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Impact of Hands-On Care on Infant Sleep in the Neonatal Intensive Care Unit

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Summary. Study Objectives: Sleep disruption is increasingly recognized in hospitalized patients. Impaired sleep is associated with measureable alterations in neurodevelopment. The neonatal intensive care unit (NICU) environment has the potential to affect sleep quality and quantity. We aimed: (i) to determine the frequency and duration of hands-on care, and its impact on sleep, for NICU patients; and (ii) to assess the incidence of respiratory events associated with handling for a cohort of sick neonates. Methods: Term and near-term neonates admitted to the NICU and at risk for cerebral dysfunction due to severity of illness or clinical suspicion for seizures underwent attended, bedside polysomnography. Continuous polysomnogram segments were analyzed and data on handling, infant behavioral state, and associated respiratory events were recorded. Results: Video and polysomnography data were evaluated for 25 infants (gestational age 39.4 ± 1.6 weeks). The maximum duration between handling episodes for each infant was 50.9 ± 26.2 min, with a median of 2.3 min between contacts. Handling occurred across all behavioral states (active sleep 29.5%; quiet sleep 23.1%; awake 29.9%; indeterminate 17.4%; $P = 0.99$). Arousals or awakenings occurred in 57% of contacts with a sleeping infant. Hypopnea, apnea, and oxygen desaturation occurred with 16%, 8%, and 19.5% of contacts, respectively. Hypopnea was most likely to occur following contact with infants in active sleep (28%; $P < 0.001$). Conclusions: Infants in the NICU experience frequent hands-on care, associated with disturbances of sleep and respiration. The potential health and developmental impact of these disturbances merits study, as strategies to monitor sleep and minimize sleep-disordered breathing might then improve NICU outcomes. **Pediatr Pulmonol. 2017;52:84–90.** © 2016 Wiley Periodicals, Inc.

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INTRODUCTION

Sleep is essential for normal health and development in children. Alterations in sleep can have a negative impact on behavior,[1] and may result in cognitive impairment.[2] Disruptions in neonatal sleep have been associated with increased distractibility in later childhood.[3] Lower-risk preterm infants with disorganized sleep, rather than more mature sleep-wake cycling, have poorer emotional regulation and cognitive development at age 5 years.[4]

Disruptions of sleep duration and quality in hospitalized patients have been described both in adult and pediatric populations. Patients treated within the intensive care unit (ICU) setting show the most profound sleep abnormalities. The patient's underlying illness, the frequency of interventions and ICU care, and the effects of medications known to alter sleep physiology may all contribute to impaired sleep.[5] The physical environment of the ICU—bright lighting, high ambient noise levels, frequent alarms, and absence of day-night differentiation—also has the potential to disrupt sleep.

The important relationship between sleep and neurodevelopment has motivated attempts to preserve infant sleep within the neonatal intensive care unit (NICU). Infants frequently spend prolonged periods of time (weeks to months) in the NICU,[6] at a stage of dramatic brain growth and development. Methods that have been proposed to reduce sleep disruption include protocols for clustering of care and the Newborn Individualized Developmental Care and Assessment Program (NIDCAP).[7]

We hypothesized that handling of infants occurs frequently, without regard to the patient's behavioral state, and results in substantial sleep disruption despite systematic attempts to provide clustered care within the NICU. The primary aim of this study was to determine the frequency and duration of hands-on caregiving, and its impact on polysomnogram-defined sleep-wake state, for newborn infants admitted to our NICU. Using the video recordings of the infant's surroundings, as routinely captured during polysomnography (PSG), we were able to continuously measure hands-on infant care and relate this to sleep state. This approach enabled evaluation of the effect of handling on infants' respiratory instability, and provided an opportunity to determine if any effects were dependent on the infants' sleep-wake state upon initiation of hands-on care. Discovery of associations between caregiving during sleep and infants' respiratory instability could help guide future models of NICU care in an effort to optimize outcomes.

MATERIALS AND METHODS

This study was approved by the University of Michigan Institutional Review Board. A parent of each enrolled infant provided written informed consent.

Participants

Term and late preterm neonates (estimated gestational age at birth $\geq$35 weeks) admitted to the NICU and at risk for cerebral dysfunction due to severity of illness or clinical suspicion for seizures were candidates for a study of neonatal neuromonitoring that included full PSG. Exclusion criteria were: presence of multiple congenital anomalies, a confirmed genetic syndrome, gestational age $<$35 weeks, or illness severity that precluded PSG recording. All subjects were stable and convalescing, although they still required NICU care. Our NICU promotes clustered care provision, but does not adhere specifically to NIDCAP models. Feeding schedules are typically every 3 hr for patients receiving tube-feedings and either regularly scheduled or infant-driven for those not dependent on tube feedings. Vital signs are typically recorded in association with feeds in infants of a gestational age and illness severity eligible for a research PSG. The present report is a secondary analysis of the neuromonitoring study; some of the subjects' quantitative PSG analyses were reported previously.[8]

Polysomnography

Enrolled infants underwent a formal, attended, bedside PSG. A sleep technologist was present for the study duration to ensure proper equipment function and to record pertinent infant behavioral observations. Monitoring included a 9-channel neonatal montage electroencephalogram (EEG), bilateral electro-oculogram, chin and bilateral anterior tibialis surface electromyogram, thoracic and abdominal excursion (by inductance plethysmography), nasal pressure, oronasal airflow (thermocouple), snoring sound, oxygen saturation, electrocardiogram, and continuous digital video. All studies were scored according to standard neonatal criteria[9] by a single, registered polysomnographic technologist experienced with neonatal recordings, and reviewed by a board-certified sleep medicine physician. Behavioral states were assigned to discrete 30 sec epochs for the duration of the PSG.

Video Analysis

Continuous 4 hr PSG segments were analyzed by individual investigators (JL, MS, and JK). Data collected on all video segments were reviewed for scoring consistency by a single investigator (JL). The 4 hr duration of video analysis was selected in order to include each behavioral state and the typical clinical care pattern. The average term infant's sleep-wake cycle lasts approximately 50–60 min, so several cycles should be included in a 4 hr PSG sample. Typical NICU patient care includes nursing assessment no less frequently than every 4 hr and most infants are fed every 3 hr, so the 4 hr study

segment included these routine facets of care for each patient. The start time of video analysis began 1 hr after PSG initiation as multiple adjustments to PSG-study equipment are often necessary at the beginning of a PSG recording. PSGs were included only if the video component captured most of the infant within the screen throughout the recording; all 25 included subjects had a full 4 hr PSG segment available for analysis.

Episodes of Contact

Handling was defined as direct contact with the infant or manipulation of their immediate environment (contact with items within the isolette). Contact start times and end times were recorded. Contacts were coded as discrete episodes if the interval between them exceeded 30 sec (to correspond with the 30 sec scoring epochs of the PSG). Apparent reasons for initiation of handling were also recorded, and classified as: clinical care provision, technical (related to the PSG recording), or uncertain. Clinical care provision included medical interventions (vital sign measurements, medication administration, physical examination, etc.) or routine infant care (diaper change, feeding, or comforting a fussy baby). Adjustments of equipment necessary for optimal signal recording for the PSG were defined as technical. Handling that appeared unprompted or without evident purpose was categorized as uncertain (e.g., epochs during which a family member held a sleeping infant's hand or a caregiver rearranged items within the isolette).

Behavioral State

The infants' PSG-defined behavioral state at the onset and end of each contact episode was recorded. The latency from the end of a handling episode until the next PSG epoch of active or quiet sleep was also recorded. These states included: awake, active sleep, quiet sleep, and indeterminate states.[9] The major features of wakefulness, active sleep, and quiet sleep for term neonates are summarized in Table 1.[10,11]

Associated Physiologic Events

To determine if handling prompted respiratory instability, hypopnea, apnea, and oxygen desaturation events during or immediately following the contact (occurring within 60 sec, two PSG epochs, of cessation of touch) were documented. Oxygen desaturation episodes were defined as SpO_2 <90% with sustained, high quality tracing on pulse oximetry monitoring. Apneic and hypopneic episodes were defined per the American Academy of Sleep Medicine Manual criteria for children.[12] Apnea was defined by a decrease in air flow by ≥90% of the pre-event baseline, for the length of at least two respiratory cycles (central apnea had an associated ≥3% decrease in oxygen saturation, bradycardia, or arousal; obstructive apnea did not require associated physiologic consequences). Hypopnea was defined as a decrease in nasal pressure by ≥30% of the pre-event baseline for a minimum of two breaths, when accompanied by a ≥3% decrease in oxygen saturation or by an arousal or awakening. To assess for sleep fragmentation due to handling, arousals from sleep, or awakening (transition from sleep to awake), within 60 sec (two epochs) of handling, but without associated respiratory events, were also recorded.

Data Analysis

The number and duration of contacts, as well as the purpose of the contact, were recorded for each handling episode for each infant. These data were analyzed according to the baseline and final behavioral state. Inter-contact intervals were calculated to evaluate the range of duration of undisturbed rest time for each infant. Respiratory events and arousals with a temporal relation to handling were recorded and analyzed in relation to the categories of contact (clinical, technical, or uncertain). Descriptive data are presented as mean ± standard deviation or median and interquartile range (IQR), as appropriate based on

TABLE 1—Comparison of Major Features of Behavioral States in the Term Neonate[1]

	Awake	Active sleep	Quiet sleep
EEG	Continuous, low to medium voltage mixed frequencies	Similar to awake EEG	High voltage bursts alternating with lower voltage interburst periods "tracé alternant"
Eye activity	Eyes open	Closed, intermittent periods of rapid eye movement	Closed, absent, or infrequent eye movement
Tone/movement	High tone/spontaneous generalized movements	Small and large body movements	Scant movements, occasional sucking, or startle
Heartbeat	High rate, irregular	Variable	Regular
Respirations	High rate, irregular	Variable	Regular

EEG, Electroencephalogram.
[1]Indeterminate sleep is designated when an infant has closed eyes but clinical and EEG features include elements of both active and quiet sleep.

the data distribution. The Chi-square goodness of fit test was used to evaluate the distribution of category of handling by behavioral state. Generalized estimating equation models, which account for dependence between individual infants' data, were used to assess associations between handling reasons and initial sleep state with occurrence of respiratory events. Linear mixed models, including random intercepts for infant to account for dependence, were used to assess the average duration of handling episodes between contacts with and without provoked respiratory events and across the different reasons for contact. All statistical analyses were performed using Stata version 13.1 (College Station, TX).

RESULTS

Video and PSG data were evaluated for 25 term or near-term infants (mean EGA 39.4 ± 1.6 weeks). The mean apnea-hypopnea index (AHI) of the 4 hr PSG segments was 13.1 ± 11.9. Subjects had a median of one apnea of duration longer than 10 sec during the 4 hr PSG (IQR = 2). Demographic, clinical, and PSG data are summarized in Table 2.

All of the infants underwent frequent handling, with 595 contacts, in total, recorded during the collective 100 hr of video analyzed. There was a median of 24 contacts per infant (IQR = 17). Most of the recordings (N = 18 of 25; 72% of contact episodes) occurred exclusively during the night shift (7 pm–7 am), so analyses by time of day were not possible.

The total duration of hands-on care lasted an average of 65.3 ± 33.0 min, or 27% of the 4 hr of PSG (range 36.2 [15%] to 185.3 min [77%]). The maximum duration between handling epochs was, on average, 50.9 ± 26.2 min. A median of 2.3 min elapsed between episodes of contact (IQR = 5.7). When only contacts initiated for clinical purposes were counted, the median inter-contact interval was 12.7 min (IQR = 8.7). The maximum duration between clinically-indicated handling episodes was, on average, 66.5 ± 37.6 min (median 58.4 min, IQR = 53.0 min), and only half of the infants (12/25) were given sufficient time to complete a full 60 min sleep-wake cycle between episodes of clinical care provision.

Contacts were most often initiated for clinical care provision (44%; technical 34%; uncertain 22%). These contacts were initiated across all behavioral states (active sleep 29.5%; quiet sleep 23.1%; awake 29.9%; indeterminate 17.4%; $P = 0.99$). Contacts for clinical care were generally of longer duration than contacts for technical reasons (mean 4.4 ± 0.6 min vs. 2.2 ± 0.6 min, $P = 0.002$). There were no differences in duration among other categories of contact.

Hands-on care resulted in arousals or awakenings in 57% of all episodes of contact with a sleeping infant. For infants who were awake at the end of a handling episode, it took a median of 4 min (eight PSG epochs, IQR = 13 epochs) to return to sleep.

Handling was frequently followed by respiratory events: hypopnea, apnea, and desaturation occurred within 60 sec in 16%, 8%, and 19.5% of all contacts, respectively (Table 3). Hypopnea preceded by handling was more likely to occur among infants in active sleep, as opposed to any other behavioral state (28% vs. 16% quiet sleep and 8% awake; overall $P < 0.001$). Handling initiated for provision of clinical care, as opposed to handling for technical or other reasons, was more likely to result in oxygen desaturation (documented with an optimal oximetry signal; 32% vs. 11% and 9%; overall $P < 0.001$), though not statistically more likely to result in apnea or hypopnea. On average, contact duration was longer for handling episodes that provoked hypopnea or oxygen desaturation than for handling that had no associated respiratory events (Table 4).

TABLE 2— Demographic, Clinical, and Polysomnography Profiles of 25 Infants

Gestational age, mean (SD), wk	39.4 (1.6)
Birth weight, mean (SD), kg	3.39 (0.56)
Sex	
Male	n = 15
Female	n = 10
Electrographic seizures during NICU admission	n = 9 (36%)
Head circumference, mean (SD), cm	34.7 (1.8)
1 min Apgar score, median (IQR)	3 (0–6)
5 min Apgar score, median (IQR)	7 (4–10)
Arousal index, mean (SD), arousal/hr sleep	23.5 (16.0)
Apnea/hypopnea index, mean (SD), event/hr sleep	13.1 (11.9)
Quiet sleep apnea/hypopnea index	7.7 (7.6)
Active sleep apnea/hypopnea index	21.9 (21.3)
Obstructive apnea index	1.1 (2.0)
Central apnea index	3.5 (4.9)
Mean % oxygen saturation during sleep, mean (SD)	96.4 (1.8)
Minimum % oxygen saturation during sleep, mean (SD)	74.4 (16.4)

DISCUSSION

Despite clinical protocols for developmentally appropriate clustered nursing care, we found that hands-on care provided to convalescent infants in a level IV NICU is frequent and often associated with respiratory instability. To our knowledge, this is the first study to employ attended PSG, the objective gold-standard for sleep-wake state monitoring, to evaluate the effects of hands-on NICU care on neonatal sleep. We report here that handling of infants in the NICU is frequent, administered across all sleep-wake states, and associated with both substantial sleep disruption and potentially consequential respiratory events.

TABLE 3— Respiratory Events Associated With Contacts, Across Sleep-Wake States

		Hypopnea[2]	Apnea	Desaturation
Sleep-wake state	Number of contacts[1]	n (% of total contacts that provoked hypopnea)	n (% of total contacts that provoked apnea)	n (% of total contacts that provoked desaturation)
Awake	173	14 (8)	6 (3)	41 (24)
Active sleep	171	48 (28)	22 (13)	29 (17)
Quiet sleep	135	21 (16)	9 (7)	20 (15)
Indeterminate	101	11 (11)	9 (9)	26 (26)

[1]Contacts were evenly distributed across sleep-wake states ($P = 0.99$).
[2]Contact with infants in active sleep were statistically most likely provoke hypopnea, compared with contacts during other sleep-wake states ($P < 0.001$).

Few published reports have assessed objective measures of sleep and sleep disturbance in relation to NICU care. In a recent case study, the relation of caregiving to sleep patterns was assessed using continuous EEG, rather than PSG, for a single patient treated with therapeutic hypothermia for hypoxic ischemic encephalopathy; findings also suggested frequent handling and resultant sleep disruption.[13] In another study, observers recorded preterm infants' sleep-wake states and movements, along with nursing cares, every 10 sec for 4 hr intervals (no PSG or respiratory events were recorded). Quiet sleep was infrequent when the infant was with a caregiver. The amount of time spent in specific sleep-wake states differed when the infant was alone versus with the nurse and also varied by type of nursing care (routine vs. procedural).[14]

Use of formal PSG to determine behavioral state and to define respiratory events is a significant strength of our study. Standard NICU cardiorespiratory monitors use time-based criteria alone to define apneic episodes (absence of respiratory effort for $\geq$20 sec). PSG has higher sensitivity and specificity to identify respiratory events through use of a combination of measured parameters. This allows for quantification of subtle respiratory changes that may have an important cumulative effect but are unlikely to be identified through standard bedside monitoring. Only three of our study subjects had more than four PSG-defined apneic events that lasted >10 sec during their 4 hr PSG segments (these outliers had 26, 32, and 39 apneas >10 sec). This suggests that clinical alarm parameters are unlikely to have signaled respiratory events for most of these infants (data are not available for bedside alarms or events >20 sec for these subjects).

TABLE 4— Association Between Risk of Provoked Respiratory Events and Duration of Handling Among 25 Near- and Full-Term Newborns

	Length of contact (minutes), mean (SE)	P-value[1]
Hypopnea	5.46 (0.74)	<0.001
No hypopnea	2.72 (0.47)	
Apnea	5.05 (1.02)	0.038
No apnea	3.04 (0.49)	
Desaturation	6.49 (0.66)	<0.001
No desaturation	2.25 (0.46)	

[1]Analysis was adjusted to account for clustering of individual subjects' data. Means provided are marginal means estimated from the final linear mixed model, with duration of contact as the outcome and event as the predictor.

The infants included in our study had both provoked and spontaneous apnea and hypopnea, even though none of these patients had clinical suspicion for sleep-disordered breathing. We are unable to comment on any unprovoked respiratory events. However, it was clear that handling of infants in active sleep was the most likely to provoke respiratory events. This finding is consistent with the known physiologic vulnerability to apnea during active sleep.[15] Our data suggest that modification of NICU hands-on care practices, specifically to avoid handling infants during active sleep, might contribute to reduction in clinically significant apneas and hypopneas. While the effects of these repeated abnormalities in respiratory patterns on neurodevelopment are not definitively known, increased number of hospital days with recorded apnea in very low birthweight infants has been associated with neurodevelopmental impairment in early childhood,[16] and persistent periodic breathing is sometimes associated with transient decreases in brain tissue oxygenation.[17]

Study of clinician behaviors can be challenging, due to the Hawthorne effect. We may have avoided this difficulty. The care teams, though aware that video is always recorded during PSGs, did not know that the video of the neonate would be analyzed to quantify hands-on care. However, this study has other limitations. Standard neonatal PSG utilizes multiple monitoring channels, which can require frequent brief repositioning to optimize the recording quality. Approximately one-third of handling episodes in our study were prompted by technical adjustments related to PSG. However, these episodes were significantly less likely to result in

desaturation than handling related to clinical care ($P < 0.001$), possibly because they were of shorter duration than clinical care ($P = 0.002$).

While our study examines the interplay of handling and sleep, the infants in our study were not insulated from other factors that could disrupt sleep, such as noise, bright lights, and medication effects. We also did not distinguish between different types of clinical care provision (e.g., feeding vs. physical examination), but it is possible that some types of care are more or less disruptive to infant sleep and respiratory patterns than others. The degree to which any of these factors contributed to our findings was not evaluated and remains unknown. Additionally, it must be acknowledged that infants in NICU often require care that cannot be deferred based on sleep-wake state. A comprehensive approach designed to optimize sleep-wake cycling for NICU patients would likely need to incorporate all facets of the caregiving environment and the patient's clinical state.

NIDCAP is a structured program of care delivered by specially trained caregivers that includes environmental modifications and behavioral assessment to provide developmentally appropriate individualized care to high risk neonates.[7] In a randomized controlled trial there was no difference in quiet sleep duration between patients provided NIDCAP versus standard NICU care.[18] NIDCAP is not utilized in our NICU, and as such this study is unable to provide evidence for or against that care model.

The newborns' tolerance of handling was associated with their baseline sleep-wake state; however, handling of neonates in this study was observed to take place evenly, across all behavioral states ($P = 0.99$). Active sleep in the neonate is characterized by behaviors that may outwardly appear similar to an awake infant, with the distinguishing feature of absent eye opening. Care providers may not be attuned to making this distinction. However, there appear to be physiologic consequences to repeated disruption of the neonatal sleep cycle, especially when active sleep is interrupted. For infants who spend weeks or months within an environment that does not foster normal sleep patterns, negative effects of disrupted sleep may be amplified.

The population of neonates that we included in our study was mainly full-term and medically stable, although they were all at risk for neurological abnormalities (which was an inclusion criteria for the main neuromonitoring study).[8] They were not considered clinically to be at high-risk for respiratory instability. Importantly, we did not include the most medically fragile patients who are typically cared for in the NICU, such as those with extreme prematurity and those with critical illness that precluded the ability to undergo PSG. Such infants commonly require even more frequent medical interventions and hands-on care; as a result, they may have less opportunity to experience normal sleep. We speculate that more premature or critically ill newborns, in comparison to those in our cohort, may experience even more profound respiratory instability associated with handling.

Within the context of providing necessary medical interventions, sleep disruption can be easily overlooked. Yet, repeated sleep disturbance may have important long-term consequences. Sleep cycling is one of the newborn infant's most highly regulated brain functions and is hypothesized to be critically important for normal neurodevelopment. The question of whether abnormal sleep leads to abnormal brain development, or abnormal brain function generates abnormal sleep is fundamental and unanswered. Brain development in relation to sleep is likely the result of interplay of the two scenarios, but sleep is a potentially modifiable factor. Our findings raise the important possibility that an opportunity may exist to enhance neurodevelopmental outcomes through interventions that optimize newborn infants' sleep.

Our study highlights measurable changes that can be observed with physical care of a sleeping neonate, and suggests that decreased handling or adjusting the timing of handling to avoid contact with infants in active sleep may be beneficial. Sleep-sensitive NICU care could potentially be guided by strategies as simple as observing whether the infant's eyes are open or closed. Simple monitoring approaches, or algorithms to improve inferences about probable sleep-wake states, based on already-recorded variables such as heart rate and respiratory patterns, might provide cost-effective strategies to optimize NICU outcomes.

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