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ORIGINAL ARTICLE

Exposure to biological maternal sounds improves cardiorespiratory regulation in extremely preterm infants

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***Objective*: Preterm infants experience frequent cardiorespiratory events (CREs) including multiple episodes of apnea and bradycardia per day. This physiological instability is due to their immature autonomic nervous system and limited capacity for self-regulation. This study examined whether systematic exposure to maternal sounds can reduce the frequency of CREs in NICU infants. *Methods*: Fourteen preterm infants (26–32 weeks gestation) served as their own controls as we measured the frequency of adverse CREs during exposure to either Maternal Sound Stimulation (MSS) or Routine Hospital Sounds (RHS). MSS consisted of maternal voice and heartbeat sounds recorded individually for each infant. MSS was provided four times per 24-h period via a micro audio system installed in the infant's bed. Frequency of adverse CREs was determined based on monitor data and bedside documentation. *Results*: There was an overall decreasing trend in CREs with age. Lower frequency of CREs was observed during exposure to MSS versus RHS. This effect was significantly evident in infants ≥33 weeks gestation ($p = 0.03$), suggesting an effective therapeutic window for MSS when the infant's auditory brain development is most intact. *Conclusion*: This study provides preliminary evidence for short-term improvements in the physiological stability of NICU infants using MSS. Future studies are needed to investigate the potential of this non-pharmacological approach and its clinical relevance to the treatment of apnea of prematurity.**

Keywords: Apnea of prematurity, maternal sounds, neonatal care

Introduction

Episodes of apnea in the preterm infant are thought to be secondary to physiologic immaturity of the autonomic nervous system and are often associated with oxygen desaturation and/or bradycardia [1–4]. Associated episodes of apnea and bradycardia are often collectively referred to as cardiorespiratory events (CREs [2,5,6]).

The underlying mechanisms responsible for disturbances in cardiorespiratory regulation in the preterm infant are unclear. Histologically, the respiratory centers of the preterm brainstem are characterized by a decreased number of synaptic connections and poor myelination [7]. In addition to these anatomical factors, the preterm brain is especially sensitive to inhibitory neurotransmitters [8]. When mild, CREs are not thought to have detrimental effects. However, more severe CREs have been shown to cause a decrease in cerebral blood flow, putting the infant at risk of hypoxic-ischemic brain injury [9]. Due to this risk, the common medical impression is that preventing frequent CREs during NICU hospitalization is better for the long-term health of the infant.

CREs can be treated pharmacologically with methylxanthines, most commonly caffeine, which act as central nervous system stimulants [10]. Although caffeine therapy is regarded as a safe and effective treatment of central apnea [1,3,4], it is not 100% effective in preventing CREs and can have adverse outcomes, such as mild tachycardia, vomiting, and restlessness [11]. Complete resolution of CREs requires maturation of central and peripheral responses to changes in arterial blood gas concentrations, a heightened ventilitory drive, and effective activation of upper airway muscles during respiration [8]. As these and other aspects of maturation progress with increasing gestational age, the incidence of apnea decreases [12].

Growing evidence suggests that postnatal cardiorespiratory regulation can be affected by environmental factors. Noise in particular, has been shown to impact cardiorespiratory regulation in newborns and to have greater effects on preterm infants with younger gestational age [13,14]. It is evident that low frequency maternal sounds, such as the mother's voice and heartbeat, are audible inside the womb early in gestation [15]. Exposure to maternal sounds may therefore be crucial for healthy fetal development [16]. However, the specific effects of maternal auditory stimulation on short-term physiological outcomes are still unclear.

The purpose of this study was to examine the effects of biological maternal sounds on the cardiorespiratory stability of extremely preterm infants. We hypothesized that infants will have significantly less CREs during exposure to Maternal Sound Stimulation (MSS) than during exposure to Routine Hospital Sounds (RHS).

Methods

Patient population

This study used a within-subject design paradigm to examine the exposure effects of MSS vs RHS on frequency of adverse CREs. Fourteen preterm infants admitted to the NICU at Brigham and Women's Hospital participated in this study. Parents gave written

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informed consent. Infants were recruited for the study if they were: (1) born between 26–32 weeks gestational age (GA); and (2) at least 27 weeks postconceptional age (PCA) at the time of study. Exclusion criteria included: chromosomal or congenital anomalies; major congenital infections; congenital hearing loss; prenatal diagnosed brain lesions; birth asphyxia; uncontrolled maternal illness; history of maternal smoking, alcoholism, and use of illicit drugs; history of significant maternal deprivation, abuse, or malnutrition. A description of patient characteristics is given in Table I.

Maternal sound recording

We recorded the mother's voice and heartbeat for each infant in a specialized recording studio at our hospital. Voice recording was done via a large-diaphragm condenser microphone (KSM44, Shure, USA) to capture a wide range of maternal vocalizations such as speaking, reading, and singing. Heartbeat recording was done via a digital stethoscope (ds32a, Thinklabs Digital Stethoscopes, USA). The maternal recordings were attenuated using a low-pass filter with a cutoff of 400 Hz to allow the highest fidelity of biological sound reproduction. The maternal recordings were loaded onto an MP3 player (Phillips Electronics, SA2RGA04KS, Netherlands) for playback inside the incubator/crib via a micro audio system, which had been validated in a previous safety and feasibility study [17].

Maternal sound stimulation

The decision to provide MSS in 30 minute intervals was based on previous recommendations for playing soothing music NICU settings (for review [18]). The prescribed dose of four times per 24 h was to ensure that the observed effect of MSS on CREs is representative of the entire 24-h period. MSS started within 7 days after birth and continued until NICU discharge. The maternal sounds were played at a safe, fixed level of 55–60 dB(A) as verified individually for each infant by a sound level meter (Bruel & Kjaer, 2250, Denmark) at the bedside. Nurses were instructed to coordinate the MSS with the infant's routine care, avoiding times of parents' visits and clinical exams. All other aspects of the infant's care remained unaffected.

Data collection

Data was collected from the infant's cardiac monitor, study documents, nursing flow sheets, and electronic medical records. The exact time of day of each CRE was recorded by the bedside nurse as part of their routine documentation. CREs were clinically defined by the occurrence of breathing cessation lasting >20 seconds and/or a drop in HR below 100 BPM (for infants <34 weeks gestation) or below 80 BPM (for infants >34 weeks gestation [19]). CREs documented as being associated with gastroesophageal reflux (occurred within 45 minutes after feeding was initiated) were excluded from our analysis. However, the final decision whether or not an event was associated with reflux was based on subjective nursing evaluation at the bedside. In addition, one infant was excluded from data analysis due to respiratory distresses associated with lactose intolerance.

Table I. Characteristics of study population.

Male gender, %	50
Maternal age (yrs)	29.8 ± 6.84
GA at birth (wks)	30.2 ± 2.07
Birth-weight (g)	1266 ± 289
Apgar 1 minute	6.1 ± 2.13
Apgar 5 minute	7.2 ± 1.85
GA at study onset	31.1 ± 2.06
PCA at discharge (d)	50.1 ± 26.52
Days on study	42.9 ± 25.07
Early-onset sepsis, %	7.1
Surfactant therapy (dexamethasone), %	64.3
Caffeine treatment (methylxanthines), %	71.4
Grade III or IV interventricular hemorrhage, %	7.1
Oxygen therapy at 36 weeks, %	14.3
Hearing failed at discharge, %	0

Note: unless otherwise notes data are mean ± SD.

Statistical analysis

Each 24-h period was divided into 22 h of RHS and 2 h of MSS (30 minute × 4 times per 24 h). Data was normalized to account for the increased probability of an apnea/bradycardia event to occur during exposure to RHS vs. BMS. The analysis accounted for repeated observations within subjects, and was restricted to 33 weeks or greater to focus on the most stable period of time when hearing sensitivity and auditory brain development were most developed [20,21] and when nearly all subjects were observed and contributed data. Spearman correlation was used for association of CRE frequency with birth-weight and GA at birth.

Results

We found an overall decreasing trend in CREs with age ($p = 0.05$) (Figure 1). A lower frequency of CREs was observed during exposure to MSS relative to RHS. This reduction was significant in infants ≥33 weeks PCA ($p = 0.03$), suggesting an effective therapeutic window for MSS when the infant's auditory brain development is most intact. Prior to 33 weeks PCA, there were mixed trends with no significant differences in CREs between the two groups (Figure 1). Therefore, cardiorespiratory outcomes prior to 33 weeks PCA between the two groups is inconclusive due to lack of sufficient data during this time period. In addition, we found no correlation between the frequency of CREs and birth-weight nor between the frequency of CREs and GA at birth,

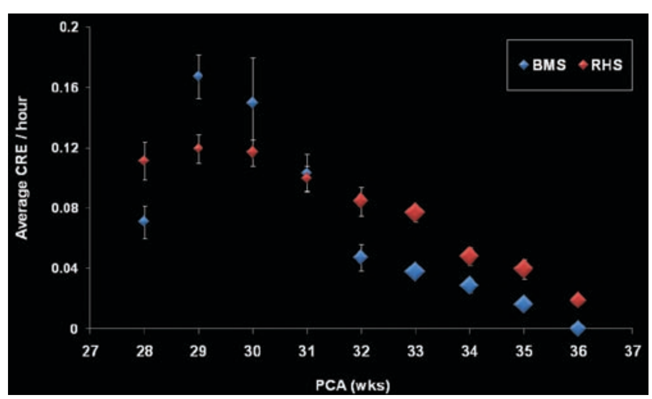

Figure 1. The mean frequency of CREs during MSS (blue) and RHS (red) is shown at each PCA. Data points include all infants observed in that particular age range. The thickness of the data points is proportional to the number of infants observed at each PCA ($N_{min} = 7$; $N_{max} = 14$). An overall decreasing trend in CREs is shown with increased PCA ($p = 0.05$). The frequency of CREs during MSS was significantly lower than during RHS ($p = 0.03$), demonstrating a significant effect for MSS beginning at 33 weeks PCA. Shown are standard errors of the mean (SEM).

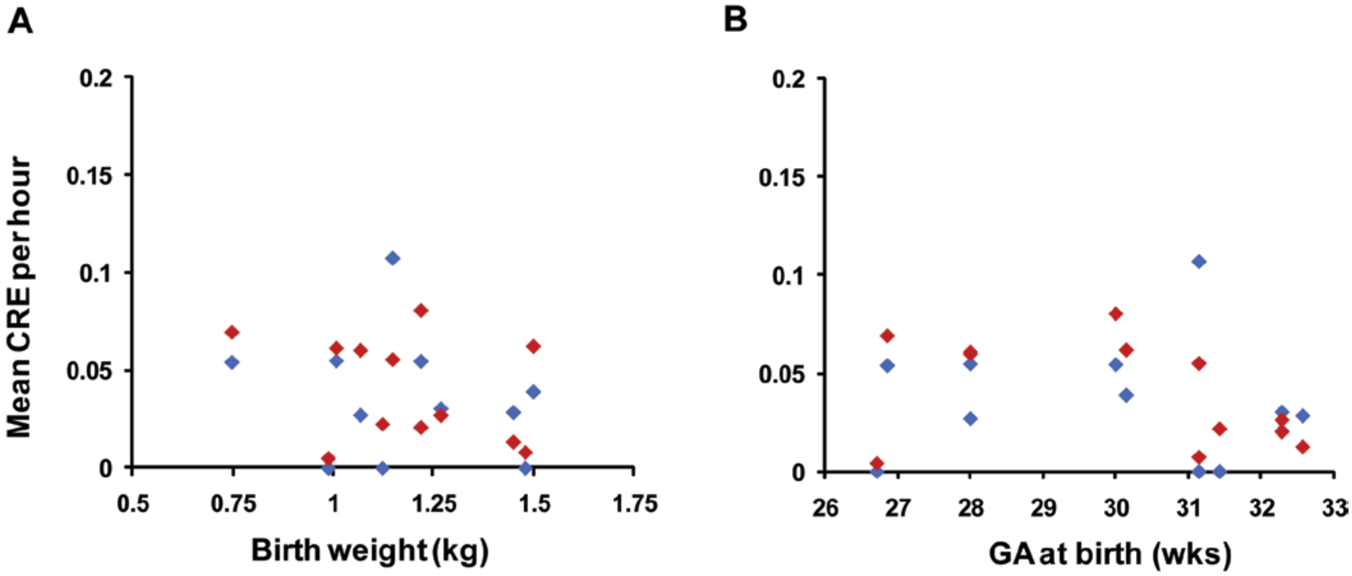

Figure 2. Plots showing mean frequency of CREs versus birth-weight (A) and versus GA at birth (B) for all infants ≤ 1500 gr. Data points represent average frequency of CREs per h for each infant throughout the entire study period during the MSS (blue) and RHS (red) conditions. Correlation of birth-weight was −0.14 ($p = 0.65$) for MSS and −0.26 ($p = 0.38$) for RHS. Correlation of GA at birth was −0.19 ($p = 0.53$) for MSS and −0.38 ($p = 0.20$) for RHS.

irrespective of whether CREs occurred during the MSS or RHS condition (Figure 2).

Discussion

This study demonstrates short-term improvements in cardiorespiratory regulation in extremely preterm infants during exposure to maternal sounds. Overall, the frequency of CREs decreased as PCA increased consistent with previous studies showing that the frequency of adverse respiratory events decreases as PCA increases [22]. However, our results show that, there was a significant reduction in the frequency of CREs during exposure to MSS beginning at 33.0 weeks through 36.6 weeks PCA.

Although the auditory system becomes partially functional from 25 to 29 weeks gestation, the ability to appropriately process sounds develops later in gestation. Tonotopic columns, necessary to receive, recognize, and react to language, music, and meaningful environmental sounds develops at ~30 weeks gestation [15]. At 34–36 weeks gestation, the fetus is capable of distinguishing different moods or emotional qualities to speech that are retained as part of accumulated memories [15]. These significant milestones in auditory development may play a crucial role in the preterm infant's ability to recognize and respond to maternal sounds. We hypothesize that as the auditory and respiratory systems mature, a therapeutic window opens allowing preterm infants to show a positive physiological response to non-invasive treatment methods, such as MSS. Once this level of maturation is reached, infants are able to both recognize MSS and respond to the more soothing auditory environment thereby enhancing their capacity for cardiorespiratory regulation.

The results of this study add to a growing body of research promoting the implementation of sensory-based developmental interventions during routine NICU care. This includes a number of studies showing the effective use of olfactory stimulation for regulating respiratory patterns [23]; the use of tactile stimulation to excite neuronal activity in the brainstem center and to stimulate respiratory activity [24]; and the use of skin-to-skin stimulation to induce calming effects on the baby's clinical and vital signs [25].

In addition to the positive short-term effects observed in the infants, this study also provides proof of feasibility that maternal sound intervention can be successfully implemented by NICU nurses without interfering with routine NICU care. The MSS seems to be especially important when the mother cannot be physically at the bedside, providing the infant with a womb-like soothing environment which may increase the capacity for self-regulation. The idea of incorporating biological maternal sounds into NICU settings may also increase family involvement and facilitate infant-mother bonding consistent with the view of family-centered [26] and developmental care [27].

Strengths and limitations

This original study examines the effectiveness of a specially-designed micro audio system installed within the infant's incubator throughout the entire NICU hospitalization. Furthermore, a therapeutic window was described and stratified by GA at which exposure to maternal sounds occurred. Our auditory intervention, here referred to as MSS, was designed to better envelop the preterm infant in a more womb-like and soothing sound environment by compensating for the loss of exposure to the maternal voice and heartbeat during hospitalization, without interfering with accepted and vital NICU practices. Despite the positive effects found, the results of this study should be interpreted with caution due to our small sample size. In addition, because our data collection was based both on monitor data and nursing documentation, it is possible that there were inconsistencies in CRE documentation due to human error. Until these results are replicated by a larger randomized controlled trial, our ability to make generalized conclusions based on the current study is still limited.

Conclusion

There is still much to learn about the exposure effects of maternal sounds and the development of the autonomic nervous system in the preterm infant. However, our results point toward potential benefits of using non-invasive strategies to compliment current medical therapies. Our findings suggest that exposure to maternal sounds as an addition to routine NICU care should be further considered and rigorously studied. More research is needed to examine the effects of maternal sounds on premature newborn infants and to further refine the specific age group that would most likely benefit from it.

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***Declaration of interest*:** The authors report no conflict of interest.

References

1. Abu-Shaweesh JM, Martin RJ. Neonatal apnea: what's new? Pediatr Pulmonol 2008;43:937–944.
2. Di Fiore J, Arko M, Herynk B, Martin R, Hibbs AM. Characterization of cardiorespiratory events following gastroesophageal reflux in preterm infants. J Perinatol 2010;30:683–687.
3. Stokowski LA. A primer on apnea of prematurity. Adv Neonatal Care 2005;5:55–70. quiz 171–4.
4. Zhao J, Gonzalez F, Mu D. Apnea of prematurity: from cause to treatment. Eur J Pediatr 2011; Sep;170(9):1097–105.
5. Di Fiore JM, Arko MK, Miller MJ, Krauss A, Betkerur A, Zadell A, Kenney SR, Martin RJ. Cardiorespiratory events in preterm infants referred for apnea monitoring studies. Pediatrics 2001;108:1304–1308.
6. Hunt CE, Corwin MJ, Baird T, Tinsley LR, Palmer P, Ramanathan R, Crowell DH, et al.; Collaborative Home Infant Monitoring Evaluation study group. Cardiorespiratory events detected by home memory monitoring and one-year neurodevelopmental outcome. J Pediatr 2004;145:465–471.
7. Miller JM, Martin RJ, Haxhiu MA. Chemical control of breathing from fetal through newborn life, In: respiratory control and disorders of the newborn. O.P. Matthew, Editor. New York: Marcel Dekker; 2003. pp 83–113.
8. Miller MJ, Martin RJ. Pathphysiology of apnea in prematurity, In: Fetal and neonatal physiology, R. Polin, W. Fox, and S. Abman, Editors. Philadelphia: WB Saunders; 2004. pp 905–918.
9. Perlman JM, Volpe JJ. Episodes of apnea and bradycardia in the preterm newborn: impact on cerebral circulation. Pediatrics 1985;76:333–338.
10. Lopes JM, Aranda JV. Pharmacologic treatment of neonatal apnea, In: Neonatal and pediatric pharmacology: therapeutic priciples in practice, S.M. Yaffe and J.V. Aranda, Editors. Philadelphia: Lipincott Williams & Wilkins; 2004.
11. Aden U. Methylxanthines during pregnancy and early postnatal life. Hand Exp Pharmacol 2001;200:373–389.
12. Henderson-Smart DJ. The effect of gestational age on the incidence and duration of recurrent apnoea in newborn babies. Aust Paediatr J 1981;17:273–276.
13. Anderssen SH, Nicolaisen RB, Gabrielsen GW. Autonomic response to auditory stimulation. Acta Paediatr 1993;82:913–918.
14. Wachman EM, Lahav A. The effects of noise on preterm infants in the NICU. Arch Dis Child Fetal Neonatal Ed 2011;96:F305–F309.
15. Graven SN, Browne JV. Auditory development in the fetus and infant. Newborn and Infant Nursing Rev 2008;8:187–193.
16. Fifer W, Moon C. The role of mother's voice in the organization of brain function in the newborn. Acta Paediatr 2008;83:86–93.
17. Panagiotidis J, Lahav A. Simulation of prenatal maternal sounds in NICU incubators: a pilot safety and feasibility study. J Matern Fetal Neonatal Med 2010;23:106–109.
18. Neal DO, Lindeke LL. Music as a nursing intervention for preterm infants in the NICU. Neonatal Netw 2008;27:319–327.
19. Finer NN, Higgins R, Kattwinkel J, Martin RJ. Summary proceedings from the apnea-of-prematurity group. Pediatrics 2006;117:S47–S51.
20. Jardri R, Pins D, Houfflin-Debarge V, Chaffiotte C, Rocourt N, Pruvo JP, Steinling M, et al. Fetal cortical activation to sound at 33 weeks of gestation: a functional MRI study. Neuroimage 2008;42:10–18.
21. Hepper PG, Shahidullah BS. Development of fetal hearing. Arch Dis Child 1994;71:F81–F87.
22. Hunt CE. Ontogeny of autonomic regulation in late preterm infants born at 34–37 weeks postmenstrual age. Semin Perinatol 2006;30:73–76.
23. Marlier L, Gaugler C, Messer J. Olfactory stimulation prevents apnea in premature newborns. Pediatrics 2005;115:83–88.
24. Gaugler C, Marlier L, Messer J. [Sensory stimulations for the treatment of idiopathic apneas of prematurity]. Arch Pediatr 2007;14:485–489.
25. Gathwala G, Singh B, Singh J. Effect of Kangaroo Mother Care on physical growth, breastfeeding and its acceptability. Trop Doct 2010;40:199–202.
26. Moore KA, Coker K, DuBuisson AB, Swett B, Edwards WH. Implementing potentially better practices for improving family-centered care in neonatal intensive care units: successes and challenges. Pediatrics 2003;111:e450–e460.
27. Butler S, Als H. Individualized developmental care improves the lives of infants born preterm. Acta Paediatr 2008;97:1173–1175.