimulation of the antagonist muscles can increase the proprioceptive input, promote the reconstruction of the cerebral cortex function, accelerate the production of detachment movements and establish normal movement patterns. Gu Tao et al. [20] used electroacupuncture to stimulate the tibialis anterior muscle to treat patients with foot drop after stroke, and the results showed that electroacupuncture improves ankle dorsiflexion by stimulating the contraction of the tibialis anterior muscle and pulling the triceps of the calf, and at the same time, the patient's gait stability is significantly improved. The results showed that the stimulation of tibialis anterior muscle movement could excite the cerebral cortex, enhance the training of ankle dorsiflexion movement, and induce detachment movement, as well as increase the input of proprioceptive stimulation.

Tension Balancing Acupuncture[21] is a method of acupuncture used by Prof Zhang Wei for post-stroke spasticity. In the treatment of foot drop, according to the disease mechanism of yin and yang imbalance, strong stimulation is targeted at the tibialis anterior muscle, and then weak stimulation is targeted at the calf triceps muscle. On the one hand, pulling the calf triceps muscle reduces muscle tension, realises the rebalancing of muscle strength and muscle tension between the antagonist and active muscles, and induces the generation of detached movement, in order to alleviate the spasm of the calf triceps and improve the muscle strength of the tibialis anterior muscle;on the other hand, the stimulation of peri-muscle proprioceptors strengthens the stimulation to the central nerves, and promotes the remodeling of central neurons as well as the restoration of proprioception[22]. There is also a study[23] that used tension balancing acupuncture to treat patients with foot drop after stroke, and the results showed that muscle tone, degree of foot inversion, and lower limb motor function improved after treatment, which further confirmed the positive effect of regulating the balance between active and antagonist muscles in the treatment of foot drop.

5. 1 The Rest

The development of foot drop after stroke is closely related to structural changes in the surrounding tissues in addition to spasticity of the calf triceps[24]. Stroke patients are often bedridden for prolonged periods of time, which in turn leads to pathological changes in muscle, tendon and joint tissues such as decreased muscle volume and collagen deposition, which further aggravate the spastic state. Some studies have shown that the earliest observed adaptive changes in muscle tissue structure begin 4h after cerebral infarction[25]. It was found[26] that chronic strain injury can stimulate the accumulation of collagen fibres in skeletal muscle, and

acupuncture treatment can delay or inhibit the accumulation of collagen fibres in skeletal muscle, and reduce the expression of TGF-β1, the initiating factor of skeletal muscle fibrosis, suggesting that acupuncture may or may not be able to inhibit the TGF-β1/CTGF pathway in order to inhibit the effect of skeletal muscle fibrosis.

The treatment of stroke patients should be intervened as early as possible after the condition is stabilised, however, the post-stroke period can be divided into different stages according to the duration of the onset of the disease, and the paralysis status of the patient changes from soft to hard paralysis due to the development of the disease, so the acupuncture points should be selected according to the characteristics of the different stages during acupuncture treatment[27].

5. 2 Short

The incidence of stroke in China is still high, and the long-term walking disability after stroke due to foot drop reduces the quality of patients' survival and brings a heavy financial burden to families. Therefore, restoring patients' daily walking ability is the centre of stroke patients' rehabilitation. In recent years, there has been some progress in the study of acupuncture treatment of foot drop after stroke, but its mechanism has not been clarified. Acupuncture therapy has the characteristics of multi-targets and multi-pathways, and this review aims to reveal the mechanism of acupuncture in treating foot drop after stroke by promoting the recovery of upper motor neurons, inhibiting the excitability of spinal motor neurons, regulating spasticity-related transmitters, and regulating the balance of muscle tone between the active and antagonist muscles, which is of great significance to the modernisation of the therapeutic means of traditional Chinese medicine. In future studies, we can conduct in-depth research based on both central and peripheral dimensions to explore more appropriate stimulation modes and stimulation amounts, and to develop the best acupuncture treatment plan for post-stroke foot drop in clinical practice.

References

[1] Yu Chuanhua, Luo Lisha, Li Mei, et al. The severity of the disease burden of stroke in China from a global perspective[J]. Journal of Public Health and Preventive Medicine, 2016, 27(1): 1-5.

[2] Dong Liangle, Li Zuowei. Recent research on acupuncture treatment of post-stroke spastic paralysis[J]. Traditional Chinese Medicine Rehabilitation, 2022, 13(15): 65-72.

[3] Qi Yujun, Shen Juan. Observation on the efficacy of acupuncture combined with rehabilitation training in treating foot drop after stroke[J]. China Acupuncture & Moxibustion , 2016, 36(07):679-682.

[4] Guo Bin, Wang Penghan, Huang Linheng, et al. Experimental study of electroacupuncture "Quchi"-"Yanglingquan" to alleviate synaptic structural plasticity in spastic state of stroke rats[J]. Chinese Journal of Rehabilitation Medicine, 2020, 35(7):787-793.

[5] Tang Yizhou, Liu Yue, Tang Yihe, et al. The efficacy of Qisheng electroacupuncture Cheng's Yunshen acupoint area to improve limb motor function in patients with post-stroke phase and its effect on serum BDNF and PDGF[J]. Journal of Acupuncture and Moxibustion, 2021, 37(11): 40-45.

[6] Tan H. Acupuncture treatment of 122 cases of post-stroke sequelae[J]. Chinese Medicine Modern Distance Education of China, 2010, 8(10):35-36.

[7] Wang Ying, Zhang Xianbao, Xiao Wei, et al. Effects of the Xiangcong prick-acupuncture method on cerebral microcirculation disorders in rats with ischaemic stroke[J]. Acupuncture Research, 2013, 38(03):220-223.

[8] Zhang Shengyu, Liu Shengbing, Xie Hongwu, et al. Effect of waking up the brain and opening up the mind acupuncture method combined with hyperbaric oxygen on haemorheology of patients with ischemic hypoxic encephalopathy[J]. Acupuncture Research, 2017, 42(06):518-521.

[9] Tian Jiancai, Yao Fei, Xie Fangfang, et al. Protective effect of electroacupuncture at Shuigou acupoint on the neurovascular unit of rats with ischaemic stroke[J]. Chinese Journal of Traditional Chinese Medicine, 2021, 36(7): 4212-4215.

[10] Qiu Lin, Liu Yanchun. Observation on the efficacy of acupuncture with rehabilitation training in treating spastic hemiplegia after stroke[J]. Henan Traditional Chinese Medicine, 2014, 34(09):1827-1828.

[11] Mezzarane R A, Nakajima T, Zehr E P. After stroke bidirectional modulation of soleus stretch reflex amplitude emerges during rhythmic arm cycling [J]. Frontiers in Human Neuroscience, 2014, 8(3):1-9.

[12] Kim J K, Jha N N, Feng Z H, et al. Muscle-specific SMN reduction reveals motor neuron-independent disease in spinal muscular atrophy model [J]. J Clin Invest, 2020, 130(3):1271-1287.

[13] Sun Fan, Xu Shouyu, Xie Guangyao, et al. Effect of acupuncture pinch point combined with rehabilitation training on lower limb H-reflex in stroke patients[J]. Zhejiang Journal of Traditional Chinese Medicine, 2014, 49(04):280-281.

[14] Fan Liubo, Tian Ying, Li Xiaojun, et al. Evaluation of the intervention effect of ziwu liu jiqi giant stabbing method on post-stroke myospasm based on sEMG[J]. Shanghai Journal of Acupuncture and Moxibustion, 2019, 38(04):399-403.

[15] Wang Fei, Wang Minji. Influence of different time of acupuncture on the therapeutic effect of patients with lower limb spasticity in stroke[J]. Liaoning Journal of Traditional Chinese Medicine, 2018, 45(1):144-147.

[16] Mayor D, Tymianski M. Neurotransmitters in the mediation of cerebral ischemic injury[J]. Neuropharmacology, 2018, 134(Pt B):178-188.

[17] Qian Xu, Ma Liangyao, Mu Jiedan, et al. Exploring the central mechanism of acupuncture for post-stroke spasticity based on the Na~+/K~+-ATPase-glutamate transporter-glutamate pathway[J]. Acupuncture Research, 2022, 47(04):283-289+320.

[18] Chen Chen, Wang Yahui, Wang Liping, et al. Progress of clinical application and mechanism of Yanglingquan acupoint in the treatment of hemiplegia in stroke[J]. Beijing Journal of Traditional Chinese Medicine, 2021, 40(06):666-669.

[19] Guo Bin, Yue Zenghui, Xie Zhiqiang, et al. Effects of electroacupuncture on the expression of both glutamate and γ-aminobutyric acid receptors in the cerebral cortex of rats in spastic state of stroke[J]. Chinese Journal of Traditional Chinese Medicine and Pharmacy, 2019, 34(01):325-327.
[20] Gu Tao, Hou Dianrui, Li Changzheng, et al. Effects of rehabilitation therapy centred on electroacupuncture antagonising muscle motor points on lower limb function and gait stability in patients with foot drop after stroke[J]. Chinese Journal of Integrative Medicine on Cardi-Cerebrovascular Disease, 2020, 18(16):2701-2704.
[21] Zhang Wei. Application of tension balance acupuncture in the rehabilitation of hemiplegia in stroke[J]. Chinese Journal of Clinicians, 2004, (06):38-40.
[22] Li Feiqin. Clinical efficacy observation of tension balance acupuncture in treating foot drop after stroke [D]. Fujian University of Traditional Chinese Medicine, 2020.
[23] Tang Jiejie, Chen Xiaokui, Huang Bin, et al. Effects of tension-balancing acupuncture combined with electroacupuncture on lower limb function and daily living ability in stroke patients with foot drop[J]. Journal of Clinical Acupuncture and Moxibustion, 2020, 36(01):40-43.
[24] Wu Xiaoyan, Lv Junling, Jin Rongjiang. Reflex-mediated and non-reflex-mediated mechanisms of post-stroke spasticity[J]. Chinese Journal of Rehabilitation Medicine, 2021, 36(01):124-127.
[25] Arasaki K, Igarashi O, Machida T, et al. Reduction in the motor unit number estimate (MUNE) after cerebral infarction[J]. Suppl Clin Neurophysiol, 2009, 60:189-195.
[26] Lei Benkai, Zhao Shuo, Xu Tao, et al. Role of TGF-β1/ERK/CTGF pathway in acupuncture intervention for exercise-induced skeletal muscle fibrosis[J]. Acupuncture Research, 2021, 46(04): 306-311.
[27] Chen Yong, Zhou Hai, Jin Tingting, et al. Observation on clinical efficacy of staged acupuncture method in treating hemiplegic patients with ischaemic stroke[J]. Chinese Acupuncture & Moxibustion, 2018, 38(10):1027-1034.