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**Post-operative pain management through music-induced analgesia: Investigating musical constructs**

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Keyword:	pain, analgesia, distraction, relaxation, harmony, rhythm, cortisol
Abstract:	<p>Distraction and attention-diversion approaches are widely integrated into pain management. Music-induced analgesia, the ability of music to reduce pain perception, is a clinically-relevant approach for managing pain, anxiety and psychological well-being. Research categorises audio-analgesic interventions as homogenous, however enquiry is required to identify which musical constructs may be therapeutically effective. This study investigated the impact of harmony and rhythm on acute, post-operative pain in a sample of 98 patients scheduled for knee surgery. Four music listening groups were compared against controls using silent relaxation. After surgery using standardised anaesthesia, participants undertook a 15-minute intervention per day of in-patient stay. Measures of pain intensity, pain interference, salivary cortisol concentration and mood were obtained. All participants showed reductions in pain from pre- to post-test, indicating silent relaxation was as effective as music listening. Salivary cortisol concentrations showed that music with high harmonicity/rhythmicity reduced cortisol concentration to a greater extent on Day 1 than music with low harmonicity/rhythmicity. These findings validate the homogenous use of auditory distraction for audio-analgesia, and importantly emphasise the core role of compositional musical constructs in maximising early post-operative recovery. Results support the need for additional psychobiological research examining the efficacy of audio-analgesic attention-diversion interventions used in pain management.</p>

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## Post-operative pain management through audio-analgesia: Investigating musical constructs

Distraction, used for pain management, has become a standardised component of integrated pain management interventions and research (Cepeda, Carr, Lau, & Alvarez, 2006; Eccleston & Crombez, 1999; Eccleston, 2001). In the context of Gate Control Theory and the subsequent Neuromatrix Theory, pain theory asserts that effective distraction can be integral to the redistribution of attentional resources, resulting in pain modulation (Melzack & Wall, 1965; Melzack, 2001). Limited capacity models of attention (Shiffrin & Schneider, 1977) posit that attention is a finite cognitive resource and that the processing of pain signals can be mediated by attentional redirection away from pain and towards absorptive tasks/stimuli (Eccleston, 1994, 1995). Distribution of attentional resources can become flawed when the required task activity exceeds available attentional capacity (Baddeley, 1986; Shiffrin & Schneider, 1977). Hence pain perception can be minimised if the distractor's attentional demands are of sufficient magnitude.

Due to the affective nature of pain, attention-diversion interventions which are emotionally resonant and multi-sensory are salient and effective in engaging attentional resources (Good et al., 2001; MacDonald et al., 2003; McCaul & Malott, 1984). Previous research has considered the use of humour (Mitchell, MacDonald, & Brodie, 2006; Weisenberg, Tepper, & Schwarzwald, 1995; Zweyer, Velker, & Ruch, 2004), relaxation (Cepeda et al., 2006; Evans, 2002a, 2002b; Good et al., 2001, 2008; Good, Anderson, Ahn, Cong, & Stanton-Hicks, 2005; Good, Anderson, Stanton-Hicks, & Makii, 2002), mathematics (Burns, 2006; Mitchell et al., 2006), art (Mitchell, MacDonald, & Knussen, 2008), virtual reality (Chan, Chung, Wong, Lien, & Yang, 2007; Hoffman et al., 2004; Wiederhold & Wiederhold, 2007),

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5 video games (Wright & Raudenbush, 2010) and music (Good, 1996; Hekmat & Hertel, 2003;  
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7 McCaffrey & Good, 2000, 2000; McCaul & Malott, 1984), collectively demonstrating that  
8  
9 pain can be modulated through attention-diversion. Research suggests that music may be  
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11 privileged in a clinical context through its innate emotional resonance, ease of use, universal  
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13 availability, familiarity, non-invasive nature and ease of administration (Lim & Locsin, 2006;  
14  
15 MacDonald et al., 2003; McCaul & Malott, 1984). Music-induced analgesia, the ability of  
16  
17 music to attenuate pain perception (MacDonald et al., 2003) is consequently at the forefront  
18  
19 of clinical attention-diversion research and has been demonstrated intra-operatively (Nilsson,  
20  
21 Rawal, Unestahl, Zetterberg, & Unosson, 2001), post-operatively (Good et al., 2005; Nilsson,  
22  
23 Rawal, & Unosson, 2003) in laboratory-induced (Hekmat & Hertel, 2003; Mitchell et al.,  
24  
25 2006), acute and chronic pain (McCaffrey & Freeman, 2003; Mitchell, MacDonald, Knussen,  
26  
27 & Serpell, 2007; Zimmerman, Pozehl, Duncan, & Schmitz, 1989).

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32 To date, the efficacy of music in pain management is equivocal; studies have demonstrated  
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34 clinically significant reductions in pain intensity (Good et al., 1999; Heiser, Chiles, Fudge, &  
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36 Gray, 1997; Hekmat & Hertel, 2003; Koch, Kain, Ayoub, & Rosenbaum, 1998), however  
37  
38 others found that music reduces anxiety and improves psychological well-being (Cadigan et  
39  
40 al., 2001; MacDonald et al., 2003). If audio-analgesic attention-diversion interventions are to  
41  
42 be explored and developed further, research is needed to address basic issues regarding the  
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44 intervention. Firstly, what constructs within the sound-source are therapeutically active?  
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46 Music is, in nature, heterogeneous, therefore there may be audio components which  
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48 precipitate greater (or lesser) pain modulation. Research has shown that preference impacts  
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50 upon analgesia, with self-selected music (preferred) or selection from a pre-prepared array  
51  
52 (quasi-preferred), demonstrating greater pain and anxiety reduction than experimenter-  
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54 selected music (non-preferred) (Hekmat & Hertel, 2003; Mitchell et al., 2006). However,  
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5 there has been no research which differentiates constructs *within* music that initiate music-  
6 induced analgesia. Secondly, music-induced analgesia has predominantly been assessed  
7 through self-report and minimal research has considered whether this is modelled  
8  
9 physiologically. Salivary cortisol, a biological marker of stress and anxiety is a potentially  
10 important indicator of psychobiological change following music-induced analgesia and  
11 attention-diversion. Music has been shown to halt cortisol elevation after psychological and  
12 pre-procedural stress (Khalfa, Dalla Bella, Roy, Peretz, & Lupien, 2003; Miluk-Kolasa,  
13 Obminski, Stupnicki, & Golec, 1994). Research has not considered the effect of music  
14 listening on cortisol as a marker of post-operative recovery.  
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26 The purpose of this research was to begin to address the questions raised by the current  
27 heterogenous results in music-induced analgesia research. This study aimed to clarify the  
28 nature of music-induced analgesia in post-operative pain management following total knee  
29 arthroplasty (full knee replacement surgery). Musical stimuli were manipulated in terms of  
30 compositional constructs and standardised pain self-reporting was supplemented by  
31 assessment of cortisol concentrations.  
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## 39 40 **Method**

### 41 42 *Participants*

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45 Patients scheduled for primary total knee arthroplasty (primary knee replacement surgery) in  
46 the Orthopaedics Department, Royal Infirmary of Edinburgh, Scotland, were approached  
47 regarding participation in the trial. Knee surgery was chosen due to the uniquely high levels  
48 of pain experienced by patients in their in-patient post-operative recovery days following and  
49 as a result of the early physiotherapy rehabilitation needed to ensure successful function of  
50 the prosthesis (Brander et al., 2003).  
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5 Participants willing to take part provided written informed consent. Trial recruitment took  
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7 place over 18 months. 122 eligible subjects were identified and 98 recruited. Randomisation  
8  
9 was according to a computer-generated pseudo-random numerical stratified schedule.

10  
11 Patients who could participate in questionnaire-based pain assessment and provide salivary  
12  
13 cortisol samples were invited to take part. Exclusion criteria included: contraindication to  
14  
15 central neural blockades, history of allergy to local anaesthetics, non-osteoarthritic chronic  
16  
17 pain or major hearing deficits (see Figure 1).  
18  
19

20  
21 Insert Figure 1 here: CONSORT Diagram  
22

### 23 24 *Design*

25  
26  
27 Patients who attained the entry criteria were randomly assigned to one of five experimental  
28  
29 groups: silent control or four possible types of music listening, using the experimental  
30  
31 constructs of Harmonicity and Rhythmicity (see Table 1; following Finlay, 2009; Krumhansl,  
32  
33 2000; Parncutt, 1989). Harmonicity is a global concept reflecting the consonance of music  
34  
35 through the harmonic series (high + or low -). Rhythmicity is the maintenance of metrical  
36  
37 (beat) regularity (high + or low -). All clinical staff and participants were blinded to  
38  
39 allocation. The correct CD was provided by the chief investigator who was, therefore, not  
40  
41 blinded. Recruiting and post-operative assessment was carried out by the chief investigator  
42  
43 and trained research nurses.  
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48 All patients undertook a pre-operative assessment at pre-admissions two weeks before  
49  
50 attendance for surgery. On each day post-surgery all assessment measures were completed  
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52 (Days 1-3). Patient controlled analgesia usage was monitored pre-intervention in the  
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54 immediate 24 hours post-operatively (Day 0).  
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### 57 58 *Music listening intervention*

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5 *Musical examples.* A battery of musical examples was created (see Appendix 1). All  
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7 examples were 12–15 minutes in length. 12–15 minutes was deemed appropriate as short-  
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9 term bursts of music listening have been proven effective in an acute pain setting (Lee,  
10  
11 Chung, Chan, & Chan, 2005; McCaffrey & Good, 2000). This time period of listening was  
12  
13 selected through interaction with nurses, doctors and consultants who considered it  
14  
15 appropriate for demonstrating the efficacy of the treatment, yet minimising intrusion into  
16  
17 clinical care and the daily activity that is required to successfully and efficiently operate an  
18  
19 orthopaedic ward.  
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23 Extracts were selected through a pilot study in which musically trained listeners and  
24  
25 musically untrained listeners were asked to rate 32 tracks for harmonicity and rhythmicity.  
26  
27 Tracks used for rating were across classical, jazz, popular, folk and ethnic music genres to  
28  
29 encompass all musical tastes. Extracts with the highest (or lowest) ratings by all participants,  
30  
31 as appropriate to grouping, were included in the final selection for use in this study (see  
32  
33 Finlay, 2009). Extracts were recorded at a sample rate of 16bits and 44.1kHz. Where multiple  
34  
35 tracks were used to create a combined length, Pro Tools LE 6.9.2 was used to merge between  
36  
37 individual extracts. All musical extracts were commercially available, did not include lyrics  
38  
39 and represented a wide range of possible genres. All record companies and copyright holders  
40  
41 were contacted and permission to use the music was granted.  
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46 *Audio equipment.* Bose QuietComfort Acoustic Noise Cancelling® headphones that utilise  
47  
48 full-spectrum noise reduction were used with a Bose portable CD-walkman. The inclusion of  
49  
50 headphones for research into music and pain has been recommended by Carroll and Seers  
51  
52 (1998) and Nilsson et al. (2001) in order to reduce environmental noise.  
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*Silent Intervention.* Around-ear noise cancelling headphones were used to provide a barrier to external sound and to minimise intrusive hospital sound as far as possible.

#### *Pain assessment*

This consisted of four structured questionnaires:

*Visual Rating Scale (VRS) and Numerical Rating Scale (NRS).* Two 11-point subjective assessments of pain intensity were completed for pain at rest (supine on the hospital bed) and on movement (controlled bending of the knee through its full range of motion, see Rakel et al, 2012), using the end-points '0 = no pain' and '10 = pain as bad as you can imagine'.

Results were averaged across both ratings types (NRS and VRS), allowing for inter-correlation and reliability checks between measures (Anderson, 2005).

*Short-Form McGill Pain Questionnaire (SFMPQ; Melzack, 1983).* The primary outcome measure was expressed as Total Pain Score (TPS) and secondary outcome measures as sensory and affective pain.

*Brief Pain Inventory (BPI Short-form; Cleeland, 1992).* Results were expressed as a single Mean Pain Interference score.

*Profile of Mood States (Profile of Mood States; McNair, Lorr, & Droppleman, 1971).* Results were expressed across mood states as a composite Total Mood Disturbance (TMD) score.

#### *Cortisol assessment*

Salivary cortisol samples were provided using the passive drool method (Gallagher, Leitch, Massey, McAllister-Williams, & Young, 2006). Samples were analysed for Salivary Cortisol Concentration at time of testing in nmol/l. All saliva samples were frozen immediately on collection and were stored at -20°C. Analysis of spun samples was performed using

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Salimetrics ER Cortisol EIA Kits (Salimetrics, 2006). Cortisol concentration was calculated using an MRX plate reader (Dynex, US).

### *Peri-operative management*

The peri-operative period was from arrival on the ward for surgery until 24 hours afterwards. Previously prescribed analgesics were continued until the day of surgery. Anaesthesia consisted of a spinal anaesthetic with single shot femoral and sciatic nerve blocks. All anaesthesia followed a standardised anaesthetic regimen and therefore was comparable between patients.

Post-operative analgesia was provided using morphine Patient Controlled Analgesic device (PCA; 1mg bolus; 5 minute lockout) overnight on Day 0, and PCA usage was monitored. Post-operative medication and anti-emetics were given as required in accordance with the standardised regimen.

### *Procedure*

*Recruitment and Pre-operative Assessment.* Patients who were scheduled for primary total knee arthroplasty were identified from the hospital waiting lists. Participants eligible for the study were approached by letter approximately two weeks before their attendance at their Pre-admissions Clinic (PAC).

On PAC arrival, all participants were invited to participate in the study and, to maintain blinding, were told that the research was an investigation into relaxation interventions used during post-operative recovery. If participants wished to continue, informed consent was taken alongside a preliminary assessment, providing baselines for all outcome measures. Subjects were randomised into groups and given the opportunity to (a) listen to one minute



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musical excerpts from the sample CD appropriate to their grouping and to select a track or (b) test the noise-reducing headphones. All participants were informed that they would receive standard care in addition to the relaxation intervention. All patients were requested to refrain from listening to their own music post-operatively and were advised that they could withdraw from the study at any time.

*Post-operative assessment.* Participants were visited daily at the same time each day and completed the VRS/NRS, SF-MPQ and salivary cortisol sample pre- and post-test. In the interim period, the study apparatus was then set up and music/silence initiated, using headphones attached to a personal CD player. During the 15 minute intervention, participants were asked either sit or lie down, to refrain from any other activity during the intervention session. Curtains were drawn around the hospital bed, visitors were asked to refrain from arriving during the relaxation session and the experimenter left the room to minimise the Hawthorne Effect . The experimenter did not discuss the relaxation with participants before or after the intervention, except as necessary to set up the apparatus. On Days 1 and 3 patients additionally completed the POMS and BPI.

*Ethics.* The study was approved by NHS Ethics (06/S1101/5) and on-site permissions were granted by the Royal Infirmary of Edinburgh Research and Development Office (2006/R/AN/06). Research was in accordance with the Helsinki Declaration of 1975 (revised 1983).

#### *Statistics: design and analysis*

This study was designed as a exploratory prospective single blind randomised trial. The primary outcome measure was pain self-report using the VRS/NRS. Secondary outcome

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measures were Total Pain Score, Mean Pain Interference, Total Mood Disturbance, Cortisol and the sub-scales of the SF-MPQ representing sensory and affective pain. There were no comparable or similar previous randomised controlled trials investigating the effects of musical constructs on post-operative pain. Initial sample size was therefore targeted at 20 per group for this project following (Cohen, 1992). Statistical analysis was carried out using SPSS v.18.

Data from the primary outcome variables was assessed using the Kolmogorov-Smirnov test and Mauchly's test of sphericity. Results were not significant, therefore data was normally distributed and sphericity assumed. Parametric statistical tests are used throughout, with means (standard deviations) presented. Internal consistency was high for all outcome measures (BPI,  $\alpha=0.79$ ; SF-MPQ,  $\alpha=0.82$ ; POMS,  $\alpha=0.78$  [55–58]. A minimum alpha level of 0.05 was used for all analyses.

One-way between-group ANOVAs (Group Allocation, 5 levels; control, 4 music types) were computed for the primary outcome measures on all days of testing. Repeated-measures ANOVAs with Bonferroni post-hoc adjustments were computed to determine the impact of Group on Day of Testing (3 levels; post-operative days 1-3) and Time of Testing (2 levels; pre- and post-test). Chi-squared analyses were used to compare proportions. All completed days of testing were used in analysis.

## Results

### *Recruitment characteristics*

Of 122 patients approached, 98 consented to take part (80.33%) and 24 did not consent. 89 participants completed the full study and 9 participants completed one or more days of testing (see Fig. 1). Approximately 20 subjects were randomly allocated to each group. 9 participants

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5 withdrew post-randomisation but consented for their complete days of data to be used in  
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7 analysis.

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10 Of the 98 participants who gave informed consent, 40 were male and 58 were female. Age  
11 and arthritic chronicity are reported in Table 2. Men and women were comparable in age at  
12 time of surgery (Males  $M=68$  years,  $SD=7.96$ ; Females  $M=68.12$ ,  $SD=8.14$ ). All participants  
13 suffered from arthritic pain and radiographic arthritis.  
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### 18 19 20 *Group distribution*

21  
22 A Pearson's chi-square test and a series of one-way ANOVAs were computed to investigate  
23 Group Distribution. There was no significant difference between groups in previous  
24 experience of arthroplasty surgery ( $\chi^2=2.190$ ,  $df=4$ ,  $p=.71$ ). Similarly, there was no  
25 significant difference between Groups in Years of pain and the Age of patients. Groups were  
26 therefore comparable in their demographics and surgical histories. Analysis of baseline pain  
27 and mood scores and cortisol concentration showed no difference between groups (see Table  
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Insert Table 2: Demographics and Baseline Pre-admission Scores

### 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 *Musical background*

67.9% ( $n=53$ ) of all experimental group participants did not consider themselves to play a  
musical instrument, though 32.1% ( $n=25$ ) had played a musical instrument in their lifetime.  
The most popular musical instrument to play was the piano (17.9%,  $n=14$ ), followed by voice  
(5.1%,  $n=4$ ). Three participants (3.8%) played folk instruments: two choosing the bagpipes  
and one playing the accordion. A further five participants had some instrumental experience;  
two participants played woodwind instruments (2.6%,  $n=2$ ), two played percussion and drum

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5 kit (2.6%,  $n=2$ ) and one played the guitar (1.3%,  $n=1$ ). 32% ( $n=8$ ) of participants who played  
6  
7 a musical instrument had done so for approximately 5–10 years and 24% ( $n=6$ ) had played  
8  
9 for over 10 years. However, only three participants still played their musical instrument  
10  
11 (12%,  $n=3$ ). Of the 25 participants who played a musical instrument, 23 (92%) had  
12  
13 undertaken a minimum of 6 months of Formal Instrumental Musical Tuition (FIMT) on their  
14  
15 chosen instrument. The majority of formally tutored participants had taken instrumental  
16  
17 lessons for between 5 and 10 years (43.5%,  $n=10$ ).  
18  
19

20  
21 Univariate between-subjects ANOVAs were conducted to investigate the impact of musical  
22  
23 experience through Group Allocation. There was no significant effect of length of time  
24  
25 (years) spent playing a musical instrument or of amount of Formal Instrumental Musical  
26  
27 Tuition (years). This indicates that the experimental groups were equally matched in their  
28  
29 distribution of formally trained musicians or participants who had played musical instruments  
30  
31 in the past.  
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#### 34 35 *PCA usage*

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38 Two one-way ANOVAs were computed on the amount of morphine-administered by patients  
39  
40 on Days 0 and Day 1 post-operatively. There was no difference between groups in the  
41  
42 amount of morphine used in the PCA on Days 0 or 1. Groups were therefore comparable in  
43  
44 the rescue analgesic they used post-surgery and pre-intervention. Mean PCA usage on Day 0  
45  
46 was 15.67 (SD=14.40, median=14) and on Day 1 was 23.62 (SD=21.03, median=18).  
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49  
50 Significance levels are shown in Table 2.3.5.

#### 51 52 *Gender differences*

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5 Repeated measures ANOVAs were used to assess the impact of gender on primary and  
6  
7 secondary outcome measures. No gender differences were found, indicating that males and  
8  
9 females were comparable in all outcome measures.  
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### 11 12 *Primary outcome measures*

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14  
15 Insert Table 3: Significance, percentage change and pre- and post-test VRS/NRS scores at  
16  
17 rest and on movement (Mean±Standard Deviation)  
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19  
20 *VRS/NRS scores: rest and movement.* As expected, pain on movement was higher and more  
21  
22 painful than pain at rest ( $p<.0001$ ), with pain scores on Movement rated as higher and more  
23  
24 painful those at rest. All VRS/NRS pre-test scores were higher than post-test scores  
25  
26 ( $p<.0001$ ), with a reduction in pain scores across the days of testing ( $p<.0001$ ). Daily  
27  
28 significance levels and descriptive statistics are shown in Table 3. There was no significant  
29  
30 main effect of group, indicating that pain was not differentially influenced by the type of  
31  
32 musical distractor or by the silent relaxation used during the intervention period.  
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### 36 37 *Secondary Outcome Measures*

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40 *Short-Form McGill Pain Questionnaire: total pain score.* Total pain scores improved over  
41  
42 the course of the study, with the highest scores on Day 1 and a gradual improvement through  
43  
44 to Day 3 ( $p<.0001$ ; see Figure 2). A series of Bonferroni post-hoc comparisons showed that  
45  
46 Days 1 and 2 were significantly different from Day 3 ( $p<.0001$  and  $p=.0304$  respectively), but  
47  
48 not from each other. Pre-test scores were significantly higher than post-test scores ( $p<.0001$ ),  
49  
50 but again, as there was no impact of group, the type of distractor did not affect total pain  
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52 scores.  
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56 Insert Figure 2 Here  
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5 *Short-Form McGill Pain Questionnaire: sensory and affective pain.* Both the Sensory and  
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7 Affective Dimensions of Pain displayed pre- to post-test reductions in pain scores (both  
8  
9  $p < .0001$ ). For Sensory pain, the magnitude of this reduction was 31% and for Affective pain  
10  
11 it was 38%. Pain scores across the course of the study showed the same pattern across Days  
12  
13 of Testing ( $p < .0001$ ) as in previous outcome measures, with Pain at Day 1 highest, with  
14  
15 significant differences between early days of testing for Sensory pain (Day 1 to Day 2  
16  
17  $p = .025$ ; Day 1 to Day 3  $p < .0001$ ; Day 2 to Day 3 not significant) and later days for Affective  
18  
19 Pain (Day 1 to Day 2 not significant; Day 1 to Day 3  $p < .0001$ ; Day 2 to Day 3  $p = .022$ ).  
20  
21 Neither dimension showed a significant main effect of Group and there were no further main  
22  
23 effects or interactions.  
24  
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27  
28 *Brief Pain Inventory: mean pain interference.* The pattern of results differed in terms of  
29  
30 Mean Pain Interference. Results showed, as before, a significant difference in Days of  
31  
32 Testing, with Day 1 higher than Day 3 ( $p = .0012$ ). However, there was a main effect of Group  
33  
34 ( $p = .021$ ) and two-way interaction between Group and Day of Testing ( $p = .026$ ), suggesting  
35  
36 that the groups did not respond similarly from day-to-day in their MPI scores (see Figure 3  
37  
38 and Table 4). Where the -- and control groups showed a progressive reduction across the  
39  
40 three Days of Testing, the ++, +- and -+ groups showed a rise from the PAC to Day 1 and  
41  
42 decline on Day 3.  
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47 Insert Figure 3 and Table 4 here  
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50 *Profile of Mood States: total mood disturbance.* Day of Testing was significant, with an  
51  
52 improvement in mood disturbance levels as the study progressed ( $p < .0001$ ). Bonferroni post-  
53  
54 hoc comparisons revealed that the difference between the days was significant at all points:  
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56 scores at the PAC were significantly different from Day 1 ( $p < .0001$ ), and Day 3 ( $p = .037$ ) and  
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Day 1 was significantly different from Day 3 ( $p=.012$ ). There was no effect of type of intervention (group) on mood disturbance.

*Cortisol.* Sixty-two participants (63.27%) agreed to provide cortisol samples in their post-operative recovery phase. The remainder of participants chose not to give saliva samples due to: inability to master technique/dry mouth (10.20%), feelings of nausea (8.16%), dislike of spitting (4.08%) or personal choice (13.27%).

Change scores for pre- to post-test cortisol concentrations were computed by subtracting the post-test scores from the pre-test scores for each Day of Testing. Group differences were displayed on Day 1, showing that the type of intervention used impacted upon levels of post-test salivary cortisol ( $p=.021$ ). A series of Bonferroni post-hoc tests comparisons revealed that the ++ group showed a significantly greater reduction from pre- to post-test scores in comparison with the -- group, whose cortisol concentrations rose after the music listening intervention ( $p=.019$ ). Similarly to the other outcome measures, cortisol concentrations reduced across the Days of Testing ( $p=.009$ ), with the highest concentrations demonstrated on Day 1. The three-way interaction between Day of Testing, Time of Testing and Group was significant ( $p=.003$ ). Post-hoc tests revealed that the ++ Group was significantly different from the -- Group on Day 1, but that the groups responded similarly on post-operative days 2 and 3. Descriptive statistics are displayed in Table 5 and Figure 4.

Insert Figure 4 here.

## Discussion

This study aimed to identify the therapeutically active properties found within audio attention-diversion for post-operative pain management. Salivary cortisol concentrations were elevated in the immediate post-operative period following the surgical stressor, and

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again reduced by discharge. Pre- to post-test analysis indicated that there were no significant overall reductions in post-test scores, suggesting that the auditory interventions were not successful in reducing endogenous cortisol concentrations in the course of the 15 minute relaxation period. However, post-hoc comparisons on Day 1 demonstrated that pre- to post-test change was significant and greatest in the ++ group and least in the -- group, indicating that the positive/negative combination of both harmonicity and rhythmicity had the greatest impact on the stress response, with harmonic and regular sound minimising cortisol production to the greatest extent. By contrast, music which was low in harmonicity and without rhythmic regularity served to increase cortisol concentrations. The between-groups variability in cortisol concentrations was most strongly evident on the first day post-operatively, implicating the first 24-hours post-operatively as the critical window for audio-analgesic benefit. It also problematises reliance on 'New Age' or 'sedative' (commonly --) music (Phumdoung & Good, 2003; Voss et al., 2004) for relaxation and suggests that ++ music (comparable to the 'pop music' genre) is of greater positive psychobiological impact. Research has demonstrated that fast-paced music elicits greater skin conductance responding than slow-paced music, suggesting that rhythmicity has a potentially activational effect, potentially regulating physiological responses (Carpentier & Potter, 2007). Though there is conflicting evidence, suggesting that pain ratings increase for faster tempi (Kenntner-Mabiala, Gorges, Alpers, Lehmann, & Pauli, 2007). Future research could integrate additional physiological measures and preferred/non-preferred musical preference groupings for greater clarity.

Beyond initial inter-group differences, cortisol concentrations were resistant to pre-test post-test change. The combination of these two findings seem conflicted: between-group divergences suggest music does differentially impact upon cortisol but the lack of post-test



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5 change indicates no response. No change is in confirmation of the post-operative pain  
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7 research by Good (2008), but conflicts with pre-procedural or laboratory-induced stress  
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9 research which showed that music did reduce cortisol concentrations in those contexts  
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11 (Khalifa et al., 2003; Miluk-Kolasa et al., 1994). Additionally, it has been shown that  
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13 cognitive-coping strategies could be used to reduce stress and lower cortisol (Hammerfald et  
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15 al., 2006). Current results may be explained by recognising that Total Knee Arthroplasty  
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17 presents a significantly greater clinical stressor than pre-surgical stress, with a more  
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19 pronounced impact on Hypothalamic-Pituitary-Adrenal (HPA) axis activity. The potential of  
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21 relaxation interventions to reduce low-level stress should not be generalised to all possible  
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23 forms of stress, particularly high-level clinical stressors.  
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28 Following surgery, pain was highest on Days 1 and 2 and diminished by Day 3. Magnitude of  
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30 post-test change in the affective pain dimension was greater than that of the sensory  
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32 dimension, suggesting that the interventions had a consistent and significant affective  
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34 psychological impact. The results of this study highlight the importance of affective pain  
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36 management and by extension, recent research has argued that audio-analgesia is dependent  
37  
38 on personal preference (MacDonald et al., 2003; Mitchell et al., 2008, 2007). The current  
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40 research did exploit preference as participants chose a preferred track from a group-  
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42 appropriate selection, but the positive effects of this could be maximised by recommending  
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44 the use of music from participants' personal collections. In this study, participants allocated  
45  
46 to the music groups were given the opportunity to select their chosen musical extract from a  
47  
48 battery of options – essentially employing a quasi-preferred selection method (Finlay, 2009).  
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50 However, the silent control group were given no choice in their use of a non-musical  
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52 relaxation intervention (Finlay & Rogers, 2014). Mitchell & MacDonald (2006) argued for  
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54 the importance of choice in enhancing self-efficacy and perceived control in audio-analgesia,  
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5 therefore it is possible that it is the variation between intervention preference levels may have  
6 influenced results. Further research should look at preferred v. quasi-preferred relaxation in  
7 order to determine whether self-selecting all interventions would further enhance results.  
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12 Pain-limited functional interference was minimised as the study progressed. By discharge,  
13 pain interference levels were below that of pre-admissions, validating the choice to proceed  
14 with the elective surgical intervention. There was some variability in between-group changes  
15 over time, with + +, + - and - + groups showing peaks in functional difficulties on Day 1,  
16 whereas the silent control and - - group demonstrated progressive, gradual reduction in pain  
17 interference. Interference was monitored at pre-test only, therefore the discrepancies between  
18 groups in their improvement in functional ability likely reflects slight differentiations in the  
19 way in which patients responded to their study and the degree of proprioceptive inhibition  
20 that occurred immediately following surgery. It is not in response to group allocation as there  
21 was no between-group main effect. The interventions/placebo responding may have served to  
22 optimise pain control, which is a primary factor in the speed at which patients return to  
23 normal function, earlier mobilisation and proficient ambulation (Lingard, Katz, Wright, &  
24 Sledge, 2004).  
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42 This preliminary research found no significant difference between music listening groups or  
43 silent control in pre- to post-test pain reduction. All groups showed lower post-test scores  
44 across every measure and dimension of pain assessment. Manipulation of the musical  
45 constructs of harmonic/rhythmicity did not differentially affect analgesic responses. Quiet  
46 (silent) relaxation was as effective as music listening in reducing post-operative pain. This  
47 suggests that constructs *within* an auditory intervention may not alter pain scores. The  
48 findings validate the inclusion of auditory distraction for post-operative pain management,  
49 but broadly do not distinguish between or prioritise any single characteristic of auditory  
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5 distraction above another (e.g. harmonicity, rhythmicity, music or silence). This suggests that  
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7 auditory distraction may be a flexible and homogenous intervention in a clinical context,  
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9 providing an opportunity for patients to self-select their attention-diversion strategy. It also  
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11 demonstrates that there is a need to separate and clearly specify differences between ‘music-  
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13 induced analgesia’ and the generic term ‘audio-analgesia’ that is regularly used to refer to  
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15 music-specific interventions (see Mitchell et al, 2006).  
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19 Results demonstrate a short-term reduction in pain states as a result of the interventions,  
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21 potentially explicable as placebo analgesia. The placebo effect is a stable and documented  
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23 psychobiological phenomenon, whereby “the placebo response is the reduction in a symptom  
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25 as a result of factors relating to a subject’s/patient’s perception of the therapeutic  
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27 intervention” (Vase et al., 2002, p.451). A placebo effect is generally considered to be  
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29 evident in clinical research if there is no differentiation between the control and experimental  
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31 groups (Vase et al., 2002). The phenomenon of placebo analgesia is a robust and validated  
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33 concept and it may play a role in the results of this study, as would be expected in any clinical  
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35 research. However, measures were taken to minimise the impact of placebo through  
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37 controlling the musical extracts chosen, refraining from discussion of the interventions until  
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39 the study conclusion and by blind randomisation of participants.  
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44 It is possible, to argue for an alternative and secondary explanation beyond the placebo effect.  
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46 Noise-reducing headphones were used for the silent control group in order to maintain  
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48 blinding and as a consequence, the audio interventions were therefore compared with a  
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50 baseline treatment as opposed to a (commonly used, unblinded) ‘no treatment’, standard care  
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52 group. Lee et al (2005) found that participants allocated to a headphone control group  
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54 reported that headphones eliminated anxiety occurring due to background noise in the ICU,  
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56 also reducing pain. It is likely therefore that the headphones facilitated separation from  
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external noise, promoted privacy, heightened internal locus of control and reduced noise-related mental fatigue for all participants, regardless of grouping (Evans, 2002b; MacDonald et al., 2003; McCaffrey & Locsin, 2002). This is evidenced in the magnitude of pain score reductions across all groups. The noise-reducing headphones used in this research were therefore an active intervention for all participants, inclusive of controls, which may potentially have minimised between-group comparisons. Future research could integrate dual control groups – headphones and standard care.

The finding that silence was as effective as music reflects the modest results reported in a meta-analysis (Cepeda et al, 2006). It could potentially be argued that in the hospital context, silence functions as a significant auditory distraction of comparable magnitude to music. The hospital environment may be viewed as one in which ‘noise pollution’ is rife. Noise pollution has been defined as an impurity of unpleasant sounds (Cabrera and Lee, 2000). With the beeping of monitoring machines and the activity of staff and other patients, noise levels are often high in hospital. The International Noise Council based with the Environmental Protection Agency in the United States have set guidelines for the noise levels in acute care areas of a hospital (including orthopaedics). Akin to a volume slightly lower than the sound of light traffic or slightly above normal conversation, daytime levels should be approximately 45 dB in the daytime and 20 dB at night (the volume of a quiet conversation) (Bayo et al., 1995). The reality has been proven quite different to the guidelines. Cabrera and Lee (2000) reported that the average noise level of acute care admissions wards at night was recorded at 67 dB.

Music and silence (though noise reducing headphones) amply mask the noise pollution from hospital equipment and activity and can have concomitant psychological, physiological and sociological benefits for the patient (see Finlay, 2013). Though it could be argued that using

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5 auditory sources would simply add to the noise pollution, in fact the opposite is true: sound is  
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7 thought to minimise noise pollution (Cabrera and Lee, 2000). Patients in this study  
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9 specifically requested additional use of the interventions for the purposes of sleep-induction,  
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11 and though it was not provided for such uses in this study, in this context, music and silence  
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13 could function as an auditory block in the immediate period before falling asleep. Other  
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15 research has confirmed that sleep quality can impact upon recovery rate. Good et al. (2002)  
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17 investigated pain and sleep quality in gynaecological surgery patients. Those participants who  
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19 had a poor night of sleep had significantly elevated pain during the day following the  
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21 disrupted night. Poor sleep preceded greater pain, but pain did not predict poor sleep. Sleep  
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23 quality was therefore directly proportional to the ensuing levels of pain experienced by  
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25 patients.  
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31 It is possible that the pre- and post-test research design may have impacted on the  
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33 significance of results as participants were required to disengage from the stimulus in order to  
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35 complete the questionnaires. The standard protocol in music-induced analgesia research has  
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37 involved the completion of pain scores immediately after a period of music listening (e.g. all  
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39 research by Good et al and MacDonald et al, 2003), as pain ratings require participants to  
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41 divert attention back to pain in order to evaluate their health status. Certainly, the issue of  
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43 durability of results and the most appropriate method of testing has been minimally  
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45 investigated in audio-analgesia literature. Research has shown that music effectively induces  
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47 affective mood changes: Panksepp and Bernatzky (2002) found that music induced desired  
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49 mood changes through positive or negative music. The induced mood persisted at 10 minutes  
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51 post-intervention, but was not statistically evident at 20 minutes. If the results of this study  
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53 were applied to pain, then they would suggest that the post-test SF-MPQ data was taken at  
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55 the peak of the response to the intervention, but the analgesic effects would thereafter have  
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5 declined quickly, hence they were not reflected in the morning and evening pain ratings.  
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7 Certainly further research is needed to clarify this area. Patients' qualitative perceptions of  
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9 the durability of music-induced analgesic effects have been addressed by Finlay (2013), who  
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11 found heterogeneity in patient views of the longevity of effects, principally related to  
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13 participants' adherence to a strictly biomedical worldview, with a rejection of the potential  
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15 role of psychological stimuli in impacting pain. Future research could consider integrating  
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17 time-delayed repeat assessments to target the length of time across which changes caused by  
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19 psychological interventions are maintained. Alternatively, it could be that there was some  
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21 short-term benefit for all patients through their feelings of involvement in research through  
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23 the Hawthorne Effect (Adair, 1984). Further research should aim to innovate in their study  
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25 designs to clarify this.  
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30 Audio-analgesia and silent relaxation are potentially effective adjunctive treatments for the  
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32 management of post-operative pain. That they were similarly effective demonstrates the  
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34 necessity of a multidisciplinary 'kit' approach to pain interventions (Pellino et al., 2005).  
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36 Cortisol concentrations responded to the interventions most strongly on the first day post-  
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38 operatively, suggesting that attention-diversion strategies may be particularly effective in the  
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40 first 24 hours after surgery and also that the use of positive and auditory interventions should  
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42 be encouraged for patient self-care. This study indicates that further investigation into  
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44 attention-diversion through sound is warranted, but pain scores should be supplemented by  
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46 biological data. The ease of use, desirability and low cost of auditory interventions for  
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48 analgesic purposes argues for their continued use in pain medicine.  
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Running Head: Post-operative pain management through audio-analgesia

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Running Head: Post-operative pain management through audio-analgesia

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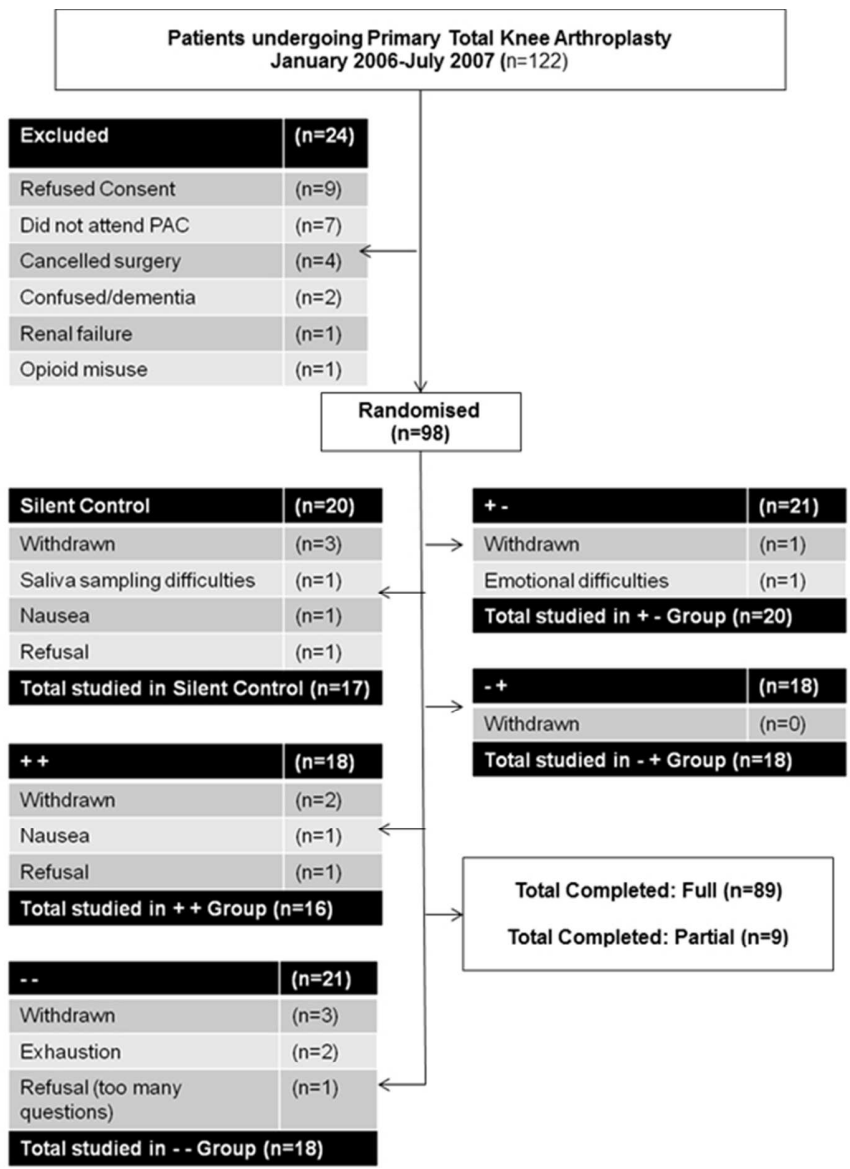


Figure 1: CONSORT Diagram



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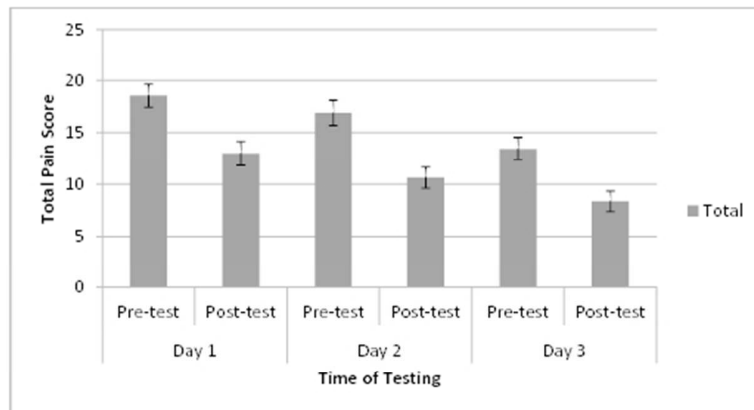


Figure 2: Total Pain Scores across Time of Testing on the Short-form McGill Pain Questionnaire  
215x279mm (72 x 72 DPI)

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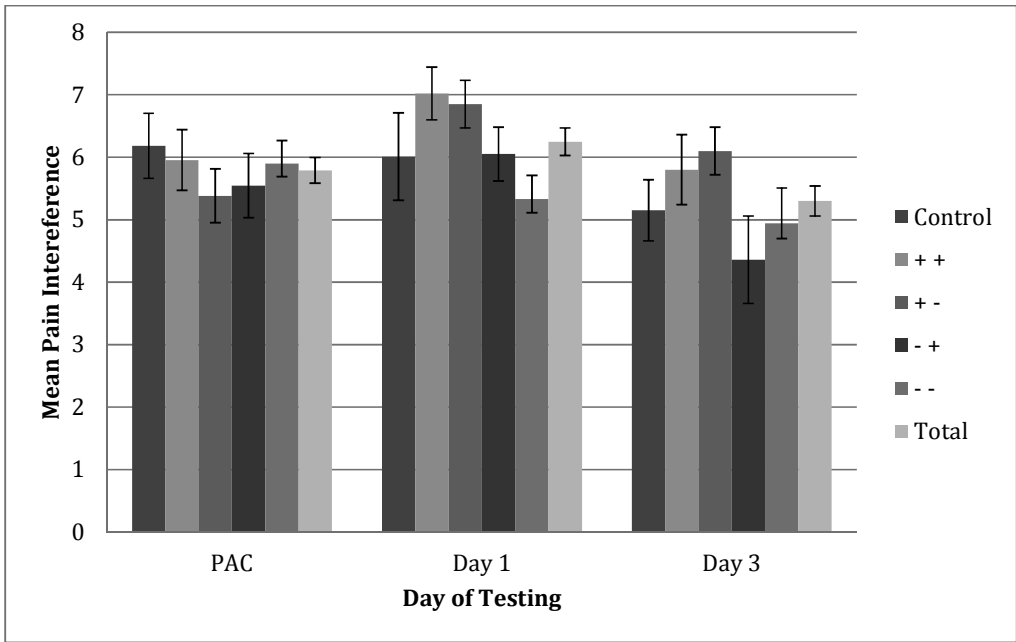


Figure 3: Mean Pain Interference according to Group Intervention (error bars show  $\pm 1$  SD)

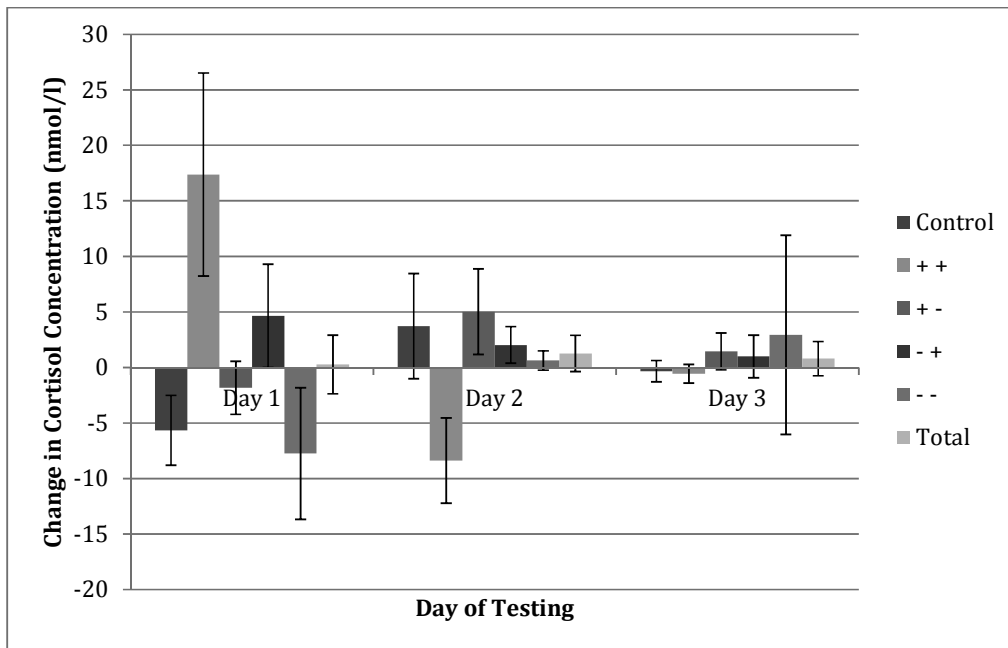


Figure 4: Pre- to Post-test change in Cortisol Concentrations. (Positive scores indicate cortisol concentrations improved and *decreased* from pre- to post-test, negative scores indicate cortisol *increased*).

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Table 1: Group Allocation

<b>Group</b>	<b>Harmonicity</b>	<b>Rhythmicity</b>
A	+	+
B	-	-
C	-	+
D	+	-
Control	Silent	Silent

For Peer Review

Baseline/Demographics	M±SD	<i>p</i> -value
Age	68.07±8.03	.92
Years of arthritic pain	10.31±10.06	.11
VRS/NRS at Rest	45.96±28.09	.49
VRS/NRS at Movement	66.60±20.81	.35
Mean Pain Interference	5.79±2.03	.74
Total Pain Score	17.11±9.25	.90
Total Mood Disturbance	5.90±27.43	.09
Cortisol (nmol/l)	11.81±13.14	.93
PCA Day 0 (ml)	15.67±14.40	.95
PCA Day 1 (ml)	23.62±21.03	.37

Table 2: Demographics and Baseline Pre-admission Scores

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Day of Testing	Rest				Movement		
	Pre-test	Post-test	% Change	<i>p</i> -value	Pre-test	Post-test	% Change
Day 1	48.68±29.14	43.49±28.43	10.66		73.99±22.43	66.51±24.65	10.11
Day 2	47.78±27.00	38.52±27.28	19.38		65.30±24.41	58.70±28.03	10.11
Day 3	37.12±23.38	30.03±22.00	19.10		60.17±22.64	52.71±23.53	12.39
Overall	44.53±26.51	37.35±25.90	16.38		66.49±23.16	59.31±25.40	10.87
Day of Testing				.0001			
Pre-test to Post-test				.0001			
Movement-Rest				.0005			

Table 3: Significance, percentage change and pre- and post-test VRS/NRS scores at rest and on movement (Mean±Standard Deviation)

Group	Mean Pain Interference				Total Mood Disturbance			
	PAC	Day 1	Day 3	p-value	PAC	Day 1	Day 3	p-value
++	5.81±2.03	6.01±2.97	5.15±2.00		8.93±35.75	24.53±32.58	13.87±25.56	
--	5.31±1.93	7.02±1.73	5.80±2.19		14.67±22.56	25.07±34.18	22.60±34.25	
- +	5.44±2.16	6.85±1.68	6.10±1.64		9.47±24.52	19.93±21.21	10.40±18.09	
+ -	5.97±1.76	6.05±1.83	4.36±2.70		-8.50±21.11	25.44±25.70	14.00±20.18	
Control	6.43±1.98	5.33±1.64	4.94±2.27		15.00±35.75	24.53±32.58	13.87±25.56	
Overall	5.77±1.96	6.25±2.07	5.30±1.19		7.26±28.30	27.23±31.21	17.13±28.81	
Day of Testing				.001				.0001
Between-Groups				.05				.127
2-way Interaction*				.05				.368

Table 4: Significance and Mean Pain Interference and Total Mood Disturbance Scores at Pre-admission (PAC), Day 1 and Day 3 (Mean±Standard Deviation). \*Indicates 2-way interaction between Day of Testing and Group

Group	p-value	Day 1			Day 2			Day 3		
		Pre-test	Post-test	% Change	Pre-test	Post-test	% Change	Pre-test	Post-test	% Change
++		33.78±37.68	11.12±6.98	67.08	9.00±4.97	19.79±12.94	-119.89	6.65±5.60	7.68±5.11	-15.49
--		15.59±7.75	27.32±25.97	-75.24	13.36±9.08	13.72±9.36	-2.69	17.70±24.93	14.76±4.94	16.61
-+		17.68±15.84	15.83±11.11	10.46	9.26±4.09	7.96±3.70	14.04	6.68±2.40	7.69±5.77	-15.12
+-		16.73±21.97	19.78±28.87	-18.23	25.96±41.99	21.02±30.24	19.03	8.49±5.19	7.55±3.92	11.07
Control		24.33±25.27	28.38±30.59	-16.65	28.15±29.54	20.21±10.34	28.21	8.28±5.48	9.99±7.91	-20.65
Overall		20.96±22.81	20.84±23.33	0.57	17.67±25.05	16.61±16.98	6.00	9.77±12.49	9.61±6.05	1.64
Day of Testing	.01									
Between-Groups*	.02									
3-way interaction**	.005									

Table 5: Salivary cortisol concentrations before and after music listening or silent control. \* Between-groups difference shown only on Day 1. \*\* 3-way interaction between Day of Testing, Time of Testing and Group.



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For Peer Review

Excerpt No.	Composer/Artist	Title	Excerpt length (mins)
<i>High Harmonicity, Low Rhythmicity (+ -)</i>			
1	Mahler	Symphony 4, Adagietto Sehr Langsam	11.54
2	Vaughan-Williams	Fantasia on a Theme by Thomas Tallis	14.41
3	Glass	Low Symphony, Movt. 1, Subterraneans	15.07
4	Lassus	Hieremiae Propheteiae de Jérémie, Lamentatio Tertia Tertii Diei Missa "Congratulamini mihî": Gloria a 6	11.42
5	Debussy	Prélude à l'après-midi d'un faune	9.02
<i>Low Harmonicity, High Rhythmicity (- +)</i>			
1	Stravinsky	Rite of Spring, Le Sacrifice	18.51
2	Mike Oldfield	Tubular Bells, Part I	15.00
3	Keith Jarrett	(If the) Misfits (Wear it)	13.15
4	Pat Metheny	Sirabhorn Unity Village	14.39
5	Miles Davis	Miles Runs the Voodoo Down	14.01
<i>High Harmonicity, High Rhythmicity (+ +)</i>			
1	Vivaldi	Le Quattro Stagioni, La Primavera	11.16
2	Dvořák	Slavonic Dances, Op. 46, No.s 1, 2, 4	16.18
3	The Rippingtons Jeff Golub Klugh & James	Tourist is Paradise Drop Top Kari	11.47
4	Kartsonakis & Bonar	Vacation in the Sun Return of the Dove Ivory Passage	12.38
5	Trad. arr. Williamson	The Scotch Cap The Lochaben Harper MacGregor's Search The Auld Jew	13.44
6	Stan Getz	I Can't Get Started	11.27
<i>Low Harmonicity, Low Rhythmicity (- -)</i>			
1	Ali Khan & Purna	Emptiness is Form	16.21
2	Pärt	Festina Lente Cantus in Memory of Benjamin Britten	15.26
3	Shakuhachi	Akita No Sugagaki Gekko Roteki	12.42
4	Tommy Smith	Into Silence, No.s 8, 9, 12, 15, 25	14.52