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Heart Rate Variability During Monochord-Induced Relaxation in Female Patients With Cancer Undergoing Chemotherapy

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Abstract

This study investigated the impact of monochord (MC) sounds, a type of archaic sound used in music therapy, on the heart rate variability (HRV) in patients with cancer undergoing chemotherapy. The HRV of patients was recorded during the first and last sessions of relaxation treatments. The time series of HRV was analyzed using methods based on the time and frequency domains. During MC-induced relaxation, low-frequency power and the ratio of low and high frequency were increased over sessions. However, changes in low and high frequency lay in different directions during relaxation caused by progressive muscle relaxation (PMR) in each session. Different activities of the parasympathetic and sympathetic nervous systems were shown during relaxation caused by either listening to MC sounds or exercising PMR. It is necessary to further investigate the relationship between the physical and psychological states induced by certain relaxation methods and specific activity of HRV.

Keywords

heart rate variability, monochord, progressive muscle relaxation, chemotherapy

Introduction

Changes to the autonomic nervous system (ANS) caused by listening to music are shown in many studies. The phenomenon "thrill" or "chill" is used to describe the music-induced strong emotional response that is associated with distinct patterns of physiological parameters such as increase in heart rate (HR), galvanic skin response, and respiration rate, while the body temperature and blood volume pulse amplitude decrease.[1] Listening to (pleasant or sad) music, which evokes emotions after aversive visual stimuli, affects the cardiovascular and respiratory activities, increasing both the vascular blood flow and respiration rate. In particular, after listening to sad music, HR and respiratory rate increase significantly in comparison with white noise; HR decreases and respiratory rate increases after listening to pleasant music.[2] On the other hand, listening to pleasant music is associated with higher HR and respiratory rate than when listening to unpleasant stimuli. However, compared with the resting condition, significant changes in autonomic response are provoked by listening to both types of music.[3] Listening to unpleasant music can cause a significant decrease in HR.[4]

Changes in physiological parameters caused by music listening can also be shown in the clinical context. The Cochrane reviews about music interventions reveal that listening to prerecorded music affects physiological parameters, whereby blood pressure and HR and respiratory rate can be reduced in patients with coronary heart disease.[5] Heart and respiratory rates were also found to be reduced in mechanically ventilated patients receiving music therapy.[6] For example, the physiological stress responses (as measured by HR and respiratory rate) as well as the level of anxiety in mechanically ventilated patients reduced significantly while listening to relaxing music.[7] These findings indicate that changes in ANS activity are evidence of physiological and psychological responses to music listening interventions.

In the case of patients with cancer, some meta-analyses show that physiological and psychological benefits can be achieved by listening to music.[8,9] For example, listening to (prerecorded) music can reduce (behavioral) anxiety, HR, respiratory rate, and blood pressure among patients with cancer. However, both reviews indicate that the results concerning the psychological and physiological responses to listening to music should be interpreted with caution and that there is a need for further investigation using adequate research methods.

In previous investigations, only the mean value of HR has been measured in various nonclinical and clinical studies.

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However, the findings reveal that the (therapeutic) effect of music cannot be verified only with a change in the mean value of HR.[2,10] Ellis and Thayer[10] report that the heart rate variability (HRV) reflects more accurately and in greater detail the activity of the ANS. The mean value of HR can be correlated with measures of HRV, while these separately can show different results. HRV is primarily related to the activity of the parasympathetic and sympathetic nervous system (PNS and SNS). This can partly reveal the relation between the states of relaxation and activity.[10-12]

Previous studies suggest that the spectral power in the high-frequency power (HF, 0.15-0.5 Hz) is typically associated with respiratory sinus arrhythmia and that it reflects the activity of the PNS,[13-17] whereas the spectral power in the low-frequency power (LF, 0.05-0.15 Hz) and LF:HF ratio mirrors the baroreflex activity.[18,19] In addition to these frequency domain measures of HRV, there are also time domain measures of HRV, such as the percentage of successive RR-interval differences $\geq$50 ms (pNN50) and the square root of the mean of the squared differences between adjacent intervals (rMSSD), which are related to the activity of the PNS.[16]

Current investigations show in different ways how listening to various types of music and playing music influence HRV. For example, Peng and colleagues showed that, after listening to preselected soft music, the LF power and LF:HF ratio were significantly lower, and HF power was significantly higher than that of the control group that rested quietly on semi-reclining chairs.[20] Further, the HF component increased significantly by listening to sedative music as compared to stimulating music, and the LF:HF ratio and LF power increased significantly by listening to both sedative and stimulating music compared with the "no music" group.[21] Listening to well-known music would lead to an increase in several components of HRV, such as HF power, rMSSD, and pNN50, and a decrease in LF:HF ratio in elderly patients with cerebrovascular disease and dementia.[22] After 30 sessions of music therapy (playing musical instruments) over 15 weeks, depression among patients with dementia decreased significantly, and the pNN50 improved in 50% of patients, whereas no such changes were witnessed in the control group.[23]

HRV could change markedly in response to diverse physical and psychological states as well as meditation, relaxation, or anesthesia. For example, during mental relaxation induced by hypnosis, an increase in LF and HF power and a decrease in the LF:HF ratio were found.[24] During the state of anesthesia, both HF and LF power reduced, whereas neither was changed by analgesia.[25] Moreover, during sedation with midazolam, HF power and LF:HF ratio were increased, which was coupled with a reduction in anxiety.[26]

Several studies show HRV activities at different states during different types of meditation, a method often used to induce relaxation. HR becomes lower during zazan (seated) meditation but higher during kinhin (walking) meditation. HF power did not change while sitting or during mental tasks and zazan meditation, but it decreased during kinhin meditation. LF power increased only during zazan and kinhin meditation but not while sitting or during mental tasks.[27] Further, LF and HF power increased during inward-attention meditation (eg, Zen meditation) as well as during resting state. However, the state of inward-attention meditation differs from the resting state in its decrease of LF:HF ratio and standard deviation of NN (SDNN) intervals and in its increase in the mean HR, the opposite of which applied during resting state.[28] After cyclic meditation (a type of meditation that combines yoga postures with supine rest), the LF power and LF:HF ratio significantly decreased, but HF power, pNN50, pNN30, and rMSSD increased significantly compared with supine rest. However, HR decreased significantly in both sessions.[29,30] During samadhi state (ie, a state of one-point concentration during meditation), LF power increased significantly.[31] These diverse results about a similar relaxation state can serve as a key for identifying specific relaxation state that can be induced by listening to certain types of music in a clinical context.

The primary aim of this study was to observe HRV changes during relaxation induced by listening to archaic monochord (MC) sounds and to compare these results against relaxation induced by progressive muscle relaxation (PMR), a standard relaxation treatment method. The MC sounds were chosen because they are often used in music therapy for relaxation in clinical settings in central Europe. Few studies describe the relaxing effect of MC sounds,[32-34] and HRV analysis has not been performed previously for MC sounds in a clinical setting. This study has a purpose to provide empirical support to the clinical use of MC sounds. Considering the equivalence in effectiveness as anxiolytic between the 2 treatments, PMR and MC,[35] we hypothesized that the HRV response caused by listening to MC sounds will be quite similar to the changes caused by exercising PMR.

Methods

Participants

This study has been conducted in the outpatient women's clinic of the University Hospital Heidelberg, Germany. The female participants who were receiving chemotherapy were informed with written information about this study. The patients were recruited and contacted for this study by the first author, a trained music therapist. After the participants agreed to sign up for this study, they were randomly assigned to 1 of the 2 relaxation treatment groups, the MC group and the PMR group. Exclusion criteria were previous experience with chemotherapy, regular practice of relaxation techniques, being over the age of 65 years, brain tumor or other metastases, other neurological diagnosis or prior brain operation, pregnancy, and mental impairment.

Procedure

During both relaxation treatments, patients remained awake in a supine position with eyes closed. Each treatment session, either listening to MC sounds or PMR exercise, lasted for 25 minutes after a 4-minute period of verbal introduction and was synchronized with the onset of chemotherapy. Both groups received their treatments via an in-ear headphone on 4 sessions.

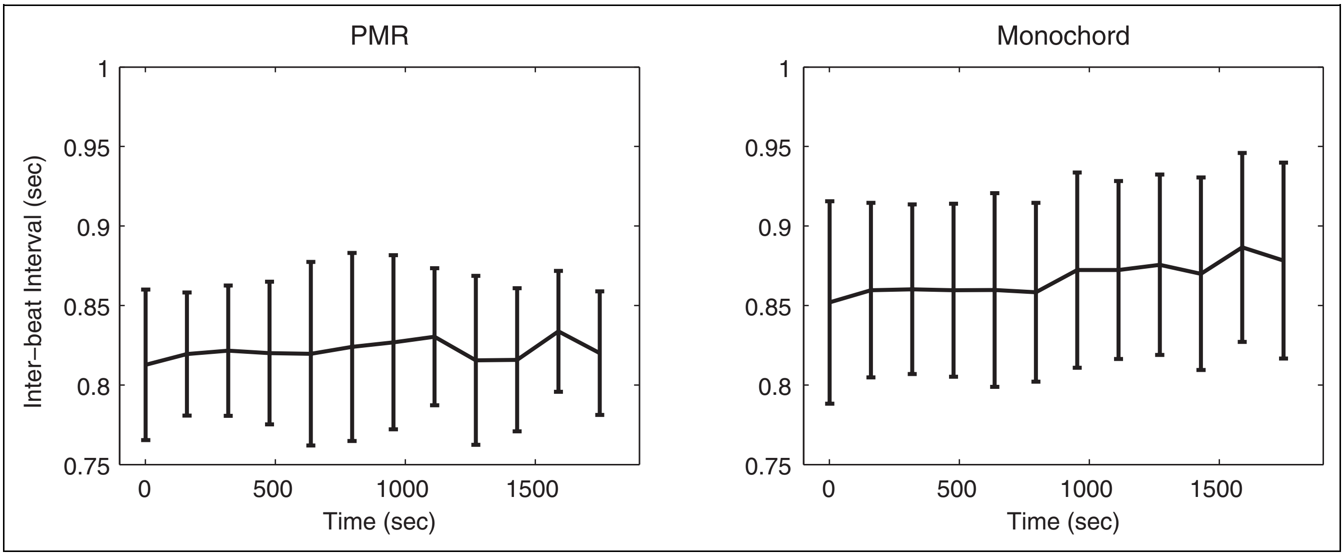

Figure 1. Change in interbeat interval. Error bar (mean $\pm$ SEM) profile of interbeat interval fluctuations within a treatment session for PMR (left) and monochord (right) group. Results were pooled across participants and sessions (pre and post). SEM indicates standard error of mean; PMR, progressive muscle relaxation.

The patients listened to prerecorded MC sounds or exercised PMR with prerecorded verbal instructions, respectively, during the second to the fifth chemotherapy session every 3 weeks when they received chemotherapy over a period of 3 months. At the first chemotherapy session, patients did not receive any relaxation treatment because most patients would like to concentrate on the chemotherapy process itself and wait until they see how they respond to the chemotherapy treatment. Usually patients waited for 1 hour before they started the chemotherapy. Along with chemotherapy, they received the respective relaxation treatment in a counterbalanced order.

Data Collection

While the participants were receiving relaxation treatments, an electrocardiogram (ECG) was recorded on both the second and the fifth chemotherapy sessions, which were separated by 10 weeks. The ECG was recorded continuously during the entire session by attaching 2 external electrodes around the left and right wrists and was amplified by a Neurowerk EEG recorder (Sigma Medizin-Technik GmBH, Germany). The sampling frequency was 128 Hz, and the analog/digital (A/D) resolution was 16 bit.

Data Analysis

The heartbeats were detected from the continuous ECG recordings by a filter-bank-based multirate digital signal processing algorithm[36] and the interbeat interval (IBI) was subsequently calculated. Any outlier or glitch was identified by studying the residuals of a forward and backward autoregressive fit and was replaced by spline interpolation; the number of such replaced beats was less than 1% of the total number of beats. Within each of the 2 sessions (referred to here as *pre* and *post* for the second and fifth chemotherapy sessions, respectively), we extracted two 5-minute phases as follows: the *begin* phase (4th-9th min) and the *end* phase (24th-29th min). These phases were selected in order to investigate the within-session effect of individual relaxation treatment. For each phase, the following HRV indices were calculated: (1) the mean spectral power in the LF band (0.04-0.15 Hz), (2) the mean spectral power in the HF band (0.15-0.4 Hz), (3) the LF:HF ratio, (4) the mean of IBI sequence, (5) the standard deviation (SD) of IBI sequence, (6) the skewness of IBI sequence, (7) the proportion of the number of pairs of adjacent intervals differing by more than 50 ms, pNN50, and (8) the square root of the mean of the sum of the squares of differences between adjacent intervals, rMSSD. The first 3 indices are frequency domain measures of HRV that are calculated based on nonparametric fast Fourier transform approach, and the last 5 are time domain measures.[12] Data preprocessing and calculation of these indices were performed by MATLAB-based scripts (MathWorks, Natick, Massachusetts). The normality was checked by the Anderson-Darling adjusted statistic.[37] For each index and for each session, we performed a mixed factorial 2×2 analysis of variance (ANOVA) with a within-subject factor phase (2 levels: begin and end) and a between-subject factor group (2 levels: MC and PMR). The level of statistical significance was set as $P < .05$. The statistical analysis was made by SPSS v. 21 (SPSS Inc, Chicago, Illinois).

Results

Thirty-eight female patients with breast and gynecological cancer participated in this study (MC group: n = 19, age ranging between 27 and 55 years and PMR group: n = 19, age ranging between 31 and 56 years). Most patients were diagnosed with mamma carcinoma except 1 patient with ovarian carcinoma in the MC group and another patient with cervix carcinoma in the PMR group. Chemotherapy was administered every

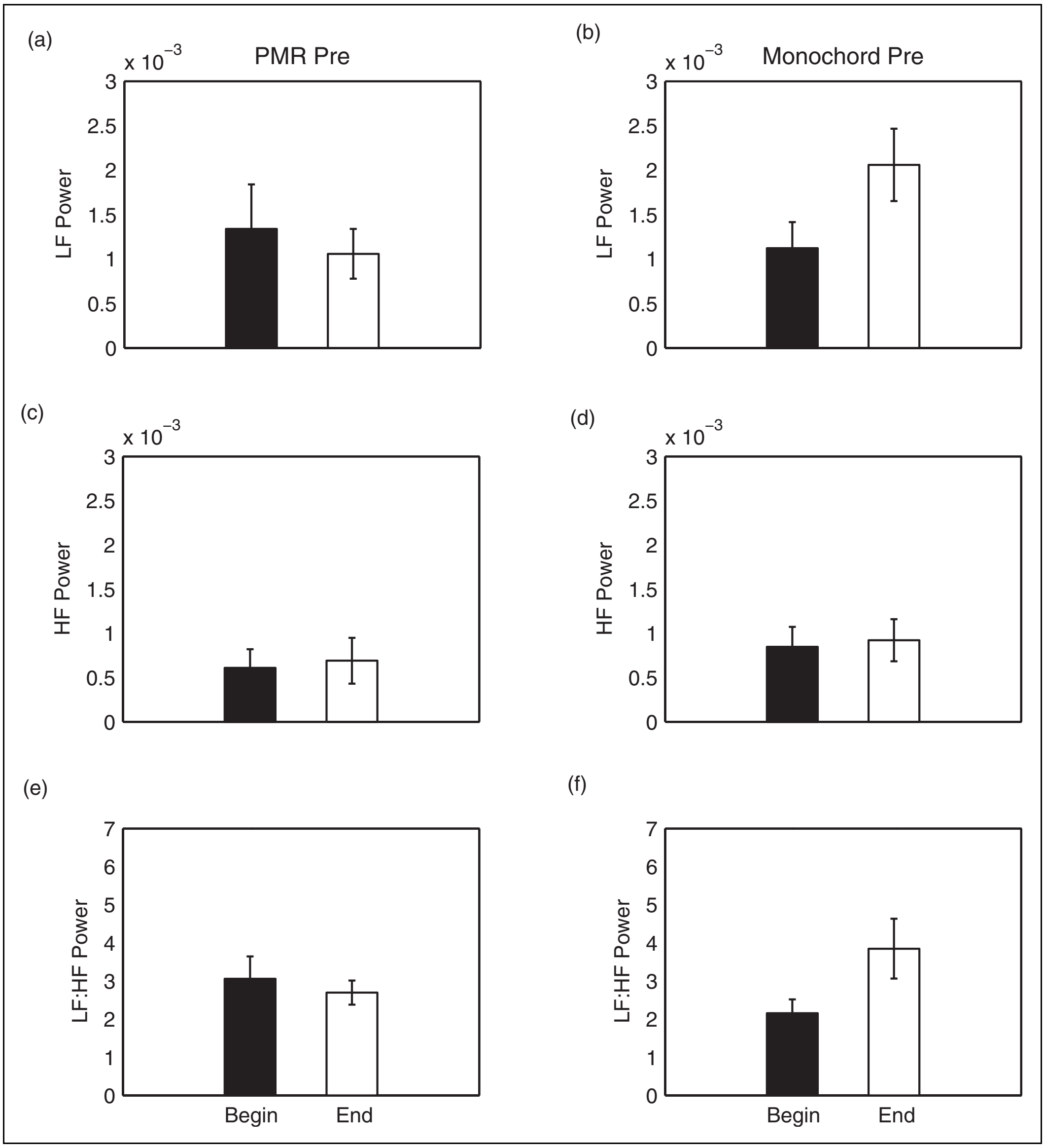

Figure 2. Change in LF power, HF power, and LF:HF ratio within the pre session. Spectral parameters—LF power (a), HF power (c), and LF:HF ratio (e)—of heartbeat interval variability for PMR group during the begin (filled bar) and the end (open) phase within the second chemotherapy (pre) session. (b), (d), (f) are the same but for the monochord group. Error bars denote SEM. SEM indicates standard error of mean; LF, low frequency; HF, high frequency; PMR, progressive muscle relaxation.

3 weeks over a period of 3 months. There were no statistically significant group differences in age and diagnosis. No participant had other psychiatric or neurological diagnosis. There were no significant group differences in terms of age, diagnosis, types of premedication and medication of chemotherapy. The ethical approval was carried out by the ethic committee of the University Hospital Heidelberg (S-365/2008).

Figure 1 shows the profile of IBI within a treatment session for both the PMR and MC groups and they seem to be quite similar. There was a minor trend toward a higher mean value of IBI (ie, slower HR) in the MC than in the PMR group, but this difference was not found to be significant. Further, the IBI in the MC group seems to be slightly more increased than that in the PMR group, particularly at the end of a treatment session.

Figure 2 shows the changes in 3 frequency domain measures of HRV in the first session (pre). In the MC group, both LF power and the LF:HF ratio increased from begin to end period of the session. A mixed ANOVA for LF power revealed an interaction effect of phase × group ($F_{1,35} = 9.26$, $P = .004$), since the LF power changes within the first treatment session was higher in the MC group (Figure 2, a and b); but no significant main effect was found for phase ($P = .16$) and group ($P = .39$). Similar analysis for HF power revealed no significant effects ($P > .40$). In LF:HF measurement, there was no main effect was found for phase ($P = .18$) and group ($P = .76$), but we found a phase × group interaction effect ($F_{1,35} = 6.59, P = .015$) since the increase in LF:HF measure from begin to end phase was much larger in MC (Figure 2f) than in the PMR group (Figure 2e).

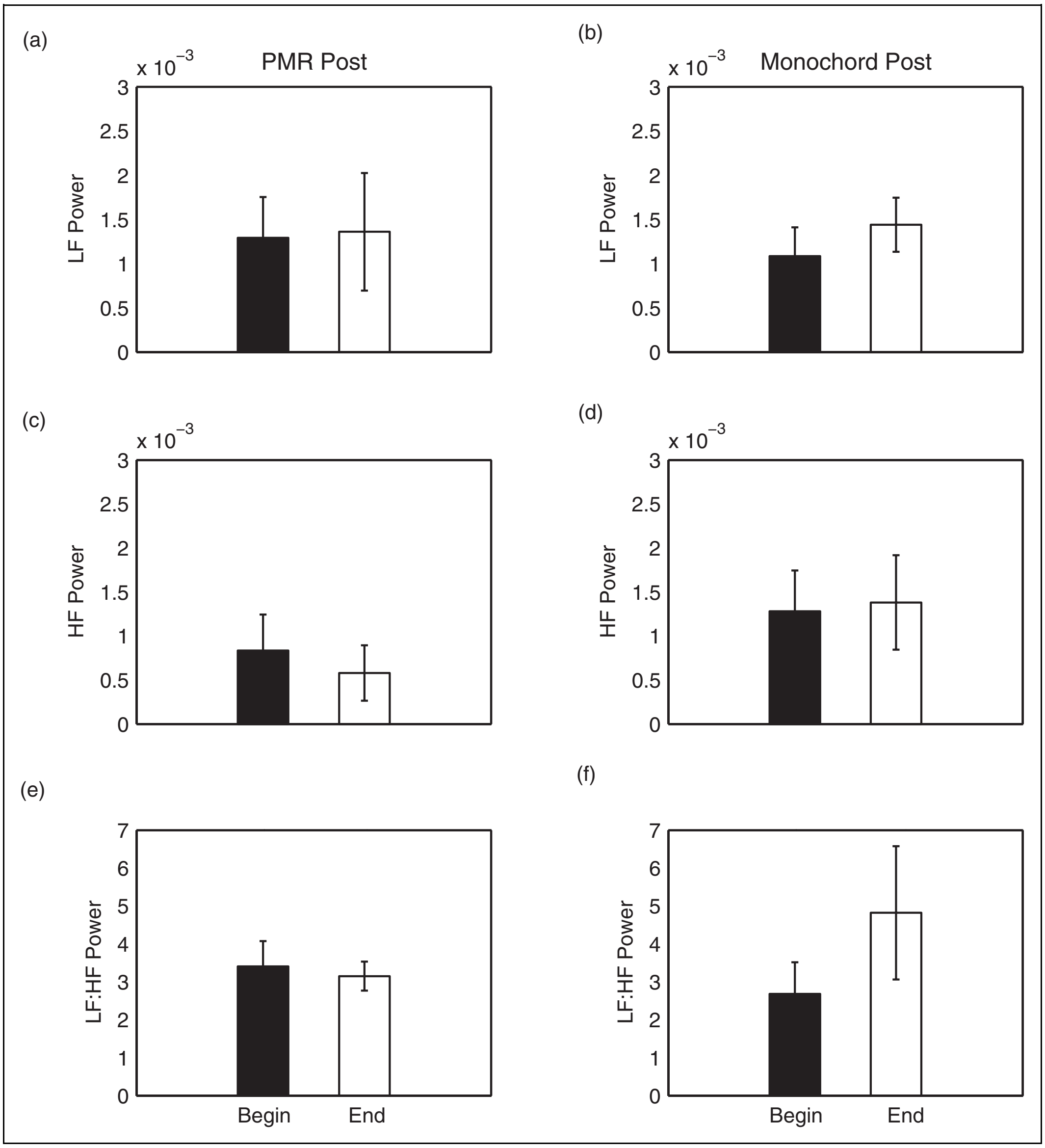

Figure 3. Change in LF power, HF power, and LF:HF ratio within the post session. Same as in Figure 2 but for the fifth (post) chemotherapy session. LF, low frequency; HF, high frequency.

Figure 3 is same as Figure 2 but for the last session (post). For LF power, we found no effect of phase ($P = .30$) or group ($P = .64$) but observed a marginal interaction between phase × group ($F_{1,35} = 4.04$, $P = .05$) since the increase in LF power measure within the last session was marginally larger in MC (Figure 3b) than that in PMR (Figure 3a). Similar analysis for HF power and LF:HF ratio revealed no significant effects ($P > .2$).

Figures 4 and 5 show the changes in 3 time domain measures of HRV for both groups during the pre and post sessions, respectively. In both treatment sessions, we did not observe any significant change with regard to the mean value between the begin and end phases. For the SD measure, only the first session, but not the last session, revealed an interaction between phase × group ($F_{1,35} = 5.68$, $P = .02$), since the difference in the SD measure within a treatment session was in the opposite direction between the 2 groups (Figure 4, c and d). Similar analysis with skew measure in the first session revealed a marginal effect of phase ($F_{1,35} = 3.77$, $P = .06$), since the skew measure was higher in the end than in the begin phase (Figure 4, e and f), and a marginal effect of group ($F_{1,35} = 3.45$, $P = .07$), since the MC group was associated with lower skew values than was the PMR group. No significant effects were observed for skew measure in the last session ($P > .3$).

Next we analyzed the percentage of successive RR-interval differences under 50 ms (pNN50), and the results are shown in Figure 6. Its values in the first (pre) session revealed no significant effects ($P > .4$), but we found a significant effect of group in the last (post) session ($F_{1,35} = 4.21$, $P = .048$), since the MC group presented a generally higher value of pNN50 than that of the PMR group (Figure 6, c and d). No differences were observed within a treatment session ($P > .2$).

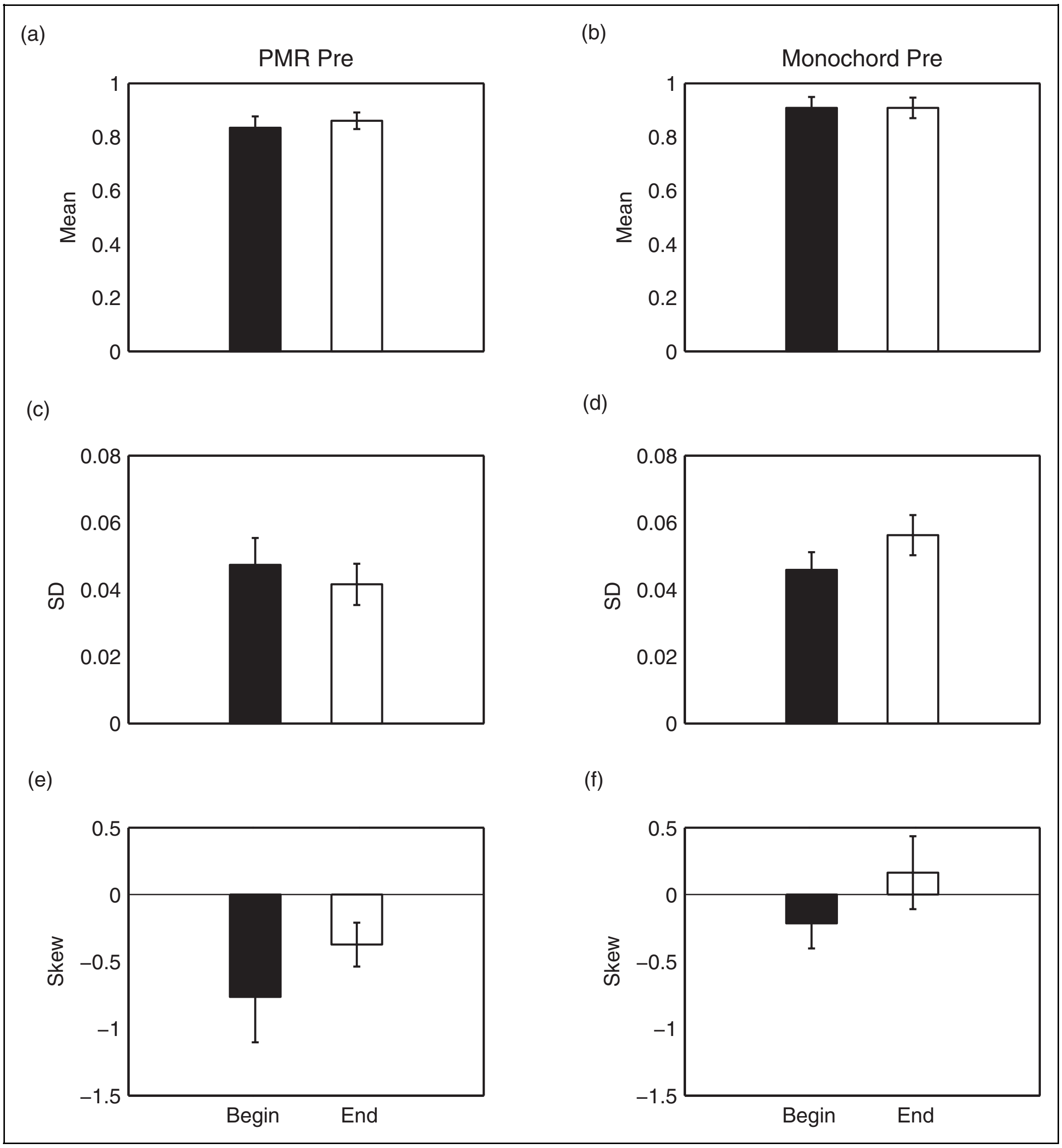

Figure 4. Change in mean, standard deviation, and skew within the pre session. Time domain parameters—(a) mean, (c) standard deviation, and (e) skew for the PMR group during the begin (filled bar) and the end (open) phase within the second chemothearpy session (pre) session. (b), (d), (f) are the same but for the monochord group. Error bars denote SEM. SEM indicates standard error of mean; LF, low frequency; HF, high frequency; PMR, progressive muscle relaxation.

Figure 7 shows the mean value of the rMSSD for both groups. For both sessions, we did not find any statistically significant effect of group or phase ($P > .2$).

Discussion

In this study, we investigated the effects of MC sounds as used in music therapeutic setting on HRV in patients with cancer; the results were compared with those of patients receiving PMR. HRV is widely believed to reflect the underlying complex dynamics and interaction between SNS and PNS of the ANS. We used a battery of HRV indices, based on time and frequency domain. Based on the targeted anxiolytic effect of the 2 treatment techniques of inducing a relaxed state, we simply expected that both treatments, MC and PMR, would deactivate SNS and activate PNS and therefore would lead to a decrease in LF power and LF:HF ratio and an increase in IBI, HF power, rMSSD, and pNN50. However, the obtained results differed from these straightforward predictions.

In the first relaxation session (pre), both LF power and LF:HF ratio were found to be increased at the end of the session compared to its beginning in the MC group but not in the PMR group. No significant changes were observed for HF power in both groups. Since the LF power measure is mostly associated with baroreflex activity and the HF being exclusively associated with PNS,[7] these results indicate a tendency toward a decreasing activation of HR and accordingly toward reduced blood pressure within the first session in the MC group. We

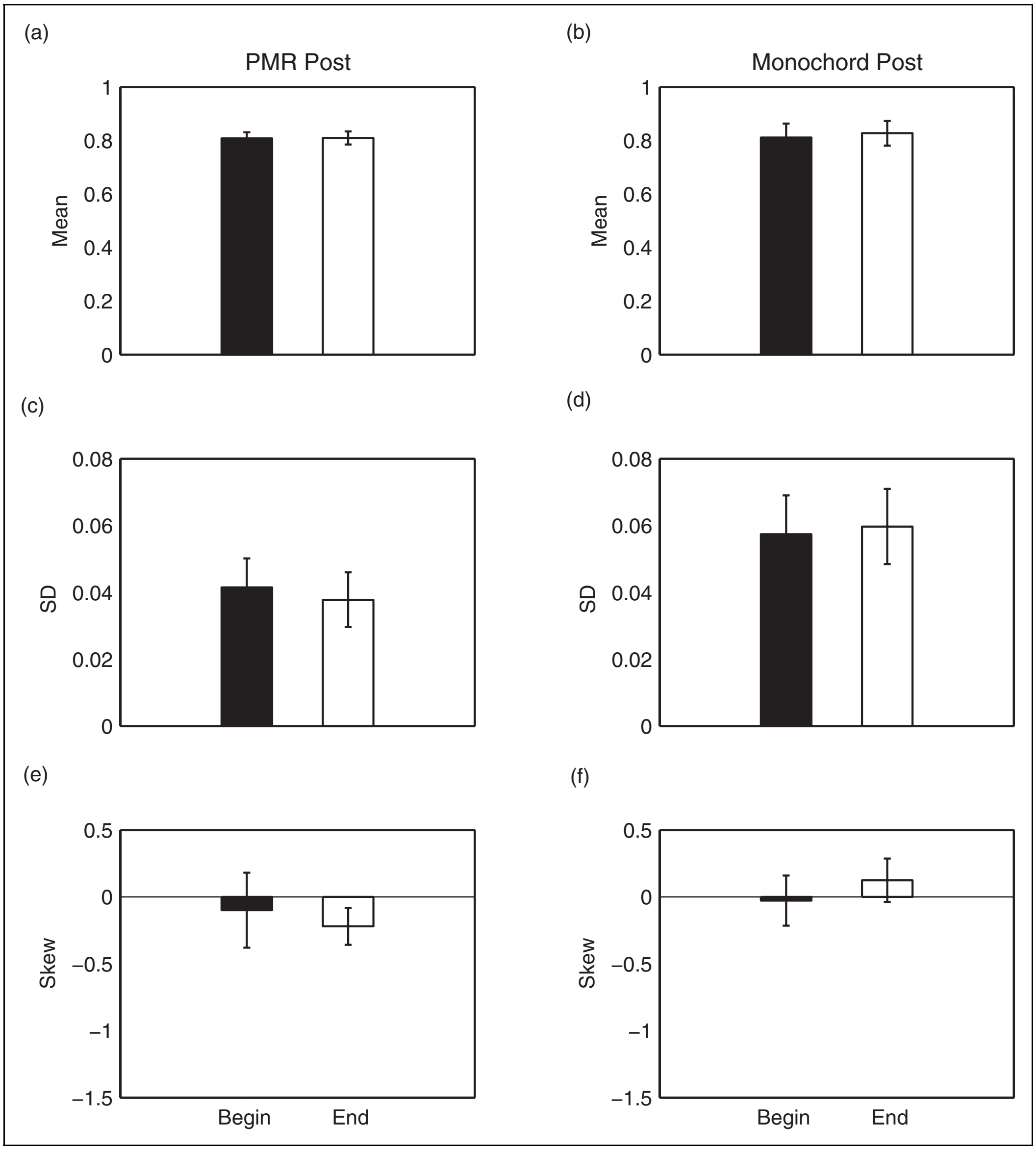

Figure 5. Change in mean, standard deviation, and skew within the post session. See Figure 4 for other details.

also observed a similar trend, though slightly less, within the last session in the MC group.

The mean HR remained relatively similar across both groups and treatment sessions. However, the variability, as measured by the SD, exhibited differences between the 2 groups; the fluctuation in the IBI sequence was found to be increased in the last phase of the MC treatment compared to its beginning phase, whereas such changes within the PMR treatment were in the opposite direction. Interestingly, this effect was only found in the first session but not in the last one. The skewness measure also produced a similar effect that was found in the first session only. We assume that the within-session differences in the MC group reflect the autonomic changes associated with MC sounds, and these differences would decrease with repeated sessions due to possible habituation to MC sounds or to decreased emotional arousal.[21] These results indicate that the impact of relaxation on the autonomic states in MC group differs from that in the PMR group. Moreover, the relaxation state caused by listening to MC sounds seems to be a different type of relaxation than that caused by listening to familiar music in previous studies.[20,22] However, it is possible that the change in the pattern of HRV caused by listening to MC sounds can be a general physical and psychological effect of musical stimuli; for example, a previous study reported an increase of similar measures (LF and LF:HF) as in ours while listening to both sedative and exciting musical excerpts.[21] The different patterns of autonomic nervous activity between the 2 groups are also supported by our pNN50 measure, which was higher in the MC group than in the PMR group. Although this measure is used primarily for diagnostic classification purposes, recent studies suggest modulations of pNN50 by a different relaxation treatment.[38,39]

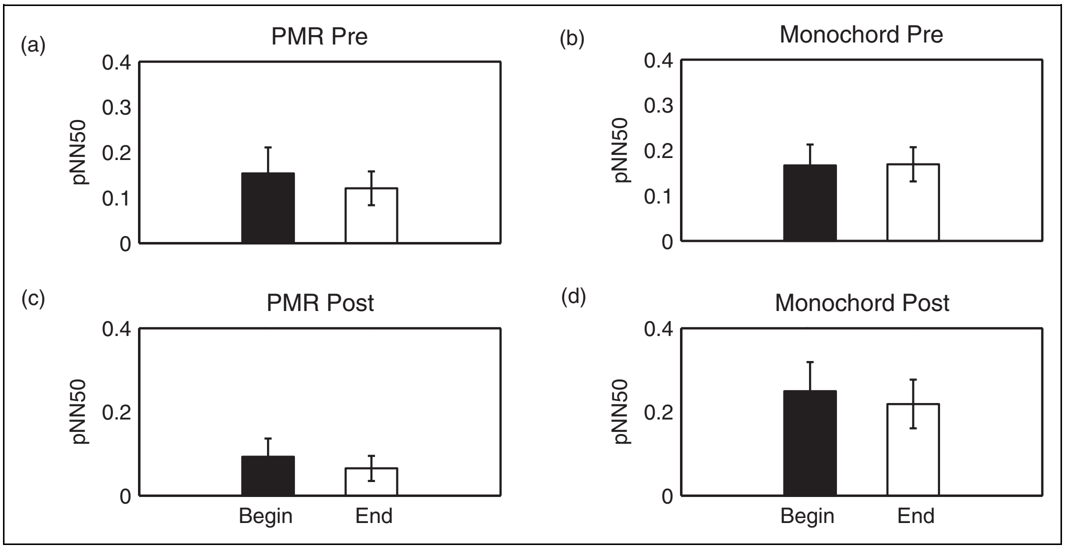

Figure 6. Change in pNN50 within the pre and post sessions for both groups. pNN50 indicates percentage of successive RR-interval differences $\geq$50 ms.

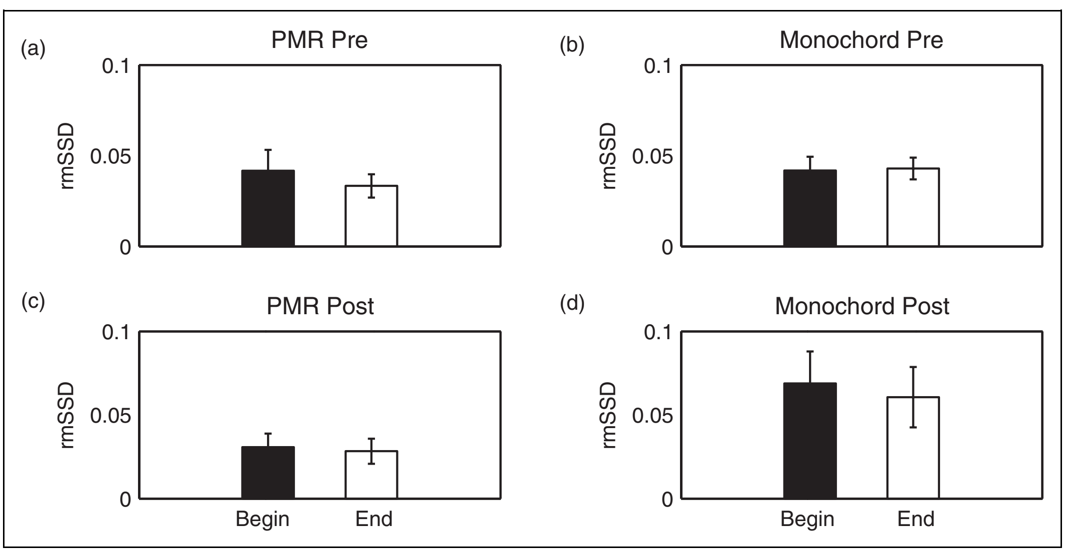

Figure 7. Change in rMSSD within the pre and post sessions for both groups. rMSSD indicates square root of the mean of the squared differences between adjacent intervals.

The results of this study—in particular regarding the induction of relaxation by listening to MC sounds—can indicate a state of relaxation in the psychological and physiological activities like other similar relaxation states. On the basis of the increase in LF power, HF power, LF:HF ratio, and pNN50, the state of relaxation caused by listening to MC sounds is not exactly comparable with other states of meditation, anesthesia, or relaxation, even though there is some similarity. It resembles most the state of sedation by midazolam due to an increase in HF power and the LF:HF ratio coupled with a significant decrease in anxiety[26] and that of zazan and kinhin meditation[27] or the samadhi state[31] due to an increase in LF power.

Unfortunately, no control group with ECG measurement was included in this study. Comparing with the resting state without audio stimuli shows a clearer tendency of HRV change, particularly with regard to the LF value even though a change was shown in the first session in the MC group. Usually, music therapists play the MC at a pace dictated by the respiration rate of patients, which strongly influences the relaxation process and the depth of relaxation achieved. In this study, we played prerecorded MC sounds and this may lead to different results compared to listening to live MC sounds. In this study, we tried to analyze the relaxing effect of MC sounds and PMR during chemotherapy. Unfortunately, we could not control all side effects of premedication and chemotherapy, which may increase or decrease HR indirectly. In this clinical study, no patient was observed with significantly accelerated or decelerated HR during chemotherapy. However, it might have been a regulated response with (pre)medication and relaxation treatment.

This study set out to compare HRV during the state of relaxation by listening to MC sounds compared against PMR, a method of inducing relaxation that has already been empirically proved. Further research needs to investigate the relationship between various states of relaxation and HRV. Considering different states of relaxation and states of consciousness can better detect the depth of relaxation for the purpose of analyzing HRV. To find out the specific physiological changes, it might be useful to compare against a control group. Moreover, it would be interesting to show the different changes in HRV achieved by similar relaxation effects from listening to MC sounds as well as from listening to minimal music or exercising meditation. Other physiological parameters, such as skin resistance, body temperature, and respiration, could be included to determine the precise physiological and mental states.

Conclusion

This study was a first attempt at investigating patients' autonomic physiological state while listening to MC sounds in comparison with those associated with PMR technique in patients with cancer. The study has shown distinct changes in HRV patterns in the patients listening to MC sounds. However, further investigation is essential in order to establish an evidence-based method for the usage of MC sounds in the clinical context.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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