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Using Music to Treat Epilepsy in Children: A Review

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Abstract

Music is a unique product of human culture. The idea of music having therapeutic effects on human health and behavior is as ancient as the writings of Aristotle and Plato. The therapeutic potential of music has largely been explored in cognitive science. Since the scientific report of the "Mozart effect" was published by Rauscher et al, much attention has been given to the therapeutic role of music in the treatment of human physiology. Although studies about music as a therapeutic option in human epilepsy are limited, emerging evidence has indicated that there may be beneficial effects of music on children with epilepsy. This review aims to summarize the current evidence of music's potential in treating epilepsy, particularly in children. It includes musical processing in the human brain, the positive effects of music on neurologic function, and music therapy in epileptiform discharges and seizure frequencies. Evidence of short-term and long-term effects on epileptiform discharges and long-term effects on refractory epilepsy is provided. Finally, the role of music components and the potential mechanisms governing the beneficial effects of music are discussed.

Keywords

children, epilepsy, epileptiform discharges, Mozart K.448, music therapy

Epilepsy is a common disease in pediatric neurology, affecting 0.5% to 1% of children.[1] Although several new antiepileptic drugs (AEDs) have been developed, one-third of children with epilepsy are resistant to medications.[2] In addition, side effects related to AEDs are not uncommon. There is a dearth of literature related to integrative strategies in childhood epilepsy.

Music has a long history of improving physical and mental illness. In 1993, a specific investigation reported by Rauscher et al[3] found that Stanford-Binet spatial task scores improved immediately after listening to Mozart's Sonata for Two Pianos in D Major, K.448 (Mozart K.448) for 10 minutes when compared with the same time of silence or relaxation instruction. Rauscher et al[3] suggested a specific effect that students scored 9 points higher on spatial tasks according to the Stanford-Binet Intelligence Scale by listening to Mozart music, and this finding received much attention. Later, the beneficial effects of listening to music were reported for several diseases: Parkinson disease by listening to relaxing music and engaging in free body expression to melodic and rhythmic music, epilepsy by listening to Mozart K.448, senile dementia by listening to familiar music or new music, and attention-deficit hyperactivity disorder by listening to self-selected music.[4-8] Music therapy for epilepsy was first reported by Hughes et al,[9] when they found reductions in epileptiform activities in comatose patients, with status epilepticus or with periodic lateralized epileptiform discharges (PLEDs) during exposure to Mozart K.448. Emerging evidence continues to demonstrate the positive effects of music on epilepsy and, in some cases, the use of Mozart's music in particular. This review aims to summarize current related literature on the effect of music as it relates to epilepsy, including musical processing in the human brain, music applications in children with epilepsy, and the current mechanisms of music therapy that contribute to treating epilepsy.

Music and the Human Brain

Music is an integral part of human life and culture. It is also a form of art and a symbol of emotion presentation. Although the human auditory cortex is located in the temporal area, listening to music is a complex process for the brain, since it triggers a sequence of cognitive and emotional responses.[10] Neural activity associated with music listening extends beyond the auditory cortex. It involves a widespread bilateral network of frontal, temporal, parietal, and subcortical areas related to attention,

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semantic and music-syntactic processing, memory, and motor functions, and even extends to the limbic and paralimbic regions related to emotional processing.[11-19] Recent progress in functional neuroimaging studies, including positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), helps us better understand the mechanisms involved in music processing. For example, activity was found in the parahippocampal gyrus and amygdala in response to the negative emotion elicited by a saxophonist improvising music before MRI scanning. The ventral striatum has been shown to respond to positive emotion elicited by a saxophonist improvising music before MRI scanning in fMRI studies.[20]

Music Application in Human Diseases

Music therapy has been used effectively as an integrative treatment in medical diseases, particularly in neurologic diseases.[8] For example, Särkämö et al[21] investigated patients with strokes who listened to their favorite music for 2 months. Results show that recovery in the domains of verbal memory and focus attention improved more significantly in the music listening group than in the control group, even 6 months after the stroke. In a study of patients with Parkinson disease,[22] listening to self-selected music resulted in improved aiming and line tracking as measured by the Vienna Test System. This study provided evidence that specific music can improve the precision of arm and finger movements. Relaxing classical music was also used in treating sleep disorders. Ninety-four students with sleep complaints participated in a music study.[23] They listened to relaxing classical music, including some popular pieces from the Baroque to Romantic periods, for 45 minutes every night at bedtime for 3 consecutive weeks; audiobooks—a CD containing 11 hours of short stories by Hungarian writers such as Frigyes Karinthy, Gyula Krúdy, Géza Gárdonyi, Zsigmond Móricz, and Mihály Babits—for 45 minutes every night at bedtime for 3 consecutive weeks; or no intervention for 3 weeks. The results show that music significantly improved depressive symptoms and sleep quality according to the Pittsburg sleep quality index. However, sleep quality and depressive symptoms did not improve in the audiobook and control groups. In addition to these studies, music has been shown to have beneficial effects on other neurologic diseases, including attention-deficit hyperactivity disorder, autistic spectrum disorder, and migraine.[7,24,25]

Music Therapy for Children With Epilepsy

Several studies have demonstrated the beneficial effects of music on childhood epilepsy, including reductions in epileptiform discharges and seizure frequencies.

Short-Term Effect on Epileptiform Discharges

Hughes et al[9] found that the epileptiform discharges reduced during listening to Mozart K.448 in 23 of 29 patients with epilepsy. The reductions were noted in patients in coma with status epilepticus or with PLEDs. Our previous study also revealed that epileptiform discharges in patients with epilepsy decreased significantly during and immediately after listening to Mozart K.448.[26] The largest decrease in discharges was observed among patients with generalized or central discharges. There was no significant difference in the epileptiform discharge between patients who were awake and those who were asleep during electroencephalogram (EEG) recordings. Both studies showed that a conscious state did not demonstrate a significant impact on the effect of Mozart K.448. In another study, Turner reported that after listening to Mozart K.448, interictal epileptiform discharges decreased in 4 patients with rolandic seizure.[5]

Long-Term Effect of Music on Epileptiform Discharges

Our previous study described 18 children with epilepsy who were clinically well controlled by AEDs and were included for the evaluation of the long-term effect of Mozart K.448 on epileptiform discharges.[27] The EEGs of the children revealed persistent epileptiform discharges for at least 6 months. Prior to music listening, there were no significant changes in epileptiform discharges after more than 6 months of AED treatment. However, significant decreases in epileptiform discharges were found after 1, 2, and 6 months (decreased by 53.2%, 64.4%, and 71.6%, respectively) of listening to Mozart K.448 when compared with the EEGs recorded before listening to music. In addition, the decrease in epileptiform discharges also showed significant difference between each of the study time points of the music intervention. This indicates that the decrease occurs in a chronologically progressive manner. When epileptic discharge foci were considered, patients with central, frontal, generalized, and temporal discharges showed significant reductions in discharge after listening to Mozart K.448 for 1, 2, and 6 months when compared with those patients with occipital discharges.[27]

Effect of Music on Refractory Seizure

Refractory childhood epilepsy accounts for 20% to 30% of epilepsy cases.[28] Although a growing number of new AEDs have been developed, the incidence of drug-resistant childhood epilepsy has not been reduced significantly.[28] Therefore, a search for alternative therapies in refractory childhood epilepsy is mandatory. We used Mozart K.448 as a therapy in the children with refractory epilepsy as well as in epileptiform discharges.[29] Eleven children with refractory epilepsy were included in the study. They listened to Mozart K.448 once a day before bedtime for 6 months. Seizure frequencies were recorded 6 months before they started listening to this music and monthly during the study period. All of the patients continued to take the AED they had been on prior to this study, during the 6-month study period. Frequency of seizures was compared before and after listening to Mozart K.448. The effectiveness of music therapy was rated as (i) seizure free, 100% remission; (ii) very good, a decrease in seizure frequency by 50% to 98%; (iii) minimal, seizure frequency of less than 50% with minimal change in seizure severity; and

(iv) unmodified or worsened, when seizure frequency and severity were found to be the same as (unmodified) or worse (worsened) than baseline, respectively.[30] The results showed that 8 of the 11 patients were either seizure free (n = 2) or had very good responses (n = 6) after 6 months of listening to Mozart K.448. The remaining 3 (27.3%) showed minimal to no effect. The average percentage of seizure reduction in all of the patients was 53.6%.

In a case report by Lahiri et al,[31] improvement in seizure control in a 56-year-old gentleman who had refractory gelastic epilepsy was also found. The patient listened to a nonspecific piece of Mozart's music for 45 minutes daily. Within days of starting to listen to Mozart regularly, he noticed a difference in the pattern of his seizures. In the 3 months during which he listened to Mozart, he did not have any secondarily generalized tonic–clonic seizures. Accordingly, Mozart music could be used as a potential add-on therapy in the treatment of patients with refractory epilepsy.

Music Components and Music Effects

There are a variety of components in virtually every kind of music, including melody, rhythm, tone, and harmony. Each of these musical elements may play an important role in the overall beneficial effect of music. To analyze the periodicity (ie, the appearance of the highest peak of voltage signals periodically) of music, Hughes et al[32] first converted musical notes into audio waveforms by converting acoustical pressure waves into voltage signals and digitizing them. The maximal points of the waves were mathematically connected to create an envelope with a sampling frequency of 0.67 Hz (period = 1.5 seconds). A fast Fourier transform (FFT) of the envelope then provided a calculation of the relative amplitude of all periodicities, from 3 to 120 seconds. The next step was an autocorrelogram of these data to better see the major periodicities. Finally, the FFT of the autocorrelogram most clearly showed the relative amplitude of the major periodicities, smoothing out the nonperiodic rhythms. A periodicity index was chosen to represent the degree of periodicity; this index is the ratio of the highest peak and the next highest peak (×10). The long-term periodicities were divided into those with major (>50% of the highest) and minor (25%-49%) peaks. For each musical selection, the major and minor peaks were counted, as was the incidence of a certain periodicity of time. Hughes et al[32] found that the long-term periodicity of melodic line in the music of Mozart and in 2 pieces by Bach was significantly more apparent and frequent when compared with the music of 55 other composers (eg, Chopin, Mendelssohn). This may account for the reduction in epileptiform discharges when listening to the music of Mozart and Bach. In another study, Zhao et al[33] report that both happy and sad melodies of equal emotional valence resulted in significantly lower pain scores during a pain test and were in contrast to the mood prediction. It indicates that the valence of music, rather than the mood it induced, appears to be a critical factor for the pain-relieving effect of music. In our previous study, the interictal discharges were reduced by an average of 24.1% in 81% of patients as patients listened to Mozart K.448.[26] The interictal discharges were defined as distinct waves or complexes distinguished from background activity when patients did not have seizure attack during the recording period. The total number of interictal discharges during each section (before, during, and after music) was divided by the duration (in minutes) of the section and compared. Changes in epileptiform discharge were expressed as ([baseline discharge − discharge during/after music]/baseline discharge) × 100. However, when we used a digitally computerized string version of the same musical stimulus, the discharges showed a slight increase by an average of 10.5%, when listening to this music.[26] A spectrogram analysis of the 2 versions, piano and string, was generated by a MATLAB program (Mathworks, Inc, Michigan). To begin to describe the differences in the 2 versions, short-time Fourier transforms of the signals were computed. A hamming window was used to truncate data of 100 seconds, which were sampled at a rate of 44.1 kHz for each spectrogram, so the resolution of bandwidth is 10 Hz. Although the 2 kinds of music had the same melody, spectrograms comparing the piano K.448 and string K.448 showed clear differences. The differences were particularly noteworthy at high frequencies (HFs). The string K.448 had much stronger HF harmonics (Figure 1A). The piano K.448 seemed to concentrate more energy in the fundamental frequency and the lower harmonics (Figure 1B).[26] Additionally, we used Mozart's Piano Sonata in C Major, K.545 (Mozart K.545), which shares similar spectrogrammatic characteristics with Mozart K.448, to investigate the effect of harmonics on epileptiform discharges in children with epilepsy (Figure 1C). Thirty-nine children with epilepsy underwent EEG examinations before, during, and after listening to Mozart K.448 and K.545, respectively, 1 week apart. There was a significant decrease in the frequency of epileptiform discharges during and immediately after listening to Mozart K.448 and K.545 (reduced by 35.7% during Mozart K.448 and 30.3% directly after; and 34.0% during Mozart K.545 and 31.8% directly after).[34] We suggest that Mozart K.448 is not the only piece of music to have beneficial effects on children with epilepsy and that listening to Mozart K.545 with similar lower harmonics can also decrease epileptiform discharges in children with epilepsy.

Mechanisms of Music Therapy for Children With Epilepsy

Recently, several theories have been introduced regarding the effects of sound on the brain. Neurotransmitter pathways may be involved in the effect of Mozart's music on epilepsy. Exposure to music is known to increase the expression of dopamine levels in the brain.[35] In recent years, there has also been evidence implying a role for dopamine in the pathophysiology of epilepsy. A PET study showed that the impaired dopamine uptake in the midbrain is hypothesized to contribute to seizures in juvenile myoclonic epilepsy.[36] In a recent animal study, Szyndler et al[37] report that pentylenetetrazole-induced seizures decreased the dopamine levels in the striatal and hippocampal areas, accompanying the induction and propagation of seizures.

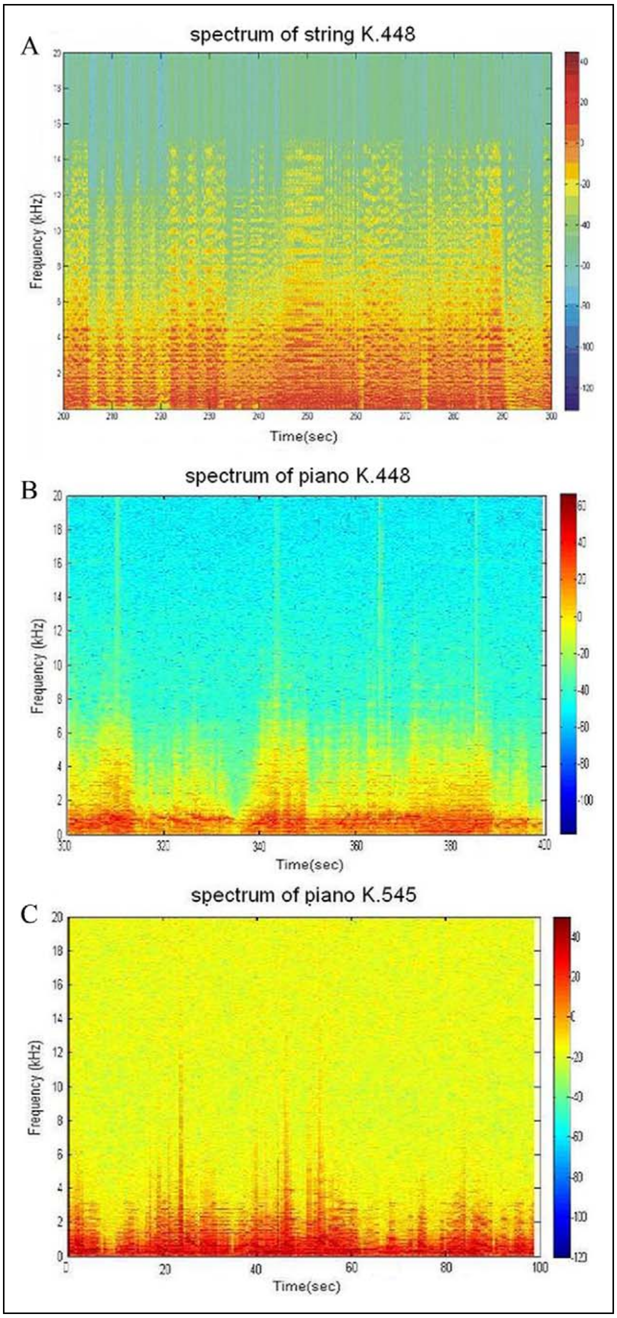

Figure 1. Spectrogram analysis for string K.448, piano K.448, and piano K.545. The differences were significant, especially at high frequencies. Spectrograms are showing high-frequency harmonics during one section of string K.448 (A), piano K.448 (B), and piano K.545 (C). Data were averaged in 10-second periods in the middle (250 seconds) of the first movement. The increase in higher harmonics in string K.448, piano K.448, and piano K.545 seemed to concentrate more energy in the fundamental frequencies and lower harmonics.

It is possible that listening to music modifies the dopaminergic pathways, contributing to the beneficial effects of epilepsy therapy. Another theory is that a "Mozart effect" might be mediated through sensory–motor circuits by the so-called mirror neurons. Mirror neurons are proposed to be a particular type of neurons that are modified when an individual performs an action and is exposed to visual/music stimulation.[38,39] The link between music and motor function is evident in some aspects of musical activity. For example, we dance to music, we move our bodies to play musical instruments, and we move our mouths and larynges to sing.[39] A recent neuroimaging study examining transcranial magnetic stimulation and behavior suggests that auditory stimulation can modulate the activity of the motor system.[40] Although there is no direct evidence to support this hypothesis, it is possible that mirror neurons mediate neuron activity by linking auditory stimulation directly to the motor cortex.[41] It seems reasonable that music may activate specific cortical functions through neuronal conduction or synaptic modulation.

It has been reported that poor health is associated with lower parasympathetic tone in several medical conditions, including diabetes, rheumatoid arthritis, and epilepsy.[42-44] Heart rate variability (HRV) analysis has been used extensively in the analysis of autonomic function.[45] In the frequency domain of HRV, a frequency band ranging from 0.04 to 0.15 Hz has been defined as a low-frequency (LF) component, which was related to the regulation of blood pressure and reflected the combined activity of the sympathetic and parasympathetic nervous systems.[46,47] The frequency band ranging from 0.15 to 0.5 Hz has been defined as the high-frequency (HF) component, which was caused by respiration and reflected the activity of the parasympathetic nervous system. In a meta-analysis study, patients with epilepsy showed lower vagal and higher sympathetic tone than the controls.[48] Mukherjee et al reported that higher sympathetic tone, lower parasympathetic tone, and more severe dysautonomia were found in patients with intractable epilepsy than in those with well-controlled epilepsy.[49] Another study demonstrated decreased HF and increased LF/HF ratio of HRV analysis in patients with epilepsy without AED therapy when compared with patients with AED therapy.[50] According to these findings, an increase in parasympathetic activity may help to improve seizure control. In our recent study, we also found that listening to Mozart music decreased epileptiform discharges and significantly increased HF, the square root of the mean squared differences of successive RR intervals (RMSSD), and the standard deviation of differences between adjacent RR intervals (SDSD).[51] Most of the patients with effective outcomes showed a decreased LF/HF ratio, LF normalized units (LF nu), mean beats per minute (bpm), and an increase in HF normalized units (HF nu), which all indicated parasympathetic activations.[51] In addition to our study, another study of patients with cancer demonstrated that a 2-hour music intervention by listening to and singing Taiwanese popular songs increased the patients' relaxation scores and parasympathetic activities.[52] Another study showed that 45 minutes of music therapy once a week in patients with cerebrovascular disease enhanced parasympathetic activities and reduced congestive heart failure events by decreasing plasma cytokine and catecholamine levels.[53] The music therapy was performed once a week for 45 minutes at least 10 times from 11:00 to 11:45 AM by 2 experienced and licensed music therapists, according to the guidelines of the Japanese Music Therapy Society. The music therapy consisted of well-known Japanese nursery rhymes, folk songs, hymns, and recent Japanese popular music.[53] These results of the preceding studies indicate that parasympathetic tone increased during music exposure, which may in part account for the reduction in epileptiform discharges in epilepsy while listening to music.

Conclusions

There is evidence that listening to Mozart's music, both short term and long term, may contribute to decreases in epileptiform discharge and seizure frequency in children with epilepsy, even in the refractory type. Not only Mozart K.448, but also music with lower harmonics, such as Mozart K.545, might decrease epileptiform discharges in children with epilepsy. Mozart and other kinds of music may have beneficial effects in treating epilepsy. Music such as Mozart's, which has frequent thematic lines and numerous sequences, should be further studied as an integrative treatment strategy in the plan of care for people with epilepsy.

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