Sleep in Critically Ill Patients Requiring Mechanical Ventilation*

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Study objectives: **To objectively measure sleep in critically ill patients requiring mechanical ventilation and to define selection criteria for future studies of sleep continuity in this population.**
Design: **Prospective cohort analysis.**
Setting: **University teaching hospital medical-surgical ICU.**
Patients: **Twenty critically ill (APACHE II [acute physiology and chronic health evaluation II] acute physiology score [APS], 10 ± 5), mechanically ventilated adults (male 12, female 8, age 62 ± 15 years) with mild to moderate acute lung injury (lung injury score, 1.8 ± 0.9) 10 ± 7 days after admission to the ICU.**
Measurements and results: **Patients were divided into three groups based on 24-h polysomnography (PSG) findings. No patient demonstrated normal sleep. In the "disrupted sleep" group (n = 8), electrophysiologic sleep was identified and was distributed throughout the day (6:00 AM to 10:00 PM; 4.0 ± 2.9 h) and night (10:00 PM to 6:00 AM; 3.0 ± 1.9 h) with equivalent proportions of non–rapid eye movement (NREM) and rapid eye movement (REM) sleep. Nocturnal sleep efficiency was severely reduced (38 ± 24%) with an increased proportion of stage 1 NREM sleep (40 ± 28% total sleep time [TST]) and a reduced proportion of REM sleep (10 ± 14% TST). Severe sleep fragmentation was reflected by a high frequency of arousals (20 ± 17/h) and awakenings (22 ± 25/h). Electrophysiologic sleep was not identifiable in the PSG recordings of the remaining patients. These were classified either as "atypical sleep" (n = 5), characterized by transitions from stage 1 NREM to slow wave sleep with a virtual absence of stage 2 NREM and reduced stage REM sleep, or "coma" (n = 7), characterized by > 50% delta or theta EEG activity with (n = 5) and without (n = 2) evidence of EEG activation either spontaneously or in response to deep painful stimuli. The combined atypical sleep and coma groups had a higher APS (13 ± 4 vs 6 ± 4) and higher doses of sedative medications than the disrupted sleep group.**
Conclusion: **Sleep, as it is conventionally measured, was identified only in a subgroup of critically ill patients requiring mechanical ventilation and was severely disrupted. We have proposed specific criteria to select patients for future studies to evaluate potential causes of sleep disruption in this population.** ***(CHEST 2000; 117:809–818)***

Key words: critical care; mechanical ventilation; polysomnography; sleep deprivation; sleep stages

Abbreviations: APACHE II = acute physiology and chronic health evaluation II; APS = acute physiology score; EMG = electromyogram; EOG = electro-oculogram; GCS = Glasgow coma scale; LIS = lung injury score; NREM = nonrapid eye movement; REM = rapid eye movement; SE = sleep efficiency; SWS = slow wave sleep; TSP = total study period; TST = total sleep time

Sleep disruption has been recognized as a complication of acute illness for at least 20 years. It is characterized by reduced nocturnal sleep efficiency and altered sleep architecture with increased wakefulness and stage 1 non–rapid eye movement (NREM) sleep, together with reduced slow wave (SWS) and rapid eye movement (REM) sleep.[1–10]

Sleep disruption in critically ill, mechanically ventilated patients may have a multifactorial cause. Acute illnesses are associated with abnormal sleep architecture.[4,5,7,9,11,12] The ICU environment, in which loud noises[13,14] and frequent care-related interruptions[14,15] are prevalent, may interfere with continuity of sleep. Medications commonly prescribed for patient comfort also have marked effects on sleep.[16] It is possible that dyssynchronous pa-

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tient–ventilator interactions may result in sleep disruption. However, there are only preliminary investigations in intubated patients requiring mechanical ventilation.[17,18]

Alteration of sleep quality and quantity can have important adverse consequences. Studies in healthy volunteers and animal models identify negative nitrogen balance,[19] reduced host immunity,[20] attenuated ventilatory responses to hypoxemia and hypercapnia,[21] and increases in oxygen consumption and carbon dioxide production.[22] Sleep disruption, therefore, could interfere with the process of liberation from mechanical ventilation by its effects on the load, control, and output of the ventilatory pump.

Clinical reports of the adverse effects of sleep disruption in critically ill patients are few and are limited by behavioral definitions of sleep[15] or incomplete polysomnographic (PSG) data.[12] Despite the clear importance of this problem, there are relatively few studies in the literature on this topic, likely because it is difficult to perform sleep studies in severely ill patients who require mechanical ventilation. Given the clinical impression that adequate sleep is important in ICU patients, and the paucity of data on sleep in critically ill, mechanically ventilated patients, we undertook a prospective cohort pilot study using 24-h PSG. Our objectives were to define the most appropriate population for future studies, to quantify sleep disruption, and to generate hypotheses about potential causes of sleep disruption to develop future research projects in this area.

Materials and Methods

Patient Recruitment

The study protocol and consent were approved by the Wellesley Central Hospital Research Ethics Committee. Written informed consent was obtained from the patient or, if the patient had evidence of an altered sensorium (inappropriate or absent response to commands), from a family member. Patients admitted to the Ewart Angus ICU between April 21, 1997, and June 30, 1998, were screened for eligibility. Selection criteria were endotracheal intubation and anticipated further mechanical ventilation of at least 24-h duration. Exclusion criteria were (1) anticipated ICU stay < 24 h, (2) very unlikely survival (prior life expectancy < 3 months, hopeless prognosis judged by two physicians, malignancy), (3) premorbid diseases that could confuse interpretation of sleep monitoring including CNS diseases and sleep disorders, (4) hemodynamic instability (BP < 90 mm Hg despite therapy), (5) general anesthetic, drug overdose, or alcohol intoxication within the preceding 24 h, and (6) enrollment in another study. General supportive care and mechanical ventilation were left to the discretion of the attending critical care team and were not altered by the investigators during the course of the study.

Sleep Studies

Patients were monitored for 24 h by continuous PSG, which included two central (C4/A1, C3/A2) ± one occipital (O1/A2 or O2/A1) channels for EEG, electrooculogram (EOG), submental and bilateral anterior tibialis electromyogram (EMG), ECG (lead I), and pulse oximetry. Techniques for gold cup electrode placement conformed to standard practices and the international 10–20 system. Sleep studies were continuously attended. Recordings were reviewed on an hourly basis by the author (A.C.) or technologist during the 24-h collection period, and if skin impedances exceeded 10 kΩ, electrodes were reapplied. Signals were acquired with a Nellcor Puritan Bennett MMC preamplifier and amplifier (NPB Melville Ltd; Ottawa, Ontario) and stored electronically on a computer hard drive with Melville Diagnostics Sandman 2.4 software. Thirty-second epochs were analyzed by a registered PSG technologist. The 24-h study period was divided into night and day periods, with nighttime defined as 10:00 PM to 6:00 AM and daytime defined as 6:00 AM to 10:00 PM.

All records were scored manually according to standard Rechtshaffen and Kales criteria. Total sleep time (TST) was defined as the total time asleep from the beginning to the end of the day or night study period (TSP). Sleep efficiency (SE) was defined as time asleep as a proportion of TSP ($SE = 100 \times TST/TSP$). Movement arousals were defined as an abrupt increase in EEG frequency accompanied by a simultaneous increase in EMG amplitude lasting for 3 to 15 s. Periodic limb movement arousals were scored if a periodic limb movement occurred within the 3 s preceding the movement arousal. EEG arousals were defined as an abrupt increase in EEG frequency lasting for 3 to 15 s without an accompanying change on the submental EMG channel. Microarousals were defined as movement arousals of 1 to 3 s duration. Awakenings were defined as EEG activation of > 15 s duration with accompanying change on the submental EMG and EOG channels. Studies with features of atypical sleep or coma (defined in results section) were reviewed in 10-s epochs by a neurologist (G.B.Y.) and classified according to reliable criteria for assessment of ICU populations.[23]

Study Population

Data were collected from the patients' charts. Lung injury was quantified with the lung injury score (LIS),[24] and severity of illness was calculated using the APACHE II (acute physiology and chronic health evaluation II)[25] on the day of admission. The acute physiology score (APS) portion of the APACHE II score was calculated on the day of the sleep study using the most abnormal values recorded during the 24-h PSG period. Administered medication doses were obtained from the nursing notes. When fentanyl was used, a conversion factor of 100 μg/mg was used to obtain the equivalent dose of morphine based on relative potency.[26] When diazepam was used, a conversion factor of 10:1 was used to obtain an equivalent dose of lorazepam.[27] Medication doses are expressed as milligrams per kilogram per hour based on the patient's total dose for the study period and admission body weight. Microbiology results were reviewed over the 7 days before the day of study. Infection was defined as a positive microbial isolate for which the patient was receiving specific antibiotic therapy. Empirical broad-spectrum antibiotic coverage was not accepted as evidence of infection in the absence of positive cultures. Blood cultures for Staphylococcus spp were considered if the microbe was isolated in both aerobic and anaerobic media. For other Gram-positive and Gram-negative organisms, fungi, and opportunistic organisms, growth in either medium or special microbiologic testing was accepted as evidence of infection.

Statistical Methods

Sample estimates are reported as means ± SD. Ninety-five percent confidence intervals for the differences between sample estimates for unpaired observations were calculated using Student's t distribution with $n_1 + n_2 - 2$ degrees of freedom and two tails according to the methods presented by Gardner and Altman.[28] All statistical calculations were performed using Microsoft Excel 97 (Microsoft Corp; Redwood, WA) formulas.

Results

Characteristics of Study Population on Day of ICU Admission

Twenty-six patients were studied from April 1997 to May 1998. We were unable to score six records, owing to technical problems. EEG recordings could not be interpreted because of electrical artifact in four of six and because of severe respiratory artifact in two of six patients. Both patients with severe respiratory artifact were very edematous. Characteristics of the study population on the day of ICU admission are given in Table 1. The majority of our patients were admitted to the ICU for respiratory insufficiency, with LIS indicating moderately severe lung injury. APACHE II illness severity also was moderate. Only three patients were unresponsive to commands (Glasgow coma scale [GCS] ≤ 8) on admission. Using the cutoffs defined for failure of individual organs in the multiple organ dysfunction syndrome score,[29] one patient had renal insufficiency defined as creatinine ≥ 350 μmol/L and two patients had thrombocytopenia defined as platelet count $\leq 80 \times 10^9$/L.

Sleep Studies

After review of 24-h PSG recordings, we categorized our results into three groups: disrupted sleep, atypical sleep, and coma. The characteristics of the patients in each group on the day of the sleep study are contrasted in Table 2.

All patients in the disrupted sleep group (n = 8) had PSG features of both NREM and REM sleep, but differed from normal with respect to the temporal distribution of sleep throughout the 24-h period, nocturnal sleep architecture, and the frequencies of arousals and awakenings (Tables 3 and 4). Daytime sleep averaged 54.4 ± 14.2% of TST during the 24-h study period. In seven of eight patients, > 33% of the TST occurred during the day (Fig 1). SE was similarly and markedly reduced during the day and night. The proportions of stage 1 and 2 NREM sleep, SWS, and REM sleep did not differ between the day and night periods. There was an increased proportion of stage 1 sleep and a reduction in the amount of REM sleep compared with age-matched control subjects.[30] The frequencies of arousals and awakenings were markedly and equally increased during the day and night periods. The most prevalent arousals were movement arousals.

The atypical sleep group (n = 5) had EEG features intermediate between sleep and coma, characterized by a virtual absence of stage 2 NREM (present in only one of five) and REM sleep (present in only two of five) (Table 5). Stage 2 NREM sleep could not be identified in four of five patients because there were no K complexes or sleep spindles, the defining EEG criteria of this sleep stage. Transitions between stages 1, 3, and 4 NREM and REM sleep occurred without intervening stage 2 NREM sleep (Fig 2). Another unique feature of this

Table 1—*Patient Characteristics on Admission to ICU**

Sex (M:F)	12:8
Age	61.7 ± 14.5
APACHE II diagnosis	
Respiratory	13
Gastrointestinal	6
Cardiovascular	1
APACHE II score	17 ± 8
APS	12 ± 7
LIS	1.7 ± 0.9
GCS	13 ± 4
Mean arterial pressure, mm Hg	74 ± 20
Bilirubin (total), μmol/L	12.7 ± 7.3
Creatinine, μmol/L	116 ± 103
Platelets, ×/10^9/L	246 ± 157

*Mean ± SD unless otherwise noted; M = male; F = female.

Table 2—*Patient Characteristics in Each Group on Day of Sleep Study**

Characteristic	Disrupted Sleep Group	Atypical Sleep Group	Coma Group
Age, yr	69 ± 10	62 ± 7	53 ± 19
M:F	6:2	2:3	4:3
ICU day	9 ± 10	13 ± 7	7 ± 2
APS	6 ± 4	13 ± 4	13 ± 4
Δ APS	−1 ± 6	1 ± 4	−4 ± 7
GCS	14 ± 3	10 ± 3	7 ± 3
LIS	1.8 ± 0.6	1.0 ± 0.0	2.0 ± 1.0
Cultures, ±	5:3	5:0	1:6
Inotropes, ±	0:8	1:4	0:7
Muscle relaxants, ±	0:8	0:5	2:5
Benzodiazepines, ±	5:3	4:1	6:1
Lorazepam dose, μg/kg/h	1.0 ± 1.0	9.1 ± 18.2	19.5 ± 27.2
Opioids, ±	5:3	3:2	6:1
Morphine dose, μg/kg/h	8 ± 19	12.3 ± 18.1	139 ± 168
Neuroleptics, ±	4:4	1:4	2:5
Haloperidol dose, mg/kg/h	0.1 ± 0.1	0.1 ± 0.1	0.3 ± 0.6

*Mean ± SD unless otherwise noted. ± = number of subjects with condition present vs with condition absent; APS = study day APS − admission APS.

Table 3—*Disrupted Sleep Group: Sleep Architecture

Study Period	TST, h	SE, %	Stage 1, %	Stage 2, %	SWS, %	REM, %
Night	3.0 ± 1.9	38 ± 24	40 ± 28	40 ± 23	10 ± 17	10 ± 14
Day	4.0 ± 2.9	25 ± 18	43 ± 26	33 ± 18	15 ± 14	9 ± 6

*Mean ± SD unless otherwise noted. All sleep stage values are expressed as percentages of TST.

group was that some patients demonstrated pathologic wakefulness. We defined this as EEG epochs in which behavioral correlates of wakefulness (such as saccadic eye movements and sustained EMG activity) coincided with EEG features of SWS (high-amplitude, low-frequency theta waves, 3 to 7 Hz), which are not seen in normal sustained wakefulness (Fig 3). The frequency of arousals and awakenings was slightly increased in this group. Three of five patients in this group regained consciousness after the study.

The coma group (n = 7) was characterized by EEG features of coma that were classified according to the system proposed by Young et al[23,31] for assessment of thalamocortical function in ICU populations. Reactivity was judged to be present if EEG activation from delta/theta or alpha/theta/spindle coma occurred either spontaneously or in response to deep pain stimuli. The most common type of abnormality (five of seven patients) was class IA, coma with > 50% delta or theta activity with reactivity. Two of seven patients had class IB coma with > 50% delta or theta wave activity without reactivity (Fig 4). Four of seven patients in the coma group, including one with class IB coma, regained consciousness after the study. None of the patients in the coma group had evidence of localizing neurologic signs at the time of enrollment. No lasting neurologic sequelae were noted in any of the surviving patients, and there was no indication that any of the nonsurvivors succumbed because of a neurologic event.

Comparison of Patient Characteristics Between Groups

Because one of the study objectives was to define the most appropriate population for future studies of disrupted sleep in mechanically ventilated patients, we combined results from the atypical sleep and coma groups in our analysis (Table 6). Our decision was made because no patients in the atypical sleep or coma groups had sleep as it is conventionally defined. The 95% confidence interval of the difference between means for APS and GCS indicated significant differences between the combined atypical sleep and coma patients and the disrupted sleep patients. APS was higher in the atypical sleep and coma groups than in the disrupted sleep group (7; 95% confidence interval, 3 to 11) and GCS was lower (−6; 95% confidence interval, −3 to −9). Pearson product-moment coefficient was calculated to assess correlation between GCS and APS; r^2 was 0.65.

Our sample size was too small to allow for univariate or multivariate analysis of factors that would correlate with disrupted sleep. We chose cutoffs that are close to the point estimate of the atypical sleep group to define a population at risk of disrupted sleep for future studies; APS < 13, GCS ≥ 10, and medications (in the preceding 24 h): lorazepam equivalent dose ≤ 10 mg/kg/h, morphine equivalent dose ≤ 10 mg/kg/h.

Discussion

This study is our first investigation of sleep in critically ill patients who are mechanically ventilated. None of the patients we studied demonstrated normal sleep. Furthermore, using standard electrophysiologic criteria,[32] sleep as it is usually defined was not present in all critically ill patients. Based on our observations, we propose criteria to select critically ill patients at risk of disrupted sleep; APS < 13, GCS ≥ 10, and sedative medication doses (in the preceding 24 h): lorazepam equivalent ≤ 10 mg/kg/h, morphine equivalent ≤ 10 mg/kg/h. We found that in those critically ill, mechanically ventilated patients in whom sleep can be monitored, the abnormalities are very similar to the abnormal sleep previously reported in other acutely ill patient populations.[1–9,11] Importantly, our data show that the severity of sleep fragmentation in these patients is of a similar magnitude to that associated with excessive

Table 4—*Disrupted Sleep Group: Sleep Fragmentation

Study Period	Arousals					Awakenings
	Movement	PLM	Micro	EEG	Total	
Night	17 ± 16	1 ± 1	2 ± 3	0 ± 0	20 ± 17	22 ± 25
Day	21 ± 20	1 ± 3	2 ± 2	1 ± 1	25 ± 21	17 ± 12

*Mean ± SD. Arousals = frequency of arousals/h; Awakenings = frequency of awakenings/h; PLM = periodic limb movements. Definitions of arousal subtypes as described in Methods.

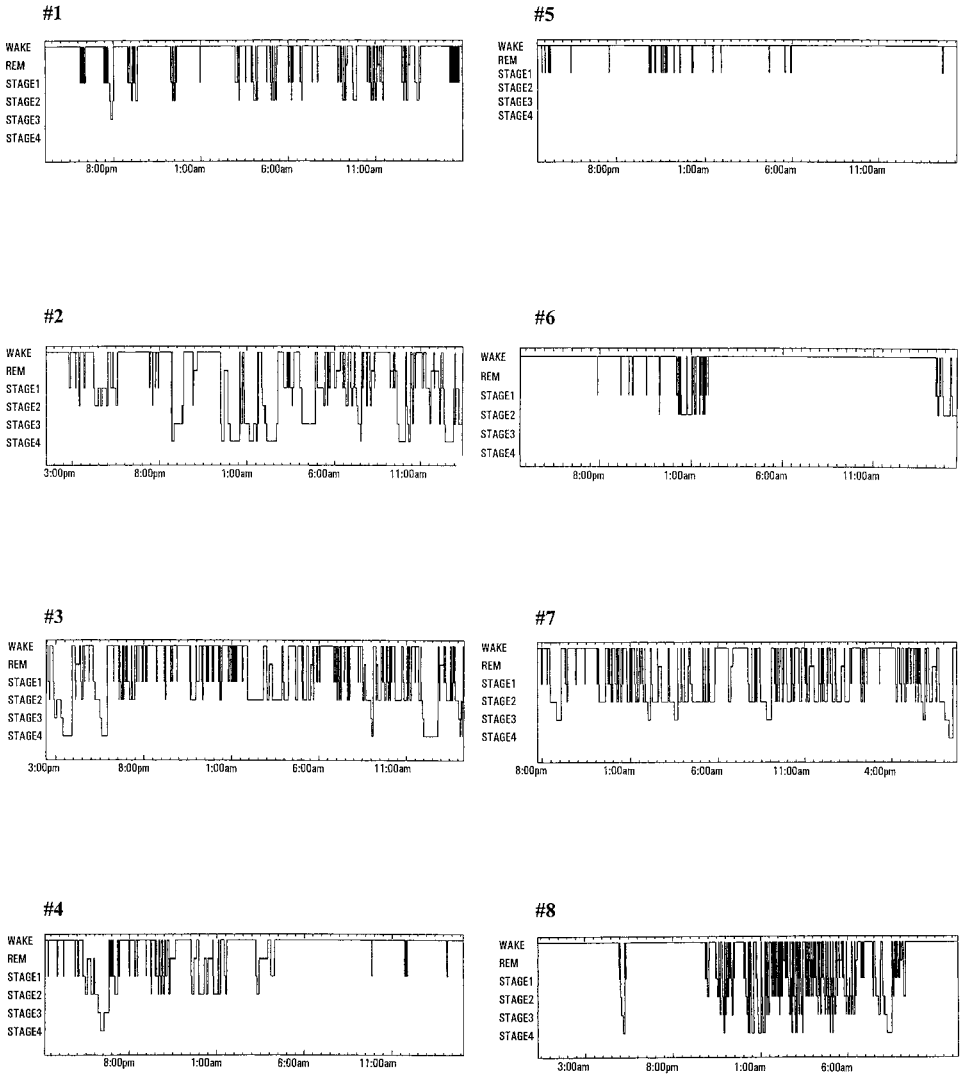

FIGURE 1. Twenty-four-hour hypnograms of the disrupted sleep group (patients 1 through 8). Vertical axis in descending sleep-stage order: wake, REM, and NREM stages 1, 2, 3, and 4. Horizontal time axis in hours. Hypnograms demonstrate (1) distribution of sleep throughout the 24-h period in all patients except patient 8, in whom sleep was predominantly nocturnal; (2) frequent awakenings; and (3) prolonged wakefulness, especially patients 4, 5, and 6.

daytime sleepiness and cognitive impairment in ambulatory sleep-disrupted patients.[33]

Our inclusion and exclusion criteria were intended to allow us to select a broad cross-section of patients who were mechanically ventilated. We excluded patients whose underlying diseases or treatments could confound interpretation of PSG recordings. For example, we excluded patients who had received a general anesthetic within the preceding 24 h, because the inhaled anesthetic agent isoflurane tran-

Table 5—*Atypical Sleep Group: Sleep Architecture and Fragmentation**

Study Period	TST, h	Pathologic Wakefulness, h	Stage 1, % TST (n)	Stage 2, % TST (n)	SWS, % TST (n)	REM, % TST (n)	Arousals	Awakenings
Night	4 ± 2	6 ± 2	37 ± 42 (3)	14 ± 32 (1)	45 ± 51 (4)	4 ± 9 (1)	5 ± 3	7 ± 5
Day	6 ± 3	10 ± 3	36 ± 36 (3)	12 ± 27 (1)	46 ± 47 (4)	4 ± 5 (2)	8 ± 5	6 ± 3

*Mean ± SD. See footnote of Tables 3 and 4 for abbreviations aned terms.

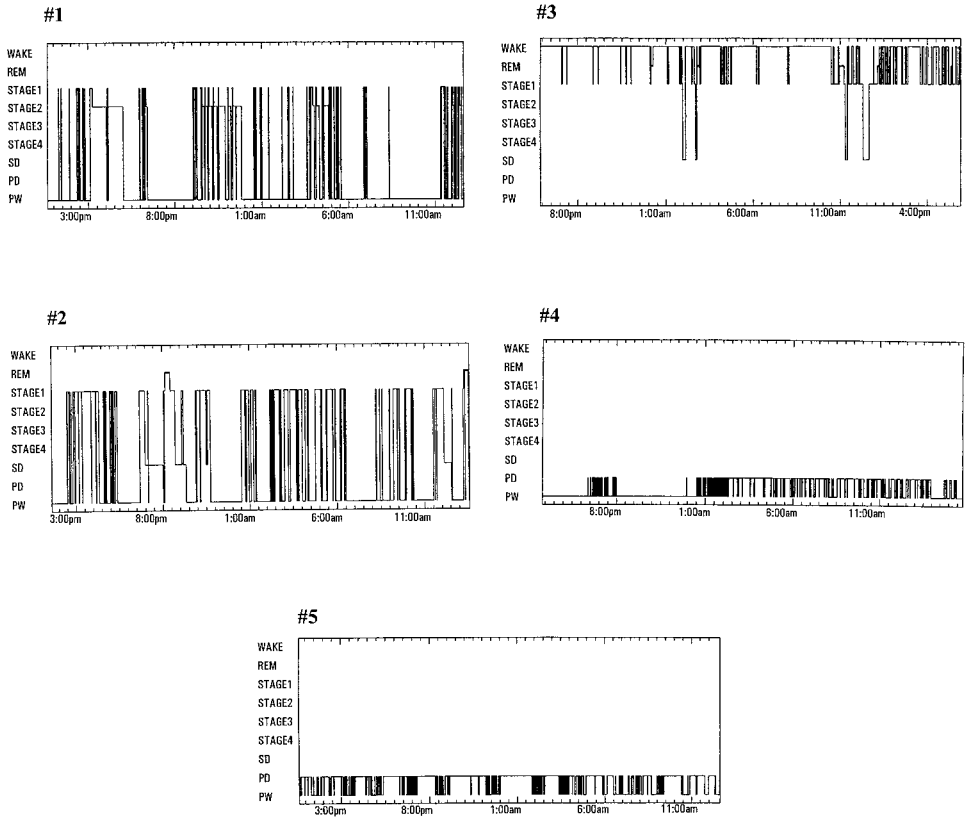

FIGURE 2. Twenty-four-hour hypnograms of the atypical sleep group (patients 1 through 5). Vertical axis in descending sleep-stage order: wake, REM, NREM stages 1, 2, 3, and 4, sleep delta (SD), pathologic delta (PD), and pathologic wakefulness (PW); see text. Horizontal time axis in hours.

siently increases stage 2 NREM sleep and decreases the proportion of SWS.[34] We also excluded patients with a history of a sleep disorder, such as narcolepsy, or CNS diseases. We were uncertain *a priori* how medications used for sedation and analgesia would affect sleep in our study patients, because literature on the effects of drugs on sleep is derived from studies of ambulatory patients and also because pharmacodynamics and pharmacokinetics in critically ill patients are difficult to predict. Consequently, we chose not to exclude patients who were receiving these medications.

In the atypical sleep (GCS, 10 ± 3; APS, 13 ± 4) and coma (GCS, 7 ± 3; APS, 13 ± 4) groups, EEG features of encephalopathy and coma instead of sleep were observed. A comparison of these patients to the sleep disrupted group showed that the only significantly different variables were APS and GCS. Because the GCS is a heavily weighted component of the APS,[25] we wondered about the extent to which the APS results might simply reflect changes in GCS. We calculated the Pearson product-moment correlation coefficient ($r^2 = 0.65$), indicating that there was indeed a moderate correlation between these factors. Analgesic and anxiolytic dosages were higher as GCS decreased, although they were not significantly different between the disrupted sleep and combined atypical sleep and coma groups. Consequently, we speculate that the EEG abnormalities we observed may have been drug-induced. None of our patients had positive blood cultures; therefore, bacteremia cannot be postulated as a cause.[31] Benzodiazepines are known to produce a decrease in alpha activity and general voltage and a slight increase in 4- to 7-Hz activity.[35] In a critically ill patient population, increasing depth of sedation with the benzodiazepine midazolam was associated with decreases in EEG spectral edge (17.61 to 10.56 Hz, $p = 0.0024$), and median frequency (4.27 to 2.56 Hz, $p = 0.0278$). The median dose of midazolam in these patients was 165 mg/24 h,[36] which corresponds to a lorazepam dose of approximately 3 mg/kg/h and is comparable to the median lorazepam dose (2 mg/kg/h) in our atypical sleep group patients. Opioids in high doses decrease EEG median frequency and spectral power. However, none of our patients (mean morphine dose, 86 ± 120 μg/kg/h) received morphine in the doses at which such changes oc-

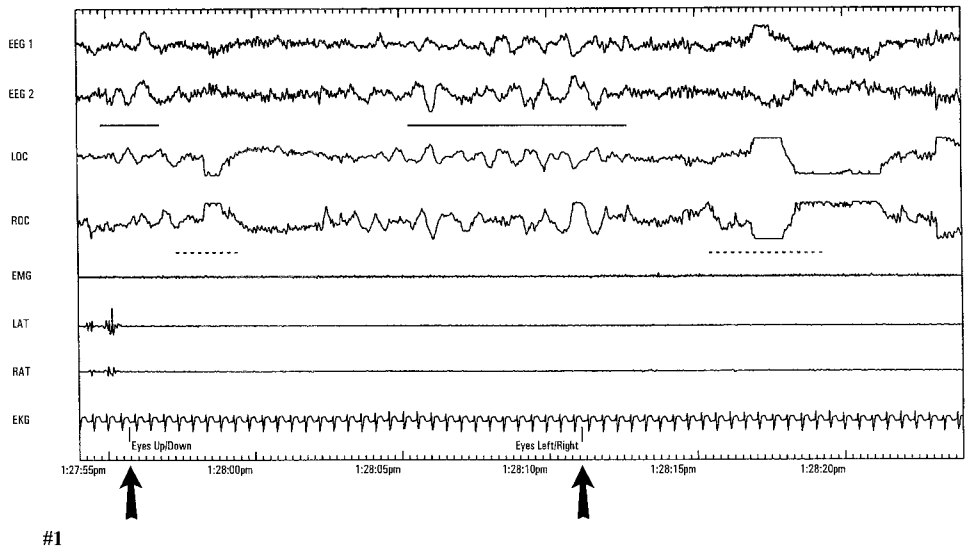

FIGURE 3. Thirty-second epoch of a patient in the atypical sleep group showing pathologic wakefulness. Vertical axis: EEG 1, EEG 2 (leads C4/A1 and C3/A2); LOC, left oculogram; ROC, right oculogram; EMG, submental electromyogram; LAT, left anterior tibialis electromyogram; RAT, right anterior tibialis electromyogram; and ECG. Horizontal time axis in hours:minutes:seconds. Note the slow-wave EEG activity (indicated by the solid horizontal bar) present during this patient's responses to biocalibration (indicated by a bold arrow).

curred during balanced anesthesia (morphine dose, ~2,600 μg/kg/h).[37] In view of this, it seems most likely that the EEG changes we observed might have resulted from benzodiazepine, rather then opiate sedation. One of seven coma and one of five atypical sleep patients had renal failure (defined by multiple organ dysfunction syndrome > 3 for the renal system) on the day of the sleep study. Uremia is another possible explanation for coma and encephalopathy in these patients, both because of primary effects of azotemia and its effect on pharmacologic clearance of sedative medications.

The sleep profiles of patients in the sleep disrupted group were similar to those previously described in diverse populations of acutely ill patients.[1–9,11] In all of these studies, SE was reduced; the lowest efficiency, 40%, was seen in a medical ICU population[3] and the highest, 89%, in postoperative herniorrhaphy patients.[6] Our study population's nocturnal SE is severely reduced in comparison with age-matched control subjects[30] and matches the lowest level previously reported in critically ill patients.[3] Despite this, it is interesting to note that the total duration of sleep during a 24-h period was close to normal. Mean TST during the day was 4.0 ± 2.9 h, and in seven of eight patients, $> 33\%$ of TST during a 24-h period occurred during the daytime. This sleep pattern has previously been reported by other investigators, who performed PSG for 24 h or longer.[1,9,11,12] Sleep architecture in acutely ill patients is characterized by variable increases in stage 1 and 2 NREM sleep and reduced SWS.[3,7] Changes in REM sleep range from mild reduction to total absence in the early postoperative period after open heart surgery.[8] Our population's marked reduction in REM sleep is comparable to previous studies of ICU patients.[1–3,7,9]

The degree of nocturnal sleep fragmentation in our sleep disrupted group patients is higher (awakening index, 22 ± 25/h) than in the most similar critically ill population (awakening index, 6.3/h), a cohort of nonintubated medical ICU patients.[3] Daytime sleep, when it was present, was also severely fragmented. This finding is clinically important because the degree of fragmentation we observed is substantially greater than that at which ambulatory patients with severe obstructive sleep apnea experience excessive daytime sleepiness, reflected by decreased sleep latency (≤ 8 min) on a multiple sleep latency test.[33] Patients with sleep fragmentation have abnormalities of cognitive function, such as significant reductions in attention, short-term memory, and verbal recall. They also have decreased calculation and problem-solving ability.[38,39] Daytime sleepiness and cognitive impairment could hinder patients' ability to cooperate with the complex activities, such as respiratory muscle training, that are required to facilitate the process of liberation from mechanical ventilation. Although evidence is limited, it is also possible that impaired sleep may contribute to the phenomenon of ICU psychosis in mechanically ventilated patients.[15] The futile cycle of

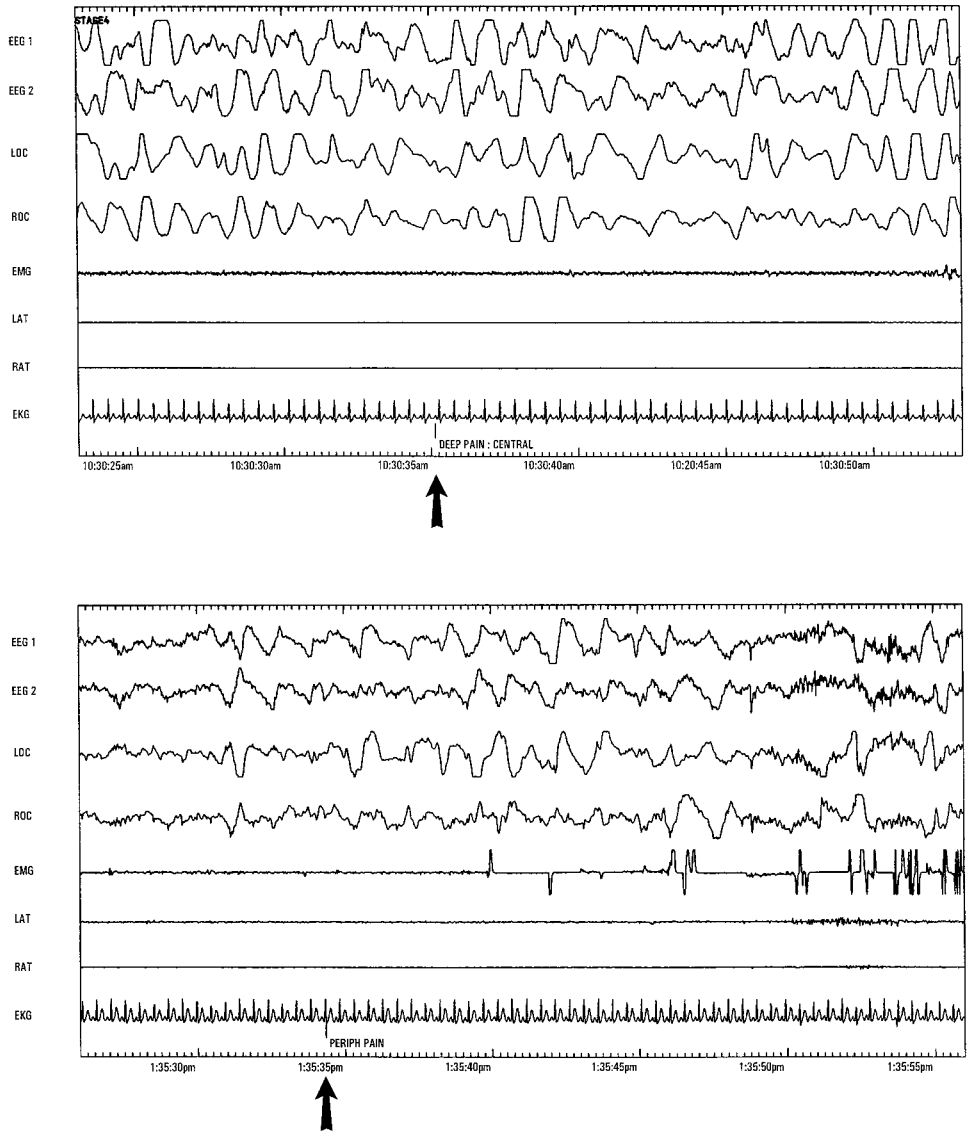

FIGURE 4. Thirty-second epochs of two patients in the coma group. Vertical and horizontal axes same as in Figure 3. *Top:* no reactivity to a painful stimulus (indicated by a bold arrow); *Bottom:* reactivity (increase in EEG activity) after a painful stimulus (indicated by a bold arrow).

delirium, patient-ventilator dyssynchrony, and sedation-induced ventilator dependency during attempts to liberate patients from mechanical ventilation is anecdotally very familiar to intensivists.

Our sleep disrupted group was studied 9 ± 10 days after admission to the ICU. Nocturnal sleep architecture has been reported to normalize as time from admission increases; general surgical patients' sleep architecture normalized by the second to third postoperative day[4–6]; the proportions of SWS and REM sleep increased and stage 2 NREM sleep decreased. The same phenomenon was seen in pediatric burn patients,[1] medical ICU patients,[3] and after myocardial infarction.[7] These observations have led to speculation that illness itself may be responsible for disrupted sleep architecture.[1,7] Our study population was recovering from illness (delta APS, −1 ± 6), yet continued to manifest disrupted sleep.

We cannot address the hypothesis that acute illness is responsible for disrupted sleep because our methodology has several limitations. We performed PSG at only one point in the ICU stay; we cannot comment whether sleep architecture and continuity changed as illness severity improved and sedative medication doses were reduced. Serial sleep studies are needed to assess this issue. In regard to other possible sleep-disrupting factors, there was no assessment of the effects of the ICU environment or patient–ventilator interaction on sleep in the current study. Indeed, because we did not collect time-

Table 6—*Intergroup Comparisons

Variable	Disrupted Sleep Group	Atypical and Coma Groups	Difference in Means	95% Confidence Interval of Difference
Age, yr	69 ± 10	57 ± 16	12	−1–+25
ICU day	9 ± 11	10 ± 6	−1	−9–+7
APS	6 ± 4	13 ± 4	−7	−11–−3
Δ APS	−1 ± 6	−2 ± 6	1	−5–+7
GCS	14 ± 3	8 ± 3	6	+3–+9
LIS	1.8 ± 0.6	1.7 ± 1.1	0.1	−0.8–+1.0
Lorazepam dose, μg/kg/h	1.0 ± 1.0	15.2 ± 23.5	−14.2	−31.8–+3.4
Morphine dose, μg/kg/h	8 ± 19	86 ± 140	−78	−184–+28
Haloperidol dose, mg/kg/h	0.1 ± 0.1	0.2 ± 0.5	−0.1	−0.5–+0.3

*Mean ± SD. Data are for the day of 24-h PSG study. Differences in means are disrupted sleep group − atypical and coma group. See footnote of Table 1 for other abbreviations.

synchronized sound and video signals, we are unable to comment on the extent to which the observed sleep fragmentation was a direct consequence of the ICU environment. For example, in one ICU cohort, noise (defined as a sound level increase of 10 dB) was responsible for up to 33% of arousals from sleep.[18] The hypothesis that a reduction in environmental sleep-disrupting factors should improve sleep quality was advanced by Hilton[9] > 20 years ago, but it remains unproved because there has never been a study of the effects of environmental interventions on objectively measured sleep. Results from some studies suggest that the hypothesis might be false, because sleep remained abnormal despite efforts to ensure an optimal environment.[5,11]

An important limitation of our methodology for assessment of sleep in mechanically ventilated patients is the considerable time and resources required to manually score 24-h PSG studies and to comprehensively assess sleep-disrupting factors such as care activities, noise, and the patient–ventilator interaction. These shortcomings should be addressed in future investigations. One approach is the use of computerized neural network processing of PSG data, which has advantages of reproducibility and speed.[40] Another would be to determine whether sleep fragmentation has the fractal characteristics of self-similarity, scaling, and fractal dimension. If sleep fragmentation in critically ill, mechanically ventilated patients has such characteristics, it might be possible to derive conclusions from a smaller subset of PSG data during successive 24-h periods, thereby reducing the resources required for scoring.

In conclusion, we have defined illness-severity guidelines that allow identification of a critically ill population in which sleep (rather than acute brain failure) occurs. We have shown that mechanically ventilated patients have changes in sleep architecture, which are characteristic of acute illness, and that they have severe nocturnal sleep fragmentation sufficient to cause significant impairment of daytime function. Future research should address the cause of these problems by using methodology for comprehensive assessment of sleep-disrupting factors and by examining the dynamic effects of changes in illness severity on sleep quality.

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