A Pacifier-Activated Music Player With Mother's Voice Improves Oral Feeding in Preterm Infants

WHAT'S KNOWN ON THIS SUBJECT: Preterm infants must develop oral feeding skills before successfully transitioning to home. Pacifier-activated devices playing selected music can improve nonnutritive sucking in preterm infants. A mother's voice is a positive auditory stimulus for infants.

WHAT THIS STUDY ADDS: A brief intervention with a pacifier-activated music player using mother's voice can decrease tube feeding duration without adverse effects on stress or growth. Operant conditioning with positive reinforcement is an effective developmental strategy to improve preterm infants' feeding skills.

AUTHORS: Olena D. Chorna, MT-BC, MM,[a] James C. Slaughter, PhD,[b] Lulu Wang, BS,[c] Ann R. Stark, MD,[d] and Nathalie L. Maitre, MD, PhD[d,e]

[a]Vanderbilt Kennedy Center, Nashville, Tennessee; [b]Department of Biostatistics, [d]Division of Neonatology, Department of Pediatrics, and [e]Department of Physical Medicine and Rehabilitation, Vanderbilt University, Nashville, Tennessee; and [c]Vanderbilt University School of Medicine, Nashville, Tennessee

Dr Maitre designed the study, obtained grant funding, carried out preliminary analyses, and reviewed and revised all drafts of the manuscript; Ms Chorna designed the study, recruited participants, performed the PAL intervention and participated in data collection and entry, and drafted the initial manuscript; Ms Wang participated in data collection and entry and drafting of the initial manuscript; Dr Slaughter designed the final statistical analyses; Dr Stark contributed to study interpretation and reviewed and revised all drafts of the manuscript; and all authors approved the final manuscript as submitted.

abstract

OBJECTIVES: We conducted a randomized trial to test the hypothesis that mother's voice played through a pacifier-activated music player (PAM) during nonnutritive sucking would improve the development of sucking ability and promote more effective oral feeding in preterm infants.

METHODS: Preterm infants between 34 0/7 and 35 6/7 weeks' postmenstrual age, including those with brain injury, who were taking at least half their feedings enterally and less than half orally, were randomly assigned to receive 5 daily 15-minute sessions of either PAM with mother's recorded voice or no PAM, along with routine nonnutritive sucking and maternal care in both groups. Assignment was masked to the clinical team.

RESULTS: Ninety-four infants (46 and 48 in the PAM intervention and control groups, respectively) completed the study. The intervention group had significantly increased oral feeding rate (2.0 vs 0.9 mL/min, $P < .001$), oral volume intake (91.1 vs 48.1 mL/kg/d, $P = .001$), oral feeds/day (6.5 vs 4.0, $P < .001$), and faster time-to-full oral feedings (31 vs 38 d, $P = .04$) compared with controls. Weight gain and cortisol levels during the 5-day protocol were not different between groups. Average hospital stays were 20% shorter in the PAM group, but the difference was not significant ($P = .07$).

CONCLUSIONS: A PAM using mother's voice improves oral feeding skills in preterm infants without adverse effects on hormonal stress or growth. *Pediatrics* 2014;133:462–468

Preterm infants must demonstrate effective oral feeding skills[1–3] before their discharge to home from the NICU. Oral feeding requires maturation of the nervous system to support coordination of oropharyngeal muscles and breathing.[4] The energy expenditure of oral feeding attempts further complicates the acquisition of oral feeding skills, and must be balanced with caloric intake to achieve sufficient growth.[5] Success at oral feedings is typically achieved at ∼34 to 36 weeks' postmenstrual age.[6] However, delays in achieving oral feedings are common and may prolong hospitalization.[4,7]

Nonnutritive sucking (NNS) is a coordinated motor skill that can be taught through practice and classic conditioning of neural responses with positive reinforcement. NNS on a pacifier promotes sucking behavior in preterm infants, improves the transition to bottle feedings, and reduces length of NICU hospitalization.[8]

Although rigorous studies in preterm infants are limited, specific types of music can positively reinforce behavioral and neural responses.[9–14] In 1 study, a pacifier-activated music player (PAM), used as positive reinforcement for feeding therapies, improved NNS, feeding rates, and growth.[15]

Similar to the effect of music, mother's voice can increase cardiorespiratory stability and growth, improve deep sleep, and shorten length of hospital stay in preterm infants.[9,16–18] However, whether use of a pacifier-activated audio device playing mother's voice has similar or greater effects has not been reported.

We designed a randomized trial to test the hypothesis that mother's voice played through a PAM during NNS would improve the development of sucking ability in preterm infants. Improved sucking ability should promote more effective oral feeding compared with routine NNS with mother's voice alone, and shorten the duration of hospitalization.

METHODS

Design

We performed a prospective, randomized, parallel group trial in preterm infants admitted to the Vanderbilt University Medical Center NICU between April 2012 and May 2013. Infants were eligible if their postmenstrual age was 34 0/7 to 35 6/7 weeks at study start, they were receiving >50% enteral feeds and <50% oral feeds in the 3 days before the study start, and they were cared for in private or semiprivate rooms. Infants were excluded if they were receiving assisted ventilation, continuous positive airway pressure, or high-flow nasal cannula >2 L/min, or if the medical team/feeding specialists considered them medically unsafe to feed orally. Infants with all grades of intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL) on cranial neuroimaging were included in the study. Infants were withdrawn from the study if they experienced a condition their medical team thought made them unsafe to feed orally or enterally during the eligibility period. The study was approved by the Vanderbilt Institutional Review Board (IRB) and informed consent was obtained from the parent(s) of each infant.

Infants were randomly assigned by using a block system to control or intervention groups. Eligible siblings were enrolled into the same group because they shared the same room in the NICU. If 1 child received the PAM intervention while the other engaged in NNS, diffusion of treatment might occur; removal of the siblings' pacifier during the pacifier-activated lullaby (PAL) was not an alternative acceptable to nursing staff. The research team enrolled participants and assigned them to groups predetermined by the randomization system. The infants' medical and nursing care teams were masked to the study group within limits of the units' standard of care. Parents did not know when/if recordings would be

played and did not keep records to suggest group assignment. All study participants, regardless of group assignment, continued with standard of care feeding procedures in the NICU, which include cue-based feeding, NNS support, skin-to-skin care, and graduated introduction of breastfeeding.

Equipment

We used a PAL (Powers Device Technologies, St Johns, FL) device, a 510k Food and Drug Administration–approved digital music delivery system that integrates a sensor, a pacifier routinely used in the NICU, and a receiver. It delivers a predetermined timed interval of auditory stimulus on detection of a suck that meets a preset pressure threshold. In addition, we used a PCM-M10 Portable Linear PCM Voice Recorder (Sony, New York, NY) to record the voice of each participant's mother. This recording served as the positive reinforcement stimulus during conditioning and was transferred to a flash memory stick for use with the PAL device. The device does not allow nutritive sucking through the pacifier.

Procedures

At enrollment, all mother-infant dyads received a set of 4 well-known children's books, 2 of which were single-story songbooks. Mothers in both groups were encouraged to read and sing to their infants whenever they were present; no time quota, schedule, or log was provided. Mothers were informed that the study's objective was to evaluate the influence of their voice on their infant's feeding ability. Mothers' daily presence at the bedside was recorded by nursing staff (masked to study group as possible, see later in this article) as part of the medical record. During the entire hospital stay, per standard of care, infants in both groups were offered pacifiers by nursing staff and mothers for NNS whenever they were

in a quiet-alert state before a feeding time.

Mothers additionally met with the music therapist to record mother's voice singing 2 preselected children's songs corresponding to the books provided. The music therapist provided the mother with the printed lyrics of the 2 songs. No melody sheets were provided. The therapist sang through each song at least once while the infant's mother listened and followed on the lyrics sheet. Mothers were given the opportunity to stop the therapist at any time to ask questions or to repeat the song. The therapist provided a variety of teaching techniques as needed, to assist each patient's mother in singing the melodies. The songs had highly repetitive rhythm and melodies, were in a major key with a range of 1 octave, and in a 4/4 meter. Neither of the melodies included dissonant intervals. The therapist simplified one of the song melodies from the original to be consistent with the previously described description. Songs were recorded and uploaded onto a streamlined digital audio software program to edit any background noise or pauses. The recording was duplicated to last for 15 minutes and put on the flash drive used directly with the PAM device.

On day 0, baseline data from the preceding 72 hours were recorded in both groups. On days 1 to 5, the therapist entered the patient room with the PAM device for 15 minutes and closed the door, regardless of the study group assignment, to mask allocation from the clinical staff. While staff were discouraged from entering during the procedure, it was not possible to prevent occasional nursing interaction due to unit standard of care. Intervention group infants received a PAM session lasting 15 minutes daily for 5 consecutive days. The intervention took place 30 to 45 minutes before the infant's scheduled care and feeding time. Infants remained

in their crib or incubator in a side-lying position for the session. The speaker component of the PAM was placed 6 inches above the infant's head at midline and sensor component of the PAM (connected to the speaker) was inserted into the infant's routinely used pacifier. When the infant's suck reached the threshold pressure, infants in the intervention group heard a lullaby sung by their mother. Pressure thresholds were identical for all participants. If the infant ceased to suck for 1 minute, the pacifier with the PAM sensor was withdrawn from the mouth and reintroduced after several seconds. If the infant dropped below a quiet alert state of arousal, an attempt was made to wake the infant by applying gentle pressure to the hands, as approved by the IRB. Infants experienced NNS only during the 15-minute intervention, and no oral or gavage feeding was attempted during the procedure. The approved IRB protocol stated that the intervention would be discontinued should the infant experience bradycardic or apneic events during the PAL intervention and that these occurrences would be reported as adverse events.

Balancing Measures

Because the additional daily activity for infants in the intervention group might result in increased caloric consumption and stress, we compared weight gain and salivary cortisol levels between groups at baseline and on day 5.

We collected saliva on all infants on the evening before the start of the intervention (day 0, immediately before their evening care time) and on the last evening of the study period (day 5). Samples were collected on infant inert-polymer cylindrical swabs that were saturated with saliva, placed in polypropylene 2-mL tubes, and immediately stored in a −80°C freezer for later assay. Cortisol levels were determined using High-Sensitivity Salivary Cortisol

Enzyme Immunoassay Kit at Salimetrics Inc (State College, PA).

Statistical Analysis

Primary outcomes included change in feeding rate between start and end of the intervention (as measured by volume of nippled nutrition intake in milliliters divided by the time in minutes for consumption) and length of hospitalization. Sample size estimate of 94 subjects was based on manufacturer claims of reduced length of stay for the device and average length of stay of preterm infants in our NICU when the study started. Using an α of 5%, we estimated that we would have 99.4% power to detect a 1 mL/min change in feeding rate and 80% power to detect a 3-day decrease in length of hospital stay. Secondary outcomes included changes in oral feeding volume and frequency after the intervention and number of days to full oral feeds. Balancing measures included discharge weight, growth rate, and change in salivary cortisol levels during the intervention. All data on hospital stay, orogastric feeding tube presence, and growth were obtained from nursing and medical records. Gender and 34- vs 35-weeks' postmenstrual age at study start were analyzed as categorical variables. All others were analyzed as continuous variables.

We summarized continuous variables by using the median, 25th, and 75th percentiles, and categorical variables using percentages. Generalized estimating equations (GEEs) were used to fit marginal linear regression models to determine if each outcome differed by randomization group. Eight twin pairs were included in this study, so we controlled for the possible nonindependence of these observations by clustering on twin identifier in the GEE linear regression models. For each outcome, we also conducted sensitivity analyses using multivariable linear regression to evaluate if adjusting for gestational age (GA) and

brain abnormality altered our conclusions. Hospital length of stay was log-transformed for analysis. All analyses were conducted by using the R statistical program, version 3.0.1 (Vienna, Austria).

An interim midpoint analysis was performed as required by the IRB. No changes to method or procedures were needed and no adverse events were reported.

RESULTS

Population Characteristics

Parents of 100 (90%) of 111 eligible infants gave consent for the study; 3 in each group were withdrawn for medical indications (Fig 1), leaving 46 and 48 infants in the intervention and control groups, respectively, available for analysis. The 2 groups were similar at baseline, including GA, age at study start, birth weight, and gender (Table 1). The groups were also matched by incidence and severity of white matter injury, including PVL and all levels of IVH. Severe brain injury was defined as IVH Grades 3 and 4[19] and/or PVL on predischarge neuroimaging. Parent presence at the bedside during the 5 days of the study was similar between groups (means and SDs for intervention versus control group were 3.8 ± 1.3 and 4.1 ± 1.2 days, respectively). Routine Auditory Brainstem Response testing in the NICU detected no hearing impairment in 45/46 and 47/48

TABLE 1 Patient Characteristics

	Intervention, $n = 46$	Control, $n = 48$	P
GA, wk, median (IQR)	30 (28–32)	30 (28–32)	.15[b]
PMA 34 completed wk at study start,[a] %	93	98	.29[b]
Birth weight, g, median (IQR)	1495 (1122–1742)	1405 (1057–1684)	.35[b]
Gender, % girls	48	52	.70[b]
White matter injury, all types, %	17	19	.86[c]
White matter injury, severe, %	4	6	.69[c]
Feeding rate at study start, day 0	0.6 (0.4–0.8)	0.6 (0.1–0.8)	.27[b]
No. of oral feedings/d at study start (IQR)	2 (1–5)	2 (0.7–4)	.27[b]

IQR, interquartile range (25th–75th).
[a] Versus PMA 35 completed weeks, respectively 7% and 2% in intervention and control groups.
P determined by using GEE linear regression controlling for [b] twins and [c] Pearson χ^2 test.

infants in intervention and control groups. Auditory Brainstem Response data were not available for the remaining 2 infants. Because all mothers' voice recordings were in the English language, 2 Spanish-speaking mothers used vocal melody instead.

Outcomes

Oral feeding rate, volume of oral intake measured during 24 hours after the last intervention, and number of oral feedings per day improved significantly in the intervention group compared with controls (Table 2). Suck pressure, measured only in the intervention group, increased by an average of 15 mm Hg between the first and fifth day of the intervention.

The PAM-with-mother's-voice group achieved full oral feeds an average of 7 days earlier than the control group (Table 3). The trend to decreased length

of hospital stay was not significant ($P = .07$). Discharge weight also did not differ between the groups. There were no improvements in significance when analyses were adjusted for white matter injury and GA.

Balancing Measures

Daily weight gain during the study period was not different between the groups, with a mean increase of 32 vs 30 g per day in the intervention and control groups, respectively ($P = .62$). Similarly, in the subset of 59 ($n = 32, 27$) infants with available data, cortisol levels remained stable across groups with no statistical differences between groups or pre-post intervention ($P = .26$).

DISCUSSION

In a group of preterm infants in the early stages of oral feeding, we showed that a PAM using mother's voice resulted in faster achievement of full oral feedings compared with NNS with a standard pacifier and random exposure to mother's voice. To our knowledge, this is the first demonstration of mother's voice used with a PAM to promote oral feeding skills. Involving mothers through music therapy to teach essential developmental skills to their infant promotes family-centered care in the NICU. Furthermore, use of recorded maternal voice as a stimulus may overcome potential lack of appropriate stimulation in single-patient rooms in modern NICUs that may contribute to neurodevelopmental abnormalities and delays.[20]
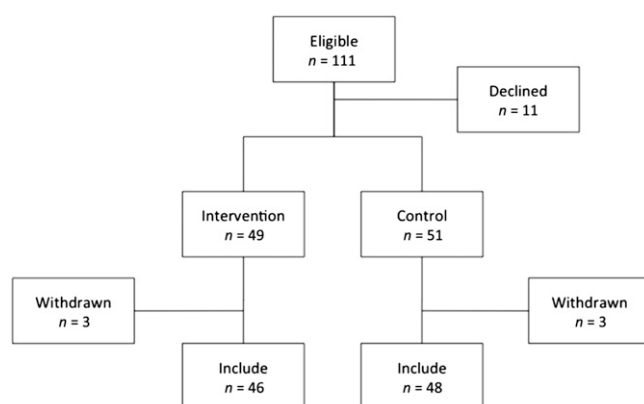

FIGURE 1
Participants.

TABLE 2 Feeding Outcomes

Measure	PAL, n = 46		Control, n = 48		P
	Pre	Post	Pre	Post	
Oral feeding rate, mL/min	0.6 (0.4–0.8)	2.0 (1.5–2.3)	0.6 (0.1–0.8)	0.9 (0.5–1.2)	<.001[a]
Oral feedings, no. out of 8/d	2 (1–5)	6.5 (4–8)	2 (0.7–4)	4 (1–7)	<.001[a]
Oral feed volume, mL/kg/d	13.3 (6.8–40.8)	91.1 (41.9–127.7)	17 (6.3–35.6)	48.1 (5.5–98.1)	.001[a]
NNS pressure, mm Hg	20 (10–30)	35 (25–60)			<.001[b]

Values are median (interquartile range).
P determined by using GEE linear regression controlling for [a] twins and [b] paired t test.

PAM with mother's voice is a developmentally appropriate successful oral feeding strategy that provides positive auditory stimulation to infants while supporting active parental roles during infant hospitalization.

Our results are consistent with other studies that demonstrated improved oral feeding in preterm infants by using various oral stimulation protocols.[4,21–23] However, these protocols differ widely in duration, techniques, providers, positioning, environment of the patient, evaluation of effectiveness, equipment, and population characteristics. These protocols are not widely used because of the variable methodologies and the high skill level required to apply them. In contrast, our use of a standardized device and an easily available stimulus during a short 5-day period makes the methodology more generalizable to a wide range of NICUs and neonatal clinicians.

Unlike other studies, we intentionally included subjects with severe white matter injury to best represent the range of patients who could benefit from this intervention. Infants with white matter injury in our study demonstrated improved feeding in spite of likely oropharyngeal or sensorimotor involvement.[24,25] These deficits commonly coexist with more obvious gross motor impairments in cases of severe white matter injury.[26–28]

Our results support the use of operant conditioning with positive reinforcement to improve the development of preterm infants' oral feeding skills. Conditioning of infant behavior, responses to stimuli, and effect on learning have been demonstrated in preterm infants as young as 32 weeks' postmenstrual age by the use of paradigms of learning, operant[13,29] and classic conditioning, and habituation.[30,31] Consistent with previous reports, our study suggests that preterm infants have the ability to learn through conditioning of neural responses with auditory stimuli-contingent reinforcement.

Our use of mother's voice as positive reinforcement makes this application of the PAM novel. Although only prerecorded female voices provided by the manufacturer are suggested for use with this device, use of maternal voice may be preferred. Previous studies with a PAM device with commercially recorded lullabies found improved NNS, weight gain, feeding rate, and decreased days of gavage feeding.[32–34] However, in very low birth weight infants exposed systematically to a recording of maternal voice and biological sounds inside the incubator, weight gain velocity was greater than in control infants.[18] Other studies recommend the use of mother's voice recordings obtained and provided according to specific guidelines.[35]

Although our study showed a trend toward shorter hospitalization in the intervention group, the results were not significant. The variability in length of hospital stay at the time of our study was greater in both groups than when we performed our power calculations. The resulting 3-day increase in the SD decreased the power to detect a difference between groups in length of hospitalization. Increased patient acuity due to an expanded referral base, increased NICU bed capacity, and an average increased length of stay during the interim period may all have contributed to this difference.

Our study has several limitations. Our findings may have been strengthened by inclusion of a third group treated with the PAM device with either a female voice that was not the mother's or an instrumental lullaby. We chose not to include such a group, as this stimulus had been conclusively studied by Standley et al.[13,15,33–35] Additionally, our purpose was to study an intervention supported by the developmental approach in the NICU to promote family-centered care. Documenting the timing and duration of mother's singing at the bedside each day for comparison with the duration of the PAM intervention would have been optimal. However, this would have unmasked the study group assignment to nursing and medical staff.

Furthermore, we kept the suck threshold that activated mother's voice consistent across all patients in the intervention group. In clinical practice, threshold can be changed to better meet an individual infant's abilities and needs. We recorded mothers' voice in English to

TABLE 3 Hospitalization Outcomes

Measure	Intervention, n = 46	Control, n = 48	P
Time to full oral feeds, d	31 (17–54)	38 (24–69)	.04
Length of hospital stay, d	41 (25–69)	50 (31–86)	.07
Discharge weight, g	2000 (1892–2228)	1990 (1902–2120)	.62

Values are median (interquartile range).
All P determined by using GEE linear regression controlling for twins.

be consistent with the study protocol, so that 2 Spanish-speaking mothers used vocal melody instead. It may be more appropriate to use the family's native language. Finally, although we had hoped to use salivary cortisol levels to assess possible stress associated with our intervention, collection of a sufficient amount of saliva was difficult, so that samples were available for analysis for only 62% of subjects.

CONCLUSIONS

Our study showed that a relatively simple, short, and reproducible intervention with a PAL sung by the infant's mother improves oral feeding skills in preterm infants, including those with brain injury. Larger studies are needed to determine whether this intervention can decrease length of hospitalization for preterm infants. Whether this therapeutic approach is applicable to other populations at risk for poor oral feeding, such as infants with congenital heart disease, prolonged respiratory illness, or neuromuscular disease, requires additional research.

REFERENCES

1. Casiro OG, McKenzie ME, McFadyen L, et al. Earlier discharge with community-based intervention for low birth weight infants: a randomized trial. *Pediatrics.* 1993;92(1):128–134

2. Darnall RA, Kattwinkel J, Nattie C, Robinson M. Margin of safety for discharge after apnea in preterm infants. *Pediatrics.* 1997;100(5):795–801

3. Merritt TA, Pillers D, Prows SL. Early NICU discharge of very low birth weight infants: a critical review and analysis. *Semin Neonatol.* 2003;8(2):95–115

4. Greene Z, O'Donnell CPF, Walshe M. Oral stimulation techniques in preterm infants - international research challenges. *J Neonatal Nurs.* 2013;19(4):168–174

5. Hans DM, Pylipow M, Long JD, Thureen PJ, Georgieff MK. Nutritional practices in the neonatal intensive care unit: analysis of a 2006 neonatal nutrition survey. *Pediatrics.* 2009;123(1):51–57

6. Rudolph CD, Link DT. Feeding disorders in infants and children. *Pediatr Clin North Am.* 2002;49(1):97–112, vi

7. Dodrill P. Feeding difficulties in preterm infants. *Infant Child Adolescent Nutr.* 2011;3(6):324–331

8. Pinelli J, Symington AJ. Non-nutritive sucking for promoting physiologic stability and nutrition in preterm infants. *Cochrane Database of Systematic Reviews* 2005 (4). Art. No.: CD001071. DOI:10.1002/14651858.CD001071.pub2.

9. Beauchemin M, González-Frankenberger B, Tremblay J, et al. Mother and stranger: an electrophysiological study of voice processing in newborns. *Cereb Cortex.* 2011;21(8):1705–1711

10. Dehaene-Lambertz G, Montavont A, Jobert A, et al. Language or music, mother or Mozart? Structural and environmental influences on infants' language networks. *Brain Lang.* 2010;114(2):53–65

11. Moon CMC, Fifer WPW. Evidence of transnatal auditory learning. *J Perinatol.* 2000;20(8 pt 2):S37–S44

12. 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(suppl 3):106–109

13. Standley JJ. Music therapy research in the NICU: an updated meta-analysis. *Neonatal Netw.* 2012;31(5):311–316

14. Loewy J, Stewart K, Dassler AM, Telsey A, Homel P. The effects of music therapy on vital signs, feeding, and sleep in premature infants. *Pediatrics.* 2013;131(5):902–918

15. Standley JMJ. The effect of music-reinforced nonnutritive sucking on feeding rate of premature infants. *J Pediatr Nurs.* 2003;18(3):169–173

16. Arnon S, Shapsa A, Forman L, et al. Live music is beneficial to preterm infants in the neonatal intensive care unit environment. *Birth.* 2006;33(2):131–136

17. Blumenfeld H, Eisenfeld L. Does a mother singing to her premature baby affect feeding in the neonatal intensive care unit? *Clin Pediatr (Phila).* 2006;45(1):65–70

18. Zimmerman E, Keunen K, Norton M, Lahav A. Weight gain velocity in very low-birth-weight infants: effects of exposure to biological maternal sounds. *Am J Perinatol.* 2013;30(10):863–870

19. Papile LA, Munsick-Bruno G, Schaefer A. Relationship of cerebral intraventricular hemorrhage and early childhood neurologic handicaps. *J Pediatr.* 1983;103(2):273–277

20. Pineda RG, Neil J, Dierker D, et al. Alterations in brain structure and neurodevelopmental outcome in preterm infants hospitalized in different neonatal intensive care unit environments. *J Pediatr.* 2014;164(1):52–60.e2

21. Fucile S, Gisel EG, Lau C. Effect of an oral stimulation program on sucking skill maturation of preterm infants. *Dev Med Child Neurol.* 2005;47(3):158–162

22. Rocha AD, Moreira MEL, Pimenta HP, Ramos JRM, Lucena SL. A randomized study of the efficacy of sensory-motor-oral stimulation and non-nutritive sucking in very low birthweight infants. *Early Hum Dev.* 2007;83(6):385–388

23. Daley HK, Kennedy CM. Meta analysis: effects of interventions on premature infants feeding. *J Perinat Neonatal Nurs.* 2000;14(3):62–77

24. Whitaker AH, Feldman JF, Lorenz JM, et al. Motor and cognitive outcomes in non-disabled low-birth-weight adolescents: early determinants. *Arch Pediatr Adolesc Med.* 2006;160(10):1040–1046

25. Perlman JM. Neurobehavioral deficits in premature graduates of intensive care—potential medical and neonatal environmental risk factors. *Pediatrics.* 2001;108(6):1339–1348

26. Vohr BR, Wright LL, Dusick AM, et al. Neurodevelopmental and functional outcomes of extremely low birth weight infants in the

National Institute of Child Health and Human Development Neonatal Research Network, 1993-1994. *Pediatrics*. 2000;105(6): 1216–1226

27. Maitre NL, Marshall DD, Price WA, et al. Neurodevelopmental outcome of infants with unilateral or bilateral periventricular hemorrhagic infarction. *Pediatrics*. 2009; 124(6). Available at: www.pediatrics.org/cgi/content/full/124/6/e1153

28. Ment LRL, Vohr BB, Allan WW, et al. The etiology and outcome of cerebral ventriculomegaly at term in very low birth weight preterm infants. *Pediatrics*. 1999; 104(2 pt 1):243–248

29. Vervloed J. Learning in preterm infants. Habituation, operant conditioning, and their associations with motor development. 1995:1–177. Available at: http://irs.ub.rug.nl/ppn/127483411. Accessed July 1, 2013

30. Hepper PG. Fetal memory: does it exist? What does it do? *Acta Paediatr Suppl*. 1996; 416:16–20

31. Colombo J, Fagen JW. *Individual Differences in Infancy*. Hillsdale, NJ: Psychology Press; 1990

32. Cevasco AM, Grant RE. Effects of the pacifier activated lullaby on weight gain of premature infants. *J Music Ther*. 2005;42 (2):123–139

33. Standley JM. *The Effect of Contingent Music to Increase Non-Nutritive Sucking of Premature Infants: An Article From Pediatric Nursing*. Pittman, NJ: Jannetti Publications, Inc; 2000

34. Standley JM, Cassidy J, Grant R, et al. *The Effect of Music Reinforcement for Non-Nutritive Sucking on Nipple Feeding of Premature Infants. (Continuing Nursing Education)(Clinical report): An Article From Pediatric Nursing*. Pittman, NJ: Jannetti Publications, Inc; 2010

35. Standley JM. Music therapy for the neonate. *Newborn Infant Nurs Rev*. 2001;1(4): 211–216

MY PURPLE SWEATER: *I have a particularly beautifully colored sweater that I love to wear. The easiest way to describe the color of the sweater is to simply say it is purple. However, there are dozens of shades of purple with different intensities and emotional attachments. The color of my sweater is somewhere between boysenberry and aubergine, but to me it is a deep, soft color that makes me feel relaxed. If, however, I lived in ancient Rome, the color would have indicated royalty.*

With the fabulous selections of colors now available to consumers for anything from socks and shoes to sweaters and shirts, we tend to forget that the development of synthetic dyes is a relatively recent phenomenon. In ancient times, clothes derived their color from natural fibers or were dyed with organic dyes. Tyrian purple was the rarest and costliest dye of them all, making it the color of royalty, nobility, and persons with lots of money trying to make a statement.

According to an article in The New York Times *(Science: October 9, 2013), the dye was derived from marine snails. While the snail does not appear purple, chromogens in protective mucus secreted by the snail, when exposed to heat and oxygen, turned purple. Thousands of snails had to be boiled for days to obtain the pigment. A Tyrian purple cloak was generally worth its weight in gold, and Tyrian purple was the most coveted and famous purple dye until early in the 20th century when cheaper synthetic dyes were developed.*

The precise process to make Tyrian purple and the exact color are no longer known. However, while it is unlikely my sweater is the same hue as Tyrian purple, I like to think that my beautiful sweater is somehow linked to a small marine animal and history.

Noted by WVR, MD