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Review

Emotional foundations of music as a non-pharmacological pain management tool in modern medicine

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ABSTRACT

This paper reviews the use of music as an adjuvant to the control of pain, especially in medical procedures. Surgery causes stress and anxiety that exacerbates the experience of pain. Self-report of and physiological measures on post-surgical patients indicate that music therapy or music stimulation reduces the perception of pain, both alone and when part of a multimodal pain management program, and can reduce the need for pharmaceutical interventions. However, multimodal pain therapy, including non-pharmacological interventions after surgery, is still rare in medical practice. We summarize how music can enhance medical therapies and can be used as an adjuvant with other pain-management programs to increase the effectiveness of those therapies. As summarized, we currently know that musical pieces chosen by the patient are commonly, but not always, more effective than pieces chosen by another person. Further research should focus both on finding the specific indications and contra-indications of music therapy and on the biological and neurological pathways responsible for those findings (related evidence has implicated brain opioid and oxytocin mechanisms in affective changes evoked by music). In turn, these findings will allow medical investigators and practitioners to design guidelines and reliable, standardized applications for this promising method of pain management in modern medicine.

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1. Introduction

The inclusion of music or rhythmic, melodic speech with medical treatments has a long history and frequently has been used to promote and maintain health as well as to alleviate pain. Historically, music has been commonly used in traditional treatments to heal and fortify the soul. Musicians were employed by the Romans and ancient Greeks in facilitating healing in spas—ritual purification and "incubation" or rest therapy approaches. In these practices, it is evident that the power of music to soothe and emotionally move was widely recognized and revered in these cultures. Contemporary medicine is taking notice of such alternative approaches to promote healing, as are an increasing number of neuroscientists.

The main goal of this review is to focus on the potential of musical therapy in the healthcare setting. Applications of music stimulation and therapy offer interesting alternative solutions to conditions and illnesses that remain largely intractable to traditional Western medicine. Although the field of music medicine

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(Spintge and Droh, 1992a; Pratt and Spintge, 1996) has long been an active area of inquiry, the mechanisms of action within body and brain are far from known.

Modern researchers have started to investigate these benefits, and have generally found that music powerfully stimulates socioemotional processes, which, in turn, positively affect moods and result in beneficial health consequences (Dileo et al., 2008; Koelsch, 2005) Music serves many functions in our lives, and we often accept it as a gift of civilized life without probing its deeper currents. At its most moving moments, it captivates our emotional apparatus to the point that the brain's autonomic nervous systems crescendo in a feeling of chills along the skin surface, perhaps the most studied, prime indicator of the emotional power of music (Blood and Zatorre, 2001; Craig, 2005; Grewe et al., 2005; Guhn et al., 2007; Panksepp, 1995).

Finding the basis of the neurophysiological effects of the affective power of music may allow us to more fully harness the utility of this powerful emotional medium to promote human welfare. Although our focus is on the use of music to control pain, first, it is useful to consider how profoundly proto-music may have been intertwined in the emotional and communicative-prosodic evolution of the human brain and mind (see Malloch and Trevarthen, 2009; Zinken et al., 2008; Panksepp, 2009, 2010; Tallal and Gaab, 2006) giving music access to the many neurochemistries known to control pain. Specifically, studies show that music can alleviate feelings of stress, distress, and depressive affects in individuals suffering from acute and chronic pain (Cepeda et al., 2006). Music stimulation may also counteract negative cognitions such as feelings of helplessness and hopelessness and the undesired stress that many patients experience in clinics or when hospitalized (Phipps et al., 2010). Music, especially through its emotional power, is bound to influence diverse brain chemistries and network activities, and we, along with many others, anticipate effects on such anti-stress systems such as endogenous opioids (Panksepp, 1995) and other neuropeptides, such as oxytocin (Nilsson, 2009a) that also mediate various positive social processes (Panksepp, 1998; Uvnäs-Moberg, 1998). It seems obvious that music would not have the power that it does if it could not touch our social-emotional nature (Panksepp and Trevarthen, 2009). And the central role of the above neuropeptides in social-emotional processes (Panksepp, 1998) is currently widely recognized (for a recent popular review, see Churchland, 2011). Convergin evidence suggests they can produce beneficial bodily effects, perhaps by alleviating negative affect and promoting positive affect, along with the secretion of various healing anti-stress factors of the body such as oxytocin (Uvnäs-Moberg, 1998) and endogenous opiates, along with modulation of widespread brain system such as biogenic amine and nitric oxide activities (Kream et al., 2010; Stefano et al., 2004).

Currently, with the increasing popularity of alternative medicine, the concept of "medicinal" music therapy is once again widely discussed (Malloch and Trevarthen, 2009), but the science of its benefits has not progressed as rapidly as its widespread acceptance (Ernst et al., 2006).

The aim here is discuss the threads of evidence that are emerging. Although neither the mechanisms by which music affects humans nor the most effective applications of music are well documented, we will focus on two trends emerging from the research, namely human problems that are heavily influenced by the auditory environment (e.g., autism), and those experiences in which feelings of suffering play a significant role (e.g., anxiety and chronic pain), which have been particulary amenable to music therapy. Indeed, the efficacy of music to reduce pain intensity or analgesic requirements, although not without controversy, is beginning to be accepted (Cepeda et al., 1998; Good et al., 1999; Koch et al., 1998).

Anxiety, which commonly accompanies the anticipation of pain, sets up a dynamic that increases the experiential impact of pain, and by addressing such stress facilitators, pain may be reduced before it becomes problematic. Indeed, for a long time music has been a staple in minor surgical procedures such as those common in dentistry (Goff et al., 1997; Aitken et al., 2002). Surgical patients treated with music therapy also commonly exhibit some alleviation of pain severity. This pain mitigation may be partly due to cognitive variables such as strengthening the individual's sense of control (Rotter, 1966), which is further amplified by expectations of self-efficacy (Bandura, 1977). Additionally, people commonly suffer during hospitalization because of isolation from their normal social and material environments. Music can decrease this burden of hospitalization: For instance, Phipps et al. (2010) have shown that music can significantly attenuate stress effects on physiological parameters, as well as pain and mood states in hospitalized patients. There were significant reductions in heart and respiration rates, perceived anxiety, depression, and total mood score in subjects who received music intervention compared to subjects who did not.

2. Pain and emotion

The processing of pain is a phenomenon involving both the periperal and central nervous systems. As the ascending nociceptive information passes through the brainstem to reach the brain, it activates a network of brainstem structures and pathways (Renn and Dorsey, 2005). The classical pain pathways ascending via the thalamus to cortical regions (insula and somatosensory cortex) are supplemented by more medial ancient pathways that directly impact the midline emotional systems concentrated in the supraspinal structures of the lower brainstem and diencephalon, including the medullary reticular formation, periaqueductal gray, parabrachial region, hypothalamus, thalamus, as well as various limbic structures and the forebrain, that mediate the perception of pain. These various brain regions are associated with autonomic, motor, discriminative, affective, cognitive, and motivational aspects of pain behaviours. Using these criteria, pain was described by the International Association for the Study of Pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. This definition means that pain is not only a sensory process but also an affective subjective phenomenon that is influenced by physiological processes and by diverse psychological and emotional processes (Renn and Dorsey, 2005).

3. Music therapy: definition

Music is a fundamental aspect of human experience, strongly linked to our "intrinsic motive" systems that is deeply ingrained in all cultures (Malloch and Trevarthen, 2009). Accordingly, it is no surprise that it has become a common element in many modern human environments, e.g., serving as a distraction during daily exercise routines, as a background facilitator in shopping malls, as an indispensible accompaniment to films, and as background music in the doctor's office. This ubiquity can lead to mistaken ideas as to what constitutes music therapy. Simply hearing or even more actively listening to music is best classified as mere music stimulation. In contrast, music therapy is the result of a deliberate, controlled procedure—a systematic protocol, the effects of which can be formally evaluated. Music therapy employs specific musical elements such as sound, rhythm, melody, harmony, dynamic and tempo to encourage or facilitate movement, positive interactions, and/or improved emotional or cognitive states (World Federation

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of Music Therapy, 2010). According to the World Federation of Music Therapy and the American Music Therapy Association (Tanguay, 2008), music therapy can be defined as the clinical and evidence-based use of music and/or its elements by a qualified music therapist to accomplish individualized goals within a therapeutic relationship with one client or a group. The aim of music therapy is to develop potentials and/or restore impaired functions of individuals so they can achieve better intrapersonal and/or interpersonal integration, which may promote a better quality of life, through prevention, rehabilitation or treatment of specific problems.

Broadly, music therapy procedures are structured as either receptive or active. Receptive music therapy frequently accompanies other forms of therapy, incorporating music chosen by the patient in consultation with a qualified music therapist. The musical interventions are often selected to arouse specific emotions, which, in turn, allow the patient to more easily access, recall, and interrogate memories with the goal of understanding the role those memories play in the patient's current circumstances. Active music therapy differs significantly from receptive therapy: this second therapeutic form requires the patient, again in conjunction with a trained therapist, to create music and sometimes bodily movements. The therapist and patient sing and/or play instruments together, and the therapist encourages the patient to improvise, at times to dance. This procedure, like receptive therapy, relies upon the emotional impact of music. A striking difference between the two forms, however, is that receptive music therapy encourages the patient to recall past events while active music therapy urges the patient to create – rather than recall – an experience, and this creation is an implicitely forward-looking exercise.

Of course, both methods have advantages and disadvantages, which is one reason that music therapists should be trained in the theories which underlie specific practices and to have clear conceptions of the objectives of therapy. Therapists must recognize the potential effect that various musical elements will elicit and how those effects may be utilized and optimized to promote the goals of therapy. Formal training in music therapy is necessary, then, because if music can facilitate positive emotions and more effective treatments, the converse possibility must also be considered. For instance, genres of music which are desirable to some are aversive to others.

4. Music medicine

In the twentieth century, the publication of an increasing number of articles describing scientifically oriented research into the therapeutic effectiveness of music attests to the rising popularity and growing acceptance of these therapies (Cunningham et al., 1997; Nickel et al., 2005; Spintge and Droh, 1992b). Results of these investigations show that music therapy is an effective intervention for patients with chronic pain, children with migraines, and patients with chronic tinnitus (Hillecke et al., 2005). Musical interventions have also been shown to reduce other forms of stress (Esch et al., 2004; Lee, 2003; Pelletier, 2004; Salamon et al., 2003a,b; Winter et al., 1994), increase relaxation (Duffy and Fuller, 2000; Kemper and Danhauer, 2005), moderate sleep disturbances (Kullich et al., 2003), and alleviate pain (Hesse, 2003; Kullich et al., 2003). These findings imply the existence of underlying commonalities, with the most prominent one being the widespread recognition that in each of these conditions, various changes in emotions may be central to therapeutic change, a perspective that is increasingly recognized (Altenmüller et al., 2007; Blood et al., 1999; Panksepp and Bernatzky, 2002).

Indeed, strategically used, music therapy has helped improve and, at times, restore many functions, for example, motor capacities in Parkinson's patients (Thaut et al., 1996; Bernatzky et al., 2004) and other motor disorders that arise from brain trauma (Bradt et al., 2010) with perhaps the most promise for pain alleviation. In a meta-analysis of pain intervention methods, Kwekkeboom et al. (2009) determined that music therapy appears to specifically target pain and fatigue. Drawing evidence from studies of pain management, many investigators propose that music should be more seriously applied to palliative medicine (Dileo et al., 2008; Aldridge, 1999). For instance, Magill (2009) found that caregivers of advanced cancer patients fared better when they employed musical therapy to reduce the relentless strain that accompanies caring for a loved one with a terminal condition. And music therapy employed as an adjuvant relieved anxiety, sadness, fear, and pain associated with conventional cancer treatments (Richardson et al., 2008) and also reduced the need for analgesics, e.g., NSAIDs and opioids, in patients receiving these drugs for pain management (Pyati and Gan, 2007). However, in a review of five studies, Bradt and Dileo (2010) found no clear evidence that music therapy improved life quality among people in end-of-life care.

If one focuses specifically on psychiatric disorders, there is some evidence from meta-analyses for the utility of music in improving communicative skills with little effect on behavioural disorders (Gold et al., 2006). A respectable therapeutic effect size has been reported in the treatment of psychotic disorders, even though neither self-selection of music nor the type of music used had any differential effect (Silverman, 2003). The overall benefits in the treatment of depression across studies are reasonably consistently positive, with larger effects with longer courses of treatment (Gold et al., 2009), and occasional studies that yield very substantial effects on both psychological as well as physiological parameters such as heart rate and blood pressure (Chan et al., 2009).

Overall, the effects of music therapy across medical problems have typically been highly variable, modest in size, and show abundant differences between studies. Perhaps the most consistent effects have been seen in the management of pain. Due to the complexity of the mechanisms responsible for music therapy effects in the treatment of psychiatric disorders, where variable effects have consistently been seen, the major goal of the present analysis will be largely limited to the treatment of chronic pain and, to a lesser extent, the alleviation of depression. This area is ripe for investigation because chronic pain and depression are highly correlated and because the interaction of these two common human ailments remains largely uninvestigated (Maratos et al., 2008).

5. Music as a non-pharmacological treatment for pain in the clinical setting

Music as a non-pharmacological treatment for pain was tested by Roy et al. (2008) and Zhao and Chen (2009). Both studies evaluated effects of valenced musical interventions upon pain perception and both studies reported that pleasant or cheerful music decreased perceptions of pain induced by heat while unpleasant or sad music increased perceptions of pain under the same conditions.

Indeed, the alleviation of pain and the reduction of anxiety which can exacerbate pain appear to be the most promising use of music therapy. Kullich et al. (2003) reported that music therapy improved both sleep and quality of life for 65 patients with acute or chronic back pain. Pothoulaki et al. (2008) found that listening to specific types of music reduced pain and anxiety in patients undergoing haemodialysis.

Importantly, music therapy for pain and anxiety has been shown to be as useful in infants and children as in adults. In two studies of infants, music played to premature babies reduces pain and encourages better oral feeding (Cignacco et al., 2007). In a meta-analysis by Klassen et al. (2008) reviewing almost four hundred studies of infants, children, preadolescents, and teenagers undergoing various medical procedures, diminished pain and anxiety were

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evident in a variety of clinical settings. The application of music therapy in children may be especially noteworthy because most pain medications, have typically not undergone systematic testing as they have in adults. As a result, the effectiveness, side effects, and dosages of pharmacological interventions for children remain less well-documented than for adults, and this lack of paediatric-specific knowledge can be problematic. Thus, music therapy may be a viable and safe non-pharmacological adjuvant to conventional pain and anxiety treatments for children. This application needs to be employed recognizing that children's brains respond to music differently than those of adults and that musical training modifies those underlying brain substrates (Koelsch et al., 2005; Seung et al., 2005).

In sum, evidence is accumulating that music can be used to promote feelings of wellbeing and to facilitate therapeutic objectives. But to most effectively employ music in these and other affectively valenced situations, e.g., pain-management, the physiological sources and neurological pathways that give rise to music's power need to be identified. Other frequently noted physiological effects that correlate closely with music therapy include effects on heart rate, respiratory rate, and oxygen saturation (Hesse, 2003; Trappe, 2009). Thus, though reactions to music are frequently considered subjective, studies suggest that cardiorespiratory variables respond to musical elements and changes in objective and somewhat predictable ways, the subjective effects of music have demonstrated objective physical as well as the well-appreciated emotional effects, both surely mediated through the brain (which we will focus on at the end of this review).

6. Music therapy in the surgical setting

Both anxiety prior to and pain after surgical procedures can be successfully relieved through music therapy, largely because both anxiety and pain can be diminished by musically-facilitated reductions of emotional distress that commonly accompany these conditions. Indeed, accompanying emotional factors influence the degree to which pain is perceived (Bernatzky et al., 2007; Peyron et al., 2000). Negative emotions, the fear and dread of pain, commonly promote suffering, and when such negative affects are diminished, the affective impact of pain commonly decreases. Seeking broad evidence for the effectiveness of music therapy, Cepeda et al. (2006) reviewed fifty-one studies. These studies evaluated pain reduction in over 3600 patients and included both patients experiencing pain from surgical procedures and patients suffering from common medical conditions that produce pain, e.g., cancer or parturition. In this metastudy, participants treated with music therapy had a 70% greater probability of reporting at least a 50% decrease in pain and lower opioid requirements than control subjects. Nevertheless, the magnitude of these benefits is small and, therefore, the clinical importance of the results remains unclear (Cepeda et al., 2006). The authors summarize by stating that listening to music offers the potential advantages of low cost, ease of provision, and safety and that more work should be done in music research as a treatment for pain. Following Cepeda et al. (2006), music should not be used as a primary method for pain relief.

In contrast, a subsequent, but smaller, metastudy by Engwall and Duppils (2009) reported that music therapy was highly effective for postoperative pain. Eighteen papers published between 1998 and 2007 were reviewed. Fifteen of those studies found that music therapy had a significant, positive effect on postoperative pain and in four of the eighteen studies the use of analgesics decreased. Although the controversies over the magnitude of musically promoted therapeutic effects is bound to continue, the consistent positive trends, whether interpreted as large or small, suggest that music as an adjuvant to more traditional therapies can consistently increase patients' feelings of well-being.

7. Music in the preoperative surgical setting

Because anxiety frequently exacerbates the perception of pain, reduction of this emotion prior to pain-inducing procedures improves patients' attitudes, ability to sleep, and quality of life. Prior to surgical procedures, psycho-physiological stress is particularly strong and music therapy has been used with notable success to counter preoperative anxiety (Cunningham et al., 1997; Heitz et al., 1992; Spintge, 2000). Significantly, listening to relaxing music decreased the level of anxiety reported by preoperative patients to a greater extent than orally administered midazolam, in a study that employed the Pittsburgh Sleep Quality Index (PSQI) to assess the sleep quality of postoperative patients (Miller et al., 2002). In this study, patients were randomly divided into a music therapy group and a control group. Groups had comparable body mass indices, sleeping indices (PSQI) and wellbeing indices before surgery. Postoperatively, PSQI values improved significantly in patients exposed to music therapy. Further, these participants showed reduced use of analgesics and needed no hypnotics or sedatives whereas three of the ten participants in the control group requested sleeping pills after surgery. Another study that monitored physiological responses rather than just subjective self-reports showed similar results (Wang et al., 2002). In this study, patients selected their own music and listened to their selections for 30 min prior to surgery. Measurements of physiological parameters including electrodermal activity, blood pressure, heart rate, cortisol levels, and catecholamine levels were generally improved compared to a control group without such intervention.

Overall, the addition of self-selection to the protocol commonly appears to be important for the effectiveness of music therapy, but apparently not among psychotics (Silverman, 2003). Mok and Wong (2003) showed that patients undergoing minor surgical procedures under local anesthetic who were allowed to choose their music exhibited significantly less stress and reduced heart rate and blood pressure compared to patients who did not listen to music. Relaxation-promoting music therapy, in combination with verbally guided relaxation sessions, has also been studied and shown to positively influence affective, cognitive, and sensory processes which, in turn, reduce the negative effects of stress on pain (Albert, 2002; Almeida et al., 2003; Kullich et al., 2003). This combination of musical and relaxation therapies reflects a supportive environment offering personal attention and social support to patients, and this environment may be the key to most effectively employing music therapy. These studies also reported a concurrent reduction in postoperative pain, suggesting that preoperative music therapy can improve postoperative outcomes.

However, though carefully selected music that includes a patient's own preferences may offer an effective method to reduce anxiety and improve quality of life, not all musical genres are equally effective in the presurgical environment. But the issues appear more complicated as personality variables and preferences may mediate any interactions between musical style and psychophysiological responses in individual listeners (Gerra et al., 1998).

8. Music in the perioperative surgical setting

Activities that take place during the perioperative period typically include hospital check-in, administration of premedications, surgical site preparation, and administration of and recovery from anesthesia as well as the surgical procedure. Though music therapy may not seem a useful adjuvant during this period, studies suggest

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that even in the perioperative period music therapy can benefit the patient. For example, after total knee arthroplasty, patients often suffer from severe pain that affects their recovery (Pellino et al., 2005). Simcock et al. (2008) monitored postoperative pain in arthroplasty patients with a Visual Analog Scale (VAS) and found that patients whose surgery was performed while the patients' musical choice played during the perioperative period in the surgical suite where the operation was about to occur and afterwards reported less pain than patients in a control group. The authors concluded that intraoperative music provides an inexpensive, non-pharmacological option to reduce postoperative pain. And in a meta-analysis of 42 randomized controlled trials of patients in perioperative settings, Nilsson (2008) found that music therapy had positive effects on patients' anxiety and perceptions of pain in approximately half of the reviewed studies. Music played during cardiovascular surgeries also appeared to influence peri- and post-operative cardiac patient outcomes (Bradt and Dileo, 2009). A study by Zalewsky et al. (1998) offers some insight into this phenomenon. The authors surveyed 118 patients whose surgery was performed while music played in the surgical suite: 95% of participants did not feel disturbed by the background music, 89% reported feeling more positive about their surgery, and 80% thought that the music supported the doctor's performance and, therefore, led to a better patient-doctor interaction.

Several recent studies have sought physiological explanations for the effects of perioperative music therapy. For instance, Nilsson (2009a) measured plasma oxytocin, heart rate, mean arterial blood pressure, oxygen pressure (PaO_2) and oxygen saturation (SaO_2) in two perioperative groups, one exposed to music therapy and a control group. Levels of oxytocin, arterial oxygen (PaO_2) and subjective relaxation levels increased significantly in the music group compared to the control group. There were no differences in heart rate, mean arterial blood pressure and (SaO_2) between the groups. According to these results, music should be offered as an integral part of a multimodal treatment.

In a similar pursuit, Nilsson et al. (2005) conducted a study of peri- and postoperative effects of music therapy on stress and immune responses during and after anesthesia. Stress responses were measured in 75 hernia patients divided into an experimental group and a control group. Plasma cortisol and blood glucose levels along with immune responses, monitored IgA levels, were tracked. A significant decrease in cortisol levels was achieved by postoperative music intervention. Patients in the music group also experienced less stress, less pain, and required less morphine than participants in the control group. However, no differences between the groups' IgA levels, blood glucose levels, blood pressure, heart rate or oxygen saturation were noted. The authors suggest these results indicate that intraoperative music therapy can decrease postoperative pain, and that postoperative music therapy can reduce anxiety, pain, and morphine consumption. In accord with the above findings, Good et al. (2005) report that multimodal pain therapy reduced pain in postoperative patients undergoing intestinal surgery. In this study, three non-pharmacological interventions – guided relaxation, self-selected music, and a combination of both – were compared to a control group. Participants exposed to one of the three treatments perioperatively reported a 16–40% decrease in postoperative pain. Authors suggest that these interventions are best employed in combination with analgesia to gain greater postoperative relief without side effects.

9. Music in the postoperative setting

Due to its duration and ability to negatively affect treatment success, postoperative pain control is the most important consideration in the utility of music as an adjuvant treatment in recovery. Postoperative pain can be particularly distressing for patients who must endure complex wound care or physical therapy. After orthopaedic surgery, wound care is often painful for patients; to counter such pain music has been effectively used by nurses to reduce distress. Hsiao and Hsieh (2009) describe the utility of music therapy to reduce acute pain experienced during wound care. Participants in this study reported a decrease in negative feelings and an increase in spiritual strength. In another study Nilsson et al. (2009b) assessed eighty children aged 7–16 years using the Colored Analogue Scale (CAS), the Facial Affective Scale (FAS), and the Short State-Trait Anxiety Inventory (STAI). Treatment consisted of simply listening to favorite musical choices one day after a surgical procedure. Data consisted of requests for pain medication and assessments of distress derived from the CAS, FAS, and STAI. Children in the music group required less morphine and their distress was reduced compared to the control group. The authors suggest that listening to music was "calming and relaxing" for the children.

In contrast, MacDonald et al. (2003) had only reported modest effects when investigating differences in pain and consumption of analgesics in postsurgical patients who had undergone hysterectomies or other minor paediatric surgeries. Patients listened to self-selected music postoperatively. Though all paediatric surgery patients in the music group reported significantly less anxiety than the control group, no such effect was evident for the hysterectomy patients.

It has also been considered that music can improve early contact between mothers and infants after caesarean delivery (Ebneshahidi and Mohseni, 2008). The sedative and emetic effects of routinely administered analgesics (opioids and benzodiazepines) may impair the immediate close contact of mother and neonate. Testing music as a means of treating postoperative pain without risking these side effects, Ebneshahidi and Mohseni (2008) monitored women recovering from a caesarean delivery. Music was self-selected and anxiety, heart rate, blood pressure, opioid requirement, and postoperative pain were measured. The experimental group listened to music after surgery for 30 min, while the control group recovered in silence. Participants who listened to music requested less opioid intervention and reported lower pain scores than controls. No differences in anxiety scores, blood pressure, or heart rate were noted.

In a study comparing the efficacy of Western and Eastern music on pain reduction, Good and Ahn (2008) created three groups of postoperative patients who had undergone gynecological surgery. Each group was treated with bed rest and analgesics. Women were placed in either a music group or a control group. Women in the experimental condition were allowed to choose instrumental piano music or traditional Korean music. Two-thirds of participants in the music group ($n = 21$, 62%) chose Korean music and one-third ($n = 13$, 38%) chose instrumental music. The third group did not receive music therapy. Patients in the experimental group listened to music four times postoperatively and reported significantly less postoperative pain than the control group. No difference in effectiveness between musical choices was found.

Table 1 provides an overview of published research on the topic of music and surgery, especially studies that emphasize the importance of creating a standardized definition of and protocol for music therapy as a non-pharmacological intervention for systematic pain management in health clinics. Most of the studies conclude that music improves quality of life and sleep and has a positive effect on heart rate. Studies also agree that music therapy reduces physiological and psychological pain and anxiety before, during, and after surgery. It also reduces stress and depression and promotes relaxation.

How are these various effects on pain mediated? It is no understatement to say they remain fundamentally unknown. To establish

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Table 1
Summary the above cited research studies of various surgeries where music stimulation was used. It is shown when the music stimulation began and which parameters were measured including the results.

Reference	Samples and design	Intervention	Music	Point of MI pre/inter/post			Measured parameters and results
Miller et al. (2002)	18 out of planned 40 patients: Group A (music program): $n = 8$, Group B (comparison group): $n = 10$		Music program including guidance for relaxation	X		X	Sleep ↑, pain ↓, hypnotics and sedatives not in A but in B
Wang et al. (2002)	People choosing self-elected music (30 min self elected music) were compared with a control group.		30 min self-elected music	X			Electrodermal activity, blood pressure, heart rate, cortisol and catecholamines –
Kullich et al. (2003)	65 patients suffering from low back pain were randomly allocated to two therapy groups: one with standardized physical therapy accompanied by music and instructions for relaxation, the other group without additional music application. A specially produced music for application with pain was listened to once daily over a period of three weeks by CD and headphones.	Low back pain	Relaxation music with a spoken relaxation text (imagery journey)				Global pain, pain on pressure ↓ Roland–Morris Disability Questionnaire ↑ Positive influence on sleep disturbances
MacDonald et al. (2003)		Minor s. on the foot, total abdominal hysterectomy	Self-selected music			X	No difference in pain and consumption of analgesics
Mok and Wong (2003)		Local anesthesia			X		Anxiety, HR, BP ↓
Good et al. (2005)	Relaxation, chosen music, and in combination, were tested for pain relief following intestinal (INT) surgery in a randomized clinical trial with 167 patients.	Intestinal s.				X	Post-test pain ↓ (16–40%)
Nilsson et al. (2005)	75 hernia patients were examined by measuring plasma cortisol, blood glucose, and immune responses by determining the IgA levels.	Hernia s.			X	X	Stress, pain, morphine ↓ IgA levels, blood glucose, blood pressure, heart rate, oxygen saturation –
Pellino et al. (2005)	65 patients were divided into two groups: a group that received usual care and a group that received usual care plus a kit of nonpharmacological strategies.	Knee arthroplasty					Opioid ↓, anxiety ↓
Ebneshahidi and Mohseni (2008)	Music can help to improve the early contact of mothers with their babies after caesarean section surgery. The sedative and emetic effects of routinely administered analgesia may impair the immediate close contact of mother and neonate and therefore were of interest.	Caesarean section s.	30 min self-elected music compared to silence			X	Opioid consumption, pain ↓ Anxiety, blood pressure, heart rate –
Good and Ahn (2008)	The experienced pain, the decision between Korean and American music, and the difference in pain relief between the unequal music styles after gynecological surgery were investigated. Women were classified in a music group, in which they could choose between American piano music and Korean ballads (both plus analgesics) and a control group with bed rest only (plus analgesics).	Gynecologicals.	American piano music, Korean ballads			X	Post-test pain ↓ No difference between the two music groups in experienced pain
Pothoulaki et al. (2008)	This study investigated the effects of preferred music listening on anxiety and pain perception in patients undergoing haemodialysis. Sixty people diagnosed with end stage renal failure undergoing haemodialysis treatment participated in this study. Preferred music listening was applied as an intervention. Anxiety and pain were measured pretest and post-test.	Haemodialysis	Self-elected music				Post-test: anxiety, pain ↓
Simcock et al. (2008)	Participants were divided into a music group, in which they selected their preferred music, and a control group.	Knee arhtroplasty	Self-elected music		X		Pain ↓.

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Table 1 (*Continued*)

Reference	Samples and design	Intervention	Music	Point of MI pre/inter/post		Measured parameters and results
Hsiao and Hsieh (2009)	Experience of a nurse using music therapy to reduce the acute pain experienced during wound care.	Wound care *after* orthopaedic s.	Individual, tailored music therapy	X		Pain, negative feelings ↓. Spiritual strength ↑.
Nilsson (2009a)	To evaluate the effect of bed rest with music on relaxation of patients who have undergone heart surgery on postoperative day one. This was a randomized controlled trial with 40 patients undergoing open coronary artery bypass grafting and/or aortic valve replacement surgery. Patients were randomly allocated to either music listening during bed rest ($n = 20$) or bed rest only ($n = 20$).	Cardiovascular s.	Soothing music	X	X	Oxytocin, PaO_2, and subjective relaxation levels ↑ Heart rate, mean arterial blood pressure, SaO_2 –
Nilsson et al. (2009b)	80 children aged 7–16 years were divided into a music and a control group, the music group listened to music after undergoing day surgery					Distress, morphine ↓

↑: improvement, ↓: reduction, –: no changes, B: bioacustic, BIS score: bispectral index, BP: blood pressure, chir.: chirurgical, CC: Chinese classic, CI: calm instrumental music, Cl: classic music, C: STAI—Chinese state trait anxiety inventory, CW: Country-Western, DBP: diastolic blood pressure, EL: easy listening, F: American indian flute, FL: famous movie songs, gyn.: gynecological, H: harp, HR: heart rate, J: slow modern Jazz, KW: classic from western regions, LB: music with slow beat, MI: music intervention, NA: new age, NRS: numerical-rating-scale, O: orchestra, P: piano, PO: piano orchestra, RASS: Richmond-agitation-sedation-scale, RL: religious songs, RM: religious music, RR: respiratory rate, s: surgery, SBP: systolic blood pressure, FS: folk songs.

some kind of interpretive framework, perhaps the most likely place to look is the effect of music on the emotional functions of the brain, especially relevant neurochemistries.

10. Therapeutic mechanisms? Music and the emotional brain

The bodily mechanisms by which music exerts its beneficial effects in various mental disorders and pain management have hardly been analyzed. Our interest in music therapy originally emerged from our interest in how the emotional power of music arises from brain mechanisms (Panksepp, 1995; Panksepp and Bekkedal, 1997; Panksepp and Bernatzky, 2002; Panksepp and Trevarthen, 2009), and obviously this is the most likely place to seek the beneficial, albeit modest, effects that have been demonstrated. Emotional states modify many bodily processes, and music has powerful effects on emotions.

Because primary-process emotions which are tightly intermeshed with a host of autonomic processes that can regulate bodily state are generated by deep brain structures, a likely place to look for explanations for music's effect is in those deep structures. Several regions in the limbic and paralimbic systems, which are centers of affective pain, show notable changes associated with listening to music. The ventral striatum, amygdala, anterior cingulate, and auditory cortices are involved in processing highly emotional musical selections (Blood et al., 1999; Blood and Zatorre, 2001). Also, novel musical stimuli heard for the first time, without any therapeutic goals, can elicit strongly positive feelings and limbic activation, just as familiar favorites do (Brown et al., 2004).

A great number of studies have demonstrated how music affects various bodily parameters (Krumhansl, 1997; Pratt and Spintge, 1996), with abundant brain effects that vary across individuals (Janata, 2005), with different levels of musical training (Koelsch et al., 2005), and with respect to the emotional content of music (Panksepp and Bekkedal, 1997). For instance, Sammler et al. (2007) have shown that the valence of perceived emotions differentially influence EEG power spectra and heart rate (HR). Unpleasant music evoked significant decreases of HR, whereas pleasant music was associated with an increase of frontal midline theta power. Since music exerts abundant effects on subcortical brain systems, it can influence diverse psychological and physiological states of the organism (Hesse, 2003; Panksepp and Bernatzky, 2002), including the brain mechanisms by which biological rewards are processed (Zatorre, 2003). Concurrently, structures associated with the endocrine system are also influenced (Kreutz et al., in press; Stefano George et al., 2004). Stefano and colleagues have shown that music listeners exhibit changes in relevant plasma signaling molecules consistent with the physiological changes associated with the reported actions of music, i.e. lower blood pressure. In their experiments with calming and relaxing music, a statistically significant increase in subjects in the music group compared to the controls was found for Inteleukin-6 (IL-6), a slight elevation of Morphine 6 glucuronide levels, while IL-1, IL-10 and cortisol values remained unchanged.

In short, there are many possibilities to consider, none of which have been worked out in any detail. In the absence of any evidence for any one critical factor, we would suggest that the most general effect might be through the regulation of painful feelings, whether physical or mental, through some of the main affective molecules of the brain. Prominent among these would obviously be brain opioids, which not only control physical pain but also the pain of social loss (for recent summary, see Panksepp, 2011). A link has been made to the modulation of endogenous opioids by music, as perhaps reflected in the psychophysiological response of chills during especially moving music (Goldstein, 1980; Panksepp, 1995). In addition, endogenous opioids are low in subjects in states of psychological pain such as depression (Watt and Panksepp, 2009; Zubieta et al., 2003). Thus, an intriguing possibility is that many of the beneficial effects of music reflect not only the emotional shifts in brain dynamics, but perhaps even more specifically the changes in distress regulating chemistries of the brain such as endogenous opioids.

A comparable case could be made for oxytocin, another chemistry that powerfully regulates social emotional processes (Panksepp, 1992, 1998) as well as the stress axis and various bodily parameters that are overactive in stress (Uvnäs-Moberg, 1998). One of the shortcomings of music-medicine research is that appropriate animal models for simulating some of the effects of music are not available. However, we would here note that exposing young chicks to music can highly reliably evoke very distinct behavioural effects and some biochemical changes in the brain of the chick (Bernatzky et al., 1997, 1998). For instance, practically any form of music will induce young chicks to laterally flick their heads, to flap their wings more than normal, and to yawn; remarkably, these same exact

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effects can be evoked by administration of oxytocin (or vasotocin, the avian form of this nonapeptide) into their ventricular systems (Panksepp, 1992). This suggests that the music may be releasing vasotocin in their brains. This is also suggested by the observation that music can reliably reduce separation-distress vocalizations in chicks and that both oxytocin and vasotocin very strongly reduce separation distress (Panksepp, 1998; p. 270, Figs. 14.8 and 14.6, respectively). Although we have never been able to convincingly demonstrate that young chicks enjoy human music, the above effects were so clear that we tried to evaluate whether the available oxytocin receptor antagonists might block the above behavioural effects of music in chicks. Regrettably, their vasotocin receptors are sufficiently different from mammalian oxytocin receptors that the available mammalian oxytocin antagonists exhibited no potency in blocking avian vasotocin receptors. Thus, the above speculations about the medically beneficial effects of oxytocin remain hypotheses for future research.

11. Conclusions

Music holds considerable promise as an adjuvant pain management therapy and in mild cases may be used to supplement, perhaps even replace, pharmaceutical interventions before, during, and after painful procedures. Indeed, as part of a multimodal pain management program, music therapy may find a place in surprisingly diverse medical settings. Thus, music as therapy has three positive characteristics: First, because music acts upon the central nervous system, specifically the deeper, more ancient parts of the brain such as the limbic system including rewarding regions such as the nucleus accumbens, and, its effects are generalized and widespread. Music's effect on many brain regions may also help activate self-repair mechanisms found throughout the brain and body that may also promote healing and mental health (Kream et al., 2010). Second, music can be used to reduce, and at times even supplant pharmaceuticals, which can reduce the cost of medical care. Third, music therapy has fewer side effects and can, therefore, be easily incorporated into a multimodal pain management program.

For future studies, it would be useful to know how long the mood effect of music persists and how specific mood changes that are specific to music are mediated (Panksepp, 1992; Panksepp and Bernatzky, 2002). A key goal should be identification of the neurochemical changes that mediate pain alleviation and other psychological effects. An example of how this can be done was in the way we pursued pre-clinical models of Auditory Integration Training for autism to try to identify how such music based treatments help autistic children (Bernatzky et al., 1997, 1998). Administration of the same treatment that autistic children were receiving to young chicks demonstrated dramatic elevations of brain norepinephrine (NE) turnover which could have easily promoted better attention since NE consistently promotes attention in animal studies. Also, as already noted, there are converging reasons to believe that music can release opioids in the brain (see Goldstein, 1980; Panksepp, 1995). Endogenous opioids have many beneficial effects in the body: it seems that ultra low doses of naltrexone, an orally available opiate receptor antagonist, can promote changes (perhaps resilience) in endogenous bodily opioid activity that can have widespread bodily and psychological effects (Brown and Panksepp, 2009). The same can be said for oxytocin (Panksepp, 1992; Uvnäs-Moberg, 1998).

Perhaps music can establish a desirable level of homeostasis in many bodily organ systems, for it is a powerful way to stimulate positive social feelings, a major factor in human happiness and well-being (Sheldon et al., 2011). Indeed, perhaps music tends to make people more social in general (Malloch and Trevarthen, 2009), for it is a well-established fact that music simply attracts people to join others in social groups. And the well-established placebo effect, which is, at least in part, mediated by brain opioid release, may reflect the fact that feelings of social support and warmth are, at least in part, mediated by brain opioids (Panksepp, 1998, 2011).

But we should also remain mindful of negative characteristics that may accompany music therapy. Most of these characteristics are due to the relative newness of the treatment in modern medicine. Without a history or an accumulation of much medical evidence, music therapy lacks guidelines, a lack which can lead to uneven application, poor compliance, and high expectations. Nor are the long-term effects of music therapy known. Obviously, to play music that does not appeal to a patient, even irritates that patient, is unlikely to be beneficial. Perhaps individually-chosen music may have better inhibitory pain-reducing effects, but that has not been adequately evaluated, and does not seem to be the case in music-assisted treatment of psychotic disorders (Silverman, 2003).

Taken together, these negative characteristics point toward the need for more and better research (see also Cepeda et al., 2006; Gold et al., 2009). Randomized, controlled studies with humans which provide clues to the biological pathways that mediate the effects of music therapy are needed for understanding the brain-body causal mechanisms involved, but obviously much of that cannot be easily accomplished without animal-models, which have been entertained so far (Panksepp and Bernatzky, 2002; Panksepp et al., 1980) but not systematically implemented in this area (but as we noted in the previous section, there are intriguing possibilities). With preclinical studies, neuroscientists could more effectively seek the physiological basis for these effects and from this knowledge generate more effective therapies. In sum, although there is increasing evidence of the effectiveness of music therapy for the treatment of various somatic and psychiatric problems, the mechanisms of the therapeutic effects remain largely unknown (Hillecke et al., 2005) although obviously the best place to seek answers is the brain.

As this paper has highlighted, one of the richest areas of exploration for the recommended studies is pain relief during the pre-, peri-, and postoperative periods. We suspect that many of the effects are due to relatively direct modulation of limbic emotional circuits with its many accompanying neurochemical effects (e.g., Blood et al., 1999; Blood and Zatorre, 2001), which may help distract people from negative feelings, modify levels and direction of vigilance, and modify the influence of past memories associated with pain. Within this conceptualization, we can easily imagine hypothalamic effects that inhibit brain corticotrophin releasing factor which would attenuate arousal of the body's pituitary–adrenal stress axis, promoting relaxation, which may automatically disrupt the pain-stress-pain feedback loop and alters the perception of pain—e.g., through activation of brain opioid and oxytocin systems.

Music may be most effective when combined with other treatment modalities. There is preliminary data suggesting that these effects can be reinforced by a combination of music and guided relaxation (Bernatzky et al., 2007; Miller et al., 2002). Ultimately, repeated application of music therapy, though both direct and learned effects, should enhance these endogenous mechanisms and this conditioning may lead to a development of competence and to a reduction of helplessness. In most cases the goal of this type of treatment cannot be expected to be complete elimination of pain and stress but rather the facilitation and management of relevant body–brain systems that help restore functionality (Nadler, 2004). Music therapy appears to be a simple, effective means of promoting these psychosomatic benefits. Such effects need to be better understood, but so far, long-term evaluation of music therapy in pain management has demonstrated improved quality of life parameters along with reduced consumption of analgesics. Likewise, in

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depression the long-term application of music therapy is more effective than short-trials (Maratos et al., 2008), and for certain problems, music therapy may compete effectively with certain psychotherapeutic maneuvers, but in combination they can synergize (Silverman, 2008).

Of course, one of the most practical aspects of music therapy is its innocuousness. With few to no side effects, this treatment can be used in diverse settings where the inclusion of pharmaceuticals is risky or unwise. Moreover, music therapy can be added to other therapies with little concern for negative interactions, and increase our understanding of the dynamic, complex connections between the mind, the brain, and the body. The possibility of turning our attention from ever increasing incidences of adverse pharmaceutical interactions to positive mind–body interactions, including the increasing use of positive social interactions and empathy, not to mention ever increasing use of mindfulness practices (Kabat-Zinn, 2003; Siegel, 2007), could be a productive use of increasingly limited financial and human resources in the increasingly expensive therapeutic techniques and practices of modern medicine. Once the phenomenology of such maneuvers is better documented, the challenge for neuroscience will be to unravel the underlying dynamics by which benefits are instantiated.

Clearly the synergistic relationship between music, emotion, and pain has the potential to be harnessed for human benefit, especially in the realm of pain management. As life expectancy has increased and once-fatal diseases have become chronic conditions, palliative care has become an important healthcare concern. Of particular interest here is the challenge of postoperative pain, which continues to trouble both patients and healthcare providers despite a variety of treatments including systemic and regional analgesia techniques (Laubenthal, 2007; Pschowski and Motsch, 2008). Appropriate pain management is still not available to the majority of patients (Breivik et al., 2006). Compounding the lack of effective pain management techniques is a dearth of peer-reviewed information on the efficacy of non-pharmacological management of pain (Nadler, 2004). In light of the need for additional techniques for pain management, the use of non-pharmacological therapies such as acupuncture, relaxation, music therapy, hypnosis, and transcutaneous nerve stimulation as a supplement, and at times a substitute, for conventional analgesic therapies, need to be more seriously considered as a viable means of achieving effective perioperative pain management. And music, as a noninvasive therapy with essentially no side effects, could be crafted into a useful non-pharmacological intervention for pain management.

The study of the effects of music on the brain is just beginning. Because of its uniquely powerful emotional qualities, we can anticipate that a fuller understanding of the neurochemical changes in the human brain that are "moved" by music, surely endogenous opioids, oxytocin and various biogenic amines, will also give us a better understanding of how higher-order emotions are organized in the human brain. Such knowledge has the potential to bridge between our understanding of the cross-mammalian primary-process emotions that are best illuminated through brain research on other animals (Panksepp, 1998) and the higher order tertiary-process emotional adjustments that are currently of greatest interest to those who study emotions in the human BrainMind. Music brings them together intimately within the brain. Humans could do the same on the playing fields of science.

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