THE MOZART EFFECT FOR EPILEPSY TREATMENT IN CHILDREN

by

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Abstract

The aim of this systematic review was to establish whether or not the Mozart Effect can lower the seizure activity in children with a history of epilepsy. An electronic literature search for “Mozart Effect,” “children,” and “epilepsy” was conducted using CINAHL Complete, Cochrane, and PubMed databases. Inclusion criteria included systematically reviewed literature all written in the English language, peer-reviewed articles, full text, abstract available, and published articles between April 1999 and September 2015. Articles written before 1999 were excluded. This search strategy identified a total of 60 articles in Science Direct and CINHAL Complete, 11 articles in PubMed, and 1 article in Cochrane. Articles not pertinent to the research topic and duplicates were removed. Nine studies were selected for analysis based on these criteria. This paper includes discussion of the limitations and strengths of each article using the Johns Hopkins nursing evidence-based practice rating scale (JHNEBP) to evaluate the level of evidence for each study and study quality. The data supports that the Mozart Effect on children with epilepsy does not cause any adverse effects. Observational studies have shown that listening to Mozart’s K.448 reduces seizure episodes in children who are not in complete control of their motor functions. The evidence is inconclusive on the Mozart Effect’s ability to reduce seizure incidence although there is strong support that epileptiform discharges are decreased with music listening. Implications Registered Nurses may consider of the Mozart Effect as an adjunct to current epilepsy treatments.

The Mozart Effect on Epilepsy in Children

Despite medical advances, we still do not have the cure to many health conditions that are affecting millions worldwide. Music therapy has many uses for people who have illnesses that cannot be treated by prescribed medicine alone. One medical condition that has been troublesome to people of all ages is epilepsy. Epilepsy is a medical condition where a person can involuntarily and unexpectedly experience a seizure at any time of their life (Chang & Lowenstein, 2003). There is no cure for epilepsy and it is a difficult chronic condition for those who have to live with it on a daily basis (Shafer & Sirven, 2013). Today many people with epilepsy are not aware of alternative treatments that do not involve medications or surgery. Various alternative treatments such as the Ketogenic diet and acupuncture have been studied and used to relieve symptoms of epilepsy. Some people have attempted to decrease their seizures with music (Pauwels, Volterrani, Mariani, & Kostkiewics, 2014). A challenge of epilepsy treatment is that sometimes nothing works.

The Mozart Effect is one form of music therapy that has been used worldwide to address a variety of conditions. The Mozart Effect, by definition, is an inclusive term referring to the transformational powers of music in health, education, and well-being. It may decreases stress, depression, or anxiety; induce relaxation or sleep; activate the body; and improve memory or awareness (NICE, 2010). Listening to classical music has been studied for its impact on attention deficit disorder, autism, dyslexia, listening disorders, and other physical and mental disorders including injuries (NICE, 2010).

The purpose of this systematic review is to evaluate the effectiveness of the Mozart Effect for children with epilepsy. At appropriate volume levels to protect hearing

(70%, <83 decibels), music has no harmful effects on children. The absence of side effects appeals to parents who are wary of the risks associated with other epilepsy treatments. Parents may be willing to explore the benefits of the Mozart Effect for their child. Further study of the Mozart Effect on seizures is important because it may be a safe alternative treatment for children with epilepsy (Liao, Jiang, & Wang, 2005).

Background

Epilepsy

Epilepsy is a medical condition where a person experiences seizures. Epilepsy can be diagnosed at any age and occurs with or without warning. The seizures come with excessive, uncontrolled electrical activity in the brain and can occur spontaneously (Warren, 2016).

Reynolds & Kinnier-Wilson (2008) reports that as early as 1581 B.C., the Babylonians believed people would get seizures due to supernatural invasion of the body by demons. Babylonians described seizures as “the falling disease” since people would fall to the ground and start to convulse for no apparent reason. Reynolds & Kinnier-Wilson further reports that it was Hippocrates that suggested that epilepsy was a brain disorder and advocated that epilepsy was not the result of supernatural forces. According to Reynolds & Kinnier-Wilson, it was only since the 19^{th} century that doctors figured out that people who have epilepsy have normal mental states.

Mukamel, Ekstrom, Kaplan, Iacoboni, & Fried (2010) describes epilepsy and normal brain function as follows. In normal brain physiology, special pumps called membrane pumps are continually at work to maintain each salt in its proper location. A nerve cell has an inner section and is bounded by a cell wall membrane. Sodium levels are higher on the outside while potassium levels are higher on the inside. The special pumps are needed to keep the salts in proper order. In epilepsy, the brain cells depolarize and changes in brain biochemistry and communication result in abnormal discharges in the brain. Normally, the brain is composed of tiny nerve cells called neurons that communicate with one another through tiny electrical pulses that do not occur at the same time (Morris et al., 2013).

According to Burneo & Jette (2016), some common causes of epilepsy include dementia, infections like meningitis, brain injury, and abnormal blood vessels in the brain. Causes of seizure activity in children include head trauma, lack of oxygen, and illness. Epilepsy can result from a family history of seizures or epilepsy, but it can develop on its own with no known etiology. Risk factors for epilepsy include history of epilepsy in the family, development of a stroke or other vascular disease, a brain infection, or having consistent seizures in childhood.

The experience of a seizure depends on the location of damage or dysfunction in the brain (Myint, Staufenberg, Sabanathan, 2006). The three most common types of seizures seen in epilepsy patients are absence (petit mal), generalized tonic-clonic (grand mal), and partial (focal). The first, absence (petit mal), is a less severe seizure type that involves a patient who has a brief loss of consciousness. The second common form is generalized tonic-clonic (grand mal) and is a more serious seizure type that deals with unconsciousness, muscle rigidity, and convulsions. Myoclonic seizures appear as sudden twitches or jerks of the arms and legs. Atonic seizures, also called drop seizures, involve the loss of muscle control where a person will suddenly collapse or fall down. The third common type of seizure, partial (focal) involves jerking muscle movements of the limbs

(Warren, 2016). There are two types of focal seizures: focal seizures without loss of consciousness (simple partial seizures) and focal dyscognitive seizures (complex partial seizures). Focal seizures without loss of consciousness involve seizures that may alter emotions or the way things feel, taste, smell, or look. Involuntary jerking can occur and sensory symptoms such as dizziness, flashing lights, and tingling. Focal dyscognitive seizures involve a loss of consciousness or awareness. This means that patients can stare into space as well as not respond to environmental stimuli. Repetitive movements of chewing, walking around in circles, and hand rubbing are common (Campellone, 2014).

Symptoms of seizure activity include temporary confusion, a staring spell, loss of consciousness or awareness, psychic symptoms, and uncontrollable jerking movements of the arms and legs due to the abnormal activity in brain cells. The type of seizure a child develops will determine what kind of symptoms they will develop. Symptoms of epilepsy vary from person to person but can involve hyper alertness and violent shaking. A child who has an epileptic seizure will normally have the same type of seizure with the symptoms that follow it. It is imperative to seek medical assistance if breathing or consciousness does not return after the seizure stops, the seizure lasts more than five minutes, a second seizure is followed immediately after the first, the child has diabetes, there is a high fever, or there was an injury during the seizure (Valente & Valente, 1998). Children are diagnosed with having epilepsy if they experience seizures more than once for no known cause. The loss of consciousness and strange behaviors can be frightening for parents to witness. Possible complications of epilepsy include permanent brain damage that could lead to a stroke, pneumonia from aspiration of food or saliva, injuries from falls, and driving accidents (Campellone, 2014).

An electroencephalogram (EEG) measures the electrical activity in the brain and is the primary test used to diagnose epilepsy. The abnormal electrical activity during the test can possibly show the location of the seizure activity in the brain (Verrusio et al., 2015). Other diagnostic tests include blood sugar, lumbar puncture, blood chemistry, and tests for infectious diseases. Blood chemistry tests are used to check for abnormal electrolyte levels like sodium and calcium. Lumbar puncture is needed to analyze spinal fluid to see if there are any infections present such as encephalitis and meningitis. CT and MRI scans are helpful with also locating where in the brain the problems are starting. Not everyone who has seizures or tests positive for any of these measures has epilepsy (Karis, 2008). Epilepsy is a difficult medical condition to diagnose and treat. Estimates indicate that at least 10.5 million children in the world have active epilepsy (Guerrini, 2006). Presently, there are three categories of treatment options: medical, surgical, and alternative.

Epilepsy Treatments

Medical. Anticonvulsants have been used as a treatment option to prevent seizures before they begin. According to the Department of Health & Human Services (2013), there are four main anti-epileptic drugs (AEDs) that are used for children who have epilepsy: carbamazepine, carbamazepine XR, lamotrigine, and topiramate. Carbamazepine is used in children ages 1-17, carbamazepine XR for ages 6-17, lamotrigine for ages 2-17, and topiramate for ages 2-17. These medications can be used as an adjunct to other treatments or as monotherapy (Goede, 2014). Carbamazepine is contraindicated in some people of Han Chinese or Thai origin. The therapeutic drug levels for carbamazepine are 4 mcg per ml to 12 mcg per ml. Adverse reactions for anticonvulsant drugs include hepatotoxicity, teratogenicity, pancreatitis, and increased risk of suicide. Carbamazepine includes the black box warnings for serious dermatologic reactions called Stevens-Johnson syndrome, aplastic anemia, and agranulocytosis. These adverse effects can be fatal.

Use of medications may be initiated after the first unprovoked seizure if a child has a neurological deficit, the EEG shows unequivocal epileptic activity, the child is considered for risk of having further seizure unacceptable, and brain imaging shows a structural abnormality (NICE, 2012). It should be recognized that some children, young people, and adults may choose not to take an AED following a full discussion of the medication's risks and benefits (NICE, 2012). Parents must also be informed that any seizure can lead to sudden death. If parents are wary of medication use in children, they must be informed that any seizure can lead to sudden death and provided information on other treatment options such as surgery.

Surgery. Surgery is a second treatment modality for epilepsy. Surgeries that have been used to decrease the epileptic seizure activity in children are Vagus Nerve Stimulation, Temporal Lobe Resection, Lesionectomy, Functional Hemispherectomy, and Extratemporal Cortical Resection (Nowell, Miserocchi, McEvoy, & Duncan, 2014). Vagus Nerve Stimulation involves surgical placement of a pacemaker-like device that stimulates the vagus nerve, which is the longest of the 12 cranial nerves and reaches the organs in the chest and abdomen. Surgeons perform a Temporal Lobe Resection on the brain to limit and control seizures of a person with epilepsy. During this surgery, surgeons remove brain tissue responsible for the seizure from the temporal lobe. This surgery is effective for treatment of temporal lobe seizures. The temporal lobe is the most common location of epilepsy seen in teens and adults. The temporal lobe is in charge of language, memory, and hearing. During a Lesionectomy a surgeon removes a damaged area in the brain called a lesion. A lesion can be an abnormal blood vessel, scar, tumor, or hematoma that is a swollen area filled with blood. During a Functional Hemispherectomy surgeons remove portions of the affected hemisphere and cut the corpus callosum (connecting the two hemispheres together). The final surgical option is an Extratemporal Cortical Resection, in which the surgeon removes the brain tissue experiencing seizure activity.

These surgical treatments have many risks and also require a period of recovery. Patients can develop brain damage from having sections of their brain removed, which can cause lasting permanent effects that are worse than what they had before with the epileptic seizures. For children, these treatments can be used but they may affect how they grow and develop into adolescents as well as into young adulthood. When part of the brain is removed, children may not develop normally. “In terms of serious adverse events, surgery caused a verbal memory decrease in 36% of operated patients and transient neurological deficit due to postoperative stroke for one patient, whereas three patients from the medical group had status epilepticus (Ryvlin, Cross, Rheims, 2014, p.1115). “Although there can be serious adverse effects due to surgery, numerous studies in the past 20 years have reported seizure freedom for at least 1 year in 53–84% of patients after anteromesial temporal lobe resections for mesial temporal lobe sclerosis; in 66–100% of patients with dual pathology; in 36–76% of patients with localized neocortical epilepsy; and in 43–79% of patients after hemispherectomies” (Spencer & Huh, 2008, p. 525).

Despite the use of several new anticonvulsants in the recent past, approximately 30% of patients with epilepsy have recurrent seizures and may experience undesirable side effects. Seizure-free outcome after epilepsy surgery is seen in approximately 61-65% infants and 58-74% young children. It is also observed that shorter seizure durations and earlier surgical intervention result in better outcome and quality of life (Parakh & Katewa, 2014). It has been shown that 58% of patients who had epilepsy surgery had significant reduction or were seizure free at the end of one year post surgery as compared to only 8% of the patients who did not have surgery. According to Parakh and Ketewa, (2014) epilepsy surgery is one of the most promising non-pharmacologic approaches in the treatment of pharmaco-resistant epilepsy. Conditions associated with focal brain lesions are mesial temporal lobe epilepsy, CNS neoplasia, focal cortical dysplasias, and vascular malformations (Parakh & Katewa, 2014).

Alternative treatments. Alternative treatment options to decrease the epileptic seizure activity in children include the Ketogenic diet and music. The Ketogenic Diet is commonly known as the Atkins diet (Kossoff, Rowley, Sinha, & Vining, 2008). It is one of the oldest treatments for epilepsy and contains a diet that is high in fat and low in carbohydrates (DiMario & Holland, 2002). Using fat as the main source of the diet allows ketones to form, which after a few months affects seizure activity. Many people enjoy listening to music for their own pleasure. Beyond pleasure, listening to music may benefit children with epilepsy (Millichap, 2015). Music is one of the few activities that involves using the whole brain. It improves physical coordination, development, pain relief, and boosts immunity (NICE, 2010). One of the best benefits of using music for prevention of seizures is that it appears to be benign and is safe to use at < 82 decibels, as well as that parents and children are likely to comply with its use.

The Ketogenic Diet*.* Martin, Jackson, Levy, & Cooper (2016) reviewed seven random controlled trials (RCTs) evaluating the Ketogenic diet with a total sample size of 427 children with epilepsy. Due to the methodological differences between the studies, a meta-analysis was not possible for their review. The quality of the evidence was low due to the small sample size and high risk of bias in the included studies. Drop-out rates varied between 30% and 77%, reportedly due to participants feeling hungry, having dietary restrictions, and the lack of efficacy of the diet. For people who have medically intractable epilepsy or people who are not suitable for surgical intervention, a Ketogenic diet remains a valid option; however, they conclude that further research is required (Levy et al., 2012).

The mechanism of the Ketogenic diet in epilepsy is not clear. This diet is indicated in patients who have pharmacologically intractable seizures. Short-term adverse effects of Ketogenic diet are constipation, dehydration, hypoglycemia, and vomiting (Hosain, La Vega-Talbott, & Soloman, 2005). Long-term adverse effects include growth retardation, gastrointestinal disturbances, renal stones, fanconi renal tubular acidosis, dyslipidemia, carnitine deficiency, and pancreatitis (Parakh & Katewa, 2014). Ketogenic diet, used with an appropriate indication and with good compliance, results in reasonable reduction in seizure frequency, improves quality of life and in some cases may eliminate the need for epilepsy surgery or adding more anti-epileptic medications. Poor compliance and lack of availability of trained dietitians continue to be major issues for families with children on Ketogenic diet (Parakh & Katewa, 2014).

The Mozart Effect. One term for the application of music for health or intellectual benefit is the Mozart Effect. The Mozart Effect is a theory that exposure to the music of Wolfgang Amadeus Mozart, especially in children, can improve the child's general intelligence (Lerch & Anderson, 2000). Mozart died December 5th, 1791, at the age of thirty-five. The sonatas he has composed have been said to have helped many people who have been suffering neurological conditions. Some of these neurological conditions include depression, anxiety, stress, memory loss, listening disorders, dyslexia, attention deficit disorder, and autism.

Rauscher, Shaw, & Ky (1993) tested The Mozart Effect at University of California Irvine. They studied whether it would help in the brain's spatial reasoning abilities. Participating college students (N=36) were to take one of three standard tests of abstract spatial reasoning immediately following listening to a sonata by Mozart, using verbal relaxation instructions, and silence. Research participants were college students who were exposed to 10 minutes of Mozart's "Sonata for Two Pianos in D Major," a monotone voice, and silence (K.448). When the research participants finished one of the three standard tests, the researchers noticed a short-term increase in spatial reasoning on the Standard-Binet IQ test. None of the students exceeded a fifteen-minute period of enhanced effect due to the music. IQ was never measured, so the study did not evaluate whether the Mozart Effect could increase a person's IQ or not.

The researchers published a short, one-paged article called "Music and Spatial Task Performance," which listed their research on how exposing college students to 10 minutes of Mozart's "Sonata for Two Pianos in D Major" helped them improve their spatial reasoning abilities because of its repetition. Tests A and B conversely done by

Hallam, Prince, & Katsarou (2002) have shown that background auditory stimuli have increased the achievement on mathematical tests. Steele, Bass and Crook (1999), psychology professors from Appalachian State University, repeated the 1993 experiment but were not able to replicate the earlier study findings. Although the experiment failed to replicate the Mozart Effect on spatial reasoning, people continue to explore the benefits of music on intellect and health.

Rauscher et al. (1997) studied three and four year olds taking eight months of private piano lessons. The children who took these private piano lessons happened to score 34% higher on spatio-temporal reasoning tests than those who were given computer lessons, singing instruction, or no lessons at all.

The Mozart Effect has also been seen to be an alternative treatment for patients who have tinnitus. Sixty-two individuals between the ages of 22 and 78 who had tinnitus for at least a year were asked to attend a one-hour cognitive behavioral counseling session as well as listen to Mozart’s K.448 for one hour per day for a month. In the next month, the patients were to listen to Beethoven’s “Für Elise” sonata for one hour per day for a month. Three tests were done to see how the patients’ tinnitus was affected: the Tinnitus Handicap Inventory, the Measure du Stress Psychologique, and a 0 to 10 visual analog scale. The study showed that the patients received better enhancement from Mozart’s sonata compared to Beethoven’s sonata (Attanasio et al. 2012).

The Mozart Effect and Epilepsy

Črnčec, Wilson, & Prior (2006) determined that the Mozart Effect had no beneficial effect on children with epilepsy. One hundred and thirty-six fifth graders listened to Mozart’s piano sonata K.448, silence, and popular music. Each student completed a mood, music questionnaire, and spatiotemporal task. The results could not be produced and there showed to be no evidence with Mozart's music decreased children's epileptic seizures.

A person living with epilepsy who wants to use the Mozart Effect to help her manage her seizures writes a blog, *The Epilepsy Journal*. Tiffany Kairos experienced many seizures and tried every known medical treatment available. When she thought all else would fail, she decided to test out the Mozart Effect for a cure. She believes more research should be taken into consideration but that this could be a possible outlook to help epilepsy sufferers. Her blog provides insight into the perspective of a patient who lives with epilepsy and her thoughts on how the Mozart Effect has benefited her (Kairos, 2015).

Dobson (2008) describes a 46-year-old patient who went through seven anti-epileptic drugs and brain surgery, which have both failed in decreasing the number of seizures he developed. This 46-year-old man started to lose his memory and learning skills due to the treatments he had been getting to help him with his neurological disorder for nine years. Surprisingly, doctors thought the only cure for saving his learning skills and memory was more surgical operations on his brain.

Before the doctors were able to operate, they noticed an increase in his motor controls. The 46-year-old man was able to smile voluntarily, and he had decreased his uncontrollable laughing fits. He was also able to go from seven seizures a month to no seizures for three months total. This improvement in the frequency of seizures also gave him control of his motor skills once again.

The mechanism of action for the Mozart's sonata effect on patients with epilepsy may relate to how the brain's neurotransmitters work. When a patient listens to music for a period of time, a hormone called dopamine increases its levels in the brain. Dopamine is a compound present in the body as a neurotransmitter that plays a role in motor control motivation, arousal, and cognition. These neurotransmitters can mainly be found in a part of the brain called the substantia nigra, which is a small midbrain area that is part of the basal ganglia. There are around 400,000 dopaminergic neurons in the human brain (Bozzi & Borrelli, 2013).

Dopamine works in two important ways, the first being that it sets an "effort threshold" for behaviors. The more the levels of dopamine increases, the higher the motor activity. Slowed reactions are caused by low levels of dopamine to the brain. The second important way in which dopamine works is through a "teaching" signal. This "teaching" signal works by having a motor response trigger higher levels of dopamine, which allows the basal ganglia circuit to facilitate a response when needed. When Mozart's sonata triggers higher levels of dopamine, therapeutic effects can happen for patients who are dealing with epilepsy (Bozzi & Borrelli, 2013).

According to Maguire (2012), patients who experience seizures may have difficulty performing daily activities such as walking and eating, but listening to Mozart's sonata K.448 resulted in fewer seizures and a more normal life (Maguire, 2015). Although the seizures that come with epilepsy are uncontrollable once you get them, knowledge of other forms of treatment like Mozart's Effect improved the lives of many and gives people hope that they can have fewer seizures.

Methodology

In order to define our research question, we used PICO to formulate an answerable question. The PICO process includes a problem, intervention, comparisons, and an outcome (Aslam & Emmanuel, 2010). The problem is childhood epilepsy. The intervention to be used is the Mozart Effect. Comparisons will be made between the Mozart Effect and other epilepsy treatments. The outcome measure will be the change in epileptic seizure frequency. A systematic review was used to evaluate available evidence of the effects of Mozart's sonatas on children who have epileptic seizure activity. Three electronic databases searched were PubMed, CINHAL Complete, and Cochrane. Inclusion criteria included systematically reviewed literature all written in the English language, peer-reviewed articles, full texts, abstracts available, and published between April, 1999 and September, 2015. Exclusion criteria included adults, any articles written before 1999, reviews, editorials, and experiments not done on children. Keywords used were 'epilepsy,' 'children,' and 'Mozart Effect.' Based on the search criteria, there were 60 articles from Science Direct and CINHAL Complete, 11 articles from PubMed, and 1 article from Cochrane. Articles were found by using a combination of at least two keywords in the search. Abstracts were reviewed and duplicate citations were removed until all the articles that met the inclusion criteria were identified. Two of the eleven articles from PubMed were excluded since one was a review and the other was an editorial, which left nine selected. Excluded articles for Science Direct and CINHAL Complete included eleven duplicates, nine reviews, five non-human studies, five non-Mozart Effect studies, thirteen non-epilepsy studies, seven conference/posters, two not children studies, and two on epilepsy effect on music studies. Six studies remained from

Science Direct and CINHAL Complete. The Cochrane study was yet to be completed protocol. Nine articles were finally chosen for this review and the Johns Hopkins nursing evidence-based practice rating scale (JHNEBP) was used to evaluate each article's level of evidence and quality. The six studies were duplicates from the PubMed search.

Analysis of Quality

The John Hopkins nursing evidence-based practice rating scale (JHNEBP) was used to evaluate the seven articles in order to determine the level of evidence and quality.

Results

A search of three databases located 16 citations. Five citations were removed due to duplication. The nine articles selected for this review all examine the Mozart Effect and epilepsy in children (see Tables 1, 2, & 3). Seven of the nine published reports were from the same research group in Taiwan. One of these seven examines the use of an EEG for prediction of epileptiform discharges using Mozart K. 448. The two remaining studies were reports from Italy. Together, there is only one Level I study and this random control trial was of low quality due to its small sample size. There were six quasi-experimental Level II studies that ranged from low to good quality. There were two Level V case studies, and both were of good quality. Each researcher rated each study independently and then discussed evidence to support the rating.

Level I

Lin, Lee, Wu, & et al. (2014) studied forty-eight children with epilepsy who had their seizures controlled only through prescribed anti-epileptic drugs. They determined that listening to Mozart's sonata for Two Pianos in D major, K.448, improved mental function of children with epilepsy. After children listened to Mozart's sonata, their epileptiform discharges instantly decreased. During a six-month trial, EEGs were used to measure each child's epileptic seizure frequency. Next, they recorded how the children were affected by seizures while listening to Mozart's K.448 at one, two, and six months. The children were required to listen to Mozart K.448 for eight minutes once a day for the six-month period. All of the children remained on their prescribed anti-epileptic drugs during this study. Researchers observed that all of the children had a decrease in seizures over a 6-month time period. Children with occipital discharges had a decrease but the reduction was not as significant as seizure activity in other regions of the brain. Those who are mentally challenged did not have as great of a decrease in seizures as those who had normal intelligence. Gender and age did not affect the frequency of seizures in these children while using the use the Mozart Effect.

Overall, the Lin, Lee, Wu, & et al. (2014) study showed that Mozart's music was able to decrease epileptic discharges in children. They reported that "72.7% of the patients with refractory epilepsy became seizure free or had a good response to Mozart K.448 (Lin et al., 2014, p.4)." Listening to Mozart K.448 once daily reduced seizure reoccurrence in music-treated patients. After 1, 2, and 6 months of music listening, 70-80% of epileptic seizures have reduced for the children who were under musical treatment. This article was a Level I randomized control trial with low quality due to insufficient sample size.

Level II

Lin, Ouyang, & Chiang (2004) conducted a study in Taiwan with nineteen Taiwanese children (eight boys and eleven girls) diagnosed with epilepsy. They used electroencephalogram (EEG) segments to measure the effect of music on children with epilepsy. The EEG segments were obtained from each child once before and once while listening to Mozart K.448's first movement. Researchers categorized each EEG segment into one of two groups: effective or ineffective. The effective group contained children with a 25% reduction in seizure activity with music. The ineffective group contained children with a less than 5% reduction rate in seizure activity. The researchers concluded that the EEG was a useful tool for predicting epileptiform discharges in children, and researchers saw promise in its use as a therapeutic model. This article was a Level II quasi-experimental study with good quality.

Lin, Lee, Wu, & et al. (2010) experimented on fifty-eight children with Mozart's Sonata for two pianos in D major, K.448. The children were between the ages of 1 year to 19 years 8 months, with 30 being males and 28 being females. The participants listened to piano K.448 before (8 minutes), during (8 minutes), and after (8 minutes) at 60-70 decibels. Forty-seven patients showed a significant decrease in epileptiform discharges while exposed to K.448. Eleven of these patients were exposed to string K.448 a week later. The results showed that interictal discharges were reduced in 81% of the patients who listened to piano K.448. Although two kinds of music had the same melody, piano K.448 and string K.448 differed in their harmonics. Interestingly, lower harmonics found in piano K.448 work better to decrease seizure activity compared to higher harmonics found in string K.448.

Lin, Lee, Wu, & et al. (2011a) conducted a study of eighteen children who had epilepsy that was well-controlled through anti-epileptic drugs (AED). EEGs were used to monitor the children for 6 months to see how their seizure activity was doing. These patients listened to Mozart K.448 over a period of 6 months for 8 minutes once a day before bedtime. Seizure activity was recorded from the EEG and compared before and after 1, 2, and 6 months of listening to Mozart K.448. “There were no significant changes in epileptiform discharges after more than 6 months of AED treatment prior to music exposure. However, significant decreases in epileptiform discharges were found after 1, 2, and 6 months of listening to Mozart K.448 when compared with EEGs before listening to music (Lin et al., 2011a, p. 323).” This article was a longitudinal Level II quasi-experimental study with good quality.

Lin, Lee, Wu, & et al. (2011b) conducted a study of eleven children with refractory epilepsy for more than one year. They demonstrated how epileptiform discharges in children with epilepsy were reduced during and after listening to Mozart K.448. The children listened to Mozart K.448 once a day before bedtime for six months. Eight of the eleven patients were seizure free or had very good responses after 6 months of listening to Mozart K.448. The other three children had little to no effect on their seizure activity. In conclusion, this article was a Level II quasi-experimental study with a pre-test post-test design. It was judged to be of low quality due to its small sample size.

In another study, thirty-nine Taiwanese children (19 boys and 20 girls) with epilepsy were studied by Lin, Lee, Wei, & et al. (2012). Each child was given an electroencephalogram (EEG) to track their seizure before, during, and after listening to Mozart K.448 for 8 minutes 22 seconds and K.545 for 9 minutes 7 seconds one week apart. The frequencies of epileptiform discharges were compared. Most patients (84.6% and 82.1% during Mozart K.448 and K.545, resp.) demonstrated decreased interictal discharge frequencies when listening to either piece of music. “There was a significant decrease in the frequency of epileptiform discharges during and right after listening to

Mozart K.448 and K.545 (reduced by 35.7 ± 32.7% during Mozart K.448 and 30.3 ± 44.4% after Mozart K.448; and 34.0 ± 39.5% during Mozart K.545 and 31.8 ± 39.2% after Mozart K.545) p. 3.” Researchers concluded that listening to Mozart K.448 and K.545 can decrease the epileptiform discharges in children with epilepsy. This is a one group longitudinal study with no control or randomization. It is a Level II quasi-experimental study with good to low quality due to small sample size but reasonable expert opinion.

Lin, Chiang, Lee, & et al. (2013) did a study on sixty-four epileptic children with epileptiform discharges. An electrocardiogram was used before, during, and after listing to Mozart K.448 or K.545. The children were exposed to K.448 for 8 minutes 22 seconds or K.545 for 9 minutes 7 seconds, depending on the patient’s preference. Each child received 60-70 decibels musical stimuli and all recordings were performed during the daytime, where they were in a state of wakefulness. Forty-one patients listened to Mozart K.448 and twenty-three patients listened to Mozart K.545. Most patients (90.2% and 82.6% during Mozart K.448 and Mozart K.545) had decreased epileptiform discharges when listening to either piece. Epileptic discharges were significantly reduced in patients with generalized seizures.

Level V

Coppola et al. (2015) studied 11 outpatients with epilepsy (7 males and 4 females) from the ages of 1.5 to 21 years old. Children were exposed to different musical compositions for their seizures. The study investigated whether or not listening to two hours a day of Mozart’s sonata for 15 days straight would lower the seizure activity they were all experiencing. After the 15-day study was conducted, the results showed that three patients reduced their seizures by 75-89%, and two other patients had a decrease in their seizures by 50-75%. The patients who were treated with Mozart’s symphonies 41 and 36, piano concerto 22 (k482), flute concerto (k314), and violin concertos 1 and 4 all had severe cerebral palsy and intellectual disability along with their epilepsy. Although not every patient’s seizures reduced during this study, all responders were able to display an improvement in their behavior. Unlike other studies in this review, the researchers used low harmonics. This article is a Level V non-experimental design with good to low quality due to small sample size but reasonable expert opinion.

Hughes, Fino, & Melyn (1999) studied the ability of patients to obtain a chronic seizure reduction effect from listening to Mozart’s music. In this case study, an eight-year-old patient was exposed to music from the time she was awake and following for a twenty-four-hour period. EEG recordings were done starting at 9:00 am on October 15, 1998 until 9:00 am the next day. Seizures that occurred by the patient were counted by the patient’s teacher and mother. Mozart K.448 was played ten minutes every hour for twenty-four hours once the patient woke up at 9:00 am that day. The patient suffered from an arteriovenous malformation on the right posterior temporal area that was operated on due to the frequent seizures she was experiencing. The eight-year-old was placed on anti-epileptic drugs (Klonopin and Topamax) to help reduce her seizures. On the day of the study, the patient was able to decrease her seizure count from 9 to 7 a day to 1 from the times she was awake. Also, she had a decrease in the number of seconds from the drop attacks. These decreased from 317 to 208 to 178 seconds. The study revealed that the eight-year-old patient was able to achieve relief from her epileptic seizures to a certain degree through the lasting effect she received from the Mozart Effect

(Hughes et al., 1999). This article was a Level V case study with good quality due to expert opinion.

Discussion

Surgical, medical, and alternative treatments are available for children with epilepsy. Anti-epileptic medications and surgical treatment for epilepsy have been beneficial for some children, but they come with potential adverse effects. Research with children is challenging due to the appropriate concerns related to exposure of children to health risks and poor outcomes. Strengths of alternative treatments include being acceptable to parents, acceptable theoretical mechanism of action, and the feasibility of music listening.

Music is an alternative treatment that appears benign and safe for use with children. Researchers in nine published articles studied Mozart's music and found it to be harmless. The safety of this intervention appeals to parents for use with children because no adverse effects to listening to Mozart's music have been reported. Case reports and underpowered studies all report a decrease in seizure frequency following periods of exposure to Mozart's music.

Combining anti-epileptic drugs and Mozart's sonatas may reduce seizure frequency. Using prescribed medications and following a music listening regimen can show a decrease in epileptiform seizure development. Additionally, consistent daily listening over time may lessen seizure frequency long term in children. As it was shown in the Lin, Lee, Wu, and et al. (2011a) Level II study, treatments for eighteen Taiwanese children who were well-controlled on anti-epileptics and listened to Mozart K.448 for 8 minutes once a day before bedtime for 6 months were able to decrease the frequency of seizures. Another Level II study done by the same researchers, Lin, Lee, Wu, and et al. (2011b), also compared the effects of anti-epileptic drugs with Mozart's music with eleven children. Eight of eleven children were seizure free (n=2) or had very good responses (n=6) after 6 months of listening to Mozart K.448 while they were still on the anti-epileptic medications.

Music changes brain wave forms on its own. Mozart's sonatas have a rhythmic effect and allow the brain to follow a steady pattern. In a report of the Level I randomized control trial study, Lin, Lee, Wu, and et al. (2014) discuss the significant decreases in epileptiform discharges observed after 1, 2, and 6 months of listening to Mozart K.448 compared to before when the 48 children did not listen to Mozart K.448. As evidenced by the study, the children developed no harmful side effects. In a Level II analysis, Lin, Lee, Wu, and et al. (2012) studied 39 Taiwanese children and reported a significant decrease in the frequency of epileptiform discharges during and immediately following listening to Mozart K.448 and K.545. Some brains respond to music better than others do. In a Level II study, Lin, Ouyang, and Chiang (2014) measured the responsiveness of brain activity to music with nineteen Taiwanese children. Those with at least a 25% reduction in seizure activity were considered responsive to music and those with less than a 5% reduction were considered not responsive.

Different harmonics (low and high) and different Mozart sonatas have been studied. In a Level II Quasi-Experimental study done by Lin, Lee, Wu, and et al. (2010) with 58 Taiwanese children were exposed to low harmonic piano K.448 and high harmonic string K.448. Forty-seven children exposed to piano K.448 greatly decreased their epileptiform discharges and did substantially better than when they were exposed to string K.448 which had high harmonics. Another Level II Quasi-Experimental study was conducted by Lin, Chiang, Lee, and et al. (2013) where forty-one children listened to K.448 and twenty-three children listened to K.545. Most participants (90.2% with Mozart K.448 and 82.6% during Mozart K.545) decreased their epileptiform discharges. Listening to either sonata can be beneficial for children with epilepsy.

The Mozart Effect has helped children with comorbidities. Children with epilepsy and severe disorders such as Cerebral Palsy and Lennox-Gastaut Syndrome were studied with the Mozart Effect. Coppola et al. (2015) conducted a Level V study where “5 out of 11 patients with drug-resistant epileptic encephalopathy associated with cerebral palsy had a ≥ 50% reduction in the total number of seizures after listening to a set of Mozart’s compositions 2 hours per day for 15 days (Lin & Yang, 2015, pg. 1).” Three of the remaining five patients had a seizure reduction of 75-89%, and the other two of the five patients had a reduction of 50-75% in seizure recurrence. Hughes et al. (1999) in their Level V study with an eight-year-old with Lennox-Gastaut Syndrome found the frequency of clinical seizures decreased from nine to seven to one over three periods of being awake.

With consideration to the level and quality of the studies available, the Mozart Effect demonstrated the greatest reduction in seizure activity when combined with anti-epileptic drugs. Due to the limitations of study design, no causal relationship between this observed reduction and the treatment can be determined. Evaluating the strength of the studies with the JHEBP demonstrated that the studies were low level and had variable quality. Many of the studies relied on expert opinion based on experience and evidence of what is known. Registered nurses need to apply knowledge and scientific evidence to improve evidence-based patient outcomes.

Combining the Mozart Effect with anti-epileptic drugs appears to be the most efficacious when considering the evidence from the nine articles reviewed in this study. This combination may allow children to reduce the number of epileptiform seizures they experience. Children can benefit from Mozart's sonatas because music is benign, music can be used with or without medications, and parents support its use for seizure reduction.

Conclusion

Music may be a simple yet powerful tool to decrease seizure activity in children. A systematic review of available evidence was performed to answer the question as to whether or not the Mozart Effect decreases seizure activity in children who have epilepsy. The data supports that the Mozart Effect on children with epilepsy does not cause any adverse effects. Observational studies have shown that listening to Mozart's K.448 reduces seizure episodes in children who are not in complete control of their motor functions. The evidence is inconclusive on the Mozart Effect's ability to reduce seizure incidence although there is strong support that epileptiform discharges are decreased with music listening. The Mozart Effect is an alternative treatment for people who do not accept the risks of surgical epilepsy treatment. Although there is no cure for epilepsy, the Mozart Effect can augment medical epilepsy treatment and possibly decrease the medication dose needed to prevent seizure activity.

Implications for Registered Nurses include offering the Mozart Effect as an adjunct to current therapies, being able to administer in school settings, and educating parents about the strengths and limitations of the research. Overall, the Mozart Effect is a safe alternative adjunctive treatment for children with epilepsy.

Future studies of the Mozart Effect would benefit from randomization, study of other races, and an increased sample size. In addition, other sonatas or repetitious music with high or low harmonics could add to our understanding of the effect music has on the management of epilepsy symptoms. Longitudinal studies would be of great interest and benefit.

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Table 1

Evaluation of Level 1 Epilepsy Studies with JHNEPB

Level I Article	# of Children	Population characteristics	Intervention	Conclusion	JHEBP Rating Scale Strength	
Lin, L.C., Lee, W.T., Wu, H.C., et al. (2014).	48	Taiwanese Unprovoked seizure with epileptiform discharges	Treatment group listened to Mozart K.448 daily before bedtime for at least 6 months.	The seizure recurrence rate was estimated to be significantly lower in the treatment group than the control group over 24 months (37.2% vs. 76.8%). Significant decreases in epileptiform discharges after 1, 2, and 6 months of listening to Mozart K.448 compared with EEGs before listening to music.	Level I Randomized Control Trial Patients were randomly placed into treatment (n=24) and control (n=24) groups. Excluded two children in treatment group due to discontinuation intervention.	Quality L Low Insufficient sample size to determine cause and effect relationship

Table 2

Evaluation of *Level II Epilepsy Studies with JHNEPB*

Level II Article	# of Children	Population characteristics	Intervention	Conclusion	JHEBP Rating Scale Strength	
Lin, L.C., Lee, W.T., Wu, H.C., et al. (2010)	58	Taiwanese Epilepsy diagnosis Ages 1 to 19 years	Children were exposed to low harmonic piano K.448 and high harmonic string K.448. Those who benefited from piano K.448 listened to string K.448 a week later after the first experiment.	Forty-seven patients exposed to piano K.448 greatly decreased their epileptiform discharges and did substantially better than when they were exposed to string K.448, which had high harmonics.	Level II Quasi-Experi mental	Quality Good
Lin, L.C., Lee, W.T., Wu, H.C., et al. (2011a)	18	Taiwanese Epilepsy diagnosis clinically well-controlled with antiepileptic drugs (AED) Persistent epileptiform discharges pm ECG for at least 6 months.	Listened to Mozart K.448 for 8 minutes once a day before bedtime for 6 months.	There were no significant changes in epileptiform discharges after more than 6 months of AED treatment prior to music exposure. Significant decreases in epileptiform discharges were found after 1, 2, and 6 months of listening to Mozart K.448 when compared with EEGs before listening to music.	Level II Quasi-Experi mental	Quality Good

Lin, L.C., Lee, W.T., Wu, H.C., et al. (2011b)	11	Diagnosed with refractory epilepsy > 1 year Receiving two antiepileptic drugs (AED)	Children listened to Mozart K.448 once a day before bedtime for 6 months; Children remained on the same AEDs during the 6-month period. 72.7% of patients became seizure-free or had a very good response to listening to Mozart K.448.	Eight of eleven patients were seizure free (n=2) or had very good responses (n=6) after 6 months of listening to Mozart K.448. The remaining (27.3%) showed minimal or no effect (effectiveness <50%; unmodified or worsened seizure frequency).	Level II Quasi-Experimental Pre-Test/Post-Test Design Recorded seizure frequencies at 6 months prior to listening to this music and monthly during the study period.	Quality Low Small sample size
Lin, L.C., Lee, W.T., Wu, H.C., et al. (2012).	39	Taiwanese (19 boys and 20 girls) Diagnosed with epilepsy	Children received electroencephalogram examinations before, during, and after listening to Mozart K.448 and K.545 one week apart. The frequencies of epileptiform discharges were compared	There was a significant decrease in the frequency of epileptiform discharges during and right after listening to Mozart K.448 and K.545 (reduced by 35.7 ± 32.7% during Mozart K.448 and 30.3 ± 44.4% after Mozart K.448; and 34.0 ± 39.5% during Mozart K.545 and 31.8 ± 39.2% after Mozart K.545).	Level II Quasi-Experimental There was one group with no control or randomization.	Quality Good to low small sample size Reasonable expert opinion.

Lin, L.C., Chiang, C., Lee, M., et al. (2013)	64	Taiwanese 31 boys 33 girls	Participants could chose to listen to either Mozart K.448 (8 min 22 sec) or Mozart K.545 (9 min 7 sec). Forty-one children listened to K.448 and twenty-three children listened to K.545.	Most participants (90.2% and 82.6% during Mozart K.448 and K.545) decreased their epileptiform discharges. Listening to either sonata can be beneficial for children with epilepsy.	Level II Quasi-Experimental	Quality Good
Lin, L., Ouyang, C., Chiang, C., et al. (2014)	19	Taiwanese 8 boys 11 girls	EEG examinations were performed in two parallel periods in each patient; before, and while listening to Mozart K.448's first movement (8 min 22 seconds) EEG data were compared by qEEG.	The qEEG has potential to predict braim response even in those without epileptiform discharges. Therapeutic effectiveness of music in patients with epilepsy can be confirmed with the qEEG.	Level II Quasi-Experimental	Quality Good

Table 3

Evaluation of Level V Epilepsy Studies with JHNEP

Level V Article	# of Children	Population characteristics	Intervention	Conclusion	JHEBP Rating Scale Strength	
Coppola, G., Toro, A., Operto, F.F., et al. (2015).	11	7 boys 4 girls Ages 1.5 to 21 Diagnosed with severe intellectual disability and Cerebral Palsy Drug resistant encephalopathy mean age, 11.9 years	Listened to Mozart 2 hours a day for 15 days. Mozart compositions presented to each person included symphonies 41 and 46, piano concerto 22 (k482), violin concertos 1 & 4, and flute concerto (k314).	Five out of the 11 had a ≥ 50% reduction in the total number of seizures after listening to a set of Mozart's compositions or 15 days. Three of the five patients had a seizure reduction of 75-89% Two of the five patients had a reduction of 50-75% in seizure recurrence.	Level V Case Study	Quality Good Expert opinion
Hughes, J.R., Fino, J.J., Melyn, M.A. (1999)	1	A 8-year old girl diagnosed with Lennox-Gastaut Syndrome	Every hour on the hour for 10 minutes when the child was awake, Mozart's music was played (Sonata for Two Pianos in D Major K.448). 24 hour monitoring with an 8-channel ambulatory EEG instrument with electrodes The number of seizures was counted by the mother and teacher while in school.	The number of clinical seizures on 10/15/98 decreased from 9 to 7 to 1 over 3 periods of being awake. The number of attacks the next day (10/16/98) was 2 in contrast to 9 on the previous day over the similar time period.	Level V Case Study	Quality Good Expert opinion

JHNEBP EVIDENCE RATING SCALES

STRENGTH of the Evidence	
Level I	Experimental study/randomized controlled trial (RCT) or meta analysis of RCT
Level II	Quasi-experimental study
Level III	Non-experimental study, qualitative study, or meta-synthesis.
Level IV	Opinion of nationally recognized experts based on research evidence or expert consensus panel (systematic review, clinical practice guidelines)
Level V	Opinion of individual expert based on non-research evidence. (Includes case studies; literature review; organizational experience e.g., quality improvement and financial data; clinical expertise, or personal experience)

QUALITY of the Evidence			
A	High	Research	consistent results with sufficient sample size, adequate control, and definitive conclusions; consistent recommendations based on extensive literature review that includes thoughtful reference to scientific evidence.
		Summative reviews	well-defined, reproducible search strategies; consistent results with sufficient numbers of well defined studies; criteria-based evaluation of overall scientific strength and quality of included studies; definitive conclusions.
		Organizational	well-defined methods using a rigorous approach; consistent results with sufficient sample size; use of reliable **and** valid measures
		Expert Opinion	expertise is clearly evident
B	Good	Research	reasonably consistent results, sufficient sample size, some control, with fairly definitive conclusions; reasonably consistent recommendations based on fairly comprehensive literature review that includes some reference to scientific evidence
		Summative reviews	reasonably thorough and appropriate search; reasonably consistent results with sufficient numbers of well defined studies; evaluation of strengths and limitations of included studies; fairly definitive conclusions.
		Organizational	Well-defined methods; reasonably consistent results with sufficient numbers; use of **reliable and valid** measures; reasonably consistent recommendations
		Expert Opinion	expertise appears to be credible.
C	Low quality or major flaws	Research	little evidence with inconsistent results, insufficient sample size, conclusions cannot be drawn
		Summative reviews	undefined, poorly defined, or limited search strategies; insufficient evidence with inconsistent results; conclusions cannot be drawn

	Organizational Expert Opinion	Undefined, **or** poorly defined methods; insufficient sample size; inconsistent results; undefined, poorly defined or measures that lack adequate reliability or validity expertise is not discernable or is dubious.

*A study rated an A would be of high quality, whereas, a study rated a C would have major flaws that raise serious questions about the believability of the findings and should be automatically eliminated from consideration.

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