Sleep Neurobiology and Critical Care Illness

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KEYWORDS

• Sleep alterations • Neurobiology • Sleep EEG pattern • Sleep organization • Circadian rhythms

KEY POINTS

- Intensive care unit (ICU) patients experience severe sleep alterations, with reductions in several sleep stages, marked sleep fragmentation, low sleep continuity, and circadian rhythm disorganization.
- The numerous sources of these sleep alterations are associated with disruptions of sleep neurobiological processes and sleep dynamics that can alter sleep restorative functions.
- Understanding the neurobiology of sleep in the ICU is a major challenge for future sleep studies in critically ill patients.

INTRODUCTION

That critical illnesses and environmental factors in intensive care units (ICUs) are associated with sleep disturbances was recognized shortly after the first ICUs were created. Many studies documented objective lack of restorative sleep.[1–4] Sleep alterations in critically ill patients differ from sleep changes observed in ambulatory patients (such as patients with sleep apnea syndrome) in pathophysiology as well as the consequences of sleep loss.

The literature regarding consequences of sleep deprivation on health is growing rapidly but ICU patients are unlikely to avoid the biological and neurobehavioral repercussions of sleep loss. To appreciate all of the phenomena triggered by sleep loss in the ICU, it is important to understand the neurobiology of healthy sleep and the specific neurobiological derangements of sleep in critically ill patients.

NEUROBIOLOGY OF THE NORMAL SLEEP CYCLE

In human beings, sleep is composed of non–rapid eye movement (NREM) sleep, which can be light NREM (stages 1 and 2) or deep sleep (stages 3 and 4). The distinction between wake and NREM sleep is made by visual analysis of a 30-second portion of an electroencephalogram (EEG): during waking, the EEG shows a mix of fast oscillations (>16 Hz) and alpha rhythm (8–12 Hz) of low amplitudes (<10 μV). During light NREM sleep (stages 1 and 2), the background EEG is characterized by slow theta oscillations (frequency between 4 and 7 Hz) and sleep spindle and K complexes. These latter regularly occur and provide the landmark of stage 2. During deep NREM sleep (also called slow wave sleep; stages 3 and 4), the EEG shows slow waves (0.5–2 Hz) of high amplitude (>75 μV). Rapid eye movement (REM) sleep is a particular sleep stage in which the EEG shows theta and

This article originally appeared in Critical Care Clinics, Volume 31, Issue 3, July 2015.
Funding sources: None.
Conflicts of interest: None.
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Sleep Med Clin 11 (2016) 105–113
http://dx.doi.org/10.1016/j.jsmc.2015.10.001
1556-407X/16/$ – see front matter

alpha rhythms. Identification of REM sleep is based on the presence of rapid eye movements identified on electro-oculograms and complete chin muscle atonia. During REM sleep, the brain is highly active, and most dreams and nightmares occur during this stage.

Human sleep is monophasic, and is programmed to occur during nighttime. The sleep-wake cycle is accurately organized and controlled. A sleep deficit elicits a compensatory increase in the intensity and duration of sleep, and excessive sleep reduces sleep propensity. This process could be represented as a sleep-pressure regulation, which would maintain this pressure between an upper and a lower limit. Sleep homeostasis can be represented by the interaction of 2 main physiologic processes. The first process is known as process S, which increases during waking and declines during sleep. Electroencephalographic slow wave activity (SWA) corresponds with an indicator of sleep homeostasis and the level of SWA is determined by the duration of prior sleep and waking. The timing and propensity to fall asleep are also modulated by a circadian process. This second process is driven by the internal clock. This circadian rhythm is sensible to external factors that help to keep the sleep-wake cycle synchronized with night-day alternation. The main external synchronizing factors are light, physical activities, meals, and social interactions.

The quantity of sleep is acutely regulated, and sleep deprivation has many neurobiological consequences. On the day following 1 night without sleep, brain performances are severely decreased. The most visible behavior is an increased tendency to fall asleep, even when the person fights to remain awake. The night following the sleep deprivation is modified and a sleep rebound usually occurs. This sleep rebound triggers a lengthening of nighttime sleep, an increase in slow wave sleep, and an increase in REM sleep.

METHODS FOR SLEEP STUDY IN INTENSIVE CARE UNIT PATIENTS

Sleep can be assessed in terms of quantity (total sleep time and time spent in each sleep stage), quality (fragmentation, sleep EEG patterns), and distribution over the 24-hour cycle.

Full polysomnography (PSG) is the only reliable tool for measuring sleep, especially in patients with marked sleep disturbances. Accurate sleep scoring requires the recording of at least 3 EEG signals (preferentially F4-A1, C4-A1, O2-A1), 2 electro-oculography signals, and a submental electromyography (EMG) signal. Additional signals are usually recorded, such as nasal and oral airflow, thoracic and abdominal belts, electrocardiogram, and pulse oximetry. Sound and light levels should be measured, although these data are not obtained routinely.

SLEEP ELECTROENCEPHALOGRAM PATTERNS IN THE INTENSIVE CARE UNIT

Sleep scoring using either the system of Rechtschaffen and Kales[5] or the recently modified rules[6] poses a specific problem in critical care patients. A variable portion of the brains of critically ill patients does not generate the usual sleep EEG patterns and habitual markers of sleep.[7–11] The presence of theta and delta EEG activities during wakefulness, rapid fluctuations between EEG features of wake and NREM sleep, rapid eye movements during stage 2, and low-amplitude fast frequencies caused by sedation and delta burst arousal pattern are often observed.[8,12,13] In a study in conscious patients (Glasgow score >8) without neurologic disease who required mechanical ventilation for lung injury, 12 of 20 patients had abnormal sleep patterns[8]; among them, 7 patients showed EEG features of coma with reactive theta-delta activity and 5 had atypical sleep with virtually no stage 2 sleep and the presence of pathologic wakefulness (a combination of EEG features of slow wave sleep and behavioral correlates of wakefulness such as saccadic eye movements and sustained EMG activity). These 5 patients had worse acute physiology scores and received a higher mean benzodiazepine dose than the patients with disrupted but recognizable sleep patterns. In a similar group of 22 patients without sedation or neurologic disease,[9] only 17 patients (77.3%) had PSG recordings that could be scored. The remaining 5 patients had an EEG pattern of low-voltage mixed-frequency waves and variable amounts of theta-delta activity; all 5 developed sepsis during the study period, suggesting that sleep abnormalities were related to sepsis encephalopathy.[9]

In a recent study, Watson and colleagues[13] found major dissociations between EEG patterns and behavior in a group of 37 ICU patients. These dissociations consisted of abnormally slow EEG frequency in the theta range (3–7 Hz), a frequency that normally indicates sleep, or even delta range in some awake patients; In contrast, they observed low-amplitude, high-frequency beta EEG activity in patients who were in coma. Some patients who were awake and interactive with research personnel showed predominately theta activity (3–7 Hz), a frequency that normally indicates sleep. One patient, awake and able to follow simple instructions, was documented to have