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COVID-19 symphony: A review of possible music therapy effect in supporting the immune system of COVID-19 patient

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Abstract

Coronavirus, the current pandemic that takes lives of 1,936,632 until the time of the paper. Scientists over the world exhibited all efforts to fight the virus. Many supplements developed to fight coronavirus by supporting the immune system which is the strongest worrier against it for now. One of the neglected strategies to enhance immunity is music therapy. Music therapy can drive immunity into different conditions. Not only able to boost and suppress immunity but also many physiological and psychological diseases are treated with music therapy. It is more than just entertainment, and research shows that music therapy may be helpful and cost-effective to support standard therapy. This systemic review tries to explore the effect of music therapy and arrives at a conclusion suggesting routine procedures to support the patient with music therapy. However, the idea of using music therapy in improving the immune system must undergo clinical and medical confirmation to be used.

Keywords: Psychology, Music therapy, Immune system, COVID-19, Coronavirus, Pandemic.

Introduction

The epidemic by a new Coronavirus, named COVID-19, initiated in late 2019 in Wuhan, China, is a worldwide public health threat [13]. The virus likely evolved in bat, a zoonotic origin, after amino acid substitution in the spike glycoprotein, as recently suggested, acquired the ability to bind to ACE2 receptor and be able to infect humans, which started the new epidemic [4]. Currently, there is no efficient treatment against the new Coronavirus. Therefore, identifying previously known antiviral drugs to fight back is urgently needed. A successful drug research strategy is to check if the current antiviral medicines are efficient in the treatment of Coronavirus infections. Several drugs, such as ribavirin, chloroquine, and two well-studied broad-spectrum antiviral drugs remdesivir, and favipiravir have been used a long time ago with SARS or MERS patients, although the efficacy of some drugs remains controversial [5]. Till now, the immune system is the only barrier against coronavirus. Before existing of an official drug or vaccine for the coronavirus, many individuals recovered due to the immune system with the aid of some vitamins to support the immunity and medications to reduce the inflammation. Although, there were some efforts to develop a vaccine [6] and discovering some potent molecules that may inhibit the virus attachment [7]. However, the official protocols aim to enhance immunity with medication. But the neglected fact that not only medication enhances immunity, but music therapy also does the same effect. Backing to the 10th BC century from western the starting from Greeks to the eastern including India and China, history proves the curative and healing powers of music therapy. The ancient Greeks are thought to have used music therapy to soothe the mentally disabled. Western thinkers from Pythagorus, Aristotle, and Plato to Schopenhauer and Nietzsche provided detailed of their interpretation of music's therapeutic forces and their confidence in its practical application to offer peace and unity, and thereby to cure mental and physical illnesses [8]. Aristotle, who has a strong background in psychotherapy, provides a theory that "after listening to music, those who suffered from uncontrollable feelings would return to their regular state, which brought their souls to happiness" [9,10]. There is also Evidence from 4000 BC of using music therapy as a tool of stress relief and is estimated to stretch back as far as Palaeolithic times [11].

The investigation of music therapy has increasingly delved deeper into the mechanisms influencing music therapy interpretation and production, investigating music psychology [12] and music cognitive neuroscience, also referred to as 'neuro musicology' [13]. The physiological basis for music-induced emotions [14,15], the neurobiology of some elements of music such as harmony [16] and the neuroanatomy of music performance have been included in this profound study [17]. And the scope of research ranged from the interpretation inside the womb of folk songs [18] to the production of opera on concert platforms [19], to the use of mainstream music in working theatres [20]. Music is an emotional language. It is known for improving mental and mood health. Any change in emotions affects the hormonal, neurophysiological, and physiological processes; thus, changes in body balance caused by music indicate the efficacy of different musical types [21]. Though still not well studied, several studies show that music therapy may promote a decrease in the stress response, a decrease in heart rate, improved tolerance to pain and suffering, change in skin behavior and muscle function, decreased anxiety, and depression. Different studies have reported this effect in musically exposed stressed patients [22-24]. On the other hand, noise stress could cause adverse effects on immunity in both human and animal models [25,26]. Several studies investigate different stress indicators, including blood pressure, pulse rate, and respiratory rate recorded measuring vital signs. These are the only anatomical measurements being used in nine of these. Several research, including [27], used vital sign assessment as proof of a transition from sympathetic to parasympathetic processes, equating a shift in immune function with a wider response to stress. In many trials, calming music was found to decrease blood pressure, pulse rate, and respiration rate. No definitive improvement was observed in just four trials. One of the first music therapy studies reports music as therapy was in 1963 when Melzack, Weisz, and Sprague report when evaluating the effect of the auditory stimulus on behavioral pain due to participants' fingertips submerged in ice water slow gradually increased discomfort in the group listening to music relative to control group [28]. In 1966, two famous scientists, Morosko and Simmons tried to shock the teeth of volunteers and found that music and white noise were effective in decreasing the pain sensation and increase tolerance [29]. In 1974, Peretti and Swenson used the Galvanic Skin Response (GSR) to assess anxiety caused during a written maze test by negative responses to participants. In this case, music lowered GSR responses dramatically [30]. The effects of music on a specific physiological mechanism such as cardiac output, respiratory rate, and blood pressure were originally reported in many studies including such as in France in 1880, America in 1899, and Russia in 1903 [31]. However, the immune system is one of the strongly affected systems in the body that can be manipulated indirectly with music.

Musically immune stimulation

As mentioned, the immune system is strongly associated with mood, psychological condition, and hormonal balance. Thus, as a result of negative mood, stress affects the immune system may cause dysregulation leads to a change in the humoral and cellular immunity and increases health risks [32]. Bittman [33] presented proof that the drummer's team has improved NK cell response, lymphokine-activated killer cell function, and dehydroepiandrosterone - cortisol balance in normal subjects, considered one of the early signs of the immune system-music interaction. Wachi [34] found that delightful music modulates immunological responses in adults 65 years of age who are demarcated. Important changes were reported in the number of lymphocytes, CD4 + T cells, T cells, and T memory cells as well as in the development of IFN- π and IL-6. Even music could reverse the immune stress induced by the immune suppressor. Not only can affect the immune response but could lead to a reversion of the effect of the medication. Music appeared to have a reversal effect as pharmacological interventions (i.e. benzodiazepines, 5 HT agonists) in immunosuppression induced by stress [35-37].

Many studies state that music minimized stress-induced hyperactivity of the hypothalamus-pituitary-adrenal [HPA] axis, including ACTH and corticosteroid production [23,38-44], and modulate norepinephrine, epinephrine, GH, PRL, and endorphin secretion [45]. This hormonal and neurotransmitter balance lowers stress and improving the condition of the immune system. Other studies show that there is a wide range of drugs that suppress the immune system, but one common immune suppressor is the negative mood. On the other hand, music is well studied as an immunity enhancer that re-regulates the immune system, increases NK cell activity, lymphokine-activated killer cell activity, lymphocytes, T cells, CD4+ T cells, and memory T cells [33,34]. Music improves the psychological state, re-balance the hormonal and neurotransmitter levels in the body, therefore improve immunity.

In the current coronavirus pandemic which began in China, there is an increasing number of infected people every day. After emerging of different vaccines that draw the immune system attention to foreign invaders, the immune system proves that it is the only and strongest barrier against the coronavirus. One promising approach is the plasma transfusion from recovered people to COVID-19 patients as many studies find that 200 ml of plasma from recovered people could neutralize the Coronavirus and lead to the disappearance of viremia in 7 days [46-49] which shows that the immune system is the only cure for such diseases.

The immune system is known to be strongly connected to psychological balance. That is when the individual mood is good which means a high level of dopamine in blood, will optimize and enhance the immune system, and a bad or sad mood will suppress immunity. So, one of the best strategies to support the immune system is to keep the mood in a good state. and some studies support the fact that dopamine is highly liked by the immune system [50,51].

The influence of music on leukocytes was investigated in six experiments [33] found that natural killer cells increased, followed by an endocrine reaction. [52] Hirokawa and Ohira [53] carried out other experiments testing the number of CD4 and CD8 cells. It was observed that inducing recorded music, analyzed by [52], increased plasma CD4+ T cell levels. The impact of music on immunoglobulins was also investigated. The most studied antibody (n = 12) has been immunoglobulin A (IgA). Some of these studies reported a rise in IgA level after a series of musical approaches with a wide range of styles and genres.

Fancourt introduces a modern model that connects Central Nervous System (CNS), Endocrine System, Autonomic Nervous System (ANS), and Immune System with them effectively to Psychological effects and Physiological effects which provides a basis for the creation of a taxonomy of study design variables linked to music and stress and traces the broad paths involved in its impact on the body [54].

Gender-dependent response

According to the physiological difference between men and women, there is a different response to music as shown in Nater *et al.*, the study [55] that reports different interactive patterns in men and women. Once met with heavy metal music, according to finger temperature and skin conductance tests, women displayed a significant gradual increase in the sympathetic nervous system (SNS) response than men's response. However, men displayed an abnormal autonomic reaction after exposure to heavy metals as demonstrated by increased salivary amylase secretion, which is caused by sympathetic and parasympathetic stimulation [55]. Several studies have suggested that the difference in sex-based psycho-physiologic responses to music might have a hormonal basis [56–59]. However, research by Trost [60] using Functional magnetic resonance imaging (fMRI) indicated that cheerful music stimulates the left striatum and insula while nostalgic sad music stimulates the right striatum and orbitofrontal cortex in both genders.

Criteria of therapeutic music

It is well known that music is related to mood and can make people feel happy, depressed, alive, or pleasant [61]. Listening to techno music (TM) or fast rhythm music [44] could cause increases in plasma norepinephrine, epinephrine, GH, PRL, cortisol, and beta-endorphin concentrations with a gradual rise in heart rate, systolic blood pressure, and significant changes in emotional response. In Gerra [62] that found that exposure to techno music increases the heart pulse rate and norepinephrine, cortisol, and adrenocorticotropic hormone secretion levels and vice versa such in the White study [63] who showed, in a group of patients in intensive care unit (ICU) when they listened to relaxing classical music, a reduction of heart rate and blood pressure. Other studies suggested that classical music has been found to improve the mood state caused by TM and increased gastric slow-wave in adults [31], but not to significantly reverse changes in hormonal concentrations [64].

An old study investigated the physiologic effect of listening to no music, fast-rhythm music, and sedative music for athletes and non-athletes during the exercise of varying intensities. Under conditions of intensive exercise, runners listening to fast rhythm music had increased plasma cortisol levels [65]. This indicates a possible metabolic advantage for the use of energetic music during exercise, considering the role of cortisol in stimulating the catabolism of energy substrates in fat, adipose, and connective tissues. McCraty's study shows the effects of music in this study was titled 'Heart Zones'. S-IgA increased by 55 percent ($p < 0.01$) when listening to the heart Zones' music alone [40].

Criteria of selected music according to [66] should be full of character, slow rate, repeated rhythm, predictable tone dynamics, pleasant harmony with no vocal content. Three songs studied by [67] are consist of 70 to 80 beats per minute and have a slow and steady, repeated rhythm as reported in the previous study. The three songs are "Canon in D major", "Love Story", and "Dance of the Iguana" played by Johann Pachelbel, Richard Clayderman, and Stevan Pasero respectively.

Valence and arousal in music have also been shown to be major factors. For calm, low tempo songs, [68] compared recorded music with four distinct tempi and moods, but only found a decrease in heart rate. [69] found that while heart rate during a stressful activity was diminished a little by high tempo music, with low tempo music there was a much greater impact. The respiratory rate was lowered only due to low tempo songs [70] found that blood pressure was not changed by soothing music when contrasting six distinct tempo pieces of music, but raised by high tempo music. The most compelling outcomes were provided by experiments that implemented more complicated controls. [71] stated, for instance, that listening to Mozart had a stronger influence on vital signs than a progressive relaxation session, and [72] found that listening to relaxing recorded music was as effective as diazepam in decreasing vital signs of anxiety.

Three specific styles of music were listened to by adults and adolescents in another study : classical, new age, and designer (designed to promote a sense of wellbeing) [73]. The respondents surveyed personal emotions at baseline and directly after listening to each style of song. Classical music reduced anxiety. Through new age music, relaxation increased dramatically and aggression, mental focus, vigor, and anxiety reduced. The subjects registered significantly more calm, mental focus, vigor, and sympathy after listening to designer music, and significantly decreased aggression, depression, exhaustion, and anxiety.

Although addressed music should be consist of 70 to 80 beats per minute with a slow and steady, repeated rhythm as reported such as "Canon in D major", "Love Story", and "Dance of the Iguana", the cultural aspect should be considered when choosing music and mentioned music example is just to clarify the type of therapeutic music.

Music therapy for COVID-19 patient

COVID-19 coronavirus disease, which is an infectious disease, and it was clear that negative feelings were mostly physiologically caused by infectious diseases and that a wide spectrum of health risks could be exacerbated or enhanced as a result of this infection. [74–76]

In Le Roux's study, he reveals that classical music, such as J. S. Bach's Magnificat in D Major BWV 243 has an effect on emotion, immunity, and endocrine parameters. In patients with specific infectious lung diseases, an experimental and control group was randomly distributed to patients. The experimental group received physiotherapy with the preferred music over a 3-day duration, while the control group only received physiotherapy. The outcome indicates major changes in parameters of the immune system, such as POMS-scale, CD4+:CD8+ ratio, cortisol, and cortisol: DHEA ratio. And music's intervention reveals contact between the mind and the body. [77]. Such experiment which conducted on a patient with infection disease, similar to coronavirus situation, may be applicable to COVID-19 patient.

Previous studies prove the therapeutic effect of music, which made music a strong candidate to be used along with medication for COVID-19 patients. A type of music administered by healthcare professionals for children also has a pain decreasing effect. The songs used consisted of age-appropriate children's songs. Yinger Provides a list of music and its purpose [78]. such strategies may be beneficial for decrease the pain resulted from the medical procedures.

As a severe case of COVID-19 patients should be placed on a respirator, One study demonstrated a significant fall in systolic and diastolic blood pressure fell causing a decrease in anxiety and depression during music therapy sessions for the patients on the respirator, as is shown in paired samples [78]. The qualitative part of the study showed that the patients remembered little of their time on the respirator which may be a good effect to remove the memories about the disease to avoid any psychological complications that may be caused by negative memories.

Recently, in some mild COVID-19 cases, it is recommended for the patient to be isolated in a room, which may increase patient anxiety and depression. The same situation reported before in Brodsky's work where music therapy was most effective in isolating hospital experiences, reducing distress, and fear-provoking hallucinations, and helping to have a more positive effect than other therapies [79].

Although several reports demonstrate the beneficial impact of classical music, it will be best to encourage the participant, as much as practicable, to select the type of music [31]. Although music therapy is deemed free of side effects, the technique should be used with the supervision of medical staff. A patient may react deeply, emotionally to a specific piece of music. Others reported a stress reduction and an increase in T-cell proliferation in mice who listened to music. In mice exposed to auditory stress, the NK activity of spleen cells also decreased during 8 days [80–83]. Such findings have been supported by

previous research on the impact of auditory stress and its negative effect on the immune system [84].

Applying music therapy way to the patient should be considered and carefully chosen in order to prevent or at least minimize infection transmission between healthy individuals and patients. A trained music therapist must deliver music interventions; the music therapist often adapts the live music experiences to the patients' needs at the time. This also presents the patient with a highly humanizing and validating experience. Furthermore, listening to self-selected pre-recorded music, introduced by the patient himself, may lead to an enhanced sense of autonomy and empowerment in a critical care setting where certain facets of care are beyond the control of the patient. [85,86]. Lee study warning from using headphones that may cause cross-contamination and nosocomial infections [87] show that speaker of personal or one-use headphones might be the best way to listen to music in case of COVID-19 patient

Conclusion

An epidemic of novel coronavirus diseases (COVID-19) in Wuhan, China has spread widely throughout the nation. The world focuses all efforts to stop the spreading of the virus using a different drug, and recently by enhancing the immune system using vitamins or plasma transfusion from the recovered person. But, one of the unnoticed supplements for the immune system is music therapy. The results of a recent investigation of music effect for medical procedural support shows that there is an urgent need for more high-quality research on the use of effective music therapy before, during, and after medical procedures, with particular emphasis on the interventions and techniques used by the music therapist [88] for patients and staff [40,89] in treating a patient with infection [77]. many studies state the improving effect of music on the immune system reported in thirteen studies [66,67]. and it seems that slow, repetitive rhythm, predictable dynamics, low tonic register, pleasant harmony such as classic music is the most effective [78] style not only in improving immunity but also in a medical procedure such in isolating room or placing the patient on a respirator [78]. Although this idea must undergo clinical trials to be proved, developing a "COVID-19 Symphony" a music track based on recent research and experiments may be urgently required to be a part of the medical protocols alongside supplements and drugs to improve mood and immunity to help the patient pass such disease with the precaution of addressing the music therapy in a personal way to prevent infection transmission without using any instrument that may transmit the infection [87].

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