How do Hormones Regulate Sleep? In-depth Analysis of the Mechanism of Action and Clinical Strategies

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Abstract. About one-third of the world's population suffers from sleep disorders, which is closely related to the development of cardiovascular diseases, diabetes, depression and other chronic diseases, which have become a health problem that needs urgent attention. Hormones play a central role in the process of regulating physiological activity and are closely related to the sleep-wake cycle. Estrogen generally has a positive promoting effect on sleep and the decrease in estradiol levels is related to the increased risk of obstructive sleep apnoea (OSA) in perimenopause and postmenopausal women. Progesterone can reduce sleep disturbance and achieve the effect of helping sleep by regulating the secretion of growth hormone. Melatonin is the most crucial hormone that connects the external light-dark environment with the internal biological clock. Its secretion has an extremely significant circadian rhythm. Cortisol secretion disorders can also lead to sleep disorders. Clinically, there are some coping strategies for sleep disorders caused by different hormone abnormalities, such as single estrogen regimens, single progesterone regimens, combined treatment regimens of estrogen and progesterone and treatments related to cortisol and melatonin. The specific choice of treatment plan should be based on clinical reality and the individual preferences of the patient, and an individualized plan should be selected. There are shortcomings in existing research. Most study samples are small and the experimental population is single. In the future, it is necessary to provide safer and more effective strategies for the prevention and treatment of sleep disorders.

Keywords: Sleep, Oestrogen, Progesterone, Melatonin, Cortisol.

1. Introduction

Sleep is a crucial physiological activity of the human body, and at least 40% of a person's life is spent in sleep. Good sleep helps to restore physical strength, promote brain development and memory consolidation, and also play an important role in the normal functioning of the immune system. However, nowadays, sleep disorders are widespread all over the world, and people's quality of life, work efficiency and physical and mental health are seriously affected by it. Statistics show that about one-third of the world's population has different degrees of sleep problems, such as insomnia, lethargy, early wake-up in the morning, etc. Sleep disorders are even closely related to the development of a variety of chronic diseases, such as cardiovascular disease, diabetes and depression, which has become a problem that people have to pay attention to.

In response to this problem, many studies choose to start from the hormone aspect. Hormones play a crucial role in regulating the physiological process. More and more research evidence shows that many hormones are closely related to the regulation of the sleep-wake cycle, and there is a complex relationship between changes in different hormone levels and sleep disorders. For example, as a hormone that secretes with a distinct circadian rhythm, melatonin can promote the body to sleep. When it secretes abnormally, it can cause sleep problems such as insomnia and day and night disorders. The secretion of cortisol also shows a tendency of rhythmic fluctuations in the day and night. If cortisol secretion is disordered and there is a lot of abnormal secretion at night, it will lead to difficulties in falling asleep, light sleep, and easy to wake up. In addition, some studies have also found that abnormal secretion of oestrogen is also related to sleep disorders. Oestrogen secretion levels will change significantly during special periods such as menstruation, pregnancy and menopause. These changes are often accompanied by symptoms of declining sleep quality, such as premenstrual insomnia, sleep disorders during pregnancy, hot flashes and sweats during menopause.

Current research progress on the relationship between hormones and sleep has not been systematically sorted out and summarized. Therefore, this article aims to systematically sort out and summarize the research progress of the correlation between different hormones and sleep disorders, hoping to provide a reference for future treatment and diagnosis.

2. Effects of Various Hormones on Sleep

2.1. Oestrogen

Oestrogen is a class of steroid-like sex hormones mainly secreted by the ovaries, which play a core regulatory role in the female reproductive, metabolic, skeletal and nervous systems [1]. Through the study of hormone-simulated false pregnancy experiments in Syrian hamsters, it was found that the total sleep time and sleep efficiency of hamsters with increased estradiol levels in "late pregnancy" decreased and the amount of activity increased. This change persisted in hamsters who continued to receive estradiol treatment "after giving birth". At the end of the experiment, the expression of cfos in the lateral anterior region of the hypothalamus and the lateral hypothalamus of hamsters who continued to receive high doses of estradiol increased significantly, indicating that the increase in estradiol levels during pregnancy was related to sleep inhibition, which may be mediated by the activation of the hypothalamic nucleus.

In addition to mouse experiments, another two experiments respectively reached new conclusions [2, 3]. Both analysed the respiratory components of Depressed Perimenopausal and Postmenopausal Women, and found that 45.23% of patients suffered from obstructive sleep apnoea (OSA), of which 43% Female apnoea hypoventilation index (AHI)≥15. Females with AHI≥15 have lower estradiol levels than women with AHI<15. Analysis shows that low estradiol levels, high body mass index, high apnoea frequency and high Hamiltonian depression score are associated with OSA, indicating that the decrease in estradiol levels may be associated with Depressed Perimenopausal and Postmenopausal Wo Men OSA risk increase is related.

2.2. Progesterone

The ovaries also secrete progesterone. Progesterone is an important steroid hormone, which is mainly secreted by the corpus luteum in the female ovaries, and is secreted in large quantities by the placenta in late pregnancy. It works together with oestrogen and is a key hormone that regulates women's menstrual cycle and maintains pregnancy and embryonic development. In recent years, a large number of papers have shown that the level of progesterone secretion can also affect sleep. Among them, points out that progesterone and its metabolites usually have the effect of promoting sleep, and the sharp decline in progesterone levels is related to sleep interruption [4, 5]. By the way, through research, it has been found that progesterone can prevent sleep disturbance in postmenopausal women, regulate growth hormone, and promote the secretion of thyroid hormone and melatonin.

2.3. Melatonin

Melatonin is a hormone mainly synthesized and secreted by the pineal gland of the human body. Its core function is to regulate the rhythm of the day and night and help the body distinguish between day and night. The secretion of melatonin is regulated by light, and the daytime light inhibits its secretion. The secretion increases significantly in the dark environment at night, and it usually peaks at 2-4 a.m. and it can directly act on the gonads and reduce the content of androgens, oestrogens and progesterone.

It inhibits the excitability of the central nervous system and reduces the difficulty of falling asleep by acting on melatonin receptors in the brain (such as MT1, MT2) [6]. Research shows that shift work can cause biological clock disorders and sleep disorders. Melatonin improves the sleep efficiency and sleep quality of shift workers by reducing the incubation period of sleep to help fall asleep faster, prolong the deep sleep stage, and reduce the number of night awakenings. The study also found that,

a one-time intake of a high dose (>5mg) of melatonin may lead to side effects such as dizziness the next day and drowsiness during the day.

2.4. Cortisol

Cortisol is a glycocorticoid secreted by the human adrenal cortex. Its core function is to help the body cope with stress, regulate metabolism, immune response and blood sugar levels. It is also known as "stress hormone". When the physiological or psychological state of the human body is in a state of tension, cortisol is rapidly secreted, providing the body with energy to cope with stress. Under normal circumstances, cortisol secretion fluctuates regularly: it peaks 1-2 hours after waking up in the morning, then gradually decreases over time, and is minimized during night sleep. Many experiments have pointed out that cortisol secretion disorder can lead to a decrease in sleep quality and other problems. A study adopted a 15-day enhanced longitudinal design. Through electroencephalogram measurement and saliva sampling, it tested whether cortisol before bedtime could predict the duration and quality of sleep, and whether these sleep parameters could predict the slope of daytime cortisol the next day. The results showed that higher bedtime cortisol foreshadowed shorter total sleep time and lower sleep efficiency. Individuals with shorter average total sleep time or lower sleep efficiency had a flatter daytime cortisol slope [7].

3. Clinical Response Strategies

The clinical response to hormone-related sleep disorders is a systematic project. The core of the strategy is to accurately identify potential hormonal imbalances and adopt various treatments to return hormone secretion to normal.

3.1. Oestradiol Treatment

At present, there are few treatments for estradiol, but some of them have been proven to be effective for specific female groups. Research has found that, oestrogen replacement therapy (ERT) can significantly help to fall asleep faster, reduce the number of night awakenings and restlessness, prolong total sleep time and improve subjective sleep satisfaction, and this improvement begins to appear 4 weeks after treatment and lasts until the end of the trial [8]. The experimental results show that the sleep improvement effect of ERT does not exist independently, but is highly related to the relief of three major symptoms. First, vasoconstriction symptoms (such as hot flashes, night sweats, and night attacks will directly interrupt sleep); second, physical discomfort symptoms (such as joint pain, muscle soreness); third, emotional symptoms (such as anxiety, Low, such emotional problems often cause difficulty falling asleep). For women who only have simple sleep problems and do not have the above-mentioned accompanying symptoms, ERT does not have a significant effect on improving their sleep. Some patients are also worried that monoestrogenic therapy might lead to cancer

3.2. Progesterone treatment

A randomized, double-blind, placebo-controlled trial with 8 healthy postmenopausal women, allowing the swomento take 300mg of progesterone or placebo at 23:00 every day for 3 consecutive weeks [9]. It was found that the blood collection procedure of the placebo group caused obvious sleep disorders, while progesterone treatment significantly reduced these interferences. The average duration of post-sleep awakening in the progesterone treatment group was reduced by 53%, the slow wave sleep time increased by nearly 50%, and the total slow wave activity increased by nearly 45%. In addition, progesterone also increases the secretion of nocturnal growth hormone and reduces the level of nocturnal thyroid-stimulating hormone, indicating that progesterone can return to normal sleep when sleep is disturbed, rather than acting as a hypnotic.

In addition, some studies have adopted a combined regimen of estrogen and progesterone to manage sleep disorders, especially in perimenopausal and postmenopausal women. Moreover, multiple studies have confirmed the efficacy of this regimen in improving sleep disorders

3.3. Melatonin Supplementation

The usual intake and supplementation of melatonin is tablets and capsules. A study conducted by the Respiratory and Sleep Centre of Beijing Chaoyang Hospital, China. The study selected 100 healthy women of childbearing age as test subjects and took them for 3 months according to different doses (0mg, 12mg, 30mg, 75mg, 300mg), The results showed that, with the increase in the dose of melatonin, the more significant the decrease in the level of sex hormones, with obvious dose dependence, the development of dominant follicles was significantly inhibited, and the diameter was significantly reduced. Long-term intake of melatonin drugs may lead to impaired reproductive function. However, in 2025, a study in a paper found that eating 40 grams of walnuts for dinner for 14 consecutive days can increase the level of melatonin in urine by 47.8%, shorten the sleep time by 22%, increase sleep efficiency by 11%, and reduce the number of sleep interruptions by 35%. This shows that the way to supplement melatonin is not only the intake of drugs, but also the maintenance of specific eating habits can also play this effect [10].

3.4. The Treatment of Cortisol

It needs to follow the laws of natural time. An open, cross-and controlled trial on 21 patients with primary adrenal cortical insufficiency [11]. The patients received standard treatment (ST, taking hydrocortisone at 8 a.m. and 4 p.m.) and hourly treatment (CT, taking hydrocortisone at 8 a.m., 4 p.m. and midnight) respectively, each treatment lasts for 8 weeks. The results show that compared with ST, CT significantly improved the sleep quality of patients. The patients in the CT group had higher sleep efficiency, fewer night awakenings, and higher quality of life scores. At the same time, it is found that the hourly treatment method that follows the natural day and night cortisol rhythm can significantly improve the sleep quality of patients, improve sleep efficiency, and reduce the number of night awakenings.

4. Conclusion

Differenet hormones significantly affect the structure and quality of sleep through specific mechanisms, and the measures required for clinical treatment are different. The decrease in oestrogen levels is associated with an increased risk of obstructive sleep apnoea in perimenopause and postmenopausal women. Oestrogen replacement therapy is only effective for some women. Progesterone treatment has been proven to effectively reduce sleep interference, reducing the duration of wakefulness after treatment by 53%, increasing slow-wave sleep time by nearly 50%, increasing total slow-wave activity by nearly 45%, and making sleep normal by regulating the secretion of growth hormone and thyroid hormone. Melatonin allows the human body to distinguish between day and night by regulating the rhythm of the day and night. Melatonin drugs may have side effects that affect reproductive function. Changing eating walnuts may have the same effect while avoiding this side effect. Disorders in the secretion of cortisol can lead to sleep disorders. High cortisol levels before going to bed will lead to a shorter total duration of sleep and a decrease in sleep quality. Hormone therapy that simulates natural rhythms can significantly improve sleep efficiency and the number of night awakenings.

The current research also has gaps and limitations. The relevant studies on estradiol have shown a variety of results, and it is not concluded that estradiol therapy must successfully improve sleep quality. In addition, melatonin drugs are widely used, but the side effect of fertility damage shows that the treatment is not perfect and still needs to be improved. What's more, most of the experiments have a small sample size, a single population, and a lack of special population data. And there are few studies on special groups such as children and pregnant women, and there is a lack of universality

conclusions; also, the treatment has not yet formed a unified standard for its long-term effect and applicable population.

Future research can be devoted to discovering the advantages and disadvantages of separate hormone therapy and hormone combination therapy and the applicable occasions, so as to explore and optimize treatment plans and produce corresponding drugs. Similarly, given the potential risks of drug intervention, exploring non-drug treatment methods such as dietary adjustment is also a valuable research direction. The promotion of these research directions will help develop safer and more effective strategies for preventing and treating sleep disorders, and provide a more reliable theoretical basis for clinical practice.

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