# Observation on the Efficacy of Acupuncture for Cognitive Function in Patients with Primary Insomnia

Liu Shuangjuan<sup>1,a</sup>, Xie Ximei<sup>1,2,b,\*</sup>

<sup>1</sup>Shaanxi University of Traditional Chinese Medicine, Xianyang, 712000, China <sup>2</sup>Xi'an Hospital of Traditional Chinese Medicine, Xi'an, 710021, China <sup>a</sup>my252501@163.com, <sup>b</sup>xieximei0830@126.com \*Corresponding author

Abstract: In order to observe the effect of acupuncture on cognitive function in patients with primary insomnia, we recruited 32 patients with primary insomnia as the acupuncture group and 30 healthy subjects as the control group. And the acupuncture group were treated with scalp acupuncture combined with body-acupuncture for 3 weeks, 5 times a week, with 2 days' rest. The control group was not intervened before and after treatment. To compare the differences of Pittsburgh Sleep Quality Index (PSQI), Brief Mental State Inventory (MMSE) and Montreal Cognitive Assessment Scale (MoCA) between the two groups. The results show that: (1) Before treatment, the PSQI score of the acupuncture group was higher than that of the control group(P < 0.05), and after treatment, the scores were decreased(P < 0.05); (2) There were differences in MMSE and MoCA scores between the two groups before treatment(P < 0.05), and after acupuncture treatment, the score was significantly advanced(P < 0.05). Ultimately our study suggest that patients with primary insomnia have mild cognitive impairment and acupuncture is effective in the treatment of primary insomnia, which can improve the sleep quality and cognitive function of patients.

Keywords: Primary insomnia; Acupuncture; Cognitive function

## 1. Background

Primary insomnia refers to insomnia caused by excluding drug abuse, mental disorders and other diseases. The clinical manifestations are difficulty in falling asleep, shallow sleep or short sleep frequency, early awakening etc., with the characteristics of recurrent and chronic persistence [1]. Some studies have found that [2,3] with the aggravation of insomnia, patients with insomnia may have a decline in cognitive function such as attention, memory and comprehension, and even increase the risk of dementia or depression. At present, the treatment of insomnia is mainly based on western medicine, but it has many side effects such as drowsiness, drug dependence, metabolic disorders [4], and there is also a lack of specific treatment for concurrent cognitive impairment. On the contrary, acupuncture, as a safe and effective treatment, has been widely used in the treatment of insomnia. Studies have shown that acupuncture has better efficacy, less adverse reactions and high patient compliance compared with western medicine [5]. However, whether it has a positive effect on cognitive dysfunction complicated by insomnia deserves further investigation. Based on this, we elaborates the clinical results of this study observing the effect of acupuncture on cognitive function in patients with primary insomnia as follows.

## 2. Methods

# 2.1 Trial design

From December 2021 to December 2022, 32 patients with primary insomnia were recruited from the Department of Encephalopathy and the Department of Acupuncture and Tuina Rehabilitation, Xi 'an Hospital of Traditional Chinese Medicine, and 30 healthy subjects from the five urban districts of Xi'an were recruited by poster. In the acupuncture group, 2 cases dropped out due to intolerance to acupuncture treatment. Finally, 60 subjects completed this study, and all subjects signed the informed consent. The study protocol has been approved by the Institutional Xi'an Hospital of Traditional Chinese Medicine (No. LLSCPJ2019049). There were no significant differences in gender and age between the two groups (P<0.05), are comparable. (Table 1).

Table 1: Baseline data

Group	Number	Gender		
		male	female	Age(years)( $X \pm s$ )
Acupuncture group	30	16	14	27.43±4.25
control group	30	13	17	26.40±3.27

## 2.2 Patients

## 2.2.1 Inclusion criteria

Patients that met all of the following inclusion criteria were enrolled:(1)The diagnostic criteria of primary insomnia were referred to the American Academy of Sleep Medicine International Classification of Sleep Disorders [6] (3rd edition).(2) referred to the Diagnostic Efficacy Criteria of TCM Diseases and Syndromes [7] issued by the State Administration of Traditional Chinese Medicine.(3)Pittsburgh sleep quality Index (PSQI) > 7 points.4)Be right-handed between 20 and 35 years of age.(4)Can understand the doctor's instructions accurately and have a high degree of compliance with the treatment.(5)Follow the voluntary principle and sign the informed consent.

Inclusion criteria for control group:(1)Be right-handed between 20 and 35 years of age.(2)All subjects had no complaints of insomnia, sleep latency < 30 minutes, and total sleep time > 6.5 hours. And clear language expression, no serious organic lesions and no mental disorders.

## 2.2.2 Exclusion criteria

Those with any of the following conditions will be excluded from the experiment: (1) Persons with other causes of sleep disorders (medications, psychiatric disorders) cannot be excluded. (2) have taken sedative and sleep AIDS, or are receiving other physical therapy.(3)Pregnant and lactating women.(4)Dizziness and severe intolerance to acupuncture treatment.(5)Combined with cardiovascular disease, liver and kidney function and other serious organic lesions.

## 2.2.3 Interventions

Acupuncture group: The acupoint selection and acupuncture operation were strictly referred to the "insomnia" treatment scheme in Acupuncture and Moxibustion [8].(1)acupoint selection:Baihui, Shenmen, Anmian, Zhaohai, Shenmai, Sanyinjiao.(2)Operation of acupuncture:The patient was placed in the supine position, and after routine disinfection with iodarone, a disposable sterile needle .The acupuncture was applied at Baihui (GV 20) for 10-20 mm, Anmian (GV 20) for 15-20 mm, Shenmen (GV 7) for 10-15 mm and Sanyinjiao (SP 6) for 20-25 mm. After deqi, the acupuncture techniques of leveling reinforcing and reducing were applied. After obtaining qi, the reinforcing method and reducing method by twining and rotating were applied respectively. During acupuncture, acupuncture was performed once every 15 minutes, and the needles were retained for 30 minutes. The above acupuncture operations were performed by the same professional acupuncture-moxibustion physician. (3)The treatment course was 5 times a week with 2 days off for 3 weeks. Control group: did not receive any intervention.

## 2.2.4 Outcome assessment

- (1) Pittsburgh Sleep Quality Index scale score (PSQI)<sup>[9]</sup>: This scale evaluates the sleep quality of patients from six aspects, with 7 as the critical point, and the higher the score, the worse the sleep quality.
- (2) Mini-mental State Examination (MMSE)<sup>[10]</sup>: The scale assesses cognitive function from 10 aspects such as memory, calculation ability, naming ability, etc. The total score of the scale is 30, and the score 27 was assessed as cognitive impairment.
- (3) Montreal Cognitive Assessment Scale (MoCA)<sup>[11]</sup>: This scale evaluates the cognitive ability of patients from 7 aspects such as language ability, abstraction ability, orientation ability, visual space and executive function. And the lower the total score, the more serious the cognitive impairment.

# 2.3 Statistical analysis

SPSS22.0 software was used for statistical analysis. Measurement data were expressed as mean  $\pm$  standard deviation. Paired sample t test was used for intra-group comparison, and two independent sample t test was used for inter-group comparison. Count data were expressed as percentage or

frequency, and comparison between groups was analyzed using the chi-square test. P < 0.05 was considered statistically significant.

## 3. Results

(1)PSQI: Before treatment, the PSQI score of the acupuncture group was higher than that of the control group (P<0.05); After treatment, the scores of each item and total score of PSQI scale in the acupuncture group were decreased(P<0.05), but the score was still higher than that of the control group (P<0.05), the results are shown in Table 2.

(2)MMSE: There were differences in MMSE scores between the two groups before treatment (P<0.05); After treatment, the MMSE score of the acupuncture group increased (P<0.05), and compared with the control group P>0.05, the difference was not statistically significant (Table 3).

(3)MoCA: Before treatment, the MoCA scale score of the acupuncture group was lower than that of the control group (P<0.05); After treatment, the scores of the acupuncture group increased(P<0.05), and compared with the control group P>0.05, the difference was not statistically significant(Table 4).

Table 2: The comparison of the effect of PSQI score

Group	Number	PSQI Score	
		Before treatment	After treatment
acupuncture group	30	13.47±2.22 <sup>a</sup>	8.23±1.90 <sup>a</sup> b)
control group	30	4.53±1.25	4.60±1.08

(Compared with pre-treatment, a: P<0.05; Compared with the control group, b:P<0.05).

Table 3: The comparison of the effect of MMSE score

Group	Number	MMSE Score	
		Before treatment	After treatment
acupuncture group	30	24.90±1.53b)	27.96±1.01 <sup>a) b)</sup>
control group	30	28.10±0.87	28.50±0.84

(Compared with pre-treatment, a: P<0.05; Compared with the control group, b:P<0.05).

Table 4: The comparison of the effect of MoCA score

Group	Number	MoCA Score	
		After treatment	After treatment
acupuncture group	30	25.87±1.81 <sup>b</sup>	28.10±0.96 <sup>a)</sup> b)
control group	30	28.40±0.82	28.37±0.80

(Compared with pre-treatment, a: P<0.05; Compared with the control group, b:P<0.05).

# 4. Discussion

Modern studies [12] have shown that quality sleep contributes to cell repair, thermoregulation, memory consolidation, and maintenance of neuroimmune-endocrine system stability. During sleep, the brain switches periodically between non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep [13], among which REM sleep is considered to play an important role in learning and memory, neurogenesis and regulation of blood-brain barrier function [14], while non-REM sleep is related to the regulation of hormone release and immune system [15]. It is obvious that sleep is closely related to cognitive function. As a common sleep disorder, primary insomnia has been gradually explained its damage to cognitive function. On the one hand, insomnia can activate glial cells, promote the release of inflammatory factors and cause inflammatory response, leading to nerve cell apoptosis and immune damage, and then affect cognitive function [16]. Moreover, the worse the sleep quality, the more proinflammatory factors are secreted [17]. On the other hand, long-term insomnia can lead to an increase in the level of  $\beta$ -amyloid protein  $(A\beta)$  in the cerebrospinal fluid, which can cause synaptic dysfunction and impaired neurotransmission, and abnormal signal transduction between neurons, which may indirectly or directly affect the memory and learning process [18]. In addition, some studies [19-21] have found that insomnia patients have structural and functional changes in brain regions, especially in hippocampus and prefrontal cortex. Hippocampus and prefrontal cortex are related to cognitive activities such as memory, executive function and logical thinking. The damage of hippocampus and prefrontal cortex may cause cognitive dysfunction in patients with primary insomnia. In conclusion, the

impairment of cognitive function caused by insomnia is the result of the joint action of many pathological factors.

In traditional Chinese medicine, primary insomnia with cognitive dysfunction is classified into the categories of "Bu mei", "Budemin" and "Chidai". In terms of treatment, traditional Chinese medicine (TCM) is mainly based on comprehensive treatment and holistic conditioning, including traditional Chinese medicine decoction, acupuncture, acupoint massage, auricular points, and traditional exercises [22]. Studies have found that acupuncture intervention can not only improve sleep, but also improve cognitive function to a certain extent [23,24]. Wang[25] observed the effect of electroacupuncture on elderly patients with insomnia and found that sleep quality and cognitive function were improved after treatment, which may be related to the increase of serum melatonin and dopamine levels. Gao [26] used acupuncture to treat insomnia, and the results showed that acupuncture had positive effects on visual space, executive function and delayed recall of patients, and the curative effect was better than western medicine. Wei [27] found that acupuncture at Neiguan (PC 6) and Zusanli (ST 36) can regulate the circadian rhythm and sleep cycle disorder of the insomnia model rats, and effectively improve the attention deficit of the rats. The mechanism may be that acupuncture is involved in regulating the expression of glial cells, reducing neuroinflammatory response and cell damage.Qiao<sup>[28]</sup> needled Baihui, Shenmen and Sanyinjiao, suggested that acupuncture may improve the cognitive function of rats by increasing the content of neurotrophic factor BDNF.As mentioned above, acupuncture is effective in the treatment of primary insomnia, and has obvious advantages in the improvement of memory, attention and executive function of patients, which is related to the regulation of neurotransmitter concentration, reduction of immune inflammatory response, up-regulation of BDNF expression and promotion of cell repair.

In this study, the acupoints Zhongbaihui and Anmian are located on the head, which can refresh the mind, calm and sleep.Baihui (GV 20) is the meeting of all Yang, located at the governor vessel, which enters the collateral brain and plays a role in dredging Yang meridians and promoting qi and blood circulation. Anmian point is an important point in the treatment of insomnia, which can calm the mind and promote sleep. Sanyinjiao is the intersection point, which can regulate the three meridians and three zang organs, nourishing the kidney and regenerating the pulp. Shenmen is the original acupoint of the shaoyin heart meridian of the hand, which is mainly associated with dementia, amnesia, and mental machine apapxia. Studies have found that [29] acupuncture at Shenmen can up-regulate serum GABA content and regulate neurotransmitters. Zhaohai and Shenmai are the eight meridians, which are used to channel Yin Qiaomai and Yang Qiaomai, respectively. The matching of the two can harmonize Yingwei [30] and guide Yang into Yin. All the acupoints match to harmonize Yin and Yang, tonify the kidney and fill the essence, calm the mind and help sleep.

We found that there was a significant difference in PSQI score before and after treatment in the acupuncture group (P<0.05), indicating that acupuncture can effectively improve the sleep quality of patients. There were significant differences in MMSE score and MoCA score between the acupuncture group and the healthy control group(P<0.05), indicating that patients with insomnia have cognitive dysfunction, which is consistent with previous studies. After treatment, the MMSE and MoCA scores were improved in the acupuncture group(P<0.05), there was no difference between groups (P>0.05), indicating that acupuncture can significantly improve cognitive function in patients with primary insomnia. This effect may be caused by two factors, one is indirectly improving cognitive function by improving sleep, and the other is directly acting on the pathological mechanism related to cognition, which needs to be further studied. In addition, this study also has some limitations, such as lack of objective efficacy indicators, no additional follow-up, and insufficient sample size, which we hope will be further improved and supplemented.

## 5. Conclusions

Our findings of this current study suggest that acupuncture may be used as an additional therapy to conventional pharmacological treatment to further improve the clinical outcomes of patients with Primary insomnia and cognitive function. Long-term and large scaled studies with more comprehensive efficacy evaluation system are still required to further verify the conclusion.

# **Conflict of Interest**

The authors declare that the research was conducted in the absence of any commercial or financial

relationships that could be construed as a potential conflict of interest.

# Acknowledgement

Funding: Our study was supported by Natural Science Foundation of Shaanxi Province (NO2020JM-699); Project of Xi'an Health and Construction Commission (NO2020yb26).

## References

- [1] Wang Y, Salas RME. Approach to Common Sleep Disorders. Semin Neurol. 2021; 41(6): 781-794.
- [2] Cousins JN, Fernández G. The impact of sleep deprivation on declarative memory. Prog Brain Res. 2019; 246: 27-53.
- [3] Sadeghmousavi S, Eskian M, Rahmani F, Rezaei N. The effect of insomnia on development of Alzheimer's disease. J Neuroinflammation. 2020; 17(1): 289.
- [4] Wilt TJ, MacDonald R, Brasure M, et al. Pharmacologic Treatment of Insomnia Disorder: An Evidence Report for a Clinical Practice Guideline by the American College of Physicians. Ann Intern Med. 2016; 165(2): 103-112.
- [5] Zhang J, Zhang Z, Huang S, et al. Acupuncture for cancer-related insomnia: A systematic review and meta-analysis. Phytomedicine. 2022; 102: 154160.
- [6] American Academy of Sleep Medicine. International classification of sleep disorders [M]. 3rd ed. Darien, IL: American Academy of Sleep Medicine, 2014: 2-3.
- [7] State Administration of Traditional Chinese Medicine. Diagnostic efficacy criteria of TCM diseases and syndromes [M]. Beijing: China Medical Science and Technology Press, 2012: 31-32.
- [8] Liang FR, Wang H. Acupuncture and moxibustion [M]. China Traditional Chinese Medicine Press, 2016: 223-224.
- [9] Xiao WD, Liu P, Ma H et al. The Reliability and Validity of Sleep Dysfunction Rating Scalein Patients with Insomnia [J]. Chinese Mental Health Journal, 2007(01): 40-41+51.
- [10] Burton L, Tyson SF. Screening for cognitive impairment after stroke: A systematic review of psychometric properties and clinical utility [J]. J Rehabil Med, 2015, 47(3): 193-203.
- [11] Chinese guidelines for diagnosis and treatment of vascular cognitive impairment. 2019 Chinese guidelines for diagnosis and treatment of vascular cognitive impairment [J]. Chinese Medical Journal, 2019, 99(35): 2737-2744.
- [12] Gomez-Gonzalez B, et al. Role of sleep in the regulation of the immune system and the pituitary hormones. Ann N Y Acad Sci. 2012; 1261: 97–106.
- [13] Saper CB, et al. Sleep state switching. Neuron. 2010; 68(6): 1023–42.
- [14] Guzman-Marin R, et al. Rapid eye movement sleep deprivation contributes to reduction of neurogenesis in the hippocampal dentate gyrus of the adult rat. Sleep. 2008; 31(2): 167–75.
- [15] Schmid DA, et al. Changes of sleep architecture, spectral composition of sleep EEG, the nocturnal secretion of cortisol, ACTH, GH, prolactin, melatonin, ghrelin, and leptin, and the DEX-CRH test in depressed patients during treatment with mirtazapine. Neuropsychopharmacology. 2006; 31(4): 832–44.
- [16] Zielinski MR, Gibbons AJ. Neuroinflammation, Sleep, and Circadian Rhythms. Front Cell Infect Microbiol. 2022; 12: 853096.
- [17] Huang XY, Xie GJ. Effect of Modified Tianwang Buxindan on Learning and Memory Function and Expression of Inflammatory Factors in Sleep Deprived Rats. Chinese Journal of Experimental Traditional Medical Formulae, 2020; 26(23): 56-62.
- [18] Chen DW, et al. Cerebrospinal fluid amyloid-beta levels are increased in patients with insomnia. J Alzheimers Dis. 2018; 61(2): 645–51.
- [19] He JW, Tu ZH, Su T, et al. Insomnia: the characteristics and mechanisms of cognitive impairment [J]. Academic Journal of Second Military Medical University, 2019, 40(09): 1015-1019.
- [20] Ma X, Jiang G, Tian J, et al. Convergent and divergent functional connectivity alterations of hippocampal subregions between short-term and chronic insomnia disorder. Brain Imaging Behav. 2021; 15(2): 986-995.
- [21] Fasiello E, Gorgoni M, Scarpelli S, Alfonsi V, Ferini Strambi L, De Gennaro L. Functional connectivity changes in insomnia disorder: A systematic review. Sleep Med Rev. 2022; 61: 101569.
- [22] Li SS, Zhao M, Sun JY et al. Research Progress on Treating Insomnia with Cognitive Dysfunction in TCM [J]. Journal of Basic Chinese Medicine, 2022, 28(11): 1887-1890.
- [23] Hu JX, Yuan F, Zhang F, et al. Research progress of functional magnetic resonance imaging in acupuncture treatment of insomnia disorder [J]. China Medical Guide, 2020, 17(30): 56-58.

- [24] Wang RY, Wang DY, Dong X, et al. Microstructural Changes of Cerebral Gray Matter in Patients with Cerebral Infarction-Related Insomnia Treated by EA [J]. JCAM, 2023, 39(02): 27-33.
- [25] Wang XQ, Qin S, Wu WZ, et al. Effect of electroacupuncture on serum melatonin and dopamine in aged insomnia [J]. Chinese Acupuncture & Moxibustion, 2021, 41(05): 501-504.
- [26] Gao QC. The effect of acupuncture on sleep quality and cognitive function in elderly patients with primary insomnia [D]. Heilongjiang University of Traditional Chinese Medicine, 2020.
- [27] Wei T. To study the mechanism of acupuncture regulating the P2X7 receptor of microglia in TRN region in insomnia rats with attention deficit [D]. Chengdu University of Traditional Chinese Medicine, 2020.
- [28] Qiao LN, Gao QL, Tan LH, et al. Electroacupuncture of Multiple Acupoints Is Significantly Superior to That of Single Acupoint in Improving Sleepby Regulating Serum Sleep-promoting and Awakening-promoting Factors in Insomnia Rats[J]. Acupuncture Research, 2018, 43(10): 651-656.
- [29] Li ZW, Yang L, Song XJ, et al. Effects of Shenmen and Sanyinjiao on sleep quality and serum GABA and 5-HT in patients with insomnia [J]. Modernization of Traditional Chinese Medicine and Materia Medica-World Science and Technology. 2022, 24(02): 860-866.
- [30] Zheng H, Gao GC, Shi XM. Thirty-two cases of narcolepsy treated by acupuncture of regulating nutrient qi and defense qi [J]. Chinese acupuncture & moxibustion, 2014, 34(02): 197-198.