Circadian Rhythm Sleep-Wake Disorders in Older Adults

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KEYWORDS

• Circadian rhythm sleep disorders • Advanced sleep phase • Delayed sleep phase • Melatonin • Circadian rhythm disruption • Alzheimer disease • Light therapy

KEY POINTS

- The circadian timing system regulates the timing, structure, and consolidation of sleep, in conjunction with a sleep-wake homeostatic process.
- There are age-related changes in the circadian regulation of sleep, in the sleep homeostatic regulation of sleep, and in the interaction between these two processes.
- Circadian rhythm sleep-wake disorders result from a mismatch between the desired timing of sleep and the ability to fall asleep or remain asleep.
- Advanced sleep-wake phase disorder and irregular sleep-wake rhythm disorder are more common in older adults than in young adults.
- Jet lag disorder and shift-work disorder are more commonly experienced by travelers and workers as they age.

INTRODUCTION

The timing, duration, and consolidation of human sleep result largely from the interaction of 2 sleep regulatory systems: the sleep-wake homeostat and the circadian timing system. When these 2 processes are aligned and functioning optimally, they allow adults to achieve a long, consolidated bout of wakefulness throughout the day and a long and consolidated sleep episode at night. Changes to either process, or a change in how the 2 processes interact, can result in an inability to fall asleep at the desired time, difficulty remaining asleep, or difficulty remaining awake throughout the desired wake episode. This mismatch between the desired timing of sleep (and wakefulness) and the ability to fall asleep and remain asleep is a hallmark of a distinct class of sleep disorders called the circadian rhythm sleep-wake disorders (CRSWDs). This article discusses the circadian timing system, the role played by the circadian system in sleep-wake regulation, typical changes in circadian regulation of sleep with aging, the CRSWDs and how age influences their diagnosis and treatment, and how neurologic diseases in older patients affect circadian rhythms and sleep.

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CIRCADIAN RHYTHM SLEEP-WAKE DISORDERS

Although surveys[1] suggest that less than 3% of the adult population have a CRSWD, the CRSWDs are often confused with insomnia, resulting in underestimates of the true prevalence. Some estimates are that up to 10% of adult patients with sleep disorders may have a CRSWD.[2] Although some CRSWDs (such as jet lag) can be self-limiting, others, when untreated, can lead to adverse medical, psychological, and social consequences for affected patients. The International Classification of Sleep Disorders classifies CRSWDs as disorders related to the timing of sleep and wakefulness, with 6 subtypes[3]: delayed sleep-wake phase disorder, advanced sleep-wake phase disorder, irregular sleep-wake rhythm disorder, non-24-hour sleep-wake rhythm disorder, jet lag disorder, and shift-work disorder (**Table 1**). The primary clinical characteristic of all CRSWDs is an inability to fall asleep, remain asleep, and/or wake at the desired time. CRSWDs arise from a problem with the internal biological clock (circadian timing system) and/or misalignment between the circadian timing system and the external 24-hour environment. This misalignment can be the result of biological and/or behavioral factors, and the rates of different CRSWDs vary across age groups.

THE CIRCADIAN TIMING SYSTEM IN HUMANS

The circadian timing system refers to near–24-hour rhythmicity in many aspects of physiology and behavior, including not only sleep and waking but hormone secretion, body temperature, and urine production.[4–6] These rhythms are features of individual cells[7] and arise through transcription-translation feedback loops.[8] Coordination of the rhythms among cells within an organ, and between the organ systems of the body, are achieved through signals from a master pacemaker in the hypothalamus, the suprachiasmatic nucleus (SCN).[9] The SCN not only coordinates the rhythmic activity of the cells and organs within the body but synchronizes the near–24-hour rhythmic activity of the body with the 24-hour cycle of the external environment, a process called entrainment. A functional circadian timing system allows the organism to predict regular changes that occur in the environment (eg, sunlight, food availability, presence of predators) and to prepare for those changes, thus providing an adaptive advantage.[10]

Because the underlying rhythmicity is close to, but not exactly, 24 hours in cycle length, it must be synchronized or entrained to the external 24-hour day on a regular basis. Entrainment of the near–24-hour circadian system to the 24-hour day occurs typically through exposure to signals from the environment, and in the case of humans (as in most other mammals) this is largely done via regular exposure to light during the day and darkness at night. Studies in healthy sighted adults have shown that the period (cycle length) of the circadian system averages around 24.2 hours across age groups.[11] This finding implies that the average adult's circadian system needs to be reset about 10 minutes earlier each day in order to remain synchronized to external clock time, and, if it is not, then the circadian system may drift out of synchrony with external clock time. One example of this desynchronization is what happens to many blind individuals. They complain of cyclic sleep-wake problems, alternating periods when they can sleep well at night and are alert during the day with times when their nighttime sleep is disturbed and they struggle to remain awake throughout the day.[12]

Although on average the circadian period is 24.2 hours, the range between individuals is about an hour, from approximately 23.5 to 24.5 hours,[11] which means that individuals with the shortest and longest periods need to reset by half an hour each day to remain entrained, and, without that regular resetting, they are even more likely than the average person to drift out of synchronization. Individuals with the shortest and longest periods are therefore most susceptible to non-24-hour sleep-wake rhythm disorder. On average, the circadian period in women is shorter than in men, and significantly more women than men have a period that is less than 24 hours.[11] This difference predisposes women to advanced sleep-wake phase disorder.

CIRCADIAN REGULATION OF SLEEP AND WAKEFULNESS

Key points

- The circadian timing system coregulates the timing, structure, and consolidation of sleep
- The circadian timing system interacts with the sleep-wake homeostat to allow consolidated wakefulness during the day and consolidated sleep at night

The circadian system is a major determinant of the timing of sleep and internal sleep structure in humans.[13] Specialized experimental techniques have been used to separate the circadian and sleep-wake homeostatic influences on sleep in order to understand how each independently influences sleep and wakefulness. Those studies have revealed that although most aspects of sleep are influenced by the biological time at which sleep