

# Maternal Voice and Infant Sleep in the Neonatal Intensive Care Unit

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abstract

**BACKGROUND:** Approximately 10% of US newborns require a NICU. We evaluated whether the NICU acoustic environment affects neonatal sleep and whether exposure to the mother's voice can modulate that impact.

**METHODS:** In a level IV NICU with single-infant rooms, 47 neonates underwent 12-hour polysomnography. Their mothers were recorded reading children's books. Continuous maternal voice playback was randomized to either the first or second 6 hours of the polysomnogram. Regression models were used to examine sleep-wake stages, entropy, EEG power, and the probability of awakening in response to ambient noise during and without voice playback.

**RESULTS:** After epochs with elevated noise, the probability was higher with (versus without) maternal voice exposure of neonates staying asleep ( $P = .009$ ). However, the 20 neonates born at  $\geq 35$  weeks' gestation, in contrast to those born at 33 to 34 weeks, showed an age-related increase in percent time awake ( $R^2 = 0.52$ ;  $P < .001$ ), a decrease in overall sleep ( $R^2 = 0.52$ ;  $P < .001$ ), a reduction in rapid eye movement sleep bouts per hour ( $R^2 = 0.35$ ;  $P = .003$ ), and an increase in sleep-wake entropy ( $R^2 = 0.52$ ;  $P < .001$ ) all confined solely to the 6 hours of maternal voice exposure. These associations remained significant ( $P = .02$  to  $P < .001$ ) after adjustment for neurologic examination scores and ambient noise.

**CONCLUSIONS:** Hospitalized newborns born at  $\geq 35$  weeks' gestation but not at 33 to 34 weeks' gestation show increasing wakefulness in response to their mother's voice. However, exposure to the mother's voice during sleep may also help protect newborns from awakening after bursts of loud hospital noise.



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**WHAT'S KNOWN ON THIS SUBJECT:** The NICU environment differs dramatically from the in utero milieu, and this may affect infant sleep. However, decreased exposure to spoken language in the NICU results in risk for developmental language delay.

**WHAT THIS STUDY ADDS:** Maternal voice exposure may insulate newborns from the impact of NICU noise by reducing the likelihood of wakefulness during and just after the highest noise levels. Impact of maternal voice may be greatest for infants born at  $\geq 35$  weeks' gestation.

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For two-thirds of each day, healthy newborns generate sleep, a complex and highly regulated neurologic function. Yet, for the 10% of US newborns who require neonatal intensive care, the factors that may promote or disturb sleep are poorly understood and rarely analyzed. Emerging evidence suggests that disturbed sleep physiology during late infancy contributes to subsequent adverse neurobehavioral outcomes<sup>1</sup> and that objective measures of neonatal sleep predict neurodevelopment.<sup>2</sup> Evaluation of sleep physiology in at-risk infants may be highly informative because sleep disruption and dysregulation are potentially modifiable. However, the optimal environment to promote ideal neonatal sleep (and whether that optimal environment differs for preterm versus term newborns) is unknown.

The NICU environment, which differs dramatically from the in utero milieu, could influence development of newborn sleep patterns. Despite a paucity of evidence regarding the impact of noise on sleep in critically ill neonates, clinical efforts are increasingly focused on reducing ambient sound in the NICU.<sup>3,4</sup> Many modern NICUs have been renovated to house individual neonates in private rooms. This quiet single-room environment might permit more sleep and better sleep. However, compelling recent data reveal the complexities inherent in efforts to optimize the NICU environment. Premature infants protected from extrinsic sound in private rooms, in comparison with infants in a multipatient open-bay NICU, more often experienced abnormal language development.<sup>5</sup> In another study, increased language exposure in the NICU was associated with better long-term language outcomes.<sup>6</sup> Therefore, simple provision of a quiet NICU environment may not be an ideal therapeutic approach. To date, the link between the acoustic milieu and

neonatal sleep regulation has not been explored for preterm or term NICU patients.

More broadly, few data are available on sleep in children's hospitals, but an increasingly robust body of literature describes disruption of adults' sleep during inpatient care. Hospital sounds, including alarms, staff conversations, over-head pages, and telephone ringtones, cause arousals from nonrapid eye movement (NREM) more than rapid eye movement (REM) sleep.<sup>7</sup> Continuous noises (eg, from a fan) are less likely to cause arousals from sleep than are intermittent, unpredictable noises (eg, from intravenous pump alarms).

In short, existing data suggest that normal quality and quantity of neonatal sleep may contribute to optimal neurodevelopment,<sup>1,2</sup> that sleep may be disrupted in the NICU by potentially modifiable environmental noise,<sup>7,8</sup> and that a quiet environment without exposure to language may have adverse neurodevelopmental impact.<sup>5,6,9,10</sup> Therefore, we aimed to assess for the first time whether enriched exposure to a unique, familiar, and potentially beneficial sound (the mother's voice) could modify objective measures of neonatal sleep physiology; whether exposure to the mother's voice may have effects that differ from the suspected adverse impact of environmental noise; and whether any such impact is modified by gestational or postmenstrual age. We hypothesized that disruption of sleep would be dampened by exposure to the mother's voice and that the effect of maternal voice exposure would be more pronounced for term (versus preterm) infants.

## METHODS

This study was approved by a Michigan Medicine Institutional Review Board. A parent of every enrolled infant provided written

informed consent. We prospectively recruited late-preterm and term neonates who required intensive care in our single-patient room NICU. Inclusion criteria were: gestational age  $\geq 33$  to 41 weeks, need for NICU admission, and stable temperature regulation in an open crib. Exclusion criteria were: congenital brain anomalies, known or suspected genetic syndromes that could be expected to result in cerebral dysfunction, severe encephalopathy that precluded sleep-wake cycling, significant airway anomalies that were likely to result in sleep-disordered breathing, and abnormal hearing screening (brainstem auditory evoked responses). Score for Neonatal Acute Physiology with Perinatal Extension-II (0 = normal;  $>37$  = elevated risk of mortality<sup>11,12</sup>) and standardized neurologic examination scores (Thompson scores; 0 = normal;  $>10$  = elevated risk for adverse neurodevelopment<sup>13</sup>) were recorded for each infant.

A 12-hour attended polysomnogram was recorded after the infant was considered by the clinical team to be medically stable (no respiratory support and able to tolerate a bedside polysomnogram). Polysomnography generally spanned the overnight and morning hours (~10 PM–10 AM). Parents were permitted but not required to remain in the patient room during the polysomnogram. A registered polysomnographic technologist at the infant's bedside recorded detailed behavioral observations during the entire polysomnogram. In addition to the 9-channel neonatal-montage EEG (expanded from the standard 6-channel montage to enable screening for subclinical seizures, which might influence sleep regulation), other channels included bilateral electrooculogram, chin surface electromyogram, chest and abdominal excursion (inductance plethysmography), nasal pressure, nasal and/or oral airflow

(thermocouples), snoring sensor, oxygen saturation, transcutaneous CO<sub>2</sub>, electrocardiogram, bilateral anterior tibialis surface electromyogram, and digital video. Polysomnograms were scored off-line by an experienced, registered polysomnographic technologist and reviewed by a board-certified sleep medicine physician. Procedures and scoring followed contemporaneously current published standards.<sup>14</sup> All infants were cared for in an open bassinet. Their care regimens and feeding schedules were maintained throughout the 12-hour polysomnogram. Neonates were generally fed every 3 hours. Infants generally remained in the bassinet for feeding and care.

During the polysomnogram recording, a digital language processing device was placed on the arm of the infant's bassinet to record the acoustic environment. By using proprietary software (Language Environment Analysis [LENA] Research Foundation, Boulder, CO; [www.lenafoundation.org](http://www.lenafoundation.org)), the audio recording was analyzed to quantify language (eg, adult word count from caregivers speaking at bedside), nonlanguage noise (eg, monitor alarms, which are coded by LENA as "television/electronic sounds"), and periods of silence.<sup>10</sup> This method has been validated for evaluation of the NICU acoustic environment<sup>9</sup> and can recognize both English and Spanish conversation, although all parents and clinical staff of included infants spoke English at bedside.

We provided the infants' mothers with 2 children's books<sup>15,16</sup> from which to read while their voices were digitally recorded. The digital voice recording was played continuously during half (6 hours) of the polysomnogram via a device placed near the foot of the infant's bassinette. Because the infants' behavioral state could be influenced by the application of the polysomnogram monitoring electrodes, we randomized the order of 6 hours usual care acoustic

environment vs 6 hours enriched maternal voice exposure such that half of the infants had their mother's voice recording played during the first 6 hours of the polysomnogram and the other half during the second 6 hours. A 1:1 randomization was performed by using an online random number table. There was no washout period between the 2 6-hour segments. The sleep technician and physician who scored and reviewed the polysomnograms, respectively, were masked to the randomization order. The LENA software classified the maternal audio recording as "television/electronic sounds" or "uncertain/fuzzy" and not as adult word counts; this allowed comparison of bedside conversation (classified as adult word counts) with versus without the maternal voice exposure.

#### Power and Sample Size Justification

On the basis of preliminary data that demonstrated a Spearman coefficient of  $\rho \approx 0.7$  for correlations between gestational age and durations of bouts of REM sleep and wakefulness,<sup>17</sup> we determined prospectively that a sample size of  $N = 47$  would provide 80% power to detect  $\rho = 0.4$  with  $\alpha = 0.05$ .

#### Analytic Approach and Statistics

We quantified standard sleep metrics<sup>14</sup> (ie, proportions of sleep-wake stages, apnea-hypopnea index [number of apneas and hypopneas per hour], and arousal index [number of arousals and awakenings per hour of sleep]) as well as transition probabilities, EEG power, and entropy measures, as previously described<sup>2,17</sup> for the 6-hour maternal voice playback and 6-hour usual care environment epochs of the polysomnograms. The calculated sleep variables included the proportion of each sleep-wake stage and the probability of changing from 1 specific sleep-wake stage to another (transition probabilities). The Walsh spectral entropy method<sup>18,19</sup> was used to measure the entropy of the

sequence of sleep-wake stage transitions; increased entropy values are suggestive of decreased predictability of the sleep-wake stage pattern. The power spectra for each 30-second polysomnogram epoch were computed from the C4-M1 channel of the EEG portion of the polysomnogram by normalizing the total periodogram power averaged across all polysomnogram epochs via the Welch method for a fast Fourier transform.<sup>20</sup> Quantitative sleep measures were regressed on gestational age at birth and postmenstrual age with adjustment for neurologic examination (Thompson) scores and average ambient noise level. Data were compared for epochs with versus without the recorded maternal voice playback exposure. Our a priori plan was to evaluate sleep measures across gestational ages. Visual inspection of the data suggested logical subgroups of 33 to 34 vs  $\geq 35$  weeks' gestation. LENA-measured adult word counts were also regressed on overall noise level and sleep-wake stage data.

For each 30-second polysomnogram epoch, the ambient noise was quantified from the digital audio file, and the sleep-wake stage was scored. The data were pooled over the participating neonates, and multinomial logistic regression was used to examine the likelihood of remaining asleep or awakening in the subsequent epoch as a function of environmental noise in the presence or absence of exposure to the maternal voice playback. Multivariable logistic regression was used to evaluate the likelihood of being asleep versus awake as a function of within-epoch peak ambient noise and exposure to the maternal recording adjusted for gestational age and neurologic examination (Thompson) scores. Relationships between gestational age, postmenstrual age, environmental noise, maternal voice

playback, and sleep were then explored separately for term and near-term ( $\geq 35$  weeks' gestation at birth) versus premature infants (33–34 weeks' gestation at birth). Bivariate analyses were conducted (Wilcoxon paired signed rank test) to compare acoustic profiles during usual care versus during maternal voice playback. All statistical models were constructed by using MATLAB (MathWorks, Natick, MA), and  $P < .05$  was used to define statistical significance.

## RESULTS

Forty-seven newborns were enrolled in the study. Clinical and demographic details are presented in Table 1.

Sound levels overall were  $\sim 1$  dBA higher during maternal speech exposure versus usual care (mean  $56.3 \pm 4.6$  vs  $55.3 \pm 5.2$  dBA, respectively;  $P < .0001$ ). The amount of language exposure, classified by LENA as adult word count, was low in both settings and did not change when the maternal voice was playing (mean  $178 \pm 213$  vs  $127 \pm 154$  words per hour;  $P = .16$  [Table 2]).

### Impact of Maternal Voice: All Subjects

#### Sleep Bout Lengths

The peak ambient noise during individual 30-second polysomnogram epochs was generally higher during versus without the maternal voice

playback exposure (mean peak noise level  $72.7 \pm 2.7$  vs  $74.4 \pm 2.9$  dBA;  $P = .0004$ ). However, overall, the infants' sleep bout lengths (durations of uninterrupted sleep) were not strongly associated with the level of background noise. In the usual care setting, shorter sleep bout length was not meaningfully predicted by louder mean noise levels (NREM sleep: linear regression adjusted  $R^2 = 0.002$ ;  $P = .7$ ; REM, sleep: adjusted  $R^2 = 0.004$ ;  $P = .04$ ). During maternal speech exposure, only a limited association emerged between shorter NREM sleep bout lengths and louder average sound levels (adjusted  $R^2 = 0.025$ ;  $P < .001$ ), and REM sleep bout lengths were not

**TABLE 1** Clinical, Demographic, and Sleep Profiles of 47 Newborn Infants

Clinical and Demographic Data	Full Sample (N = 47)	33–34 Weeks' Gestation (n = 27)	$\geq 35$ Weeks' Gestation (n = 20)
Gestational age at birth, wk, mean $\pm$ SD	35.5 $\pm$ 2.0	34 $\pm$ 0.48	37.5 $\pm$ 1.5
Legal age at time of polysomnography, d, mean $\pm$ SD	6.6 $\pm$ 5.4	5.7 $\pm$ 2.4	7.8 $\pm$ 7.7
Postmenstrual age at time of polysomnography, wk, mean $\pm$ SD	36.4 $\pm$ 2.3	34.9 $\pm$ 0.56	38.6 $\pm$ 1.8
Birth wt, g, mean $\pm$ SD	2502 $\pm$ 541	2190 $\pm$ 299	2925 $\pm$ 507
Sex, n			
Female	27	17	10
Male	20	10	10
5 min Apgar score, median (IQR)	9 (8–9)	9 (8–9)	8 (7–9)
Neurologic examination (Thompson) score, median (IQR)	0 (0–2)	0 (0–2)	0 (0–2)
SNAPPE-II score, median (IQR)	5 (0–16)	0 (0–5)	11 (5–23)
Primary NICU diagnosis, n			
Prematurity	29	26	3
Respiratory	10	1	9
Hypoglycemia	5	0	5
Other <sup>a</sup>	3	0	3
Sleep data			
Polysomnogram summary results, n			
Normal	16	8	8
Primary sleep apnea of infancy	20	11	9
Central sleep apnea	4	3	1
Obstructive sleep apnea	2	2	0
Hypoventilation	2	1	1
Other	3	1	1
AHI, mean $\pm$ SD	22.6 $\pm$ 14.7	22.2 $\pm$ 17.3	16.5 $\pm$ 8.4
REM sleep AHI	33.0 $\pm$ 16.3	36.2 $\pm$ 21.3	26.2 $\pm$ 14.6
NREM sleep AHI	13.1 $\pm$ 14.4	17.0 $\pm$ 18.4	7.7 $\pm$ 4.4
Obstructive apnea index, mean $\pm$ SD	3.3 $\pm$ 5.4	4.9 $\pm$ 6.7	1.4 $\pm$ 0.9
Central apnea index, mean $\pm$ SD	6.4 $\pm$ 8.0	8.4 $\pm$ 9.9	3.6 $\pm$ 2.6
Hypopnea index, mean $\pm$ SD	12.5 $\pm$ 7.4	13.0 $\pm$ 8.1	11.4 $\pm$ 7.0
Time with O <sub>2</sub> saturation (<90%), %, mean $\pm$ SD	5.4 $\pm$ 9.5	4.2 $\pm$ 6.6	7.0 $\pm$ 12.4
Total sleep time spent in REM sleep, %, mean $\pm$ SD	49.5 $\pm$ 8.0	50.2 $\pm$ 5.6	49.4 $\pm$ 8.9
Total sleep time spent in NREM sleep, %, mean $\pm$ SD	34.1 $\pm$ 7.6	35.7 $\pm$ 5.1	31.2 $\pm$ 8.1
Total sleep time spent in indeterminate sleep, %, mean $\pm$ SD	16.4 $\pm$ 7.0	14.2 $\pm$ 4.9	19.3 $\pm$ 5.0
Total recording time spent awake, %, mean $\pm$ SD	15.4 $\pm$ 7.1	12.8 $\pm$ 5.5	17.8 $\pm$ 7.1

AHI, apnea-hypopnea index; IQR, interquartile range; SNAPPE-II, Score for Neonatal Acute Physiology with Perinatal Extension-II.

<sup>a</sup> Other diagnoses included: sepsis (n = 1), hypoxic-ischemic encephalopathy (n = 1), and intraventricular hemorrhage (n = 1).

**TABLE 2** Classifications by LENA Software of Audio Segments During Usual NICU Care and Maternal Voice Playback Exposure

	All Subjects (N = 47)			33–34 Weeks' Gestation (n = 27)			≥35 Weeks' Gestation (n = 20)		
	Usual NICU Care, Mean ± SD	With Voice Playback, Mean ± SD	Wilcoxon Paired Signed Rank Test, P <sup>a</sup>	Usual NICU Care, Mean ± SD	With Voice Playback, Mean ± SD	Wilcoxon Paired Signed Rank Test, P <sup>a</sup>	Usual NICU Care, Mean ± SD	With Voice Playback, Mean ± SD	Wilcoxon Paired Signed Rank Test, P <sup>a</sup>
	Time classified as overlapping vocals, %	0.82 ± 0.85	1.1 ± 1.4	.32	0.6 ± 0.7	1.0 ± 1.5	.37	1.1 ± 0.9	1.3 ± 1.2
Time classified as television and electronic media, %	6.8 ± 12.0	16.3 ± 29.7	.07	3.4 ± 6.6	9.7 ± 24.2	.22	11.5 ± 15.8	25.2 ± 34.4	.17
Time classified as noise, %	39.6 ± 26.7	6.6 ± 12.2	<.0001	38.3 ± 28.6	6.3 ± 15.0	<.0001	41.3 ± 24.6	7.0 ± 10.8	.0001
Time classified as silence, %	31.1 ± 32.9	19.5 ± 24.8	<.0001	37.6 ± 34.4	27.1 ± 27.4	.0006	22.4 ± 29.4	9.3 ± 16.6	.01
Time classified as noise uncertain and/or fuzzy, %	18.2 ± 15.2	52.6 ± 27.9	<.0001	17.3 ± 16.6	52.7 ± 29.4	<.0001	19.3 ± 13.4	52.4 ± 30.9	.0006
Adult word count (words per hour)	177.5 ± 213.3	126.6 ± 154.0	.16	165.0 ± 214.0	101.2 ± 125.6	.30	194.4 ± 216.6	160.9 ± 183.6	.30
Mean epoch sound, dBA	55.1 ± 3.4	56.2 ± 3.2	.001	54.3 ± 3.6	55.5 ± 3.4	.01	56.2 ± 2.9	57.1 ± 2.8	.04
Peak epoch sound, dBA	72.7 ± 2.7	74.4 ± 2.9	.0004	72.0 ± 2.4	73.7 ± 3.1	.009	73.7 ± 2.8	75.4 ± 2.2	.02

<sup>a</sup> Wilcoxon paired signed rank test comparing the 6 h of usual care to 6 h of maternal voice playback exposure.

affected (adjusted  $R^2 = 0.002$ ;  $P = .14$ ).

### Maintenance of Sleep After Loud Noises and During Noises of Various Levels

The probability was higher during versus without the maternal voice exposure for the neonate to stay asleep in the epochs after elevated peak noise levels (model  $R^2 = 0.62$ ; Table 3, Fig 1). Similarly, the probability of the infant being asleep during any given polysomnogram epoch was higher during maternal voice exposure in comparison with usual care (multivariable logistic regression:  $\beta = .07$ ;  $P = .001$ ) after adjustment for peak noise ( $\beta = -.11$ ;  $P < .001$ ), gestational age ( $\beta = .1$ ;  $P < .001$ ), and Thompson score ( $\beta = .03$ ;  $P < .001$ ).

### Arousals and Apnea-Hypopnea Indices

The arousal index during sleep tended to decline only modestly with advancing gestational age (linear regression model adjusted  $R^2 = 0.03$ ;  $P = .1$ ) and postmenstrual age (adjusted  $R^2 = 0.08$ ;  $P = .03$ ). Arousal index increased slightly with versus without the maternal voice playback ( $19.7 \pm 8.5$  vs  $18.0 \pm 7.4$ , respectively;  $P = .01$ ). Similarly, the apnea-hypopnea index declined with advancing gestational age (adjusted  $R^2 = 0.06$ ;  $P = .047$ ) and postmenstrual age (adjusted  $R^2 = 0.07$ ;  $P = .03$ ) but was not altered by exposure to the maternal voice recording ( $21.9 \pm 15.8$  during maternal voice exposure vs  $22.2 \pm 16.2$  without maternal voice exposure;  $P = .9$ ).

### Term and Near-Term Versus Preterm Infants

Associations of quantitative sleep measures with increasing gestational age varied with maternal voice exposure for the 20 neonates born at  $\geq 35$  weeks' gestation but not the 27 born preterm at 33 to 34 weeks' gestation (Table 4, Fig 2). During the voice exposure, among neonates born at  $\geq 35$  weeks' gestation, increasing



**TABLE 3** The Nominal Multinomial Logistic Regression Model Reveals That the 47 Neonates Were More Likely To Stay Asleep After Loud Ambient Noise When They Were Exposed to Their Mothers' Voice Recordings (Model  $R^2 = 0.62$ )

	$\beta$	$P$
Intercept	6.7	<.0001
Sound level, dB	-.035	<.0001
Maternal voice exposure	1.85	.016
Sound $\times$ maternal voice exposure interaction	-.026	.009

Note: maternal voice exposure was modeled as a binary variable, which was one (1) when the voice playback was off and zero (0) when the playback was on.

gestational age was associated with increased percent time awake ( $R^2 = 0.52$ ;  $P < .001$ ) and more clearly decreased REM sleep ( $R^2 = 0.2$ ;  $P < .001$ ) than NREM sleep ( $R^2 = 0.19$ ;  $P = .04$ ). Similarly, advancing gestational age was associated with increased wakefulness bout duration ( $R^2 = 0.42$ ;  $P < .001$ ) but not REM or NREM sleep bout duration, fewer REM sleep bouts per hour ( $R^2 = 0.35$ ;  $P = .003$ ), and increased sleep-wake entropy ( $R^2 = 0.52$ ;  $P < .001$ ). These associations remained significant after adjustment for Thompson scores and average ambient noise level (adjusted model  $R^2 = 0.30$ – $0.58$ ; each  $P < .004$ ). Without the voice playback, none of these associations were significant. EEG power at 2 to

4 and 4 to 8 Hz increased with gestational age in both age groups ( $R^2 = 0.14$ – $0.47$ ;  $P = .01$  to  $<.001$ ), and this was not changed by the voice playback. For infants born at  $<35$  weeks' gestation, no other associations emerged between sleep measures and gestational age with or without maternal voice exposure.

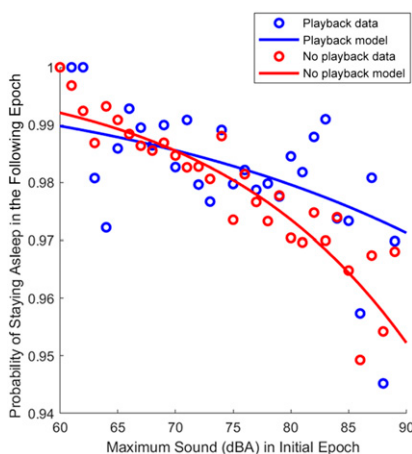
Parallel analyses were conducted between postmenstrual age and sleep parameters adjusted for Thompson scores and average noise level. Among neonates born at  $\geq 35$  weeks' gestation, during the maternal voice exposure, the proportion of wakefulness rose with increasing postmenstrual age ( $R^2 = 0.34$ ;  $P = .002$ ) but no other associations emerged. Without the voice exposure, this association was not significant. There were no statistically significant associations between postmenstrual age and sleep-wake variables among infants born at  $<35$  weeks with or without the maternal voice playback.

## DISCUSSION

Results of these quantitative, gold-standard recordings of sleep, ambient noise, and maternal voice exposure suggest that sounds can be remarkably loud in the NICU (even in a single-patient-room design) and that these sounds can influence neonatal sleep. Furthermore, exposure to the mother's voice (here by recording, but presumably in person as well) may insulate newborns from some of the impact of NICU noise by reducing the likelihood of wakefulness during and just after

the highest noise levels. The impact of maternal voice in our data was not uniform across all gestational ages studied; starting at  $\sim 35$  weeks' gestation at birth, in contrast to earlier gestational ages, newborns of advancing ages showed steadily increased amounts of wakefulness during maternal voice exposure. After 35 weeks' gestation (and aside from periods of loud ambient noise during sleep), newborns may become progressively more alert for their mothers' voice as they approach term. Finally, our results also suggest that patterns of sleep-wake cycle development and the relationship of sleep to the sensory environment are altered by preterm birth because the neonatal sleep variables were more strongly associated with gestational age at birth than postmenstrual age at the time of the polysomnogram. Overall, these remarkable results could have important implications for care of NICU patients during the earliest days after birth and advance our understanding of newborn dependence on parental interaction.

Moreover, even beyond the first days of life, we speculate that the NICU sensory environment, which differs dramatically from the in utero milieu, may disrupt the stimulus-sensitive plasticity of the immature brain and contribute to abnormal developmental outcome, at least in some vulnerable infants. As a result of physiologic dysmaturity, development of sleep patterns may differ for term versus late-preterm infants at equivalent postmenstrual ages.<sup>21,22</sup> This could explain why our results reveal that the influence of the NICU acoustic environment on neonatal sleep variables is more highly associated with gestational age at birth than with postmenstrual age at the time of the polysomnogram. Animal models have demonstrated the critical, time-specific role of the acoustic environment during auditory cortex organization.<sup>23,24</sup> Others have reported that when played to preterm



**FIGURE 1**

For 30-second polysomnogram epochs with high peak noise levels, the probability of the newborn remaining asleep in the subsequent epoch was modified by exposure to maternal voice playback (model  $R^2 = 0.62$ ; sound  $\times$  maternal voice exposure interaction:  $P = .009$ ). The results depicted here were computed from data pooled across all polysomnogram epochs for all of the neonates included in the study.

**TABLE 4** Selectively for Late-Preterm and Term Infants ( $\geq 35$  Weeks' Gestational Age), As Opposed to Preterm Infants ( $< 35$  Weeks' Gestational Age), Maternal Voice Exposure Appeared to Have Increasing Tendency To Promote Wakefulness as Gestational Age Increased

GA as a Predictor	Among the 20 Infants With $\geq 35$ Weeks' GA, Adjusted for Thompson Score and Average Ambient Noise Level		Among the 27 Infants With $< 35$ Weeks' GA, Adjusted for Thompson Score and Average Ambient Noise Level	
	Without Recording	With Recording	Without Recording	With Recording
Time awake, %	$\beta = .02$ ; model $R^2 = 0.18$ ; $P = .09$	$\beta = .06$ ; model $R^2 = 0.48$ ; $P = .003$	$\beta = .01$ ; model $R^2 = -0.03$ ; $P = .56$	$\beta = -.04$ ; model $R^2 = -0.01$ ; $P = .45$
Wake bout duration	$\beta = 53.2$ ; model $R^2 = 0.63$ ; $P < .001$	$\beta = 94.2$ ; model $R^2 = 0.59$ ; $P < .001$	$\beta = 27.1$ ; model $R^2 = 0.07$ ; $P = .19$	$\beta = -3.6$ ; model $R^2 = 0.03$ ; $P = .32$
Overall sleep, %	$\beta = -.02$ ; model $R^2 = 0.19$ ; $P = .09$	$\beta = -.06$ ; model $R^2 = 0.48$ ; $P = .004$	$\beta = -.01$ ; model $R^2 = -0.03$ ; $P = .56$	$\beta = .04$ ; model $R^2 = -0.01$ ; $P = .45$
REM sleep bouts per hour	$\beta = -.17$ ; model $R^2 = 0.05$ ; $P = .29$	$\beta = -.26$ ; model $R^2 = 0.41$ ; $P = .009$	$\beta = -.28$ ; model $R^2 = -0.09$ ; $P = .85$	$\beta = -.01$ ; model $R^2 = -0.03$ ; $P = .53$
Sleep-wake entropy	$\beta = -.03$ ; model $R^2 = 0.05$ ; $P = .28$	$\beta = .05$ ; model $R^2 = 0.48$ ; $P = .003$	$\beta = -.06$ ; model $R^2 = 0.05$ ; $P = .24$	$\beta = -.08$ ; model $R^2 = -0.07$ ; $P = .27$

GA, gestational age.

infants, recorded maternal sounds are associated with improvements in apnea of prematurity<sup>25</sup> and increased time in the quiet alert state.<sup>26</sup> Among preterm infants born at 25 to 32 weeks, exposure to audio recordings of the mother's voice and heartbeat for 45 minutes 4 times per day in the first month of life in comparison with usual NICU care was associated with larger auditory cortex size 30  $\pm$  3 days after birth.<sup>27</sup> For late-preterm infants, exposure to a lullaby recording (not sung by the infant's mother) was associated with improvements in the qualitative cycling patterns thought to represent sleep-wake cycles on amplitude-integrated EEG.<sup>28</sup> Our study now adds objective evidence, through quantitative polysomnographic and sound analyses, that changes in the NICU acoustic environment (such as enriched maternal voice exposure) can influence sleep physiology for newborn infants. Although this study did not include long-term follow-up, previous work by our group and others has suggested that better quality and efficiency of sleep during the newborn period is associated with improved neurodevelopmental outcomes in cognitive, motor, and language domains.<sup>2,29</sup>

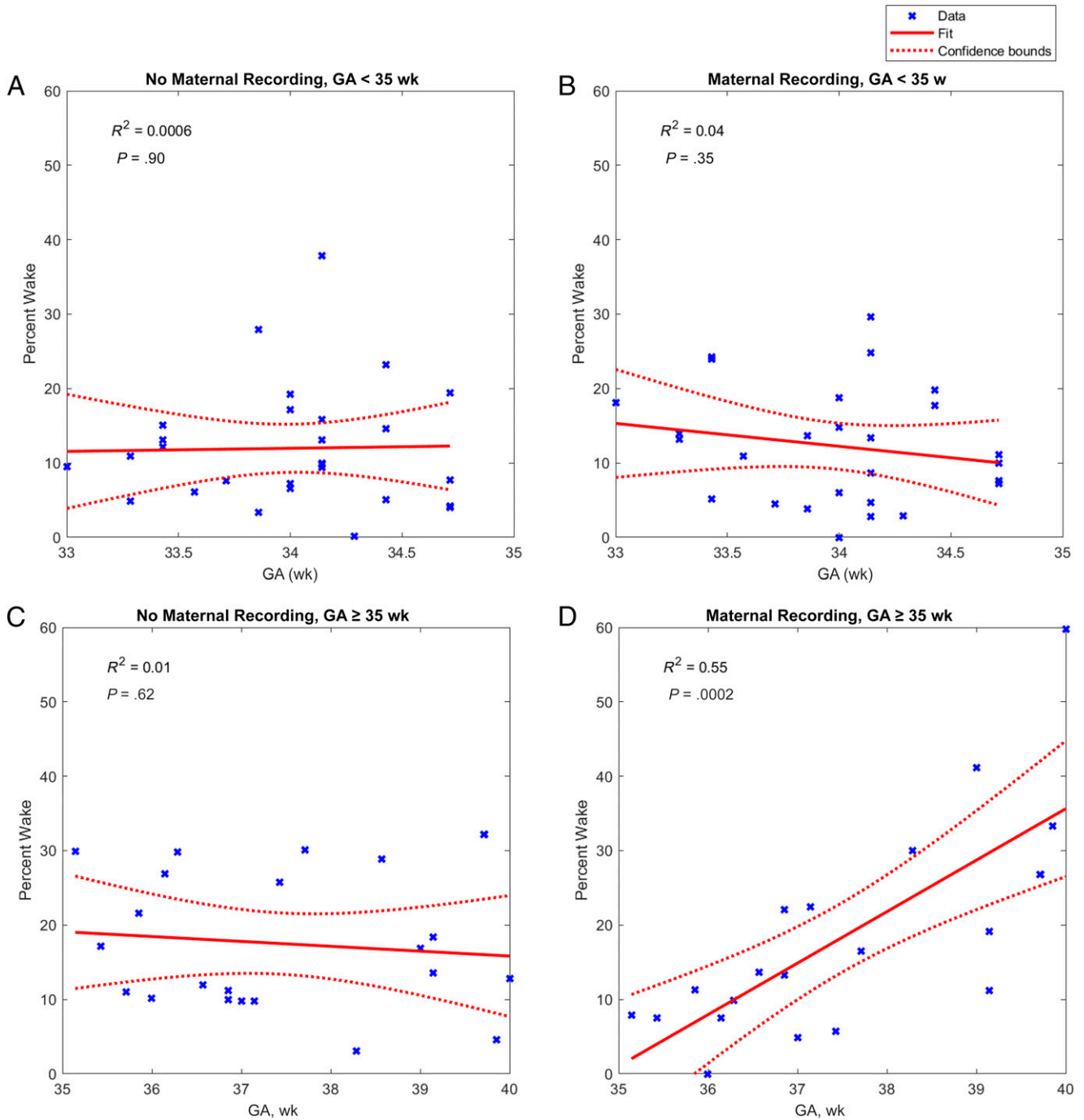
Compelling recent data revealed that, unexpectedly, neonates cared for in a single-room NICU with low parent visitation rates versus an open-bay NICU design were at much higher risk

for abnormal language development.<sup>5</sup> Linguistic outcomes were also better for formerly preterm toddlers whose parents reported noisier rather than quieter NICU environments after adjustment for relevant clinical and socioeconomic variables.<sup>30</sup> Increasing language exposure during NICU admission is also associated with better long-term language development.<sup>6</sup> Recently published data reveal that aiming for silence in the NICU is unrealistic,<sup>4,31</sup> and simply providing a quiet NICU environment may not be an ideal therapeutic approach. We theorize that an ideal balance between opportunity for sleep-wake cycling and appropriate language exposure could help to optimize outcomes.

Importantly, our current and previous results<sup>3</sup> as well as data from others<sup>6,32</sup> reveal that adult word count is low in the NICU. Although the present findings reveal an association between increased adult word count and higher overall sound levels, this does not mean that conversation was the major driver of overall NICU noise (eg, sound might be higher because the infant was crying, and the caregiver may be more likely to speak if an infant is crying). It is necessary for infants to have language exposure to optimize language development, so it is reasonable to encourage clinicians and families to speak at bedside without excessive concern

that they are disrupting the infant's ability to sleep. However, the potential advantages of necessary language exposure as well as ambient NICU noise required for care targeted selectively to periods of wakefulness rather than sleep remains to be tested. Such care is often provided to older hospitalized patients who, in the absence of such courtesy, could complain about the sleep disturbance and consequent daytime sleepiness. Although infants will not complain, the possibility exists that their developmental trajectory could reflect the impact of sleep disruption.

In the current study, we used gold-standard attended bedside polysomnography to characterize objective measures of neonatal sleep in association with the NICU acoustic environment and maternal voice exposure. However, this study does have some limitations. We evaluated the immediate impact of sound exposure on the infant and cannot know the long-term effect of intermittent language enrichment on longitudinal maturation of sleep-wake cycling or neurodevelopment. Infant responsiveness to sound and language might be hypothesized to be associated with immediate brain function and potentially to predict neurodevelopmental outcomes; long-term follow-up of the present cohort is planned. We analyzed the impact of the acoustic environment, but



**FIGURE 2**

A, For 27 infants born at <35 weeks' gestation, there was no association between the proportion of wakefulness and advancing gestational age (GA; model  $R^2 = 0.0006$ ;  $P = .9$ ). B, For 27 infants born at <35 weeks' gestation, there was no association between the proportion of wakefulness and advancing GA, and this was not influenced by exposure to the maternal voice recording (model  $R^2 = 0.04$ ;  $P = .35$ ). C, In the absence of maternal voice playback, the proportion of wakefulness similarly did not change with GA for 20 infants born at  $\geq 35$  weeks' gestation (model  $R^2 = 0.01$ ;  $P = .62$ ). D, When infants born at  $\geq 35$  weeks' gestation were exposed to the maternal voice recording, the proportion of wakefulness increased significantly with GA (model  $R^2 = 0.55$ ;  $P = .0002$ ).

additional factors such as handling of the infant<sup>33</sup> or neuroactive medications also can influence sleep. Comprehensive approaches to

optimize sleep for NICU patients will need to account for these manifold elements of intensive care. Although the overall sound intensity was high

during the polysomnograms and tended to be slightly louder during the maternal voice exposure, we found no evidence that the maternal



voice playback increased abnormal respiratory events. Of note, even with peak noise as high as 90 dB, the probability for most neonates to remain asleep was high. Epoch-to-epoch sleep scoring in our analyses evaluated for awakenings and not for arousals; loud noises could have a physiologic impact, short of waking the neonate in the subsequent epoch. Whether exposure to live spoken words has a different effect on language development than exposure to the recorded maternal voice is not known. The LENA software classified the maternal voice recording as “uncertain/fuzzy” rather than adult word counts. Still, we show that exposure to the voice recording was associated with measureable changes in sleep physiology.

## CONCLUSIONS

Given the results of the current study in combination with other published data that suggest consequential long-term impact of healthy early-life sleep or its

disruption, a pressing need exists for additional high-quality research to define optimal outcome-relevant conditions for sleep in the NICU and to identify any simple opportunities for intervention. Our findings suggest that to be effective, such interventions will need to be tailored to the infants’ gestational and perhaps postmenstrual age. Moreover, part of the strategy may need to provide the newborn with basic parental voice exposure or other experiences that would have been taken for granted in utero. We anticipate that a greater quantitative understanding of sleep-wake patterns and their associations with the NICU acoustic environment will lead to intervention studies that are focused on improvements in neonatal sleep regulation and ultimately achievement of better neurodevelopmental outcomes for these highly vulnerable patients. More broadly, such research also could open opportunities to improve long-term outcomes for all

infants aside from those who require a NICU stay. Conceivably, the timing and volume of noise and parental language exposure and their influence on sleep obtained during the first days of life outside the uterus could have important implications for every new family.

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## ABBREVIATIONS

LENA: Language Environment Analysis  
NREM: nonrapid eye movement  
REM: rapid eye movement

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