ACTA PÆDIATRICA
NURTURING THE CHILD

Acta Pædiatrica ISSN 0803–5253

REGULAR ARTICLE

The influence of music on aEEG activity in neurologically healthy newborns ≥32 weeks' gestational age

Monika Olischar (monika.olischar@meduniwien.ac.at)[1,2], Helen Shoemark[2,3], Trudy Holton[2], Manfred Weninger[1], Rod W Hunt[2,3,4]

1.University Childrens Hospital, Neonatology, Vienna, Austria
2.The Royal Childrens Hospital Neonatology, Melbourne, Vic., Australia
3.Murdoch Childrens Research Institute, Melbourne, Vic., Australia
4.Department of Paediatrics, The University of Melbourne, Melbourne, Vic., Australia

Keywords
Amplitude-integrated electroencephalography, Music, Neonates, Quiet sleep, Sleep–wake cycling

Correspondence
Monika Olischar, M.D., Department of Neonatology, The Royal Childrens Hospital, Flemington Road, Parkville, Vic. 3052, Australia.
Tel: +61-3-9345-5000 |
Email: monika.olischar@meduniwien.ac.at

Department of Neonatology, University Childrens Hospital, Waehringer Guertel 18-20, 1090 Vienna, Austria.
Tel: +43-1-40400-3232 |
Fax: +43-1-40400-6453 |

Received
24 September 2010; revised 9 January 2011; accepted 17 January 2011.

DOI:10.1111/j.1651-2227.2011.02171.x

ABSTRACT

Aim: Music is increasingly being used in neonatal intensive care units to aid neurodevelopmental care. The aim of this pilot study was to examine the possible effects of music on quiet sleep (QS) in neurologically healthy newborns.

Methods: Twenty newborns ≥32 weeks' gestational age admitted to the neonatal intensive care unit at The Royal Children's Hospital in Melbourne for specialist consultation were randomly assigned to experimental or control groups. Ten subjects were exposed to music (*Music for Dreaming*, (Sound Impressions, Pty. Ltd.) using a CD player (50–55 decibel A). Amplitude-integrated EEG was recorded on the BrainZ Monitor (BRM2, Version 8.0, Natus). Background pattern, presence and quality of sleep–wake cycles (SWC) were assessed before and after exposure to music.

Results: All 20 subjects showed continuous background patterns with developing SWC. Whereas no subject in the control group showed differences in their QS and eight patients in the intervention group showed lower minimum amplitudes of their QS after music exposure. Also, the length of QS and interval between QS epochs became progressively longer in all ten subjects of the intervention group.

Conclusion: We report a trend to more mature SWC in subjects who were exposed to music when compared to controls suggesting that there might be a small effect of music on quiet sleep in newborns.

BACKGROUND

Auditory capability is one of the earliest discriminative abilities of the foetus (1). The human cochlea and peripheral sensory end organs complete their normal development by 24 weeks' gestation. Ultrasonographic observations of blink-startle responses to vibro-acoustic stimulation are first elicited at 24–25 weeks of gestation and are consistently present after 28 weeks, indicating maturation of the auditory pathways of the central nervous system (2). At birth, the term infant can recognize his/her mother's voice as well as melodies heard during the final trimester of foetal life. Evidence indicating preference for native language as early as day 2 of life has also been published (3,4).

For the premature infant, we know that excessive noise is correlated with decreases in oxygen saturation, increases in heart rate and sleep disturbances (5–7). A controlled auditory environment may protect sleep, support stable vital signs, improve speech intelligibility and reduce potential adverse effects on auditory development (8).

It has been suggested that recorded music is a valuable resource in the neonatal intensive care unit (NICU) to reduce stress and increase physiological stability, to provide better growth rates and to facilitate neurosensory maturation (9). Music is an intentional auditory stimulus with organized elements including melody, rhythm, harmony, timbre, form and style. Music soothes, and the existence of lullaby is evidence of the innate acceptance that music quietens babies (10). A recent survey with regard to common forms of stimulation during the neonatal period at NICUs in the United States showed that music was used in 72% of hospitals (11). Additionally, stimulation may enhance the development of associative cortical tissue via sensory-motor activation (12). Studies using near-infrared spectroscopy suggested that auditory stimulation in newborn infants induced neuronal activation in their frontal lobe (13).

The amplitude-integrated electroencephalography (aEEG) is now increasingly used in NICUs with demonstrated clinical value in the monitoring of the newborn infant's brain function (14). Standard criteria for assessing

Abbreviations
aEEG, Amplitude-integrated electroencephalography; dBA, Decibel A; NICU, Neonatal intensive care unit; QS, Quiet sleep; RCH, The Royal Children's Hospital; SWC, Sleep–wake cycling.

sleep–wake states include evaluation of respiration, cardiac activity, movements and rapid eye movements. In aEEG, sleep–wake cycling (SWC) appears as a sinusoidal pattern with varying bandwidth and continuity, more discontinuous during quiet sleep (QS) than during wakefulness and active sleep. The average duration of quiet sleep periods is 24–28 min between 32 and 36 postconceptional weeks. It is slightly longer at night, but is otherwise relatively stable and appears not to be affected by developmental care interventions (15).

Sleep is a vital component of healthy neurological development in the newborn infant. However, in the NICU, sleep is repeatedly disrupted by essential procedures and unrelated ambient noise. Recorded music has been employed in the NICU as an auditory stimulus to mask aversive auditory stimuli with observable success in infants both transitioning to sleep and remaining asleep. However, the mechanism by which this is achieved is unclear.

In pursuit of further evidence, the application of the aEEG may provide a clearer picture of the impact of recorded music on newborn brain activity during sleep. The hypothesis of this pilot study was music would lead to reduction in disturbance of state regulation for the newborn infant with an increase in the amount of QS.

The aim of this pilot study was therefore to evaluate the influence of music on aEEG activity (background pattern and SWC) in neurologically healthy neonates born ≥32 weeks' gestational age. This pilot study was designed to inform future studies that are planned to investigate the influence of music on aEEG activity in sick newborns requiring intensive care treatment.

PATIENTS AND METHODS

From January 2009 to December 2009, twenty neurologically healthy infants admitted to the NICU at The Royal Children's Hospital Melbourne (RCH), with minor non-neurological abnormalities requiring further investigation (isolated surgical anomalies not affecting the central nervous system or admission for the assessment of non-neurological problems), were recruited for this study. SWC on aEEG is consistent and easily discernable from 32 weeks' gestational age onwards (15). Therefore, we aimed to recruit patients born after 32 weeks within the first 6 weeks of life to avoid the bias of previous exposure to auditory influences. Patients were eligible for inclusion in this study if they were neurologically healthy neonates born ≥32 weeks' gestational age, required investigation or specialist consultation for a non-neurological condition and were less than six completed weeks of postnatal age. Neurological examination was performed on admission by the neonatal registrar on duty, and patients were recruited in the order they were admitted to the NICU. Infants were excluded if they were born <32 weeks' gestational age, had neurological conditions or syndromes known to affect neurodevelopment or required mechanical ventilation.

Participants were randomly assigned to either experimental or control groups using simple random allocation by means of sealed sequential numbered envelopes. After parental informed consent was obtained, the principal researcher requested a sealed envelope from a staff member not involved in the study. The envelope was opened, and the allocation was documented on a list, and signed by both researcher and staff member as witness. Ten infants were randomized into the experimental group (musical stimulation) and 10 subjects into the control group – these infants were monitored by aEEG without any musical stimulation. This actual number of infants was chosen because of the number of admissions of stable and neurologically noncompromised patients not requiring intensive care treatment within the study period of 1 year.

As the investigation was focused on sleep, a lullaby was selected for its sedative quality. Lullaby melody has more descending contours, fewer contour changes and a higher-median pitch than other songs (16). The lullaby is rhythmically simple and has a lilting meter. Lullabies are repetitive, simple and slow and are identified as 'soothing' and 'soft' (17).

Music stimuli appropriate for the NICU demonstrate the infant-preferred characteristics of limited accompaniments, simple rhythms, consistent dynamic levels, steady tempos, lilting melodies and a structured and organized form that is soothing and comforting (18–23).

The specific source of music in this case was *Brahms' Lullaby* from the Australian produced *Music for Dreaming*, (Sound Impressions, Pty. Ltd.; http://www.musicfordreaming.com/index.html). This recording of instrumental lullaby music was arranged to meet the recommendations about music as a stimulus for premature infants at the time of production (Cherie Ross, producer, personal communication). Standley et al. (22) report that this music was favoured by nurses above 12 other lullaby recordings. Hanson-Abromeit (19) found that when using specific criteria for selecting sedative music for infants in NICU, NICU nurses and music therapists selected *Brahms' Lullaby* (*Music for Dreaming*) as the best choice.

Music was administered to the infants using a Sony Discman and speakers arranged at 30 cm from the infant's head. Prior to the commencement of music, the sound level was checked at the infant's ear with a hand-held Lutron SL-4022-calibrated sound level meter to ensure the ambient level was quiet enough to add music. Sound levels were monitored throughout the aEEG recording. The music was presented in line with the American Academy of Pediatrics recommendations for sound in NICU – thus around 50–55 decibel A weighted scale (dBA).

The music was presented after one SWC on aEEG for approximately 20 min. aEEG was recorded on the BrainZ Monitor (BRM2, Version 8.0; BrainZ Instruments, Auckland, New Zealand) from the standard application of central (C3, C4) and parietal (P3, P4) positions from the international 10–20 system. The aEEG was applied by placing five small sticky electrodes (neonatal sensor set manufactured for BrainZ Instruments Ltd.) on the infant's head (two on each side and one down towards the neck) and the leads connected to the aEEG monitor. The participant was continuously monitored by the same researcher who opened the envelope (HS or TH). The background pattern, presence and quality of the QS were assessed offline by two blinded researchers (RH and MO) unaware of the group allocation, using the aEEG and raw trace from both hemispheres for analysis. The assessment focused on the background of the aEEG and a comparison of the first QS with the following QS epochs to determine whether music had an influence on their appearance.

Sleep–wake cycles are described as smooth sinusoidal variations, mostly in the minimum amplitude. The broader bandwidth represents discontinuous background activity during quiet sleep, while the narrow bandwidth corresponds to the more continuous activity during wakefulness and active sleep. SWC develops with increasing maturation, and from 31 to 32 weeks' gestational age, quiet sleep periods are clearly discernable in the aEEG trace as distinct periods with increasing bandwidth. At term, these periods represent tracé alternant EEG patterns (14). The average duration of quiet sleep periods is 24–28 min between 32 and 36 postconceptional weeks, and slightly longer at night, but otherwise relatively stable and not affected by incubator covers (24) or developmental care intervention (14).

For comparison of aEEG activity before and after musical stimulation, we aimed to obtain data for one SWC before music and two to three SWCs after music. To ensure three to four SWCs were captured, the aEEG monitor was applied for up to an hour prior to music delivery and left in place for up to 4 h afterwards. Traces were analysed offline and classified as follows, according to the classification system of Hellstrom-Westas et al. (14):

- No SWC: no cyclic variation of the aEEG background.
- Immature SWC: some, but not fully developed, cyclical variations of the lower amplitude present, but not developed when compared with normative gestational age representative data.
- Developed SWC: clearly identifiable sinusoidal variations between discontinuous and more continuous background activity, with cycle duration ≥20 min.

Because we did not know whether qualitative differences in aEEG (background pattern and quality of SWC) before and after the delivery of music to the neonate would be evident, an additional quantitative analysis of recorded QS periods has been performed: QS epochs were analysed in terms of duration (determination of start of QS by visual perception only, then calculation of length of QS period in minutes), minimum and maximum amplitudes (by counting the 10 lowest and the 10 highest amplitudes within one QS period) and frequency of appearance (length of trace between two QS epochs in minutes), and the first SWC was compared to all the following ones.

One of the investigators (HS, TH) was present during the study period to observe the baby's behaviour and account for the acoustic environment to which the infant was exposed (e.g. ward rounds, arrival of a new patient or family members and ambient noise and monitor alarms). Additional information was collected from observations including type of room and bed in which the baby was cared for (indicative of auditory environment).

At the point of recruitment, mothers were asked about their music-listening experience during pregnancy, and whether music had been played to their infant since birth. Information collected from the medical record included contact information, gender, gestational age at birth, admission diagnosis, current medication and results from previous neurological examinations.

Statistical analysis was conducted in SPSS (PASW Statistics for Mac, v18). Continuous variables measuring amplitude and duration of SWC were analysed with *t*-test for independent samples. Linear regression was also performed adjusting for duration of sound intensity during SWC. A p-value of 0.05 was considered statistically significant. The study was approved by the Human Research Ethics Committee at RCH, and informed consent was obtained in all cases.

RESULTS

A total of 20 subjects were included in the study. Patients' characteristics are summarized in Table 1. Both groups were similar, except for their behavioural state as measured by Prechtl's method at the time of aEEG recording (25). In the intervention group, nine subjects were in State I (quiet sleep) compared to only six subjects in the control group. Patients in the intervention group were admitted to NICU at RCH for further investigation of reflux (n = 2), micrognathia (n = 2), respiratory distress (n = 2), Hirschsprung's disease (n = 1), bilious vomiting (n = 1), colitis (n = 1) and fever (n = 1). Patients in the control group were admitted for bronchiolitis (n = 3), bilious vomiting (n = 2), colitis

Table 1 Patient's baseline characteristics

Group	Gestational age at birth (median and range)	Day of life (median)	Behavioural state	Time of day	dBA before 1st SWC (median)	dBA after 1st SWC (median)	Music during pregnancy
Intervention group	37.7 (33 + 2 to 41 + 2)	15.3 (3–32)	State I n = 9 State II n = 1	Day n = 3 Night n = 7	48.3 (45.3–50.3)	54.0 (52.1–54.8)	Incidentally n = 5 2–3×/day n = 2 Every day n = 3
Control group	38.1 (36 + 0 to 42 + 0)	17.6 (2–42)	State I n = 6 State II n = 4	Day n = 6 Night n = 4	48.5 (46.0–51.3)	50.8 (45.0–53.4)	Incidentally n = 7 Every day n = 3

SWC = sleep–wake cycles.

(n = 1), reflux (n = 1), jitteriness (n = 1), fever (n = 1) and inguinal hernia (n = 1). None of them required intensive care treatment, surgery or showed any evidence of neurological compromise. Although the impact of the variability of diseases on sleep quality remains unclear, we tried to standardize our study setting by monitoring the patients while they showed similar behavioural states (State 1 or 2).

The auditory environment was reported below 50dBA prior to the addition of music, and physiological parameters were within normal limits in all subjects and during every study period. All subjects were nursed in open cots, and they were all located in two bed rooms. All staff members on duty were alerted to the beginning of a study period of a newly included patient, and therefore, they were able to avoid ward rounds at the bedside of a study patient during aEEG monitoring. None of our subjects were disturbed by new admissions.

Amplitude-integrated electroencephalographies were recorded for 3.5 h (range 3–6 h) in the intervention group and for 4.4 h (range 3–7.75 h) in the control group. All 20 subjects showed a normal continuous background activity and well-developed SWC. aEEG characteristics are summarized in Table 2. QS periods did not differ significantly between groups except for a lower mean minimum amplitude in the intervention group (5.8 μV) when compared to controls (7.7 μV), suggesting more easily discerned sleep–wake cycling in the music-exposed infants ($t = 1.84$, $p = 0.08$). This result remained statistically nonsignificant after adjustment for sound intensity during the study period ($p = 0.29$). There was no significant difference in mean maximum amplitude of SWC between music-exposed (24.8 μV) and control (24.7 μV) infants ($t = 0.79$, $p = 0.9$). Whereas none of the patients in the control group showed differences in their QS periods throughout the whole measurement and eight patients in the intervention group showed lower minimum amplitudes of their QS epochs after music exposure (Fig. 1). Also, patients in the control group did not show any alteration in the time between QS periods ($t = 1.68$, $p = 0.11$), whereas duration of the pattern between QS became progressively longer in all ten subjects of the intervention group. These two observations made QS periods in the intervention group more easily discernable.

DISCUSSION

To our knowledge, this is the first study analysing the impact of music on SWC and QS in term and near-term infants. We did not show any statistically significant differences between music-exposed and control infants but the numbers of subjects were small in this pilot study. We were able to demonstrate a trend towards more discernable SWC after music exposure. Previous studies have demonstrated an increase in the mean amplitude of the lower margin of aEEG with increasing maturity, and we are unable to explain why we should have found a decrease in those infants exposed to music. However, we have demonstrated a trend towards a significant difference between the two groups, and with easier discernability of sleep wake cycling

Table 2 Characteristics of QS epochs, excluding the first sleep–wake cycles before an eventual musical stimulation

Group	Number of QS epochs (median)	Duration of QS epoch (in min, median)	Minimum amplitude (in μV, median)	Maximum amplitude (in μV, median)	Duration between QS epochs (in min, median)
Intervention group	2.7 (2–4)	19.2 (13.5–22.7)	5.8 (2.3–8.5)	24.8 (21.3–26.75)	49.9 (25–88)
Control group	2.8 (2–5)	19.2 (15.5–22.8)	7.7 (3.4–11.5)	24.7 (22.5–27.5)	53.2 (21–82)

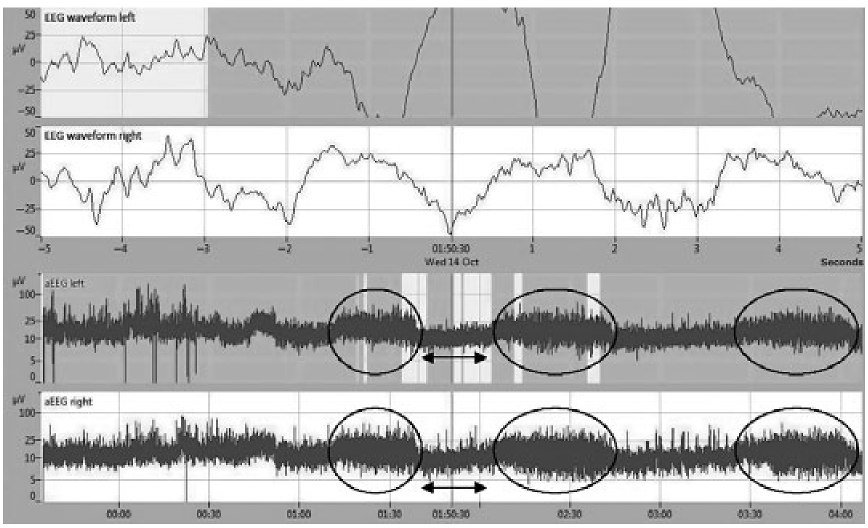

Figure 1 Trace of patient in the intervention group showing three QS periods (encircled). The second and third QS periods (after music exposure indicated by arrow) show lower minimal amplitudes when compared to the first sleep–wake cycles (before music exposure).

argue that this may reflect improved or more mature sleep integrity.

Recently, Perania et al. (26) showed that a hemispheric functional asymmetry for music perception is present at birth. Activation with right-hemispheric dominance was observed in the primary, secondary and higher-order auditory cortices in newborns. This right-hemispheric dominance indicates that the newborn brain responds to musical information quite specifically and that these areas are already recruited with right-hemispheric dominance by newborns for the processing of musical information (26). Therefore, we believe that infants were able to process the music presented. SWC is present in healthy term newborns and is a sign of neurological integrity (27), and the presence of SWC pattern on aEEG is therefore considered a good prognostic sign (28). In term infants with hypoxic-ischaemic encephalopathy, the presence, time of onset and quality of SWC correlated with recovery from the hypoxic-ischaemic insult. The time of onset of SWC has a predictive value for neurodevelopmental outcome in these infants (29). Our results show that music tends to change the appearance of SWC by lowering minimum amplitude. SWC becomes more sinusoidal through reduction in minimum amplitude and therefore more easily discernable. This suggests that music might be a positive stimulus to the newborn brain.

It has been noted that reports of applied recorded music in the NICU lack rigorous articulation of parameters including duration of stimulus, validation of loudness and rationale for music selection (30,31). This was an observational study, and the music stimulus was prepared according to the AAP recommendations.

In this pilot study on a small number of neurologically healthy newborns, we did not expect to show any statistically significant differences. Furthermore, a main limitation of our study was that only one SWC before and two to three SWC after the musical stimulation were recorded and analysed. As SWC shows physiological variations of length and bandwidth, the variability limits the interpretation of the findings. However, the sample size and study time were considered by the investigators to be adequate to determine whether there was any impact of music on sleep in these infants. Trends towards significant reductions in minimum amplitude suggest improved maturation of SWC.

These results have to be interpreted with caution because of the limitation of aEEG to differentiate between sleep stages, active sleep and wakefulness. aEEG only allows analysis of quiet sleep periods and their frequency only. Other parameters often analysed in relation to sleep including respiration rate, heart rate variability and eye movements were not evaluated in this study. Furthermore, the patients were not all analysed at the same time of the day and changes in SWC might reflect the differences in day and night rhythms, although the presence of circadian rhythm in infants at this gestation is debated (32). It is also possible that musical stimulation presented to infants at an intensity level recommended within guidelines for NICUs may be too quiet to have any significant impact on the infants quiet sleep behaviour. Our subjects were not newborn and had already been exposed to relatively noisy ex utero environments so they may have undergone some auditory adaptation.

Further studies may focus specifically on the preterm infant – 32- to 36-week gestation with or without pathology. At this gestation, the time of day that the infants are studied is likely to confound the results, but study at similar times of the day for each infant would eliminate this as a potential confounder.

Nevertheless, improved discernability of SWC in infants following exposure to music suggests improved sleep integrity and may mediate improved neurological behaviour and outcome. This finding requires further interrogation in a larger study.

CONCLUSION

Given the increasing application of recorded music in the clinical setting, we believe we should monitor its impact. This pilot study examined the utility of the aEEG to measure the impact of a simple presentation of recorded music on the sleep of newborn infants. We have shown that SWC becomes more easily discernable, through reduction in minimum amplitude of QS periods, in subjects who were exposed to music when compared to controls. A more detailed examination of the immediate impact and potential long-term benefit of music in the sick newborn infant is indicated.

References

1. Cheour-Luhtanen M, Alho K, Sainio K, Rinne T, Reinikainen K, Pohjavuori M, et al. The ontogenetically earliest discriminative response of the human brain. *Psychophysiology* 1996; 33: 478–81.
2. Birnholz JC, Benacerraf BR. The development of human fetal hearing. *Science* 1983; 222: 516–8.
3. De Casper AJ, Fifer WP. Of human bonding: newborns prefer their mothers' voices. *Science* 1980; 208: 1174–6.
4. Moon C, Cooper RP, Fifer WP. Two-days-olds prefer their native language. *Infant Behav Dev* 1993; 16: 495–500.
5. Kellman N. Noise in the intensive care nursery. *Neonatal Netw* 2002; 21: 35–41.
6. Morris BH, Philbin MK, Bose C. The full-term and premature newborn: physiological effects of sound on the newborn. *J Perinatol* 2000; 20: S54–9.
7. Sparshott MM. The "sound" of neonatal intensive care: effect of noise levels in the neonatal unit on the sleep patterns of sick preterm infants. *J Neonat Nurs* 1995; 2: 7–9.
8. Graven SN. Sound and the developing infant in the NICU: conclusions and recommendations for care. *J Perinatol* 2000; 20(Pt 2): S88–93.
9. Dieter JN, Emory EK. Supplemental stimulation of premature infants: a treatment model. *J Pediatr Psychol* 1997; 22: 281–95.
10. Standley JM. A meta-analysis of the efficacy of music therapy for premature infants. *J Pediatr Nurs* 2002; 17: 107–13.
11. Field T, Hernandez-Reif M, Fejo L, Freedman J. Prenatal, perinatal and neonatal stimulation: a survey of neonatal nurseries. *Infant Behav Dev* 2006; 29: 24–31.

12. Poggel DA, Kasten E, Sabel BA. Attentional cueing improves vision restoration therapy in patients with visual field defects. *Neurology* 2004; 63: 2069–76.
13. Sakatani K, Chen S, Lichty W, Zuo H, Wang YP. Cerebral blood oxygenation changes induced by auditory stimulation in newborn infants measured by near-infrared spectroscopy. *Early Hum Dev* 1999; 5: 229–36.
14. Hellström-Westas L, Rosen I. Continuous brain-function monitoring: state of the art in clinical practice. *Semin Fetal Neonatal Med* 2006; 11: 503–11.
15. Hellström-Westas L. Continuous electroencephalography monitoring of the preterm infant. *Clin Perinatol* 2006; 33: 633–47. vi.
16. Unyk A, Trehub S, Trainor L, Schellenberg E. Lullabies and simplicity: a cross cultural perspective. *Psychol Music* 1992; 20: 15–28.
17. Trehub S, Unyk A, Trainor LJ. Adults identify infant-directed music across cultures. *Infant Behav Dev* 1993; 16: 193–212.
18. Bates D, Brez C, Kaplan R. Sink or swim: Wading through the literature to develop music therapy protocols in the NICU. Concurrent session at the annual meeting of the American Music Therapy Association, Minneapolis, MN, 2003, November.
19. Hanson-Abromeit D. Developmentally based criteria to support recorded music selections by neonatal nurses for use with premature infants in the neonatal intensive care unit. Dissertation Abstracts International, 67, 2003: 1143.
20. Loewy J. Musical sedation: mechanisms of breathing entrainment. In: Azoulay R, Lowey J, editors. Music the breath and health: advances in integrative music therapy. New York: Satchnote Press, 2009: 209–16.
21. Shoemark H. Singing as the foundation for multi-modal stimulation. In: Pratt R, Grocke D, editors. Music medicine 3, music medicine and music therapy: expanding horizons. Victoria, Australia: The University of Melbourne, 1999: 140–52.
22. Standley JM. Music therapy for premature infants in neonatal intensive care: physiological and developmental benefits. *Earl Child Connect* 2001; 7: 18–25.
23. Standley JM. Music therapy with premature infants: research and developmental interventions. Silver Spring, MD: American Music Therapy Association, 2003.
24. Hellström-Westas L, Inghammar M, Isaksson K, Rosen I, Stjernqvist K. Short-term effects of incubator covers on quiet sleep in stable premature infants. *Acta Paediatr* 2001; 90: 1004–8.
25. Visser GH, Mulder EJ, Prechtl HF. Studies on developmental neurology in the human fetus. *Dev Pharmacol Ther* 1992; 18: 175–83.
26. Perania D, Saccumana MC, Scifob P, Spadae D, Andreollia G, Rovellif R, et al. Functional specializations for music processing in the human newborn brain. PNAS Early Edition; February 22, 2010; doi:10.1073/0nas.0909074107(0).
27. Verma UL, Archbald F, Tejani NA, Handwerker SM. Cerebral function monitor in the neonate. I: normal patterns. *Dev Med Child Neurol* 1984; 26: 154–61.
28. Hellström-Westas L, Rosen I, Svenningsen NW. Cerebral function monitoring during the first week of life in extremely small low birthweight (ESLBW) infants. *Neuropediatrics* 1991; 22: 27–32.
29. Osredkar D, Toet MC, van Rooj LG, van Huffelen AC, Groenendaal F, de Vries LS. Sleep-wake cycling on amplitude-integrated electroencephalography in term newborns with hypoxic-ischemic encephalopathy. *Pediatrics* 2005; 115: 327–32.
30. Neal DO, Lindeke LL. Music as a nursing intervention for preterm infants in the NICU. *Neonatal Netw* 2008; 27: 319–27.
31. Gray L, Philbi MK. Effects of the neonatal intensive care unit on auditory attention and distraction. *Clin Perinatol* 2004; 31: 243–60.
32. Serón-Ferré M, Torres C, Parraguez VH, Vergara M, Valladares L, Forcelledo ML, et al. Perinatal neuroendocrine regulation. Development of the circadian time-keeping system. *Mol Cell Endocrinol* 2002; 186: 169–73.