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THE ROLE OF SLEEP ARCHITECTURE AND CIRCADIAN RHYTHMS IN HEALTH: A REVIEW OF DISORDERS AND INTERVENTIONS ACROSS AGE GROUPS

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ABSTRACT

This review explores the critical influence of sleep architecture and circadian rhythms on health across all life stages, highlighting the functions of REM and NREM sleep in memory, metabolism, and emotional stability. It examines factors such as aging, lifestyle changes, hormonal fluctuations, and modern environmental stressors that disrupt sleep quality and contribute to disorders like insomnia, sleep apnea, and mood disturbances. Each life stage presents unique sleep-related challenges: children and adolescents often face neurodevelopmental and behavioral impacts, adults encounter elevated risks of cardiovascular and metabolic diseases, and elderly individuals experience fragmented sleep linked to cognitive decline. Gender-specific issues such as those arising from menstrual cycles, pregnancy, and menopause further illustrate the relationship between hormonal shifts and sleep quality. This review also underscores the impact of contemporary lifestyle factors, such as artificial lighting, digital device usage, and irregular schedules, on circadian rhythms, increasing the prevalence of chronic conditions including metabolic syndrome and depression. Effective management strategies—including cognitive behavioral therapy, light exposure control, and lifestyle adjustments—are essential to maintaining sleep health and promoting public well-being. Addressing sleep health as a public health priority can reduce the burden of sleep disorders and enhance quality of life.

INTRODUCTION

1. Introduction to Circadian Rhythms and Evolutionary Adaptation

Life on Earth has developed to evolve to the 24-hour sun day, with organisms, which include humans, internalizing those each day cycles thru circadian rhythms. Circadian rhythms, which comply with a more or less 24-hour period, assist synchronize organic and behavioural methods with the outside environment, optimizing the timing of physiological functions.

Sleep Phases and Cycles

Sleep is composed of two main phases:

1. REM (Rapid Eye Movement) and
2. NREM (Non-Rapid Eye Movement).

REM sleep is characterized by dreaming and heightened brain activity and recurs multiple times throughout the night.

NREM is divided into three stage N1 - (light sleep), N2 - (intermediate), and N3 - (deep sleep).

A full sleep cycle lasts around 90 minutes, during which we transition from non-rapid eye movement (NREM) sleep to rapid eye movement (REM) sleep. This cycle typically repeats 4 to 6 times throughout the night**.**

Key Influences on Sleep Quality and Stages

Factors such as depression, aging, brain injuries, medications, and circadian rhythm disorders can significantly alter sleep stage duration and overall sleep quality. These changes often impact both NREM and REM phases, affecting restorative functions and cognitive health.

Sleep-Regulating Mechanisms

Sleep-promoting mechanisms rely on neurotransmitters like GABA and adenosine. GABA, the main inhibitory neurotransmitter in the CNS, encourages sleep by suppressing wakefulness centers. Adenosine, another key compound, dampens wakefulness by inhibiting neurons that keep us alert. In contrast, wakefulness is supported by neurotransmitters such as acetylcholine, dopamine, norepinephrine, serotonin, histamine, and hypocretin. Together, these chemicals boost alertness and help maintain wakefulness.

Sleep architecture changes significantly across the lifespan

Newborns and infants (0–1 year) sleep 16–18 hours daily, with REM cycles of about 50 minutes, developing circadian rhythms by 2–3 months. Toddlers and young

children (1–9 years) gradually reduce sleep from 13 to 11 hours, with more deep sleep (N3) and emerging sleep preferences. Adolescents (10–18 years) need 9–10 hours but have less deep sleep due to hormonal changes that may cause daytime sleepiness. Adults (18+ years) need 7–8 hours, spending more time in lighter sleep (N2) as they age, while older adults (65+) experience more awakenings and earlier sleep-wake times. Elderly adults (65+) often have shorter, lighter sleep and advanced circadian rhythms.

Functions of sleep: Sleep serves multiple essential functions, including neural development, memory consolidation, metabolic waste clearance, energy conservation, and synaptic network organization. These processes underscore the necessity of each sleep stage in maintaining health and cognitive performance.

Clinical Significance and Testing

Polysomnography is the gold standard for diagnosing sleep disorders, including conditions like sleep apnea and REM sleep behavior disorder. These disorders can significantly impact both the quality and duration of sleep. Insomnia, for example, interferes with the ability to fall or stay asleep, while sleep apnea causes interruptions in deep sleep due to airway obstructions. Other conditions such as narcolepsy lead to abrupt transitions into REM sleep, and somnambulism (or sleepwalking) typically occurs during N3 (deep) sleep.

Impact of Substances on Sleep: Substances such as alcohol, benzodiazepines, and barbiturates suppress REM and N3 stages, affecting sleep quality. Benzodiazepines, however, are sometimes used to manage night terrors and sleepwalking by raising arousal thresholds in these sleep stages.

Alterations of circadian rhythms may leads

1. **Artificial light exposure:** Modern lighting disrupts natural day-night cycles, impacting circadian rhythms and increasing health issues, particularly in industrialized settings.
2. **Night shift work:** Night workers have higher rates of cancer, cardiovascular disease, and mood disorders due to circadian misalignment.
3. **Jet Lag and Social Jet Lag:** Time-zone shifts and inconsistent weekend sleep schedules misalign circadian rhythms, affecting mood and well-being.
4. **Circadian Disruption and MDD:** Night shift work and circadian misalignment are associated with higher depression risks. Biological rhythm disruptions often align with MDD symptoms, like altered melatonin and cortisol rhythms.
5. **Mood Disorders and Circadian Disruption:** Disruptions are linked to SAD, bipolar disorder, and PTSD, with physiological evidence of circadian regulation of mood-related brain areas.
6. **Modern Light Exposure and Lifestyle:** Nighttime device usage has increased, correlating with rising mood disorders due to circadian disruption.
7. **Behavioral Interventions:** Reducing evening light exposure, setting consistent schedules, and limiting screen time can help align circadian rhythms and improve mental health.

Circadian System and Light's Impact on Mood Regulation

1. **Pathways linking light exposure to mood:** Night light exposure influences mood through retinal cells (ipRGCs) that connect to mood-regulating brain areas.
2. **Melatonin and Light's Influence on Mood**:** Darkness-triggered melatonin helps synchronize clocks, though its absence may not solely drive mood disruptions.
3. **Light and Mood Disruption:** Studies on nocturnal animals show night light impacts mood independently of sleep disruption.
4. **Circadian control of glucocorticoid secretion:** Daily glucocorticoid rhythms, crucial for glucose homeostasis, are linked to stress responses. Night light disrupts the HPA axis, increasing cortisol-related mood disorders.
5. **Implications for mood regulation:** Night light can disrupt mood by interfering with circadian rhythms, affecting brain areas tied to mood and indirectly dysregulating systems like the HPA axis. Managing light exposure may help mitigate circadian-related mood disturbances.

Sleep architecture changes significantly across the lifespan

Typical Sleep Patterns in Infants and Children

The circadian rhythm is an internally regulated cycle, with its central pacemaker located in the suprachiasmatic nuclei of the anterior hypothalamus. Light from the retina serves as the primary input to this system, while its output regulates key processes such as the sleep-wake cycle, body temperature, and melatonin secretion. By approximately 3 months of age, the circadian system matures, with melatonin levels becoming detectable in infants' urine. At birth, infants exhibit two primary sleep states: active sleep (which is the precursor to REM sleep) and quiet sleep (the precursor to NREM sleep). As the brain matures, the electroencephalogram (EEG) patterns evolve, and by 6 months, clear distinctions can be made between the stages of NREM sleep (from light sleep, NREM 1, to deep sleep, NREM 4) and REM sleep.[4]

The Causes That Effect the Sleep Patterns of Infants and Children

1. **Definition and Subtypes of Childhood Insomnia**

The International Classification of Sleep Disorders (ICSD) initially classified pediatric insomnia as "behavioral insomnia of childhood" (BIC) and later integrated it into chronic insomnia in its third edition. Pediatric insomnia is characterized by three subtypes:

- **Sleep-onset association type:** The child depends on specific stimuli or conditions to initiate or return to

sleep, leading to significant delays without these factors.
- **Limit-setting type:** The child exhibits bedtime stalling or refusal due to inadequate limit-setting by caregivers.
- **Mixed type:** This encompasses difficulties with sleep-onset associations combined with bedtime resistance.[5]

2. Definition of pediatric insomnia

Pediatric insomnia is defined as repeated difficulty with sleep initiation, duration, or quality, despite having appropriate time and opportunity for sleep. This condition results in daytime functional impairment for the child and/or family. Common sleep problems include difficulty initiating and maintaining sleep. In young children, these are often referred to as "bedtime problems and night waking," whereas older children and adolescents typically identify these issues as insomnia. Furthermore, insomnia and sleep disturbances can increase the risk of depression and self-harm behaviors in children and adolescents.[6]

3. Spectrum of sleep disorders in children

Sleep is vital for human biology, and disturbances can affect cognitive, emotional, and physical well-being. Sleep problems in infancy and early childhood are generally related to initiating and maintaining sleep. Children typically require 16 to 18 hours of sleep in their first year, gradually decreasing to about 10 hours during childhood and adolescence. Sleep disorders can indicate neurophysiological alterations and lead to behavioral changes.[7]

4. Pediatric sleep disturbances

Behavioral insomnia of childhood (BIC) is the most common cause of pediatric insomnia, affecting both sleep initiation and maintenance.[8]

5. Causes of pediatric sleep disorders
- **Biological causes:** Hyper-arousal and hypersensitivity, especially in children with autism spectrum disorders (ASDs), as well as dysregulated neurotransmitters like GABA, melatonin, and serotonin, can contribute to insomnia.
- **Medical causes:** Conditions such as gastrointestinal issues, pulmonary diseases (e.g., asthma), and upper airway pathologies (e.g., snoring and obstructive sleep apnea) can lead to sleep disorders. Studies show that children with atopic dermatitis often experience disturbed sleep, impacting their quality of life. Children with Down syndrome frequently face sleep challenges, including insomnia and disruptive awakenings. Neurological conditions like headaches, epilepsy, and restless legs syndrome can also influence sleep.
- **Behavioral causes:** Factors such as electronic device usage, caffeine and alcohol intake, irregular bedtimes, and insufficient physical activity can cause or exacerbate sleep disorders, often overlapping with biological causes related to dependence on external factors for sleep.[8]

6. Obstructive sleep apnea

Children with sleep disorders, particularly severe sleep-disordered breathing (SDB), can experience significant medical and behavioral issues, including heart complications and growth problems. Less severe SDB is associated with attention issues, hyperactivity, cognitive impairments, and emotional instability. Obstructive sleep apnea syndrome affects about 1% to 3% of children, with up to 43% experiencing substantial sleep disturbances. Common parasomnias like sleep terrors, sleepwalking, and bruxism are reported in 15% to 29% of children, and insomnia affects around 17% of children aged 3 to 14 years.[9] Children with Down syndrome are at higher risk for obstructive sleep apnea due to anatomical factors, with obesity and adenotonsillar hypertrophy contributing to this risk.[10] Reports of sleepiness are less common in preschoolers than in older children, and excessive weight correlates with higher SDB scores among overweight children.

In adolescence

1. General sleep patterns

During adolescence, sleep duration tends to decrease, particularly between the ages of 10 and 12. This period often sees an increase in sleep disturbances due to inadequate sleep duration, irregular sleep patterns, and abnormal schedules. The quality of sleep can be objectively measured using techniques like polysomnography and wrist actigraphy, with the latter requiring specialized software. For subjective assessments, the Sleep Disturbance Scale for Children (SDSC) is frequently employed.[11]

A study found that participants monitored with wrist actigraphy had an average sleep duration of 6.6 hours. Among these, 51.6% of children reported sleep disturbances, with the SDSC identifying issues in 71.7% of cases, and 34.9% experiencing insomnia. These results align with research in Jakarta, where a 62.9% prevalence of sleep disturbances was noted. The SDSC showed 80.6% sensitivity and 37.9% specificity when compared to wrist actigraphy. The results showed the sensitivity of SDSC was 80.6%, the specificity was 37.9%, the positive predictive value was 58.1% and negative predictive value was 64.7%.[11]

Excessive technology use, especially smartphones and televisions, has significantly contributed to adolescent insomnia. Sleep disturbances disrupt the quantity, quality, and timing of sleep, impairing daytime functioning and contributing to various health issues. They are correlated with obesity, hormonal imbalances, and high-altitude living. Effective management strategies include cognitive therapy, avoiding triggers, and medication to normalize sleep patterns.[12]

2. Restless Legs Syndrome (RLS)

Restless Legs Syndrome (RLS) is characterized by an uncontrollable urge to move the legs, particularly during periods of rest, and is more pronounced at night. It affects approximately 2% to 6% of children, with limited research on its prevalence. A study focusing on adolescents aged 12 to 20 found that 8.4% exhibited RLS symptoms, leading to increased sleep difficulties (odds ratio of 3.1) and lower quality of life. Notably, the cognitive and sleep impacts were independent of ADHD, which was excluded from the study.[13]

Similar to findings in younger children, where sleep disturbances were prevalent, this emphasizes the need for attention to technology use to improve sleep quality.

3. Obstructive Sleep Apnea Syndrome (OSAS)

Obstructive sleep apnea syndrome (OSAS) affects 2% of women and 4% of men aged 30-60, with a significant portion of cases undiagnosed. Characterized by airflow interruptions and oxygen desaturation during sleep, OSAS can lead to snoring, fatigue, and cognitive issues, increasing risks for cardiovascular diseases and accidents. A study found that 55.8% of participants had OSAS, with a higher apnea-hypopnea index (AHI) observed when supine.[14] Positional therapy showed promise, but adherence was low due to discomfort. Behavioural sleep disorders, such as bedtime resistance and excessive daytime sleepiness, affect 20-30% of children in the U.S. Notably, sleep issues are common among children with psychiatric disorders, with significant associations with ADHD, autism spectrum disorders, and mood/anxiety disorders.[15]

4. Delayed Sleep Phase Syndrome (DSPS)

Delayed Sleep Phase Syndrome (DSPS) is increasingly recognized as a cause of insomnia in adolescents, often beginning in childhood. It is influenced by social, psychological, environmental, and biological factors. Traditional treatments have been largely ineffective, while strategies allowing for later sleep onset have shown promise. Effective treatments include light therapy, melatonin supplementation, and vitamin B12.[16]

5. Depression

Depression affects approximately 4-5% of children, with over a third experiencing sleep disturbances. A study involving 12,520 children in sleep clinics revealed that those with sleep issues, particularly insomnia, were significantly more likely to exhibit severe depressive symptoms. Factors such as age, gender, and specific sleep disorders were identified as predictors of depression. Recognizing these factors is crucial for timely intervention, as almost 5% of children expressed suicidal thoughts.

Sleep disturbances in adolescents are multifaceted, with various contributing factors and health implications. Recognizing and addressing these issues through early interventions, appropriate therapies, and lifestyle modifications can improve sleep quality and overall well-being.[17]

In men

1. Infertility in men

Infertility affects around 15% of couples worldwide, with male factors contributing to 20-30% of cases. Sleep deprivation (SD) is linked to reduced sperm quality and negatively impacts reproductive hormones. SD disrupts the hypothalamic-pituitary-adrenal (HPA) axis and immune function, leading to increased anti-sperm antibodies and oxidative stress, ultimately compromising fertility.

A study on Vitamin C's effects indicated its potential in alleviating the negative impacts of SD on male fertility. In sleep-deprived rats, SD reduced sperm count, viability, and motility, while increasing abnormal sperm forms. Vitamin C supplementation improved testosterone levels, reduced oxidative stress, and countered inflammatory cytokines, supporting spermatogenesis and preserving testicular structure.[18]

Additionally, research on 981 healthy Chinese men found that late bedtimes and insufficient sleep negatively impacted semen quality. The optimal sleep duration for fertility was identified as 7.0 to 7.5 hours, with early bedtimes associated with better semen quality. However, the link between longer sleep durations and semen quality remains unclear.[19]

Sleep disturbances pose a significant public health issue, with gender disparities noted in a study of Jordanian residents. Women reported more sleep disturbances, influenced by hormonal factors, socioeconomic status, and technology use. Interestingly, older women experienced fewer issues than younger women, while men on fixed night shifts generally slept better than those on rotating schedules. This highlights the complex interactions of gender, age, and lifestyle choices in sleep health, indicating a need for targeted interventions to improve sleep quality across demographics.[20]

In women

1. Menstrual cycle

The menstrual cycle has two key phases: the follicular phase (characterized by low estrogen and almost absent progesterone) and the luteal phase (marked by high progesterone levels). Hormones such as estrogen and progesterone influence neurotransmitters like serotonin and GABA, impacting sleep quality. Sleep disturbances often worsen with dysmenorrhea during the follicular phase and premenstrual syndrome (PMS) symptoms, such as cramps and mood changes, during the luteal phase. Sleep is crucial for overall health, affecting metabolism, immune function, and memory.[21] Disturbances can lead to lifestyle diseases (e.g., obesity, hypertension) and are linked to hormonal fluctuations.[22] Young women, particularly college students in Korea, often experience sleep deprivation due to academic

stress, exacerbating PMS and dysmenorrhea symptoms. Poor sleep quality is identified as a key factor worsening menstrual pain and requires sleep-focused interventions.[23] Increased mobile phone use among younger women is associated with poor sleep quality, potentially impacting reproductive health through hormonal disruption. While research hasn't found a direct link between mobile phone use and menstrual disturbances, it emphasizes the need for further studies.[24] Additionally, shift work disrupts circadian rhythms, contributing to menstrual issues and highlighting the importance of addressing sleep patterns to improve reproductive health.[25]

2. Pregnancy and Infertility

Up to 80% of pregnant individuals experience insomnia in the third trimester, often due to hormonal changes, physical discomfort, and stress.[26]

Common sleep disorders include obstructive sleep apnea, insomnia, restless leg syndrome, and GERD, which are linked to complications like gestational diabetes, hypertension, preeclampsia, preterm birth, and postpartum depression.[27,28] Maternal sleep apnea is associated with lower Apgar scores and more frequent NICU admissions, while insomnia increases emergency room visits and preterm births by 70%.[29] A study with nearly three million births found that infants of mothers with sleep disorders had higher risks of negative outcomes. Cognitive Behavioral Therapy for Insomnia (CBTI) and Continuous Positive Airway Pressure (CPAP) are recommended for managing insomnia and sleep apnea, but research on their effectiveness during pregnancy is still limited.[29] Sleep hygiene education, which teaches better sleep habits, has shown positive effects on sleep quality, though more research is needed to confirm its benefits in reducing adverse outcomes.[30] Poor sleep quality negatively affects IVF outcomes, including pregnancy and live birth rates.[31] Women with recurrent implantation failure (RIF) or recurrent miscarriage (RM) report poorer sleep quality and shorter sleep duration compared to fertile women, suggesting that sleep may influence reproductive success.[32] Adequate sleep is essential for infants' cognitive, emotional, and physical development, and can influence long-term obesity risk. Safe sleep practices are critical to prevent sudden infant death syndrome (SIDS), with the American Academy of Pediatrics recommending room-sharing for the first six months. Research indicates that independent sleep after six months is linked to better sleep quality, suggesting that promoting independent sleep could improve long-term sleep health.[33]

3 Menopause

During menopause, women commonly experience sleep disturbances such as insomnia and irregular breathing patterns, often due to decreased estrogen and progesterone levels.[34] Hormone therapy (HT) can alleviate symptoms, particularly hot flashes, but subjective sleep improvements may not always align with objective measures. Fragmented sleep during menopause affects 40-70% of women, worsened by hot flashes and age-related changes. Micronized progesterone has been shown to improve sleep continuity and REM sleep without the cognitive side effects associated with other sleep medications.[35] Factors such as neurological issues, metabolic imbalances, and partner-related problems can further impact sleep quality.[36] Despite increased sleep disturbances during menopause, the direct relationship between hot flashes and sleep issues remains unclear, suggesting that aging may play a significant role.[37] In conclusion, understanding the interplay of hormonal and behavioral factors across different life stages emphasizes the need for comprehensive sleep assessments in women's healthcare to enhance overall quality of life.

3. Metabolic disorders

Sleep is a vital physiological process that significantly impacts overall health, particularly metabolic and liver health. Disruptions such as insufficient sleep, insomnia, and obstructive sleep apnea are notable risk factors for metabolic dysfunction-associated steatotic liver disease (MASLD), which is becoming a global epidemic linked to severe complications like cirrhosis and cardiovascular disease. Improving sleep quality presents a modifiable preventive measure against MASLD.[38]

A prospective cohort study showed that short sleep duration on work and free days increases MASLD risk, while longer sleep averages reduce it. Factors like sleep debt, late sleep times, and early awakenings were associated with higher risk, particularly regarding liver fibrosis progression linked to late workday sleep.[39]

Moreover, poor sleep patterns-including short duration and insomnia also influence metabolic health, contributing to conditions like type 2 diabetes and obesity. Alarmingly, over half of university students exhibit metabolic risk factors, underscoring the need for early interventions. Studies have shown that poor sleep quality correlates with metabolic syndrome risk, particularly among women who snore frequently. Thus, addressing sleep disorders and enhancing sleep quality are essential public health strategies for preventing and managing metabolic disorders.[40]

6. Bone mineral density

Osteoporosis is a significant public health concern, especially in Japan, where about 10% of the population and nearly 40% of women over 70 are affected. This prevalence increases healthcare costs and burdens caregivers, underscoring the need for preventive measures to support bone health. Traditionally, age, gender, BMI, smoking, and physical inactivity were considered the main modifiable factors influencing bone health. However, recent research indicates that sleep is also a critical component in maintaining bone mineral density (BMD). Studies suggest that sleeping less than five to seven hours per night may increase the risk of

osteoporosis. A recent study examining sleep duration and insomnia among health check-up participants found that about 80% reported sleeping less than seven hours nightly. Surprisingly, shorter sleep duration did not correlate with lower BMD, nor did insomnia show a significant impact.[41] Individuals sleeping less than five hours tended to have higher BMIs and lower physical activity levels, hinting at a broader link between sleep and overall health. These findings contrast with earlier research that indicated inadequate sleep could negatively affect BMD, emphasizing the need for further studies. Limitations such as self-reported sleep duration and inadequate micronutrient data may have influenced the results. Globally, osteoporosis affects over 200 million people, contributing to increased mortality and healthcare costs. Although hormonal changes due to insufficient sleep like decreased melatonin and growth hormone may play a role, the cross-sectional nature of current studies limits causal conclusions.[42] More research is needed to clarify the relationship between sleep and bone health.

7. Depression

Depression is a significant public health issue, particularly affecting women, with a prevalence of 10.4% among U.S. women aged 20 and older compared to 5.5% in men. Chronic depression severely impacts quality of life and is projected to become the leading cause of disease burden by 2030. Sleep plays a crucial role in mental health, yet around 40% of U.S. adults and 67% of young adults aged 19 to 29 report insufficient sleep, with young women experiencing these issues at double the rate of young men. Research indicates a strong link between sleep disturbances and depression, especially among young women, who also face higher rates of depression related to lower educational attainment and poverty. Additionally, depression often co-occurs with other health issues like diabetes. It is essential to routinely screen young women with sleep disturbances for depression and adopt a holistic approach to improve both sleep quality and overall well-being.[43]

CONCLUSION

This review underscores the critical role of sleep in maintaining health across all life stages. Disruptions in sleep architecture, including REM and NREM stages, impact memory, metabolism, immunity, and emotional well-being. Factors such as aging, lifestyle, and hormonal changes exacerbate conditions like insomnia, sleep apnea, and mood disorders. In childhood and adolescence, inadequate sleep affects neurodevelopment and emotional regulation, with issues like insomnia and sleep apnea leading to cognitive and behavioral challenges. For adults, sleep disturbances increase the risk of cardiovascular and metabolic issues, while elderly individuals face fragmented sleep linked to cognitive decline. Gender-specific sleep problems, such as those related to menstruation, pregnancy, and menopause, highlight the impact of hormonal fluctuations on sleep quality and overall well-being. Modern lifestyle factors, such as artificial light and irregular work schedules, disrupt circadian rhythms, contributing to chronic health conditions like metabolic syndrome and depression. Interventions like cognitive behavioral therapy, controlled light exposure, and lifestyle adjustments are essential to improving sleep health. Ultimately, prioritizing sleep health can significantly enhance individual well-being and public health. A holistic approach, considering biological, psychological, and environmental factors, is vital for addressing the growing prevalence of sleep disorders. Future research and increased awareness can drive improvements in sleep-related health outcomes.

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