

# *The Mechanism of Acupuncture in Patients with Sleep Disorders after Stroke*

Qiuyu Li<sup>1</sup>, Ximei Xie<sup>2,\*</sup>

<sup>1</sup>*School of Acupuncture and Tuina, Shaanxi University of Traditional Chinese Medicine, Xianyang 712046, China*

<sup>2</sup>*Department of Acupuncture and Tuina, Xi'an City hospital of Traditional Chinese Medicine, Xi'an 710021, China*

\*Corresponding author: xiximei0830@126.com

**Keywords:** Sleep disorder after stroke, Acupuncture, Sleep-wake functional area, Cerebral blood flow, Neurotransmitters, Cytokines, Melatonin, Review.

**Abstract:** To discuss the mechanism of acupuncture in the treatment of sleep disorder after stroke in recent years. Comprehensive literatuer found that acupuncture treatment of sleep disorder after stroke are mainly concentrated in relive sleep-wake function area of the damage, improve cerebral blood flow perfusion, adjust the neurotransmitter release, adjust the levels of inflammatory cytokines and so on ways to improve the symptoms of sleep disorder after stroke, promote the patient recover. This paper reviews and analyzes the literature on the treatment of post-apoplexy sleep disorders by acupuncture, in order to provide theoretical basis and reference for the majority of medical staff in the clinical treatment of post-apoplexy sleep disorders by acupuncture, and promote the development of acupuncture therapy in the field of post-apoplexy sleep disorders.

## 1. Introduction

In recent years, post-stroke sleep disorder has become one of the common complications of acute stroke. The clinical manifestations are excessive sleep, insomnia, heterogeneous sleep, sleep cycle disorder and other types. It not only affects the quality of life of patients, but also hinders the recovery of patients' neural function<sup>[1]</sup>. Western medicine treatment of sleep disorders after stroke is mainly anti-insomnia drugs. Most patients have good short-term efficacy, but some patients do not have a long-term effect is not obvious, and there are drug dependence, drug side effects and other disadvantages. Some scholars<sup>[2]</sup> believe that sleep disorders after stroke may be stroke damage to sleep-related brain structure, resulting in reduced brain blood flow and slow blood flow rate, It leads regulates the secretion of central nervous transmitters and a non-specific inflammatory response. In addition, sleep disorders after stroke may also be related to reduced melatonin secretion, emotional depression, psychological and social environment. A large number of clinical practices have proved that<sup>[3]</sup>: acupuncture treatment of sleep disorders after stroke is significantly effective, easy to operate, and has no toxic side effects, which can be used as an important way for the treatment of sleep disorders after stroke in traditional Chinese medicine. The mechanism and effects of acupuncture on

sleep disorder after stroke are summarized as follows:

## 2. Effects of orthoacupuncture treatment on sleep-wake function

Normal sleep-wake function is primarily associated with the thalamus, circadian rhythms, and neurotransmitters. Areas of sleep-wake function in the brain, such as the hypothalamus, basal ganglia, and the inferior frontal lobe, may be impaired after stroke<sup>[4]</sup>. Among them, the thalamus is the regulatory center of bipolar sleep-wake, and its damage may cause various sleep-wake disorders and circadian disorders<sup>[5]</sup>. After stroke, the sleep-awakening function area in the body is damaged, and a large number of free radicals are generated in the brain, causing lipid peroxidation to further damage the brain tissue. In addition, the intracellular Ca<sup>2+</sup> balance is unbalanced after stroke, and the intracellular Ca<sup>2+</sup> overload can also cause brain damage wound. Ma Yuxia et al<sup>[6]</sup> found that points such as acupuncture and Guan could quickly adjust the Ca<sup>2+</sup> content in neurons in the CA1 region of the hippocampus after ischemia / reperfusion, inhibit intracellular calcium overload and maintain calcium homeostasis. Lin Ruirong<sup>[7]</sup> found that acupuncture Baihui point can significantly improve the glucose uptake of the hypothalamus, pituitary and other brain areas in the middle cerebral arteries, improve the glucose metabolism in the thalamus, accelerate the energy conversion caused by thalamic tissue nerve cells, thus promoting the recovery of thalamic nerve tissue. This may be related to the ability of acupuncture to reduce damage in sleep-wake function areas, protect brain cells, and repair neural function.

## 3. Effect of acupuncture treatment on cerebral blood flow reperfusion

The brain conducts the precise control of the brain blood flow through the cerebral blood flow regulation function, to maintain the dynamic balance of the brain metabolism, and to support the brain homeostasis and the execution of the function<sup>[8]</sup>. Studies have shown that<sup>[9]</sup>: stroke patients may reduce cerebral blood flow, blood flow speed, and blood volume during sleep, causing rapid eye movement sleep that requires increased blood flow and metabolism to produce sleep disorders. Needle therapy has a certain curative effect in patients with sleep disorders after stroke, which can improve the low perfusion symptoms of cerebral blood flow, increase the cerebral blood flow, promote nerve cell repair and stem cell proliferation, and accelerate the repair of nerve damage. Li Shichen et al<sup>[10]</sup> research shows that: acupuncture therapy can be Accelerate the blood flow rate of ischemic stroke patients, and improve the cerebral blood flow circulation of patients. Ma Mei et al<sup>[11]</sup> believe that acupuncture and cong can reduce endothelin levels, reduce blood pressure, relieve cerebral vascular tension; acupuncture clearance can improve cardiac output, improve blood flow speed, inhibit thrombosis. This may be related to the ability to promote cerebral vasodilation, increase cerebral blood flow, and improve cerebral blood circulation after acupuncture.

## 4. Effects of acupuncture treatment on neurotransmitter secretion

The metabolites of monoamine neurotransmitters accurately regulate the nervous system and the cardiovascular system, and play a very important role in the physiological activities of sleep<sup>[12]</sup>. Neurological tissue damage after stroke, leading to the secretion of monoamine neurotransmitters, mainly including serotonin (5-HT), norepinephrine (NE) and dopamine (DA), and 5-HT, NE, DA are also the main neurotransmitters related to sleep-awakening function, its metabolism disorder can cause further aggravation of brain injury, is one of the important mechanisms leading to sleep disorders after stroke. 5-HT is the nerve involved in the regulation of neural function The transmitter, a sleeping factor, whose levels can induce rapid entry into sleep<sup>[13]</sup>. NE acts on the relevant receptors in regulating arousal and mental activities. DA promotes arousal and behavioral excitation, and its

reduced levels can reduce the number of arousal and improve sleep quality in [14-15]. Song Shuling et al [16] found that after the use of ear acupoint pressure combined with acupuncture and cong, the serum 5-HT level was significantly increased and the DA level was significantly reduced. Miao Wenli et al [17] found that acupuncture can restrict dopamine production and increase norepinephrine production, and thus carry on brain tissue protect. Ou Xiang, Xu Bin et al. [18-19] reported that when the content of monoamine neurotransmitters (NE, DA) in the rat ischemic brain tissue is significantly increased, the electric needle can significantly reduce the content of monoamine neurotransmitters in the ischemic brain tissue, and can also effectively regulate the disorder of monoamine neurotransmitters in the process of cerebral ischemia and reperfusion. This may be related to the effective regulation of neurotransmitter secretion after stroke and significantly improving sleep quality after acupuncture.

## 5. Effect of acupuncture on inflammatory cytokines

Inflammatory cytokines (interleukin (IL), tumor necrosis factor (TNF-)), as the important cytokines of immune regulation, play an important role in the activation, differentiation and other processes of immune cells, with pro-inflammatory and anti-inflammatory characteristics [20]. After stroke, the inflammatory molecules of ischemic and damaged brain tissue activate infiltrating immune cells, trigger sterile inflammatory responses, and activate a variety of immune cells (neutrophils, macrophages, and lymphocytes) through a series of inflammatory mechanisms, transforming their function from inflammation to repair [21]. Experiments confirmed [22-23], pro-inflammatory cytokines IL-1, IL -6, The level of TNF-and upregulation of the anti-inflammatory cytokine IL-10 could alleviate the volume and improved neural functional outcome of cerebral infarction in tMCAO rats. Wang Jinhai et al [24] gave rapid puncture treatment with bilateral "anterior oblique" in the head needle of cerebral ischemia model, which found that IL-6, IL-1 expression, IL-10 were significantly increased and the volume of cerebral infarction decreased. This may be related to acupuncture improving the collateral circulation of cerebral infarct areas and regulating the levels of inflammatory cytokines to alleviate the inflammatory response after cerebral infarction.

## 6. Effect of acupuncture treatment on melatonin levels and sleep-wake rhythm

Melatonin (MT) is an indole hormone secreted by the pineal gland, which changes in low day and high night in the body endocrine [25-26]. It has been shown that this specific circadian change in melatonin can change the sleep-wake circadian rhythms in a time-dependent manner and thus affect the human sleep cycle [27]. Other studies have shown that melatonin regulates sleep mainly through its interaction with melatonin receptor 1a (MT1) and melatonin receptor 1b (MT2) to regulate sleep disorders, restore circadian rhythm, and improve sleep quality [28]. After a stroke, insufficient melatonin secretion causes circadian disturbances leading to sleep Sleep Disorder [29]. The study of Yao Haijiang et al [30] found that the serum level of melatonin in the model rats increased significantly after electroacupuncture. Liu Zhen et al [31] found that the electric needle can significantly change the sleep-wake circadian rhythm disorder in insomnia rats, which is consistent with the level of melatonin changes in the serum of rats after acupuncture. This may be related to acupuncture regulating melatonin levels and protecting the central nervous system. In addition, Sherina et al [32] research showed that after the acupuncture insomnia rat model of Baihui, Shenmu, Sanyang intersection and other acupoints, MT was contained in the ventrolateral hypothalamus of the insomnia rat Quantity and MT1 and MT2 m RNA expression were significantly increased. It shows that the efficacy of acupuncture for insomnia is exact, and the mechanism of improving sleep may be realized by regulating MT content and MT1 and MT2 mRNA expression in the ventrolateral hypothalamus of insomnia rats.

## 7. Brief summary

Needle is the characteristic treatment of traditional Chinese medicine treatment, and stroke is the advantageous disease of acupuncture treatment, and its curative effect is certain. Needle treatment can protect and repair the ischemic brain tissue after stroke from multiple aspects. This paper provides ideas and objective theoretical basis for acupuncture for treatment of sleep disorders after stroke. However, the mechanism of acupuncture for sleep disorders after stroke remains to be deeply studied.

## Acknowledgements

**Fund Project:** This project is funded by Shaanxi Natural Science Foundation (NO: 2020JM-699); Shaanxi University of TCM Project (NO: 2020FS04); Xi'an Health Commission Project (NO: 2020yb26); Xi'an TCM Hospital Project (NO: YJ201941); Key Specialty of Traditional Chinese Medicine, Shaanxi Administration of TCM Development (2012) No.55, etc.

First author: Li Qiuyu (1995-), female, master student, E-mail: 3111822861@qq.com.

\*Corresponding author: Xie Ximei (1978-), female MD, deputy chief physician, master tutor. Research direction: Research on acupuncture and treatment of geriatric diseases and immune system diseases. E-mail: xieximei0830@126.com

## References

- [1] Wang Jie, Chen Xingsheng. *Progress in acupuncture treatment for sleep disorders after stroke [J]. Guangxi Traditional Chinese Medicine*, 2015, 06: 8-10
- [2] Jiao JiuCun. *Clinical observation of 80 cases with insomnia in sputum heat and internal insomnia after cerebral infarction [J]. Hebei Traditional Chinese Medicine*, 2015, 37 (1): 44-45
- [3] Hu Zhen, Ni Guangxia. *Overview of acupuncture treatment for sleep disorders after stroke [J]. Journal of Traditional Chinese Medicine*, 2016,44 (3): 78-81
- [4] Hu Zhen, Ni Guangxia. *Overview of the mechanism of acupuncture for sleep disorders after stroke [J]. Journal of Traditional Chinese Medicine*, 2016,11: 975-978.
- [5] Shao Bin, Huang Kaiye, Wang Jianbin, et al. *Effect of acupuncture on daytime function in patients with sleep-wake disorder after stroke: a randomized controlled trial (English) [J / OL]. World Journal of Acupuncture-Moxibustion: 1-10 [2021-03-22]. <http://kns.cnki.net/kcms/detail/11.2892.R.20210306.1334.002.html>.*
- [6] Ma Yuxia, Wang Shu, Shi Xuemin. *Electrical modulation of L type calcium channels in the CA1 region of rat hippocampus after cerebral ischemia / reperfusion injury [J]. Shandong Journal of Traditional Chinese Medicine*, 2007,26 (6): 407-409.
- [7] Lin Ruirong. *Electric needle and magic lamp imaging aged small animals Effects on learning and memory function in cerebral ischemia / reperfusion rats. Fuzhou: Journal of Fujian University (Medical edition) 2017; 1-102.*
- [8] Wang A, Ortega-Gutierrez S, Petersen NH. *Autoregulation in the Neuro ICU [J]. Curr Treat Options Neuroly*, 2018, 20(6): 20.
- [9] Wang Xing, Zheng Meisheng, Chen Xiaojing, et al. *Analysis of related factors of cerebral infarction sleep disorder in the basal nuclear region [J]. Journal of Integrated Traditional Chinese and Western Medicine Cardiovascular and cerebrovascular Diseases*, 2007,5 (9): 907-908.
- [10] Li Shichen, Zhang Lei, Dou Feng Quan. *Effect of head acupuncture combined with Western medicine in acute ischemic cerebral infarction [J]. Chinese TCM Emergency*, 2016,25 (4): 732-734.
- [11] Ma Mei, Xu Yan. *Efficacy of acupuncture and acupuncture on convalescent ischemic stroke and its effect on ET-1 and CGRP levels [J]. Chinese Journal of Modern Medicine*, 2015,25 (30): 57-61.
- [12] Julie, Cheung, Lee Tlin. *Effect of spiaddition on learning and memory and hippocampal monoamine neurotransmitters in sleep deprived rats [J]. Chinese Journal of Experimental Medicine*, 2012,18: 219-222.
- [13] Wu Xuefen, Zheng Xuena, Guo Xin, et al. *Progress in the effect of acupuncture on 5-HT, and its receptor, and HPA axis-related hormones in insomnia rats [J]. Chinese Chinese Medicine Journal*, 2018,19 (1): 91-92.
- [14] Zhou Yanli. *Experimental study on the effect of different acupoints of acupuncture points on neurotransmitters 5-HT and DA in insomnia model rats [J]. Chinese Journal of Basic Medicine of Traditional Chinese Medicine*, 2012,12 (8): 81-82.
- [15] Li Mei, Hu Linlin, Zhang Yonghua. *Combined with Zopillone to treat anxiety insomnia and effects on serotonin and dopamine levels [J]. Chinese Journal of Experimental Formulology*, 2015,21 (17): 161-162.

- [16] Song Shuling, Zhou Xiangjuan, Zheng Liqiang. Effect of ear hole compression combined with acupuncture on sleep quality and neurotransmitters in patients with sleep disorders after stroke [J]. *Journal of Modern Integrated Traditional Chinese and Western Medicine*, 2021,30 (03): 290-293.
- [17] Miao Wenli, Gao Weibin. Effects of acupuncture on monoamine neurotransmitters and related neurological disorders [J]. *Clinical Journal of Acupuncture*, 2008,24 (12): 47-48.
- [18] Ou Xiang, Yuan Hong. Immunomodulatory effect of acupuncture therapy on stroke [J]. *Needle study*, 2005,30 (2): 125-127.
- [19] Xu Bin, Lu Renyun, Ni Guangxia, et al. Effect of electricity targeting monoamine transmitters and their metabolites in the rat striatal thalamus with cerebral ischemia and reperfusion [J]. *Chinese Journal of Chinese Medicine*, 2001,8 (8): 27-28.
- [20] Zhu Hua, Tao Wuxian, Xiong Xiaoxing. The anti-inflammatory effect of interleukin in ischemic stroke and its mechanism [J]. *Medical Review*, 2020,26 (20): 3976-3980 + 3986.
- [21] Nakamura K, Shichita T. Cellular and molecular mechanisms of sterile inflammation in ischaemic stroke [J]. *J Biochem*, 2019,165(6): 459-464.
- [22] Mizuma A, Yenari MA. Anti-inflammatory drugs used to treat stroke reperfusion injury. *Frontier Neuroscience*, 2017, 8: 467.
- [23] Protti GG, Gagliardi RJ, Forte WC, et al. Interleukin-10 can prevent progressive injury in the acute phase of ischemic stroke. *Arq Neuropsiquiatr*, 2013, 71: 846-851.
- [24] Wang Jinhai, Zhang Tingzhuo, Li Xinglan, et al. Effect of acupoint acupuncture on cytokine expression and cerebral infarction volume related to parahippocampal inflammatory response in rats with focal cerebral palsy. *Needle study*, 2019,44 (6): 405-411.
- [25] Zhao Chaoying, Wu Xumin, Yao Xiaoman, et al. MLT for Sleep Improvement Trial Study [J]. *Chinese Journal of Food Sanitation*, 1998, (5): 11-12.
- [26] Zhang Lianlong, Zhang Qingzhu, Zhang Jintian, et al. Progress in melatonin prevention and treatment of geriatric-related diseases [J]. *Chinese Journal of Gerontology*, 2001, (5): 397-399.
- [27] Gao Yundong, Geng Jinrong. Progress in clinical research on melatonin. *Chinese Journal of Hospital Pharmacy*, 2001, (3): 173-174.
- [28] Lewy AJ, Ahmed S, Jackson JM, et al. Melatonin shifts human circadian rhythms according to a phase-response curve [J]. *Chronobiol Int*, 1992,9(5):380-392.
- [29] Guo Jinliang, Wang Danni, Ni Yan, et al. Progress of TCM research on sleep improvement based on melatonin synthesis and secretion [J/OL]. *Chinese Journal of Traditional Chinese Medicine*: 1-10 [2021-03-28]. <http://kns.cnki.net/kcms/detail/21.1546.r.20201106.1518.004.html>.
- [30] Yao Haijiang, Song Hongtao, Mo Yuping, et al. Effects of electrical targeting of body temperature and melatonin circadian rhythm in rats with chronic stress-induced depression models [J]. *Chinese Acupuncture*, 2014,34 (7): 685-689.
- [31] Liu Zhen, Zhao Na, Xie Chen, et al. Effect of electricity on sleep-wake circadian rhythms and melatonin rhythms in insomnia rats [J]. *Chinese Journal of Traditional Chinese Medicine*, 2016,31 (9): 3695-3699.
- [32] Sherina, Xie Zhiqiang, Guo Xin, et al. Effect of selected acupoint acupuncture on melatonin content and receptor gene expression in the ventrolateral hypothalamus [J]. *Chinese Journal of Chinese Medicine Information Medicine*, 2018, 25 (12): 40-44.