SLEEP PHYSIOLOGY

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Abstract

Sleep is a complex and essential biological process that plays a fundamental role in maintaining physical and mental health. This paper provides a comprehensive overview of the physiological mechanisms underlying sleep, including circadian rhythms, sleep homeostasis, sleep stages, neural regulation, and sleep disorders. The circadian rhythm, controlled by the suprachiasmatic nucleus, regulates the sleep–wake cycle in response to environmental light, while sleep homeostasis reflects the body's need for sleep based on prior wakefulness. Sleep is divided into two main phases: non-rapid eye movement (NREM) and rapid eye movement (REM), which alternate cyclically throughout the night. NREM sleep is primarily associated with physical restoration, whereas REM sleep plays a key role in memory consolidation, emotional processing, and cognitive function. The neural control of sleep involves complex interactions between the hypothalamus, brainstem, thalamus, and cortical networks. Additionally, this paper discusses common sleep disorders such as insomnia, obstructive sleep apnea, narcolepsy, and somnambulism, highlighting their impact on overall health. Understanding sleep physiology is essential for recognizing the importance of sleep and improving approaches to sleep-related disorders.

Keywords: Sleep physiology, circadian rhythm, REM sleep, NREM sleep, sleep disorders

Introduction

Sleep is a fundamental biological process essential for maintaining the normal functioning of the human body. Despite appearing as a passive state, sleep is an active and highly regulated physiological process involving complex interactions between neural, hormonal, and metabolic systems. Its importance extends beyond rest, playing a critical role in physical recovery, cognitive performance, emotional regulation, and overall health.

The significance of studying sleep physiology has increased in recent years due to the growing prevalence of sleep-related disorders and their impact on quality of life. Disruptions in sleep are associated with a wide range of health problems, including metabolic, cardiovascular, and neurological conditions. Therefore, understanding the mechanisms that regulate sleep is essential for both clinical practice and preventive healthcare.

This paper focuses on the physiological mechanisms underlying sleep, with particular emphasis on circadian rhythms, sleep homeostasis, sleep stages, and neural regulation. The circadian system, controlled by the suprachiasmatic nucleus of the hypothalamus, synchronizes the sleep–wake cycle with environmental light–dark patterns. In parallel, sleep homeostasis regulates the need for sleep based on prior wakefulness, ensuring a dynamic balance between sleep and alertness.

The objective of this paper is to provide a comprehensive overview of sleep physiology and its regulatory systems, as well as to discuss the main stages of sleep and their functional significance. Additionally, common sleep disorders are briefly presented in order to highlight the clinical relevance of normal sleep mechanisms.

By analyzing these aspects, this work aims to emphasize the importance of sleep as a vital component of human health and to contribute to a better understanding of its physiological basis.

Body of Manuscript

2.1 Sleep Physiology : Sleep is regulated by two key biological mechanisms: the circadian rhythm and sleep homeostasis. These systems interact to control the timing, duration, and quality of sleep.
The circadian rhythm is an internal 24-hour biological clock regulated by the suprachiasmatic nucleus (SCN) of the hypothalamus. It synchronizes physiological processes such as hormone secretion, body temperature, and the sleep–wake cycle with environmental light–dark changes. Light exposure inhibits melatonin secretion, promoting wakefulness, whereas darkness stimulates melatonin production and facilitates sleep.
Sleep homeostasis reflects the body's need for sleep based on prior wakefulness. During wakefulness, substances such as adenosine accumulate in the brain, increasing sleep pressure. During sleep, particularly deep sleep, these substances decrease, restoring physiological balance.

2.2 Stages of Sleep: Sleep is a dynamic process divided into two main phases: non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. These stages occur in cycles that repeat several times throughout the night.

2.2.1 NREM Sleep: The N1, N2, and N3 stages constitute non-rapid eye movement (NREM) sleep and account for approximately 75% of total sleep time. These stages are characterized by a gradual transition from light to deep sleep, accompanied by progressive changes in brain activity, physiological functions, and level of consciousness.
Stage N1 is the initial stage of sleep and is considered very light sleep. It occurs during the transition from wakefulness to sleep and typically lasts 1–5 minutes. During this stage, brain activity shifts from alpha waves to low-amplitude theta waves. The body begins to relax, although muscle tone is still present and breathing remains regular. Brief muscle contractions, known as *hypnic jerks*, may occur, and individuals often experience a sensation of falling. This is the stage in which a person can be easily awakened and may not perceive it as actual sleep.
Stage N2 represents a deeper level of sleep and is the longest stage, accounting for approximately 45–50% of total sleep time. During this stage, physiological functions slow significantly: heart rate decreases, body temperature drops, and muscles relax further. Brain activity is characterized by two distinct patterns: *sleep spindles* and *K-complexes*. Sleep spindles are short bursts of neural activity associated with information processing and protection of sleep from external stimuli, while K-complexes are high-amplitude waves that help stabilize sleep and contribute to memory consolidation. Bruxism (teeth grinding) may also occur during this stage. As the night progresses, the duration of N2 sleep gradually increases.
Stage N3 is the deepest stage of NREM sleep and is also known as *slow-wave sleep*. It is characterized by the presence of delta waves, which have low frequency and high amplitude. This stage is essential for physical restoration, as processes such as tissue repair, muscle growth, growth hormone secretion, and immune system strengthening occur. It is very difficult to awaken a person during this stage, and if awakened, they often experience temporary confusion and fatigue, known as *sleep inertia*. Phenomena such as sleepwalking (somnambulism), night terrors, and involuntary urination may also occur during this stage. N3 sleep is more prominent in the first half of the night and decreases as sleep cycles progress.

2.2.2 REM Sleep: REM sleep is one of the most important stages of sleep and accounts for approximately 20–25% of total sleep time in adults. It typically begins about 90 minutes after sleep onset and recurs several times throughout the night, with progressively longer durations in later cycles. This stage is characterized by high brain activity similar to wakefulness, while the body is in a state of temporary muscle paralysis (atonia), which prevents the physical enactment of dreams.
One of the main features of REM sleep is the presence of vivid and intense dreaming. Cerebral activity increases significantly, and brain oxygen consumption may rise by up to 20%, indicating high neuronal metabolism. During this stage, eye movements are rapid and repetitive, while breathing and heart rate become more irregular. Despite this increased brain activity, skeletal muscles remain relaxed and almost completely immobile, except for the muscles involved in breathing and eye movements.
REM sleep plays a crucial role in cognitive and emotional functions. It is closely associated with memory consolidation, particularly emotional and procedural memory, as well as learning and creativity. Additionally, REM sleep contributes to emotional processing and the reduction of psychological stress, supporting overall emotional stability.
During this phase, neurochemical changes also occur, such as increased levels of acetylcholine (ACh), which stimulate brain activity. At the same time, the autonomic nervous system becomes more active, leading to fluctuations in blood pressure and heart rate. Another characteristic phenomenon is genital tumescence (penile or clitoral), which occurs regardless of dream content.
In conclusion, REM sleep is essential for mental health and optimal brain function. It complements the restorative processes that occur during NREM sleep by providing not only physical rest but also the reorganization and processing of information in the brain.

2.3 Neural Control of Sleep: Sleep is not controlled by a single anatomical center in the brain, but rather by a complex and integrated network of neural structures that interact to regulate its initiation, maintenance, depth, and rhythm. However, the hypothalamus is considered the primary region in sleep regulation, as it contains nuclei involved both in promoting sleep and synchronizing the sleep–wake cycle with circadian rhythms.
One of the most important structures is the ventrolateral preoptic nucleus (VLPO), which plays a key role in initiating sleep. Its neurons secrete inhibitory neurotransmitters, mainly GABA and galanin, which suppress the systems responsible for wakefulness, including monoaminergic and cholinergic centers in the brainstem and hypothalamus. In this way, the VLPO acts as a “functional switch” that facilitates the transition from wakefulness to sleep.
Another essential structure is the suprachiasmatic nucleus (SCN), known as the body’s “biological clock.” The SCN receives direct input from the retina through the retinohypothalamic tract and synchronizes biological rhythms, including the sleep–wake cycle, according to the light–dark cycle. Although it does not directly induce sleep, it determines the biological timing when the organism is predisposed to sleep. Through its connections with the pineal gland, the SCN regulates the secretion of melatonin, a hormone that promotes sleep onset.
In addition to the hypothalamus, the brainstem plays a crucial role in regulating consciousness and the transition between wakefulness and sleep, particularly through the ascending reticular activating system (ARAS). This system consists of neuronal groups in the midbrain, pons, and medulla oblongata, which project to the thalamus, hypothalamus, and cerebral cortex. The

ARAS is responsible for maintaining wakefulness, alertness, and cortical activity. Its neurons use excitatory neurotransmitters such as norepinephrine, serotonin, dopamine, histamine, and acetylcholine. During sleep onset, the activity of this system decreases, while during wakefulness it increases, demonstrating that sleep is an active and regulated process rather than a passive state.

The thalamus also plays an important role, especially during NREM sleep, acting as a filter for sensory information reaching the cerebral cortex. During deep sleep, this transmission is significantly reduced, effectively isolating the brain from external stimuli. An important component is the thalamic reticular nucleus (TRN), which is involved in generating sleep spindles characteristic of stage N2.

The cerebral cortex and thalamocortical networks also contribute to sleep regulation. During NREM sleep, cortical activity becomes more synchronized and appears on EEG as slow waves, whereas during REM sleep, brain electrical activity resembles that of wakefulness. REM sleep is primarily controlled by brainstem structures, particularly in the pons, where circuits regulate dreaming, rapid eye movements, and muscle atonia.

From a functional perspective, sleep regulation is often explained by the “flip-flop switch” model, in which sleep-promoting and wake-promoting systems mutually inhibit each other. Dominance of the VLPO leads to sleep, while activation of wake-promoting systems maintains consciousness. This mechanism explains the rapid and stable transitions between sleep and wakefulness.

An important role in stabilizing wakefulness is also played by orexin (hypocretin), a neuropeptide produced in the lateral hypothalamus. Orexin helps maintain wakefulness and prevents sudden transitions into sleep; its deficiency is associated with disorders such as narcolepsy.

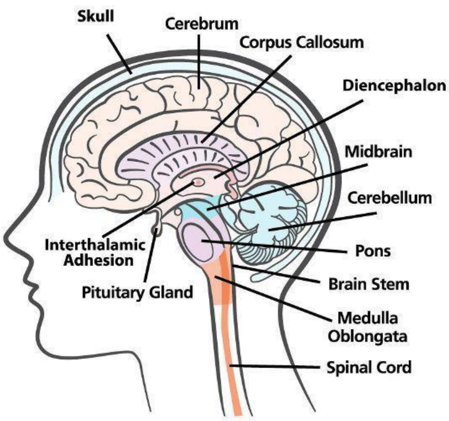

Figure 1. Centrals of sleep in the brain

2..4 Sleep Cycle: The sleep cycle represents a periodic process in which the body repeatedly passes through different stages of sleep during the night. A complete cycle includes the transition from non-REM (NREM) sleep to REM sleep and typically lasts about 90–110 minutes. During a normal night, an individual usually goes through 4–6 such cycles.

The sleep cycle begins with the stages of NREM sleep. Initially, the individual enters stage N1, which represents the transitional phase from wakefulness to sleep and is characterized by a gradual reduction in brain activity, muscle relaxation, and slowing of physiological processes. Sleep then progresses to stage N2, where it becomes more stable and deeper. In this stage, heart rate and body temperature decrease, while brain activity is characterized by specific structures such as sleep spindles and K-complexes, which help stabilize sleep and process information. Following this, the body reaches stage N3, known as deep or slow-wave sleep. This stage is essential for physical recovery, as processes such as tissue repair, muscle growth, and immune system strengthening occur.

After completing the NREM stages, the body transitions into REM (Rapid Eye Movement) sleep. In this phase, brain activity increases and resembles that of wakefulness, while the body experiences temporary muscle paralysis. REM sleep is associated with vivid dreaming and plays a key role in memory consolidation, learning processes, and emotional regulation.

Throughout the night, the structure of sleep cycles changes progressively. In the early cycles, deep sleep (N3) predominates and is more important for physical recovery. In later cycles, REM sleep duration increases and is more closely associated with cognitive and emotional functions. This organization of sleep cycles is essential for optimal brain function and overall well-being.

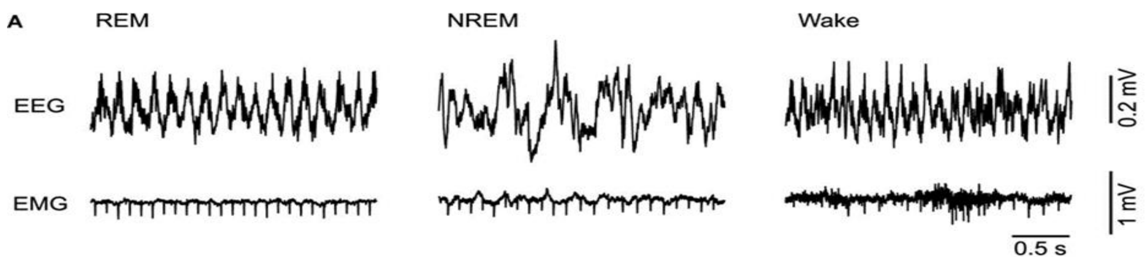

Figure 2. Sleep cycle showing progression of NREM and REM stages

2.5 Sleep disorders : Sleep disorders, also known as disturbances of sleep, are conditions that affect the quality, duration, or normal rhythm of sleep. These disorders can negatively impact both physical and mental health, leading to fatigue, decreased concentration, irritability, and impaired daily functioning.

Sleep problems are common and are often behavioral in origin, influenced by factors such as a child's temperament and development, parenting style, parent–child interactions, and environmental conditions. Additionally, parasomnias may occur, which are undesirable episodic behaviors associated with sleep. Nightmares occur during REM sleep, usually in the early morning, and are most common in school-aged children, although they are also observed in approximately 1.9–3.9% of preschool children.

2.6 Clinical Conditions:

2.6.1 Insomnia: Insomnia is a general term for conditions that cause difficulty in falling asleep or maintaining sleep. It is the most common sleep disorder and is typically associated with psychological stress, poor sleep environments, irregular sleep schedules, or excessive mental, physical, or chemical stimulation.

2.6.2 Obstructive Sleep Apnea (OSA): Obstructive sleep apnea is a disorder characterized by repeated episodes of interrupted breathing during sleep due to airway obstruction, often caused by obesity or weakened pharyngeal muscles. When the airway collapses, breathing stops, and hypoxia forces the body to awaken from deep sleep to resume breathing. When this occurs repeatedly throughout the night, restful sleep becomes impossible.

OSA is classified into three severity levels:

[1] Mild: 5–14 apnea episodes per hour
[2] Moderate: 15–30 episodes per hour
[3] Severe: more than 30 episodes per hour

The primary treatment is positive airway pressure therapy, including:

[1] Continuous Positive Airway Pressure (CPAP)
[2] Bilevel Positive Airway Pressure (BiPAP)

CPAP provides continuous pressure to keep the airway open, while BiPAP alternates between two pressure levels, improving ventilation. Additional treatments include mandibular advancement devices and surgical interventions such as uvulopalatopharyngoplasty, adenotonsillectomy, and maxillomandibular advancement. However, the main treatment remains non-surgical positive airway pressure therapy.

2.6.3 Central Sleep Apnea: Central sleep apnea is similar to obstructive sleep apnea but differs in its underlying cause. It results from reduced or absent respiratory drive during sleep due to dysfunction in the brain's respiratory control mechanisms. Conditions associated with central sleep apnea include congenital central hypoventilation syndrome (Ondine's curse) and congestive heart failure.

When breathing becomes ineffective, the body awakens from deep sleep to correct hypoxia. Treatment options include CPAP, BiPAP, adaptive servo-ventilation, and pharmacological therapy such as acetazolamide or theophylline.

2.6.4 Mixed Sleep Apnea (Complex Sleep Apnea): Mixed sleep apnea is a combination of obstructive and central sleep apnea. It occurs when patients with obstructive sleep apnea develop central sleep apnea symptoms after treatment with CPAP during a sleep study.

Treatment usually involves CPAP therapy at lower pressure levels.

2.6.5 Ghrelin–Leptin Imbalance: Sleep duration plays an important role in maintaining body weight. An imbalance between two key hormones regulating hunger—leptin and ghrelin—is associated with altered sleep patterns. Leptin, produced by adipose tissue, reduces appetite and regulates energy balance. Ghrelin, produced in the gastrointestinal tract, stimulates appetite.

Short sleep duration is associated with decreased leptin and increased ghrelin levels, which may lead to increased appetite and higher body mass index (BMI). This imbalance is often associated with obstructive sleep apnea, as increased BMI is a major risk factor for its development. The primary intervention is maintaining consistent sleep of 7–8 hours per night.

2.6.6 Narcolepsy: Narcolepsy type 1 occurs when there is a near-complete loss of neurons that produce orexin (hypocretin). The mechanism of narcolepsy type 2 is less clear but is thought to involve a partial loss of these neurons.

During normal REM sleep, orexin levels decrease, reducing activity in the reticular activating system (RAS) and promoting muscle atonia. In narcolepsy type 1, insufficient orexin leads to instability between sleep and wake states. The RAS fails to consistently maintain wakefulness and cannot properly inhibit sleep-promoting systems such as the VLPO.

This results in sudden transitions between sleep and wakefulness and allows REM-related phenomena to occur during wakefulness. Symptoms include excessive daytime sleepiness, cataplexy, and sometimes hallucinations triggered by strong emotions. Many individuals with narcolepsy also experience insomnia.

2.6.7 Somnambulism (Sleepwalking): Somnambulism is a condition that combines elements of sleep and wakefulness, resulting in sleepwalking. It occurs when an individual performs actions or walks without conscious awareness and has no memory of the event.
Although not fully understood, it is associated with increased slow-wave sleep and sleep deprivation, and there is evidence of a genetic component. The primary treatment involves the use of benzodiazepines.

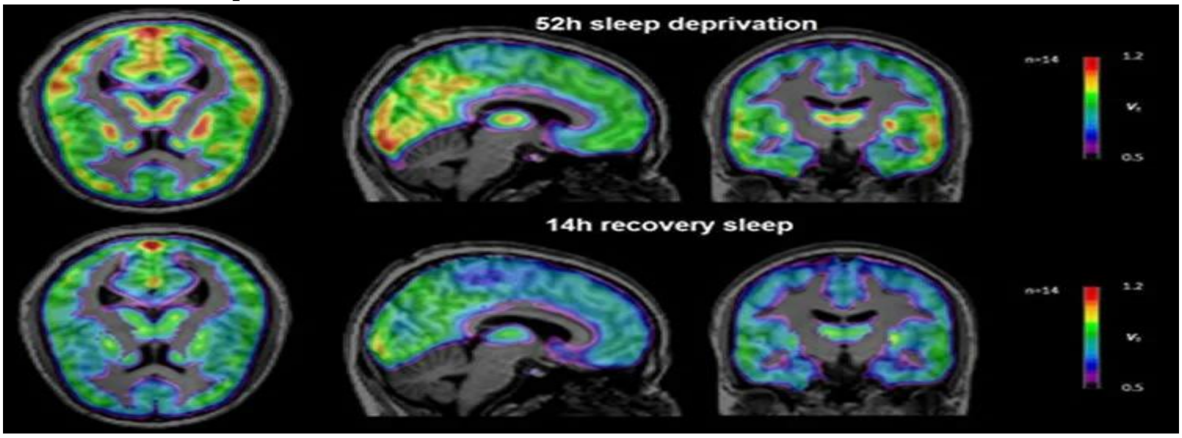

Figure 3. Sleep deprivation

Conclusions

Sleep is a fundamental biological process essential for maintaining physical health, cognitive performance, and emotional stability. It is a complex and highly regulated process involving the interaction of neural, hormonal, and physiological mechanisms that control the sleep–wake cycle.
The different stages of sleep, including NREM and REM sleep, play distinct yet complementary roles in restoring the body and optimizing brain function. NREM sleep is primarily associated with physical recovery, tissue repair, and immune function, while REM sleep is crucial for memory consolidation, learning, and emotional regulation.
Disruptions in normal sleep patterns can lead to a variety of sleep disorders, such as insomnia, sleep apnea, and narcolepsy, which can significantly impair daily functioning and overall health. These conditions highlight the importance of maintaining proper sleep hygiene and understanding the underlying physiological mechanisms of sleep.
In conclusion, sleep is not merely a passive state of rest but an active and essential process that supports overall well-being. A deeper understanding of sleep physiology is important for improving clinical approaches to sleep disorders and promoting better health outcomes

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