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Experimental muscle pain and music, do they interact?

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Background: Music is used to evoke audio analgesia during dental procedures, but it is unknown if experimental pain and music interact. This study aimed to explore the multisensory interaction between contrasting types of music and experimentally induced muscle pain.

Methods: In 20 healthy women, 0.3 mL sterile hypertonic saline (5.8%) was injected into the masseter muscle during three sessions while contrasting music (classical and black metal) or no music was played in the background. Pain intensity was assessed every 15 seconds with a 0-100 mm visual analogue scale (VAS) until pain subsided. Pain spread (pain drawings), unpleasantness (VAS), anxiety (VAS), and pain quality (McGill Questionnaire) were assessed after the last pain assessment.

Results: Pain of high intensity was evoked at all sessions with a median (interquartile range) peak pain intensity of 78 (30) in the black metal music, 86 (39) in the classical music, and 77 (30) in the control session. The pain duration was 142 (150) seconds in the black metal music, 135 (150) seconds in the classical music, and 135 (172) seconds in the control session. The corresponding pain-drawing areas were 42 (52), 37 (36), and 44 (34), arbitrary units respectively. There were no differences in any of these variables (Friedman's test; *P´s* > .368), or in unpleasantness, anxiety, or pain quality between sessions (*P´s* > .095).

Conclusions: Experimentally induced muscle pain does not seem to be influenced by contrasting types of background music. Further studies exploring the multisensory integration between music and experimental muscle pain are needed.

KEYWORDS

analgesia, anxiety, facial pain, music, pain measurement

1 | INTRODUCTION

Pain is defined by the International Association for Pain (IASP) as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[1] Hence, pain is a complex and subjective experience, including several aspects such as physiological, sensory, affective, cognitive, behavioral, and sociocultural components.[2]

In a systematic review, chronic pain was estimated to affect as many as 34% of the population world-wide,[3] with musculoskeletal pain accounting for the vast majority. In the orofacial region, temporomandibular disorders (TMD) are the most

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frequent musculoskeletal conditions with a prevalence of 5%-12%.[4] Epidemiological and psychophysical studies show that women experience more recurrent pain than men.[5] Chronic pain is associated with significant disability. Indeed, musculoskeletal pain conditions, along with mental health and behavioral conditions, are the leading cause of global disability.[6] The etiology to chronic pain is considered multifactorial, and the biopsychosocial model is the most predominant explanation.[7] Because of the complex interaction of biological, psychological, cultural and social factors in chronic pain patients, multimodal treatment is recommended. As the term implies, multimodal treatment includes a variety of different therapies, such as pharmacological treatment, physiotherapy, behavioral therapy, and other adjunctive therapies. One such treatment that is offered at many pain clinics is music therapy.[8]

Music can be defined as an "art concerned with combining vocal or instrumental sounds for beauty of form or emotional expression, usually according to cultural standards of rhythm, melody, and, in most western music, harmony".[9] It has existed for thousands of years as an integral part of most cultures and has followed people in different life events. For example, archeologists have found prehistoric music instruments that date 40 000 years back.

There are different mechanisms by which music can induce both basic and complex emotions in listeners. These mechanisms are not unique for music but share similar psychological mechanisms as other emotions. Induction of both positive and negative emotions can depend on factors such as cultural impact, induction speed and degree of volitional influence, modularity, dependence on musical structure, information focus, ontogenetic development, and key brain regions.[10] Music activates pathways in various areas of the brain, such as the cingulate and the insular cortex, hypothalamus, prefrontal cortex, amygdala, and hippocampus.[11] Different substances like endorphins, endocannabinoids, dopamine, and nitric oxide seem to affect impressions of music.[11] Also, pleasurable music can lead to the release of dopamine in striatal reward systems and this could be a possible explanation why music is so valued in all human societies.[12] However, music can also cause negative sensations and emotions such as sadness, pain, and worry,[13] and noise can cause discomfort and evoke pain, for example migraineurs with phonophobia.[14]

Multisensory integration refers to the process in which the brain is able to co-process and co-modulate various kinds of incoming stimuli in order to create a single perception of the environment.[14] This ability of the human brain is essential for humans to meaningfully interpret the complexity of their environment.[15] Music affects the perception of pain in a complex way. Parts of the auditory and pain systems cross each other in several regions of the reticular formation and lower thalamus,[16] and the regional brain networks mediating reward and anxiolytic effects overlap with regions involved in analgesia.[10,12]

Music therapy has a long history, and numerous studies have demonstrated its effectiveness in pain management. For example, audio analgesia in dental procedures was initially reported 50 years ago.[16] A systematic review with meta-analysis concluded that music interventions may provide an effective complementary approach for the relief of acute, procedural, and cancer/chronic pain in the medical setting.[8] Different types of music, such as classical, Spanish guitar, and synthesizer, have been used with different effects on the outcome, although a recent meta-analysis suggested that the analgesic effect does not depend on a specific type of music.[17] Rather, results from human experimental studies indicate that self-chosen music seems to have better analgesic capacity than researcher-chosen music. However, it is not known whether the effect is due to the musical capacity or just expectations because the music is familiar.[18]

The aim of this study was to investigate whether contrasting kinds of researcher-chosen music can affect the experience of experimental muscle pain in the orofacial region. The hypothesis was that tuneful music would be preferred over tuneless music and thus be associated with lower pain ratings.

2 | MATERIALS AND METHODS

2.1 | Participants

Healthy female participants were recruited to this study through advertisement on the website: www.studentkaninen.se and by posting flyers at Karolinska Institutet Huddinge, Södertörn University, Huddinge and Stockholm University, Stockholm.

Since the effect on the background music on pain was unknown, the sample size was based on previous experimental studies using hypertonic saline to induce pain.[19] A power calculation showed that 17 participants would yield a power of 80% at a significance level of 5% given a mean difference of 20% (SD 20%) between groups. To compensate for dropouts, 20 women were included.

Inclusion criteria were age over 18 years and good general health. Exclusion criteria were (a) any current pain from the orofacial region, (b) a diagnosis of painful TMD according to the Diagnostic Criteria for TMD (DC/TMD),[4] (c) frequent or chronic headache, (d) diagnosed systemic muscular or joint diseases, such as fibromyalgia or rheumatoid arthritis, (e) whiplash-associated disorder, (f) neuropathic pain or neurological disorders, (g) pregnancy or lactation, (h) severe psychiatric conditions, such as depression or bipolar disease, (i) use of any kind of medication except for contraceptives 48 hours preceding the study day.

This study took place at the Department of Dental Medicine, Karolinska Institutet, Huddinge, Sweden. The project followed the guidelines according to the Declaration of Helsinki and was approved by the Regional Ethical Review Board in Stockholm (number 2015/1659-31/2). Verbal and written information of the study were given to the participants, and their written consent was obtained before study commencement.

2.2 | Experimental protocol

The study design was an experimental randomized study with the volunteer as her own control. The study included three separate sessions that were performed in a randomized manner. The

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randomization list was generated by a computer (http://www.randomization.com) and facilitated by a researcher otherwise not participating in data collection (ME). The participants sat in a conventional dental chair during the entire experiment. The participants were screened with a shortform of the DC/TMD Axis II questionnaire,[4] including the Symptom Questionnaire, Graded Chronic Pain Scale (GCPS), Patient History Questionnaire (PHQ-4), Perceived Stress Scale (PSS-4), Oral Behaviors Checklist (OBC-6), and Jaw Functional Limitations Scale (JFLS) and were then examined clinically to confirm that they did not fulfill any DC/TMD pain diagnosis. The current day of the menstrual cycle was recorded. At each session, hypertonic saline was injected into the masseter muscle during contrasting background conditions. The sessions were separated by a minimum of one week to allow time for tissue repair before the next injection. Clinical palpation of the masseter before injections confirmed that the muscle was pain-free. The participants were informed that pain was influenced by many factors, such as cognitive and emotional factors as well as gender, and that the purpose of the research was to investigate these effects and were hence unaware of the genre of the music that would be played at two of the sessions. After the injection, the participant was asked to assess the pain evoked.

2.3 | Auditory stimuli

Each session included one of three different conditions; two with contrasting types of background music and one without any music. The two musical pieces were chosen to represent contrasting genres. For one session, it was determined that the music was to be noisy and tuneless to evoke feelings of unpleasantness and agony and that possibly would enhance pain. The music piece selected was black metal, which is an extreme subgenre of heavy metal music. This type of music is characterized by "fast tempos, a shrieking vocal style, heavily distorted guitars played with tremolo picking, raw (lo-fi) recording, unconventional song structures, and an emphasis on atmosphere."[20] The song played was "Hvite Krists Dod" by the Norwegian group Satyricon.[21] For the other session, the music was selected to be tuneful and soft to evoke feelings of pleasure and relaxation. The classical music piece "Spiegel im Spiegel" by the Estonian composer Arvo Pärt was selected.[22] The music was played in the background from the time point when the participant stepped into the room and continued until pain subsided. The volume of the music was adjusted to be similar for both pieces and was the same for all participants. Since the participants' music preferences could differ, they were asked after the experiment how they liked the music using a 5-point verbal scale (1 = "disliked a lot," 2 = "disliked a little," 3 = "neutral," 4 = "liked a little," 5 = "liked a lot").

2.4 | Injections

The injections of hypertonic saline were carried out in a standardized point of the relaxed masseter muscle. This point corresponded to the most prominent part of the masseter muscle on the dominant side, felt during palpation while the muscle was contracting, that is, in the midline and approximately 2 cm superior to the inferior mandibular border. The hypertonic saline solution was prepared from a concentrated stock solution of sodium chloride (Natriumklorid Braun 34 mg/mL, Melsungen, Germany) that was mixed in a 1:4 proportion with sterile water (Distansapoteket Falun 2016-01-27, Sweden) shortly before injection.

2.5 | Assessment of pain

Pain intensity was assessed with a 0-100 mm visual analog scale (VAS) marked with the endpoints "No pain" and "the worst pain experienced"[23] every 15th second until pain subsided. The maximal pain intensity (VAS peak) and pain duration (VAS dur, seconds) were recorded, and the area under the curve (VAS AUC) was calculated in arbitrary units (au).

Pain drawings were used to assess pain spread and pain area caused by the injection. The participants were asked to encircle the maximal distribution of pain (pain area) on a lateral view of the head (the side of injection), one for extra-oral assessments and one highlighting the teeth and jaws for both extra-oral and intra-oral assessments. Participants chose one of the views depending on if they felt the pain in the teeth and jaw or just in the muscle. To calculate the pain area, a transparent sheet with 1.5 × 1.5 mm squares was placed over the pain drawing and the number of full squares inside the border of the drawing was counted. Squares that were partly inside the border were added to full squares, that is two half squares or three 1/3 squares were considered as one full square. The area (pain drawing area) was expressed in au. The participants were further questioned if pain was referred to distant sites, and if so where to.

To assess the quality of the evoked pain, the McGill Pain Questionnaire (MPQ) was used. This is a multidimensional pain questionnaire designed to measure the sensory, affective, and evaluative aspects of pain.[23] It consists of 20 classes of adjectives that are ranked according to severity, and the participant chose the ones that best described their pain. The total score was calculated and used in analyses. In addition, the unpleasantness and anxiety evoked by injections were assessed with a 0-10 NRS (no unpleasantness/anxiety to maximal unpleasantness/anxiety).

2.6 | Menstrual cycle

The phase of the participants' menstrual cycle was assessed by asking them about the timing of their cycle, counted from the first day of the last menses. The menstrual cycle was divided into five phases: menstrual (days 1-5), follicular (days 6-11), preovulatory (days 12-16), luteal (days 17-23), and premenstrual (days 24-28).[24]

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2.7 | Statistics

Data were analyzed with the SigmaPlot for Windows, version 14.0 (Systat Software Inc). Shapiro-Wilk's test was used to test the normality of the data. Since all pain variables were not normally distributed, non-parametric statistics were used. Data are reported as median and interquartile range (IQR). To analyze differences in pain intensity over time, Friedman's test was used for each session separately, with Dunn's test as posthoc test. Friedman's test was also used to analyze most other variables between sessions. The music preference was dichotomized into "liked" ("liked a little" and "liked a lot") and "disliked" (disliked a little" and "disliked a lot") and the proportions analyzed with McNemar's test. Correlations between pain intensity and music liking, menstrual cycle day, and anxiety levels were tested with Spearman's test. The level of significance was set at $P < .05$.

3 | RESULTS

The mean age of the participants was 24.5 (SD 5.4) years. None had any current pain (Characteristic Pain Intensity: 0 (0)) and all other scores showed normal values (PHQ-4:1 (2), PSS-4:4 (4), OBC: 6 (3.5), JFLS: 0 (0). No participant dropped out of the study.

The pain evoked by injections is shown in Table 1 and Figure 1. The injections evoked pain of high intensity at all sessions (Friedman test, $P < .001$) that lasted 0-21 min, and differed from baseline during 105s at all sessions (Dunn's test; $P < .05$).

There were no significant differences in VAS peak, VAS dur, or VAS AUC between the different sessions (Table 1) and no order effect. The number of women in each phase of the menstrual cycle during the different sessions varied between 1 and 8 (Table 2).

The pain induced was localized to the area over the masseter muscle and spread to adjacent sites (Figure 2). Ten participants reported referred pain in the black metal session and nine each in the classical and no music sessions. The most frequently reported sites were the teeth, eyes, ears, and temple. There was no difference in the pain drawing area between sessions (Table 1).

There was no difference between sessions with regards to pain quality, unpleasantness, or anxiety evoked by injections (Table 1). VAS peak and anxiety correlated at all sessions (Figure 3).

Only 15% of the participants liked the black metal piece compared to 89% that liked the classical piece (McNemar's test, $P < .001$). There was no correlation (Spearman's test) between music preference and VAS peak. There were no correlations between day of the menstrual cycle and VAS peak.

4 | DISCUSSION

In this study, we used a battery of methods to assess both sensory and emotional aspects of hypertonic saline-evoked experimental pain to investigate the multisensory interaction between pain and music in healthy women. We hypothesized that tuneless and noisy music, such as black metal, played in the background while pain was induced experimentally would enhance the pain experience, while tuneful and soft classical music would reduce the pain. However, there were no differences in any pain variable assessed between sessions with contrasting background. Thus, our hypothesis was rejected.

The findings were unexpected as music is well established as an adjuvant for pain relief for example during dental procedures[16] and the overall positive effects on pain are reported in a meta-analysis.[17] On the other hand, listening to noise has been found to evoke pain in migraineurs.[14] Several studies have also shown that music reduces experimental pain. However, in both clinical and experimental studies, there is considerable variability in the results and different methodological approaches have been used. Factors that have been discussed as varying between studies include type of music, who chooses the music, expectancy, and placebo control.[18] Other factors that may influence experimentally induced pain include method of inducing pain, for example, chemical or mechanical, and outcome measures, for example if pain intensity or unpleasantness is assessed. Regarding the music genre, two very different genres were selected namely classical and black metal, with no music as control. Even if the analgesic effect

TABLE 1 The maximal pain intensity (VAS peak), pain duration (VAS dur) and pain area under the curve (VAS AUC) as well as pain drawing area, pain quality (McGill) unpleasantness, and anxiety, evoked by hypertonic saline injection into the masseter muscle of 20 healthy women during contrasting background music conditions

	Black metal	Classical	No music	*P*-value
VAS peak (0-100)	77.5 (30.0)	86.5 (39.0)	77.0 (30.0)	0.368
VAS dur (s)	142.5 (150.0)	135.0 (150.0)	135.0 (172.5)	0.476
VAS AUC (au)	444.0 (430.5)	273.0 (412.0)	290.5 (366.8)	0.212
Pain drawing area (au)	41.5 (51.5)	37.0 (35.5)	44.0 (34.3)	0.393
McGill (0-81)	18.5 (15.0)	17.0 (9.0)	18.0 (17.8)	0.095
Unpleasantness (0-100)	68.0 (38.0)	70.5 (44.0)	64.0 (59.0)	0.262
Anxiety (0-100)	20.0 (45.5)	14.0 (53.0)	6.0 (59.3)	0.465

Note: Data show median (IQR) values.

IQR, interquartile range (75% percentile minus 25% percentile).

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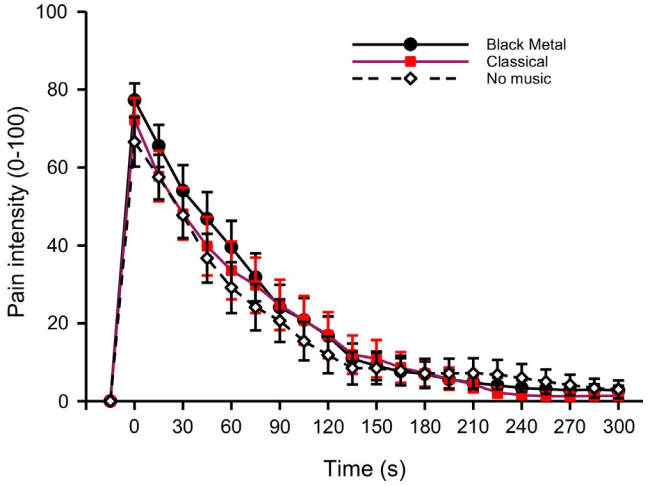

FIGURE 1 The mean (SEM) pain intensity evoked by injection of hypertonic saline (5.8%) into the masseter muscle of 20 healthy women during contrasting background conditions, black metal, classical music, and no music. The injections evoked pain of similar intensity at all sessions (Friedman test, $P < .001$) that differed from baseline during 105 s at all sessions (Dunn's test; $P < .05$). The graph shows the first 300 s

TABLE 2 The number of the participants under different phases of the menstruation cycle at three different sessions, in which experimental pain was evoked by hypertonic saline injection into the masseter muscle of 20 healthy women while playing contrasting background music or no music (control)

	M	F	PO	L	PM
Black metal	2	1	3	8	4
Classical	7	4	3	2	1
No music	0	4	5	5	3

Note: M = Menses; day 1-5, F = follicular phase; day 6-11, PO = periovulatory; day 12-16, L = luteal phase; day 17-24, and PM = premenstrual; day 24-28 from the first day of menstruation. Two participants were not included because of use of contraceptive pills.

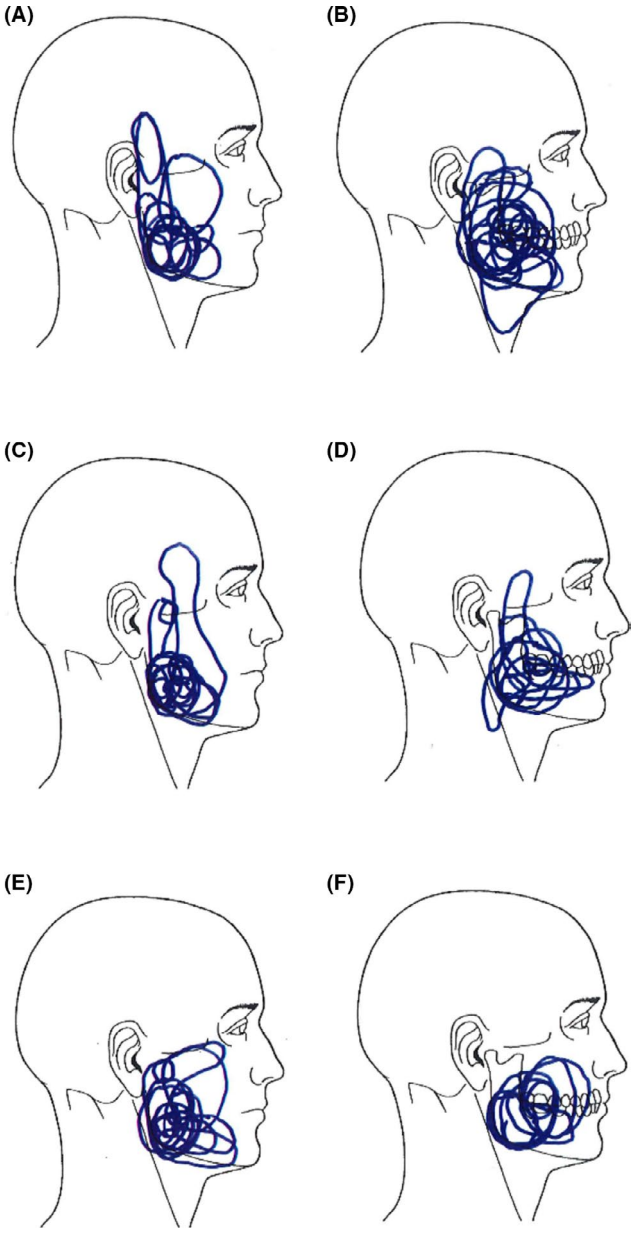

FIGURE 2 Superimposed pain drawings after injection of hypertonic saline (5.8%) into the masseter muscle of 20 healthy women during contrasting background music conditions, black metal, classical music, and no music. A and B, black metal session, extra-oral and intra-oral, respectively, (C) and (D) classical session, and (E) and (F) no music session. There were no significant differences in pain areas between sessions

did not seem to be associated with a specific music genre,[17] most previous studies have used soft, relaxing music, such as classical or Spanish guitar. Hence, it was postulated that comparing classical music with black metal which is regarded as unpleasant and agitating would generate contrasting responses. Another consideration is the autonomy for the participant to choose the music. It seems that the analgesic effect is greater when the participant chooses the music as opposed to listening to researcher-chosen music.[25-27] However, if the participant is able to choose the music, personal preference and familiarity to the music may explain the analgesic effect and not the music per se.[18,28] Our results seem to support this point. Also, to control for this factor the participants were asked whether they liked the music played. A majority (89%) stated that they liked the classical piece, in contrast to the black metal, that only a few (15%) enjoyed. With respect to expectation, two previous studies have shown that participants listening to preferred, well-loved music compared to non-preferred or non-musical sounds expect, but also experience better pain relief.[26,27] To minimize the positive expectations, the participants in this study were not told that music would be played during the sessions and the music was researcher-chosen. On the other hand, they were aware that they would receive a painful hypertonic saline injection, which likely resulted in negative expectations. The significant correlations between anxiety and pain intensity at all sessions support this explanation. Studies have shown that expectation of a placebo hypoalgesia and nocebo hyperalgesia

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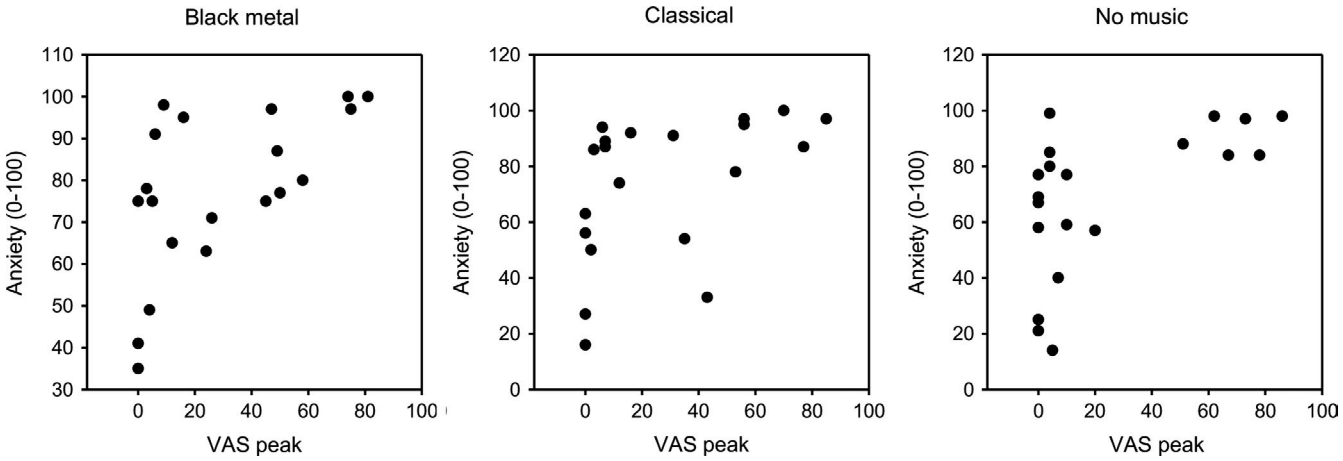

FIGURE 3 Correlations between the maximal pain intensity and anxiety evoked by injection of hypertonic saline (5.8%) into the masseter muscle of 20 healthy women during contrasting background music conditions, black metal, classical music, and no music. All correlations were significant (Spearman test; black metal and classical: r_s = .642, P = .002; no music: r_s = .530, P = .016)

differently influences pain perception.[29] Villareal and coworkers showed that the pain-reducing effect was superior to control (no music) for active distraction, music, and environmental sounds, but that there was no difference between music and sounds.[30] In this study, we included a session with just the normal sounds in the environment as control. To summarize, our experimental results support that other factors beyond the music per se are more important for the analgesic effects of music.

There were some strengths and limitations in this study that should be addressed. First, only women were included and hence the results cannot be readily translated to men. Second, the experiments were not undertaken during the same menstrual phase for all participants, which may have affected the results.[5] Nevertheless, we recorded the day from the last menses at all visits and there were no correlations between the menstrual cycle day and pain intensity at any of the sessions. Another limitation was the relatively small sample size and one can argue that the lack of positive results could be due to lack of power. On the other hand, there were only minor differences between sessions for most of the outcome measures; therefore, increasing the sample size might not have influenced the results. Also, the participants served as their own controls, which is a strength since it reduces the number of variables. One should also bear in mind that even if the hypertonic saline injections evoke pain with similar characteristics as clinical myalgia, the pain evoked is acute and lacks many of the features of chronic myalgia, which is much more complex. Thus, the results from this experimental study may not be translated to clinical practice.

With respect to the limitations of this study, we conclude that experimentally induced pain in the masseter muscle of healthy female participants was not influenced by two contrasting types of background music. However, more studies about the multisensory integration between music and experimental muscle pain are needed.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

AUTHOR CONTRIBUTION

Malin Ernberg: Conceptualization; Formal analysis; Methodology; Project administration; Resources; Software; Supervision; Visualization; Writing-original draft. **Dina Al-Khdhairi:** Data curation; Formal analysis; Investigation; Writing-review & editing. **Kseniya Shkola:** Data curation; Formal analysis; Investigation; Writing-review & editing. **Sofia Louca Jounger:** Investigation; Supervision; Writing-review & editing. **Nikolaos Christidis:** Conceptualization; Investigation; Methodology; Project administration; Supervision; Writing-review & editing.

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