Sleep Architecture in Mechanically Ventilated Pediatric ICU Patients Receiving Goal-Directed, Dexmedetomidine- and Opioid-based Sedation

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Abstract

This single-center prospective observational study aimed to evaluate sleep architecture in mechanically ventilated pediatric intensive care unit (PICU) patients receiving protocolized light sedation. We enrolled 18 children, 6 months to 17 years of age, receiving mechanical ventilation and standard, protocolized sedation for acute respiratory failure, and monitored them with 24 hours of limited (10 channels) polysomnogram (PSG). The PSG was scored by a sleep technician and reviewed by a pediatric sleep medicine physician. Sixteen children had adequate PSG data for sleep stage scoring. All received continuous opioid infusions, 15 (94%) received dexmedetomidine, and 7 (44%) received intermittent benzodiazepines. Total sleep time was above the age-matched normal reference range (median 867 vs. 641 minutes, $p = 0.002$), attributable to increased stage N1 and N2 sleep. Diurnal variation was absent, with a median of 47% of sleep occurring during night-time hours. Rapid eye movement (REM) sleep was observed as absent in most patients ($n = 12$, 75%). Sleep was substantially disrupted, with more awakenings per hour than normal for age (median 2.2 vs. 1.1, $p = 0.008$), resulting in a median average sleep period duration (sleep before awakening) of only 25 minutes (interquartile range [IQR]: 14–36) versus normal 72 minutes (IQR: 65–86, $p = 0.001$). Higher ketamine and propofol doses were associated with increased sleep disruption. Children receiving targeted, opioid-, and dexmedetomidine-based sedation to facilitate mechanical ventilation for acute respiratory failure have substantial sleep disruption and abnormal sleep architecture, achieving little to no REM sleep. Dexmedetomidine-based sedation does not ensure quality sleep in this population.

Keywords
- intensive care units
- pediatric
- sleep stages
- polysomnography
- sleep
- rapid eye movement
- dexmedetomidine
- hypnotics and sedatives

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Sleep disruption is common among children receiving sedation and mechanical ventilation for acute respiratory failure in the intensive care unit (ICU).[1] Polysomnogram (PSG)-based studies show that these children have decreased rapid eye movement (REM) sleep, decreased slow-wave sleep (SWS), frequent arousals and awakenings, and loss of circadian cycling (day/night variation).[1] Sleep deprivation has numerous transient and cumulative physiologic effects, including impaired glucose metabolism, growth hormone inhibition, decreased respiratory function (including respiratory muscle fatigue and decreased response to hypercapnia), increased inflammatory cytokine levels, altered immune function, increased sympathetic tone, inattention, decreased cognitive function, and hallucinations.[2] These consequences are especially worrisome in critically ill patients, who are already at risk of muscle wasting, impaired nitrogen balance, delayed ventilator weaning, healthcare-acquired infections, sleep disruption, delirium, and cognitive and psychiatric sequelae following ICU discharge.[2–7] Most ICU nurses and physicians agree that poor sleep is common among critically ill patients and negatively impacts recovery.[8]

Exposure to sedative medications common in the ICU, including propofol,[9] ketamine, opioids, and benzodiazepines, is associated with abnormal sleep architecture, including frequent sleep disruption and decreased or absent SWS and REM sleep.[1,2,10] Dexmedetomidine is an α-2 agonist with sedative properties initially approved for use in the United States in 1999, with pediatric-specific labeling added in 2013. It has been enthusiastically adopted for continuous intravenous sedation in the pediatric ICU (PICU) setting due to its favorable side effect profile, including limited respiratory depression[11] and its association with lower rates of delirium compared with continuous sedation with midazolam in adult ICU trials.[12] In short-term use (up to 6 hours), adults and children receiving dexmedetomidine have electroencephalogram (EEG) tracings indistinguishable from physiologic stage 2 sleep.[13,14] Clinical studies in adults have observed increased total sleep time, improved diurnal variation, and reduced sleep fragmentation with nighttime dexmedetomidine infusion compared with no dexmedetomidine[15,16] and with its use as a continuous sedative or pain treatment.[17,18] These observations have led clinicians to hope that dexmedetomidine-based sedation would facilitate physiologic sleep in PICU patients,[1] but whether it does so during typical clinical use in children receiving sedation and mechanical ventilation is unknown.

We aimed to quantitatively evaluate sleep architecture in children requiring mechanical ventilation for acute respiratory failure receiving standardized, nurse-directed sedation targeted to a light depth using opioids and limited benzodiazepines, with or without dexmedetomidine, and using standard clinical sleep scoring methodology from a limited (10 channels) PSG. We compared quantitative measures of sleep architecture and sleep disruption to published age-matched normative values, hypothesizing that critically ill children would have abnormal sleep architecture and more frequent sleep disruption compared with reference values in healthy children. We also evaluated associations between quantitative measures of sleep architecture and demographic and clinical characteristics and sedation exposures.

Methods

Study Design and Setting

This prospective observational study was performed in the Seattle Children's Hospital PICU. Seattle Children's Hospital is a tertiary academic pediatric hospital with 403 inpatient beds, and pediatric residency and critical care medicine fellowship training programs. Patients receive ICU care beyond the neonatal period in a 32-bed PICU or a separate cardiac ICU. Our PICU employs a nurse-directed sedation protocol originally adopted in 2008.[19] In addition, a multidisciplinary Sedation Committee provides recommendations regarding delirium prevention, which since 2013 have included an analgesia-first approach, limiting benzodiazepines and other deliriogenic medications, and maintaining light sedation whenever possible.[20] Ventilated patients requiring sedation receive opioid infusions with or without dexmedetomidine. Intermittent benzodiazepine doses are given only for agitation that cannot be managed with these medications and nonpharmacologic measures. Delirium screening is performed twice daily at noon and midnight using the Cornell Assessment of Pediatric Delirium (CAPD) tool.[21]

Inclusion criteria were age 6 months to 17 years, within the first 5 days of receiving mechanical ventilation through an endotracheal tube for an acute respiratory indication, and receiving standard sedation guided by the sedation protocol. Exclusion criteria included developmental disability (pediatric cerebral performance category [PCPC][22] ≥ 3), receiving treatment for a diagnosed sleep disorder, acute or historical neurologic injury, lack of an English-speaking parent available for consent, expected to extubate in < 24 hours, sedated with a continuous propofol infusion, not anticipated to survive the current illness, presence of limitation of care orders, concurrently enrolled in another study, or PICU attending refusal. This study was approved by the Seattle Children's Hospital Institutional Review Board, including a waiver of patient assent due to the presence of mechanical ventilation and sedation.

Study Screening, Enrollment, and Data Collection

The PICU patients were screened Monday through Friday during business hours for eligibility. We screened and enrolled patients from March 25, 2016 to October 30, 2019. Eligible patients were reviewed with the primary attending and, if deemed appropriate, approached by the study team. Following written parental consent, enrolled children underwent 24 hours of limited PSG monitoring, including eight EEG leads (F3, F4, C3, C4, O1, O2, M1, and M2), two electrooculographic leads, two chin electromyographic (EMG) leads, and two limb EMG leads (bilateral anterior tibialis). The bedside PSG montage was left off so that providers could not see it. Educational resources regarding the study and the PSG procedure were provided for bedside nursing and respiratory therapy staff on enrollment. We obtained detailed clinical data on enrolled patients from the electronic medical record. Severity of illness

was quantified by Pediatric Risk of Mortality III (PRISM3) score.[23] Depth of sedation was described by daily modal Richmond Agitation Sedation Scale (RASS) scores.[24]

Analysis

PSG data were scored for sleep staging using American Academy of Sleep Medicine (AASM) criteria[25] by a sleep technologist and reviewed by a board-certified pediatric sleep medicine physician (J.W.), who were blinded to the patient's sedative regimen. AASM criteria define arousals as characteristic EEG frequency changes that last for at least 3 seconds after 10 seconds of sleep. Demographics, clinical characteristics, and sleep metrics (total sleep time, nocturnal sleep time, sleep stage times and percentages, sleep period durations, arousal index, and awakening index) are presented using descriptive statistics. Night time sleep metrics were calculated from 9 PM to 7 AM. Age-specific normal values for sleep metrics were abstracted from multiple references,[26–33] using the mean of abstracted values if multiple values were available. If values specific to a patient's age were not available, we abstracted values from the closest age range with available data. These age-specific normative values were compared with individual study results using a paired Wilcoxon's signed-rank test. Univariate analyses to evaluate associations between clinical and sedative exposures and sleep times used Fisher's exact tests for categorical data, Wilcoxon's rank-sum tests for comparisons of continuous data by categorical exposures, and Pearson correlation coefficient or linear regression for continuous exposures. We used Stata SE 14.2 (StataCorp LP, College Station, Texas, United States) for all analyses and considered a two-sided p-value of <0.05 as significant.

Results

The majority of patients meeting inclusion criteria ($n = 353$) were excluded ($n = 295$, 84%), primarily due to acute or historical neurologic injury (43%; ►**Fig. 1**). Additional common reasons for exclusion included not having an English-speaking parent available (13%), intubation for a nonrespiratory indication (11%), and anticipation of extubation within 24 hours (11%). Of 58 eligible patients, 40 (69%) did not participate, most often because parents declined approach by study staff or declined participation ($n = 33$, 83%; usually citing either that the study offered no potential for direct benefit or concern for discomfort during EEG lead placement). We enrolled 18 patients who completed the 24-hour PSG. In total, 16 of the 18 patients (89%) had scorable PSG data. One patient had a history of stable, chronic liver disease, and presented with respiratory failure due to septic shock. She did not have clinically apparent encephalopathy, but her PSG could not be scored for sleep stages due to features suggestive of hepatic encephalopathy. One additional recording could not be retrieved due to technical issues.

Among 16 patients with usable PSG data, the median age was 2.5 years, and 50% had medical comorbidity (►**Table 1**). The majority were receiving acute mechanical ventilation for respiratory failure due to bronchiolitis or viral pneumonia

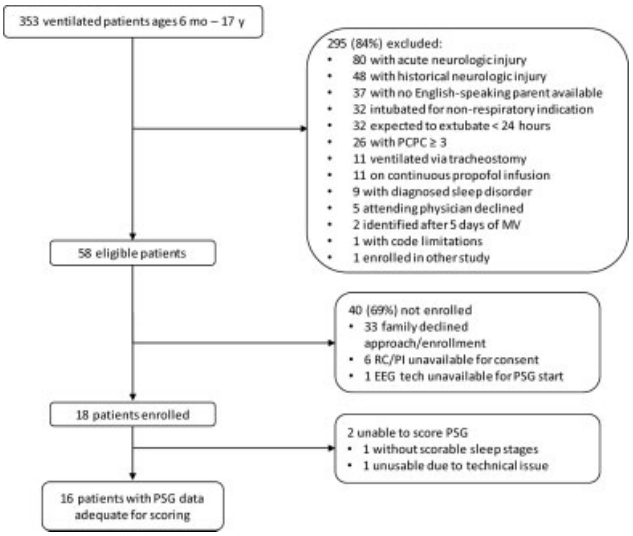

Fig. 1 Study participant enrollment flow diagram. EEG, electroencephalogram; MV, mechanical ventilation; PCPC, pediatric cerebral performance category; PSG, polysomnogram; RC/PI, research coordinator or primary investigator.

(56%), followed by bacterial pneumonia (25%). The majority were supported using a spontaneous mode of ventilation on the study day (pressure support, $n = 11$, 69%). For sedation on the study day, all received a continuous opioid infusion, 15 (94%) received a continuous dexmedetomidine infusion, and 7 (44%) received intermittent benzodiazepines. Few patients received adjunctive sedation with intermittent doses of propofol ($n = 3$) or ketamine ($n = 2$), and few received intermittent pharmacologic paralysis ($n = 3$). Depth of sedation was generally light, with a median daily modal RASS score of -1 ("drowsy"; interquartile range [IQR]: -2 to -1, range $= -3$ to $+2$) during the 24-hour PSG monitoring. No patients received melatonin or antipsychotic medications; one patient received a norepinephrine infusion and seven (44%) received steroids. Most patients had at least one positive delirium screening score (CAPD $\geq$ 9, 81%) during the 24-hour PSG. Patients were enrolled early in their ICU stay on a median of one day following ICU admission (IQR: 1–2).

Sample hypnograms from the enrolled patients are displayed in ►**Fig. 2**. Qualitatively, sleep was highly fragmented for nearly all study patients, without recognizable circadian variation. Quantitatively, total sleep time over the 24-hour study period was nearly equally distributed between day and night periods, with a median of 47% (IQR: 41–59%) of total sleep time occurring at night. Patients spent limited time in REM stage sleep (►**Fig. 3**; ►**Table 2**), and 12 patients (75%) achieved no REM sleep. One patient (6%) achieved no SWS, while three patients had individual periods of SWS lasting for 2 hours or more. Compared with normal parameters for sleep in age-matched peers, study patients had increased total sleep time and increased time in stage N1 and stage N2 sleep, with comparable duration of SWS but fewer minutes of REM sleep over the 24-hour study (►**Fig. 3**; ►**Table 2**). They had shorter sleep period

Table 1 Demographic and clinical characteristics of study patients

	n (%) or median (IQR) *n* = 16
Female	9 (56%)
Age, y	2.5 (1.1–11.5)
Race	
Black/African American	1 (6%)
White/Caucasian	10 (63%)
Other	4 (25%)
Declined to answer	1 (6%)
Ethnicity	
Hispanic	2 (13%)
Non-Hispanic	13 (81%)
Declined to answer	1 (6%)
Baseline PCPC	
1 (normal)	14 (88%)
2 (mild disability)	2 (13%)
Medical comorbidity[a]	8 (50%)
Primary admission diagnosis	
Bronchiolitis/viral pneumonia	9 (56%)
Bacterial pneumonia	4 (25%)
Airway abnormality (abscess, tonsilitis, and foreign body aspiration)	2 (13%)
Sepsis-associated PARDS	1 (6%)
Admission PRISM score	3 (0–12)
Unscheduled admission	12 (75%)
Ventilation mode[b]	
Synchronized intermittent mandatory ventilation	5 (31%)
Pressure support ventilation	11 (69%)
Sedative exposure[b]	
Opioids, any	16 (100%)
Opioids, mg/kg/day	1.9 (1.2–3.6)
Dexmedetomidine, any	15 (94%)
Dexmedetomidine, mcg/kg/day	11.9 (9.2–19.5)
Benzodiazepines, any	7 (44%)
Benzodiazepines, mg/kg/day	0 (0–0.2)
Depth of sedation (mode RASS[b])	−1 (−2 to −1)
Delirium[b,c]	13 (81%)
ICU length of stay, d	8.8 (5.3–10.8)

Abbreviations: ICU, intensive care unit; IQR, interquartile ratio; PARDS, pediatric acute respiratory distress syndrome; PCPC, pediatric cerebral performance category; PRISM, pediatric risk of mortality score; PSG, polysomnogram; RASS, Richmond Agitation Sedation Scale.

[a]Including osteogenesis imperfecta, acute myelogenous leukemia, Pompe disease, esophageal atresia, craniofacial syndromes, aplastic anemia, and bronchopulmonary dysplasia.

[b]During the 24-hour PSG study period.

[c]Positive delirium screening based on having any Cornell Assessment of Pediatric Delirium score ≥9 during the PSG study period. The screening score is performed on all ICU patients every 12 hours as standard of care.

durations (median 25 vs. 72 minutes, $p = 0.001$) and more awakenings per hour. Median arousal index was lower for study patients compared with age-matched normal values, in contrast to the other measures of sleep fragmentation, although this difference did not reach statistical significance.

Gender, age, race, ethnicity, unscheduled admission, admission diagnosis, and mode of ventilation were not associated with any of the sleep parameters studied in univariate analysis. Presence of delirium on the study day was associated with longer cumulative duration of SWS (median 285 minutes among those with delirium vs. 26 minutes among those without; $p = 0.009$). Patients with PCPC = 2 (mild cognitive dysfunction) had a lower number of arousals per hour of sleep time (arousal index) compared with those with normal baseline cognitive status (median 1.3/hour vs. 5.3/hour, $p = 0.026$). Increasing severity of illness was also associated with lower arousal index (average decrease of 0.4 per increase in PRISM3 score by 1, $p = 0.02$) and a longer average sleep period duration (mean 2.4 additional minutes per increase in PRISM3 score by 1, $p = 0.016$.) Total sleep time and minutes and proportion of REM sleep were not associated with any clinical or demographic measures studied.

Certain sleep parameters were associated with other sleep parameters. Minutes of REM sleep during the 24-h PSG were higher among patients with more awake time and lower among patients with longer total sleep time (►**Table 3**). The three patients who achieved any REM sleep had lower median total sleep time than those not achieving any REM sleep (669 vs. 1201 minutes, $p = 0.05$). This was illustrated by a 5-year-old patient who achieved the most REM sleep (►**Fig. 2**, panel C), who also remained awake during the entire daytime period. Minutes of SWS during the 24-h PSG were increased among those with longer total sleep time and decreased among those with more frequent awakenings.

Sedation exposures were associated with certain sleep parameters. Patients with higher exposure to dexmedetomidine had fewer minutes in REM sleep during the 24-h PSG, although this difference was not statistically significant (R-squared = 0.19, $p = 0.09$). This difference was illustrated by the 5-year-old patient achieving the most REM sleep (►**Fig. 2**, panel C), who also received the least amount of sedative medications during the PSG, including no benzodiazepines, no dexmedetomidine, and the lowest dose of opioid among the study cohort at 0.4 mg/kg/day. Patients with longer duration of SWS during the 24-hour PSG study period than expected for age ($n = 9$, 56%) had higher median dexmedetomidine exposure (16.5 vs. 9.5 mcg/kg/day, $p = 0.023$), but had no differences in other sedative exposures. Total duration of SWS was also associated with depth of sedation, with an average of 184 additional minutes in stage N3 sleep for each decrease in modal RASS by 1 (R-squared = 0.25, $p = 0.049$). Ketamine exposure was associated with increased time in light sleep and with increased awakening index, and propofol exposure was associated with increased arousal index (►**Table 3**). Opioid, benzodiazepine, diphenhydramine, and paralytic agent exposures were not associated with any sleep parameters.

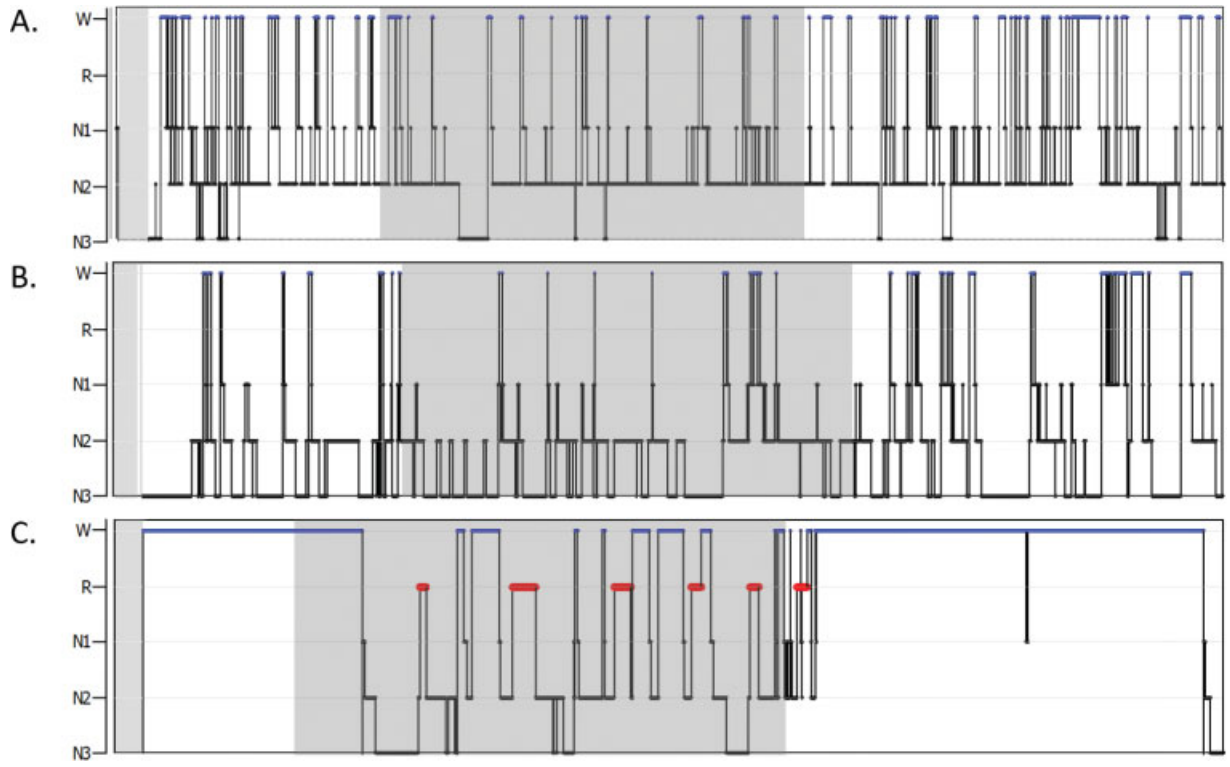

Fig. 2 Sample hypnograms from three mechanically ventilated pediatric intensive care unit patients receiving protocolized sedation including opioids with or without dexmedetomidine, targeted to a light depth of sedation. Patient details. (**A**) An 8-year-old male, with retropharyngeal abscess and shock in the setting of aplastic anemia. Ventilated in PS mode, received 1.2 mg/kg morphine equivalents, 12.9 mcg/kg dexmedetomidine, propofol and ketamine on the study day, achieving modal RASS −2 ("light sedation"). (**B**) An 8-month-old female, with *Haemophilus influenzae* pneumonia in the setting of respiratory syncytial virus bronchiolitis. Ventilated in PS mode, received 1.2 mg/kg morphine equivalents and 10.1 mcg/kg dexmedetomidine on the study day, achieving modal RASS −2 ("light sedation"). (**C**) A 5-year-old female with rhinoviral/enteroviral viral pneumonia and Pompe disease. Ventilated in PS mode, received 0.3 mg/kg morphine equivalents on the study day, achieving modal RASS −1 ("drowsy"). Shaded box = nighttime (9 PM–7 AM). N1, stage 1 (light) sleep; N2, stage 2 (light) sleep; N3, stage 3 (deep) sleep, or slow wave sleep; PS, pressure support; R, rapid eye movement sleep; RASS, Richmond Agitation Sedation Scale; W, wake.

Discussion

Pediatric patients receiving sedation to facilitate mechanical ventilation for acute respiratory failure, targeted to a light level of sedation using opioids with or without dexmedetomidine, have substantially disrupted sleep. Their sleep was predominantly light (stage N1 and stage N2), and few patients achieved REM sleep during the study period. While some patients failed to achieve any SWS, others had abnormally prolonged periods of SWS. Sleep periods were generally short, with frequent arousals and awakenings. Diurnal variation in sleep pattern (circadian rhythm) was absent.

Prior studies evaluating sleep architecture in sedated, mechanically ventilated pediatric patients using PSG involved no patients treated with dexmedetomidine and were conducted when a deeper level of sedation was more commonly targeted.[1] In our study, children achieved an average light level of sedation using dexmedetomidine, opioids, and limited benzodiazepines, and demonstrated increased total sleep time, increased stage N1 and N2 sleep, extremely fragmented sleep with abnormal sleep architecture, and REM deprivation. These observations are consistent with EEG findings in healthy individuals receiving dexmedetomidine, which are indistinguishable from N2 sleep.[13,14] Our observations are also consistent with PSG studies in critically ill adults receiving dexmedetomidine, who demonstrate increased N1 and N2 sleep but with very little to no REM sleep and SWS,[15,16] with the exception of a single study that observed increased SWS in nonventilated critically ill adults receiving dexmedetomidine.[18] Animal model data demonstrate that dexmedetomidine suppresses REM sleep, followed by rebound increases in REM and NREM sleep after discontinuation.[34] While dexmedetomidine may promote light (stage N1 and N2) sleep, critically ill patients receiving dexmedetomidine still experience highly fragmented sleep and REM deprivation.

Patients in our study did achieve more SWS compared with prior PICU sleep studies, with a median of 26% of total sleep time spent in stage N3 versus 0 to 8%.[35,36] Increasing SWS duration was associated with deeper levels of sedation by RASS score, and patients with abnormally long periods of SWS had higher average dexmedetomidine exposure, suggesting an association with sedation. However, increased duration of SWS was also associated with increased sleep fragmentation. The few patients in our study who achieved REM sleep had lower total sleep time than those who did not, suggesting that increased daytime wakefulness may preserve circadian signaling, resulting in less REM suppression. These observations indicate that longer total sleep time in the sedated, critically ill

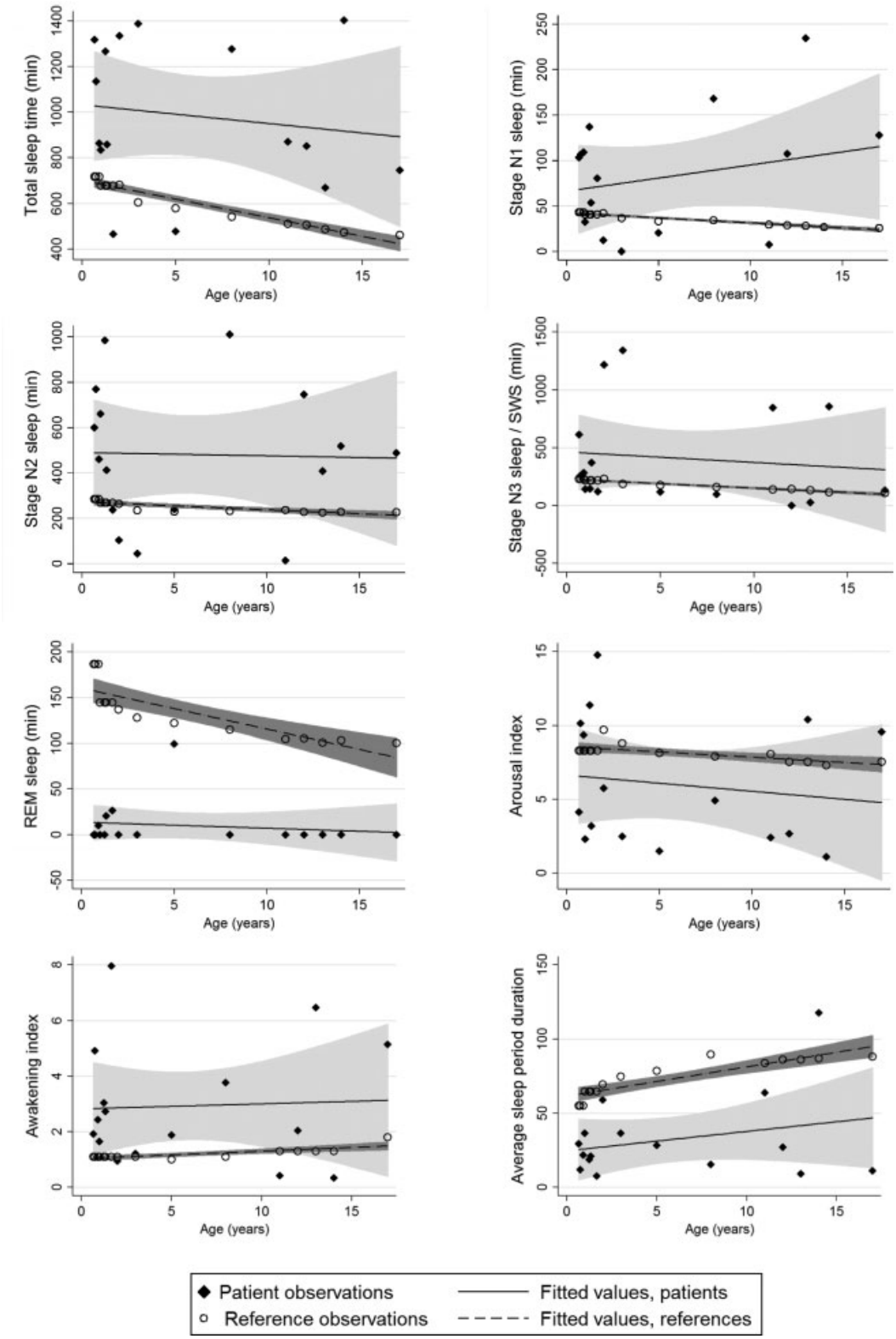

Fig. 3 Observed sleep characteristics by age over 24 hours for study patients compared with age-matched normative values. Fitted values from linear regression. Shaded areas represent 95% confidence intervals. Average sleep period duration is presented in minutes. Arousal and awakening index = number events per hour of sleep time. Min, minutes; REM, rapid eye movement; SWS; slow wave sleep.

patient may counterintuitively be associated with more abnormal sleep architecture and poor sleep quality.

Many additional factors contribute to fragmented, poor quality sleep in the ICU population. For ventilated patients, ventilator dyssynchrony, inadequate ventilation, and central apneas are all associated with sleep fragmentation.[37] Lack of exposure to daylight, exposure to artificial light during nighttime hours, noise, frequent hands-on assessments,

Table 2 Polysomnogram results. Sleep characteristics and sleep staging over 24 hours for 16 pediatric patients requiring sedation and mechanical ventilation for acute respiratory failure

Measure[a]	Median (IQR)	Reference range[b]	*p*-Value[c]
TST	867 (790–1297)	641 (508–679)	0.002
Night time sleep time	438 (413–578)	548 (481–579)	0.07
% of TST	47 (41–59)	89 (85–95)	0.0004
Stage N1 sleep	92 (24–119)	39 (29–41)	0.02
% of TST	9 (3–13)	6 (6–6)	0.1
Stage N2 sleep	474 (238–702)	250 (228–268)	0.02
% of TST	52 (41–73)	40 (40–46)	0.2
Slow wave sleep (stage N3)	202 (122–731)	200 (139–223)	0.3
% of TST	26 (14–54)	31 (28–32)	0.8
Rapid eye movement (stage REM)	0 (0–5)	132 (105–144)	0.0004
% of TST	0 (0–1)	21 (21–22)	0.0004
Arousal index	4.5 (2.5–9.9)	8.3 (7.7–8.3)	0.06
Awakening index	2.2 (1.4–4.3)	1.1 (1.1–1.3)	0.008
Sleep period duration	25 (14–36)	72 (65–86)	0.001

Abbreviations: IQR, interquartile range; REM, rapid eye movement; TST, total sleep time.
[a]All sleep measurements in minutes unless otherwise indicated.
[b]Published reference ranges vary and are specific to age, sex, and developmental stages. Median (IQR) ranges presented are specific to the ages of the patients enrolled in this study, based on published reference data.[26–33]
[c]Comparing each patient's result to age-matched norms[26–33] using a paired Wilcoxon's signed-rank test.

Table 3 Univariate associations of sleep parameters and sedation exposures

Sleep parameter[a]	Associated with sleep parameter[a]	Average change if associated parameter increases by 1[b]	R-squared	*p*-Value[b]
REM	TST	−0.04	0.38	0.02
N3	TST	0.8	0.32	0.01
N3	N1	−4	0.44	0.005
N3	N2	−0.8	0.37	0.013
N3	Awakening index	−8.4	0.01	0.038
Awakening index	Arousal index	0.3	0.69	0.002
Sleep parameter[a]	Associated with sedation exposure[a]	Average sleep parameter change if sedation exposure increases by 1[b]	R-squared	*p*-Value[b]
N3	Modal RASS score	−184	0.25	0.049
N2	Ketamine	117	0.27	0.04
Arousal index	Propofol	10.6	0.06	0.035
Awakening index	Ketamine	12.7	0.06	0.007

Abbreviations: N1, stage 1 sleep; N2, stage 2 sleep; N3, stage 3 (deep) sleep, or slow wave sleep; RASS, Richmond Agitation Sedation Scale; REM, rapid eye movement; TST, total sleep time.
[a]Sleep stages presented in minutes. Arousal and awakening indices equal the number of events per hour of total sleep time. Sedation exposures analyzed in mg/kg/day.
[b]Coefficients and *p*-values presented from linear regression, except where otherwise indicated.

nighttime enteral feeding, neurologic dysfunction, and common ICU medications including vasoactive agents all further disrupt circadian rhythms.[38,39] Unfortunately, trying to restore circadian rhythm with melatonin or melatonin receptor agonists has not been clearly effective.[40] No studies have evaluated the effect of melatonin in adult or pediatric ICU patients on sleep architecture or fragmentation by PSG, although at least two such studies have been planned in critically ill adults.[41]

Most of the patients in this study had screening scores consistent with delirium. These patients had longer SWS than those without delirium, and the duration of SWS was in turn associated with the depth of sedation, suggesting that SWS in these patients may have been a feature of sedation instead of a

feature of physiologic sleep. Delirium frequently coexists with abnormal sleep in ICU patients. The neuropsychiatric effects of sleep deprivation can mimic features of delirium; however, it is unclear to what extent sleep deprivation might influence the development of delirium.[42] Rigorous and longitudinal studies are needed to develop a better understanding of the relationship between sleep and ICU delirium and to identify effective interventions for improving both.

We struggled with a low rate of enrollment despite thorough screening and multidisciplinary support for the study among ICU staff, primarily due to a high rate of exclusions for acute or historical neurologic injury. Among the relatively few eligible patients, parents/caregivers frequently declined participation, citing concern for patient discomfort during the PSG setup. Unfortunately, sleep architecture is difficult to study without PSG, particularly in sedated patients. Clinical sleep scoring does not correlate with PSG findings.[43] In critically ill adults, actigraphy overestimates total sleep time and underestimates sleep fragmentation.[44] Algorithmic EEG-based monitors, such as the Bispectral Index, also have poor correlation to actigraphy and patient assessments of sleep[45] and poor capability to distinguish wakefulness, light sleep, and REM sleep when compared with PSG.[46] Novel methods of evaluating sleep in critically ill patients, such as in a recent study evaluating circadian rhythm and loss of normal spectral frequency bands during sleep in critically ill children,[47] will need to be developed to support future sleep research in the ICU setting.

This study has important limitations. In addition to small sample size, we observed only one 24-hour period per patient early in the ICU stay, which precludes any evaluation of how sleep might change over the ICU stay. This period of observation may not be generalizable to other phases of ICU care, such as weaning and convalescence. While 24 hours has been the most common period of time evaluated for PSG-based studies in ICU patients, permitting evaluation of both day and nighttime sleep in patients who lack circadian rhythm; this time frame reduces the ability to identify which exposures precede disrupted sleep and which may be a consequence of it. At the time of this study, our ICU had not established a formal sleep hygiene protocol, so patient care, noise, and light disruptions may not have been rigorously minimized. We excluded patients with acute or prior neurologic injury and moderate or worse cognitive dysfunction, given the potential difficulties in applying sleep scoring criteria to these patients and the likelihood that they experience abnormal sleep at baseline; however, these patients are also at risk of sleep deprivation and its effects.

Conclusion

Mechanically ventilated, critically ill children receiving sedation targeted to a light depth have substantially fragmented sleep with limited to no REM sleep and highly variable SWS, despite common use of dexmedetomidine. As we observed very few associations between sedation exposures and sleep parameters, it remains unclear whether any specific approach to sedation management optimizes sleep, although daytime wakefulness was associated with increased REM sleep. Due to technical challenges and cost, little research has evaluated the effectiveness of various interventions on sleep architecture and fragmentation in the context of pediatric critical illness, sedation, and mechanical ventilation. Technical advancements in this field are needed to support more rigorous evaluation of clinical outcomes related to sleep disruption and of potential interventions to improve sleep in critically ill patients.

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Conflict of Interest
None declared.

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