Combining Kangaroo Care and Live Harp Music Therapy in the Neonatal Intensive Care Unit Setting

Ayelet Schlez MD, Ita Litmanovitz MD, Sofia Bauer MD, Tzipora Dolfin MD, Rivka Regev MD and Shmuel Amon MD

1Department of Neonatology, Meir Medical Center, Kfar Saba, Israel
2Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

ABSTRACT: Background: Music therapy has been recommended as an adjuvant therapy for both preterm infants and mothers during their stay in the neonatal intensive care unit (NICU), and has been shown to have beneficial effects. Objectives: To study the usefulness of combining live harp music therapy and kangaroo care (KC) on short-term physiological and behavioral parameters of preterm infants and their mothers in the NICU setting. Methods: Included in this study were stable infants born between 32 and 37 weeks of gestation, with normal hearing. Mother-infant dyads were randomly assigned to KC and live harp music therapy or to KC alone. Using repeated measures, neonatal and maternal heart rate, oxygen saturation and respiratory rate were recorded along with neonatal behavioral state and maternal anxiety state. Maternal age, ethnicity, education, and love of music were documented. Results: Fifty-two mother-infant dyads were tested. Compared with KC alone, KC and live harp music therapy had a significantly beneficial effect on maternal anxiety score (46.8 ± 10 vs. 27.7 ± 7.1, respectively, P < 0.01). Infants' physiological responses and behavior did not differ significantly. No correlation was found between mothers' age, ethnicity, years of education and affinity for music, and anxiety scores (P = 0.2 to 0.5 for all four variables). Conclusions: KC combined with live harp music therapy is more beneficial in reducing maternal anxiety than KC alone. This combined therapy had no apparent effect on the tested infants' physiological responses or behavioral state.

KEY WORDS: anxiety, behavioral state, harp, live music therapy, neonatal intensive care unit, preterm infants

A range of anxiety reduction techniques have been developed to reduce preterm infants’ anxiety and improve their physiological and neurobehavioral outcomes [1] while hospitalized in the neonatal intensive care unit, including NIDCAP (newborn individualized developmental care and assessment program) [2], family-centered care [3], skin-to-skin contact, i.e., kangaroo care [4,5], and control of external stimuli combined with music therapy [6]. Given that music is a useful tool in stress reduction of preterm infants [7], combining modalities as a means to increase their soothing effect has been the subject of recent studies [8,9].

KC and music therapy are well-established, safe, inexpensive and easily implemented therapies. Lai et al. [9] combined recorded music and KC applied to preterm infants and showed that this therapy reduced maternal anxiety. No effect was noted in the physiological and behavioral parameters of the infants. Arnon and co-workers [10] demonstrated the superiority of live music therapy over recorded music or no music therapy in inducing reductions in heart rate and anxiety behavior in preterm infants in the cot position.

These findings prompt the question whether combining KC and live music, in our case harp music therapy, as compared with KC alone, may improve the short-term physiological and behavioral parameters of mother-infant dyads in the NICU setting. We hypothesized that combining harp music therapy and KC would lead to a more beneficial effect than applying KC alone for both maternal and infant physiological parameters and for neonatal behavioral state and maternal anxiety.

PATIENTS AND METHODS

A prospective randomized intervention was initiated during a 4-month period ending 31 January 2008. Inclusion criteria were clinically stable infants born between 32 and 37 weeks of gestation and having normal hearing confirmed by measurement of distortion product otoacoustic emission. Exclusion criteria were: a) observed hyper-responsiveness to live music therapy, as opposed to other sounds and noises, and defined as crying when music starts and relaxing when music stops; b) congenital anomaly that mainly affects hearing, such as craniofacial anomalies; c) medication intake such as phenobarbital, furosemide and gentamycin, which might interfere with the reaction to musical stimuli; and d) brain anomalies associated with neurological disorders such as grade 3-4 intraventricular hemorrhage and periventricular leukomalacia. Maternal inclusion criteria were ability to hear, literary ability to read and answer an anxiety questionnaire, and no signs or medical history of postpartum depression.

KC = kangaroo care
NICU = neonatal intensive care unit
The study was approved by the Institutional Review Board of Meir Medical Center and conducted in conformity with the principles of research established by the Helsinki Declaration. Before enrolment, the parents received verbal information on the study objectives and design and gave written informed consent to participate in the study.

PROCEDURE
A within-subject, crossover, repeated design was used with mother-infant dyads acting as their own controls. The mothers were sitting at the infants’ bedside in the feed-and-grow area that serves stable preterm infants. The infant was placed in the kangaroo position, assuring skin-to-skin contact with the mother. Each therapy session began 30 minutes after feeding to ensure a relaxed infant and to test the intervention with no disturbances such as hunger. As recommended [7], the infants received either KC alone for 30 minutes or KC combined with live harp music therapy for 30 minutes. According to the randomization schedule, both therapies were performed in the afternoon after finishing the medical and nursing rounds, were in alternating order 3 to 5 days apart to allow for a washout period [11], and used the same music. Monitor alarms were silenced and the door was closed.

Live harp music was performed by a single experienced musician providing music therapy in the NICU [10]. The music, shown in earlier studies to be beneficial [10,12], was played at a distance of 1 to 2 meters from the infant-mother dyad. Given that the infants were mainly of Jewish and Arab origin with different cultural and musical backgrounds, a blend of Eastern and Western melody was chosen, appropriate to most families attending the Meir Medical Center, a regional referral center for the Sharon area and its vicinity. Live music comprised simple improvised melodies in the style of lullabies with soothing and repetitive wordless melodic lines that have become a recognized musical art [12], using major and harmonic minor modes with the latter mode being used in both Jewish and Arab music. To entrain the listener towards a calm and meditative state, the tempo of the music was at a soothing 60 to 70 beats per minute, matching the resting adult heartbeat.

OBJECTIVE SOUND MEASUREMENTS
Music and background sound levels were measured 10 cm from the infant’s ear with a sound analyzer and a decibel scale filter (407790 Octave Band Sound Analyzer, type 2 Integrating Sound Level Meter and Decibel-A Scale Filter, respectively; Extech Instruments, Melrose, MA, USA). Before each recording, the sound level meter that simulated typical reception of sound in the human ear was adjusted by a sound analyzer and a decibel scale filter (407744 Sound Level Calibrator, Extech Instruments), according to the manufacturer’s instructions, at a range of 30 to 130 dB and a frequency of 25 to 10,000 Hz. To minimize the effect on mother-infant reactions and allow for a comfortable listening volume of approximately 50–65 dB with a maximum 1-second duration of Lmax without causing hyper-alertness or adverse effects [6], the ambient noise was controlled at the lowest possible level, approximately 40 dB.

INFANT AND MATERNAL MEASURES
For accuracy, neonatal and maternal heart rates, oxygen saturation levels and respiratory rates were recorded continuously and documented every 2 minutes during all sessions. Similar to the practice used elsewhere [2,10], a 7-point scale to assess infants’ behavioral state (deep sleep, light sleep, drowsy, quiet awake or alert, actively awake and aroused, highly aroused, upset, or crying, and prolonged respiratory pause > 8 seconds) [2] and a self-report questionnaire, comprising 20 descriptive statements for measuring maternal anxiety symptoms (i.e., state-trait anxiety inventory scale) [13] were used at the beginning and the end of each intervention. Higher scores indicate greater anxiety, with a possible score of 20 to 80 points. Additional maternal measures were age; ethnicity (Arab/Jews); education (8 years – elementary school, 8–12 years – high school, and > 13 years – college/university degree); and affinity for music measured by a 5-point scale estimating the length of time spent listening to music a day (1, 2, 3, 4, and 5 hours) [Table 1].

<table>
<thead>
<tr>
<th>Table 1. Study population characteristics (N = 52)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ethnic origin</strong></td>
</tr>
<tr>
<td>Jews/Arabs (N)</td>
</tr>
<tr>
<td><strong>Infants</strong></td>
</tr>
<tr>
<td>Male/female (N)</td>
</tr>
<tr>
<td>Gestational age (wks)</td>
</tr>
<tr>
<td>Postnatal age (days)</td>
</tr>
<tr>
<td>Birth weight (g)</td>
</tr>
<tr>
<td>AGA/SGA (N)</td>
</tr>
<tr>
<td>Weight at testing (g)</td>
</tr>
<tr>
<td>Bronchopulmonary dysplasia (N)</td>
</tr>
<tr>
<td><strong>Mothers</strong></td>
</tr>
<tr>
<td>Age (yrs)</td>
</tr>
<tr>
<td>Education (yrs, N)</td>
</tr>
<tr>
<td>1–8</td>
</tr>
<tr>
<td>8–12</td>
</tr>
<tr>
<td>≥ 13</td>
</tr>
<tr>
<td>Affinity for music** (hrs, N)</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
</tbody>
</table>

*When applicable data are presented as median (range)
** A 5-point scale was initiated to measure the length of time spent a day listening to music.
AGA = appropriate for gestational age, SGA = small for gestational age
Data were recorded by a single physician (A.S.), who remained at the bedside throughout each session. Data were analyzed in a blinded fashion by S.A., who was unaware of treatment allocations.

**STATISTICAL ANALYSIS**

Statistical analysis was performed using the SPSS for Windows version 14.0 (SPSS Inc., Chicago, IL). The comparisons were made using paired Student’s t-test or repeated measures analysis of variance, when appropriate for distribution normality. Categorical data were analyzed using the chi-square test. Multiple t-test comparisons with Bonferroni adjustment and Kruskal-Wallis ANOVA test were used to compare the medians of the two modes of therapy. Multiple regression analysis was calculated with the STAI scores considered as dependent variable, and maternal age, ethnicity, education, and affinity for music as independent variables. Data were presented as mean ± SD or median and range in parentheses when applicable.

Power analysis was calculated to estimate the sample size required for the study. To achieve a power of 0.8 at α = 0.05 and one-tailed with a medium effect size of 0.610 and a medium required for the study. To achieve a power of 0.8 at ± SD or median and range in parentheses when applicable.

Power analysis was calculated to estimate the sample size required for the study. To achieve a power of 0.8 at α = 0.05 and one-tailed with a medium effect size of 0.610 and a medium correlation ($r = 0.50$) among two repeated measures using the $F$-test, a sample size of 48 mother-infant dyads sufficed.

**RESULTS**

Of 72 preterm infants who were screened for the study, 15 were excluded: 3 for medical reasons (intraventricular hemorrhage grade 3 or 4) and 12 due to parental refusal to participate. Of the latter parents, four showed lack of interest and eight did not want their baby to be part of the research study. In another five cases, the data were insufficient for statistical analysis. The final study population comprised 52 mother-infant dyads. There were 24 male and 28 female infants, with a median gestational age of 32 weeks (range 26–36 weeks) and a median postnatal age of 35 days (range 12–76 days). The median age of the mothers was 30 years (range 19–46 years). Other characteristics of infants and mothers are shown in Table 1.

The mean sound level during KC with music therapy was within the pre-study recommendations (50–65 dB). There was a significant difference between sound levels during KC alone (40.6 ± SD 3.6 dB, range 38.3–44.7) and KC combined with live harp music therapy (58.1 ± SD 7.9 dB, range 50.3–64.2) ($P < 0.05$).

Table 2 lists the differences in heart rate, oxygen saturation and respiratory rate of infants and mothers during KC alone and KC with live harp music therapy, showing no clinical difference in these parameters between the two modes of therapy. The behavioral scores of the infants also remained unchanged. Compared with KC alone, KC combined with live harp music therapy had a significant beneficial effect on maternal anxiety state (before intervention: KC 53 ± SD 11.3 and KC combined with music therapy 55.3 ± SD 9.2; after intervention: 46.8 ± SD 10 vs. 27.7 ± SD 7.1, respectively, $P < 0.01$).

The data showed that maternal age, ethnicity, education, and affinity for music did not correlate with the STAI scores ($P = 0.2$ to 0.5 for all four variables).

**DISCUSSION**

We performed KC in the feed-and-grow area and included for study only stable and normal-hearing infants born between 32 and 37 weeks of gestation. The quiet noise-controlled environment was within recommended limits [6] with sound levels at approximately 40 dB. This was achieved by closing the doors, silencing the monitor’s alarm, and reminding the parents and medical personnel to keep their voices down. In this manner, music could be played at a mean comfortable volume of 58 dB, without causing hyper-alertness or other adverse effects [6]. This follows the recommendations of Standley [7] that music can be implemented in the NICU either as recorded lullaby music in the infant’s isolette beginning at 28 weeks of gestation or as live music at 32 weeks adjusted gestational age in an area where ambient noise can be reduced to minimal levels. All of these make the NICU a feasible environment for both kangaroo care and music therapy.

We chose to measure key indicators of infants’ responses to sound, including heart rate, oxygen saturation and behavioral state that are considered responsive to auditory stimuli [7], are commonly used in studies on the effects of music therapy on preterm infants [7,9], and are directly affected by infants’ behavioral state [11,14]. Furthermore, measure-
ments of behavioral state are important because they characterize the underlying functioning of the brain and reflect infants’ ongoing responses to acoustic stimulation [15]. It was hypothesized that combining live harp music therapy with KC would lead to a more beneficial effect than applying each modality alone for both mothers and infants [9]. However, these assumptions were only partially supported by the findings, showing that adding live harp music therapy during KC helped mothers to relax and maintain the infants’ stable physiological responses. No changes in the cardiorespiratory parameters of either the mothers or the infants were noted. Regardless of the differences in the methodological approach, these findings are in agreement with those of Lai and collaborators [9], who compared recorded lullaby music played to mothers during KC. This significantly beneficial effect on maternal anxiety is very important for parents and especially for mothers who experience the stress of physical separation after birth [16,17] and need to be soothed to increase bonding with their offspring. Our findings have shown that the soothing effect of KC with harp music therapy can apply to all mothers in the NICU setting, regardless of their age, ethnicity, education, and affinity for music.

A feasible explanation for the lack of effect of KC combined with live harp music therapy on the physiological measures and behavioral score of the infants is the stability of their autonomic systems, showing less heart rate variability during KC, an impact that may even last during painful stimuli such as the heel-stick test [18,19]. During KC, the mother’s skin-to-skin contact with the preterm infant provides multisensory stimulation including emotional, tactile, proprioceptive, vestibular, olfactory, auditory, visual and thermal stimulation in a unique interactive way that can significantly lessen or mask any other stimulus, including music in any form [9,20]. Furthermore, the tactile-sensory system develops sooner than the auditory system does, already in utero. Thus, testing the auditory system with music that is not fully developed, along with KC, which uses the tactile and vestibular systems that develop earlier in uterine life [6], may explain the response to KC with or without musical stimuli. Also of note is that contrary to a previous study [10], in the current study we did not add a female voice to live music therapy. It seems that the female voice may resemble that of the mother, and even if born prematurely the infant begins to recognize it and to develop a preference for its sound, making the sound of a female voice and music more beneficial than that of a musical instrument alone.

In conclusion, applying live harp music during mother-infant kangaroo care and music therapy is feasible within the NICU milieu, and the combination significantly reduced maternal anxiety responses. However, it had no apparent effect on infants’ physiological parameters and behavioral states. These outcomes may stem from the ability of KC to mask music or from the lack of a female voice added to harp music. No correlation was found between maternal age, ethnicity, education and affinity for music, and anxiety scores, implying that the soothing effect of KC combined with music therapy for mothers, who are in need of support at a stressful time for the family, is universal regardless of their characteristics and personal beliefs, traits or preferences. Further studies using music therapy to reduce anxiety should focus on finding the best combination of interventions for preterm infants and mothers/parents and should comply with a specific study design to measure the effect of music in the NICU setting.

Acknowledgment
The authors thank Sunita Stanislow, MA, Kfar Saba, Israel, for providing valuable information on the elements and rhythm of harp music and for playing the harp.

Corresponding author:
Dr. S. Arnon
Dept. of Neonatology, Meir Medical Center, Kfar Saba 44281, Israel
Phone: (972-9) 747-2225
Fax: (972-9) 747-1189
e-mail: shmuelar@clalit.org.il

References
Brain stimulation by transcranial magnetic stimulation

Transcranial magnetic stimulation (TMS) is a non-invasive clinical method of stimulating the human brain, which has been tested for the treatment of depression and other neurological disorders. Depending on the stimulation protocol used, TMS can increase or decrease cortical excitability; however, how it does so is poorly understood. Benali et al. used electrophysiological recording techniques and immunohistochemistry to analyze the changes that occur in the rat brain after different repetitive TMS protocols. They found that two theta-burst stimulation (TBS) protocols that were previously shown to modify human cortical excitability in opposite ways also affected rat cortical activity and protein expression. Although both intermittent and continuous TBS affected cortical inhibitory neuronal systems, the cell types affected, and thus the overall effects of the stimulation, differed. These findings sound a note of caution because such impairment of the cortical inhibitory system may also take place in the human cortex. They also raise the critical question of whether these novel and increasingly popular high-frequency TMS protocols are really safe for use in human cognitive or clinical neuroscience.

J Neurosci 2011; 31: 1193

Eitan Israeli

Mutations and therapy in pancreatic cancer genes

Pancreatic neuroendocrine tumors (PanNETs) are aggressive human cancers that often develop silently and progress to untreatable metastatic disease prior to diagnosis. Using an exome sequencing strategy to identify recurrent somatic mutations in PanNETs, Jiao et al. found that the most commonly mutated genes, affecting nearly 45% of the tumors, encode proteins implicated in chromatin remodeling. About 15% of the tumors had mutations altering the mammalian target of rapamycin (mTOR) signaling pathway. mTOR inhibitors are already being tested as cancer therapies, so the mutational status of the PanNETs could help to identify which patients are most likely to respond to these drugs.

Science 2011; 331: 1199

Eitan Israeli

Detecting rejection by DNA from dying cells in blood

Tissue biopsies used to detect graft rejection in organ transplant recipients are invasive and expensive and can cause serious complications. Reporting the development of a non-invasive method to monitor the health of heart transplants, Snyder et al. confirmed that they could detect DNA from transplanted hearts released by dying cells in recipients’ peripheral blood. In female recipients of male hearts, the Y chromosome can be used to identify circulating donor DNA. But detecting donor DNA in sex-matched transplant recipients is much trickier. To get around this problem, the researchers used high-throughput shotgun sequencing to obtain a signature of the single nucleotide polymorphisms in heart donor and recipient DNA. They then used this information to detect changes in the amount of donor-specific DNA in patient plasma that reflected cardiac graft rejection confirmed by biopsy. The technique is not restricted to sex-mismatched grafts and can also be used to monitor treatment response after a rejection episode. Confirming these results in a larger patient cohort and extending the technique to other solid organ transplants may facilitate dynamic monitoring of graft health and early intervention to stem graft rejection.

Proc Natl Acad Sci USA 2011; 108: 6229

Eitan Israeli