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Impact of Music on Pediatric Oncology Outpatients

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Abstract

Music is widely used to enhance well-being. We wished to assess music's effect on pediatric oncology outpatients. Patients who had leukemia and were in maintenance or consolidation outpatient treatment served as their own control at two visits. At visit 1, children rested for 20 min; at visit 2, for 20 min they listened to music designed to increase vitality and improve heart rate variability (HRV). At both visits, parents completed before and after treatment visual analog scales (VAS) of their child's relaxation, well-being, vitality, anxiety, stress, and depression; patients' heart rates were monitored during treatments to calculate HRV. The 47 patients with complete VAS data and 34 patients with usable HRV data were similar. At baseline, VAS scores for negative states were low (average <2.5 of 10) and positive states were high (average 7> of 10). Relaxation improved more with music than rest ($p < 0.01$). The HRV parasympathetic parameter was significantly lower with music than rest. No other differences were significant. Further studies are needed to better delineate the relationship between subjective and objective measures of well-being among patients who are not in severe distress.

Cancer and its treatment are generally considered stressful (1–3). Oncology patients often use music as a nonpharmacologic therapy to reduce stress, improve mood, and decrease pain (4–6). Music may also offer potent physiologic and psychological benefits for very sick children (7,8). The extent to which music is helpful for outpatients who are less acutely ill is unknown.

Given developmental differences, it is difficult for children to provide reliable self-reports on their stress or well-being. Parental reports are often used as proxies for the child's symptoms and quality of life (9,10). However, parent-proxy reports of health-related quality of life are only moderately correlated with child's reports (11–13). These discrepancies suggest that objective measures would be useful to augment parental proxy reports of well-being.

Several studies suggest that a subjective sense of well-being is reflected in increased parasympathetic activity compared with sympathetic activity in the autonomic nervous system (14–16). Heart rate variability (HRV), that is, the variability of the cardiac interbeat interval (IBI), is a noninvasive, sensitive measure of autonomic balance (17,18). Improvements in HRV parameters (such as the SD of the IBI, SDNN) and power spectrum measures, including total power (TP), very low frequency (VLF), low frequency (LF), and high frequency (HF), have been reported in animal and adult studies as reflecting severity of illness, response to therapy or decreased stress (19–23). In pediatric patients, HRV parameters such as SDNN and TP are lower in patients with more severe pain and traumatic

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injuries (24,25). Increases in HF values are thought to reflect increased vagal tone, greater parasympathetic activity, and more relaxation.[1]

Music can impact HRV and perceived stress (26–28). For example, specially designed music (HeartZones by Doc Childre) significantly increased TP, while adult and adolescent subjects reported feeling increased vitality and reduced anxiety, fatigue, and stress (29). It is unclear how these findings translate to pediatric oncology outpatients who are more ill than healthy subjects but less ill than many patients involved in clinical studies of music or music therapy. The effects of music on autonomic activity and balance in pediatric oncology outpatients are largely unknown. Furthermore, much of the research on the effects of music has focused on music therapy, which involves a therapist who conducts an assessment, provides individualized treatment, and seeks feedback and may alter interventions as needed to achieve desired outcomes. Given the expense of formal music therapy, many clinical settings simply use recorded music or a radio to entertain or distract children during clinic visits.

We conducted this study to answer the question: how does specially designed music that improves HRV and subjective feelings of well-being in healthy adolescents affect pediatric oncology outpatients? Specifically, how does it affect parental proxy reports of subjective stress and well-being in the patients and how does it affect standard HRV parameters reflecting sympathetic and parasympathetic activity? The null hypothesis was that the music would have no significant effect on any HRV parameter or on any parent-completed visual analog scale (VAS) of reported well-being.

METHODS

To address these questions, we conducted a prospective cohort study at the pediatric oncology unit of Brenner Children's Hospital (BCH) in Winston-Salem, North Carolina between May 2004 and May 2007. Each patient served as his or her own control.

Subjects were eligible, if they had been diagnosed with acute lymphoblastic leukemia or acute myelogenous leukemia, received their primary oncology care at BCH, were in remission, had completed the induction phase of therapy, and had an English-speaking parent. Because of slower than expected patient accrual associated with lower diagnosis rates than in prior years, criteria were expanded in the last 6 mo to include any pediatric oncology patient who was not undergoing induction therapy. Patient age, gender, diagnosis, and treatment information were extracted from the medical records and verified by the pediatric oncologist.

At two routine clinic visits, patients participated in 40-min monitoring sessions: Visit 1 (usual care plus rest in a quiet room) and visit 2 (usual care, plus rest in a quiet room while listening to music for 20 min). At the beginning and end of each study session, the child's parent completed 0–10 point VAS with numeric and verbal anchors; typically, the parent asked the child to help complete these questionnaires. The VAS surveys assessed three positive and three negative states: relaxation, well-being, and vitality or energy (scored from 0, 10 with 10 being best) and anxiety, stress, and depression (scored from 0–10 with 10 being the worst). Patients received a small ($5 the first year and $10 in subsequent study years) gift certificate at each visit as an incentive and thanks for their participation.

The music used for the intervention was 20 min of Doc Childre's HeartZones compact disk (CD). This music was selected because it had previously been reported to enhance a sense of vitality, reduce stress, and improve HRV (29). In addition, given the differences in musical preferences among patients and families, we wished to use a standard intervention that would be equally unfamiliar to all participants; in fact, no patient or family member reported having heard the CD previously. The length of intervention was selected after a pilot period to determine the length of time that young children could remain relatively still; despite the relatively short intervention, it was still too long for some of the children, resulting in fewer children who contributed complete HRV data. The music was played on a CD-player “boom box” in a quiet treatment room. Volume was adjusted as desired by the patient and his or her parent.

During the intervention, subjects wore a MiniMitter 2000 monitoring unit (MiniMitter Co, Inc., Bend, OR). This unit consisted of two electrocardiograph electrodes placed on the anterior chest wall, attached to a transmitter unit, which was belted around the participant’s chest. A wireless receiver collected telemetric HRV data.

HRV was measured by several parameters. The SD of the interbeat interval (SDNN) is the most widely used measure of HRV. Commonly used parameters derived from the IBI power spectrum analyses include TP, which can be divided into HF, LF, and VLF power oscillations. HF oscillations (0.15–0.4 Hz) are thought to be markers of parasympathetic and particularly vagal autonomic tone. LF oscillations (0.04–0.15 Hz) reflect sympathetic and, to a lesser extent, parasympathetic tone; VLF oscillations (0.0033–0.04 Hz) reflect mostly sympathetic tone (17).

Data files for each individual session were stored in a secure location, and electronically transferred for analysis. We picked the central 15 min to reduce artifacts from motion during monitor placement and removal. Data were filtered before analysis by identifying and excluding IBI outliers if any lay outside a range of one half to twice the mean IBI for that individual (30). Any session in which more than 20% of IBIs were identified as outliers was omitted from further HRV analysis. After filtering, the data were analyzed using software was developed using Matlab (The Mathworks, Natick, MA) based on standard calculations for SDNN. Power spectrum calculations were performed using the Lomb periodogram, source code for which was obtained from PhysioNet archives with 500 frequency points over the range 0.0033–0.4000 Hz (31). The HRV analysis was completed without knowledge of the patient’s age, gender, ethnicity, or treatment stage; the analyst was also unaware of the responses to the VAS assessing psychosocial characteristics.

Statistical analyses included simple descriptive statistics. To test the effect of music on changes in VAS score, only data from those children with both pre- and post-VAS scores at both the baseline and music sessions were used. Pre- and post-change scores were calculated. To test the effect of music on HRV parameters, only data from those children with usable HRV data from both the baseline and music sessions were used. Differences were compared for the rest and music visits using a nonparametric sign test.

This study was approved by the Wake Forest University School of Medicine Institutional Review Board. Informed consent was obtained from parents of all infants enrolled.

RESULTS

During the study period, 68 patients were eligible and 67 enrolled; 4 patients dropped out before completing a baseline visit. The 63 patients who completed a baseline visit are compared with the 47 who had complete VAS data and 34 who had usable HRV data for both the baseline and music intervention visit in Table 1. Three of those who dropped out before the first study visit cited not wanting to spend extra time at the end of the clinic visit to participate in the study; one died before the first study visit. The most common reason the patients gave for not participating in the second study visit was that they did not want to stay an extra 40 min beyond their usual clinic visit to participate. Ten of the 13 patients who had VAS data but did not have usable HRV data were male and disliked sitting still for the HRV data collection. Baseline VAS scores were similar (average within 0.1 point for every parameter) for patients who continued and those who did not continue to participate in the study (data not shown).

Scores for the VAS scales for subjective well-being were generally high (mean and median 7 or more out of 10) at baseline for both the rest and music visits (Table 2). Similarly, scores on the VAS scales for negative states (anxiety, stress, and depression) were low (mean and median less than 2.5 out of 10) at baseline for both the rest and music visits. The average time between rest and music visits was 35 d. The score for relaxation fell (less relaxed) 0.4 points with rest and rose (more relaxed) 0.9 points with music, reflecting greater relaxation with music ($p < 0.01$). The other five VAS parameters were similar for the rest and music visits.

The values for HRV parameters for both rest and music visits are shown in Table 3. The ranges and variability for each parameter were quite wide at baseline. The resting heart rate ranged from 56.7 to 169.3 bpm. Similarly, SDNN scores ranged from 20.5 to 138.3 and TP ranged from 52.4 to 4251.8 at baseline. There were no significant differences in any HRV parameter except HF power, which was about 50% lower with the music than the rest visit. Because the change in HF was the reverse of expectations, we conducted additional analyses.

Additional analyses of the HRV data included visual inspection of the individual HRV recordings for all patients. Not only was HF lower on the music than the rest visits, HF fell over the course of each music intervention and was lower at the end of sessions than at the beginning, supporting a temporal relationship between music and changes in HF. In addition, to adjust for the effects of multiple comparisons and the close relationships between various HRV parameters, a multivariate logistic regression modeling using all HRV parameters was conducted by an independent statistician, Dr. Douglas Lake. This analysis also found that, even while controlling for changes in SDNN, TP, LF, and VLF, the drop in HF with music compared with rest conditions was still statistically significant ($p < 0.05$).

DISCUSSION

This study builds on earlier studies that reported either objective or subjective measures of well-being to include both types of responses to a specific type of music among pediatric oncology patients (4–6,32,33). We found a significant improvement in reported relaxation with this music, even though the music was unfamiliar and even though the patients had a high level of well-being and low level of distress at baseline. Paradoxically, this music was associated with a lower value for objectively measured HRV parameter, HF that is generally associated with parasympathetic autonomic activity and subjective relaxation.

There are several potential reasons for not finding a greater effect on subjective well-being with music in this study. First, there may have been a ceiling effect; patients reported high levels of well-being and low levels of distress at baseline. Second, reports by parental proxy may not be sensitive to subtle changes in a child's subjective sense of well-being (10,11). To maintain standardized data collection in a study with a wide pediatric age range, we had parents complete all VAS scales; to enhance the sensitivity of parental reports, parents asked their children for help completing the VAS questionnaires. Third, to bolster recruitment and retention among patients who were eager to leave clinic rather than stay to participate in a time-consuming study, we used the brief VAS instruments rather than longer questionnaires that may have greater sensitivity for detecting subtle differences. On the other hand, VAS correlates well with longer instruments for pain and quality of life in pediatric patients (34). Future studies may increase their power to detect an impact on subjective well-being by including patients who report more distress at baseline and older patients who are able to report their own subjective states rather than relying on parental proxy. However, such studies will not provide insight into the impact of music on well-being in younger or less distressed patients who comprise a substantial portion of the pediatric oncology population. Finally, it is possible that there is poor agreement between parent ratings and objective measures of well-being or that parents projected their own feelings of relaxation onto their children who were, in fact, not particularly relaxed as they listened to this music. It may be that parents experience more stress from the child's treatment than the child does, and that this is the reason why relaxation was the only VAS measure affected in this study.

Given the wide variation in HRV parameters at baseline, we analyzed patients as their own controls to reduce the impact of the between-patient variability. This is important because previous studies have shown marked changes in HRV with age; HRV parameters generally increase from infancy through adolescence, peak in late adolescence or early adulthood and decline with aging (35–37). Values for the HRV parameters in this study were similar to those in an earlier study of HRV in pediatric oncology patients (38). Additionally, to bolster sample size, we included a broad age range of patients, many of whom also had comorbid conditions such as asthma and hypertension that might affect HRV. Again, using patients as their own controls protects against confounding by these factors. However, using patients as their own controls does not completely correct for changes over time with different treatment stages, and larger studies will be needed to control for these potential contributors to variation.

The drop in HF with music was unexpected and led us to conduct additional analyses to verify the observation. Based on studies of the effect of massage and meditation on HRV in adults, music was expected to lead to increased parasympathetic activity, reflected in an increased HF (39,40). The findings from this study suggest the opposite for pediatric oncology outpatients, that is, that sitting in a clinic treatment room listening to this particular music decreased HF, the HRV parameter associated with parasympathetic or vagal activity. This finding may reflect the fact that patients were unhappy with being asked to sit still and listen to unfamiliar music; unlike adults who might relish the opportunity to rest quietly for 30–40 min, children may instead prefer more active forms of stress management. It is possible that listening to music that is more familiar and not being asked to keep still would have had different autonomic effects in a pediatric population.

This study examined the effect of one particular type of recorded music and does not address the impact of music therapy or the therapeutic value of an additional therapist. Although we intentionally chose a standardized music that was unfamiliar to the patients, clinicians seeking a significant clinical impact may instead use music preferred by patients. Such choices would be expected to have greater impact on subjective well-being, would be clinically appropriate, and may help fidgety children remain more still to optimize collection of physiologic data. Furthermore, the sample was quite diverse. Different children had received different doses of doxorubicin and other potentially cardiotoxic medications at different time intervals before the study; future studies using much larger samples should control for the effects of cardio-toxic medications in the analysis.

Despite its limitations, this study has value for future research. It demonstrates that it is possible to assess both subjective and objective measures of well-being, although restriction to patients ages 10 and older (who can report on their own subjective well-being) or female patients (who have fewer movement artifacts in short HRV recordings) may improve data collection. Like this one, future studies in pediatric oncology patients would benefit from using patients as their own controls unless the sample size is quite large given the heterogeneity in this population. Future studies and clinicians may also need to ask patients

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at the outset what kinds of music they find most helpful and use those; more than one dose and longer follow-up may also assist in detecting effects. Furthermore, the research design was not counter balanced in terms of control or intervention order; future studies should balance the order of interventions to control for the possibility that patients might become more relaxed and comfortable over time as they become more used to the procedure.

Music is widely used clinically to promote well-being. In a pediatric oncology outpatient population experiencing low levels of stress and normal HRV values, the specific music provided in this study enhanced subjective relaxation, but decreased parasympathetic activity measured by HRV. The paradoxical relationship between subjective and objective measures in response to music in this study requires further evaluation in pediatric oncology patients.

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Abbreviations

CD	compact disk
HF	high frequency
HRV	heart rate variability
IBI	interbeat interval
LF	low frequency
SDNN	standard deviation of the interbeat interval of the ECG
TP	total power
VAS	visual analog scale
VLF	very low frequency

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Table 1

Participant description

	Patients with a baseline visit, N = 63 (%)	Patients with complete VAS data for both visits, N = 47 (%)	Patients with complete HRV data for both visits, N = 34 (%)
Age			
Mean ± standard deviation (yrs)	9 ± 5.3	10.4 ± 5.1	9.5 ± 4.9
Median (yrs)	8	10.7	9.4
Range (yrs)	0.8, 17.9	0.8, 17.9	0.8, 17.6
Gender—% male	40 (63)	28 (60)	18 (53)
Race			
African American	12 (19)	11 (23)	8 (24)
White	47 (75)	34 (72)	24 (71)
Mixed/other	4 (6)	2 (4)	2 (6)
Ethnicity—Hispanic	4 (6)	2 (4)	1 (3)
Diagnosis			
ALL	50 (79)	36 (77)	26 (76)
Other	11 (21)	11 (23)	8 (24)
Comorbidities (some patients had none, while others had more than one)—any	24 (38)	19 (40)	14 (41)
Asthma/allergies	9 (14)	7 (15)	4 (12)
Congenital/genetic	6 (11)	4 (10)	2 (7)
Hypertension	3 (5)	3 (6)	3 (9)
Stage of treatment			
Continuation	24 (38)	16 (34)	15 (44)
Consolidation	31 (49)	25 (53)	15 (44)
Other	8 (13)	6 (13)	4 (12)
Ever treated with doxorubicin	38 (61)	33 (70)	26 (77)

ALL indicates acute lymphoblastic leukemia; HRV, heart rate variability; VAS, visual analog scale.

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Table 2

Changes in VAS scales for 47 patients who had complete data at rest and music visits

	Rest		Music		
VAS scales: Mean (SD) median (range)	**Pre**	**Change**	**Pre**	**Change**	***p** for comparing baseline and music changes**
Positive feelings—higher scores are more positive					
Relaxation—mean (Std Dev)	7.2 (2.3)	−0.4 (1.7)	7.2 (2.0)	+0.9 (1.1)	<0.001
Median	7	0	7.1	0.4	
Vitality—mean (SD)	7.0 (2.4)	0 (1.5)	7.1 (2.3)	+0.1 (1.3)	0.14
Median	7	0	7.4	0	
Overall well being—mean (Std Dev)	7.1 (2.2)	+0.33 (0.1)	7.4 (2.3)	+0.17 (1.65)	0.70
Median	7	0	8.0	0	
Negative feelings—higher scores are more negative					
Stress—mean (SD)	2.4 (2.8)	−0.7 (2.5)	2.0 (1.7)	−0.7 (1.7)	0.49
Median	1.2 (0–10)	0	0	0	
Anxiety—mean (SD)	2.3 (2.6)	−0.2 (1.9)	2.5 (2.8)	−0.3 (1.1)	0.54
Median	1.0 (0–10)	0	1.2	0	
Depression—mean (SD)	0.9 (1.7)	+0.1 (1.5)	0.7 (1.3)	−0.1 (0.8)	0.99
Median	0 (0–7.50)	0	0	0	

* Using nonparametric sign test.

VAS indicates visual analog scale; SD, standard deviation.

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Table 3

HRV parameters for 34 patients with complete, analyzable data

HRV parameter: Mean (SD)	Rest	Music
HR—BPM	102.4 (20.4)	104.5 (15.3)
SDNN	55.5 (21.4)	51.1 (19.1)
Total power	762.7 (183.4)	747.3 (158.0)
Very low frequency (VLF)	147.8 (97.7)	144.8 (63.7)
Low frequency (LF)	444.1 (166)	471.3 (120.2)
High frequency (HF)*	184.3 (106.1)	146.7 (74.8)

*Using nonparametric sign test, $p = 0.002$.

BPM indicates beats per minute; HR, heart rate; HRV, heart rate variability; SDNN, standard deviation of the interbeat interval of the ECG.