







Effects of music therapy

on the autonomic nervous system in patients with COVID-19: a clinical crossover trial

Efectos de la musicoterapia sobre el sistema nervioso autónomo en pacientes con COVID-19: un ensayo clínico cruzado

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Abstract

Background: Music therapy is a process in which health is stimulated and promoted by exposing oneself to musical experiences. In COVID-19, music therapy has been used in physical and neurological rehabilitation. However, the evidence describing the relationship between music and the autonomic nervous system is limited.

Methods: A clinical crossover trial was carried out to evaluate the association between the activity of the sympathetic and parasympathetic nervous system in this population when exposed to sound stimulation through strictly selected pieces of music. Instrumental work of 8 minutes and 34 seconds in duration, composed and produced specifically for the purposes of intervention and research in the treatment of COVID.

Results: A total of 27 patients were included in the study, of which 13 underwent the music-silence sequence and 14 the silence-music sequence in a first study period, later the patients were analyzed in the opposite sequences in a second study period. A greater effect of music therapy on the sympathetic nervous system was evidenced in both sequences of studies in the intervention and control group ($p=0.078$). The stress index presented greater activity in both sequences when receiving musical notes compared to silence ($p=0.089$).

Conclusion: Music presents a greater stimulation of the sympathetic nervous system, and silence on the parasympathetic system.

Keywords: COVID-19; SARS-CoV-2; Music therapy; Crossover trial.

Resumen

Introducción: La musicoterapia es un proceso en el que se estimula y promueve la salud al exponerse a experiencias musicales. En COVID-19, la musicoterapia se ha utilizado en la rehabilitación física y neurológica. Sin embargo, la evidencia que describe la relación entre la música y el sistema nervioso autónomo es limitada.

Métodos: Se realizó un ensayo clínico cruzado para evaluar la asociación entre la actividad del sistema nervioso simpático y parasimpático en esta población cuando se exponen a la estimulación sonora a través de piezas musicales estrictamente seleccionadas. Obra instrumental de 8 minutos y 34 segundos de duración, compuesta y producida específicamente con fines de intervención e investigación en el tratamiento de la COVID.

Resultados: Se incluyeron en el estudio un total de 27 pacientes, de los cuales a 13 se les realizó la secuencia música-silencio y 14 la secuencia silencio-música en un primer periodo de estudio, posteriormente los pacientes fueron analizados en secuencias opuestas en un segundo periodo de estudio. Se evidenció un mayor efecto de la musicoterapia sobre el sistema nervioso simpático en ambas secuencias de estudios en el grupo intervención y control ($p=0,078$). El índice de estrés presentó mayor actividad en ambas secuencias al recibir notas musicales en comparación con el silencio ($p=0,089$).

Conclusión: La música presenta una mayor estimulación del sistema nervioso simpático, y el silencio sobre el sistema parasimpático.

Palabras clave: COVID-19; SARS-CoV-2; Terapia musical; Ensayo cruzado.

Introduction

The infection by coronavirus type 2 that causes severe acute respiratory syndrome (SARS-CoV-2) is currently a threat to worldwide public health due to its fast spread and degree of morbidity and mortality^{1,2}. Vaccination has allowed the control of the disease, reduced the mortality rate and relieving health systems^{2,3}. However, cases of mild SARS-CoV-2 infection and hospitalization for moderate coronavirus 2019 disease (COVID-19) persist in fewer numbers^{3,4}, which leads to an increase in the number of patients with associated mental illnesses to viral tropism at the level of the central nervous system or stressful and invasive medical interventions⁵.

Music therapy (MT) is a process in which health is stimulated and promoted by exposing oneself to musical experiences and interactions that occur in front of auditory perception⁶. The adjuvant management of multiple physical and mental illnesses and associated sequelae is increasing, focused mainly on motor sensory rehabilitation, cognitive performance, changes in mood and behavior⁶. One of the main therapeutic targets is mainly explained by its impact on the autonomic nervous system (ANS) and modulation in neurotransmitters^{6,7}.

In COVID-19, MT has been used in physical and neurological rehabilitation, mainly in patients with sequelae after neuronal hypoxic damage associated with viral tropism and therapeutic complications due to intubation or pharmacological management⁸⁻¹⁰. However, the available medical literature that evaluates the impact of MT on the ANS in patients with active SARS-CoV-2 infection^{11,12} is limited, making it essential to develop clinical studies that evaluate the clinical outcomes and effects on the nervous system of this medical and musical process. The objective of this study is to describe the variability that causes MTs in the ANS of mild and moderate COVID-19 patients.

Methodology

A clinical crossover trial was carried out to evaluate the association between the activity of the sympathetic and parasympathetic nervous system in this population when exposed to sound stimulation through strictly selected pieces of music. Patients diagnosed between August 2020 and November 2021 with COVID-19 requiring hospitalization were included.

Eligibility criteria

Patients older than 18 years of age and with positive reverse transcription polymerase chain reaction tests for SARS-CoV-2 infection were included. Sensorineural or conduction hearing impairment and being under mechanical ventilation support were exclusion criteria in this study. Before agreeing to participate in the study, the participants were fully informed of the associated risks and discomforts, and subsequently gave their written informed consent.

Exposure to MT

All the participants were evaluated in two groups: music therapy-silence (MS) and silence-music therapy (SM) in two

different study periods; each patient was exposed to both groups during the study. Patients are randomly assigned to the two groups of MS and SM sequences, the comparison of which forms the basis for confirmatory analysis. The effects of MT on ANS in both groups were evaluated based on the within-subject difference between the two treatments with respect to the outcome variable. A previous familiarization with the study situation was carried out to avoid that the patients who receive the MS treatment in period 1 and the SM treatment in period 2 (or vice versa) show differences in the result despite being the same patients, because of the effects of time.

Characteristics of the piece of music

Instrumental work of 8 minutes and 34 seconds in duration, composed and produced specifically for the purposes of intervention and research in the treatment of COVID.

Timbre and instrumentation: - Pads: Permanent and sustained sound from vocal samples and analog synthesizers that simulate a constant flow of air. They have a harmonious role. - Sequencer: Percussive, enveloping, ascending and descending sound that creates a sensation of continuous movement and displacement. It has a rhythmic role. - Piano room: Acoustic piano sound within a large room that generates a feeling of large and deep space. It has a melodic role.

Rhythm: There is no defined pulse, which generates a feeling of freedom. The rhythms of the sequencer and the melody are not connected or related to each other and there is no defined periodicity. It seeks to create a feeling of relaxation and comfort by not introducing a fixed rhythm or a certain metric.

Harmony: The work is unimodal and multitonal. The single mode is Ionian based on the diatonic scale, but it hovers over 4 different major keys to create some variety over the 8 minutes. Progressions towards 4, 6, 3 and 2 degrees are used with the use of suspended chord variations, minor chords 9 and 11 and major chords with the added 9.

Melody: Following the guidelines of interval music therapy, the melody moves through consonant intervals such as the perfect 4, 5 and 8, narrative intervals of 3 and 6, and displacement intervals such as the major 2. In this way, dissonant intervals such as 2 minor, 4 augmented or 7 major are avoided, seeking an exclusive connection with sensations of fullness (8), closing, and opening (4 and 5), personal history (3 and 6) and capacity for change (2 major).

Variables

The effect of MT and silence on the sympathetic and parasympathetic nervous system was evaluated, as well as the stress index that these sequences will cause in patients.

Statistical analysis

For confirmatory statistical analysis of a crossover trial, we performed an "ordinary" unpaired t-test, evaluating the probability that the absolute value of a (centrally) distributed t parameter with N-2 degrees of freedom exceeds the calculated absolute value of the T test statistic^{13,14}. Data were collected in an Excel spreadsheet and analyzed using the licensed SPSS statistical program.

$$T = \sqrt{\frac{mn}{N}} \frac{\bar{C}(X) - \bar{C}(Y)}{\sqrt{(SQ_{CX} + SQ_{CY}) / (N - 2)}}$$

Ethical considerations

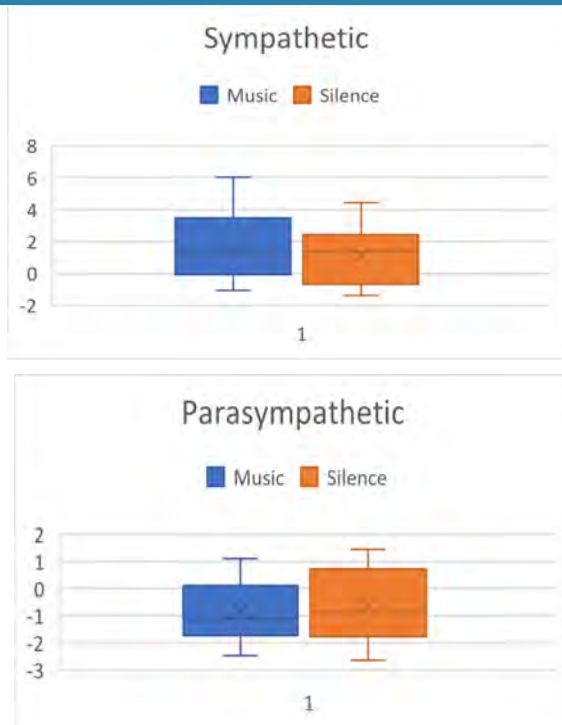
The study protocol was reviewed and approved by the ethics and research committee of the institution where the study was carried out, obtaining informed consent.

Results

A total of 27 patients were included in the study, of which 13 underwent the MS sequence and 14 the SM sequence in a first study period, later the patients were analyzed in the opposite sequences in a second study period.

A greater effect of MT on the sympathetic nervous system was evidenced in both sequences of studies in the intervention and control group ($p=0.078$) Figure 1. Regarding the parasympathetic nervous system, the SM sequence presented a higher activity in both study groups ($p=0.670$).

Figure 1. Sympathetic and parasympathetic nervous system



The stress index presented greater activity in both sequences when receiving musical notes compared to silence ($p=0.089$) Figure 2.

Figure 2. Stress index



Discussion

Our study described the impact of MT compared to silence on the ANS, showing a greater activity of musical pieces on the sympathetic nervous system, with an increase in the stress index. On the contrary, the sequences that began with silence generated greater activity on the parasympathetic nervous system.

Music acts as a powerful sensory stimulus by activating the brain and retraining the nerves, presenting anxiolytic effects⁶⁻⁸. The research using recorded music in its various forms of singing or making music, listening to music, or live MT by music therapists for specific groups of patients as interventions has been used to relieve stress, in addition, the potential effects of music research on the release of the stress-inducing hormone cortisol are beneficial⁶⁻⁸.

The stimulation of music in the context of a stressful situation increases coping capacity and reduces levels of perceived psychological stress, by reducing cortisol levels in patients undergoing stressful procedures in hospital^{9,10}. Music effects of listening to music or making active music, such as singing or playing instruments, have been found to have perceived benefits in the literature, including physical relaxation leading to a feeling of happiness, positivity, and increased sense of physical and emotional well-being^{6,10}.

MT is a form of human interaction and since the last century it has been formally used as an adjunct and alternative therapeutic resource in various clinical settings such as pain control, physical recovery after surgery, and even in end-of-life care. life, among others^{6,9,10}. One of the mechanisms and hypotheses to explain the effects of music is due to the acoustic stimulus that is processed by the auditory cortex and the limbic system. This structure establishes direct and indirect bidirectional connections with the endocrine, immune, and autonomic nervous systems, regulating their activity. A possible decreased secretion of substances and hormones by these complex systems such as catecholamines and cortisol downregulates blood pressure, pulse, and immune and inflammatory responses, in addition, upregulation of endogenous endorphins regulates pain perception and increases well-being and motivation, achieving better physiological and psychological conditions.

Anxiety can impose harmful effects on the course of recovery and the general well-being of a person, increasing the stimulation of the sympathetic nervous system, increasing the work of breathing and fatigue, impacting unfavorably on the clinical evolution of patients requiring supplemental oxygen¹⁵. A deterioration in the regulation of the ANS can generate numerous systemic responses, including arterial and venous constriction, myocardial stimulation, and bronchoconstriction^{10,15}; the latter causes elevated airway resistance, increased work of breathing, muscle tension leading to increased oxygen consumption, and generalized fatigue.

Constant stimulation of the sympathetic nervous system can also result in increased breathing and heart rates, related to psychological stressors, such as fear and anxiety¹⁶. In addition, prolonged activation of the stress response due to a disease state and associated treatment can cause a state of immunosuppression, implying a possible higher rate of complications, prolonged hospital stays, and an unfavorable impact on patient mortality^{15,16}. In our study, a predominance in the stimulation of sympathetic activity associated with music was evidenced, although these data may be related to a deterioration in the clinical condition of the patients due to a greater adrenergic discharge, in patients who had an active infection could be related to hypercatabolic and persistent inflammatory state.

Limitations

Among the weaknesses of our study are the fact that the information was obtained in a single health center and a small number of patients, which could reduce the generalizability of the results and could only be extrapolated to populations with similar characteristics. The people of the research team have experience in the proper collection and interpretation of this type of data. Future studies are needed to characterize the current situation of MT more clearly in patients hospitalized for severe COVID-19 and in the period of weeks and months during recovery from prolonged illness.

Conclusion

Music presents a greater stimulation of the sympathetic nervous system, and silence on the parasympathetic system. Future studies are needed to evaluate a higher population density with different severity of the disease.

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