REVIEW

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Music and Medicine: Promoting Harmony for Health

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ABSTRACT

A multitude of clinical trials measuring hemodynamic and psychological parameters have shown the beneficial effects of music on health. However, there are no clear instructions on how to utilize the potential benefits of music to improve health outcomes. Moreover, whether the effect of music is transient or enduring has yet to be determined. To address the effect of music on vital parameters and emotional well-being of patients we provide an overview of methods and findings of some studies that have evaluated the physiological or psychological impacts of music. This review puts forward a proposed model for fostering an individualized approach that can examine the therapeutic effects of music.

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THE HISTORY OF MUSIC AND MEDICINE

Music has been an integral part of human life since the ancient past. As a powerful tool to express emotions, music has been used in the daily life of human beings for relaxation, stress reduction, dance, socialization, entertainment, ritual, and religious ceremonies.[1]

Music's effects on human health have been appealing yet controversial. The connection between music and medicine has been explored in the modern era. The combination of art and science recognizes the interconnected nature of these disciplines aiming to work synergistically.[2]

The relationship between music and physiological and psychological function was evaluated in several studies, and these studies have shown the potential but inconsistent benefits of music to improve health outcomes in various patient populations. Conclusive data are lacking, in part due to the challenges related to the subjective nature of musical preferences and the design of trials. A renewed interest in the application of music in health and raising awareness about the potential health benefits of music as a safe and non-pharmacological tool can lead to further recognition and can establish the value of music in improving health outcomes.[3]

CELEBRITIES AS ADVOCATES FOR HEALTH INITIATIVES

Medical conditions of famous individuals have resulted in greater awareness about their specific conditions. Basketball superstar, Magic Johnson publicly announced that he was affected with the human immune deficiency virus, which helped raise awareness about the condition and millions of dollars for research and therapy.[4]

The famous actress and human rights activist, Angelina Jolie revealed that she had undergone bilateral mastectomy after she was found to have a mutation in the BRCA1 gene. Her experience helped raise awareness about the importance of genetic testing for those who are at risk.[5] The pop

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star Selena Gomez publicly spoke about her diagnosis of lupus, resulting in greater awareness about how this condition can affect the body, including how it can affect the kidneys and lead to kidney failure and the need for kidney transplantation.[6]

Stevie Wonder,[7] Michael Jackson,[8] and Elvis Presley[9] were among other famous musicians who were known to struggle with medical conditions, resulting in raising awareness about specific disorders.

Toni Braxton shared her lupus journey with a team of kidney health experts and discussed lupus, kidney health, and the importance of routine testing. She is encouraging individuals with lupus nephritis to keep up with their health checks via the "Get Uncomfortable" campaign.[10]

Inspired celebrities, especially those who are involved in the music industry, can play a crucial role in raising awareness, injecting enthusiasm, and increasing funding to thoroughly evaluate the effectiveness of music. By producing solid evidence, specific guidelines can be established to apply music in health settings.

The Louis Armstrong Department of Music Therapy (musicandmedicine.org) was originally established and funded by the Louis Armstrong Educational Foundation, Inc through Mount Sinai in 1994. It applies music to improve physical symptoms and assesses the patient's unique mind-body connection, with licensed music therapists using current techniques in music psychotherapy and the management of pain and stress. [11]

CLINICAL SIGNIFICANCE

- Music may offer physiological and psychological impacts on humans.
- Establishing centers of music for health in academia can help develop inter-disciplinary approaches to unravel the power of music.
- Raising awareness about the potential health benefits of music can lead to further studies and establishing guidelines to employ music in health setting.

HOW DOES MUSIC EXERT ITS EFFECTS ON THE HUMAN BODY?

Music can induce mental and physical effects on the human body. The exact underlying mechanistic effects of music are not well understood.

The neural pathways from stimulation of the cochlea to activation of cells in the medial geniculate nucleus of the thalamus and then relayed to the primary auditory cortex (in Heschl's gyrus in the superior temporal lobe) are well identified, along with generally tonotopic organization within the primary auditory cortex.[12] Subsequent projections from the H gyrus to other cortical regions within the temporal cortex and other subcortical and limbic regions have been identified; however, there is little consensus on how these regions participate in the cognitive, emotional, and visceral responses to music stimulation[13,14]

A learned cognitive response may underpin the music effectiveness. A patriotic song may bring a sense of togetherness and boost morale. The learning process may be similar to the learning that takes place in unborn babies with exposure to their mother's heartbeats. At the molecular level, music can increase dopamine and serotonin activities and modulate cellular responses via epigenetic mechanisms.[15] Further studies are needed to understand the mechanism of action for music in health settings.

WHICH PATIENT POPULATIONS CAN BENEFIT FROM MUSIC?

A very diverse range of patient populations have been shown to benefit from music, including those suffering from cancer,[16] hypertension,[17] lung disease,[18] Parkinson disease,[19] pain,[20] depression,[21] and anxiety,[22] However the effect of music in different patient populations can be inconsistent due to different methodology in exposure to music, type and severity of the medical condition, and personal preferences. Large scale, well-conducted studies tailored to specific patient population and individual preferences are needed to establish guidelines for use of music to improve health outcomes.

MUSIC EFFECTS ON THE HEART AND BLOOD PRESSURE

An analysis of baseline electrocardiogram (ECG) of 80 healthy individuals found 4 ECG waves amplitude (RS complex and T wave of lead aVL, the R wave of lead II and maximal RS complex of chest leads) as discriminating variables among different personalities. To eliminate the effect of other variables that could change ECG amplitude with no effect on emotional personality, the investigators computed ratios of ECG amplitudes and developed ECG base index (E_k). All E_k values were lower in the group with a low emotionality score compared with the group with a high emotionality score. To validate the relationship between the cardiac signature (E_k) and music-evoked emotions, 17 healthy individuals were presented with alternating pleasant and unpleasant musical excerpts, with time durations ranging between 45 and 60 seconds, and brain activity was monitored using functional magnetic resonance imaging (fMRI). Brain activity in the structures known to be involved in the processing of emotion to either pleasant or unpleasant excerpts was related to E_k. The results suggested that higher E_k values (measured before fMRI) were significantly correlated with stronger emotional response in amygdala ($P < .0001$, $r = 0.68$) and hippocampal formation ($P < .0005$, $r = 0.42$) in response to pleasant vs unpleasant music.[23] Further studies are required to explore the relationship of music-evoked emotions and physiological effects and to develop objective methods to measure the response to music.

Music evoking higher level of emotional arousal can lead to increased heart rate (HR) and respiratory rate (RR) by activating the sympathetic autonomous nervous system through its effect on the cortical fore-brain structures involved in emotion, including the hypothalamus and amygdala. Tranquilizing music, alternatively, can decrease the HR by activating parasympathetic autonomous nervous system.[14,24,25]

During musical frissons (involving shivers and piloerection), both HR and RR increase.[26] Moreover, HR and RR tend to increase in response to music compared with silence, and HR appears to decrease in response to unpleasant music compared with pleasant music.[27]

One study of 37 subjects who had well-controlled hypertension found that music as an auditory stimulus has a synergistic influence on heart rate dynamics with antihypertensive medication. The intervention in the experimental group was the music playing for 60 minutes at the same intensity after oral antihypertensive medication administration. Reduced values of resting HR in the interventional group (P = .0014) were found in comparison to the control group.[17]

Antihypertensive medications had more intense effect on HR when combined with music intervention compared with the control condition. This effect may be related to the parasympathetic nervous system; however, antihypertensive class is not discussed in this study.

A randomized controlled study examined the change in heart rate from baseline for a group listening to music vs a control group with no music intervention. Sixty subjects were randomly assigned to 3 groups of 3 music types for 25 minutes duration of listening: Mozart, J. Strauss, and ABBA. A significant decrease in heart rate across all 3 music types was noted compared with baseline (Mozart − 5.6 ± 9.8 bpm with 95% confidence interval [CI], − 8.2 to − 3.1; Strauss − 4.7 ± 9.3 bpm with 95% CI, − 7.1 to − 2.3; ABBA − 3.0 ± 7.4 bpm with 95% CI). The effect on lowering the heart rate was greater in Mozart's and Strauss' music compared with ABBA's music (baseline vs Mozart P < 0.001; baseline vs Strauss P < 0.001; baseline vs ABBA P = 0.003).[28] The relevant factors for a positive effect were music piece with a high degree of periodicity, music popularity, a pleasant key, a catchy melody line, few changes in volume or rhythm, the absence of sung words, and harmony sequences that are not rousing.[28] A significant decrease in systolic blood pressure (SBP) was found when listening to music by Mozart (4.7 ± 8.6 mm Hg, P < .001, 95% CI, − 6.9 to − 2.5) and Strauss (3.7 ± 9.2 mm Hg, P = .003, 95% CI, − 6.1 to − 1.4), but no relevant changes were seen with ABBA (1.7 ± 8.8 mm Hg, P .151, 95% CI, − 3.9 to 0.6). Decrease in diastolic blood pressure (DBP) was equally significant after listening to Strauss and Mozart (P = .004), but not changed after listening to ABBA.[28] A meta-analysis review investigated the effects of music in hypertensive patients.[29] The results showed a significant reduction (P < .0001) in SBP by an average of 6.58 mm Hg. A reduction of 5 mm Hg has been associated with a 13% reduced risk for stroke.[30] Further studies are needed to assess the long-term effects of music on blood pressure control.

MUSIC EFFECTS ON RESPIRATORY FUNCTION

Intubated patients on mechanical ventilation in the intensive care unit (ICU) usually have high levels of stress and anxiety, which can contribute to patient-ventilator dyssynchrony.[31] Patient-ventilator dyssynchrony is defined as a mismatch between the patient's neural breathing and demand flow by the breathing rate and volume that the mechanical ventilator is delivering to the patient. It can lead to serious complications such as hypoxia, barotrauma, discomfort, and prolonged mechanical ventilation, which may lead to poor outcomes in ICU patients.[31] Analgesic medications are often prescribed to mechanically ventilated patients to reduce pain and anxiety and promote ventilator synchrony; however, these treatments have multiple adverse effects such as bradycardia, hypotension, immobility, gut dysmotility, weakness, and delirium when given at high doses for prolonged periods.[31,32] A randomized controlled trial enrolling 373 patients from 12 ICUs in the United States tested whether listening to self-initiated patient-directed music can reduce anxiety and sedative exposure during ventilator support.[33] Reduction in anxiety in the patient-directed music experimental group was shown compared with usual care. The patient-directed music group had also reduced sedation intensity (β = −.18 (−.36, −.004), P = .05) and reduced sedative frequency (β = −.21(−.37, −.05), P = .01) compared with the standard care group. More studies are required to evaluate the effects of music on mechanical ventilation in critically ill patients. In addition to potentially improving clinical outcomes, use of music in ICU setting may be beneficial from a cost effectiveness standpoint.

MUSIC EFFECTS ON PAIN RESPONSE AND MOOD

In a crossover study of 400 patients in Turkey, effect of listening to music during shock wave lithotripsy on the patient's pain control, anxiety levels, and satisfaction was examined.[34] Patients undergoing 2 sessions of shock wave lithotripsy were divided into 2 groups: one group listened to Turkish folk, classical, popular, or slow music for the first session but not in the second, and the other group listened to music in the second session but not the first. In both groups, the State-Trait Anxiety Inventory-State Anxiety score and Visual Analog Scale pain scores were lower in the music listening intervention session (P < .001). The use of music in this clinical setting showed increased patient compliance and reduced analgesic requirements during procedures (Table 1).

STUDIES WITH MUSIC IMPACTS ON PATIENTS WITH KIDNEY DISEASES

Music therapy may be an alternative therapy to reduce anxiety and depression in chronic kidney disease patients beside

Table 1 Studies of Music Effects on Biometric and Psychological Measures from Different Geographic Regions

Biometrics Psychological Measures	Author	Geographic Region	Genre	Findings
Electrophysiological cardiac activity	Koelsch et al, 2007[23]	Germany	Unpleasant or pleasant excerpts	*Significant correlation between EK values and changes to left amygdala and the hippocampal formation
Heart rate	Koelsch and Jancke, 2015[27]	USA, Europe	Not specified	↑ HR to musical frissons ↓ HR to unpleasant music ↑ HR to exciting music compared with tranquilizing music
	Trappe and Voit G, 2016[28]	Germany Brazil	Mozart, Strauss, ABBA Instrumental music	↓ HR* ↓ HR*
Blood pressure	Do Amaral, et al, 2016[29]	Turkey	Classical music	↓ SBP* and ↓ DBP*
	Trappe and Voit, 2016[28]	Germany	Mozart, Strauss, ABBA	↓ SBP* and ↓ DBP*
Respiratory rate/activity	Koelsch and Jancke, 2015[27]	USA, Europe	Not specified	↑ RR increased to exciting music compared with tranquilizing music ↑ RR during musical fissions
	Laczika K, et al, 2013[35]	Austria	Classical Music; Mozart's Piano Concerto No. 14, KV 449	Respiratory coupling between music, musicians and listening audience, creating respiratory synchronicity between participants
Anxiety and depression	Jasemi et al, 2016 [36]	Iran	Relaxing light music (sea, rain and water sound)	↓ depression* ↓ anxiety*
	Chlan et al, 2013 [33]	USA	Relaxing instrumental music (piano, harp, guitar, and Native American flute)	*↓ Visual Analog Scale anxiety scores for patients on mechanical ventilators ↓ sedative intensity for patients on mechanical ventilators *↓ sedative frequency for patients on mechanical ventilators
Pain	Akbas et al, 2016 [34]	Turkey	Turkish folk, classical, popular, or slow music	↓ STAI-SA anxiety* ↓ VAS pain scores*

DBP = diastolic blood pressure; HR = heart rate; RR = respiratory rate; SBP = systolic blood pressure; STAI-SA = State Trait Anxiety Inventory-State Anxiety; VAS = Visual Analog Scale.
*Significant finding.

conventional pharmacological and non-pharmacological treatments.[37]

A randomized controlled study on chronic kidney disease patients receiving conventional care in hemodialysis clinics evaluated the therapeutic effect of music on anxiety and vital parameters, including SBP, DBP, HR, RR in 60 patients.[38] The experimental group received a classical song for music selection; it was played on individual headphones for 30 minutes, after the first 30 minutes of dialysis. State anxiety was evaluated in both groups by the State-Trait Anxiety Inventory. The experimental group scored lower on the state anxiety scale after the intervention, whereas the control group had virtually no change in their anxiety score; between group comparisons showed a significant difference ($P = .03$). A comparison between the two groups demonstrated that the reduction levels in HR and RR were lower in the experimental group vs control group ($P = .007$ and $P = .01$, respectively). The reduction levels of SBP and DBP were comparable between groups. However, the study was limited due to the small sample size.

Another study of 60 patients with end-stage kidney disease on hemodialysis evaluated the effect of self-selected music on anxiety and perceived pain.[39] The experimental group listened to self-selected music through a personal portable music device for the duration of the hemodialysis; anxiety (State-Trait Anxiety Inventory) and pain questionnaires (McGill Pain Questionnaire) were taken before and after dialysis treatment. A decrease in state anxiety score was noted in the experimental group, and an increase in state anxiety score was noted in the control group. There was a significantly higher perceived pain intensity in the control group before and after dialysis ($P < .001$), whereas the experimental group did not have within-group differences, supporting the effectiveness of preferred music listening.

Table 2 Music Therapy and Patients on Hemodialysis Treatment

Country	Authors	Genre	Duration and Timing of Treatment	Physiological and Psychological Findings for Music Therapy Group
Turkey	Koca and Kutlu, 2014 [42]	Turkish art music (violin and piano)	30 minutes of listening time at the beginning of the third hour of dialysis treatment	↓ perception of pain* ↓ nausea scores
Greece	Pothoulaki et al, 2008 [39]	Patient Preferred Music from genres: popular music, Greek folk music, ethnic music, jazz, classical, soundtracks from films, and new age music	Entire duration of dialysis treatment	↓ scored anxiety*
Spain	Melo GAA et al, 2018 [38]	Soft classical song, "Spring" from Vivaldi's *Four Seasons*: low amplitudes, simple and direct rhythms, and frequencies of ≈ 60 to 70 beats per minute	30 minutes of listening time within the first hour of dialysis treatment	↓ state anxiety score* ↓ HR* ↓ RR* ↓ SBP and ↓ DBP
Brazil	Hagemann et al, 2019 [40]	Music therapist — guitar and vocals	75 minutes, twice a week	↓ intensity of depression symptoms* ↑ QOL scores*
Taiwan	Lin et al, 2012 [41]	Patient-preferred music	Entire duration of dialysis treatment (4 hours), 3 times a week	↓ frequency and severity of adverse reactions* ↓ RR* ↑ oxygen saturation* ↑ finger temperature*
Italy	Burrai, et al, 2019 [43]	Live singing by trained musical vocalist	15 min of live singing during 6 consecutive hemodialysis sessions	↓anxiety and depression ↑quality of sleep ↓pain, itching, and cramps

DBP = diastolic blood pressure; HR = heart rate; QOL = quality of life; SBP = systolic blood pressure.
*Significant finding.

A music therapy intervention on 23 hemodialysis patients was conducted, where participants attended 2 weekly 75-minute music therapy sessions consisting of guitar and vocals performed by a music therapist for a month, totaling 8 sessions.[40] Participants were divided into groups of 4 and evaluated for depression symptoms and quality of life (QOL) before and after the intervention. There was a decrease in intensity of depression symptoms ($P < .001$) and improvement of QOL scores: functional capacity pain, general health, vitality, mental health, symptom problem list, and overall health.

Another study conducted a randomized controlled trial of 88 maintenance hemodialysis patients in a 1:1 ratio. The experimental group created their own music playlists during week 1 and listened to the playlist throughout each hemodialysis session on week 2. After 1 week of using music as a therapeutic intervention, there was a reduction in the frequency and severity of adverse reactions during hemodialysis ($P < .001$) and reduction in RR and increased temperature and oxygen saturation ($P < .001$)[41] (Table 2).

FUTURE DIRECTIONS

Music impacts hemodynamic measures, including RR, HR, BP, and neurologic function.[44] More studies are needed to support the efficacy of mind-body interventions as promising therapies for the treatment of comorbid physical and mental illness.

Research trials to evaluate the effects of music on health outcomes should consider music genre, duration, and even exploring new modalities for delivering music, such as use of personal portable and virtual reality devices and self-selected music through special music channels dedicated to different patient populations. It is also important to account for differences within populations, such as socioeconomic demographics, ethnicity, age, race, and sex, when interpreting study findings and music choices.

In addition to conventional pharmacological treatment, music can play a strong role as an affordable, noninvasive therapy tool to improve health outcomes. However, standardization of music interventions, music choice, delivery methods and outcome measures are among the challenges.

CENTERS OF MUSIC FOR HEALTH: AN INTERDISCIPLINARY APPROACH

Music is an easily accessible yet underappreciated tool with the potential to improve health outcomes. Establishing centers of music for health in academia and industry can help

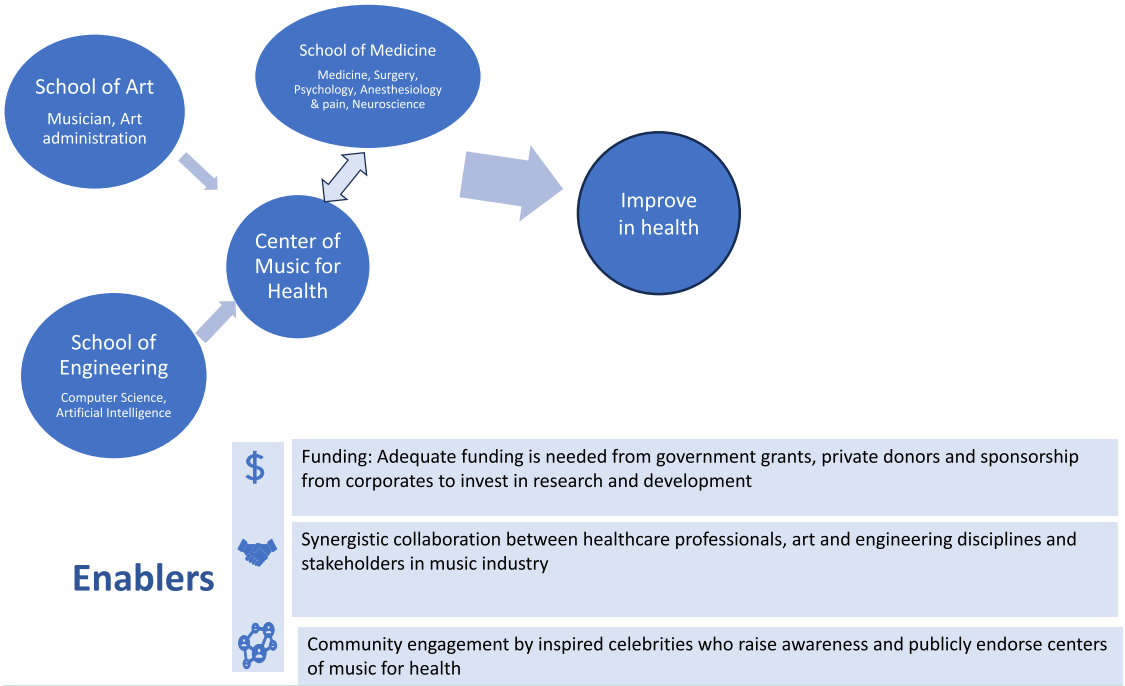

Figure Innovative collaboration between different departments within schools of medicine and health sciences and other disciplines such as art, computer science, and information technology can aid in the development of music centers for health by incorporating music technology to assess the effect of choice and dose of music and develop effective delivery methods of music for health benefits. By producing solid evidence, specific guidelines can be established to apply music in health settings.

develop inter-disciplinary approaches to unravel the power of music. Innovative collaboration between different departments within schools of medicine and health sciences, such as internal medicine, surgery, psychology, neurology, pain management, palliative care, and precision health, can help with creating validated tools to measure outcomes that are clinically meaningful. Moreover, collaborations with other disciplines such as art, computer science, and information technology can help with better understanding and incorporating of music technology to assess the effect of choice and dose of music and develop effective delivery methods of music for health benefits. Collecting health data associated with the use of music and employing artificial intelligence can complement conventional clinical trials to assess the impact of music.

Conducting large scale prospective controlled trials dedicated to assessing the effect of music on health outcomes is challenging; however, government- and industry-sponsored trials should be encouraged to include lifestyle information such as diet, exercise, and patterns of listening to music. The signals from such studies will set the stage for dedicated trials to assess the effect of music on health outcomes.

Adequate funding is needed from government grants, private donations, and corporate sponsorship to invest in research and development. Synergistic collaboration between healthcare professionals, art and engineering disciplines, and stakeholders in the music industry play an important role in the development of centers of music for health. Community engagement can be enhanced by inspired celebrities who raise awareness and publicly endorse centers of music for health via social media and their public appearances and offer special performances for the cause. Celebrity ambassadors who believe in the power of music can attract attention to support music centers for health.

Establishing centers of music for health will inspire faculty and trainees from different disciplines to collaborate and bring different perspectives on how to utilize an easily accessible tool for health benefits of potentially billions of people (Figure 1).

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