Randomized clinical trial examining the effect of music therapy in stress response to day surgery

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Background: Music therapy could reduce stress and the stress response. The aim of this study was to investigate the role of music therapy in alleviating stress during day surgery.

Methods: Sixty patients undergoing day surgery were randomized to one of three groups, each containing 20 patients. Before and during surgery, patients in group 1 listened to new age music and those in group 2 listened to a choice of music from one of four styles. Patients in group 3 (control group) heard the normal sounds of the operating theatre. Plasma levels of cortisol and subpopulations of lymphocytes were evaluated before, during and after operation.

Results: Plasma cortisol levels decreased during operation in both groups of patients who listened to music, but increased in the control group. Postoperative cortisol levels were significantly higher in group 1 than in group 2 (mean(s.d.) $14\cdot21(6\cdot96)$ versus $8\cdot63(2\cdot72)$ ng/dl respectively; $P < 0\cdot050$). Levels of natural killer lymphocytes decreased during surgery in groups 1 and 2, but increased in controls. Intraoperative levels of natural killer cells were significantly lower in group 1 than in group 3 (mean(s.d.) $212\cdot2(89\cdot3)$ versus $329\cdot1(167\cdot8)$ cells/µl; P < 0.050).

Conclusion: Perioperative music therapy changed the neurohormonal and immune stress response to day surgery, especially when the type of music was selected by the patient.

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Introduction

Surgery is a well recognized cause of stress^{1,2}. Although day surgery is associated with better patient compliance, it still causes stress^{3,4}. Anxiety and metabolic, neurohormonal and immune system changes are implicated in the stress response^{5,6}, and such changes have been observed in response to surgery^{7–9}. Cardiovascular alterations, and increased plasma levels of cortisol and natural killer (NK) lymphocytes have been reported to be associated with stress^{5,10–14}.

Several studies have shown that music therapy can inhibit stress, reducing anxiety and neurohormonal responses to psychological stress^{15–18}, as well as preoperative anxiety^{19–22} and postoperative pain^{23–27}. Some authors have allowed patients to select the type of music^{19–22}, whereas others prefer to use new age^{23,27} or classical¹⁵ music. However, the results of these studies are not strictly comparable as different methods of investigation have

been used and the most suitable type of music is still a matter of debate. The effectiveness of music therapy may depend on the type of music adopted in relation to the emotional perception of the patient. The aim of this trial was to examine the role of music therapy in reducing stress associated with day surgery, by evaluating changes in plasma levels of cortisol and NK lymphocytes. The effect of different types of music (new age or patient-selected) was also examined.

Methods

Between January and December 2005, 582 patients had an elective operation in the day surgery unit of Pescina Hospital, University of L'Aquila. All of these patients were eligible and were informed about the study. Sixty agreed to participate, 30 men and 30 women of mean age 65 (range 25–85) years.

After they had given written informed consent, patients were randomized to one of three groups by the staff nurse using a list of randomized numbers. Each group had 20 patients (Fig. 1). Patients in group 1 listened to a compilation of relaxing new age music via headphones before and during surgery. Those in group 2 chose a music programme from four CD compilations (classical, country, pop or dance music) on the morning of admission for day surgery and listened to their choice via headphones before and during surgery. Patients in group 3 (controls) were subjected to the typical sounds of the operating theatre during day surgery. Patients in the music therapy groups listened to music from 1 h before surgery until the end of operation. Surgery was performed between 09.00 and 13.00 hours, and patients were discharged between 18.00 and 20.00 hours. No general anaesthetics or analgesics were administered during operation.

The preoperative anxiety level of all patients was evaluated on admission to hospital at 08.00 hours, using the Hamilton Anxiety Scale (normal score less than 18)²⁸. This rating scale consists of 14 items, each defined by a series of symptoms.

A sample of blood was collected by venepuncture immediately before, during and 3 h after surgery. Cortisol levels were measured by fluorescence polarization immunoassay (normal range 4·2–38·4 ng/dl). Lymphocyte counts were measured using the immunofluorescence multitest method and a FACSCalibur flow cytometer (Becton Dickinson, Franklin Lakes, New Jersey, USA). These included T lymphocytes (CD3) (normal range

690–2540 cells/μl), suppressor cells (CD8) (normal range 190–1140 cells/μl), helper cells (CD4) (normal range 410–1590 cells/μl), NK cells (CD6) (normal range 90–590 cells/μl) and B lymphocytes (CD19) (normal range 90–660 cells/μl). Blood pressure, heart rate and respiratory rate of all patients were recorded at the same times.

Postoperative pain was assessed by visual analogue scale and doses of analgesic required. All investigators were blinded to group assignments.

Statistical analysis

Statistical power analysis²⁹ was used to calculate that each group would need 20 patients in order to detect a true 5 ng/dl difference in mean cortisol between the highest and lowest group at the 0.005 level of significance with 90 per cent power if the standard deviation in each group was 4 ng/dl (from the experience of the Clinical Pathology Units regarding immunoassay of cortisol). Data were expressed as mean(s.d.) and analysed by two-factor repeated-measures ANOVA, with time and treatment as the two factors. Duncan's test was used for *post hoc* comparison. SAS® version 9.1 software (SAS Institute, Cary, North Carolina, USA) was used for the statistical analysis.

Results

The three groups were comparable with respect to sex, age, indication for and type of surgery, and type of anaesthesia (*Table 1*). The Hamilton test score was normal in all

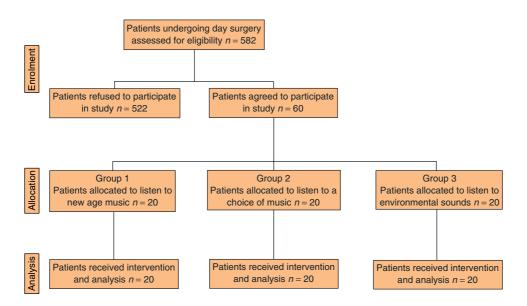


Fig. 1 Study flow chart

Table 1 Patient characteristics, anaesthetic and surgical factors

	music	Choice of	No music
Age (years)*	57(17)	54(15)	55(19)
Sex ratio (M:F)	10:10	9:11	11:9
Indication for surgery			
Orthopaedic disease	6	5	8
Inguinal hernia	5	5	4
Varicose vein	5	5	4
Proctological disease	4	5	4
Type of surgery			
Inguinal hernia repair with mesh and	5	5	4
plug			
Saphenous vein stripping	5	5	4
Lateral internal sphincterotomy	4	5	4
Incision transverse carpal ligament	3	3	4
Reduction of fractures and stabilization	3	2	4
Type of anaesthesia			
Local	17	16	18
Epidural	3	4	2
Duration of surgery (min)*	57(5)	60(4)	54(7)
	(-)	(-)	(.)

^{*}Values are mean(s.d.).

patients before the operation (mean(s.d.) score 7(3), 11(4) and 8(5) in groups 1-3 respectively).

Preoperative plasma levels of cortisol were within the normal range in all groups. The plasma level of cortisol showed a different profile over time in the three groups (Table 2). In patients who had new age music, cortisol levels decreased during operation and increased after surgery. In patients who chose the style of music they had, levels decreased progressively until discharge. In the patients with no music, levels increased during surgery and decreased thereafter. Two-factors repeated-measures ANOVA showed a significant effect of time (F = 6.42, P = 0.003) and a significant treatment-time interaction (F = 2.63, P = 0.040). Postoperative cortisol levels were significantly lower in patients who chose the music style than those listening to new age music (P < 0.050).

NK lymphocyte levels decreased during surgery in both groups who had music but increased in the group without music (Table 3). They decreased after surgery in the control group, but not in either of the music therapy groups. Two-factors repeated-measures ANOVA showed a significant effect of time (F = 8.00, P < 0.001) and a significant treatment-time interaction (F = 2.51, P =0.045). Intraoperative NK cell counts were significantly lower in those listening to new age music than those without (P < 0.050).

There were no significant differences between the three groups in levels of T, suppressor, helper or B lymphocytes,

Table 2 Music therapy and plasma levels of cortisol in 60 patients undergoing day surgery

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Cortisol levels (ng/dl)	Group 1 New age music (n = 20)	Group 2 Choice of music (n = 20)	Group 3 No music $(n = 20)$
Preoperative	15·51(2·58)	14·84(3·64)	14·73(4·39)
Intraoperative	12·59(4·24)	12·40(3·66)	15·80(6·25)
Postoperative	14·21(6·96)	8·63(2·72)*	12·08(6·96)

Values are mean(s.d.). Duncan's test after a two-factor repeated-measures ANOVA found an interaction between treatment and time. *P < 0.050versus group 1.

Table 3 Music therapy and plasma levels of natural killer lymphocytes in 60 patients undergoing day surgery

Natural killer lymphocyte levels (cells/μl)	Group 1 New age music (n = 20)	Group 2 Choice of music $(n = 20)$	Group 3 No music $(n = 20)$
Preoperative	259·6(151·0)	329·2(122·8)	311.6(166.8)
Intraoperative	212·2(89·3)*	238·6(107·6)	329.1(167.7)
Postoperative	214·3(65·9)	234·6(55·5)	239.1(141.5)

Values are mean(s.d.). Duncan's test after a two-factor repeated-measures ANOVA found an interaction between treatment and time. *P < 0.050versus controls.

or in blood pressure, heart rate or respiratory rate. Sex, age, type of operation and type of anaesthesia had no effect on plasma levels of cortisol or lymphocytes.

One patient each in groups 1 and 2 and two patients in group 3 reported postoperative pain, but there were no significant differences in pain scores or analgesic consumption.

Discussion

In this study, music played before and during day surgery reduced patients' stress response. Plasma levels of cortisol and NK lymphocytes, which increase during stress^{5,10,12-14,16}, were found to decrease during surgery in patients who listened to music. Music of a style selected by patients had a greater effect on cortisol levels, whereas only new age music had a significant effect on NK lymphocyte levels during surgery. The selected music appeared to be more effective overall, as it was associated with lower postoperative plasma levels of cortisol, but the difference in NK cell counts between the two music therapy protocols was not significant.

Other studies of the effect of music therapy in acute psychological stress¹⁶⁻¹⁸ and after operation²³ showed reduced levels of salivary or urinary cortisol after music therapy, similar to the present findings. On the other

hand, an investigation of the effect of drum music on the response of the immune system to non-surgical stress showed an increase in NK lymphocyte count³⁰.

The type of anaesthesia may affect plasma cortisol levels^{31,32}. Decreased levels of cortisol have been demonstrated during epidural anaesthesia³¹ and after administration of benzodiazepine³³ and analgesics³⁴. Local anaesthesia was used predominantly in the present study, and cortisol values were not related to the type of anaesthesia.

Anxiety before surgery may be another cause of decreased plasma cortisol levels³⁵, but all of the present patients had normal preoperative anxiety scores. Therefore the reduced levels of cortisol and NK lymphocytes in patients having day surgery while listening to music suggest that music therapy can reduce surgical stress.

The mechanism of this effect is unknown. However, nitric oxide may be the mediator chiefly responsible for reducing anxiety and stress in response to music therapy, probably as part of a complex interrelationship between emotion centres within the central nervous system³⁶; further studies are necessary to confirm this.

Music therapy did not significantly decrease postoperative pain in the present study, in contrast with previous findings^{19,24–27}. However, pain scores and postoperative analgesic requirements were low in all groups of patients in this study, even though half of the surgical procedures were orthopaedic or proctological, which are typically associated with considerable postoperative pain. The use of minimally invasive surgical techniques, the choice of anaesthesia (mainly local anaesthetic) and the nursing care within the day surgery unit may all have contributed to the low levels of postoperative pain.

Music therapy may improve patient care for day surgery. Allowing the patient to choose the music appears to have a larger positive effect.

References

- 1 Pierantognetti P, Covelli G, Vario M. [Anxiety, stress and preoperative surgical nursing.] *Prof Inferm* 2002; 55: 180–191.
- 2 Mitchell M. Patient anxiety and modern elective surgery: a literature review. *7 Clin Nurs* 2003; **12**: 806–815.
- 3 Grieve RJ. Day surgery preoperative anxiety reduction and coping strategies. Br J Nurs 2002; 11: 670–678.
- 4 Palese A, Burlon A, Rizzato M, Dritti P, Matuella D, Conte L. [The perception of anxiety and stress in day surgery: a comparison among patients, family members and nurses.] *Prof Inferm* 2004; **57**: 102–108.
- 5 Bourdarne N, Legros JJ, Timsit-Berthier M. [Study of the stress response: role of anxiety, cortisol and DHEAs.] *Encephale* 2002; 28: 139–146.

- 6 De Kloet ER. Hormones and the stressed brain. Ann NY Acad Sci 2004; 1018: 1–15.
- 7 Pickar D, Cohen MR, Dubois M. The relationship of plasma cortisol and beta-endorphin immunoreactivity to surgical stress and postoperative analgesic requirement. *Gen Hosp Psychiatry* 1983; **5**: 93–98.
- 8 Sari R, Sevinc A. The effects of laparoscopic cholecystectomy operation on C-reactive protein, hormones, and cytokines. *J Endocrinol Invest* 2004; **27**: 106–110.
- 9 Le Blanc-Louvry I, Coquerel A, Koning E, Maillot C, Ducrotte P. Operative stress response is reduced after laparoscopic compared to open cholecystectomy: the relationship with postoperative pain and ileus. *Dig Dis Sci* 2000; 45: 1703–1713.
- 10 Herbert TB, Cohen S, Marsland AL, Bachen EA, Rabin BS, Muldoon MF et al. Cardiovascular reactivity and the course of immune response to an acute psychological stressor. Psychosom Med 1994; 56: 337–344.
- 11 Steptoe A, Fieldman G, Evans O, Perry L. Cardiovascular risk and responsivity to mental stress; the influence of age, gender and risk factors. *J Cardiovasc Risk* 1996; **3**: 83–93.
- 12 Perna FM, Schneiderman N, LaPerriere A. Psychological stress, exercise and immunity. *Int J Sports Med* 1997; 18(Suppl 1): S78–S83.
- 13 Larson MR, Ader R, Moynihan JA. Heart rate, neuroendocrine and immunological reactivity in response to an acute laboratory stressor. *Psychosom Med* 2001; 63: 493-501.
- 14 Isowa T, Ohira H, Murashima S. Reactivity of immune, endocrine and cardiovascular parameters to active and passive acute stress. *Biol Psychol* 2004; 65: 101–120.
- 15 Smith JC, Joyce CA. Mozart versus new age music relaxation states, stress and ABC relaxation theory. J Music Ther 2004; 41: 215–224.
- 16 Miluk-Kolasa B, Obminski Z, Stupnicki R, Golec L. Effects of music treatment on salivary cortisol in patients exposed to pre-surgical stress. *Exp Clin Endocrinol* 1994; 102: 118–120.
- 17 Fukui H, Yamashita M. The effects of music and visual stress on testosterone and cortisol in men and women. *Neuro Endocrinol Lett* 2003; **24**: 173–180.
- 18 Khalfa S, Bella SD, Roy M, Peretz I, Lupien SJ. Effects of relaxing music on salivary cortisol level after psychological stress. *Ann N Y Acad Sci* 2003; 999: 374–376.
- 19 Augustin P, Hains AA. Effect of music on ambulatory surgery patients' preoperative anxiety. AORN J 1996; 63: 750: 753-758.
- 20 Wang SM, Kulkarni L, Dolev J, Kain ZN. Music and preoperative anxiety: a randomized, controlled study. *Anesth Analg* 2002; **94**: 1489–1494.
- 21 Mok E, Wong KY. Effects of music on patient anxiety. *AORN J* 2003; 77: 396–397, 401–406, 409–410.
- 22 Cooke M, Chaboyer W, Schluter P, Hiratos M. The effect of music on preoperative anxiety in day surgery. J Adv Nurs 2005; 52: 47-55.
- 23 Nilsson U, Unosson M, Rawal N. Stress reduction and analgesia in patients exposed to calming music

- postoperatively: a randomized controlled trial. *Eur J Anaesthesiol* 2005; **22**: 96–102.
- 24 Good M, Stanton-Hicks M, Grass JA, Cranston Anderson G, Choi C, Schoolmeesters LJ et al. Relief of postoperative pain with jaw relaxation, music and their combination. Pain 1999; 81: 163–172.
- 25 Renzi C, Peticca L, Pescatori M. The use of relaxation techniques in the perioperative management of proctological patients: preliminary results. *Int J Colorectal Dis* 2000; 15: 313-316.
- 26 Nilsson U, Rawal N, Unosson M. A comparison of intra-operative or postoperative exposure to music: a controlled trial of the effects on postoperative pain. *Anaesthesia* 2003; 58: 699–703.
- 27 Voss JA, Good M, Yates B, Baun MM, Thompson A, Hertzog M. Sedative music anxiety and pain during chair rest after open-heart surgery. *Pain* 2004 112:; 197–203.
- 28 Hamilton M. The assessment of anxiety states by rating. Br J Med Psychol 1959; **146**: 917–919.
- 29 Cohen J. Statistical Power Analysis for the Social Sciences (revedn). Academic Press: New York, 1977.
- 30 Bittman BB, Berk LS, Felten DL, Westengard J, Simonton OC, Pappas J *et al.* Composite effects of group drumming music therapy on modulation of

- neuroendocrine-immune parameters in normal subjects. *Altern Ther Health Med* 2001; 7: 38–47.
- 31 Kasachenko VM, Briskin BS, Evstifeeva OV, Savchenko ZI. [The impact of the type of anaesthesia on stress-realizing and stress-limiting mechanisms of the immune system in gerontological patients at abdominal surgeries.] *Eksp Klein Gastroenterol* 2004; **105**: 58–61, 105.
- 32 Ram E, Vishne TH, Weinstein T, Beilin B, Dreznik Z. General anaesthesia for surgery influences melatonin and cortisol levels. *World J Surg* 2005; **29**: 826–829.
- 33 Duggan M, Dowd N, O'Mara D, Harmon D, Tormey W, Cunningham AJ. Benzodiazepine premedication may attenuate the stress response in day case anesthesia: a pilot study. Can 7 Anesth 2002; 49: 932–935.
- 34 Wang ZY, Wang CQ, Yang JJ, Sun J, Huang YH, Tang QF *et al.* Which has the least immunity depression during postoperative analgesia morphine, tramandol, or tramandol with lornoxicam? *Clin Chim Acta* 2006; **369**: 40–45.
- 35 Pearson S, Maddern GJ, Fitridge R. The role of preoperative state-anxiety in the determination of intra-operative neuroendocrine responses and recovery. Br J Health Psychol 2005; 10: 299–310.
- 36 Salamoi E, Kim M, Beaulieu J, Stefano GB. Sound therapy induced relaxation: down regulating stress processes and pathologies. *Med Sci Monit* 2003; **9**: RA96–RA101.

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