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REVIEW

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Sleep in the intensive care unit

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Abstract Abnormalities of sleep are extremely common in critically ill patients, but the mechanisms are poorly understood. About half of total sleep time occurs during the daytime, and circadian rhythm is markedly diminished or lost. Judgments based on inspection consistently overestimate sleep time and do not detect sleep disruption. Accordingly, reliable polygraphic recordings are needed to measure sleep quantity and quality in critically ill patients. Critically ill patients exhibit more frequent arousals and awakenings than is normal, and decreases in rapid eye movement and slow wave sleep. The degree of sleep fragmentation is at least equivalent to that seen in patients with obstructive sleep apnea. About 20% of arousals and awakenings are related to noise, 10% are related to patient care activities, and the cause for the remainder is not known; severity of underlying disease is likely an important factor. Mechanical ventilation can cause sleep disruption, but the precise mechanism has not been defined. Sleep disruption can induce sympathetic activation and elevation of blood pressure, which may contribute to patient morbidity. In healthy subjects, sleep deprivation can decrease immune function and promote negative nitrogen balance. Measures to improve the quantity and quality of sleep in critically ill patients include careful attention to mode of mechanical ventilation, decreasing noise, and sedative agents (although the latter are double-edged swords).

Keywords Sleep · Critical illness · Mechanical ventilation · Artificial respiration · Arousal

Introduction

In his roman-a-clef, "Ravelstein", the Nobel Laureate Saul Bellow [1] describes being admitted to an intensive care unit and receiving mechanical ventilation:

"I was now the dying man. My lungs had failed. A machine did my breathing for me. Unconscious, I had no more idea of death than the dead have. But my head (I assume it was my head) was full of visions, delusions, and hallucinations. These were not dreams or nightmares. Nightmares have an escape hatch...."

Despite the obvious importance of sleep and its desirability in a patient with a serious illness, we know nothing of the visions, hallucinations and dreams experienced by a critically ill patient such as Bellow. Indeed, we know little of the sleep experienced by a critically ill patient. But we do know that sleep is commonly disrupted in critically ill patients [2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16], and that sleep disruption may adversely affect patient outcome [8, 17]. In this review, we discuss the nature of sleep disturbances in critically ill patients, potential causes, and possible therapies.

Normal sleep and circadian rhythm

Healthy young adults experience two distinct states of sleep: rapid eye movement (REM) sleep and non-REM (NREM) sleep. REM sleep accounts for about 25% of sleep time and is characterized by episodic bursts of rapid

Table 1 Studies of sleep in critically ill patients

More than 24 h	Number of patients	Patient type	Sleep staging	Arousals and awakenings per hour	Mechanical ventilation (%)
Polysomnography performed over 24 h					
Hilton [2]	10	Medical	Yes	Not listed	Not listed
Aurell [3]	9	Postoperative	Yes	Not listed	Some patients
Gottschlich [4]	11	Burn patients	Yes	>63	100
Cooper [5]	20	Medical	Yes	39	100
Freedman [6]	22	Medical	Yes	>11	100
Valente [7]	24	Head trauma	Yes	Not listed	100
Gabor [8]	7	Medical	Yes	22	100
Polysomnography performed only at nighttime					
Johns [9]	5	Postoperative	Yes	Not listed	Not listed
Orr 10	9	Postoperative	Yes	Not listed	Not listed
Broughton [11]	12	Medical	Yes	>21	NA
Knill [12]	12	Postoperative	Yes	>21	Not listed
Edwards [13]	21	Medical	Yes	Not listed	95
Aaron [14]	6	Medical	Yes	>19	Not listed
Parthasarathy [15]	11	Medical	Yes	58	100
Richards [16]	64	Medical	Not listed	Not listed	0
Polysomnography not performed					
Woods [18]	4	Postoperative			Not listed
Helton [19]	62	Not listed			Not listed
Tweedie [20]	15	Medical and postoperative			80
Kong [21]	60	Medical			100
Hurel [22]	223	Medical and postoperative			0
Freedman [23]	203	Medical and postoperative			0
Simini [24]	162	Medical and postoperative			0
Treggiari [25]	40	Postoperative			0
Walder [26]	17	Postoperative			60
Shilo [27]	8	Medical			50
Olson [28]	843	Medical and postoperative			Not listed
Topf [29]	97	Postoperative			Not listed
Nelson [30]	100	Medical			60
Mundigler [31]	24	Medical and postoperative			100
McKinley [32]	14	Medical and postoperative			0

eye movements, irregularities in respiration and heart rate, and paralysis of major muscle groups with the exception of the diaphragm and upper airway muscles. NREM sleep is divided into four stages (1, 2, 3 and 4). The progression of sleep from stage 1 through to stage 4 is accompanied by a progressive increase in the arousal threshold (the ability to wake in response to a stimulus). Stage 1 occurs at sleep onset and is also a transitional state between sleep stages. Up to 50% of the night is spent in stage 2 sleep, which is characterized by spindles and K complexes on the electroencephalograph (EEG). Progression of stage 2 is accompanied by the gradual appearance of high-voltage slow wave activity on the EEG (greater than 75 μV and less than 2 Hz). When such slow-wave activity exceeds 20% of the time in a 30-s epoch, sleep is categorized as stage 3; when it exceeds 50%, sleep is categorized as stage 4. Slow wave sleep is considered the most restorative. NREM sleep normally cycles with REM sleep every 90 min. The cycling of sleep and wakefulness, in turn, is regulated by a biological clock that operates over a 24-h period (circadian rhythm). In addition to sleep, the biological clock regulates several physiological, behavioral, and biochemical rhythms. Hormone secretion (cortisol, growth hormone), body temperature, immune function, coronary artery muscle tone, and bronchial smooth muscle tone, to name a few, exhibit marked circadian variability.

Abnormalities of sleep in critically ill patients

Just as with ambulatory patients, sleep in critically ill patients is assessed in terms of quantity, distribution over 24 h, and lack of continuity. Also assessed is the type and depth of sleep—rapid eye movement (REM) and non-REM (stages 1, 2, 3 and 4)—and the pattern from day to day in the distribution of sleep over a 24-h period (circadian rhythm). Accurate measurement of sleep quantity and quality requires reliable polygraphic recordings. Judgments based on inspection consistently overestimate sleep time [3] and do not detect sleep disruption [3, 13]. Table 1 classifies research reports on sleep in critically ill patients into studies involving polysomno-

graphic recordings over 24 h [2, 3, 4, 5, 6, 7, 8], polysomnographic recordings during nighttime alone [9, 10, 11, 12, 13, 14, 15, 16], and studies without polysomnographic recordings [18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32]. Also indicated is the type of patient population, whether patients were receiving mechanical ventilation, and whether sleep stages and disruption were adequately reported. Of the 28 studies listed in Table 1, 15 employed polysomnography [2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16], and 7 included continuous recordings for 24 h or longer [2, 3, 4, 5, 6, 7, 8]. These studies reveal that almost half of total sleep time in critically ill patients can occur during the daytime [5, 8].

Investigators differ in their conclusions as to whether critically ill patients are sleep deprived. Three groups of investigators found that critically ill patients have a normal or near normal total sleep time, an average of 7–10.4 h a day [4, 5, 6]. Three other groups of investigators found a decrease in total sleep time, 3.6–6.2 h a day [2, 3, 8]. The investigators in one of the studies revealing decreased sleep time had deliberately restricted sedatives and hypnotics [3], although patients received sedatives in the other two studies that revealed sleep deprivation [2, 8]. Even in the studies revealing adequate amounts of sleep, the investigators noted large variations in total sleep time among the patients. Cooper and co-workers found that some patients slept for hardly an hour and other patients for nearly 15 of 24 h [5] (Fig. 1). Total sleep time in the study of Freedman and co-workers varied from 1.7 to 19.4 h [6]. Patients falling in the lowest quartile for total sleep time in these studies are clearly suffering from major sleep deprivation. In addition to variation in sleep quality from patient to patient, sleep quality may vary from night to night within a patient as a result of changes in acuity of illness [33], pain, and sedative and analgesic infusions. As such, sleep deprivation occurs in many, if not all, critically ill patients. To achieve better clarification of the frequency and severity of sleep deprivation, longitudinal studies in a large number of patients are needed; it will be essential to control for the effects of sedation, analgesia, and acuity of illness when conducting such studies.

In 11 critically ill patients, Parthasarathy and Tobin [15] noted 19 arousals (abrupt shifts in EEG frequency lasting more than 3 s) and 35 awakenings (EEG features compatible with wakefulness) per hour. Total sleep disruption, 54 arousals and awakenings per hour, was more than twice that seen in healthy individuals similarly instrumented. Cooper and co-workers [5] also reported frequent sleep disruption, with 42 arousals and awakenings per hour, and Gabor and co-workers [8] reported somewhat less frequent disruption, 22 arousals and awakenings per hour. With the exception of the three preceding studies [5, 8, 15], the remaining investigators who obtained EEG recordings in critically ill patients did not specify the sum of arousals and awakenings [3, 7, 9, 10, 16], making it impossible to compare studies in that respect (Table 1). The degree of sleep fragmentation in studies of critically ill patients, however, is equivalent to that in patients with obstructive sleep apnea [34].

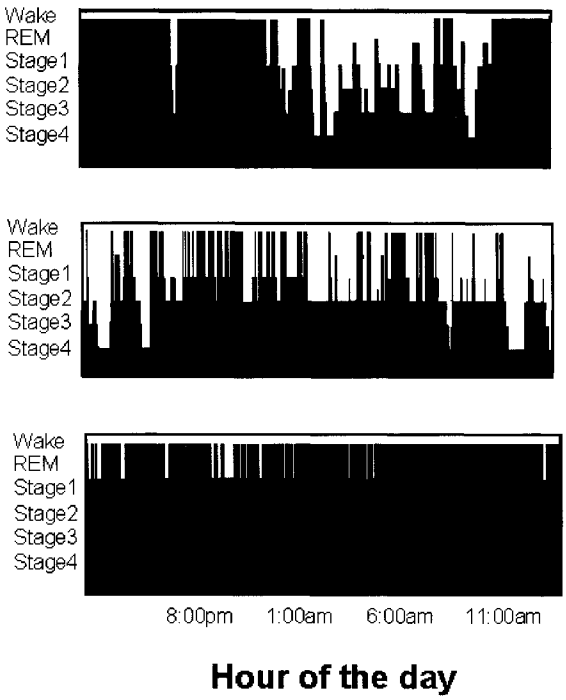

Fig. 1 Sleep stages, along the vertical axis, over a 24-h period in three critically ill patients with disrupted sleep. The hypnogram in patient 1 (*top*) reveals a normal nocturnal sleep pattern. Patients 2 (*middle*) slept for 65% of time, predominantly stages 1 and 2, and wakened repeatedly. Patient 3 (*bottom*) had isolated episodes of stage 1 sleep but was awake for most of 24 h. (Modified from [5] with permission)

Sleep is normally divided into rapid eye movement (REM) and non-REM (NREM) sleep. Critically ill patients spend 6% or less of sleep time in REM sleep as opposed to the normal of 25% [5, 6, 12]. The decrease in REM sleep has been attributed to medications (narcotics) [12], lack of sustained sleep needed to reach REM sleep [6], disturbance of circadian rhythm, underlying disease, and endotoxin release [35, 36]. The reduction in REM sleep might also be an adaptive response to critical illness because REM is a time of sympathetic-parasympathetic imbalance and increased susceptibility to breathing abnormalities. Critically ill patients also experience less of stages 3 and 4 of NREM, which are characterized by stable respiratory control and are devoid of sympathetic-parasympathetic imbalances.

Critically ill patients may not exhibit the EEG features of sleep and wakefulness conventionally seen in ambulatory patients [5]. Cooper and co-workers found that 7 of 20 mechanically ventilated patients were in coma and 5 patients did not exhibit EEG characteristics of stage 2 sleep (spindles or K complexes). Four patients

exhibited pathological wakefulness (a combination of behavioral correlates of wakefulness and EEG features of slow wave sleep), occupying 26–68% of the 24-h recording. Only 8 of the 20 patients demonstrated EEG characteristics of sleep, and even these patients had an average of 39 arousals and awakenings per hour [5] (Fig. 1).

Obtaining reliable EEG recordings is difficult in critically ill patients. Electrical interference (60 Hz) arising from equipment such as infusion pumps or ventilators [37] is common; interference also arises from muscle contractions in agitated patients [38]. To achieve satisfactory EEG signals, which may consist of only a few micro volts, it is necessary to apply electrodes to appropriate areas of the scalp; the skin also requires careful preparation to ensure low contact impedance (preferably less than 5 Ohms). To further minimize interference, all wires between a patient and preamplifier must be as short as possible [37]. Additional challenges in conducting research studies are avoiding a change in sedative medications, curtailing unnecessary visits by hospital personnel, and minimizing agitation.

A few investigators have studied circadian rhythms in critically ill patients. Mundeglier and co-workers [31] measured urinary 6-sulfatoxymelatonin every 4 h over 24 h. Compared with 7 non-septic critically ill patients and 21 healthy volunteers, the amplitude of circadian fluctuation in this melatonin metabolite was markedly lower in 17 critically ill patients suffering from septic shock.

Relationship between sedation and sleep

Critically ill patients are often given sedatives to increase patient comfort, decrease anxiety and agitation, and promote amnesia and sleep [25, 39]. Continuous infusion of sedatives, however, may prolong the duration of mechanical ventilation by 2.5 days and prolong ICU stay by 3.5 days [40]. The effect of sedative agents on the depth of sedation has been rigorously studied [39, 41, 42], although little is known about its effect on sleep quality in critically ill patients [43]. Over a 5-day period, 40 non-intubated critically ill patients were randomized to nocturnal midazolam and propofol [25]. On a 10-point self-rating scale, both groups reported a tendency towards improved sleep quality: from 6.3 to 7.2. The infusions were titrated to achieve a score of 3 or greater on the Ramsay sedation scale (a score of 3 indicates that a patient is asleep but awakens with a brisk response to a glabellar tap or a loud auditory stimulus) [42]. Self-perception of sleep quality was not different for propofol and midazolam (range 0.1–9.7; mean of 7.2). Some patients continued to rate sleep quality close to zero on the fifth day. These data indicate that self-perception of sleep quality can be poor with high dosages of sedatives despite achieving adequate levels of sedation. Severe sleep fragmentation may also occur in mechanically ventilated patients despite sedatives and analgesics [4, 5].

Some of the discrepancies between bedside assessment of sedation and subjective scoring of sleep may reflect known limitations in the Ramsay sedation scale [43]. Kong and co-workers studied the efficacy of midazolam and isoflurane in reducing plasma levels of catecholamines when similar levels of sedation (on the Ramsay scale) were achieved. Although both agents achieved comparable levels of sedation, isoflurane, but not midazolam, lowered the plasma levels of catecholamines from baseline [21]. The persistently elevated catecholamines in the patients receiving midazolam may have produced sleep disruption, although the explanation is no more than a possibility because polysomnography was not performed.

Benzodiazepines, narcotic analgesics, and propofol are commonly used to sedate critically ill patients [39]. Benzodiazepines improve behavioral aspects of sleep. They decrease the time needed to fall asleep, decrease awakenings, increase sleep duration, and increase sleep efficiency (duration of sleep as a percentage of time in bed). Benzodiazepines, however, also increase the number of spindles, increase cortical EEG frequency (at low doses), decrease EEG amplitude and frequency (at high doses), *and* suppress REM and slow wave sleep [44]. Although the clinical importance of these EEG alterations is not totally clear, an ideal hypnotic should not disturb the normal sleep pattern. Narcotics can also suppress REM sleep, cause a dose-dependent slowing of EEG, and suppress slow wave sleep—the most restorative stage of sleep [12, 44, 45]. In sum, a medicated state may resemble sleep on the surface, but may not provide the physiological benefits associated with true sleep.

Factors contributing to sleep disruption

Noise and hospital staff

The level of noise in the ICU ranges from 50 to 75 dB, with peaks of up to 85 dB [8, 26, 46, 47, 48, 49, 50, 51, 52]. This level of noise is comparable to that in a factory (80 dB) or a busy office (70 dB), and is louder than noise in a bedroom (40 dB) [51]. (The decibel scale is logarithmic, and an increase of 10 dB represents a doubling of noise.) When studying the relationship between ICU noise and sleep disruption, investigators commonly attribute arousals to noise when they occur within 3 s of a measurable (greater than 15 dB) increase in noise [5, 6]. In these studies, 11–20% of arousals were attributed to noise [5, 6]. Because critically ill patients have frequent arousals and awakenings (20–68 per hour, Table 1) some arousals may mistakenly be attributed to noise. In a study of healthy volunteers subjected to audio recordings

of ICU noise, a greater than normal number of awakenings and less REM and total sleep time were observed [50, 53]. Findings in healthy subjects, however, may not apply to critically ill patients, who may have a higher arousal threshold secondary to sleep deprivation, sedative agents, or coma.

Gabor and co-workers [8] recorded audio and video signals in synchrony with polysomnography in seven patients receiving mechanical ventilation. Twenty percent of the arousals and awakenings were related to noise peaks, and only 10% were related to patient care activities. The cause of 68% of arousals and awakenings could not be identified [8].

Mechanical ventilation

About 40% of patients in an ICU receive mechanical ventilation [54], but investigations into the precise mechanisms of the effect of mechanical ventilation on sleep are only commencing. Mechanically ventilated patients experience considerable sleep disruption, with as many as 20–63 arousals and awakenings per hour [4, 5, 8]. At first glance, a comparison of mechanically ventilated patients with spontaneously breathing critically ill patients should provide a reasonable method for investigating the effect of mechanical ventilation on sleep (Table 1). Such comparisons might prove misleading for a number of reasons. First, acuity of illness may be greater in ventilated patients than in spontaneously breathing patients. Second, spontaneously breathing patients are vulnerable to obstructive apneas, which will be prevented by an endotracheal tube. Third, factors associated with ventilation, such as masks, tracheal tubes, suctioning, mouth guards, nasogastric tubes, and physical restraints, may contribute to sleep fragmentation [55]. Fourth, sedatives and analgesics are more likely during mechanical ventilation. An attractive way to study the effect of mechanical ventilation on sleep might be to study tracheostomized patients while connected and disconnected from a ventilator over a short time period.

Notwithstanding methodological concerns with the studies, data suggest that the mode of ventilation can influence sleep quality [56, 57]. Meza and co-workers [56] showed that pressure support induces central apneas in healthy subjects during sleep. In a study of 11 critically ill patients during one night of sleep, Parthasarathy and Tobin observed greater sleep fragmentation during pressure support than during assist-control ventilation: 79 versus 54 arousals and awakenings per hour (Fig. 2). Six of the 11 patients developed central apneas during pressure support, but not during assist-control ventilation [15]. Heart failure was more common in the patients who developed apneas than in the patients without apneas: 83% versus 20%. The findings emphasize that research on sleep in critically ill patients needs to be controlled for the ventilator mode. In these 11 patients, the most important determinant of apneas was the difference between PCO_2 during resting breathing and the patient's apnea threshold. When a patient's resting PCO_2 was close to the apnea threshold, central apneas were more likely to develop. The addition of dead space caused a further increase in resting PCO_2 above the apnea threshold and decreased the sum of arousals and awakenings from 83 to 44 events per hour (in the patients who developed central apneas during pressure support). Sleep efficiency (time asleep as a percentage of study duration) increased from 63 to 81% with the addition of dead space (Fig. 2).

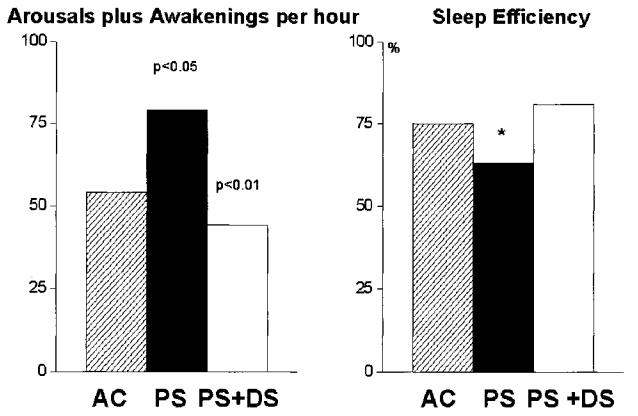

Fig. 2 Sleep fragmentation (*left panel*) and sleep efficiency (*right panel*) during assist-control ventilation and pressure support with and without dead space. Sleep fragmentation, measured as the number of arousals and awakenings, was greater during pressure support (*solid bars*) than during assist-control ventilation (*hatched bars*) or pressure support with dead space (*open bars*). Sleep efficiency (*right panel*) was also lower during pressure support (*solid bars*) than during assist-control ventilation (*hatched bars*) or pressure support with dead space (*open bars*). (Modified from [15] with permission)

Other factors

Factors that contribute to sleep abnormalities in critically ill patients include acute illness [2, 3, 11, 12], pain, light, and patient discomfort [17]. Noxious stimuli that contribute to patient discomfort and arousal include increased respiratory effort [58, 59], hypoxemia [58], and hypercapnia [58]. Swings in intrathoracic pressures are potent stimuli for inducing arousals in healthy subjects [60] and in patients with upper airway resistance syndrome [34].

Clinical implications

Clinical outcomes

Sleep fragmentation may influence morbidity and mortality in critically ill patients. Patients in coma and pa-

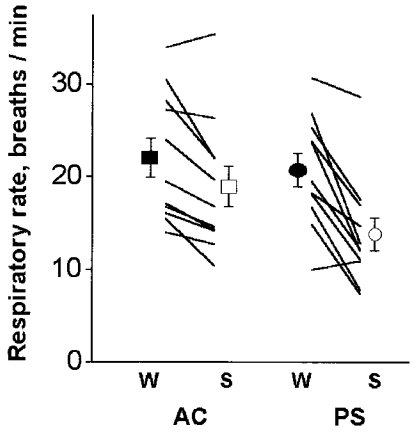

Fig. 3 Respiratory rate during assist-control ventilation (*AC*) and pressure support (*PS*) in 11 critically ill patients. For each mode, the lines connect the mean value for each patient during wakefulness (*W*, *left*) and sleep (*S*, *right*). Compared with wakefulness, group mean respiratory rate was lower during sleep (*closed symbols*) than during wakefulness (*open symbols*). The difference between sleep and wakefulness was greater for pressure support than for assist-control ventilation. (Modified from [15] with permission)

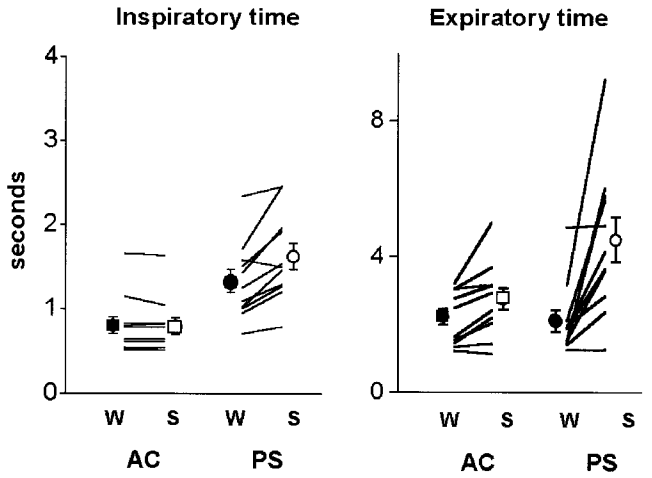

Fig. 4 Inspiratory time (*left panel*) and expiratory time (*right panel*) during assist-control ventilation (*AC*) and pressure support (*PS*) in 11 critically ill patients. The lines connect the mean value for each patient during wakefulness (*W*, *left*) and sleep (*S*, *right*). During pressure support, group mean inspiratory time and expiratory time were greater during sleep (*closed symbols*) than during wakefulness (*open symbols*). The difference between sleep and wakefulness was greater for pressure support than for assist-control ventilation. (Modified from [15] with permission)

tients who lack well-defined EEG characteristics of stage 2 sleep have higher acute physiological scores than do patients with identifiable but fragmented sleep [5]. Some investigators have reported no association between the acuity of illness and sleep disruption [6]. As such, the contribution of acuity of illness to sleep disturbances is unclear. Animal data suggest that sleep deprivation may lead to death [61]. It is thought that death is unlikely to result with sleep deprivation in human subjects [62, 63], but the consequence of sleep deprivation has been studied only in healthy subjects and not in critically ill patients.

Among 24 patients with post-traumatic coma, 5 of 6 patients who had organized sleep patterns survived as opposed to 3 of 7 patients who had low voltage theta-delta or mixed frequency activity without definable features of sleep; functional outcome was also better in the patients with organized sleep patterns [7]. Freedman and co-workers found that 5 of 22 patients exhibited EEG features of mild to moderate encephalopathy before other features of sepsis manifested [6]; none of the non-septic patients demonstrated such EEG features.

Ventilator settings

Physicians typically adjust ventilator settings during the daytime and without knowing whether a patient is asleep or awake. Compared with wakefulness, sleep caused a 33% decrease in respiratory rate during pressure support and a 15% decrease in rate during assist-control (Fig. 3) [15]. The level of pressure support is commonly titrated to respiratory rate, which provides reasonable guidance as to a patient's inspiratory effort [64, 65]. If, however, physicians titrate pressure support to respiratory rate while the patient is asleep, patient effort will increase considerably on awakening.

Changes in ventilator settings are commonly based on arterial blood gas measurements. End-tidal CO_2 was greater in 11 critically ill patients during sleep than during wakefulness: by 11% during pressure support and by 5% during assist-control ventilation. Patients who repeatedly slip in and out of sleep display marked fluctuations in end-tidal CO_2. The coefficient of variation of end-tidal CO_2 was 8.7% during pressure support and 4.7% during assist-control ventilation [15]. In some patients receiving pressure support, end-tidal CO_2 can be as much as 7 mmHg higher during sleep than during wakefulness. Differences in PCO_2 between sleep and wakefulness of this magnitude may cause physicians to change ventilator settings when a change is not necessary. Consequently, under-ventilation or over-ventilation may result [66]. Compared with wakefulness, sleep caused a 23% increase in inspiratory time and a 126% increase in expiratory time in patients receiving pressure support (Fig. 4). The increase in inspiratory time that accompanied change from wakefulness to sleep was also associated with an increase in tidal volume, and the likely accompaniment of hypocapnia may explain the development of apneas during pressure support [67, 68]. These findings indicate that the effect of sleep on breathing pattern and gas exchange has important implications for research on patient-ventilator interaction.

Cardiorespiratory consequences

In ambulatory patients, sleep fragmentation can result in elevations of arterial blood pressure, elevations of urinary and serum catecholamines, arrhythmias, progression of cardiac failure, and even death [69, 70]. Sleep-disordered breathing might cause similar abnormalities in critically ill patients, although direct evidence is lacking. Apneas and hypopneas cause hypoxemia [16], which, in turn, may produce sympathetic activation and arrhythmias in critically ill patients; evidence on this issue, however, is anecdotal [71] and inconclusive [72].

Sleep fragmentation induced by auditory stimuli can increase nocturnal blood pressure in dogs [73]. In patients who have central sleep apnea, the major cause of oscillations in blood pressure is ventilatory oscillations, with a significant contribution from arousals [73]. These investigations [73, 74] suggest that arousals may elevate nocturnal blood pressure, secondary to increases in sympathetic activity, and contribute to cardiovascular complications [75]. Preliminary data suggests that sleep fragmentation in critically ill patients may be associated with elevations in blood pressure [76], but the effect on morbidity and mortality is unknown.

The effect of sleep deprivation [77] on the ventilatory responses to hypoxia and hypercapnia is controversial [78]. Sleep deprivation has long been believed to depress chemoreceptor function [78]. Spengler and colleagues [78], however, recently found that sleep deprivation did not alter the hypercapnic ventilatory response in healthy subjects. The situation in critically ill patients has not been studied. Blunting of the chemoreceptor response can decrease the ability of the respiratory system to compensate for respiratory loads during or after the withdrawal of mechanical ventilation [68].

At least some postoperative patients experience an increase in REM sleep on the third to fourth postoperative day secondary to the earlier suppression of REM sleep by anesthetics and analgesics [12]. Because REM sleep is characterized by unstable breathing patterns and sympathetic-parasympathetic imbalances, the increase in REM sleep in the early postoperative period may aggravate the risk of postoperative atelectasis, pneumonia, hypoxemia, and cardiovascular morbidity.

Neurological consequences

Sleep deprivation may contribute to delirium and agitation [19, 79]. In a study of 62 critically ill patients, Helton and colleagues [19] noted that 24% experienced severe sleep deprivation and 16% experienced moderate deprivation. One third of the patients with severe sleep disruption suffered from delirium, 10% of patients with moderate sleep disruption suffered from delirium, but only 3% of patients with adequate sleep had delirium. The study has limitations. Sleep was assessed at the bedside by nursing staff rather than polysomnography. No intervention was performed, and a cause and effect relationship between sleep deprivation and delirium cannot be inferred. Agitation can cause elevations in plasma catecholamines [21]. Large doses of sedative agents are often used in agitated and delirious patients; when the agitation resolves, however, the sedative agent may remain in adipose tissue and interfere with weaning from mechanical ventilation.

Immunological and metabolic consequences

Sleep deprivation can unfavorably alter immune function [80, 81, 82, 83, 84, 85, 86]. In 42 healthy volunteers, Irwin and co-workers found that sleep deprivation resulted in almost a 50% decrease in natural killer cell activity and a 50% decrease in lymphokine killer cell activity. One night of sleep returned natural killer cell activity to baseline.

Sleep deprivation can promote negative nitrogen balance and increase energy expenditure [62, 63, 87]. In six healthy volunteers, 24 h of sleep deprivation produced a 7% increase in nitrogen excretion. Some subjects experienced as much as a 20% increase in nitrogen excretion. It is not known whether similar changes occur in critically ill patients.

Long-term consequences

Critical illness may have long-term consequences on sleep [22]. When 329 patients were interviewed 6 months after discharge from an ICU, 223 (67%) reported severe alterations in sleep. The lack of a control group makes it impossible to distinguish the role of critical illness from previous health status, underlying medical diagnosis, persistent disability, or other factors.

Strategies to decrease sleep disruption

Gabor and co-workers studied the effect of reducing noise in six healthy volunteers while they slept in an ICU [8]. The average level of noise was 51 dB in an open ICU and 43 dB in an isolated single room (the respective peak levels were 65 and 54 dB). Total sleep time was greater in the isolated room than in the open ICU, 9.5 versus 8.2 h, although the number of arousals and awakenings were virtually identical in the two settings (14 to 15 events per hour) [8]. In six healthy volunteers attempting to sleep in a noisy environment, Wallace and co-workers found that use of earplugs increased REM sleep (20 versus 15%) and decreased REM latency (107 versus 148 min), although the number of awaken-

ings was not affected (25 versus 27 per hour). Because only 20% of sleep fragmentation in critically ill patients appears to be attributable to noise [8], reducing noise in the ICU may be of limited value.

Shilo and co-workers undertook a double blind, placebo-controlled study of melatonin in eight critically ill patients with chronic obstructive pulmonary disease [27]. The authors conclude that melatonin achieved greater sleep time and less fragmentation, although the conclusions are not well supported by the data.

Conclusion

Research into sleep disorders in ambulatory patients over the last 30 years has provided us with a strong set of physiological principles. The time is ripe for applying these principles to critically ill patients. A major challenge, as with most research in critically ill patients, is the difficulty in controlling for confounding influences in order to achieve high fidelity recordings.

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