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Sleep and Melatonin

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Abstract – Sleep and melatonin are closely connected. Melatonin is a hormone naturally produced by the body, and it plays a crucial role in controlling sleep patterns. Its primary function is to maintain and synchronize the body's biological clock, influencing various biological and physiological processes. Additionally, melatonin contributes significantly to enhancing sleep quality. Among its essential roles are promoting cell renewal, bolstering the immune system, and regulating both sleep cycles and body temperature.

Keywords – Sleep, Melatonin, Biological Clock, REM, NREM

I. INTRODUCTION

In recent years, there has been a growing global interest in researching the hormone melatonin. Its main role is to safeguard and regulate the body's biological clock, actively participating in numerous biological and physiological processes. People with sleep issues often consider using melatonin as a medication due to its low levels. After application, it has been observed that melatonin improves sleep quality without affecting the total duration of sleep. The secretion of melatonin is contingent on the light sensitivity of pinealocyte cells. Sleep plays a crucial part in ensuring our health and well-being. Quality sleep contributes significantly to preserving both our mental and physical health, thereby helping us maintain an overall high quality of life.

II. SLEEP

Sleep is a vital and intricate behavioral state that plays a crucial role in maintaining neurological, somatic, and psychological health throughout our lives. It is influenced by the structural and functional condition of the brain, which can have both positive and negative effects on neuropsychological performance.

Certain sleep processes are active and involve significant interactions within the brain. Sleep profoundly impacts our overall quality of life. Chronic sleep disorders have been associated with conditions like coronary heart disease and depression, leading to a potential reduction in long-term well-being [1], [2].

The effects of sleep extend to all physiological systems, and in research settings, sleep is commonly characterized by measuring central nervous system activity. This involves using electrodes to evaluate brain activity (electroencephalogram, EEG), eye movements (electrooculogram, EOG), and muscle activity (electromyogram, EMG) to assess brain functions. Since the 1930s [3], sleep researchers have systematically described various sleep stages or states by analyzing combinations of visually observed EEG, EOG, and EMG signals.

A. Stage of Sleep

Sleep is a complex and dynamic process. It encompasses two distinct stages, as defined by Rechtschaffen and Kales [4]: Rapid Eye Movement (REM) sleep and Non-Rapid Eye Movement (NREM) sleep. NREM sleep can be further subdivided into four stages.

NREM sleep is generated in specific regions of the brain, namely the medulla and basal forebrain, while REM sleep is generated in the pons and basal forebrain. Wakefulness, on the other hand, is facilitated by neurons in the brainstem reticular formation, projecting non-specifically to the thalamocortical system, and by neurons in the ventral pathways that facilitate the posterior hypothalamus and basal forebrain [5].

NREM sleep is often referred to as quiet or slow-wave sleep, while REM sleep is characterized by rapid eye movements and also known as paradoxical, active, or rapid sleep. In humans, NREM sleep can be categorized into four stages based on electroencephalographic patterns. NREM-I and II are sometimes called light sleep, whereas NREM-III and IV are referred to as slow-wave sleep or deep sleep [6], [7].

Stage I is an intermediary period between being awake and falling asleep. It is often referred to as light sleep or dozing. In a polysomnogram, the duration of Stage I during regular sleep ranges from 0.5 to 7 minutes. During this stage, breathing becomes slow and steady, the heart rate decreases, and slow eye movements can be observed. Electromyogram (EMG) readings indicate relatively high muscle tone. Reactivity to external stimuli diminishes during Stage I. Mental processes also undergo changes, with thoughts not lingering for long, and short dreams may occur. Interestingly, many individuals may subjectively feel awake during this phase.

Stage II During this slightly deeper phase of sleep, the clarity of thoughts starts to diminish. Eye movements typically cease, and muscles relax with low tonic EMG activity, leading to minimal body movement.

Stages III and IV are collectively known as deep sleep, delta sleep, or slow-wave sleep. It represents the deepest stage of sleep and is characterized by a high threshold for waking reactions. If someone attempts to wake a person during this stage, it often results in heightened drowsiness or immobility (sleep inertia) immediately after awakening, and the individual may feel confused [7], [8].

REM Sleep: Also known as rapid eye movement sleep or paradoxical sleep, it is characterized by muscle atonia, except for essential skeletal muscles like the diaphragm, along with rapid eye movements. REM sleep occurs in cycles, alternating with NREM sleep, with intervals of about 60 minutes in infants and approximately 90 minutes in adults. In certain REM sleep episodes, eye movement activity is highly pronounced, whereas in other instances, eye movements may be minimal or absent. These two distinct states of REM sleep are labeled as phasic REM sleep and tonic REM sleep. Around 80% of individuals who wake up from REM sleep can recall their dreams [9].

III. PINEAL GLAND

The pineal gland, present in the brains of vertebrates, is a structure with a reddish-gray color that produces the hormone melatonin. Melatonin plays a role in regulating sleep-wake patterns and influencing seasonal functions. This small gland extends as a single part of the brain and is located between the posterior commissure and the dorsal habenular commissure, attaching to the posterior wall of the third ventricle. The size and position of the pineal gland vary among different species. In humans, it constitutes a relatively small proportion compared to body weight. In adults, its weight is approximately 100-180 mg, resembling a cone shape, with dimensions of 5-9mm in length, 3-6mm in width, and 3-5 mm in depth, enclosed by the pia mater [10], [11].

Pinealocytes are the primary cell type responsible for secreting melatonin. When observed under a light microscope, these cells show prominent nucleoli, lobulated nuclei, and irregular borders. In close proximity to pinealocytes, numerous synaptic bodies are believed to be involved in axo-dendritic synaptic communication. The melatonin produced by pinealocytes is released into the systemic bloodstream or cerebrospinal circulation at the same rate it is synthesized within the cell, and there is no storage of secretion granules [11], [12], [13].

IV. MELATONIN

Melatonin, a hormone produced by the pineal gland predominantly during the night, has long been linked to regulating the sleep-wake cycle [14], [15]. Melatonin production follows a circadian rhythm and occurs at night in all species. In mammals, the suprachiasmatic nucleus (SCN) governs this rhythm, and disruptions to the SCN can lead to a loss of the circadian pattern of melatonin release. The circadian rhythm is

primarily synchronized with the light-dark cycle [16], [17].

In various species, melatonin secretion is associated with the duration of the night, with longer nights leading to extended melatonin secretion [18]. Light plays a crucial role in suppressing and regulating melatonin release, particularly at the beginning and/or end of the dark phase. Melatonin secretion also exhibits seasonal variations, being released later during summer and earlier during winter. Short-day lengths are linked to prolonged melatonin secretion, while long-day lengths result in shorter melatonin secretion. The physiological response to day length and signal interpretation varies among species. In animals, a preceding long-day period before the short-day melatonin signal triggers the development of the reproductive cycle. Short but adequate exposure to light can suppress melatonin secretion. In humans, a light dose of 2500 lux is required to suppress melatonin secretion at night, with green light being the most effective [10], [19].

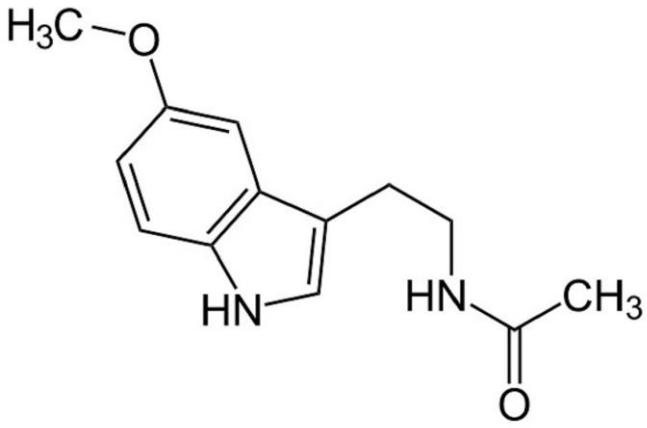

Fig. 1 Melatonin

V. The Relationship Between Melatonin and Sleep

Melatonin's effects on sleep are primarily attributed to its chronobiological influence. The impact of melatonin secretion on sleep is more related to the initiation, quality, and timing of sleep rather than the overall duration of sleep. It is believed that melatonin achieves this by exerting a hypothermic effect and participating in thermoregulation. Sleep is not a prerequisite for melatonin secretion; darkness alone is enough to trigger its release. The increased melatonin secretion leads to a decrease in body temperature (through vasodilation), inducing a feeling of sleepiness, but it does not directly act as a hypnotic.

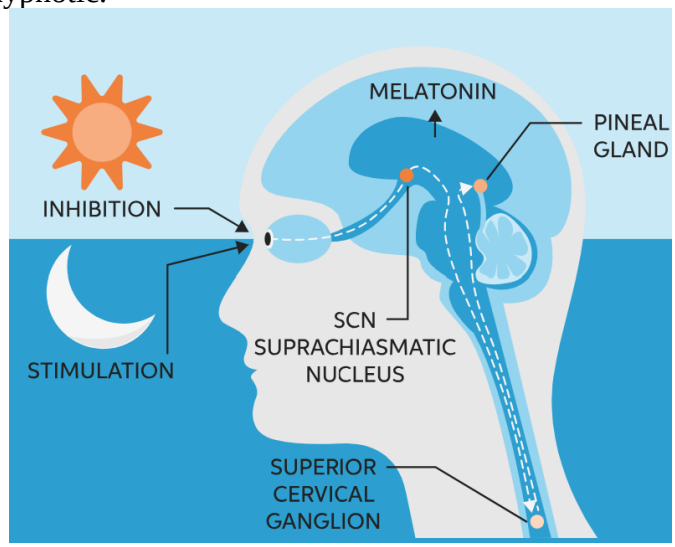

Fig. 2 Melatonin secretion [25]

The role of melatonin in the brain's electrical activity is well understood. Following melatonin administration, there is an increase in alpha waves observed in the electroencephalogram (EEG), particularly. Individuals with sleep disorders tend to have lower serum melatonin levels compared to those without such conditions. In adults, administering 5 mg of oral melatonin has been reported to enhance REM sleep duration and improve sleep quality [21]. Garfinkel's study [22] revealed that low melatonin levels in individuals aged 55 and above were associated with sleep disturbances, and administering 2 mg of melatonin at night did not alter total sleep duration but improved sleep quality [11], [23], [24].

VI. Conclusion

Melatonin, a hormone released during darkness, appears to provide insights into various unanswered questions associated with dark conditions. By incorporating the promising potential of in vivo approaches alongside in vitro melatonin research, we anticipate that numerous enigmatic aspects of melatonin will be clarified in the future, leading to new possibilities for diagnosis and treatment.

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