



Original Article

Sleep-Wake Disturbances After Acquired Brain Injury in Children Surviving Critical Care



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ABSTRACT

Background: Sleep-wake disturbances are underevaluated among children with acquired brain injury surviving critical care. We aimed to quantify severity, phenotypes, and risk factors for sleep-wake disturbances.

Methods: We performed a prospective cohort study of 78 children aged ≥ 3 years with acquired brain injury within three months of critical care hospitalization. Diagnoses included traumatic brain injury ($n = 40$), stroke ($n = 11$), infectious or inflammatory disease ($n = 10$), hypoxic-ischemic injury ($n = 9$), and other ($n = 8$). Sleep Disturbances Scale for Children standardized T scores measured sleep-wake disturbances. Overall sleep-wake disturbances were dichotomized as any total or subscale T score ≥ 60 . Any T score ≥ 70 defined severe sleep-wake disturbances. Subscale T scores ≥ 60 identified sleep-wake disturbance phenotypes.

Results: Sleep-wake disturbances were identified in 44 (56%) children and were classified as severe in 36 (46%). Sleep-wake disturbances affected $\geq 33\%$ of patients within each diagnosis and were not associated with severity of illness measures. The most common phenotype was disturbance in initiation and maintenance of sleep (47%), although 68% had multiple concurrent sleep-wake disturbance phenotypes. One third of all patients had preadmission chronic conditions, and this increased risk for sleep-wake disturbances overall (43% vs 21%, $P = 0.04$) and in the traumatic brain injury subgroup (52% vs 5%, $P = 0.001$).

Conclusions: Over half of children surviving critical care with acquired brain injury have sleep-wake disturbances. Most of these children have severe sleep-wake disturbances independent of severity of illness measures. Many sleep-wake disturbance phenotypes were identified, but most children had disturbance in initiation and maintenance of sleep. Our study underscores the importance of evaluating sleep-wake disturbances after acquired brain injury.

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Introduction

Acquired brain injury from a neurological diagnosis accounts for more than 20% of admissions to pediatric intensive care units.^{1,2} Each year tens of thousands of children require specialized pediatric neurocritical care (PNCC) to treat the primary neurological insult and minimize secondary brain injury in an effort to improve outcomes.³ Despite specialized care, acquired brain injury is the leading cause of death and long-term morbidity among children requiring critical care.^{1,4,5} Chronic morbidities include physical, cognitive, emotional, and psychosocial impairments termed post-intensive care syndrome.^{6,7}

Healthy sleep is vital for brain maturation and normal development, and is likely even more important after neurological injury or illness given that sleep facilitates neuronal healing and reduces inflammation.^{8–12} Sleep-wake disturbances (SWDs) in otherwise healthy children are known to impair quality of life, reduce participation in social activities, and impair cognitive function.^{13–15} Many of the impairments found in children with SWD overlap with those of children with postintensive care syndrome. SWDs including insomnia, somnolence, and sleep-related breathing disorders are reported in survivors of brain injury, but to date have been poorly quantified in children after critical care hospitalization.^{8,16,17} Our prior work showed SWDs were a common subjective complaint in children with various neurological diagnoses treated in a critical care follow-up clinic.¹⁸ Most research has focused on traumatic brain injury (TBI), and very few studies have reported SWD outcomes in children with injuries more severe than concussion.¹⁷ Those that included children hospitalized with mild complicated, moderate, or severe TBI requiring PNCC rarely used a validated sleep questionnaire^{19–22} and most were not originally designed for the purpose of collecting sleep data.^{19,22} Therefore the severity of SWDs and phenotypes of the SWDs are largely under-evaluated and under-reported in prior studies limiting the ability to adequately identify risk factors and design targeted intervention studies.

To address these important knowledge gaps surrounding SWDs in survivors with acquired brain injury, we evaluated SWDs at two institutions with longitudinal critical care programs treating children in specialized multidisciplinary clinics. On the basis of our clinical experience, we hypothesized SWDs would be prevalent and severe after acquired brain injury. We aimed to quantify overall SWDs, severity and phenotypes of SWDs, and risk factors for SWDs after PNCC hospital discharge using a multidimensional sleep questionnaire.

Materials and Methods

Study design

We evaluated SWDs one to three months after hospital discharge (December 2017 to October 2018) in a prospective cohort study of children aged three to 18 years with acquired brain injury. Evaluations were performed as part of routine clinical care in each institution's coordinated follow-up clinic. More than two thirds of all PNCC survivors complete a clinic visit and referral patterns and follow-up rates at each program have been previously described.^{18,23} The Institutional Review Board at each institution approved the study under a waiver of informed consent.

Population characteristics

Both institutions are tertiary children's hospitals and accredited level I pediatric trauma centers with multidisciplinary critical care follow-up programs that include pediatric critical care, pediatric

neurology, and pediatric neuropsychology faculty. Consecutive children who completed a follow-up visit were included. For the analysis, diagnoses were grouped into five unique subgroups: TBI; stroke (hemorrhagic and ischemic); infectious or inflammatory (meningitis, encephalitis, and demyelinating); hypoxic-ischemic (cardiac arrest and extracorporeal life support); and other (carbon monoxide, hemolytic uremic syndrome, severe sepsis, hippocampal necrosis after polypharmacy ingestion, and refractory status epilepticus). The primary diagnosis was used in patients with multiple diagnoses (e.g., patients with seizures because of meningitis were classified as infectious).

Demographic and clinical characteristics were collected from electronic medical records. Preadmission chronic conditions were grouped into system categories given the large number of individual diagnoses (Supplemental Table 1). The presence of any chronic condition was dichotomized for analysis. Pediatric Index of Mortality-2 score and critical care interventions (intubation, noninvasive ventilation, central venous catheterization, arterial catheter placement, intracranial pressure monitoring, continuous antiepileptic infusion, neurosurgical intervention, hemodynamic resuscitation or vasopressor use, and in-hospital cardiopulmonary resuscitation) were evaluated as markers of illness severity. Interventions were not counted if only used during operative management and were discontinued before return or admission to the pediatric intensive care unit (e.g., intubation during operation only). Functional assessments were made by attending physicians using the Functional Status Scale (FSS).²⁴ Glasgow Coma Scale measured TBI severity (mild complicated 13 to 15, moderate 9 to 12, and severe 3 to 8). Location and type of TBI and concurrent non-brain traumatic injuries were identified from radiology reports.

Outcomes

Sleep outcomes were measured at follow-up visits using the Sleep Disturbances Scale for Children (SDSC), a parent-reported 26-item validated multidimensional questionnaire for use in children aged 3 to 18 years.^{25,26} Each question is scored 1 to 5 with higher scores reflecting more disturbance. The SDSC provides six subscale scores and a total composite score that can each be converted to *T* scores to reflect risk of clinical sleep disorders.²⁵ In our study, SWDs were defined as a *T* score ≥ 60 in any of the SDSC total or subscale scores, corresponding to moderate or greater risk of clinical sleep disorders and ≥ 1 standard deviation (S.D.) from healthy population means.²⁵ SWD group was used to compare demographic and clinical characteristics. Severe SWDs were defined as *T* scores ≥ 70 (≥ 2 S.D. from normal). Phenotypes of SWDs were identified by the six SDSC subscales: disorders of initiation and maintenance of sleep (e.g., insomnia); sleep breathing disorders (e.g., sleep apnea); disorders of arousal (e.g., nightmares); sleep-wake transition disorders (e.g., sleep talking, bruxism); disorders of excessive somnolence (e.g., daytime sleepiness); and sleep hyperhidrosis (e.g., night sweats).

Statistical analysis

Descriptive statistics were used to describe the population including percent for categorical variables and median with interquartile range for continuous variables as data were not normally distributed in our sample. SDSC total and subscale score mean and S.D. for our cohort were compared with unpaired *t* tests to prior published data on SDSC total and subscale means among healthy children (historical control subjects).²⁵

Demographic and clinical characteristics were compared between dichotomized SWD groups. We used χ^2 tests for categorical

variables and Mann-Whitney *U* tests to compare continuous variables. Multiple logistic regression was used to identify variables associated with SWDs among the overall cohort and results reported as adjusted odds ratio with 95% confidence interval. We controlled for diagnosis subgroup (“other” as reference diagnosis category), gender, age, Medicaid, non-White race, Hispanic ethnicity, and the presence of any preadmission chronic condition based on the significance in the bivariate analysis ($P < 0.05$) and prior reports of risk factors for SWDs in children.¹⁷ The full model results are reported (Supplemental Table 2) as it showed good calibration (Hosmer-Lemeshow $P = 0.9$) and discrimination (area under the curve = 0.80) and outperformed reduced models (using area under the curve) derived from stepwise regression.

A descriptive analysis evaluated SWD phenotypes using SDSC subscales and SWDs by diagnosis subgroup. A secondary analysis was performed to explore demographic and clinical variables by SWD group with the same tests as mentioned previously for the TBI subgroup. Analyses were conducted using SPSS (version 24.0; IBM

Corporation, Armonk, NY). All tests were two-tailed and significance defined as $P < 0.05$. When multiple pairwise comparisons were made within variable groups, a Bonferroni adjustment was used to define significance level.

Results

A total of 78 children were evaluated in clinic a median of 1.8 months (interquartile range 1.3, 2.8) postinjury. Most patients had TBI ($n = 40$) followed by stroke ($n = 11$), infectious or inflammatory disease ($n = 10$), hypoxic-ischemic injury ($n = 9$), and other diagnoses ($n = 8$). Table 1 shows demographic and clinical characteristics. Preadmission chronic conditions were found in 26 (33%) patients and varied by diagnosis subgroup (Supplemental Table 1). Severity of illness and length of stay were variable, but two thirds required at least one critical care intervention and half were intubated (Table 1). No significant differences were found between institutions in diagnosis, severity, or any interventions.

TABLE 1.
Demographic and Clinical Characteristics by Sleep-Wake Disturbance Group

Characteristics	All, N = 78 (%)	No SWD, n = 34 (%)	SWD+, n = 44 (%)	P Value
Age in years, median (IQR)	9.9 (6.8, 14.1)	8 (6, 11)	10.7 (7.6, 15)	0.03
Male gender	47 (60)	18 (53)	29 (66)	0.35
Preadmission chronic condition	26 (33)	7 (21)	19 (43)	0.04
Race				0.61
White	63 (81)	26 (77)	37 (84)	
Black	6 (8)	4 (12)	2 (5)	
Other, multiple races, or unknown	9 (12)	4 (12)	5 (11)	
Hispanic ethnicity	13 (17)	4 (12)	9 (21)	0.38
Medicaid insurance	35 (45)	17 (50)	18 (41)	0.42
Diagnosis category				0.13
Traumatic brain injury	40 (51)	19 (56)	21 (48)	
Stroke	11 (14)	4 (12)	7 (16)	
Infectious and inflammatory disease	10 (13)	1 (3)	9 (21)	
Hypoxic-ischemic injury	9 (12)	6 (18)	3 (7)	
Other	8 (10)	4 (12)	4 (9)	
Pediatric Index Mortality-2; median (IQR)	-3.7(-4.1, -3)	-3.1(-4.1, -3)	-4(-4, -3.1)	0.49
Intensive care interventions				
Monitoring only	27 (35)	8 (24)	19 (43)	0.07
Intubation	39 (50)	19 (56)	20 (46)	0.36
Noninvasive ventilation	10 (13)	7 (21)	3 (7)	0.07
Central venous line	29 (37)	15 (44)	14 (32)	0.27
Arterial line	31 (40)	14 (41)	17 (39)	0.82
Bolt	5 (6)	1 (3)	4 (9)	0.27
External ventricular drain	6 (8)	2 (6)	4 (9)	0.60
Infusion for seizure control	12 (15)	4 (12)	8 (18)	0.44
Neurosurgical intervention	21 (27)	11 (32)	10 (23)	0.34
Hemodynamic resuscitation or vasopressor	25 (32)	12 (35)	13 (30)	0.59
Cardiopulmonary resuscitation in-hospital	8 (10)	5 (15)	3 (7)	0.26
Inpatient nutrition				0.43
Any parenteral	5 (6)	3 (9)	2 (5)	
Any nasogastric or nasojejunal	17 (22)	10 (29)	7 (15)	
Oral only	56 (72)	21 (62)	35 (80)	
Inpatient consults				
Physical therapy	52 (67)	20 (59)	32 (73)	0.20
Occupational therapy	47 (60)	19 (56)	28 (64)	0.49
Speech therapy	20 (26)	9 (27)	11 (25)	0.88
Psychology	26 (33)	7 (21)	19 (43)	0.05
Inpatient rehabilitation discharge	11 (14)	7 (21)	4 (9)	0.15
New tracheostomy	6 (8)	3 (9)	3 (7)	>0.99
New gastrostomy	3 (4)	2 (6)	1 (2)	0.41
Hours of mechanical ventilation, median (IQR) n = 39	16.7 (4, 37.2)	17.4 (6.3, 28)	15.5 (3.1, 35.8)	0.68
Hospital length of stay in days, median (IQR)	7.4 (2.1, 20.8)	6.8 (1.8, 29.6)	7.4 (2.8, 16.7)	0.61
PICU length of stay in days, median (IQR)	2.8 (1.4, 11.9)	2.8 (1.0, 13.0)	2.5 (1.5, 7.9)	0.78
Clinic Functional Status Scale, median (IQR)	6 (6, 7)	6 (6, 6)	6 (6, 7)	0.30

Abbreviations:

IQR = interquartile range

PICU = pediatric intensive care unit

SWD = sleep-wake disturbance

Values are prevalence or median when stated. Values in the parentheses represent group percentage or IQR when stated. Mann-Whitney *U* tests were used for continuous variables and χ^2 tests for categorical variables.

Average SDSC total score was 39.4 (S.D. 10.4) for the overall cohort and was significantly higher than the average for healthy children in published cohorts²⁵ (35.1, S.D. 7.7; $P < 0.001$; Table 2). The distribution of standardized *T* scores for the SDSC total score is shown in Fig 1.

SWDs were identified in 44 (56%) patients with acquired brain injury and were severe in 36 (46%) patients. Table 1 shows demographic and clinical characteristics compared by SWD group. FSS at follow-up ranged from 6 to 12, and $\geq 75\%$ had good functional outcomes (FSS, 6 to 7). Older median age and the presence of preadmission chronic conditions were significantly associated with SWDs. There was no association in bivariate analyses between SWDs and institution or other demographic and clinical characteristics. Using multiple logistic regression controlling for demographic characteristics and diagnosis, the presence of a preadmission chronic condition was the only variable significantly associated with SWDs, portending fivefold increased odds of SWDs among the overall cohort (adjusted odds ratio, 5.4; 95% confidence interval, 1.3 to 21.9).

SWD phenotypes

All SWD phenotypes measured by the SDSC were identified. Multiple SWD phenotypes were found in 30 (68%) of the 44 patients with SWDs. Table 2 shows the overall cohort had significantly higher average scores in the total score and several subscales when compared with healthy children. Overall, the disorders of initiation and maintenance of sleep phenotype was most common with 37 (47%) patients having disturbance and 26 (33%) having severe disturbance (Fig 2). Sleep-wake transition disorders ($n = 18$, 23%) and somnolence ($n = 15$, 19%) were also prevalent phenotypes in the overall cohort. Sleep breathing disorder ($n = 8$, 10%), arousal disorder ($n = 8$, 10%), and hyperhidrosis ($n = 5$, 6%) phenotypes were less common. Among patients with any SWD, 37 (84%) showed disturbance in the disorders of initiation and maintenance of sleep subscale.

SWDs by diagnosis group

Prevalence of SWDs varied by diagnosis, but SWDs were found in $\geq 33\%$ in each subgroup. SWDs were found in nine (90%) patients with infectious and inflammatory diseases, seven (64%) patients with stroke, 21 (53%) patients with TBI, four (50%) patients with other diagnoses, and three (33%) patients with hypoxic-ischemic injury. The disorders of initiation and maintenance of sleep phenotype was most commonly disturbed among all diagnosis groups (Table 3).

More than half of patients with TBI had SWDs and showed significant differences from published results in healthy children (Table 2).²⁵ No association between SWDs and severity, mechanism, or location of TBI was found (Table 4). Type of intracranial injury was not statistically different between SWD groups. Preadmission chronic conditions were strongly associated with SWDs in the TBI population (52% with SWDs versus 5% without SWDs, $P = 0.001$). The most prevalent preadmission conditions identified in TBI were attention deficit hyperactivity disorder (ADHD) and behavioral disorders ($n = 5$), but this was not statistically different between SWD groups. The disorders of initiation and maintenance of sleep subscale was disturbed in 17 (43%) patients with TBI and severely disturbed in 13 (33%) patients. Sleep-wake transition disorders (25%) and somnolence (20%) phenotypes were also common. Phenotypes did not vary between mild complicated, moderate, and severe patients with TBI.

Discussion

Among children with acquired brain injury treated in critical care follow-up clinics after discharge, SWDs are highly prevalent and often severe. Risk of SWDs was increased in children with preadmission chronic conditions, but SWDs were not associated with severity of injury measures. Many SWD phenotypes were found, some varying by diagnosis, and multiple SWD phenotypes coexisted in most patients. The disorders of initiation and maintenance of sleep phenotype was most common and nearly universally identified in patients with SWDs. These disturbances were also frequently severe and may serve as a target for future intervention studies seeking to improve outcomes in critical care survivors with acquired brain injury.

Our study adds to the literature showing that SWDs are important outcomes in survivors of critical care and brain injury. This study is the first to describe SWDs after many PNCC diagnoses. Case reports of SWDs in children with stroke, meningitis, and hypoxic-ischemic injury are reported, although SWDs have not been systematically evaluated in these populations after critical care.^{27,28} Our rates of SWDs among children with TBI are similar to prior reports showing high rates of somnolence, insomnia, and overall disturbances after pediatric TBI when compared with control subjects.^{17,19–22} One prior study used the SDSC in a PNCC population, showing significantly worse SWDs in children after TBI compared with healthy control subjects, and reported similar total SDSC scores to our population.¹⁹ SWDs are also reported in broader populations of children surviving critical care, with high rates similar to our study, and much higher than healthy children.^{29,30}

TABLE 2.

Comparison of the Overall Acquired Brain Injury and Traumatic Brain Injury Cohorts to Healthy Control Subjects Reported for the Sleep Disturbances Scale for Children

SDSC Scale	Healthy Control Sample, ²⁵ N = 1157	Overall Cohort, N = 78	TBI Subgroup, N = 40
SDSC total, mean (S.D.)	35.1 (7.7)	39.4 (10.7) [*]	38.6 (9.7) [†]
Disorders of Initiation and Maintenance of Sleep, mean (S.D.)	9.9 (3.1)	13.2 (5.3) [*]	12.7 (4.7) [*]
Sleep breathing disorder, mean (S.D.)	3.8 (1.5)	3.9 (1.7)	3.5 (1.0)
Disorders of arousal, mean (S.D.)	3.3 (0.8)	3.6 (1.7) [†]	3.3 (1.0)
Sleep-wake transition disorders, mean (S.D.)	8.1 (2.4)	8.7 (3.1) [†]	8.8 (3.7)
Hypersomnolence, mean (S.D.)	7.1 (2.6)	7.5 (2.5)	7.6 (2.8)
Sleep hyperhidrosis, mean (S.D.)	2.9 (1.7)	2.5 (1.1)	2.6 (1.0)

Abbreviations:

S.D. = standard deviation

SDSC = Sleep Disturbances Scale for Children

TBI = traumatic brain injury

Healthy control subjects obtained from Bruni et al. validation study.²⁵

^{*} $P < 0.001$ when compared with healthy control populations in the published literature. All comparisons with unpaired *t* tests.

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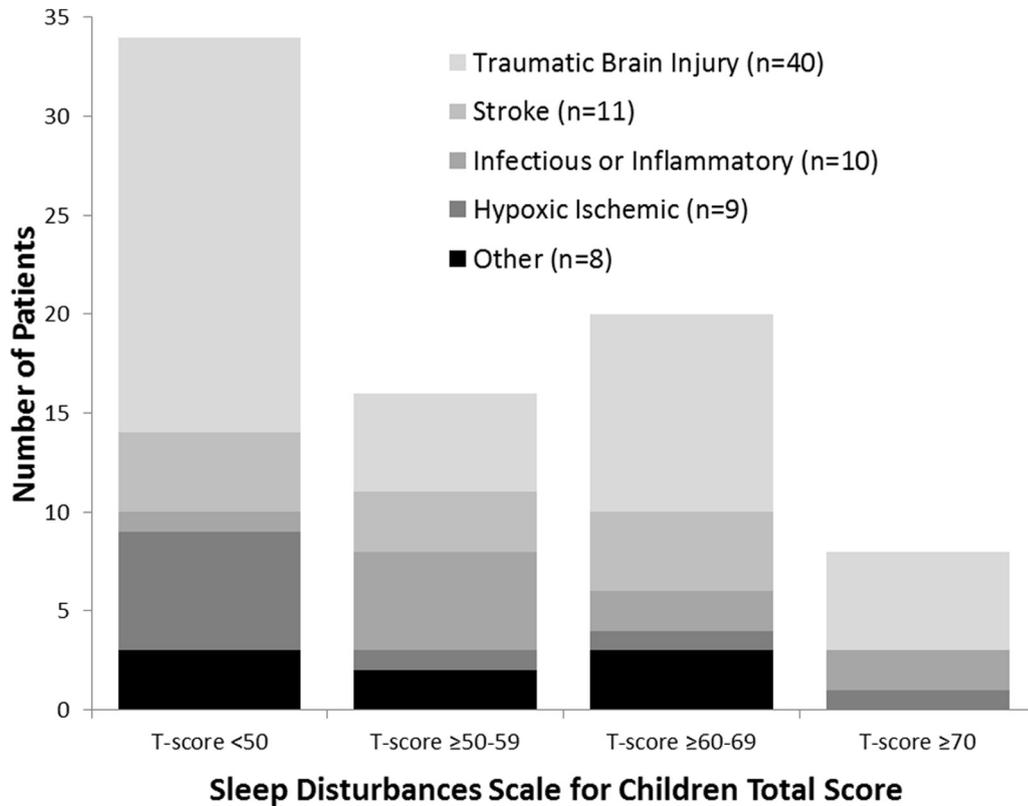


FIGURE 1. Distribution of standardized *T* scores for the Sleep Disturbances Scale for Children total score is shown separated by primary diagnosis.

Taken together, results highlight the importance of evaluating SWDs in all PNCC survivors.

Our study additionally evaluated SWD phenotypes, showing the disorders of initiation and maintenance of sleep subscale was abnormal in most children with SWD after acquired brain injury.

This subscale suggests insomnia or circadian rhythm disturbances are contributing to SWDs in children surviving PNCC. Insomnia has been described in up to 60% of adults with TBI and after concussion.⁸ Poor sleep efficiency and impaired onset and maintenance were reported using actigraphy in 15 children with moderate and

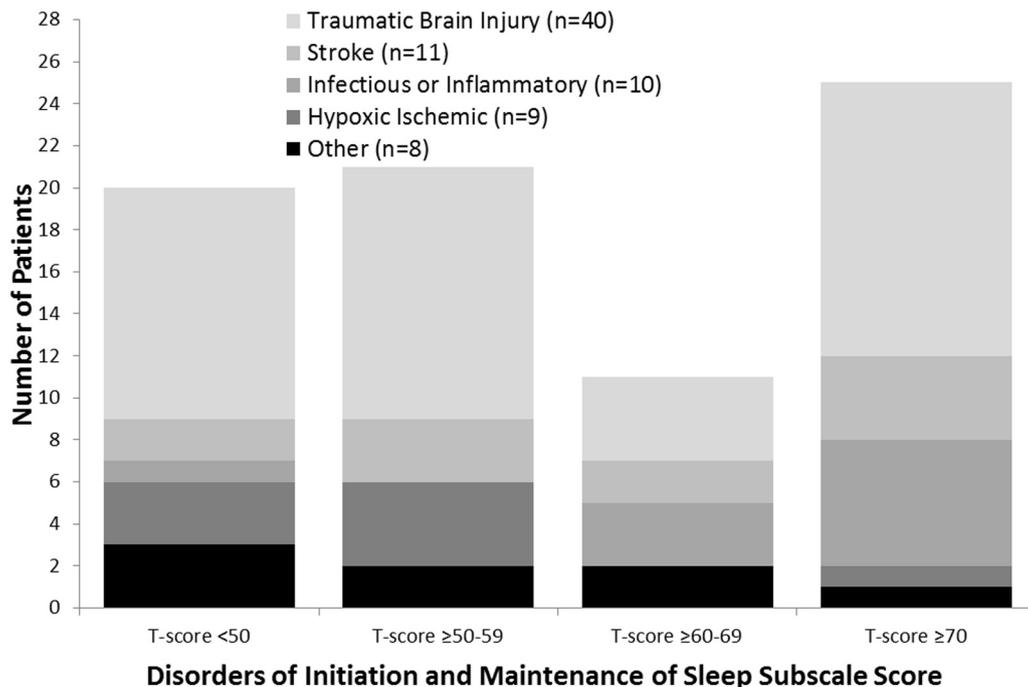


FIGURE 2. Distribution of standardized *T* scores for the Disorders of Initiation and Maintenance of Sleep subscale is shown separated by primary diagnosis.

TABLE 3.
Sleep-Wake Disturbance Phenotypes by Diagnosis Group

Phenotype	All, N = 78	TBI, n = 40	Stroke, n = 11	Infectious or Inflammatory, n = 10	Hypoxic-Ischemic, n = 9	Other, n = 8
Total score						
Median (IQR)	36.5 (32, 46)	34 (30.5, 45)	42 (32.5, 46)	41.5 (37, 47)	32 (32, 37)	37 (33, 46.5)
N (%) disturbance	28 (36)	15 (38)	4 (36)	4 (40)	2 (22)	3 (38)
N (%) severe	8 (10)	5 (13)	0	2 (20)	1 (11)	0
Disorders of Initiation and Maintenance of Sleep						
Median (IQR)	12 (9, 16)	11 (8.5, 16.5)	14 (10, 17)	16 (13, 18)	11 (8, 12)	11.5(9, 13.5)
N (%) disturbance	37 (47)	17 (43)	6 (55)	9 (90)	2 (22)	3 (38)
N (%) severe	26 (33)	13 (33)	4 (36)	6 (60)	2 (22)	1 (13)
Sleep breathing disorders						
Median (IQR)	3 (3, 4)	3 (3, 4)	3 (3, 5)	3.5 (3, 6)	3 (3, 4)	3.5 (3, 4.5)
N (%) disturbance	8 (10)	2 (5)	1 (9)	3 (30)	1 (11)	1 (13)
N (%) severe	4 (5)	1 (3)	1 (9)	1 (10)	1 (11)	0
Disorders of arousal						
Median (IQR)	3 (3, 3)	3 (3, 3)	3 (3, 3)	3 (3, 5)	3 (3, 4)	3 (3, 4.5)
N (%) disturbance	8 (10)	2 (5)	0	3 (30)	1 (11)	2 (25)
N (%) severe	8 (10)	2 (5)	0	3 (30)	1 (11)	2 (25)
Sleep-wake transition disorders						
Median (IQR)	8 (7, 10)	7 (6, 10.5)	7 (6.5, 8)	9 (7, 11)	8 (7, 10)	9 (7, 10)
N (%) disturbance	18 (23)	10 (25)	1 (9)	4 (40)	2 (22)	1 (13)
N (%) severe	6 (8)	5 (13)	0	0	1 (11)	0
Hypersomnolence						
Median (IQR)	7 (5, 9)	7 (5, 9)	7 (6.5, 7.5)	7.5 (5, 9)	6 (5, 8)	6 (5.5, 9.5)
N (%) disturbance	15 (19)	8 (20)	1 (9)	2 (20)	2 (22)	2 (25)
N (%) severe	7 (9)	6 (15)	0	1 (10)	0	0
Sleep hyperhidrosis						
Median (IQR)	2 (2, 3)	2 (2, 3)	2 (2, 3.5)	2 (2, 2)	2 (2, 2)	2 (2, 3)
N (%) disturbance	5 (6)	3 (8)	1 (9)	0	0	1 (13)
N (%) severe	1 (1)	0	1 (9)	0	0	0

Abbreviations:

IQR = interquartile range

TBI = traumatic brain injury

Total and subscale scores from the Sleep Disturbances Scale for Children; disturbance defined as T score ≥ 60 ; severe defined as T score ≥ 70 .

severe TBI consistent with insomnia.²² Circadian rhythm disturbances are less well described in the brain injury.⁸ Patients with visual impairment may be at increased risk of circadian disruption,³¹ although none of our patients had complete blindness or cortical visual impairment at follow-up. Hospitalized patients do have altered levels of melatonin and circadian rhythms while inpatient due to cares, medications, and persistently high ambient light levels,^{32,33} and patients with brain injury have greater alterations compared with other hospitalized patients.^{34,35} It is possible that children in our cohort have acquired circadian rhythm disturbance from brain injury compounded by the hospital environment, but more research is needed to distinguish these phenotypes and investigate the relative contribution of brain injury and the therapeutic environment. Both insomnia and circadian rhythm disturbances have been treated successfully in pediatric populations,^{36,37} but interventions to treat these SWDs after critical care have not been studied.^{27,38,39} It remains unknown if interventions during or after hospitalization to improve sleep could augment recovery after discharge for pediatric acquired brain injury.

Risk of SWDs was significantly increased with preadmission chronic conditions in our cohort. We found similar rates of chronic conditions in PNCC patients in prior studies.³ Chronic conditions, such as epilepsy, asthma, ADHD, and autism are associated with SWDs.^{37,40} We did not measure baseline SWDs to determine effects of preinjury SWD or potential association with preadmission chronic conditions. A small number of our patients had any one of these individual chronic conditions limiting our ability to determine if specific preadmission conditions were associated with SWD. One prior study did show children with TBI and concurrent ADHD had worse SWDs than ADHD control subjects 1 to 4 years after injury.⁴¹ The acquired brain injury may compound preinjury SWDs or increase risk of SWDs among those with pre-existing chronic conditions. However, most children in our study were

previously healthy and prevalence of SWDs was higher than reports in healthy children, which suggests the acquired brain injury and hospital course, rather than solely preadmission conditions, explain our findings.

Older age was associated with SWDs in bivariate analysis. Adolescents and teens are reported to have high rates of baseline SWDs, which may explain the trend for increased SWDs with older age in our study. Estimates show 30% to 40% of teenagers may have clinically important SWDs at baseline, whereas estimates are lower in preschool to adolescence.⁴² Older children may have more insight into sleeping problems, more effectively communicate problems to caregivers, or have behavioral differences in screen-time, caffeine intake, and sleep schedules contributing to these findings. Prior studies in TBI show inconsistent results with respect to age and SWDs, and our analysis did not find age to be an independent risk factor when controlling for confounders in multivariable analysis. In addition, most prior studies focus on narrower age ranges and have small sample sizes, thereby limiting direct comparison to our study.^{17,20-22,43}

We found overall SWDs were not associated with measures of severity of illness, including need for critical care interventions, functional outcome, or discharge to inpatient rehabilitation. Prior studies of heterogeneous pediatric critical care cohorts also failed to show associations between SWDs and severity of illness markers or length of stay.^{29,30} Although not associated with SWDs in our study, some of the markers we used for severity of illness (e.g., critical care interventions) have been associated with delusional memories, delirium, and risk for post-traumatic stress,⁴⁴⁻⁴⁶ all of which may impact sleep. Evaluation of these important outcomes as mediators of SWDs after discharge should be evaluated in future studies.

In the TBI subgroup, our study also found overall SWDs were not associated with Glasgow Coma Scale on admission, loss of consciousness, or type or location of intracranial injury, and is

TABLE 4.
Clinical Characteristics by Sleep-Wake Disturbance Group Among Patients with Traumatic Brain Injury

TBI Patient Characteristics	No SWD, N = 19 (48%)	SWD+, N = 21 (52%)	P Value
Admission GCS median (IQR)	12 (7.5, 15)	12 (9, 15)	0.83
Severity of TBI			0.86
Mild complicated	8 (42)	10 (48)	
Moderate	5 (26)	6 (29)	
Severe	6 (32)	5 (24)	
Age in years	9.8 (6.2, 12.9)	10.1 (8, 13)	0.31
Preadmission chronic condition	1 (5)	11 (52)	0.001
Any critical care intervention	13 (68)	9 (43)	0.11
Male gender	11 (58)	17 (81)	0.11
Mechanism			0.26
Motor vehicle occupant	5 (15)	3 (7)	
All-terrain vehicle	1 (3)	1 (2)	
Fall	7 (21)	6 (14)	
Auto-pedestrian or auto-bicycle	1 (3)	6 (14)	
Bicycle or scooter	3 (9)	5 (11)	
Penetrating	2 (6)	0	
Other traumatic injuries	12 (63)	12 (57)	0.70
Type of injury*			
Skull fracture	7 (37)	14 (66)	0.06
Subdural	5 (26)	7 (33)	0.63
Epidural	2 (11)	3 (14)	0.72
Subarachnoid	8 (42)	8 (38)	0.8
Contusion	10 (53)	12 (57)	0.78
Diffuse axonal injury	3 (16)	4 (19)	0.79
Location of brain injury*			
Frontal	9 (47)	11 (52)	0.75
Parietal	8 (42)	10 (48)	0.73
Temporal	6 (32)	6 (29)	0.84
Occipital	5 (26)	8 (38)	0.43
Loss of consciousness	10 (53)	12 (57)	0.16
Other non-brain injuries	12 (63)	12 (57)	0.7
Inpatient rehabilitation discharge	2 (11)	3 (14)	0.72
Clinic Functional Status Scale, median (IQR)	6 (6, 6)	6 (6, 6)	>0.99

Abbreviations:

IQR = interquartile range

GCS = Glasgow Coma Scale

SWD = sleep-wake disturbance

TBI = traumatic brain injury

Mann-Whitney *U* tests were used for continuous variables and χ^2 tests for categorical variables

* Multiple responses possible in a single patient.

consistent with prior work showing SWDs are pervasive after all severities of TBI.^{8,17,19} We additionally found no difference in SWD phenotypes based on severity of TBI. Although some adult studies suggest differences based on severity,⁸ prior literature in pediatric populations with injuries more severe than concussion are limited and have variable results. Osorio et al.²⁰ found increased daytime sleepiness in adolescents with moderate or severe TBI compared with mild complicated TBI. Shay et al.²¹ evaluated young children and found no difference in daytime sleepiness based on severity of TBI, but did show increased bedtime resistance in patients with severe TBI. Daytime fatigue was also similar in children by TBI severity in other studies.^{47–49} Differences between available studies and our findings are likely explained by different populations, measurement tools, and limited sample sizes. Associations between sleep phenotypes and injury characteristics should be assessed in future studies with larger populations using validated measures of SWDs to inform targeted intervention studies.

Given known associations between SWDs and poor academic achievement, depression, and obesity in otherwise healthy children, SWDs represent a substantial problem.^{13–15,37} SWDs impair neuronal development and healing,^{9–12} a function even more critical in the developing brain and after injury. SWDs offer a potentially modifiable target to improve recovery after acquired brain injury, and our results underscore the importance of systematically evaluating sleep in these children.

Although our study includes data from two centers, our centers are unique in the presence of coordinated critical care follow-up programs. Most institutions do not have similar programs,⁵ and care of children with morbidities after brain injury is often left to general practitioners and subspecialists. Our unique clinical population limits generalizability, but our results show a need for increased awareness of SWDs after acquired brain injury in PNCC survivors. Our study has several other limitations to consider including lack of preinjury sleep measures, parent-reported questionnaires to define sleep outcomes, short-term follow-up, and lack of objective measures of SWDs to supplement the questionnaire data. Prevalence of SWDs in our study was high suggesting a large increase in prevalence even if baseline disturbances are present. In addition, questionnaires may not capture the true prevalence of SWDs relying on recall and estimation of events. The SDSC represents one of the only validated multidimensional tools to measure sleep in pediatric patients,⁵⁰ but future studies should use objective measures like actigraphy and polysomnography to supplement patient and parent report. Our follow-up evaluations were limited to 1 to 3 months after discharge, so the trajectory of SWD after PNCC remains largely unknown, although studies in TBI have documented persistence of SWDs several years after injury.^{17,51} Despite these limitations, our study highlights an important problem in survivors with acquired brain injury for which future research is needed.

Conclusions

SWDs are an important morbidity affecting more than 50% of children surviving critical care with acquired brain injury in the months after discharge, and are frequently severe. Phenotypes consistent with insomnia or circadian rhythm disturbances were most common, but all SWD phenotypes were found in our cohort. SWDs can impair physical, cognitive, and psychosocial functions, and our study showed SWDs were pervasive in all diagnoses and regardless of severity of acute injury, which underscores the importance of evaluating SWDs after discharge. More research is needed to identify effective interventions to prevent and treat SWDs and determine if treating SWDs can also augment recovery from acquired brain injury in other important domains.

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Supplementary data

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