Disrupted sleep patterns and atypical electroencephalograms in children admitted to the pediatric intensive care unit: an observational cohort study

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Abstract

Purpose: To describe sleep (disruptions) in critically ill and non-critically ill hospitalized children, by comparing sleep parameters to reference ranges of healthy children.
Methods: Observational cohort study in a tertiary, university children's hospital. Twenty-five critically ill children with expected PICU stay ≥ 48 hours who underwent 24-hour polysomnography (PSG) and 120 non-critically ill children who underwent diagnostic PSG between May 2017 and June 2021 for suspected sleep disordered breathing (SDB) were included. In both groups, nighttime sleep parameters were determined and compared to age-specific reference ranges obtained from literature.

Results: Among critically ill children, comparison to reference ranges showed reduced rapid-eye-movement (REM) sleep (24, 96%) and, in those with discernable non-REM stages, reduced non-REM 3 sleep (4 of 6, 67%). Median nighttime sleep accounted for 50.9% (interquartile range (IQR) 49.5–55.5) of total 24-hour sleep. Moreover, EEG abnormalities were prominent (19, 76%), including abundant slow-wave activity (9, 36%), lacking sleep spindles (6, 24%) and/or K-complexes (2, 8%) and abnormal background EEG with persistent theta and delta activity (2, 8%). In non-critically ill children with suspected SDB, comparison to reference ranges showed reductions in REM sleep (age ≤ 6 months), reduced mean sleep period duration (age ≥ 1 year), and low sleep efficiency and high awakening index in older children.
Conclusions: Critically ill children exhibit disrupted sleep architecture, loss of day-night variation and atypical EEG. Non-critically ill children mainly exhibit fragmented and reduced sleep. These findings foster better understanding of how critical illness and the hospital environment affect sleep in children.

What is Known – What is New

- Sleep in the PICU is frequently disrupted, but detailed PSG data in critically ill children are limited, often exclude young infants and patients with CNS injury, and lack EEG assessment.
- This study compares sleep parameters of critically ill and non-critically ill hospitalized children to reference ranges of healthy controls.
- Critically ill children show reduced REM and N3 sleep, sleep fragmentation, loss of day-night variation and EEG abnormalities.

Introduction

Sleep may play a pivotal role in recovery from illness, considering its essential roles in tissue repair, immune function, cognitive function, pain management and hormonal regulation.[1–3] However, critically ill children admitted to the pediatric intensive care unit (PICU) are at risk of disrupted and even abnormal sleep due to pathological, environmental and pharmacological factors.[4–6] While these children may frequently exhibit the behavioural state of sleep on account of continuous sedation, this apparent sleep may restorative qualities.[7] Unfortunately, detailed understanding of what sleep during critical illness and sedation in a hospital environment entails in children is currently lacking.[7, 8]

Only five studies have described sleep in the PICU using gold standard overnight polysomnography (PSG) testing, reporting sleep fragmentation, reduced rapid-eye-movement (REM) sleep and a loss of circadian rhythm.[9–13] However, these studies typically excluded infants under three months of age and children with central

nervous system (CNS) injuries, who comprise a substantial portion of PICU admissions. Such exclusions may be motivated by the difficulty of sleep scoring in the presence of atypical electroencephalogram (EEG) patterns, although none of the studies reported on this.[14–16] Previously published automated sleep scoring algorithms using EEG also performed poorly in critically ill children as compared to non-critically ill children, suggesting fundamental differences in sleep and EEG patterns.[17–19] Relative contributions of critical illness, sedation and the hospital environment to these differences are yet to be disentangled.

The present study describes sleep (disruptions) in critically ill children, including young infants and patients with CNS injury, and in non-critically ill hospitalized children, by comparing parameters of sleep quality and quantity with age-specific reference ranges. Underlying EEG patterns are assessed for atypical features to determine sleep scoring feasibility. The findings provide insight into how critical illness and the hospital environment may contribute to sleep disruptions.

Methods

Study design

Observational cohort study conducted at Erasmus MC Sophia Children's Hospital, Rotterdam, The Netherlands in accordance with the 1975 Helsinki Declaration and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[20] Two populations were studied: critically ill children and non-critically ill children with suspected sleep disordered breathing (SDB), hereafter referred to as PICU and SDB group, respectively. Sleep measurements in the PICU group were obtained during two clinical studies: the Critical Clock study (Netherlands Trial Register (NTR): NL8533) investigating circadian rhythm; and the ContInNuPIC study (NTR NL7877) investigating intermittent feeding with overnight fasting. Both studies were approved by the appropriate review committees (NL72302.000.19, "ContInNuPIC", 2020; NL72597.078.20, "Critical Clock", 2020). Written informed consent was obtained from patients and/or parents or legal guardians. Separate consent was obtained for PSG. In the SDB group, sleep measurements were obtained from a retrospective database, with consent waived by the Erasmus MC Medical Ethics Committee (MEC-2021-0121, "Sleep studies", 2021).

Study population

PICU group

In the PICU group, eligible patients were critically ill children (aged term to 18 years) admitted to the PICU with expected stay ≥ 48 hours. Exclusion criteria for ContInNuPIC mainly concerned contra-indications for prolonged fasting.[21] Exclusion criteria for Critical Clock were the diagnosis of a syndrome associated with severe mental retardation (trisomy 21 was not an exclusion criterion), hydrocortisone use in the three days prior to admission, melatonin use within 24 hours prior to admission, weight < 2.0 kg and patients expected not to receive an arterial line. The criteria were intended to exclude pre-existent circadian rhythm disruptions and to minimize the burden of blood sampling. Both studies also excluded patients transferred from another PICU, patients participating in trials with conflicting study procedures and previously included patients. In addition to sleep measurements, medical records were screened for the following: age, gender, private room or ward, diagnosis upon admission, Pediatric Index of Mortality 3 (PIM3) score, Pediatric Logistic Organ Dysfunction 2 (PELOD-2) score from the day of PSG, CNS injury, sedative and norepinephrine dosage during the PSG (cumulative dose from noon to noon),

ventilator support and duration of PICU stay. Duration of mechanical ventilation and PICU stay were counted from the day of PSG and censored on study day 31 as this was the follow-up limit. Duration of PICU stay was only counted when patients required critical care, i.e. not when they were awaiting transfer. Death was treated as a competing risk factor and also censored on day 31.

SDB group

In the SDB group, sleep measurements were obtained from non-critically ill children who underwent PSG for diagnostic purposes between May 2017 and June 2021. Age categories were established: 0–2 months, 2–6 months, 6–12 months, 1–2 years, 3–4 years, 5–8 years, 9–12 years and 13–18 years.[22] Fifteen recordings of distinct patients were randomly collected per age category (120 in total). If patients had undergone multiple PSGs, the last one was used. In addition, medical records were screened for age, gender, PSG indication and possible diagnosis of epilepsy or neurocognitive impairment.

Sleep measurement

All PSGs were recorded at 250 or 256 Hz (Brain RT, OSG, Rumst, Belgium or Morpheus, Micromed S.p.A., Treviso, Italy) and scored conform the American Academy of Sleep Medicine (AASM) criteria.[23] In the PICU group, patients underwent sleep measurement with 24-hour PSG using optional EEG derivations.[23] Sleep scoring was performed by a European Sleep Research Society certified and experienced sleep technologist (KB) and reviewed by a clinical neurophysiologist (DS). Both were blinded to subject characteristics other than age and gender. In the SDB group, sleep measurements were conducted with recommended EEG derivations in a high or medium care unit.[23] Scoring was performed by sleep technicians under supervision of a clinical neurophysiologist. All sleep was scored into REM and non-REM (NREM) stages 1–3 (N1-3). The transitional sleep stage for young infants (age < 2 months) is not used in our center. Epochs meeting criteria for transitional sleep were instead scored as NREM sleep. If abnormalities affected EEG features used for sleep scoring, scoring was based on remaining features. Not scoring or scoring epochs as unclassified NREM sleep (N) was minimized. Scored sleep measurements were extracted for analysis from RT Software Suite v4.05.00.

Sleep characteristics

Parameters of sleep quality and quantity were derived from scored PSGs. Total sleep time (TST) was calculated for the entire recording in the SDB group and for both the entire recording and for nighttime in the PICU group. Other parameters were calculated for nighttime only for maximal comparability to reference ranges. Nighttime was defined as 21:00 to 07:00 for the PICU group, and as mean PSG start time until mean PSG end time for the SDB group. Sleep parameters included the proportion of sleep stages for REM, NREM, N1, N2 and N3 relative to nighttime TST; sleep proportion (nighttime TST as a proportion of TST in entire recording, corrected for daytime and nighttime measurement duration); sleep period (continuous sleep between two wake epochs); sleep period duration (time from first to last sleep epoch), awakening index (number of awakenings per hour of TST of entire recording) and sleep efficiency (nighttime TST as a proportion of sleep period duration).

Reference ranges of sleep parameters were obtained from studies with PSG-based sleep measurement, as detailed in Supplemental Methods A.[24–27]

Statistical analysis

Descriptive statistics were reported as count (percentage) and mean (standard deviation (SD)) or median (first quartile, third quartile (Q1-Q3)). The primary outcome was the deviation from normal sleep during critical illness, assessed by comparing the PICU group to reference ranges.[24–27] The secondary outcome was deviation from normal sleep in the SDB population, assessed by comparison of mean (SD) sleep parameters per age group to the reference ranges. Sleep parameter values were considered abnormal when exceeding the mean with 2 SD, the 5th to 95th percentile or the range, whichever was reported. Nighttime sleep proportion ≥ 50% of total sleep signified no day-night variation. Analyses were conducted in python (version 3.11) and R (version 4.3.0), with packages listed in Supplemental Methods B.

Results

Study population

Between May 2020 and July 2022, 140 and 25 PICU patients were included in the ContInNuPIC and Critical Clock study respectively. Sleep measurements were feasible in 34 patients and ultimately 25 measurements conducted in distinct patients were included (Supplemental Figure S1). Characteristics of the PICU and SDB group are reported in Table 1. In the PICU group, age varied between 3 days and 17 years, with median 3.6 (1.0, 20.4) months. Six patients (24.0%) had CNS injury and five (20.0%) encephalopathy. Most PICU patients received sedative medication, primarily midazolam (16, 64.0%) and various opioids (18, 72.0%). In the SDB group, characteristics varied across age categories (Table 2). In total, 35 children (29.2%) had neurocognitive impairment and eight (6.7%) had a history of epilepsy. PSG was mainly indicated for suspected airway obstruction (62, 51.7%). Fifteen children (12.5%) were already asleep when PSG recordings started. Twelve (10.0%) children had obstructive sleep apnea (OSA) during PSG, of which five severe, three moderate and four mild.

Table 1
Patient characteristics of the PICU and SDB group

Characteristic	PICU group		SDB group
Sample size	25		120
Female gender	13 (52.0%)		59 (49.2%)
Age (months)	3.6 (1.0, 20.4)		36.7 (6.1–107.7)
Indication of PICU admission/PSG recording			N/A
Cardiac/cardiothoracic surgery	8 (32.0%)		0 (0.0%)
Abdominal surgery	1 (4.0%)		0 (0.0%)
Respiratory/pulmonary	7 (28.0%)		11 (9.2%)
Infectious	4 (16.0%)		0 (0.0%)
Neurological/neuromuscular	3 (12.0%)		16 (13.3%)
Metabolic	1 (4.0%)		0 (0.0%)
Oncological	1 (4.0%)		0 (0.0%)
Airway obstruction	0 (0.0%)		62 (51.7%)
Central sleep apnea	0 (0.0%)		15 (12.5)
Day of sleep measurement	3 (2, 7)		N/A
Type of room (multi-patient ward)	17 (68.0%)		7 (5.0%)
Study group			
ContInNuPIC: intervention (nighttime fasting)	7 (28.0%)		N/A
ContInNuPIC: control (day and night feeding)	14 (56.0%)		N/A
Critical Clock	4 (16.0%)		N/A
PIM3 score	-3.57 (-4.45, -1.87)		N/A
PIM3 mortality risk	0.03 (0.01, 0.13)		N/A
PELOD-2 score	7 (6, 9)		N/A
Mechanical ventilation during measurement (including non-invasive BiPAP)	20 (80.0%)		N/A
Sedative use[3]	n	Dose	
Esketamine (mg/kg/day)	7	6.05 (4.03, 9.80)	N/A
Fentanyl (µg/kg/day)	2	(3.85, 4.22)	N/A

Data are presented as n (%) or median (Q, Q3) where applicable (N/A indicates not applicable). BiPAP = Bilevel Positive Airway Pressure; CNS = central nervous system; PELOD = Paediatric Logistic Organ Dysfunction; PICU = pediatric intensive care unit; PIM3 = Paediatric Index of Mortality 3.

Characteristic	PICU group		SDB group
Midazolam (µg/kg/day)	16	3.53 (2.33, 4.57)	N/A
Morphine (µg/kg/day)	14	229 (137, 242)	N/A
Propofol (mg/kg/day)	1	2,97	N/A
Remifentanil (µg/kg/day)	4	167 (108, 223)	N/A
Norepinephrine[3] (mg/kg/day)	4	3.80 (2.01, 223)	N/A
Length of PICU stay (days)	12.5 (5, 26.25)		N/A

Data are presented as n (%) or median (Q, Q3) where applicable (N/A indicates not applicable). BiPAP = Bilevel Positive Airway Pressure; CNS = central nervous system; PELOD = Paediatric Logistic Organ Dysfunction; PICU = pediatric intensive care unit; PIM3 = Paediatric Index of Mortality 3.

Table 2
Demographic characteristics of the control group

Age category	Neurocognitive impairment	History of epilepsy	PSG indication				OSA
			Airway obstruction	Neuromuscular disease	Pulmonary disease	Central sleep apnea	
0–2 months	5 (33.3%)	2 (13.3%)	10 (66.7%)	4 (26.7%)	0 (0.0%)	4 (26.7%)	2 (13.3%)
2–6 months	8 (53.3%)	1 (6.7%)	5 (33.3%)	3 (20.0%)	2 (13.3%)	4 (26.7%)	2 (13.3%)
6–12 months	3 (20.0%)	0 (0.0%)	4 (26.7%)	1 (6.7%)	5 (33.3%)	2 (13.3%)	1 (6.7%)
1–3 years	4 (26.7%)	0 (0.0%)	12 (80.0%)	3 (20.0%)	1 (6.7%)	1 (6.7%)	3 (20.0%)
3–5 years	3 (20.0%)	3 (20.0%)	12 (80.0%)	1 (6.7%)	0 (0.0%)	1 (6.7%)	1 (6.7%)
5–9 years	6 (40.0%)	1 (6.7%)	9 (60.0%)	2 (13.3%)	0 (0.0%)	0 (0.0%)	2 (13.3%)
9–13 years	3 (20.0%)	1 (6.7%)	4 (26.7%)	0 (0.0%)	2 (13.3%)	1 (6.7%)	0 (0.0%)
13–18 years	3 (20.0%)	0 (0.0%)	6 (40.0%)	2 (13.3%)	1 (6.7%)	2 (13.3%)	1 (6.7%)
Total	35 (29.2%)	8 (6.7%)	62 (51.7%)	16 (13.3%)	11 (9.2%)	15 (12.5%)	12 (10%)

Data are presented as n (%). Note that there are 15 children per age category and 120 children in total. PSG = polysomnography; OSA = obstructive sleep apnea.

Sleep characteristics in critically ill children

Results of primary analysis showed deviations from normal sleep during critical illness (Table 3 and Supplemental Table S2). Nighttime TST appeared normal, with only four (16.0%) children sleeping less, but day-night variation was absent as median nighttime sleep was only 50.9% (49.5, 55.5) of 24-hour TST. This led to high TST over 24 hours. REM sleep was considerable reduced in nearly all (24, 96.0%) patients and occasionally (6, 24.0%) absent, while NREM sleep was increased (20, 80.0%). In nine patients where NREM stages were discernable we observed more N1 (5 of 9, 55.6%) and N2 (4 of 9, 44.4%) but less N3 sleep (6 of 9, 66.7%). Reduced N3 sleep was prominent in patient with CNS injury (3 of 6, 50.0%), alongside reduced REM (6 of 6, 100.0%) and increased NREM or N1 and N2 sleep (4 of 6, 66.7%). In young infants up to one month, similar patterns in REM and NREM sleep were observed, with normal (4 of 6, 66.7%) to high (2 of 6, 33.3%) sleep efficiency. In patients older than one month, sleep efficiency was mainly reduced (10 of 19, 53.0%).

Table 3
Selection of sleep parameters of critically ill children compared to literature reference ranges

Participant/Age	Nighttime TST min (%24h TST)	REM %TST	NREM %TST	N1 %TST	N2 %TST	N3 %TST	SE % SPT
1. 0–1 months	378 (49.0)	44.8	55.2	0.0	0.0	0.0	63.1
2. 0–1 months	413.5 (49.5)	17.9	82.1	0.0	0.0	0.0	69.0
3. 0–1 months	545.5 (49.4)	37.5	62.5	0.0	0.0	0.0	91.0
4. 0–1 months	534 (50.9)	0.7	99.3	0.0	0.0	0.0	89.9
5. 0–1 months	435 (57.0)	29.4	70.6	0.0	0.0	0.0	72.6
6. 0–1 months	393 (51.1)	30.8	69.2	0.0	0.0	0.0	65.6
7. 1–2 months	405 (54.5)	24.0	76.0	0.0	0.0	0.0	71.0
8. 1–2 months	357.5 (65.8)	36.1	63.9	0.0	0.0	0.0	60.1
9. 1–2 months	437 (48.5)	25.3	74.7	0.0	0.0	0.0	72.9
10. 2–6 months	260.5 (50.6)	18.2	81.8	0.0	0.0	0.0	43.5
11. 2–6 months	543.5 (50.6)	8.5	91.5	0.0	0.0	0.0	91.0
12. 2–6 months	433 (55.7)	10.3	89.7	0.0	0.0	0.0	85.6
13. 2–6 months	385.5 (49.4)	8.7	91.3	0.0	0.0	0.0	64.3
14. 2–6 months	223.5 (44.1)	5.4	0.0	11.4	4.0	79.2	38.5
15. 2–6 months	517 (55.2)	13.7	39.1	0.0	13.4	33.8	86.2
16. 2–6 months	83 (29.2)	0.0	100.0	0.0	0.0	0.0	14.1
17. 6–12 months	366.5 (55.5)	0.0	2.9	38.6	47.1	11.5	62.3
18. 1–3 years	578.5 (51.3)	4.5	0.0	14.6	52.5	28.4	96.5
19. 1–3 years	459.5 (56.5)	11.3	0.0	16.2	53.2	19.3	77.4
20. 5–9 years	390 (50.6)	8.5	0.0	26.7	57.7	7.2	67.5
21. 9–13 years	342.5 (59.0)	0.0	0.0	42.2	54.2	3.6	57.1
22. 13–18 years	552 (50.3)	0.0	73.9	0.0	21.8	4.3	92.1
23. 13–18 years	261 (44.5)	3.8	0.0	11.1	54.4	30.7	43.5
24. 13–18 years	323 (56.4)	0.0	0.0	46.1	50.6	3.3	53.9

Selection of nighttime sleep characteristics (columns) of individual patients (rows, in order of increasing age) and the corresponding values which are either in range (black), below range (blue) or above range (red) with regard to reference ranges of healthy controls. Grey values represent values for which no valid reference range was found. Up two months of age, we assumed differentiation of different NREM stages is not yet present in healthy children. The complete table is available in the supplements. NREM = non-rapid-eye-movement sleep (N); REM = rapid-eye-movement sleep; SE = Sleep efficiency; SPT = sleep period time; TST = total sleep time

Participant/Age	Nighttime TST min (%24h TST)	REM %TST	NREM %TST	N1 %TST	N2 %TST	N3 %TST	SE % SPT
25. 13–18 years	575 (51.8)	0.0	100.0	0.0	0.0	0.0	95.9

Selection of nighttime sleep characteristics (columns) of individual patients (rows, in order of increasing age) and the corresponding values which are either in range (black), below range (blue) or above range (red) with regard to reference ranges of healthy controls. Grey values represent values for which no valid reference range was found. Up two months of age, we assumed differentiation of different NREM stages is not yet present in healthy children. The complete table is available in the supplements. NREM = non-rapid-eye-movement sleep (N); REM = rapid-eye-movement sleep; SE = Sleep efficiency; SPT = sleep period time; TST = total sleep time

Sleep scoring in critically ill children

Among PICU patients, 19 (76.0%) had abnormalities in the underlying EEG. Nine (36.0%) patients exhibited excessive slow wave activity during wake. In these patients, epochs with a marked increase in slow waves were scored N3, while remaining epochs were scored based on the presence of other features. Eight patients (32.0%) lacked specific EEG features expected for their age. Sleep spindles, expected after nine weeks, were absent in six out of seventeen patients in this age category; and K-complexes, expected after six months, were absent in two out of nine patients in this age category.[23] In four (16.0%) patients, EEG abnormalities precluded distinction of NREM sleep stages, although these should have been discernible at their age. Two of these patients, both with severe CNS injuries, displayed atypical EEG patterns with abundant theta and delta activity without sleep spindles or K-complexes. All hypnograms are available in Supplemental Figure S2, the last hypnogram showing an older patient (patient Y) in whom NREM stages could not be distinguished.

Sleep characteristics in non-critically ill children

Results of secondary analysis, deviations from normal sleep in non-critically ill hospitalized children, are presented in Table 4 and Supplemental Table S3. Children in the SDB group showed reduced proportions of REM sleep up to six months of age, lower sleep efficiency and higher awakening index above the age of nine years and shorter mean sleep period duration in all age groups for which reference values were available.

Table 4
Selection of mean sleep parameters in the control group compared to literature reference ranges

Age group	TST	REM	NREM	N1	N2	N3	SE
	min	%TST	%TST	%TST	%TST	%TST	% SPT
0–2 months	498.7	34.4	59.5	*0.5*	*0.0*	*5.6*	71.7
2–6 months	524.6	32.0	*20.1*	*5.4*	*14.0*	*28.5*	81.7
6–12 months	535.0	28.7	*0.0*	*11.5*	*27.5*	*32.2*	85.5
1–3 years	493.3	22.6	0.0	15.1	28.9	33.4	83.9
3–5 years	540.5	21.6	0.0	9.5	27.3	41.6	89.6
5–9 years	507.0	21.5	0.0	9.0	35.6	33.9	86.0
9–13 years	408.8	16.2	0.0	14.9	32.7	36.3	77.1
13–18 years	412.7	17.9	0.0	13.2	38.0	30.8	82.2

Selection of sleep characteristics (in columns) per age category (in rows, in order of increasing age) and the corresponding values which are either in range (black), below range (blue) or above range (red) with regard to reference ranges of healthy controls. Grey values represent values for which no valid reference range was found. Values were considered abnormal when they exceeded either mean with 2 standard deviations, the 5th to 95th percentile range or the range, whichever was reported in the respective article. AI = awakening index; NREM = non-rapid-eye-movement sleep (N); REM = rapid-eye-movement sleep; SE = Sleep efficiency; SPD = average sleep period duration; SPT = sleep period time; TST = total sleep time

Discussion

This observational study describes sleep (disruptions) in critically ill and non-critically ill hospitalized children aged 0 to 18 years. Through inclusion of young infants and children with CNS injury, and by reporting on the underlying EEG, this study addresses critical gaps in pediatric sleep research. Critical illness was associated with disrupted sleep, specifically reduced duration, high fragmentation and reduced REM and N3 sleep. Underlying EEGs showed frequent abnormalities, with abundant slow waves, absence of prominent sleep features and non-discernible NREM sleep. In non-critically ill children with suspected SDB, sleep was mainly disrupted by high fragmentation and occasionally reduced REM sleep.

The findings obtained here align with previous sleep studies in critically ill PICU patients, reporting higher 24-hour TST, loss of day-night variation and reduced REM sleep.[9–13] Our study adds that young infants in the PICU tend to experience higher sleep efficiency and fewer awakenings, whilst CNS injured patients experienced less REM and N3 sleep, as compared to healthy reference ranges. Sleep efficiency is rarely reported in the PICU as it requires clearly defined sleep onset and wake periods. Yet, it was included here as a measure of sleep continuity. To account for disrupted circadian rhythm, we calculated sleep efficiency from the first to last sleep epoch during nighttime. Despite its limitations in critically ill populations, our findings of low sleep efficiency and high awakening index, particularly in children over one year, align with adult literature and one pediatric study.[8, 13]

In contrast, findings on NREM sleep and in particular N3 sleep in critically ill children deviate from previous studies. While generally N3 sleep was reduced when NREM stages were discernable, there was considerable

interpatient variability (e.g. one patient spent almost 80.0% of TST in N3 sleep). Dervan et al. reported normal mean proportions of N3 sleep with similar interpatient variability as observed here, while Zhao et al. reported means of 61.1% and 83.1%.[12, 13] These discrepancies may reflect the challenge in distinguishing pathological slow wave activity from physiological N3 sleep, potentially leading to mislabeling.[23] Therefore, the present study uniquely reported on underlying EEGs. Slow waves were in abundance among critically ill children, requiring an adaptation of sleep scoring, and may reflect sedation or analgesics, hypercapnia and/or encephalopathy.[28–31] Importantly, sedatives may reduce environmental sensitivity, lowering the awakening index and prolonging mean sleep periods, even for increased illness severity.[12]

The observed abnormalities in underlying brain activity and overall difficulty experienced during sleep scoring in critically ill children raises concern whether the observed sleep was truly restorative sleep. The abnormal EEG patterns observed in two older patients with CNS injuries resembled non-typical sleep stages At1 and At2 described by Watson et al., which are associated with encephalopathy.[16] While their classification offers guidance for handling the most abnormal EEG patterns, it remains difficult to distinguish restorative sleep from sedation induced or pathological states. Perhaps more importantly, findings of the present study raise the question whether critically ill patients retain the capacity for healthy (restorative) sleep, and whether the hospital environment harbors modifiable targets to improve this.

The hospital environment and iatrogenic factors likely contribute to sleep disruptions.[32, 33] In non-critically ill children exposed to a high or medium care unit, we observed reduced REM sleep up to six months of age. Normally, REM sleep typically reduces from around 50.0% in the neonatal period to a stable 20.0% at two years of age.[34] In non-critically ill children aged one year and older, mean sleep period durations were reduced and in the ages nine to eighteen years sleep efficiency was reduced due to high fragmentation. While these disruptions may be due to underlying sleep disorders, such as SDB/OSA, the influence of the hospital setting and/or PSG cannot be dismissed. Disrupted sleep can exacerbate the stress response, impair cognition and weaken the immune system, potentially prolonging admission and increasing complication risk.[12, 35–38] Increased illness severity may also enhance the homeostatic process driving sleep, creating a vicious cycle in which critical illness and sleep disruption reinforce one another. It seems imminent that strategies to optimize sleep in the PICU may contribute to individual recovery trajectories and, potentially, outcomes.

The present study has several strengths. Firstly, our study is the first to include patients of all ages and a wide variety of (critical) illnesses. Including a non-critically ill group provided insight into relative contributions of illness and the hospital environment to sleep disruption. Finally, the use of 24-hour PSG enabled evaluation of day-night variation, reflecting circadian rhythm. However, several limitations must be acknowledged. First, sleep is a dynamic process that changes as children grow and mature, which we aimed to describe as comprehensively as possible. The study was designed to be longitudinal, but logistical constraints resulted in single sleep measurements per patient, obtained on day 1, 3, 7 or 14 of the study. The SDB group is not a healthy population, but was nonetheless selected for methodological and ethical reasons. As fifteen children in the SDB group were already asleep when PSG started, their sleep efficiency and sleep period duration may not be accurate, therefore we averaged across age categories. Furthermore, the small sample size and heterogeneity of the cohort did not permit statistical analysis. Lastly, reference ranges were limited by differential measurement conditions and reporting standards.

The present study provides valuable insight into how critical illness and the hospital environment disrupt sleep in children, which may bear implications for the standard of pediatric (critical) care. Much work remains to clarify the exact role of sleep in short- and long-term recovery from critical illness. An important step in future research is the development of patient-friendly, automated sleep measurement tools.[39–41] Such tools would facilitate larger, longitudinal sleep studies in the PICU, enable bedside monitoring and support personalized interventions. However, these tools require understanding and consensus on how to interpret atypical EEG patterns in critically ill children. Finally, establishing comprehensive pediatric reference values is essential, by including all sleep characteristics and preferably obtaining them over 24 hours to assess sleep disruptions.

Conclusion

This observational study describes sleep in critically ill and non-critically ill hospitalized children, as compared to healthy reference ranges. Critically ill children in the PICU, including young infants and CNS injured patients, exhibited EEG abnormalities, loss of REM and N3 sleep, high fragmentation and absent day-night variation. Non-critically ill children mainly showed high fragmentation and reduced sleep efficiency. Findings suggest underlying illness and sedative medications disrupt sleep, with the hospital environment likely contributing. Further research is needed to clarify how sleep affects both short- and long-term recovery from critical illness.

Abbreviations

AASM
American Academy of Sleep Medicine
AI
Awakening index
CNS
Central nervous system
EEG
Electroencephalography
IQR
Interquartile range (Q1, Q3)
MEC
Medical Ethics Committee
NREM
Non-rapid-eye-movement
OSA
Obstructive sleep apnea
PELOD-2
Pediatric Logistic Organ Dysfunction 2
PICU
Pediatric intensive care unit
PIM3
Pediatric Index of Mortality 3
PSG
Polysomnography

REM
Rapid-eye-movement
SDB
Sleep disordered breathing
SE
Sleep efficiency
SD
Standard deviation
SPD
Sleep period duration
SPT
Sleep period time
STROBE
Strengthening the Reporting of Observational Studies in Epidemiology
TST
Total sleep time

Declarations

Authorship statement

The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Competing interest statement

The authors have nothing to disclose.

Ethics approval statement

This study was performed in line with the principles of the Declaration of Helsinki. The ContInNuPIC trial was approved by the Dutch national review board, the Central Committee on Research Involving Human Subjects (NL72302.000.19). The Critical Clock study and the use of diagnostic and follow-up polysomnograms were approved by the Erasmus MC Medical Ethics Review Committee (NL72597.078.20, MEC-2020-0333 and MEC-2021-0121, respectively).

Patient consent statement

All ContInNuPIC and Critical Clock trial participants and/or their parents or legal guardians provided written informed consent to participate in this study and to publish individual data. Given the potential discomfort of the

application and removal of the electrodes, separate consent was asked for the PSG on the day of measurement. Consent for the use of diagnostic and follow-up polysomnograms was waived due to the retrospective nature.

Data availability statement

Individual patient data reported in this article can be shared in the context of a collaboration, after de-identification, to researchers who provide a methodologically sound proposal and after approval by the internal scientific committee. Proposals should be addressed to the corresponding author. Data requestors must sign a data transfer agreement to gain access.

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