

Sleep disorders in Parkinson's patients

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Abstract. Sleep disorder is one of the most common non-motor symptoms of Parkinson's disease and can occur at any stage of the disease. Clinical symptoms are decreased total sleep time, decreased sleep efficiency (difficulty falling asleep, easy awakening, etc.), rapid eye movement, excessive daytime sleepiness, often accompanied by cognitive impairment, thinking and emotional disorders, etc. It is a huge burden, so it is crucial to pay attention to sleep disorder in Parkinson's patients. This article introduces the pathogenic mechanism and treatment methods of insomnia, restless legs syndrome, sleep apnoea and excessive daytime sleepiness.

Keywords: Parkinson's disease, sleep disorders.

1. Introduction

Parkinson's disease is neurodegenerative disease common in middle-aged and elderly people, and its clinical manifestations are more obvious resting tremor, dystonia, bradykinesia and other motor symptoms. In addition to motor symptoms, Parkinson's disease is often accompanied by non-motor symptoms such as cognitive impairment, abnormal sense of smell, psychosis, and sleep disorder [1].

Sleep disorder are the most common non-motor symptoms of Parkinson's disease, including insomnia, restless legs syndrome (RLS), sleep-disordered breathing (SDB), and excessive daytime sleepiness (SDM), which can occur in any Parkinson's disease. stage. According to reports, the incidence of sleep disorder in Parkinson's disease is as high as 60%-98%, and up to 60% of patients suffer from sleep disorder even long before any obvious motor symptoms, which seriously reduces the quality of life of patients [2].

Insomnia

Insomnia refers to the difficulty in falling asleep, intermittent sleep at night, and early awakening when there is sufficient sleep time, causing patients to be in a trance and memory loss during the day [3].

Insomnia is the most common sleep disorder in Parkinson's patients. According to research, about 30% to 80% of Parkinson's patients have insomnia symptoms, which are often manifested as intermittent sleep at night and early awakening, which seriously affects the quality of life of patients [4]. There are many related causes of insomnia symptoms in Parkinson's patients, which may be the result of one or more factors. These include changes in sleep-wake cycles, nocturnal motor symptoms versus non-motor symptoms, medications, age or gender, etc.

The degeneration of the brainstem sleep-wake center and the hypothalamic-cortical pathway is an important cause of insomnia in Parkinson's patients. During the patient's illness, the medulla oblongata and pontine tegmentum have degenerated, and then the cortical parts have gradually degenerated, and the degeneration of these parts will affect the sleep-wake mechanism. Neurotransmitters that regulate sleep and wakefulness include acetylcholine, dopamine, serotonin, gamma-aminobutyric acid, and norepinephrine. Degeneration of some parts of Parkinson's patients, such as damage to serotonin in the raphe nucleus and norepinephrine in the locus coeruleus, can lead to the disruption of the normal sleep structure and cause insomnia [5].

Nocturnal motor symptoms and non-motor symptoms are also one of the causes of disease. Common motor symptoms in Parkinson's patients include resting tremor, dystonia, and limb pain. Non-motor symptoms such as Parkinson's patients are often accompanied by mental symptoms such

as depression, anxiety, hallucinations, frequent urination at night, pain, etc [6,7]. Psychiatric symptoms may be caused by decreased dopamine, serotonin, and norepinephrine functions in the limbic system in Parkinson's patients [8].

Nocturnal motor symptoms and non-motor symptoms seriously affect the nocturnal sleep of patients with Parkinson's disease, resulting in patients prone to insomnia

Some drugs can cause insomnia in patients. Parkinson's patients need to take medicines during treatment, but these medicines often come with more serious side effects. For example, lower doses of dopaminergic drugs can promote sleep by activating D1 receptors, and higher doses of dopaminergic drugs can activate D2 receptors to make patients more awake and cause insomnia [9]. Taking selegiline at night can cause difficulty waking and falling asleep [10].

2. Treatment

Patients with insomnia should choose appropriate drugs according to different symptoms. For patients with nocturnal exercise and non-motor symptoms, multi-aminergic agonists (eg, rotigotine, pramipexole immediate-release, and ropinirole), melatonins (melatonin, melatonin extended-release) can be selected) treat. Patients with insomnia often suffer from anxiety, depression and other psychological emotions, which aggravate the degree of illness. For these patients, nisamide, agomelatine, and levodopa-carbidopa enteral gel can be selected for treatment [11].

Non-drug therapy: (1) Cognitive behavioral therapy: Cognitive behavioral therapy should be recommended first for patients with Parkinson's disease insomnia. Talk therapy is usually given to patients within 10-12 weeks to help patients get out of negativity and establish new behaviors, including sleep education, sleep restriction, stimulation therapy, relaxation therapy, etc. Cognitive-behavioural therapy for non-motor symptoms of Parkinson's disease: a clinical review (2) Physical exercise: According to studies, Parkinson's patients with regular moderate and high-intensity exercise rehabilitation therapy under the guidance of professionals can improve sleep disorders [12]. For example, doing steady and gentle exercises such as Qigong and Tai Chi at ordinary times is a feasible treatment method [13,14] . (3) Light therapy: Light therapy is an artificial simulation of natural light, and the treatment of Parkinson's patients is achieved through the intensity and irradiation time of light, which may be related to the regulation of circadian rhythm. Light therapy can improve patients' sleep disorders, mood, etc., and has a positive effect on patients with Parkinson's disease insomnia [15]. (4) Deep brain stimulation therapy: Deep brain stimulation therapy modulates neural nuclei through electrical circuit stimulation to achieve therapeutic effects. Deep brain stimulation therapy is a regulated and relatively safe treatment method that can treat the motor symptoms of Parkinson's disease, thereby improving sleep quality, while reducing drug dosage and drug side effects [16].

restless legs syndrome

Restless legs syndrome is often characterized by intense nighttime lower extremity discomfort that the patient seeks to relieve by exercising the lower extremity and exacerbated by resting or resting [17].

Research has shown that restless legs syndrome is 2 to 3 times more common in PD patients than in the general population [19]. Restless legs syndrome may be associated with damage to dopaminergic neurons, which has parallels with Parkinson's disease. However, there are still many debates about these two diseases, such as whether there is the same pathogenic mechanism, and whether there is a secondary condition between restless legs syndrome and Parkinson's disease [18]. The current research status suggests that restless legs syndrome may be related to dopamine neuron damage, iron deficiency, genetics, gender and other factors.

Iron deficiency is also related to the pathogenic factors of restless legs syndrome. Parkinson et al. determined that the content of iron in the brain of patients with restless legs syndrome in Parkinson's disease is low, which may be due to the internal and external central nervous system [19]. Iron deficiency will cause the body to reduce the combination with hemoglobin, weakening the oxygen

transport capacity, and the patient is prone to anemia and hypoxia. A study showed that patients with restless legs syndrome (untreated) were more prone to hypoxia than healthy people in the high-altitude Himalayas, suggesting that iron deficiency may be the cause of restless legs syndrome of factors [20].

Women may also be associated with restless legs syndrome, possibly because women are more likely to show upper and lower limb movement posture disorders during sleep [21].

Drug treatment: The restless legs syndrome in PD patients is recommended to be treated with levodopa, but the minimum effective dose is recommended for treatment, otherwise the condition may be aggravated. In addition, other dopaminergic agonists and α -2- δ calcium channel ligands (gabapentin, pregabalin) can also be used for treatment [22].

Nonpharmacological Treatment: Sleep education is a treatment method that is built on changing a patient's sleep habits. Some patients do not have good sleep habits, such as playing with electronic products before going to bed, taking drugs that cause excitement before going to bed, irregular work and rest, etc., which will aggravate the disease. Sleep education intervention for patients can effectively improve sleep quality. Moderate amount of aerobic exercise such as swimming, jogging, etc. can also help sleep [23,25].

3. sleep-disordered breathing

Sleep-disordered breathing is a disease in which patients breathe abnormally during sleep, including obstructive sleep apnea, central sleep apnea, restricted pulmonary insufficiency, etc., most of which are obstructive sleep apnea 20% to 60% of Parkinson's patients have obstructive sleep apnea [26]. Obstructive sleep apnea is caused by sleep-related upper airway muscles 4 to 8 Hz oscillations and lung volume limitation [27]. Bahia et al. found that upper airway dysfunction associated with Parkinson's disease can cause upper airway obstruction, which is more than three times that of normal people, indicating that Parkinson's patients can induce obstructive sleep apnea [28]. Studies have shown that as Parkinson's patients spend more time with the disease, they have fewer changes in body movement at night and more lying on their backs during sleep, which aggravates the condition of obstructive sleep apnea. The reason for this is that the tongue blocks the airway due to gravity during sleep. The sleep apnea index decreased when changing to the side [29,30].

Neuronal degeneration is an important cause of sleep-disordered breathing with Parkinson's disease. Alpha-synuclein has been implicated in the pathogenesis and dysfunction of Parkinson's disease. Under normal circumstances, molecular chaperones can hinder the interaction of α -synuclein with mitochondria, which is weakened by hypoxia in patients with sleep-disordered breathing, and α -synuclein can also damage the mitochondrial membrane structure and cause inflammation. reactions that may cause Parkinson's disease. For example, alpha-synuclein causes the degeneration of dopaminergic neurons, leading to a predisposition to Parkinson's disease [31,32].

Drug therapy: Currently, there are relatively few drug treatments for sleep-disordered breathing. Dopaminergic agonists can relieve muscle tone. Levodopa may improve airway obstruction.

Non-drug treatment: (1) Continuous positive airway pressure is the most effective method for the treatment of obstructive sleep apnea. Its mechanism is to improve the number of sleep apnea in patients at night, increase blood oxygen saturation, and then alleviate the problem of sleep apnea [33]. (2) The mandibular extension treatment device is a kind of treatment for some patients who cannot use continuous positive airway pressure. It can improve the oxygen content and the number of apnea, and can replace continuous positive airway pressure [34].

4. Excessive daytime sleepiness

Excessive daytime sleepiness means that the mind should be kept awake and awake during the day, but patients often show mental exhaustion and uncontrollable sleepiness [35]. 29%-49% Parkinson's patients have symptoms of excessive daytime sleepiness. At present, excessive daytime sleepiness is

mainly related to orexin, a neurotransmitter secreted by the hypothalamus, which plays an important role in regulating sleep. Orexin in Parkinson's patients activates the inhibitory area of REM sleep behavior disorder, but in patients with orexin deficiency, CeA releases the inhibition of the hyponucleus locus coeruleus in this area, thereby causing muscle paralysis and making patients prone to daytime sleepiness.

Excessive daytime sleepiness may result from abnormalities in the parts of the brainstem that regulate sleep and wakefulness. The principle is that lesions in the parts of the brain related to sleep and wakefulness cause dopamine, serotonin activation, 5-HT and norepinephrine functions in the limbic system to decrease; in addition, the central inhibitory transmitter adenosine in non-REM sleep And cholinergic neurons such as the dorsolateral dorsal tegmental nucleus also changed.

Multiple awakenings during the night and sleep deprivation may also lead to excessive daytime sleepiness. Multiple other sleep disorders (eg, insomnia, restless legs syndrome, obstructive sleep apnea syndrome), movement disorders (eg, tremors, difficulty turning in bed), and other non-motor symptoms (eg, pain, depression, nocturnal polyuria, and hallucinations) It can also cause daytime sleepiness. Bhat S, Chokroverty S. Hypersomnia in neurodegenerative diseases.

Dopaminergic drugs aid in sleep and increase the risk of excessive daytime sleepiness.

Drug treatment: a small amount of dopaminergic drugs can treat excessive daytime sleepiness in Parkinson's patients; the use of the wake-promoting drug modafinil can treat sudden sleep symptoms with less side effects, in addition to melatonin, oxybutyric acid Sodium, etc. can also treat diseases.

Non-drug treatments: Common non-drug treatments include light therapy, cognitive behavioral therapy, and transcranial magnetic stimulation. Transcranial magnetic stimulation stimulates the brain through electrical stimulation of the cerebral cortex. This method has a certain therapeutic effect on excessive daytime sleepiness associated with Parkinson's disease.

5. Conclusion

Sleep disorder is a common non-motor symptom of Parkinson's disease. Patients often have comorbidities, which seriously affect our quality of life and require early prevention and treatment. At present, the mechanism of Parkinson's sleep disorder has not been fully studied, and some of the mechanisms are still unclear. For the treatment of sleep disorders in Parkinson's disease, drug therapy and non-drug therapy can be selected, but drug therapy is often accompanied by more serious side effects. It is recommended to build corresponding animal models according to different types of sleep disorders. On the one hand, it is of great significance to study the mechanism of different types of sleep disorders, and on the other hand, to study the influence of drugs on diseases, improve the pertinence of drugs and reduce side effects.

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