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SCIENTIFIC INVESTIGATIONS

Sleep disturbances in infants and young children following an acquired brain injury

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Study Objectives: Sleep disturbances impact over half of older children and teens with acquired brain injury (ABI) following critical care hospitalization but are underevaluated in infants and young children. Given the importance of sleep in brain development and healing after injury, we hypothesized sleep disturbances would be associated with worse neurodevelopmental outcomes in infants with ABI.

Methods: We performed a retrospective cohort study of 68 children aged 2–32 months following critical care hospitalization for ABI. The Brief Infant Sleep Questionnaire assessed sleep disturbances. Bayley Scales of Infant and Toddler Development, third edition and Adaptive Behavior Assessment System, third edition assessed developmental and adaptive functioning outcomes, respectively. *t* tests compared sleep characteristics in infants with ABI to historical healthy controls. Spearman's correlation evaluated relationships among sleep and outcomes. Multiple linear regression investigated relationships controlling for demographic and ABI characteristics.

Results: Compared to healthy controls, children with ABI had shorter nighttime sleep duration ($P = .01$), longer daytime sleep duration ($P < .001$), and longer duration of nighttime awakenings ($P < .001$). Duration of night awakenings negatively correlated with Bayley Cognitive scores (Spearman's correlation = −.40). Night awakenings negatively correlated with worse Adaptive Behavior Assessment System, third edition General Adaptive Composite scores (Spearman's correlation = −.42). When controlling for demographic and ABI characteristics, ≥ 3 awakenings was significantly associated with worse Adaptive Behavior Assessment System, third edition General Adaptive Composite (β = −11.3; 95% confidence interval = −19.2, −3.5).

Conclusions: Sleep disturbances are associated with poorer outcomes in infants and toddlers after ABI. Sleep is vital to recovery and a potentially modifiable target to improve outcomes.

Keywords: sleep, development, infant, toddler, acquired brain injury

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Acquired brain injury (ABI) is a prevalent cause of morbidity in young children, and sleep disturbances are observed in over half of children ages 3 years and above with ABI. Sleep disturbances following hospitalization for ABI are associated with poorer health outcomes and quality of life in older children, consistent with the known importance of sleep to healthy brain development and healing. However, sleep is underevaluated in infants and young children with ABI and may represent a modifiable target to improve outcomes.

Study Impact: Our study showed sleep disturbances were prevalent after ABI in infants and young children. Importantly, sleep disturbances in our ABI cohort, particularly increased night awakenings, were associated with significantly worse adaptive and developmental outcomes.

INTRODUCTION

Acquired brain injury (ABI) is a prevalent cause of mortality and morbidity in young children.[1] ABI is the result of a variety of primary etiologies including but not limited to trauma, stroke, seizure, infection, and cardiac arrest that require specialized critical care services to optimize outcomes.[2] In fact, ABI from primary neurologic diagnoses accounts for 20% of all pediatric critical care admissions and more than 60,000 hospital admissions annually.[3,4] Incidence of ABI is bimodally distributed, with high frequencies of occurrence among young children birth to 2 years of age and adolescents, primarily due to traumatic injuries.[4,5] Children of all ages with ABI are known to experience long-term morbidities across physical, cognitive, emotional, and social health domains.[6–8] Many studies show young age at injury is an important risk factor for poorer outcomes after ABI,[9,10] likely due to the critical periods of brain development disrupted by the injury and resultant change in developmental trajectories. A recent study showed that 1 in 3 children suffered significant neurodevelopmental morbidity following an ABI.[11] Unfortunately, to date, few modifiable risk factors or effective interventions to improve outcomes have been identified for infants and young children following ABI.

Sleep disturbances are reported in more than half of children over age 3 years with ABI[12,13] and may represent a modifiable factor key to recovery following ABI.[14] Children with a broad

spectrum of ABI severity are at risk for sleep wake disturbances, which can persist years after injury and subsequently impact a variety of health outcomes and health-related quality of life.[12,15] Disrupted sleep following ABI in older youth and adult populations most commonly consists of insomnia and excessive daytime sleepiness, and has been associated with weakened executive function and poor health-related quality of life following ABI.[12,16] Similarly, sleep deprivation has been correlated with poorer emotional regulation, cognition, health-related quality of life, mood, and academic performance in previously healthy school-aged children and adolescents.[15] However, the burden of sleep disturbances in infants and young children is underevaluated in the ABI population.[12]

Adequate sleep is essential for normal brain development and maturation, making young children particularly vulnerable to long-term consequences of sleep disturbances and sleep deprivation.[1,17] Sleep is critical to processes restoring cellular homeostasis, memory consolidation, synaptic pruning, and neuronal migration.[18] Prior studies have demonstrated the functional implications of poor sleep on neurodevelopment of healthy infants and young children, including 1 study showing children with 3 or more nighttime awakenings had significantly lower cognitive functioning.[19] In healthy preschoolers, quality of sleep is associated with cognitive function, and worse sleep is associated with problematic behavioral outcomes such as aggressiveness, hyperactivity, and emotional dysregulation.[20,21]

Understanding sleep disturbances in infants and young children following ABI could help identify modifiable factors important for neurodevelopmental outcomes following ABI and help to guide interventions aimed at optimizing recovery. As such, the objectives of this study were to (1) describe sleep characteristics in infants and toddlers who were hospitalized in the pediatric intensive care unit (PICU) for ABI, (2) compare sleep in our ABI population with sleep in healthy infant and toddler historical controls, and (3) examine the relationship between sleep disturbances and neurodevelopmental outcomes within our cohort. Given the importance of sleep to healthy development in childhood, we hypothesized sleep disturbances after ABI would be associated with worse neurodevelopmental outcomes.

METHODS

Procedure and participants

This retrospective cohort study was performed at Oregon Health & Science University. We included 68 infants and toddlers aged 2–32 months (mean = 11.03, standard deviation [SD] = 8.25) who received care in the Pediatric Critical Care and Neurotrauma Recovery Program (PCCNRP) clinic after surviving critical care hospitalization for ABI from October 2017 to May 2021. Included participants completed a follow-up visit at the PCCNRP between 1 and 3 months after hospital discharge. PCCNRP referrals, follow-up patterns, and program details were previously described.[22,23] Briefly, the PCCNRP receives systematic referrals for children with primary ABI diagnoses (trauma, cardiac arrest, stroke, neurological infections, refractory status epilepticus) and as needed referrals from clinical teams for other diagnoses. Follow-up rates are consistently > 70% following hospital discharge. Procedures were approved by the Institutional Review Board.

Demographic and clinical variables

We recorded demographic information and markers of severity of ABI on presentation from the electronic health record. We categorized admission diagnosis based on PICU attending documentation: traumatic brain injury; hypoxic ischemic injury from cardiopulmonary arrest; status epilepticus; infectious or inflammatory disease; stroke; or other (including extracorporeal support for sepsis, pulmonary hypertension, or hemophagocytic lymphohistiocytosis; osmotic demyelination syndrome; hydrocephalus; traumatic amputation with hemorrhage but without head trauma). Illness and injury severity were approximated by length of stay in the hospital and PICU, admission Glasgow Coma Scale, discharge to rehabilitation or nursing facility, and need for any critical care interventions (mechanical ventilation, neurosurgical intervention, vasopressor infusion, central venous line placement, arterial line placement, intracranial pressure monitor, dialysis, therapy for refractory status epilepticus, extracorporeal support, or in-hospital cardiopulmonary resuscitation). Premorbid chronic neurodevelopmental disorders (developmental delay, autism spectrum disorder) and medical conditions (congenital heart disease, pulmonary hypertension, gastrointestinal malformations, genetic conditions, epilepsy, and neurologic and neuromuscular conditions) were recorded. Presence of any chronic condition was dichotomized for analysis consistent with prior work.[22,24,25] Functional Status Scale scores preadmission, at discharge, and at follow-up assigned by a PICU attending were also recorded from medical records using previously described methodology.[24] Change from baseline Functional Status Scale was dichotomized as no change or change ≥ 1 point for analysis.

Sleep measures

We utilized the Brief Infant Sleep Questionnaire (BISQ) to evaluate sleep in this population (see Appendix A in the supplemental material). The BISQ is a widely utilized questionnaire consisting of 13 questions assessing the child's sleep during the previous 2 weeks in ages 0–32 months. The following variables are included: age and sex of child, birth order, night sleep duration, day sleep duration, number of night wakings, duration of night wakings, nocturnal sleep onset time, settling time, method of falling asleep, location of sleep, body position during sleep, and role of person who completed the questionnaire. Location of sleep and body position during sleep were recorded as measures of sleep safety for infants < 12 months of age. Data from the BISQ show significant correlation with data from actigraphy devices and sleep diaries.[26] A longitudinal study comparing frequency and duration of night wakings in infants aged 3–18 months evaluated BISQ, actigraphy, and sleep diaries observing significant correlations between all 3 measures.[27] Parents or legal guardians completed the BISQ during their child's PCCNRP follow-up visit 1–3 months after hospital discharge.

Developmental measures

Developmental and adaptive functioning outcomes were assessed at the follow-up appointment. The Adaptive Behavior Assessment System, third edition (ABAS-3) provides a comprehensive assessment of a child's adaptive skills compared to children of the same age. It is widely used to evaluate for developmental delays, intellectual disabilities, social and motor impairments, and neuropsychological disorders. For children aged 0–5 years, parents/caregivers complete a questionnaire to provide information about the child's adaptive behaviors. The questionnaire contains 241 items for children ages 2–5 years and 170 for those 0–1 year of age. Items and results standardize scores in Conceptual, Social, and Practical domains as well as an overall General Adaptive Composite (GAC), which summarizes performance across all domains. The ABAS-3 has shown good performance in a variety of clinical populations including children with intellectual disabilities, as well as validity in detecting neurodevelopmental disabilities.[28,29] The Conceptual Composite includes the subscales of communication, functional preacademics (only for those aged 2–5 years), and self-direction skills; the Social Composite includes the subscales of leisure and social skills; and the Practical Composite includes the subscales of community use (only for those aged 2–5 years), home living (only for those aged 2–5 years), health and safety, and self-care skills. Also, there is an additional motor subscale that is included in the overall GAC but not any of the other domains. All composite, domain, and subscales scores are normalized by patient age. We defined a clinically important score as scores < 90 on the GAC, corresponding to a "low average" categorization or worse adaptive skills, as this is used to trigger early intervention referrals in the clinical program.

The Bayley Scales of Infant and Toddler Development, third edition (Bayley-III) is a standardized measure of development. It provides subscale scores including language (49 items in the receptive domain and 48 in the expressive domain), cognitive (91 items), and motor (66 items in fine motor and 72 in gross motor) domains. It also includes an optional parent-completed social–emotional scale and adaptive behavior scale derived from the ABAS-2. The Bayley-III is widely used to assess for autism spectrum disorder and other developmental disabilities in children aged 16 days–42 months[30] and has been shown to have strong predictive validity in detecting developmental delays in this age group.[31] We defined Standard Scores < 90 as clinically important across the three developmental subscales, corresponding to a "low average" categorization or worse. We use the "low average" or worse categorization because it triggers referral to early intervention services in clinical practice for the ABI cohort. Bayley outcomes were corrected for prematurity when applicable per test manual scoring instructions.

Statistical analysis

Despite known differences in sleep patterns in infants < 12 months and toddlers, we observed minimal variation in measured sleep characteristics on the BISQ among children ages 2–32 months in our ABI sample. Thus, infants and toddlers were grouped together for most data analyses. Infant-specific sleep measures such as sleeping arrangement and body position were examined in infants aged < 12 months only. Descriptive statistics were used to summarize results for the cohort. Data with a non-normal and normal distribution were described using median with interquartile range and mean with SD, respectively.

t tests were used to compare sleep in infants and toddlers with ABI with that of healthy infants from a historical control cohort.[26] Infants and toddlers with ABI were grouped by < 3 or ≥ 3 nighttime awakenings as the primary sleep disturbance exposure variable due to the previously observed association between ≥ 3 awakenings and poorer outcomes in healthy children.[19] This prior work identified a nonlinear relationship in infants and toddlers between frequency of awakenings and developmental outcomes, but both age groups had lower Bayley outcomes with ≥ 3 nighttime awakenings.[19] Three or more awakenings is also more than 1 SD above normal across ages in healthy children.[32] Seven patients had missing data for this question, and were included in the < 3 category for comparative analyses. We used chi-square with Fisher's exact correction for expected cell counts < 10 and Mann-Whitney *U* tests as appropriate to compare variables across sleep disturbance groups based on nighttime awakenings to assess for confounding variables. ABAS-3 GAC was evaluated as the primary outcome, and other measures were explored as secondary outcomes. Spearman's correlation (r^s) assessed relationships between sleep characteristics and neurodevelopmental outcomes (ABAS-3 GAC, ABAS-3 Domain Composites, Bayley-III Composite scores). Missing data were excluded pairwise.

We evaluated demographic and clinical characteristics' association with ABAS-3 GAC using simple linear regression. We used multiple linear regression to determine if sleep disturbances predicted adaptive functioning on the ABAS-3 GAC when controlling for demographic and clinical variables. A priori we chose to include age given expected differences in healthy sleep patterns. Other covariates were identified in bivariate analyses at a significance level of $P < .10$. Covariates for the final multivariable model included age, preadmission chronic conditions, primary trauma diagnosis, length of stay, and any worsening from preadmit Functional Status Scale. Length of stay was significantly skewed and was categorized by quartiles for entry into regression models, with longest quartile length of stay corresponding to ≥ 10 days in the hospital. All variables were dichotomized to reference all other patients for the variable in regression models. Regression results were reported as β-coefficients with 95% confidence interval. Variables were tested for collinearity and multicollinearity in the multivariable model. No variables were excluded as the variance inflation factors were all < 5 and correlation coefficients < 0.6. Backward regression was explored to assess overfitting, comparing r^2 to adjusted r^2 at each level of variable entry, with differences ranging 3–5% between models. Minimal differences in adjusted r^2 between models were noted, and we reported results of the full model. All analyses were performed using Statistical Package for the Social Sciences (IBM Corp. IBM SPSS Statistics for Macintosh, Version 27.0. Armonk, NY: IBM Corp) and significance was defined as $P < .05$.

RESULTS

Sample characteristics

We evaluated 68 infants and young children following ABI (**Table 1**). Most (62%) were male with a median age of 7.4 months (interquartile range = 4.7, 14) and mean age of 11.0 months (SD = 8.3). Etiology of ABI included 43 (63%) trauma, 7 (10%) infectious, 3 (4%) hypoxic ischemic encephalopathy from cardiac arrest, 4 (6%) stroke, 5 (7%) refractory status epilepticus, and 6 (9%) other diagnoses. Half of the sample required critical care intervention, including 31% requiring intubation. Nine (13%) patients had preadmission chronic conditions including 3 (4%) with preexisting developmental delay.

Sleep characteristics and comparison to healthy controls

Twelve (18%) children with ABI had ≥ 3 nighttime awakenings defining the sleep disturbance group. There was no significant difference in demographic characteristics, measures of severity of presentation, or interventions received in the PICU between groups (**Table 1**). Median age in children with ≥ 3 nighttime awakenings was not significantly different from those with < 3 awakenings, and the proportion of infants < 12 months of age also did not differ significantly between sleep disturbance groups. Significantly more parents who reported that their child's sleep was a problem on the BISQ had a child with ≥ 3 nighttime awakenings (50% vs 13%, $P = .003$). Average night sleep duration in children with ABI was 9 hours (SD 1.8), with only 11 (16%) sleeping for the recommended minimum duration of 11 hours per night.[33] Of the 46 infants < 12 months old, 13 (28%) reported cosleeping with parents and 13 (28%) reported sleeping on their stomach (see **Table S1**).

As shown in **Table 2**, compared to healthy children, children with ABI had significantly shorter average night sleep duration ($P = .014$), longer average day sleep duration ($P < .001$), and increased average duration of nighttime awakenings ($P < .001$). On average, nighttime sleep duration was 40 minutes shorter and duration of nighttime awakenings was twice as long in children with ABI compared to healthy children. Mean frequency of nighttime awakenings was not significantly different between healthy and ABI populations ($P = .68$). Average age of the healthy cohort (mean = 12.30 months, SD = 5.51 months) was slightly older than the ABI population (mean = 11.0 months, SD = 8.25 months); however, as noted, sleep outcomes did not vary by age within the ABI cohort.

Sleep disturbances and outcomes

Overall cohort scores on the ABAS-3 and Bayley-III measures fell within normal limits. Clinically important scores were found in 13% on ABAS-3 GAC, 12% on Bayley-III Cognitive, 18% on Bayley-III Language, and 12% on Bayley-III Motor composite scores. As seen in **Table 3**, number of night awakenings was significantly and negatively correlated with ABAS-3 GAC ($r^s = -.42$), ABAS-3 Practical Composite ($r^s = -.52$), and ABAS-3 Social Composite ($r^s = -.41$). Duration of night awakenings negatively correlated with Bayley-III Cognitive outcomes ($r^s = -.40$).

Regression model

Table 4 displays the results of simple regressions showing associations between ABAS-3 GAC and demographic and clinical characteristics. Children with nontrauma diagnoses, preadmission chronic conditions, seizure during admission, longer duration length of stay, and sleep disturbance had worse ABAS-3 GAC scores (all $P < .05$). When controlling for age, preadmission chronic conditions, seizure, primary trauma diagnosis, length of stay, and any worsening from preadmission Functional Status Scale, sleep disturbance with ≥ 3 nighttime awakenings was associated with significantly lower scores for ABAS-3 GAC (β = −11.3; 95% confidence interval = −19.2, −3.5; **Table 5**). Sleep disturbance group was the only significant variable in the full model and contributed 16% to the overall model variance, with a full model adjusted $r^2 = .3$.

DISCUSSION

In our sample, nearly 1 in 5 infants and children with ABI following critical care hospitalization exhibited important sleep disturbances, defined as 3 or more nighttime awakenings, and 84% were not meeting the recommended nightly duration of sleep during the acute phase of recovery. Moreover, sleep characteristics in our ABI cohort differed significantly from healthy control populations. The results suggest that ABI negatively influences sleep in this age group, particularly evidenced by shorter nighttime sleep duration and longer duration of nighttime awakenings. Importantly, we found worse sleep correlated with poorer outcomes on adaptive and developmental measures and that having 3 or more night awakenings was strongly associated with worse overall adaptive skill functioning, even when controlling for other demographic and clinical covariates.

The current findings suggest a need for increased screening, education, and intervention for sleep in this vulnerable patient population as sleep disturbances may represent a modifiable target to improve outcomes following ABI. Prior studies show that sleep is integral to normal brain development and the healing of the brain following injury.[1,17] This is likely due to restorative sleep being associated with gray and white matter volumes in the dorsolateral, hippocampal, and prefrontal cortexes, which play a role in executive functioning, learning, memory, and emotional and behavioral regulation.[34] Sleep is critical to processes restoring cellular homeostasis, memory consolidation, synaptic pruning, and neuronal migration.[18] Additionally, deep slow-wave sleep is integral in clearing waste from the brain in the recently described glymphatic pathway, which is likely even more important in the injured brain.[35]

Much of the extant literature regarding ABI and sleep is focused on older children, with limited studies examining sleep disturbances after ABI in infants and young children. More specifically, sleep disturbances have been reported in 24% of infants with inflicted traumatic brain injury at 5-year follow-up.[36] Similarly, in a neonatal ICU population following hypoxic ischemic brain injury, Edmonds et al found that sleep difficulties persisted 2 years after injury.[37] Similar associations between brain injury and sleep disturbances, particularly sleep

Table 1—Demographics and clinical characteristics of children with ABI and comparison by sleep disturbance groups with < 3 or ≥ 3 nighttime awakenings.

	Total (n = 68)	< 3 Nighttime Awakenings (n = 56)	≥ 3 Nighttime Awakenings (n = 12)	*P*
Age at evaluation, median months (IQR)	7.4 (4.7, 14.0)	8.1 (3.8, 17.3	6.6 (2.4, 12.1)	.53
Age at evaluation < 12 months	46 (68%)	37 (66%)	9 (75%)	.55
Male sex	43 (62%)	35 (63%)	8 (67%)	.79
Race				.79
White	54 (79%)	45 (80%)	9 (75%)	
African American	0 (0%)	0 (0%)	0 (0%)	
Asian American	2 (3%)	1 (2%)	1 (3%)	
American Indian	1 (2%)	1 (2%)	0 (0%)	
Multiracial	5 (7%)	4 (7%)	1 (8%)	
Not reported	6 (9%)	5 (9%)	1 (8%)	
Hispanic ethnicity	11 (16%)	10 (18%)	1 (8%)	.42
Medicaid insurance	36 (53%)	29 (52%)	7 (58%)	.68
Primary diagnosis				.69
Traumatic brain injury	43 (63%)	35 (63%)	8 (67%)	
Cardiac arrest	3 (4%)	2 (3%)	1 (8%)	
Stroke	4 (6%)	4 (7%)	0	
Infectious	7 (10%)	5 (9%)	2 (17%)	
Status epilepticus	5 (7%)	4 (7%)	0	
Other	6 (9%)	5 (9%)	1 (8%)	
Chronic condition, any	9 (13%)	8 (14%)	1 (8%)	.58
Medical	7 (10%)	6 (11%)	1 (8%)	>.99
Developmental	3 (4%)	2 (3%)	1 (8%)	.45
FSS > 6 at admission	4 (6%)	3 (5%)	1 (8%)	.69
Any FSS worsening	15 (22%)	13 (23%)	2 (17%)	.62
GCS at admission, median (IQR)	15 (15,15)	15 (14, 15)	15 (15,15)	.22
Hospital length of stay, days, median (IQR)	2.6 (1.2, 10.0)	3.8 (1.4, 12.3)	1.2 (0.6, 8.5)	.53
Critical care intervention, any	34 (50%)	29 (52%)	5 (42%)	.53
Intubation	21 (31%)	20 (36%)	1 (8%)	.09
Neurosurgery	12 (18%)	9 (16%)	3 (25%)	.46
Central line	16 (24%)	14 (25%)	2 (17%)	.54
External ventricular drain	3 (4%)	3 (5%)	0 (0%)	.41
Hemodynamic resuscitation	10 (15%)	8 (14%)	2 (17%)	.83
ECMO	3 (4%)	3 (5%)	0 (0%)	.41
Dialysis	2 (3%)	0 (0%)	2 (4%)	.51
Targeted temperature	4 (6%)	4 (7%)	0 (0%)	.34
Osmolar therapy	3 (4%)	3 (5%)	0 (0%)	.41
Seizure during admission	15 (22%)	13 (23%)	2 (17%)	.62
Required NG/NJ feeds	16 (23.5)	15 (27%)	1 (8.3)	.17
Rehabilitation discharge	2 (3%)	2 (4%)	0 (0%)	.51
Parent-defined sleep problem[a]	13 (19%)	7 (13%)	6 (50%)	.003

[a]Parent-defined sleep problem based on responses to Brief Infant Sleep Questionnaire question "Do you consider your child's sleep a problem?" ABI = acquired brain injury, ECMO = extracorporeal membrane oxygenation, IQR = interquartile range, FSS = functional status scale, GCS = Glasgow coma scale, NG = nasogastric, NJ = nasojejunal.

Table 2—Comparison of sleep in pediatric ABI cohort to historical cohorts of healthy children.

	Healthy Cohort[a] (n = 57)	ABI Cohort (n = 68)	*P*
Nighttime sleep duration, hours, mean (SD)	9.67 (1.08)	9.01 (1.84)	.01
Daytime sleep duration, hours, mean (SD)	2.32 (.79)	3.18 (1.61)	<.001
Number of nighttime awakenings, mean (SD)	1.83 (1.45)	1.73 (1.24)	.68
Duration of nighttime awakenings, hours, mean (SD)	.34 (.34)	.72 (.65)	<.001

Comparison of sleep in infants and toddlers with ABI with a historical cohort of healthy children. Welch's *t* tests were used to compare groups. [a]Historical control cohort of healthy children reported in Sadeh.[26] ABI = acquired brain injury, SD = standard deviation.

onset and maintenance difficulties, are reported in over half of older children and teens following ABI.[25,38] A recent systematic review showed that at least 20% of older children following traumatic brain injury hospitalization had difficulties falling or staying asleep and also had fatigue, daytime tiredness, and nightmares and showed the available evidence supports the role of sleep disturbances in worsening of cognitive, behavioral, and quality of life outcomes.[12] Shay et al reported that children aged 3–6 years with traumatic brain injury had significantly more sleep problems at 6 months after injury than those with orthopedic injury, and this was associated with worsened executive function and behavioral outcomes.[21] Additionally, Tham et al identified an association between subjective report of sleep problems and poor communication and self-care up to 2 years postinjury in children 2–17 years old.[39] There is also a well-developed literature showing negative functional consequences in otherwise healthy older children and adolescents with inadequate sleep, aligning well with our findings.[15]

While the aforementioned research is important, the paucity of literature in infants and young children regarding the impact of sleep disturbances is particularly alarming when considering birth to 4 years is among the highest risk periods for pediatric ABI,[40] the high rates of morbidity following ABI in young children,[41] and the importance of sleep to healthy brain development and healing after injury. Prior work in children with ABI following critical care hospitalization within the first 3 months of hospital discharge showed 36% with new neurodevelopmental morbidity as diagnosed by a pediatric neuropsychologist.[2,22] Relatedly, a recent study examined neurodevelopmental outcomes in previously healthy infants who received pediatric critical care for management of bronchiolitis, showing abnormal Bayley-III scores in the majority of these infants at long-term follow-up.[42] This finding highlights the notion of secondary brain injury even outside primary neurologic admission diagnoses occurring in critically ill children due to factors such as inflammation, hypoxia, ischemia, and neuroactive medication exposure, among others. In infants and young children with primary neurologic diagnoses, particularly in traumatic brain injury, long-term morbidity in physical, cognitive, and psychosocial outcomes are well-described.[2,6,8] In particular, studies have observed persistent deficits in adaptive and cognitive behaviors including motor, visual processing, and language problems.[8] Current literature suggests risk factors for worse neurodevelopmental morbidity after ABI in infants and young children include young age at injury, increased duration of coma, seizures during hospitalization, and critical care interventions.[2,9,10,43] Unfortunately, many of these known risk factors are not modifiable, hindering development of effective interventions to improve neurodevelopmental outcomes.

Well-described functional implications of sleep disturbances support its role as a modifiable risk factor in young children with ABI. With this in mind, our study shows that those with ABI demonstrated shorter sleep duration and poorer sleep quality compared to healthy infants and children. Further, most young children with ABI in our sample did not meet the recommended nightly sleep duration,[33] spent more time asleep during

Table 3—Correlation between sleep variables and outcomes in infants and young children with acquired brain injury.

	Nighttime Sleep Hours	Daytime Sleep Hours	Number of Night Awakenings	Duration of Night Awakenings	Minutes to Fall Asleep
ABAS General Adaptive Composite	.014	−.122	−.421*	−.078	−.131
ABAS practical	.076	−.048	−.519**	.048	−.047
ABAS social	.085	−.125	−.406*	.044	−.063
ABAS conceptual	.068	−.027	−.190	.086	−.211
Bayley Cognitive	−.028	−.196	.012	−.401*	−.094
Bayley Language	−.355*	−.011	.057	.106	−.055
Bayley Motor	−.124	−.174	−.055	.049	−.070

Spearman correlation between sleep variables and adaptive and developmental outcomes in infants and young children with ABI. *Spearman correlation is significant at the 0.05 level (two-tailed). **Spearman correlation is significant at the 0.01 level (two-tailed). ABAS = Adaptive Behavior Assessment System.

Table 4—Simple linear regression evaluation of ABAS General Adaptive Composite with demographic and clinical characteristics.

Covariate	β-coefficient (95% CI)
Infant age < 12 months	0.5 (−7.0, 8.0)
Male sex	3.2 (−4.0, 10.0)
White race	4.7 (−3.9, 13.3)
Hispanic ethnicity	3.0 (−6.5, 12.5)
Medicaid insurance	2.2 (−4.9, 9.2)
Preadmission chronic condition present	−11.6 (−21.3, −1.9)
Trauma diagnosis	7.6 (0.8, 14.5)
Critical care intervention, any	0.1 (−7.0, 7.1)
Intubation	−2.9 (−10.5, 4.7)
Seizure during admission	−9.9 (−17.8, −2.1)
Length of stay, longest quartile	−10.6 (−18.0, −3.3)
Any worsening in Functional Status Scale	−7.8 (−15.9, 0.4)
Sleep disturbance (≥ 3 nighttime awakenings)	−10.0 (−18.6, −1.4)

Covariates dichotomized to reference all other patients within each variable for regression analysis. ABAS = Adaptive Behavior Assessment System, CI = confidence interval.

the daytime, and spent more time awake during the night than their healthy counterparts. Interestingly, our study also identified important safety concerns in nearly half of our ABI cohort including cosleeping with parents/caregivers, sleeping on their stomach, and not following the American Academy of Pediatrics recommendations for safe sleep.[44] In addition to increased screening for sleep disturbances in the ABI population, further exploration of this finding regarding safety practices is warranted to help identify areas for educational interventions in the ABI cohort to ensure safe sleep after hospital discharge.

Table 5—Multivariable model for ABAS General Adaptive Composite standard score.

Covariate	β-coefficient (95% CI)
Infant age < 12 months	0.9 (−5.6, 7.3)
Preadmission chronic condition present	−6.7 (−17.1, 3.7)
Trauma diagnosis	2.9 (−4.4, 10.1)
Length of stay, longest quartile	−5.8 (−18.3, 6.7)
Seizure during admission	−3.2 (−14.6, 8.2)
Any worsening in Functional Status Scale	1.0 (−9.0, 10.9)
Sleep disturbance (≥ 3 nighttime awakenings)	−11.3 (−19.2, −3.5)

Model statistics: $F = 3.11$; model P value = .01; adjusted $r^2 = .28$. Infant age included a priori; other covariates selected by entry in bivariate analysis at $P < .1$. Covariates dichotomized to reference all other patients within each variable for regression analysis. ABAS = Adaptive Behavior Assessment System, CI = confidence interval.

Our study also demonstrated an important association between increased sleep disturbances and lower adaptive and developmental scores at follow-up in the acute phase of recovery, consistent with our hypothesis and aligning with prior examinations of healthy infants. Other researchers have similarly reported that infants with a lower proportion of night sleep showed worse performance on working memory tasks[45] and that 3 or more nighttime awakenings was significantly associated with poorer cognitive and language development according to the mental development index in otherwise healthy children.[19] Similarly, our study identified an association between 3 or more night awakenings and significantly lower adaptive functioning scores following ABI. This finding suggests that poor sleep in the ABI population may lead to overall daily life challenges. More specifically, skills within the ABAS-3 Practical and Social Composites appeared most vulnerable to sleep disturbance in our cohort. Questions within those ABAS-3 composites focus on tasks germane to safety in the community, participating in the home environment, cooperating with parentally enforced safety measures, exhibiting early-life intellectual curiosity via play, and socially engaging with others. Those adaptive skills make sense conceptually when thinking about them in concert with our observation of night awakenings being associated with early-life cognitive skills directly assessed via the Bayley-III. The Bayley-III Cognitive scores reflect assessment of play, participation in a stimulating environment, and social engagement, which are the building blocks of early cognition.

Our study found that total sleep duration was not as predictive of developmental scores as other measures, such as duration and frequency of nighttime awakenings. This implies that quality and pattern of sleep in infants and children with ABI may play a larger role in functioning.[19,45] While quality of sleep is often measured through sleep efficiency in adults, it is less often measured or accounted for in infants and young children. Sleep efficiency refers to the amount of time spent actually sleeping vs total time in bed, accounting for sleep latency, wake after sleep onset, and total duration of nighttime sleep.[46] In adults, sleep efficiency is routinely associated with poorer functional and global health outcomes and is the target for many effective interventions in sleep disturbances like insomnia.[47] Future research should consider overall measures of sleep efficiency to determine relationship with neurodevelopmental outcomes and highlight the most important areas to target for intervention.

Future research should also consider the potential role of parent–child interactions in the development and maintenance of sleep problems following ABI. In healthy populations, frequent and prolonged night wakings are associated with reliance on parental presence (eg, soothing, holding, rocking) to fall asleep at bedtime and following night wakings.[48] Parents of children with recent or ongoing medical problems may be especially likely to be overly responsive to night waking due to feelings of worry or guilt.[49] Such dynamics have been identified in multiple pediatric populations and may be exacerbated by the conditions of hospitalization.[50] Understanding the possible contribution of parent–child interactions to night wakings, as well

as the perspectives of parents whose child received critical care for ABI, are therefore important goals for developing appropriate interventions.

Limitations

Our study has several limitations to consider. It is a single-institution, retrospective cohort study with a small sample size due to the unique population of interest. Heterogeneity in pediatric ABI populations is unavoidable, and there are known geographical and institutional differences in populations and acute treatments in pediatric critical care and ABI populations, which may limit generalizability of our findings.[3] Additionally, sleep measures were parent-reported, allowing increases in the likelihood of response bias due to parent perceptions which are influenced by parent demographic backgrounds, societal norms, and other factors such as being overly responsive to nighttime awakenings after a hospital admission. Furthermore, use of subjective report measures such as BISQ cannot diagnose sleep-disordered breathing, which could contribute to nighttime awakenings. Future studies should assess objective measures of sleep. We additionally evaluated nighttime awakenings as our primary exposure variable in order to compare with prior literature; however, exploration of other variables such as sleep efficiency or cutoffs for duration of nighttime awakenings may also reveal important associations in future work. Relationships between sleep disturbances and developmental outcomes were also limited to short-term follow-up, and baseline evaluations from prior to hospitalization were not available. Further longitudinal research is necessary to understand long-term implications of sleep disturbances following ABI.

CONCLUSIONS

Sleep disturbances are a common sequela following ABI in infants and young children in the months following hospital discharge and are associated with poorer adaptive and developmental outcomes. Sleep is vital to healthy brain development and repair following injury, suggesting sleep disturbances represent a modifiable target to improve outcomes. Sleep is underevaluated in infants and toddlers despite its known association with the cognitive and functional performance of older children with ABI. Identifying the role of sleep in ABI recovery for infants and young children will help guide clinical interventions and follow-up care to improve long-term outcomes in this population.

ABBREVIATIONS

ABAS, Adaptive Behavior Assessment System
ABI, acquired brain injury
Bayley, Bayley Scales of Infant and Toddler Development
BISQ, Brief Infant Sleep Questionnaire
GAC, General Adaptive Composite
PCCNRP, Pediatric Critical Care and Neurotrauma Recovery Program
PICU, pediatric intensive care unit
r^s, Spearman's correlation
SD, standard deviation

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