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Isn’t there room for music in chronic pain management?

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Abstract

Chronic pain with its comorbidities, such as depression, insomnia, and social deprivation, is a major cause of disability and health-economic burden. Insufficient response to pain medication and potentially serious adverse effects have led the majority of chronic pain patients to seek relief from non-pharmacological remedies. Along with this trend, pain research has paid increasing interest in critical evaluation of various complementary treatments. Music-based treatments have emerged as an efficacious and safe means to enhance the management of acute and chronic pain. We review the current position of music-based interventions in the treatment of chronic pain and present explanations for the analgesic effects of music through modulation of the primary nociception and discuss the contribution of the mesolimbic dopaminergic system to the affective component of pain perception. We propose ways to translate the novel theoretical understanding into clinical practice in different health care settings, primary health care in particular, and discuss the preconditions of successful implementation. We argue that music interventions provide low-cost, easily applicable complementary pain treatments not requiring heavy utilization of health care resources. Finally, we provide research and quality improvement frameworks and make suggestions to cover the gaps of existing evidence.

Perspective

This article addresses the current evidence for analgesic effects of music interventions, discusses its neurobiological basis and evaluates potential use of music in treating chronic pain patients in different health care settings. We also propose directions for future research to cover shortages in the currently published data.

Keywords: chronic pain, neuropathic pain, music-induced analgesia, music interventions, music

Introduction

Chronic pain affects over 40 per cent of the general population and is recognized as an extensive problem in the community[10,11], with combined direct and indirect costs exceeding half a trillion dollars per year in the US alone[21]. In the Global Burden of Disease study[53], chronic pain emerged as one of the leading causes of disability. It also has a clear impact on employment: 19 per cent of patients with chronic pain report having lost their job and 29 per cent have changed their entire job or job responsibilities because of the pain[7]. Additional socio-economical dimensions of chronic pain include comorbidities, such as depression, insomnia and anxiety, and imminent risk of dependency on opioids.

Opioid medication, even when prescribed for severe refractory pain by strict medical indications, not infrequently leads to adverse effects, and in worst cases induces hyperalgesia, i.e. activates pronociceptive pathways resulting in central sensitization to pain[8]. Opioids also modulate the reward circuit of the brain, predisposing the patient to prolonged opioid use, in some cases to abuse, overdosing and addiction. The result is a vicious pain cycle, much the opposite to the intended goal. Most pain patients receive pharmacotherapy, but despite the wide array of medical treatments, 46 per cent still experience constant pain and report inadequate analgesia[4,7]. Indeed, 69 per cent of patients with chronic pain report using non-drug remedies to treat their pain[7]. Along with this trend and due to the health-economical factor, increasing interest among pain scientists has been focused on non-pharmacological treatments[34]. Obviously, the optimal management of pain calls for multifaceted strategies based on critical evaluation of efficacy and safety. Here, our goal is to review the literature on music interventions for chronic pain and to propose ways to translate the theoretical understanding into clinical practice in primary health care. We discuss the preconditions of successful implementation and provide a series of questions to map the relation of an individual patient to music to promote personalized music-based interventions in treating chronic pain. Finally, we propose research to cover the gaps of existing evidence and to provide a basis for quality improvement of chronic pain practice performance through music interventions.

Music emerging as a means to manage chronic pain

The unmet needs of patients with chronic pain have raised the demand to pursue new cost-effective, safe, easily applicable, and customizable treatments, both independent of and complementary to traditional treatments. Earliest reports on use of music in procedural anesthesia and analgesia were published over half a century ago[39]. A study from 1960 reported music and noise to be effective in suppressing acute pain during dental procedures[14]. In 2015, Jenny Hole and colleagues reported in *The Lancet* their meta-analysis[20] of 72 randomized controlled trials (RCTs), showing that perioperative music listening significantly reduces postoperative pain and anxiety, and use of analgesics, as well as increases patient satisfaction. Another meta-analysis published in 2020 revealed that music interventions significantly reduce opioid requirement, improve the outcome of surgical patients and potentially reduce medical costs[12].

Studies on the effects of music interventions on chronic pain were first reported in the 1990s[33,44]. Since then, growing research evidence suggests that music may be beneficial in treating patients with chronic pain. In 2017, Eduardo A. Garza-Villarreal and colleagues reported a meta-analysis[15] of 14 RCTs showing that music reduces chronic pain in general, as well as anxiety and depression, regardless of the etiology of the pain. It is noteworthy, that in 79 per cent of the studies showing efficacy of music on chronic pain, the intervention was mere music listening that could be implemented in clinical practice with minimal costs. Even higher analgesic effect was achieved by listening to self-selected music.

Pain network and music network of the brain

Processing of chronic pain and associated secondary disturbances in the brain involves a network defined by areas of somatosensory, insular and cingulate, as well as frontal and posterior parietal cortex, which functionally consist of both sensory-discriminatory and affective and cognitive-evaluative components[13,50]. This network, rather than being strictly specific for pain, may represent a general mechanism by which we detect, focus attention, and respond to any salient stimulus. The ascending spinothalamic tracts, both nociceptive and non-nociceptive, and the descending inhibitory system modulate the perception of pain[50] (Figure 1). Further modulation is

provided by multiple central processes affecting the pain experience: previous experiences, fears and expectations contribute to the affective characteristics of pain and guide the interpretation of its meaning and intensity[6]. Chronic pain may induce severe anxiety and thereby decrease functional ability irrespective of the pain intensity[23]. Anxiety often precedes the pain onset, whereas depressive disorders usually follow the pain[23].

Music-induced analgesia has been demonstrated in healthy participants exposed to experimental pain[31,32,41,42] and in patients with acute[20] and chronic pain[15,16]. Yet, the mode of action of music on pain has remained elusive until recently. Functional neuroimaging evidence suggests that music-induced analgesia relates to its capability to modulate the descending pain modulatory system as well as the emotion circuitry[25] of the brain (e.g., amygdala, cingulate cortex)[2,9,38,51]. Functional and structural neuroimaging studies in healthy subjects have provided evidence for large-scale involvement of bilateral network in the neural processing of music, comprising, for example, somatosensory and prefrontal areas, amygdala and cingulate cortex as well as the insula[24,48,49,55,56], all of which overlap strongly with the pain network (Figure 1).

Beyond directly modulating nociceptive mechanisms, music may ease off pain by ameliorating anxiety and depression (Figure 1). Subjectivity is clearly an important factor for these effects: neuroimaging studies have shown that pleasurable music strongly activates the brain reward system by stimulating the mesolimbic dopaminergic circuitry and release of dopamine, which correlates with the intensity of the listener´s experience[55]. In chronic pain, reduced dopaminergic activity has been hypothesized to mediate increased pain[50]. In turn, self-selected music has been shown to be the most efficient in reducing pain and depression[15], feasibly through stimulatory effects on the dopaminergic circuitry[55]. Similar effects have been observed in healthy subjects whose mental health has been shaken during the COVID-19 pandemic. Data from over a thousand individuals revealed that musical leisure activities mitigated depression and enhanced well-being during the pandemic[30]. Listening to music may also provide distraction[26] and sense of control[6], both of which can decrease pain via the descending pain modulatory system. Finally, a systematic review concluded that music may improve sleep[22], disturbances of which are part of classical symptom triad in patients with chronic pain[7].

It seems obvious that the analgesic effects of music cannot be fully dissected apart, that is, music most likely ameliorates pain through multiple functional levels[27], including cognition – diverting the patient's attention to a competing stimulus, and emotion – inducing pleasure and positive emotions. Structurally this correlates with modulation of pain network by overlapping music networks (Figure 1). This provides the opportunity for more individually tailored music interventions in treating chronic pain. In conclusion, it is easy to imagine that a drug with similar efficacy and safety would be widely used in treating patients with chronic pain.

From research to practice - preconditions of successful implementation

Common clinical experience is that music interventions or music therapy are only rarely included in pain treatment plans and are offered mostly for patients in pediatric neurology units[45]. Yet, music interventions have emerged as promising rehabilitation strategies in several other neurological diseases during the past decade[47] and have been included in the current American guideline for adult stroke rehabilitation and recovery[54] and in the British guideline for management of dementia[35]. In these neurological entities, music improves mood and ameliorates depression[47]. Despite the increasing evidence for analgesic effects of music, the medical profession has been slow to reap and capitalize on its benefits. Music should not be seen as a substitute for pharmacological or other non-pharmacological treatments, but rather as part of holistic pain management that, when implemented, could improve its quality (Figure 2). Music may modulate factors that usually are beyond the reach of conventional drug therapy, such as fear and catastrophizing.

Overcoming the translation barrier from research knowledge to clinical practice is a challenge. From the patients´ point of view, music interventions as part of chronic pain management should ideally be provided close to their home. Yet, implementation of novel treatments takes effect in academic pain centers, which in most health care systems do not offer long-term rehabilitation services. Primary health care takes the main responsibility of chronic pain management and would be a natural implementer of music interventions, which do not require major investments or heavy utilization of health care staff resources. A nurse specializing in pain management would be an optimal actor between the doctor and the patient to

provide continuity in supervision and encouragement. Music-based rehabilitation should be systematically offered to the patients and in willing cases be incorporated in the treatment plan. There is no validated clinical questionnaire for individual mapping of potential benefits of analgesic effects of music-based interventions observed in study cohorts. While a formulation and validation of one should be of future research interest, to support the implementation, we have outlined a series of questions mapping the parameters of music that should be considered and might be suitable for a particular patient (Table 1). Examples include both passive and active formats, such as daily music listening hours, music-guided motion or dancing, singing or instrument playing, or musical group activities tailored to the patient's condition. While music listening or singing are accessible to most pain patients, instrument playing might not be a viable option for patients with widespread pain, reduced grip strength, osteoarthritis, or malposition. When applicable, instrument playing, singing and dancing might support physical rehabilitation.

Collaboration with parties outside the health care system (e.g., social services, community colleges, volunteers) might be worthwhile. Pleasurable musical activities in groups, for example choir singing, could provide additional benefits by offering livelier social integration and peer support, to compensate for social limitations and imminent isolation[7] (see Figure 1). It is clear that the effects of a single or sporadic music treatment are limited, wherefore music should become a part of regular self-care. Optimal effective dosage of music for pain patients has not been investigated, although in several studies on other patient groups even a short daily exposure (15 min to an hour) has been sufficient to result in measurable responses[47].

Implementation of music interventions in a hospital setting meets further requirements, particularly for patients with low level of consciousness or cognitive decline. Music preferences should be easily ascertained by interviewing the patient or relatives. Incorporating music listening in ward routines and treatment procedures requires careful consideration[52], since interventions must not hamper or disturb communication of the personnel. Interestingly, music is frequently played during surgical procedures, and some research evidence suggests facilitation of the surgeon´s operational work by surgeon-selected music[1,37]. A question to be resolved is whose preference decides the music selection.

It should be borne in mind that patients' individual music attribute preferences may significantly differ: The patient's preferred music might feature low (e.g., gentle and sensual) vs. high (e.g., strong and tense) arousal, negative vs. positive valence, and different levels of depth (emotional intensity, complexity of music)[18], all of which could influence different analgesic mechanisms (e.g., distraction, relaxation, dopaminergic activity)[5]. In general, listening to preferred music seems to be more effective in reducing pain intensity and increasing pain tolerance[5]. The patient's affective response to the music, not the music itself, seems crucial to the level of music-induced analgesia, not the music itself. Therefore, while patients' preferred music will provide valid and natural starting point for utilizing music in chronic pain treatment plans, it would be beneficial to consider music attributes in the axes of arousal, valence, and depth to achieve the optimal outcome. If the desired outcomes are not achieved in the follow-up, choosing music with different attributes is encouraged.

Beyond music attributes, the social dimension of music might play a significant role in music-induced analgesia. Group-based interventions could provide analgesic benefits beyond the reach of individual treatments, as shown for healthy subjects: group singing elevates oxytocin levels and mood compared to individual singing[17]. These effects could provide important additions in modulating pain experience in patients with chronic pain. In ideal world, both individual and group-based interventions would be carried out by a certified music therapist. This could possibly further amplify the beneficial effects of music[28], owing to the therapeutic relationship considered as common and crucial mechanism of change in psychotherapy practice. A music therapist could also help adapt treatments and accomplish individualized analgesic goals within a therapeutic relationship or deliver music-based interventions in a group setting, when appropriate. However, the reality is that music therapists are not routinely available in pain-treating units and their recruitment may counteract the argument of music-based treatment being cost-effective. Yet, music therapist as a consulting supervisor of the regular pain treatment team would be a worthwhile contribution to improved management of chronic pain patients.

Music interventions in pain management appear to be safe and do not require musicality, yet, they may not be suitable for all patients. Auditory hypersensitivity, migraine or other types of intense pain may diminish the tolerance to auditory stimuli. In addition, neurological musical disorders, such as amusia and musical anhedonia,

may hamper the benefits of music interventions. While the prevalence of both congenital amusia and musical anhedonia is less than 5 per cent[29,40], acquired amusia affects up to one third of chronic stroke patients[43,46], calling for assessment of these deficits, as music interventions are considered. Despite amusia, singing-based interventions evidently provide a promising rehabilitation tool for pain, as processing of vocal music seems to be, at least partly, preserved in amusic brain[48].

Future directions of research

The US Department of Health and Human Services proposal for National Pain Strategy defines effective pain management as a moral imperative, a professional responsibility, and everyone´s duty in health care professions[36]. Unambiguously, these imperatives are currently not met in chronic pain management. This is reflected in increased use of health services: 60 per cent of patients with chronic pain have seen their doctor two to nine times within the last six months, similar number of patients have suffered from pain for more than 5 years, and approximately 30 per cent of the patients report severe pain[7]. Considering the limited efficacy of prescribed pain medication and uncontrollable use of over-the-counter medication, non-pharmacological treatments that reduce the need for medication decrease the risk of adverse effects and economize health care costs.

Chronic pain can have neuropathic characteristics[19]. Evidence is still completely lacking on the effect of music on neuropathic pain. In April 2021, the Clinical Trials database (clinical.trials.gov) registered only one ongoing or upcoming study on neuropathic pain using music therapy in combination with a capsaicin skin patch. Another largely uncovered area is the primary headaches, migraine particularly.

In future research, studying music in connection with different clinical entities of chronic pain[3] should help us understand the mode of action of music in relation to mechanism-based pain classification[4]. Moreover, effects of music interventions on immunological responses, tissue recovery and prevention of pain chronification should be addressed. Longitudinal information, which is largely lacking, is needed to determine the frequency and quantity of music interventions and the long-term cost-effectiveness.

In conclusion, further studies on the effects of music interventions on pain, particularly more accurate information on its interaction with the pain network, are clearly needed. Nevertheless, even the current status of evidence strongly supports implementation of music-based treatments. They are health-economically feasible, increasingly available through telemetric/video connection, and allow tailored prescription to meet individual needs and therefore could provide a significant respond to the challenge of effective pain treatment both in the pandemic and post-pandemic world.

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Table and Figure legends

Table 1. Clinical questions mapping and promoting implementation of music-based interventions in treating chronic pain.

PAIN	1	What type of chronic pain does the patient have?	While the effects of music-based interventions have been extensively studied on chronic pain, specific management of neuropathic or nociplastic pain and headaches with music-based interventions have not been systematically studied.
	2	Does the patient report adequate analgesia?	Improve pain management plan, map depressive symptoms, reassess and adjust pain management plan as needed.
	3	Does the patient's pain change with time or associate with certain activities?	Provocation of pain by particular activities might provide a window of opportunity to focus music listening interventions. Limitations due to the cause of the pain should be considered in individual planning.
	4	Does the patient have a comorbid depression, anxiety, and/or insomnia?	Chronic pain is often accompanied with depression, anxiety and insomnia that negatively affect pain experience. Soothing music could be used to target anxiety and insomnia whereas stimulating and rewarding music could be used to target depressive symptoms in chronic pain.
MUSICAL PREFERENCES	5	What type of music (e.g., genre, mood, tempo) does the patient prefer to listen to? What music attributes are preferred by the patient?	Self-selected music seems to be more effective in treating chronic pain and different musical characteristics might provide different effects. Analyze the patient´s personal music attributes (arousal, valence, depth). For example, rhythmic music might help during exercising, whereas calm music might help relax. More rewarding music has been associated with increased dopaminergic activity.
PRACTICE OF MUSIC	6	Does the patient like to listen to music, play an instrument, sing, or dance?	While music listening might be accessible to most patients, instrument playing might not be a viable option for patients with reduced grip strength, osteoarthritis, or malposition. Yet, instrument playing/singing/dancing might support physical rehabilitation.
	7	Is the music listening passive or active?	Does the patient focus on listening to the music or is it a background activity? Music might provide distraction, help relax, support walking and exercising. Encourage active listening, if passive listening seems ineffective in amelioration of pain.
	8	What other activities does the patient usually combine with music listening?	Is it customary for the patient, for example, to listen to music, while exercising or relaxing? Is the patient, perhaps unconsciously, applying gate-control through these associated activities? Does the patient´s music listening usually occur in solitude, with someone else or in a group?
EXPERIENCE AND ATTITUDE	9	Does the patient experience pain relief when listening to music, playing an instrument, singing, or dancing?	Has the patient already utilized music in pain management? How could the response be enhanced?

	10	If the patient has not used music as a part of the pain management plan, would he/she consider trying?	Consider the patient´s own beliefs and expectations. Consider peer support in conjunction with music-based pain management. Make sure the patient understands that music-related therapies may complement, but do not replace conventional treatments. Pain treatment plans must be developed together with the patient. Uncommittable goals, objectives and interventions are likely to hamper pain management, compliance, and clinician-patient relationship.
FEEDBACK	11	In the follow-up, have music-based interventions produced the desired effects?	If positive outcomes have been achieved, encourage the patient to continue using music in pain management. If not, has there been negative outcomes? Has the patient adhered to the treatment plan? Consider revising the plan, the music attributes (arousal/valence/depth), individual/group-based format of delivery.

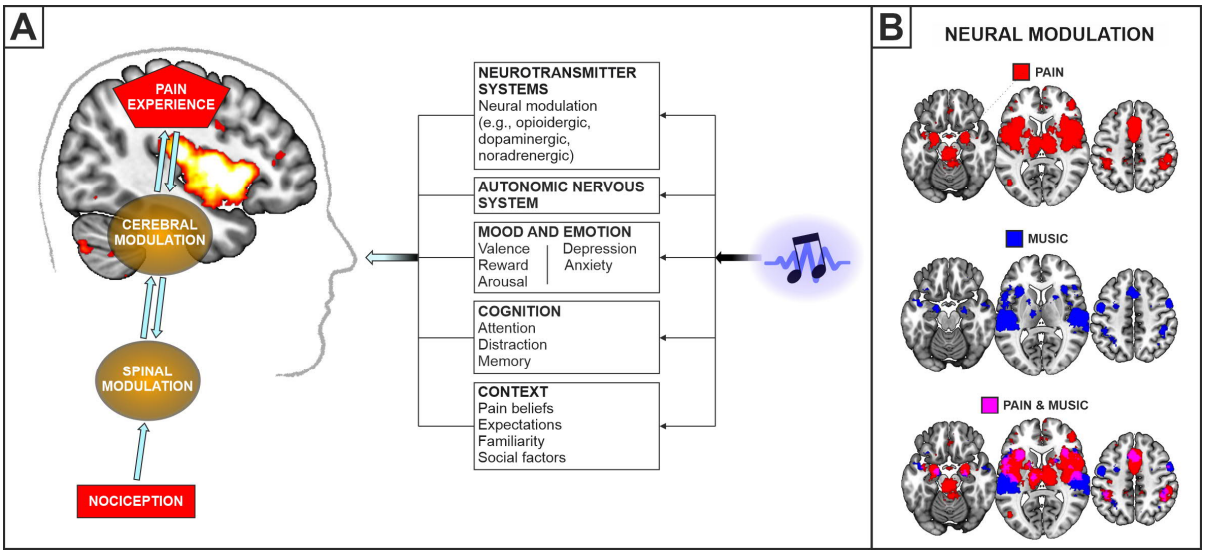

Figure 1. Illustration of the (A) main factors affecting the pain experience and influencing nociception and their suggested relation to music (adapted from the work by Lunde *et al.*[27] and Tracey and Mantyh[50]), and (B) neural overlap between the pain network and music network in the brain based on data-driven meta-analysis of fMRI studies on pain and music from Neurosynth.org.

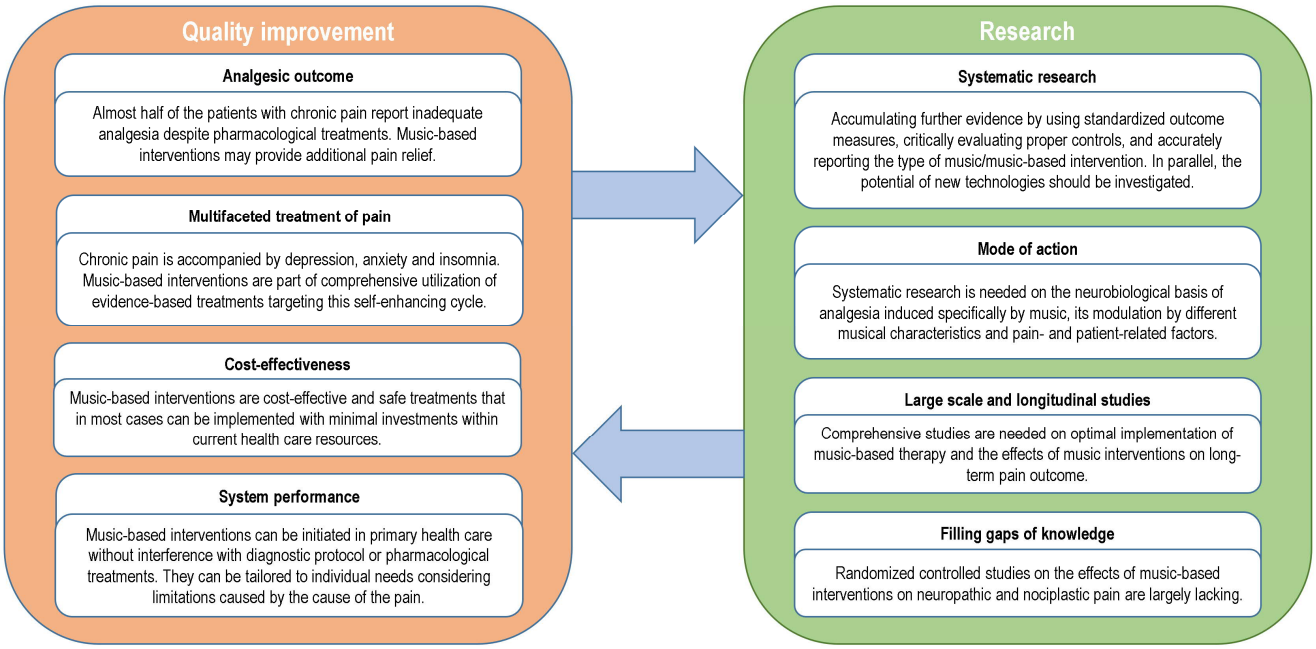

Figure 2. Quality improvement framework and research directions targeting increased implementation of music in pain management.