Sleep Loss and Circadian Rhythm Disruption in the Intensive Care Unit

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KEYWORDS

• Sleep deprivation • Sleep loss • Circadian rhythm • Circadian misalignment • Delirium • Intensive care unit • Critical illness

KEY POINTS

- Patients in the intensive care unit (ICU) present on admission with sleep disruption due to acute and chronic medical conditions.
- Sleep disruption includes sleep loss, decrements in N3 sleep, decrements in rapid eye movement (REM) sleep, and circadian misalignment.
- ICU admission reinforces and perpetuates sleep disruption because of environmental, patient, and illness-related factors.
- Clustered care initiatives show promise in improving patient outcomes; this includes decreases in delirium rates.
- Inclusion of other ICU care protocols such as daily sedative interruption and early mobilization may support sleep prolongation, normalization of sleep architecture, and circadian reentrainment.

INTRODUCTION

Critical illness leading to ICU admission creates and propagates a syndrome of sleep loss, poor sleep quality, and circadian misalignment. This syndromic entity is summarized with the term sleep disruption in the context of this review article. Causality is diverse and includes physiologic, psychological, and environmental factors (**Fig. 1**). This syndrome affects virtually all critically ill patients, including mechanically ventilated, nonventilated, septic, nonseptic, and less and more severely ill patients, as well as healthy volunteers exposed to recordings of the ICU environment.[1]

Sleep is a periodic, reversible state of cognitive and sensory disengagement from the external environment. Normal adult sleep occurs overnight and lasts 7 to 9 hours; the sleep period consists of four to six 90- to 100-minute periods during which non-REM (NREM) and REM sleep alternate in a cyclical fashion. NREM sleep includes sequential progression through stages N1, N2, and N3, which grossly correlate to the depth of sleep. In general, N1 comprises 2% to 5% of overnight sleep, N2 comprises 45% to 55% of overnight sleep, and N3 comprises 15% to 20% of overnight sleep. N3 is otherwise known as slow wave sleep (SWS) and is considered necessary for anabolic

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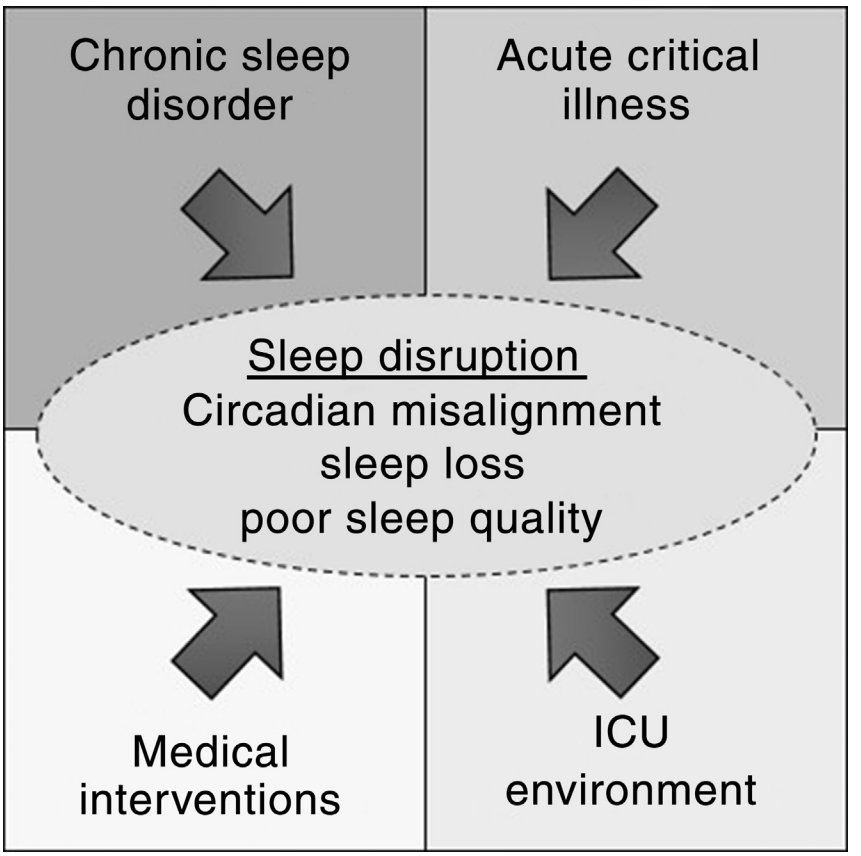

Fig. 1. Causes and perpetuating factors for sleep disruption in the intensive care unit.

cellular recovery. REM sleep occupies 20% to 25% of the total sleep period and is considered to have a critical role in cognition and memory formation.[2,3]

Circadian rhythms are oscillations in biological function that follow a 24-hour cycle and are endogenously generated.[4] These rhythms influence an array of behaviors and physiologic parameters and arise from a genetically based chronometer called the molecular clock that is present in most nucleated cells.[5] This molecular clock is composed of a group of transcription factors and transcription factor regulators that have a feedback effect on one another to produce circadian oscillations in their own transcription. Molecular clock proteins have wide effects on transcriptional activity and metabolism, directly or indirectly causing up to 50% of genes to oscillate body-wide.[6–9] The complement of genes that oscillate in any given organ are largely unique to that organ (outside of the core molecular clock genes themselves),[7,10] indicating that circadian rhythms are heavily embedded in organ physiology. The clocks within individual cells are synchronized at the organ level through incompletely understood mechanisms. Systemic cues including body temperature, autonomic tone, and circulating hormones such as cortisol are thought to play a role.[11,12] These global cues in turn are under control of a master circadian clock that resides in the neurons of the suprachiasmatic nucleus (SCN).[13] The SCN receives innervation directly from the retina, and its clock is thereby directly pegged to the day-night cycle. The SCN projects to multiple central nervous system regions, including areas of the hypothalamus that regulate arousal, metabolism, and hormone release from the pituitary and pineal glands.[13]

The amount (total sleep time), quality (N3 and REM fractions), and timing (circadian alignment) of sleep are important to human health; all 3 elements are disrupted in the ICU. Studies using 24-hour polysomnography (PSG) in mechanically ventilated and nonventilated patients in the medical ICU (MICU) demonstrate severely reduced overall sleep time, decreased N3, limited REM sleep, frequent arousals, and increased sleep during daytime hours.[1,14–17] Similar findings have been observed in patients in the surgical ICU[18] and in healthy subjects exposed to recordings of the ICU.[19]