

# Sleep Neurobiology and the Critical Care Environment

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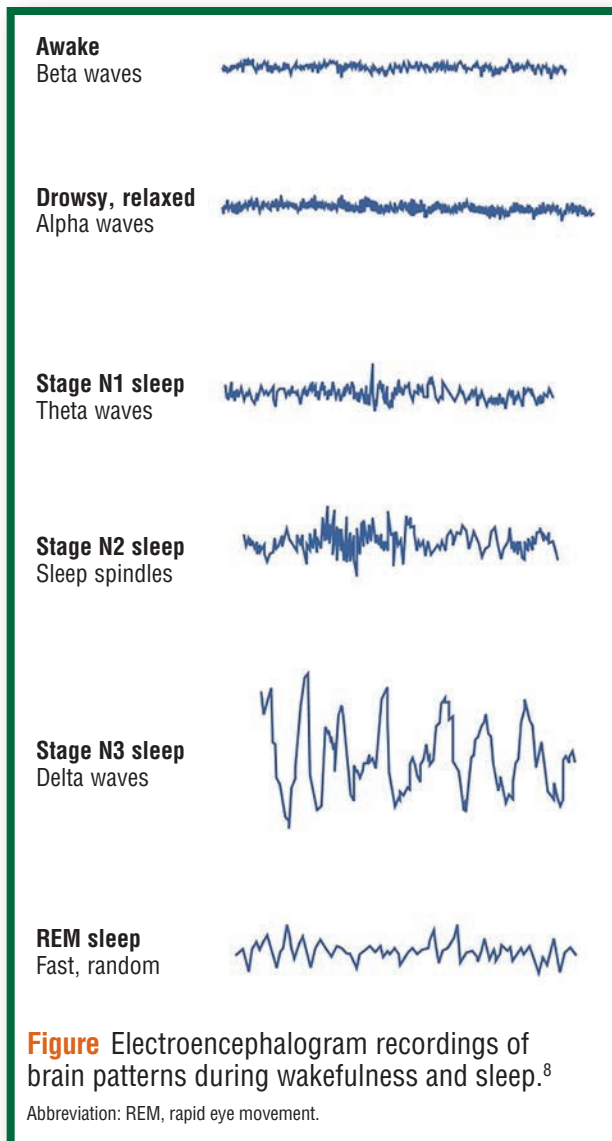
**TOPIC** Sleep in the intensive care unit can be poorly consolidated and highly fragmented. This review examines the neurobiology of normal and abnormal sleep, with a focus on the changes that occur in the intensive care unit environment.

**CLINICAL RELEVANCE** Patients in the intensive care unit demonstrate a lack of rapid-eye-movement sleep and an inability to effectively transition from light to deep stages of sleep. These abnormalities can adversely affect hemodynamic parameters and physiological and psychological outcomes.

**PURPOSE** To describe the brain mechanisms and electroencephalographic characteristics of wakefulness and the different stages of sleep. This review also describes how sleep can be altered by hospitalization in the intensive care unit and how nurses can design interventions that improve sleep and outcomes.

**CONTENT COVERED** The review examines sleep mechanisms, including brain electrical activity, regulatory centers in the brain, and circadian and diurnal patterns of sleep and hemodynamic function. Nursing interventions for specific patient risk factors in the intensive care unit are proposed. (*Critical Care Nurse*. 2020; 40[4]:e1-e6)

**A**bnormal sleep complicates the recovery of patients hospitalized in intensive care units (ICUs). When researchers analyzed electroencephalogram (EEG) recordings, patients were found to sleep for approximately 5 to 9 hours a day in the ICU.<sup>1-3</sup> Total sleep duration of patients in the ICU, according to these studies, was similar to reported sleep duration in healthy populations, but the studies in ICU patients demonstrated evidence of pathological EEG characteristics during sleep.<sup>1,2,4</sup> The consensus among studies was that ICU sleep was highly fragmented. The researchers found EEG evidence of frequent arousals from sleep, a lack of rapid eye movement (REM) sleep, and an inability to transition effectively from the light stages of non-REM sleep (N1 and N2) to the deep stage (N3).<sup>2,4-6</sup> These sleep abnormalities can negatively impact physical and psychological health. This review describes the neurobiology of abnormal sleep in patients in the ICU. The purpose of this review is to assist nurses in identifying high-risk patients who require interventions to reduce ICU-induced sleep dysfunction.



## Sleep Consolidation, Transitions, and Neural Activity

Consolidated sleep occurs during a prolonged, uninterrupted period of sleep and demonstrates cyclical transitions among the sleep stages. Factors related to the ICU and illness can impair the ability to consolidate sleep,

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resulting in frequent awakenings and restless, nonrestorative sleep.<sup>7</sup> The EEG activities characterizing each behavioral state are illustrated in the Figure. Rhythmic oscillations in neural activity in the cortex are fast (approximately 14-30 Hz) when patients are alert. As a patient begins to fall asleep, the frequency of oscillations slows, transitioning the brain through a relaxed state (alpha rhythm, 9-13 Hz) to a light sleep stage (N1, characterized by theta rhythm, 4-8 Hz). Electroencephalogram activity shifts toward a higher-amplitude and lower-frequency pattern as the depth of sleep increases. An EEG pattern characterized by a cortical wave frequency of less than 4 Hz (defined as delta waves) is indicative of the deepest stage of sleep (N3), also called slow-wave sleep.<sup>9</sup> The normal sleep transition pattern begins with a gradual transitioning from N1 to N2 to N3; these periods of non-REM sleep alternate cyclically with shorter bouts of REM sleep. Rapid-eye-movement sleep is characterized by a low-amplitude, high-frequency EEG pattern accompanied by muscle atonia and rapid movements of the eyes.<sup>10</sup>

Neurons in the basal forebrain, thalamus, hypothalamus, and pons control brain activity during sleep and wakefulness.<sup>10-12</sup> These networks are regulated by neurotransmitters including  $\gamma$ -aminobutyric acid (GABA), glutamate, orexin, and acetylcholine.<sup>11</sup> Basal forebrain GABAergic neurons fire preferentially during non-REM sleep, and GABAergic projections arising from the ventrolateral preoptic area of the hypothalamus inhibit wake-promoting hypothalamic and pontine nuclei when the patient falls asleep. Populations of cholinergic neurons in the basal forebrain and pons are active during REM sleep and during wakefulness. Glutamatergic neurons in the lateral hypothalamus, which also release orexin, become active as the patient awakens.<sup>12</sup>

## Changes in Non-REM and REM Sleep in the ICU

The progression of non-REM sleep is characterized by 2 distinct EEG waveforms: K-complexes (brief peaks in brain activity) and sleep spindles (bursts of oscillatory activity). K-complexes are generated in the cerebral cortex, and sleep spindles are generated by the reticular nucleus of the thalamus.<sup>4,13</sup> K-complexes and sleep spindles mark the transition from N1 to N2 sleep and suppress activation of the cortical networks involved in alertness. K-complexes and sleep spindles have been

proposed to play a role in memory consolidation and information processing.<sup>13,14</sup> Researchers who examined the EEG characteristics of patients in the ICU during non-REM sleep reported that patients in the ICU may not demonstrate K-complexes and sleep spindles, and they found that the absence of K-complexes and sleep spindles was associated with an elevated mortality risk.<sup>4</sup> The inability to produce these EEG features could indicate dysfunction of the corticothalamic networks that generate these rhythms, which may be caused by brain injuries or the effects of ICU therapies and medications.

The EEG characteristics of REM sleep are generated by neurons in the pons, mainly the pontine tegmentum and locus coeruleus.<sup>15</sup> Unlike N3 sleep, which is characterized by slow, synchronized EEG oscillations, REM sleep involves low-amplitude, fast, and desynchronized EEG activity. Periods of REM sleep can involve surges of sympathetic activity that cause increases in blood pressure.<sup>9</sup> Electroencephalogram activities demonstrate a circadian pattern—REM sleep, for example, increases as nighttime sleep progresses, and REM sleep bouts are longest during the end of the sleep period (usually in the early morning hours). Although the physiological significance of REM sleep has not been fully defined, available data suggest that REM sleep may be important for a variety of functions, including metabolism, memory consolidation, immune function, and tissue repair.<sup>9,15,16</sup> Several studies indicate that patients in the ICU have reduced REM sleep time, and a complete absence of REM sleep has been associated with mechanical ventilation, sedation, and administration of neuromuscular blocking agents.<sup>2,5</sup> Benzodiazepines and opioids are also known to suppress REM sleep.<sup>17</sup>

### Circadian Rhythms, Sleep Stage Transition Structure, and Hemodynamic Instability

Cardiovascular regulatory centers in the medulla receive signals from the hypothalamic and pontine sleep-wake regulatory networks.<sup>10</sup> Medullary neurons that augment blood pressure are inhibited during non-REM sleep, and as a result, sympathetic innervation of the heart and blood vessels reaches the lowest levels during N3 sleep.<sup>10,18,19</sup> The propensity for N3 sleep typically increases during the night, and in most individuals blood pressure exhibits a circadian rhythm with the highest values during the day and the lowest levels

during the night. Circadian (24-hour) and diurnal (light/dark) patterns in sleep and hemodynamic parameters are regulated by a group of light-sensitive neurons, the suprachiasmatic nuclei, found above the optic chiasma of the hypothalamus.<sup>19</sup> Exposure to artificial light and irregular sleep schedules in the ICU can alter activity of the suprachiasmatic nuclei.<sup>20</sup>

There is considerable interest in understanding how sleep and circadian patterns influence ICU outcomes. Defining the interactions among control centers in the brain that regulate sleep, circadian rhythms, and cardiorespiratory function is necessary for understanding why the early morning hours may be a high-risk time for life-threatening events in hospitalized patients.<sup>21,22</sup> Animal model find-

ings suggest that **The absence of sleep spindles and K-complexes is associated with mortality.** the timing

and structure of sleep may influence the stability of cardiovascular and respiratory parameters. For example, in 1 study, animals demonstrated 24-hour rhythms in the propensity for sleep apnea; sleep apnea was most severe when the animals had frequent sleep stage transitions and awakenings from sleep.<sup>23</sup> In another study, animals developed hypertension when they were deprived of REM sleep.<sup>24</sup>

In humans, the early morning hours are normally associated with an increase in the number of transitions among N1, N2, N3, REM sleep, and wakefulness. Periods of REM sleep also tend to be more frequent and longer during the early morning hours. Hemodynamic variability is greater during REM sleep than during non-REM sleep.<sup>9</sup> Intensive care unit environments can alter circadian rhythms, especially when the brightness of artificial lighting is not adjusted to mimic natural day and night periods. Although the physiological mechanisms remain to be determined, it is possible that circadian mechanisms regulating sleep stage transitions, particularly those involving REM sleep, affect hemodynamic stability in the ICU setting.

In many ICUs, laboratory and diagnostic testing, wound care, and bathing are scheduled between 12 AM and 4 AM, a period when the circadian drive for sleep is elevated. Knauert et al<sup>25</sup> examined the effects of reducing nonurgent bedside care between 12 AM and 4 AM. Patients were randomized to a usual-care group or a group with reduced interruptions during this time. The researchers did not record EEGs and therefore could not make conclusions about how the protocol affected sleep

**Table 1** Nursing considerations for identifying and improving disordered sleep in the ICU

Patient risk factor	Associated sleep dysfunction	Nursing intervention
Daytime sleep and nighttime wakefulness	A misaligned circadian rhythm results in fragmented, poorly consolidated sleep.	Mimic natural light-dark periods in the ICU when possible.
Mechanical ventilation and sedation	ICU therapies contribute to an impaired ability to obtain REM sleep and to transition effectively from light to deep non-REM sleep.	Prioritize management of respiratory conditions to facilitate decreasing or discontinuing therapies that alter EEG phenomena.
Preexisting sleep disorders such as sleep apnea	Intermittent hypoxia fragments sleep and causes frequent awakenings. Blood pressure may become chronically elevated during sleep and wakefulness.	Monitor for and treat sleep apnea in spontaneously breathing patients with continuous positive airway pressure.
Treatment-resistant hypertension or hypotension	Hemodynamic patterns may be influenced by abnormalities in non-REM or REM sleep.	Consider sleep dysfunction as a possible contributor to hemodynamic disorders. Schedule patient care to allow consolidated periods of sleep during the night when possible.
Insomnia and anxiety related to the hospitalization	Long sleep latency (ie, prolonged time spent attempting to fall asleep) increases anxiety.	Ask patients directly about sources of anxiety that are hindering sleep. Provide psychosocial support and comfort measures (eg, eye masks, earplugs) tailored to the patient's needs to enhance the ability to fall and stay asleep.
Signs of delirium or posttraumatic stress	Sleep deprivation and abnormal EEG characteristics of sleep and wakefulness can cause confusion and emotional distress.	Remove environmental stimuli contributing to confusion or stress (eg, turn off television). Schedule care to promote sleep during the night when possible. Teach patients/families strategies for promoting consolidated sleep after ICU discharge.

Abbreviations: EEG, electroencephalogram; ICU, intensive care unit; REM, rapid eye movement.

architecture, but comparisons of the usual-care and intervention groups revealed that the latter group had approximately 20 more minutes per hour of uninterrupted time to rest.<sup>25</sup> Demoule et al<sup>26</sup> tested the hypothesis that using earplugs and an eye mask could improve sleep in the ICU. Patients underwent EEG monitoring. Earplug and eye mask use were associated with a significant reduction in the number of awakenings from sleep and a trend toward an increased percentage of deep sleep (N3). The study also found that 30% of patients did not tolerate wearing these devices, however, suggesting that earplugs and an eye mask may be a useful intervention for only a subset of patients.<sup>26</sup> To date, no studies have been designed to examine whether reducing sleep interruptions alters hemodynamic activities or long-term outcomes in ICU patients. Sleep and circadian factors also have not yet been investigated for potential effects on the optimal dosing of vasoactive

**The early morning hours may be a high-risk time for life-threatening events.**

medications administered in the ICU. These areas are important topics for future research in the ICU.

## Nursing Interventions

Table 1 summarizes patients' risk factors for disordered sleep and proposes nursing interventions. The Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU do not recommend routinely using EEG monitoring in ICUs to quantify sleep. However, the 2018 guidelines emphasize the importance of developing new sleep hygiene interventions.<sup>27</sup> Even without EEG monitoring, nurses can recognize the behavioral and hemodynamic characteristics of healthy and unhealthy sleep. Studies about sleep in the ICU have focused mainly on initiatives for reducing noise and dimming lights, but these interventions do not fully address the challenges patients have when sleeping in the ICU. Anxiety was highlighted as a key theme in a qualitative study about ICU sleep,<sup>28</sup> and patients with the highest risk factors for dysfunctional

**Table 2** “Intensive Care Unit,” by Adrien Stoutenburg<sup>29</sup>

In one corner of the ward  
somebody was eating a raw chicken.  
The cheerful nurses did not see.  
With the tube down my throat  
I could not tell them.  
Nor did they notice the horror show  
on the TV set suspended over my windowless bed.  
The screen was dead  
but a torn face was clear.

I did not see my own  
in a mirror for weeks.  
When it happened,  
when I dared to face my face  
after the ravaging,  
it was not mine  
but something whittled, honed down  
to a sly resemblance.  
It, even the mirror, the pale room,  
the oxygen tank  
neat and black as a bomb  
in its portable crate—  
all was hallucination.

But the bloody rooster,  
the stray pieces of bodies  
slung into dreamless nooks,  
the white-haired doll whimpering  
on a gift counter—  
those were real.

I keep living there.  
Foolish. I am home. Half safe.

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sleep (eg, patients who are receiving mechanical ventilation, are sedated, or are cognitively impaired) have been largely unable to describe their ICU experiences. The relationship between delirium and poor sleep, for instance, is understudied, especially with respect to long-term health consequences. As an example, in her poem “Intensive Care Unit,” Adrien Stoutenburg<sup>29</sup> depicted her experience with disordered sleep and wakefulness (Table 2). In the ICU a “windowless bed” and “dreamless nooks” haunted her, but the most striking aspect of her poem is that the ICU environment affected her even after she returned home.<sup>29</sup> The poet described a phenomenon consistent with research about posttraumatic stress after ICU discharge.<sup>30,31</sup> Posttraumatic stress may be particularly prevalent when patients have traumatic injuries and prolonged hospital stays.

## Summary

Intensive care unit therapies and environmental factors have an important influence on the neurobiology and perceptions of sleep. Simply increasing patients’ sleep time may not restore the characteristics of normal sleep, especially when ICU therapies, anxiety, and post-traumatic stress are affecting the ability to rest. In these cases, nursing interventions that more directly address the physiological and psychological factors altering sleep are necessary. Sleep is a critical, and often overlooked, factor affecting outcomes in the ICU. [CCN](#)

Financial Disclosures  
None reported.

## See also

To learn more about sleep in the critical care setting, read “Factors Influencing Patients’ Sleep in the Intensive Care Unit: Perceptions of Patients and Clinical Staff” by Ding et al in the *American Journal of Critical Care*, 2017;26(4):278-286. Available at [www.ajconline.org](http://www.ajconline.org).

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