RESEARCH ARTICLE

Effects of Music on Immunity and Physiological Responses in Healthcare Workers: A Randomized Controlled Trial

Hui-Ling Lai[1,2*†], Kuang-Wen Liao[3], Chiung-Yu Huang[4], Pin-Wen Chen[5] & Tai-Chu Peng[1]

[1]Department of Nursing, Tzu Chi University, Hualien, Taiwan

[2]Department of Nursing, Buddhist Tzu Chi General Hospital, Hualien, Taiwan

[3]National Chiao Tung University, Department of Biological Science and Technology, Hsin-Chu, Taiwan

[4]Department of Nursing, I-Shou University, Taiwan

[5]National Cheng Kung University, Institute of Art Studies, Taiwan

Abstract

Research-based evidence supports the effectiveness of soothing music in improving stress-related psycho-physiological indices in a clinical setting. However, there is currently insufficient scientific knowledge of the effects of music on immune markers of stress in humans. Therefore, the aims of the study were to compare the effects of music and quiet rest on the levels of interleukin-6 (IL-6), tumour necrosis factor-α (TNF-α), interleukin-10 (IL-10), heart rate and mean arterial pressure among healthcare workers. By using a randomized controlled trial design, 60 nurses were randomly assigned to the stimulating or sedating music or rest groups for 30 min. Participants' psychoneuroimmunological parameters were measured using enzyme-linked immunosorbent assays. General estimating equation was used to analyse data. Results revealed that IL-6, TNF-α and IL-10 were not detectable in this population. No significance differences in heart rate were found among the three groups. However, the stimulating music group had significantly higher mean arterial pressure levels than the sedating music group but no differences between the quiet rest group and the sedating music group. Music with different tempi had little effect on mean arterial pressure. Any effect of music on immune markers of stress requires further research. Copyright © 2012 John Wiley & Sons, Ltd.

Introduction

Stress is one of the major factors affecting our health in the 21st century (WHO, 2010). Studies indicate an inverse association between stress and immune function (Stojanovich, 2010). The stress response is essentially protective, but it also exerts immune system depression. Stress leads to immunological response and alterations in normal body homeostasis. Thus, stress has long been considered a psychological factor with a major impact on disease development (Stojanovich, 2010).

Research on psychoneuroimmunology, that is, the study of relationships between the psychological, nervous and immunological systems of the body, has demonstrated linkage between stress and diminished immunity over the past 25 years. As early as the 1950s, studies were conducted, which considered that physical and mental disturbances were the result of stress and immunological factors (Solomon & Moos, 1964). Nowadays, it is well established that inflammatory cytokines released peripherally have profound effects on mood and behaviour (DellaGioia & Hannestad, 2010). Cytokine imbalances in the peripheral blood compartment have implications for physiological and psychological functional changes (Miller, 2009).

Nilsson's study (2008) demonstrates that listening to music, one of the mind/body interventional techniques, has proven effective for stress management, from which vital signs are the most extensively investigated variables. Music intervention, an inexpensive technique, can maximize relaxation and reduce stress and therefore has a necessary role in stress management (Nilsson, 2010). Different tempi of music have differential effects on psycho-physiological responses (Gerra et al., 1998),

with unclear consequences on physiological responses and immune factors. Researchers have therefore proposed that future studies ought to investigate exactly what patterns of music are linked to improved patient well-being (Batt-Rawden, 2010).

Psychoneuroimmunological theory for this study

There is no succinct model to explain the complexity of the immune system. Three decades ago, Ader (1980) introduced the theory of psychoneuroimmunology and reported the implied relationship between a stressor and immunologic response. Ader (2000) conceptualized the relationship as a bidirectional pathway between the brain and the immune system consisting of the hypothalamic–pituitary–adrenal system and the sympathetic nervous system. Ader (2000, p. 173) postulated, 'Both pathways exist because each system produces chemical signals recognized by surface receptors on lymphocytes and other immune cells with their activation or interruption influencing immune response'. Cytokines are derived from lymphocytes and monocytes. Th1 lymphocytes produce TNF-α to assist in cellular immunity. Th2 lymphocytes secrete IL-6 and IL-10 and promote humoral immunity.

Tissue damage or pathogens activate monocytes and macrophages to release pro-inflammatory cytokines including IL-6 and TNF-α (DellaGioia & Hannestad, 2010). Leukocytes are activated and recruited to the site of injury by stimulation of pro-inflammatory cytokines. Insufficient or excessive pro-inflammatory cytokine response can increase risk for inflammatory diseases. The magnitude of pro-inflammatory cytokine response to immune activation is modulated via several mechanisms including the local release of anti-inflammatory mediators, such as IL-10, by activated immune cells to suppress macrophage activation and prevent excessive production of pro-inflammatory cytokines.

Stress and immunity

Stress has been defined as 'a demand made upon the adaptive capacities of the mind and body' (Fontana, 1989, p.3). Stress can influence secretory IgA levels (Benham, Nash, & Baldwin, 2009). Psychological stress inhibits immune responses (DellaGioia & Hannestad, 2010). Nunez *et al.* (2002) demonstrated that music effectively reversed the adverse effects of stress on lymphocyte numbers and function in rodents. However, confirmation of this effect in humans is limited because of a lack of sufficient scientific research.

Occupational stress has a significant effect on psychological distress (Klainin, 2009). Healthcare workers, especially nurses in particular, may bear significant psycho-physiological stress. The changes in psycho-physiological responses may in turn cause an imbalance in circulating cytokine levels. Study has revealed that a certain level of anxiety is common in nurses (Lai, Lin, *et al.*, 2008). Persistent and unrelenting stress often leads

to anxiety. Anxiety will vary in duration and in intensity and fluctuate over time as a function of the amount of stress that impinges upon an individual and that individual's interpretation of the stressful situation as personally threatening. For the purpose of this study, nurses were recruited as participants.

Currently, no published studies examined the effects of music on cytokines in humans. Therefore, the main purpose of this study was to examine whether musical intervention influenced pro-inflammatory and anti-inflammatory cytokines [interleukin-6 (IL-6), tumour necrosis factor-α (TNF-α) and interleukin-10 (IL-10)] and influenced heart rate and mean arterial pressure. For the purpose of the study, we hypothesized that music with different tempi would have different effects on IL-6, TNF-α, IL-10, heart rate and mean arterial pressure.

Methods

Study design

A randomized controlled trial was conducted to examine the effects of various types of music on IL-6, TNF-α and IL-10, as well as heart rate and mean arterial pressure among nurses who were arranged to a mental arithmetic task to increase their anxiety levels (Tomaka, Blascovich, Kelsey, & Leitten, 1993).

Participants

Purposive sampling was used to recruit participants. Sixty healthy nurses at a hospital in Taiwan were recruited using an intranet e-mail announcement. Prior the study, all participants read and signed an informed consent form, which detailed the experimental procedures and the benefits and potential risks related to their participation. Each participant received a book coupon equal to NT$600 (about US$25) for their voluntary involvement in the study.

Power analysis was used to estimate sample size. To achieve a power of 0.8 at $\alpha = 0.05$, two-tailed, with an effect size 0.5 (Lane, 1992), correlation ($r = 0.65$) among repeated measures (Lai *et al.*, 2006), the size of each group was computed to be 19. Five per cent of attrition was added; therefore, 20 subjects were needed for each group. In order to qualify for participation in the study, participants were required to have a self-rated anxiety score of ≥ 40 on state anxiety measured by the State Anxiety Inventory (Spielberger, 1977) and to have no history of asthma, cancer treatment in the past year or psychotic illness. Over a 4-month period, a total of 60 participants were contacted and were all qualified to participate.

Measures

Participant characteristics

The participants' characteristics including age, education, marital status, health status and disease as well

as trait anxiety were measured by researcher-designed questionnaire and standardized instruments. The State-Trait Anxiety Inventory (Spielberger, 1977), used to measure trait anxiety, was valid and reliable. The trait anxiety scale consists of 20 questions that assess how the respondents 'generally feel'. This anxiety scale consists of 20 self-reported scales, with each Likert-type scale running from 1 to 4, where a score of 20 indicates the absence of anxiety and a score of 80 indicates high anxiety. The alpha coefficient of Chinese version was 0.90 in this study.

Heart rate and mean arterial pressure

A blood pressure monitor (DINAMAP ® ProCare Monitor 200, GE Company, NY, USA) was used to measure heart rate and blood pressure. This blood pressure monitor met the AAMI/ANSI standard (American National Standards Institute 1992) and had an accuracy of ± 5 mmHg, with a standard deviation range of 2.12–6.29 mmHg (within the AAMI standard of 8 mmHg).

IL-6, IL-10 and TNF-α measurement

The concentrations of IL-6, IL-10 and TNF-α in the samples were measured separately by enzyme-linked immunosorbent assay (ELISA) kits from R&D Systems Inc (ELISA, Endogen, USA) (detection limit: 10 pg/mL). All samples were stored at $-20\,°C$ before testing. The reagents, samples and working standards were brought to room temperature and were prepared according to the manufacturer's directions. ELISA was performed following the manufacturer's instructions. Each sample was run in duplicate and read on an automated ELISA reader (450/540 nm wavelength).

Test anxiety

The Test Anxiety Inventory (TAI) was previously tested for validity and reliability and was used to measure test anxiety of mental arithmetic tasks. The TAI, with an internal consistency 0.92, is a 20-item self-report measure that uses multiple-choice answers in a Likert format to assess participants' anxiety and discomfort in test-taking situations. Scores on the TAI range from 20 to 80 points. Higher scores indicate higher levels of test anxiety (Speilberger, 1980). Permission for use of the TAI in Mandarin was given by Professor Speilberger for use in this study. The TAI was used to examine if the mental arithmetic tasks would induce stress. The scores of test anxiety were used as a covariate in the study. The Cronbach's alpha of the Chinese version of TAI in this study is 0.84.

Music likeability

The participants' musical likeability was measured using a visual analogue scale (VAS). The scale used consisted of a horizontal line 10 cm in length and fitted with a scale. Zero centimetres represented 'dislike a lot', while 10 cm represented 'like a lot'. Previous studies on the effects of music on test anxiety by means of a VAS scale showed 1-week test-retest reliability of 0.77 and a 2-week test-retest reliability of 0.73 (Lai, Chen, *et al*., 2008).

Procedures

The study was approved by the Institutional Review Board prior to commencement. The study took place in a music study room. All participants came to the study after the day shift. After participants arrived at the study room at the appointed time, researchers assessed their eligibility to participate in the study. They were fully instructed on the procedures of the study (Figure 2). Informed consent was obtained from each of them. Participants also completed a State-Trait Anxiety Inventory as well as a health survey indicating that they did not have any known medical problems and that they were not taking medications that would affect the physiological assessments. Participants were individually seated in the study room. They were asked to rest for 10 min while the assistant prepared the equipment. Research assistants aided participants and were responsible for operating blood pressure monitors to record heart rate and mean arterial pressure. At baseline, 5 mL of blood was acquired from each participant to obtain the baseline values (T1) for IL-6, IL-10 and TNF-α. Each participant was asked to draw a lot to determine which group the participants would be assigned to. All lots are packed in a jar that was prepared by another person. Therefore, researchers did not know beforehand which group each participant would be assigned to. Researchers responsible for statistical analysis also were not aware of which group the collected data belonged to. Both approaches were aimed to decrease the error rate.

Previous studies have demonstrated that a standard mental arithmetic task reliably generates physiological responses (Tomaka *et al*., 1993) and that acute stress can alter aspects of immune function in humans (Weisse *et al*., 1990). Therefore, in order to test the effect of various types of music on the mediation of physiological parameters, a serial mental arithmetic was imposed on participants and was considered an immunosuppressive agent. The stress-inducing exercise participants were given consisted of a facedown, size A4 index card on which was written a four-digit number. When signalled to begin by the research assistant, the participants turned over the card revealing the number and proceeded to subtract 7 serially from that number for 2 min. A digital metronome was set at 60 beats/min and at a volume of 90 dB (80 dB is normal conversation) throughout the entire mental arithmetic process to create a tense atmosphere. Participants were instructed to try to perform the task as quickly as accurately as possible and were asked to count out loud (Andren & Hansson, 1980). The mental arithmetic lasted 23 min and consisted of four 2-min mental arithmetic periods including the subtractions

from the values 1539, 2737, 5529 and 2527 by intervals of 7 for the first two sets and by intervals of 13 for the last two sets. Each task was preceded by a 5-min rest period. Performance on mental arithmetic tasks was tracked for accuracy by the assistant.

The TAI was assessed immediately after the mental arithmetic tasks were completed, and 5 mL of blood was drawn as the second pre-test data (T2). Measurements were recorded for heart rate and blood pressure and at the same time. Intervention of music or quiet rest was started immediately after the mental arithmetic tasks were carried out. Participants were seated on the sofa resting or listening to music for 30 min according to their assigned groups. During the intervention, subjects were asked to turn off their mobile phones. After the intervention, 5 mL of blood was drawn as the post-test data (T3). The room temperature was maintained comfortably at 25–26 °C. The study was carried out between 6 PM and 8 PM. This was exactly the time during which nurses ended their day shift, which facilitated their participation in the study. The whole procedure lasted at least 75 min.

Experimental intervention

Interventions consisted of listening to sedating or stimulating music or quiet rest. An auto-reverse multi-laser disc player (UX-P450, JVC, Japan) and wireless stereo headphones (Camma HR-805, Taiwan) were used for listening to the music. Four sedating musical pieces included in the study were (1) Beethoven: Piano sonata No. 14 Moonlight, (2) Beethoven: Romance for Violin No. 2 in F major and (3) Mozart: Andante from Piano Concerto No. 21 in C Major (CM music Records Co. 1992, Taipei). The fourth piece was composed and recorded by the authors (P-W. and H-L.) of this study (Figure 1). The musical tempos ranged from 60 to 80 beats/min (slow) and had minor tonalities, smooth melodies and no dramatic change in volume or rhythm

(Figure 2). Participants did not know that one of the sedating musical pieces was made by the researchers. All the sedative music pieces used in the study were demonstrated in previous studies to have beneficial effects on stress among adults undergoing root canal treatments (Lai, Hwang, *et al.*, 2008) and text anxiety (Lai, Chen, *et al.*, 2008).

The stimulating musical pieces played had tempos ranging from 100 to 130 beats/min (MAXI Kingdom, 12 Alpha Music Co. 1992, Taipei). Sixteen stimulating musical pieces included in the study were (1) Gabry Ponte: Time to rock, (2) Celina: Light and shadow, (3) Rollerbaby: Geisha Dreams, (4) Dj Ali: Stomp, (5) D Control: Clown-song, (6) Jessica Jay: Chi Chi Quita, (7) Dj Sam Feat: Heaven, (8) Reanimator: Live is life, (9) Lady Bouncer: Dirty Mary, (10) Eiffel: Cosa restera, (11) Lion Project: Happy Children 2002, (12) Butterfly: She moves, (13) Kim Lukas: Clouds, (14) Hands up: Sugababy (15) Yamboo: Kalinka and (16) Cocktail: Kakadu. The music had stimulating qualities including fast tempos, syncopations, major tonalities and percussive qualities. All the participants were seated on a comfortable sofa. The participants in the quiet rest group had no music or headphones.
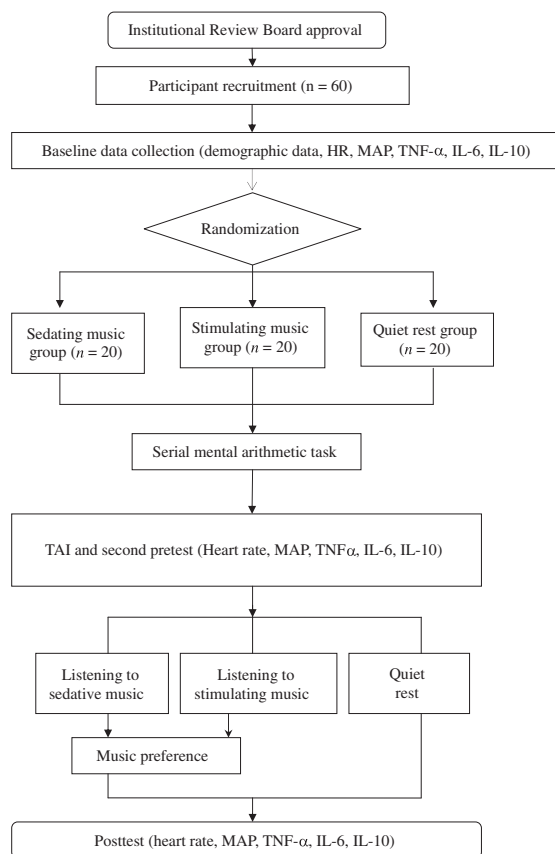

Figure 1. Excerpt from researchers' composition of sedating music

Figure 2. Study flowchart. MAP: mean arterial pressure; TNF-: tumour necrosis factor-; IL-6: interleukin-6; IL-10: interlenkin-10

Intervention protocol

The intervention protocols were carried out individually as follows: (1) participants were seated on a comfortable sofa, and a blood pressure cuff was fastened on their left upper arm to measure heart rate and blood pressure. (2) Venipuncture was performed with an intravenous catheter in the right arm to collect 5 mL of blood into a plasma-separated test tube as the baseline (T1), and another 5 mL was drawn again as the second pre-test data (T2). (3) Headphones were placed on the participants, and a thin blanket was used to cover the participant's abdomens and upper legs. (4) Participants in the music groups were instructed how to adjust the volume of the headphones, according to personal preference. (5) Participants in the quiet rest group sat on a comfortable sofa for 30 min without any music. (6) After 30 min, 5 mL of blood was drawn at the end of the intervention (the post test, T3). Participants in both music groups were then asked to evaluate their music likeability using a VAS recorded by the assistant.

Data analysis

Data was analysed using PASW 18.0 for Windows (SPSS Inc., Chicago, IL, USA). Demographics were compared using t-test and a χ^2 test. ANOVA was used to determine the differences at different time points for each group. Fisher's skewness coefficient was used to check the normality of the data (Pett, 1997). Generalized estimating equation analysis was used to control for changes in time and baseline values. Post hoc multiple comparisons with the least significant difference correction were used to determine group differences in relaxed indices at each time points. The level of significance was set at a p-value of 0.05.

Results

Description of participants

Participant age ranged from 21 to 42 years [mean standard deviation (SD), 27.28 ± 5.2 years]. Participants

were all female. The majority were single ($n = 48$, 80%), and 50% of them had graduated from a university ($n = 30$, 50%). Only one subject had master's degree. All participants reported being in good general health and were free from symptoms of current or recent infection.

Comparability of groups

At first pre-test (T1), there were no group differences in participants' characteristics, trait anxiety, heart rates and mean arterial pressure. However, IL-6, TNF-α and IL-10 were not detectable in all participants. All the levels of these immune factors reported were below the detection limit of the assays. These immune factors were therefore not used for further statistical analysis.

With the use of paired t-tests, there was no significant difference between baseline (T1) and the second pre-test scores (T2) for heart rate and mean arterial pressure among the three groups. We also found that there were no significant differences of test anxiety among groups (Table I) as well as no correlation between test anxiety and any of the outcome parameters (T2) examined in the study. Both findings revealed that the mental arithmetic task did not load additional stress on the participants. The baseline data of heart rate and mean arterial pressure as well as test anxiety scores were all used as covariates in this study.

Heart rate and mean arterial pressure

Generalized estimating equation was used to determine group differences in post-test scores of heart rate and mean arterial pressure. Our study found that there were no significant differences in heart rate among the three groups. However, significant group differences were found for mean arterial pressure (Table II). While controlling for pre-test score and test anxiety, the results demonstrated that the group effect was significant ($\chi^2 = 6.31$, $p = 0.04$). With the use of post hoc least significant difference comparisons for the group effect, there were significant differences between

Table I. Scores of psychoneuroimmunological parameters in different time points by group ($n = 60$)

Psychoneuroimmunological parameters	Total ($n = 60$)		Stimulating music ($n = 20$)		Sedating music ($n = 20$)		Quiet rest ($n = 20$)		F	p
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
Heart rate at T1	75.37	8.87	76.10	9.41	74.1	7.72	75.9	9.66	0.301	0.741
Heart rate at T2	71.65	9.01	73.15	8.99	68.6	8.03	73.2	9.60	1.76	0.18
Heart rate at T3	70.25	8.22	72.00	9.41	68.35	6.66	70.40	8.37	0.99	0.38
MAP at T1	86.12	9.90	86.08	9.71	85.08	8.00	87.18	9.78	0.260	0.772
MAP at T2	84.76	9.23	86.63	8.79	82.75	9.13	84.88	9.81	0.88	0.82
MAP at T3	83.0	9.45	84.68	11.02	81.35	7.64	82.96	9.58	0.614	0.545
TAI	45.28	9.72	42.2	8.54	48.55	11.36	45.1	8.37	2.23	0.12

T1 = baseline measurement, T2 = second pre-test (after mental arithmetic task), T3 = post-test (after intervention).
SD: standard deviation; MAP: mean arterial pressure; TAI: Test Anxiety Inventory.

Table II. General estimating equation estimating group difference (*n* = 60)

Outcome measure	Group	Estimate	SD	95% Wald CI	Wald	p	Post hoc
MAP	Stimulating	85.861	0.986	(83.928, 87.793)	6.311	0.043*	Stimulating > sedating (*p* = 0.02)
	Sedating	82.703	0.894	(80.951, 84.455)			
	Quiet rest[†]	83.070	1.096	(80.922, 85.217)			
Heart rate	Stimulating	72.004	1.445	(69.173, 74.835)	2.976	0.226	None
	Sedating	69.393	1.008	(67.416, 71.369)			
	Quiet rest[†]	71.453	1.097	(69.303, 73.603)			

SD: standard deviation; MAP: mean arterial pressure.
[†]Reference group.
*$p < 0.05$.

the stimulating and sedating music groups (*p* = 0.02). These results indicate that the stimulating music group had higher mean arterial pressure levels than the sedating music group. However, there were no differences in the mean arterial pressure levels between the quiet rest group and the sedating music group (Table II, Figure 3).

Likeability of music between two music groups

By using Student's *t*-test, the sedating music group had significantly higher scores for music likeability ($M = 8.05 \pm 1.54$) than did stimulating music group ($M = 6.65 \pm 1.84$) ($t = -2.61$, *p* = 0.013), indicating that participants in the sedating music group had higher scores of the likability of music than the participants in the stimulating music group.

Discussion

Cytokine levels

The study is one of very few to look at the immune effects of music. With the use of the high sensitivity R and D kits, the levels of the immune factors measured were below the detection limit of these assays. Although non-detectable amounts are not uncommon

in plasma or serum, the possible reasons for the undetectable may be because the half-lives of these cytokines are quite short. Cytokines may begin to break down as soon as the blood is drawn. Moreover, a shift in cytokine pattern could occur over the measurement period tested, and generation of cytokines is a complex process where the cytokines produced lag in appearance from the stimulating event. Moreover, the unexpected findings of the effects of music on cytokines may be also because the nurses did not have much anxiety as we expected.

During an exhaustive literature search, we found that there are no similar previous studies available to compare and contrast the results of our study. However, previous studies revealed that positive emotional style (Prather, Marsland, Muldoon, & Manuck, 2007) and psychosocial resources (Sjogren, Leanderson, Kristenson, & Ernerudh, 2006) are negatively associated with the production of IL-6 and IL-10, while plasma levels of IL-6 are positively associated with depression (Sjogren *et al.*, 2006). In this respect, listening to sedating music could play a role in the improvement of well-being (Krout, 2007). Among first-line nurses, depressive symptoms and insomnia are common (Lai, Lin *et al.*, 2008). Immunosuppression is reported in people who experience depressive symptoms (Miller,
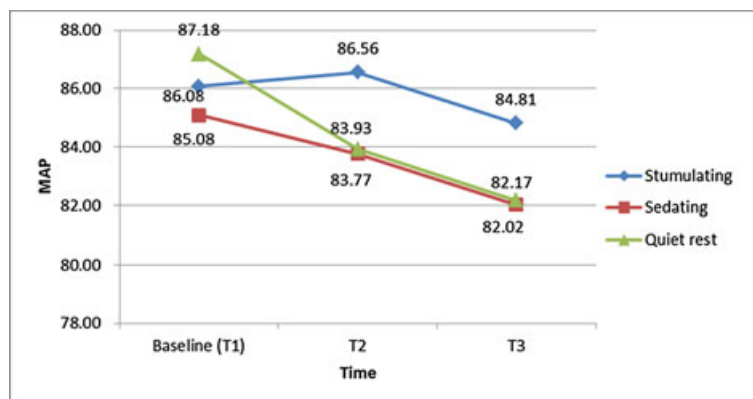

Figure 3. Changes in mean arterial pressure (MAP) levels among groups at different time points. T1 = baseline measurement. T2 = second pre-test (after mental arithmetic task) and T3 = post-test (after intervention)

2010) and insomnia (Opp, 2009; Irwin, Carrillo, & Olmstead, 2010) in response to stressors. Detection of any effects of music on immunity requires further research.

Mental arithmetic tasks and stress responses

In order to test the effect of various types of music on the influence of physiological parameters, a serial mental arithmetic was imposed on the participants. We found it surprising that the serial mental arithmetic task did not successfully load stress onto the participants in the study manifested in no differences of heart rate and mean arterial pressure between before and after mental arithmetic. Conversely, Andren and Hansson (1980) found that a mental arithmetic task increased blood pressure from resting levels. This discrepancy could be because the research assistant was a colleague of the participants. The friendship could have decreased participants' tension, even though a standard procedure was performed.

Music, heart rate and mean arterial pressure

Our study showed little effect of music on mean arterial pressure. This finding is similar to that of a recent study reported by Lai, Hwang, *et al.* (2008), in which music had no favourable effect on heart rate or blood pressure for subjects under the stress of a medical procedure. Nilsson (2008) performed a meta-analysis evaluating 42 relevant randomized controlled trials and concluded that only 27% of music intervention groups had significantly reduced heart rates and decreases in blood pressure. The impact of music on vital signs was inconclusive. A possible key reason for this inconsistency among studies could be explained by the different study populations, the nature of the stressor and sample sizes. Other reasons for the inconsistency may be because findings of such studies is hampered by the heterogeneity of methods, from study populations, the procedures undertaken and the choice of a comparison group to whether or not the music was preferred or not preferred by participants.

The study also found no significant effect of quiet rest on mean arterial pressure compared with both music groups. However, we found that mean arterial pressure was higher in the stimulating music group than in the sedating music group. This result is in line with a study by Gerra *et al.* (1998), which found that fast music significantly increases heart rate and systolic blood pressure. Consequently, these findings would suggest that stimulating music should be used with caution for stress management.

Likeability of music and music effectiveness

We played two types of music in the study. The sedating music group had significantly higher scores on music likeability than did the stimulating music group. Participants listening to sedating music appeared to have lower mean arterial pressure than those listening to stimulating music (Figure 3; Table I). Sedating music tends to increase a sense of well-being (Nilsson, 2010). Although subjects in the present study did not have the opportunity to choose their own preferred music, a Cochrane review has found that the positive effects of music were similar in studies in which patients selected the type of music and those in which patients did not (Cepeda, Carr, Lau, & Alvarez, 2006).

On the basis of these results, the notion that music likeability is vital to stress reduction is supported (Lai, 2004; Lai & Good, 2005). Indeed, this is not surprising, given the differences in the 'soothing' quality of the prescribed music (Lai & Good, 2002) compared with stimulating music. We suggested that rhythm, in particular, influences the characteristics of music and, as such, produces the anticipated outcome (Lai & Good, 2002).

Limitations and recommendations for future studies

A randomized controlled trial was used in this study to improve study power. This study design allowed for the measurement of the dependent variable via objective ways in order to ascertain the main causes. The findings of this study should be interpreted with caution. The participants were all women; it is intriguing to speculate on gender disparities for the effect of music. We suggest recruiting male participants in future studies. Even though the mechanism of the effect of music is not fully understood, it should not interfere with the application of music as an intervention, along with medical treatment, to provide holistic care. The likeability of music listeners should be measured as baseline data and should be considered taking into account in data analysis in further studies. Research that examines the classification of music according to its effects on psycho-physiological index is important in order to establish scientific evidence.

Conclusion

Interleukin-6, tumour necrosis factor-α and interleukin-10 were not measureable in healthy nurses. Music with different tempi had little effect on mean arterial pressure. Any effect of music on other immune factors of stress requires further research.

Acknowledgements

Conflict of interest

No conflict of interest is declared by the authors.

REFERENCES

Ader, R. (1980). Presidential address: Psychosomatic and psychoimmunologic research. *Psychosomatic Medicine*, *42*, 307–322.

Ader, R. (2000). On the development of psychoneuroimmunology. *European Journal of Pharmacology*, *405*, 167–176.

Andren, L., & Hansson, L. (1980). Circulatory effect of stress in essential hypertension. *Acta Medica Scandinavica*, *648*(Suppl.), 69–72.

Batt-Rawden, K. B. (2010). The benefits of self-selected music on health and well-being. *The Arts in Psychotherapy*, *37*, 301–310.

Benham, G., Nash, M. R., & Baldwin, D. R. (2009). A comparison of changes in secretory immunoglobulin: A following a stress-inducing and stress-reducing task. *Stress and Health*, *25*, 81–90.

Cepeda, M. S., Carr, D. B., Lau, J., & Alvarez, H. (2006). Music for pain relief. *Cochrane Database Systematic Review*, (2): CD004843.

DellaGioia, N., & Hannestad, J. (2010). A critical review of human endotoxin administration as an experimental paradigm of depression. *Neuroscience and Biobehavioral Reviews*, *34*, 130–143.

Fontana, D. (1989). Managing Stress. London: British Psychological Society and Routledge.

Gerra, G. Zaimovic, A. Franchini, D. Palladino, M., Giucastro, G., Reali, N.,. . . Brambilla, F. (1998). Neuroendocrine responses of healthy volunteers to techno-music: Relationships with personality traits and emotional state. *International Journal of Psychophysiology*, *28*, 99–111.

Irwin, M. R., Carrillo, C., & Olmstead, R. (2010). Sleep loss activates cellular markers of inflammation: Sex differences. *Brain, Behavior, and Immunity*, *24*, 54–57.

Klainin, P. (2009). Stress and health outcomes: The mediating role of negative affectivity in female health care workers. *International Journal of Stress Management*, *16*(1), 45–64.

Krout, R. E. (2007). Music listening to facilitate relaxation and promote wellness: Integrated aspects of our neurophysiological responses to music. *The Arts in Psychotherapy*, *34*, 134–141.

Lai, H. L. (2004). Music preference and relaxation in Taiwanese elderly people. *Journal of Geriatric Nursing*, *25*(5), 286–291.

Lai, H. L., Chen, C. J., Peng, T. C., Chang, F. M., Chen, M. L., Huang, H. Y., & Chang, S. C. (2006). Randomized controlled trial of music during kangaroo care on perinatal anxiety and preterm infants' responses. *International Journal of Nursing Studies*, *43*, 139–146.

Lai, H. L., Chen, P. W., Chen, C. J., Chang, H. K., Peng, T. C., & Chang, F. M. (2008). Randomized crossover trial studying the effect of music on examination anxiety. *Nurse Education Today*, *28*(8), 909–916.

Lai, H. L., & Good M. (2002). An overview of music therapy. *The Journal of Nursing*, *49*(2), 80–84.

Lai, H. L., & Good M. (2005). Music improves sleep quality in older adults, *Journal of Advanced Nursing*, *49*(3), 234–244.

Lai, H. L., Hwang, M. J., Chen, C. J., Chang, K. F., Peng, T. C., & Chang, F. M. (2008). Randomised controlled trial of music on state anxiety and physiological indices in patients undergoing root canal treatment. *Journal of Clinical Nursing*, *17*(19), 2654–2660.

Lai, H. L., Lin, Y. P., Chang, H. K., Wang, S. C., Liu, Y. L., Lee, H. C.,. . . Chang, F. M. (2008). Intensive care unit staff nurses: Predicting factors for career decisions. *Journal of Clinical Nursing*, *17*(14), 1886–1896.

Lane, D. (1992). Music therapy, gift beyond measure. *Oncology Nursing Forum*, *19*(6), 863–867.

Miller, A. H. (2009). Mechanisms of cytokine-induced behavioral changes: Psychoneuroimmunology at the translational interface. *Brain, Behavior, and Immunity*, *23*, 149–158.

Miller, A. H. (2010). Depression and immunity: A role for T cells? *Brain, Behavior, and Immunity*, *24*, 1–8.

Nilsson, U. (2008). The anxiety- and pain-reducing effects of music interventions: A systematic review. *AORN Journal*, *87*(4), 780, 782, 785–794, 797–807.

Nilsson, U. (2010). Music: A nursing intervention. *European Journal of Cardiovascular Nursing*. DOI:10.1016/j.ejcnurse.2010.06.004

Nunez, M. J., Mana, P., Linares, D., Riveiro, M. P., Balboa, J., Suarez-Quintanilla, J.,. . . Freire-Garabal, M.

(2002). Music, immunity and cancer. *Life Sciences*, *71*, 1047–1057.

Opp, M. R. (2009). Sleep and psychoneuroimmunology. *Immunology and Allergy Clinics of North America*, *29*(2), 295–307.

Pett, M. A. (1997). Nonparametric statistics for health care research: Statistics for small samples and unusual distributions. Thousand Oaks, CA: Sage.

Prather, A. A., Marsland, A. L., Muldoon, M. F., & Manuck, S. B. (2007). Positive affective style covaries with stimulated IL-6 and IL-10 production in a middle-aged community sample. *Brain, Behavior, and Immunity*, *21*, 1033–1037.

Sjogren, E., Leanderson, P., Kristenson, M., & Ernerudh, J. (2006). Interleukin-6 levels in relation to psychosocial factors: Studies on serum, saliva, and in vitro production by blood mononuclear cells. *Brain, Behavior, and Immunity*, *20*, 270–278.

Solomon, G. F., & Moos, R. H. (1964). Emotions, immunity, and disease. *Archives of General Psychiatry*, *11*, 657–674.

Speilberger, C. (1980). Test Anxiety Inventory. Palo Alto, CA: Consulting Psychologist Press.

Spielberger, C. (1977). State-Trait Anxiety Inventory Form Y. Menlo Park, CA: Mind Garden Incorporated.

Stojanovich, L. (2010). Stress and autoimmunity. *Autoimmunity Reviews*, *9*(5), A271–A276.

Tomaka, J., Blascovich, J., Kelsey R., & Leitten, C. L. (1993). Subjective, physiological and behavioral effects of threat and challenge appraisal. *Journal of Personality and Social Psychology*, *65*(2), 248–260.

Weisse, C. S., Pato, C. N., McAllister, C. G., Littman, R., Breier, A., Paul, S. M., & Baum, A. (1990). Differential effects of controllable and uncontrollable acute stress on lymphocyte proliferation and leukocyte percentages in humans. *Brain, Behavior, and Immunity*, *4*(4), 339–351.

World Health Organization (2010). Global health diplomacy: Negotiating health in the 21st century. Retrieved from http://www.who.int/dg/speeches/2008/20081021/en/ [30 April 2010]