

# Research Progress of Post-Stroke Sleep Disorders

Shanshan Zhang<sup>1, a</sup> and Qiming Zhang<sup>2, b\*</sup>

<sup>1</sup>Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
<sup>2</sup>Medical Experimental Center of China Academy of Chinese Medical Sciences, Beijing 100102,
China

<sup>a</sup>nec757@163.com, <sup>b</sup>Zhang\_917@126.com \*corresponding author

**Keywords:** Stroke, Sleep Disorder, Pathogenesis, TCM Therapy

**Abstract:** Stroke has a high incidence trend, and not only has a high mortality relatively, but also has a high disability rate, however, sleep disorder is one of the more common clinical manifestations of stroke, patients. Sleep disturbances can increase the risk of stroke, and stroke can also cause insomnia. For sleep disorders, on the one hand, it can aggravate the disease of stroke patients and delay the recovery of symptoms and reduce the quality of patients' life seriously, on the other hand, it can also increase the risk of stroke recurrence. This article summarizes the characteristics and efficacy of traditional Chinese medicine in the disease name, etiology and pathogenesis and traditional Chinese medicine treatment of sleep disorders Stroke in recent years, and these three aspects can provide basis and guidance for clinical using.

Stroke is the main clinical type of cerebrovascular disease, which lives with heart disease and malignant tumor constituting the three major fatal diseases. In according to investigations, the incidence of sleep disorders after stroke in China is about 20%-77%. [1] And in according to foreign reports, the incidence of sleep disorders in patients with ischemic stroke is as high as 78%.[2] Sleep disorders after stroke affect the rehabilitation of motor and language functions, and meanwhile it can lead to social dysfunction. Not only that, sleep disturbances after stroke can also increase the risk of elevated blood pressure or recurrent stroke. However, both patients and medical staff still have insufficient awareness and attention to sleep disorders in clinical practice, which results in a low diagnosis rate of sleep disorders in stroke patients and delayed treatment.[2] The clinical research experience of TCM on sleep disorders after stroke has been more summarized, and the clinical effect is obvious, which deserves to be further and further promotion in the clinical.[3]

# 1. The Cognition of TCM on Sleep Disorders after Stroke

According to traditional Chinese medicine, sleep disorder after stroke belong to the categories of "not squinting", "not lying down", "not sleeping" and so on. The main symptoms are difficulty in squinting in sleeping all night or easy to wake up, and then difficulty in sleeping after waking up.[4]

The imbalance of Yin and Yang caused by stroke is an important pathogenesis of sleep disorder. If Yin and Yang are not harmonious, Yin does not melt Yang, Yang does not enter Yin, then the mind floats over and the soul goes astray, which can cause alarm and forget, insomnia and anxiety or somnolence and snoring. Dazzled and the lower energizer fail to keep can cause urinary incontinence and drowning insomnia; The Qi is not smooth and difficult to traffic that can cause snoring sleep; When the heart and kidney are imbalance, the fire and water are disordered that can cause insomnia and more dreams. The viscera's Yin and Yang Qi and blood insufficiency which caused by Stroke, and Yuan God's loss of nutrition, dazzling all are another pathogenesis of sleep disorders.[5]

Other scholars think that patients after stroke will appear the retention of evil influences and disturbance of consciousness, which lead to serious imbalance of Yin and Yang and viscera organs. This is an important pathogenesis of sleep disorders. If the phlegm turbidity obstructs, and the mind traps, then the spirit will be depressed and manifest sleepiness; If the phlegm turbidity upgoings and dazzled, then the body will manifest more dreams and be difficult to fall asleep and lying restless; If phlegm turbidity brews longer, turn heat into fire, phlegm heat disturbance and dazzled wandering, then will behave as sleepwalking, nightmare, dream language, dream fear and etc; If blood stasis, blocked channels ,Qi and blood is loss of nutrition and the mind upsetting, then the body can appear limb pain, numbness, sobriety and clonus, which can lead to insomnia, matt gets sleepless, waking up early and even sleepless night.[6] Table 1 summarises etiology and pathogenesis and clinicial characteristicsof post-stroke sleep disorders.

Etiology	Pathogenesis	Clinicial characteristics	
Turbid phlegm block	Perplexed one's mind	Lethargy and drowsiness	
Phlegm turbid upward disturbance	Perplexed one's mind  Dreamy, difficult to fall asleep, restles lying down		
Long accumulation of turbid phlegm	Turn heat into fire, phlegm-heat disturbance	Sleepwalking, nightmares, dream words, dream terrors	
Blood stasis block	The meridians are blocked, the qi and blood are not nourished, and the mind is disturbed.	Limb pain, numbness and distension, clonus, and cramps lead to insomnia, restlessness in sleeping at night, early awakening, and even sleeplessness all night.	

Table 1. Etiology and pathogenesis and clinical characteristics of Post-Stroke sleep disorders

### 2. The Cognition of Modern Medical on Sleep Disorders after Stroke

Stroke is the main clinical type of cerebrovascular diseases. It includes ischemic stroke and hemorrhagic stroke. They have some common clinical features, they are sudden onset, and localized or disseminated brain function defects rapidly. It is a group of cerebrovascular diseases caused by organic brain injury [7]. The International Classification of Sleep Disorders (ICSD-3) divides sleep disorders into 7 main types (Table 2).

Table 2. Classification of Sleep Disorders

(1) Insomnia		
(2) Sleep disordered breathing		
(3) Disturbance of circadian sleep arousal		
(4) Central sleep increased		
(5) Abnormal sleep		
(6) Sleep-related movement disorders;		
(7) Other sleep disorders, includes multiple overlapping sleep disorders and environmental-related		
sleep disorders.		

Sleep disorders generally occur during the acute phase of stroke. Most of the patients with unconsciousness disorder on admission occurred within 3-5 days after admission, and most of the patients with conscious disorder occurred within 3 days after awakening, and some patients occurred within 4-14 days. Clinical data show that sleep disorders are common within 3-4 months after the occurrence of stroke, and sleep disorders in stroke last from 1 month to 3 years and accompanied by an average duration of 9.63 months.[10]

Through the observation of sleep disorders in clinical stroke patients, it was found that the location and lesion scope of stroke were closely related to the occurrence of sleep disorders after stroke, but the nature of stroke (bleeding or infarction) was less related. Among the stroke sites that were correlated with sleep disorders, they are thalamus, cerebral hemisphere, basal ganglia, brainstem and cerebral cortex in sequencely. The incidence of sleep disorders in hypothalamic stroke is higher than that in cortical stroke and cerebellar stroke. The incidence of sleep disorder in patients with cerebral hemorrhage is higher than that of cerebral infarction. The more severe the neurological deficit, the higher the incidence of sleep disorders.[8]

The damage to the thalamus, hypothalamus, midbrain tegmentum, and upper pons behind in stroke, where even has a small injury that may cause severe damage to the ascending reticular activating system (ARAS), causing severe and persistent hypoarousal. In patients with cerebral deep hemispheric (subcortical) and thalamic stroke, increased sleep can be accompanied by corresponding bedtime behaviors, including yawning, stretching, eye closing, body curling, putting the body into a normal sleep posture, and complaining of continuous sleep desire. When subcortical, thalamus, midbrain and pontine tegmentum are infarcted, insomnia can be accompanied by sleep and wake reversal, then showing insomnia and agitation at night and increased sleep during the day. Increased sleep and excessive daytime sleep [9]. The location and lesion scope of stroke were closely related to the occurrence of sleep disorders after stroke (Table 3).

Table 3. The location and lesion scope of stroke and the occurrence of sleep disorders

Location and lesion scope of stroke	Pathogenesis	Clinicial characteristics
Thalamus, hypothalamus, midbrain tegmentum and upper pons behind	Severe damage to the ascending reticular activating system	Severe and persistent hypoarousal
Cerebral deep hemispheric	Corresponding bedtime	Yawning, stretching, eye
(subcortical) and thalamic stroke	behaviors	closing, body curling
Subcortical, thalamus, midbrain and pontine tegmentum	Sleep and wake reversal,	Insomnia and agitation at night and increased sleep during the day.

Brainstem breathing regulating center, frontal lobe and basal ganglia, internal capsule, and other parts of the brain tissue damage are multifactorial [11]. (Figure 1)

Acute ischemic stroke leads to decreased nocturnal sympathetic depression and increased secretion of epinephrine and cortisol, and insular cortical involvement, which then leads to circadian disturbance and sleep disturbance.[13] Circadian disruption can cause a series of hemodynamic, neuropathic (hypersympathetic activity), metabolic (such as insulin resistance) inflammatory or oxidative changes (such as C-reactive protein, tumor necrosis factor-A, interleukin-6 and increased levels of adhesion molecules) which leads to diabetes and platelet aggregation increased, fibrinolytic activity decreased, endothelial damaged and atherosclerosis chaged, which all increase the risk of stroke.[12]

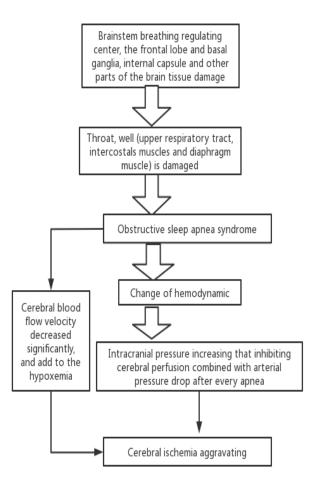


Figure 1. Brainstem breathing regulating center, the frontal lobe and basal ganglia, internal capsule damage and pathogenesis

The humoral regulatory mechanism of sleep disorders after stroke: It has been clear that  $\gamma$ -aminobutyric acid, 5-hydroxytryptamine (5-HT), norepinephrine, and acetylcholine are involved in the regulation of sleep and wake.5-HT-ergic neurons in the head of raphe nucleus are involved in generating and maintaining NREM sleep, while NA neurons in the tail of locus ceruleus and Ach neurons in the low brain stem tegmental region are triggered by 5-HT-ergic neurons in the tail of raphe nucleus to produce REM sleep.[14]

#### 3. The Treatment of Sleep Disorders after Stroke

# 3.1. The Modern Medicine Treatment of Sleep Disorders after Stroke

Currently, the drugs used to treat sleep disorders include mainly benzodiazepines, new non-benzodiazepines, and antidepressants. Benzodiazepines can shorten the time to fall asleep, reduce the number and time of awakenings and increase the total sleep time, but also affect the normal sleep physiological structure. Long-term using of benzodiazepines can lead to dependence, daytime sleepiness, rebound insomnia, and withdrawal symptoms. Patients with insomnia caused by psychological factors or secondary to depression mainly choose antidepressants, but these drugs have poor safety, long half-life and easy -to-appear anticholinergic and other adverse reactions.[15]

# 3.2. Traditional Chinese Medicine Therapy for Sleep Disorders after Stroke

Chaihu Keel and Oyster soup can improve patients' sleep quality and shorten patients' sleep time, and lengthen sleep time and improve sleep efficiency and alleviate sleep disorders and improve daytime function.[16]

Gardenia tempeh soup can protect e brain tissue and promote blood circulation to relieve sleep disorders by relieving fever and calming down.[17]

Xuefuzhuyu soup can reduce the platelet aggregation rate in patients with cerebral infarction, and reduce the degree of carotid artery stenosis, and play a role in the treatment of sleep disorders by improving the hemorheology and brain blood supply in patients with insomnia and blood stasis syndrome after stroke.[18]

Huanglian ejiao soup can improve nerve arc reflex functionand repair damaged neurons. Meanwhile, it can improve oxygen and blood supply to the brain and protect nerve cells to improve microcirculation, then promote blood circulation and reduce the level of inflammatory factors and then improve the body function of patients significantly.[19]

Baihe Dihuang soup may be beneficial to improve the survival rate of new nerve cells in the brain and appear more new cells to be mature, differentiate, and integrate into the hippocampal network, then improve their impaired function gradually.[19]

Ganmai Dazao soup has an analgesic effect and central inhibitory effect to a certain extent, and can lengthen the sleep time, sleep rate, and reduce the number of convulsions significantly. [20]

Auricular point therapy is an important part of Chinese acupuncture and moxibustion. Stimulating auricular points can obstruct channels and qi and blood operations to stimulate the cerebral cortex and improve cerebral blood supply effectively, and then can treat insomnia, dreams, irritability or other diseases.[21]

Acupuncture stimulation modulates monoamine neurotransmitters in the prefrontal cortex and increases norepinephrine levels. Meanwhile, other researches have shown that acupuncture treatment can increase nocturnal melatonin production and reduce insomnia and anxiety [22].

In addition, acupoint and massage, foot bath in Chinese medicine, pressure bolus in auricular point, acupoint application, five elements music and relaxation training and other TCM characteristic nursing techniques have no dependence and withdrawal reaction and few side effects compared with drug therapy, [23] and they can effectively improve patients' sleep quality and promote nerve function repair and reduce the incidence of secondary stroke. Traditional Chinese Medicine Therapy for Sleep Disorders after Strokeare multifactorial(Figure 2).

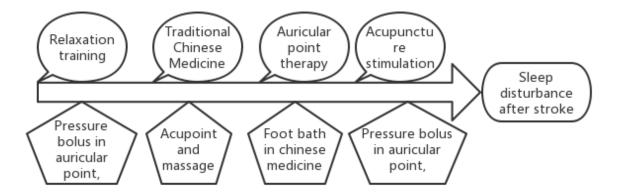


Figure 2. Traditional Chinese medicine therapy for sleep disturbance after stroke

# 4. Summary

Sleep disturbance after stroke is a common clinical complication of stroke. It is necessary to identify and evaluate sleep disturbance after stroke early. Modern medical treatment of insomnia drugs has a certain curative effects after stroke, but there are adverse reactions. Conversely,the Chinese medicine treatments may have an advantage to treat sleep disorders after stroke is that they apply to individualized treatment in different TCM syndrome types, and it has more advantages such as safe, reliable and affordable, which can clearly improve the patient's sleep quality and the quality of life and achieve good clinical curative effect, In a word it's worthing to reference for clinical doctors.

#### **Funding**

No funds.

#### **Data Availability**

No new data is used or generated.

#### **Conflict of Interest**

There is no conflict of interest between the two authors.

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