



THE ROLE OF PHYSICAL THERAPY IN THE MANAGEMENT OF CHILDREN WITH
EPILEPSY.

By

ABDULSALAM MOHAMMED YAKASAI

S150933

DOCTOR OF PHYSICAL THERAPY

abdulpeace1@gmail.com/a.yakasai@manualosteopath.com

JUNE,2016

CHAPTER ONE

BACKGROUND: An epileptic seizure is the transient occurrence of signs or symptoms due to abnormal electrical activity in the brain, leading to a disturbance of consciousness, behavior, emotion, motor function or sensation (Nunes et.al 2012). Epilepsy is not a single diagnosis but is a symptom with many underlying causes (NICE,2013). Epileptic seizures and epilepsy syndromes should be classified according to the description of seizure, the seizure type, the epilepsy syndrome and the etiology. The seizure type(s) and epilepsy syndrome, etiology and comorbidity should be accurately determined because failure to classify the epilepsy syndrome correctly can lead to inappropriate treatment and persistence of seizures (Scottish intercollegiate guidelines network, 2015).

STATEMENT OF THE PROBLEM: Every function in our bodies is triggered by messaging systems in our brain. What a patient with epilepsy experiences during a seizure shall depend on what part of his/her brain that is affected and epileptic activity starts, and how widely and quickly it spreads from that area. It affects consciousness, behavior, emotion, motor and sensory functions which compromised health related quality of life. Consequently, there are several types of seizures and each patient will have epilepsy in his/her own unique way (Nordqvist, 2015).

Neuroprotective and antiepileptogenic approaches have been extensively explored for preventing and treating epilepsy (Acharya, Hattiangady, & Shetty. 2008). Although the most commonly used therapeutic approach to control seizures is pharmacological, non-pharmacological therapies, including complementary and alternative medicine, are often used by people with epilepsy (Sirven, Drazkowski, Zimmerman, Bortz, Shulman,& Macleish,M, 2003; Schachter,2008; Arida Scorza,Scorza &Cavalheiro, 2009). Among them, acupuncture, botanical/herbals, chiropractic care, magnet therapy, prayers, stress management, and yoga are frequently employed (Sirven,2007). It is interesting to note that neither people with epilepsy nor health care professionals usually include physical exercise programs as a complementary therapy. This reluctance may be due to fear that exercise will cause seizures, stigma, or lack of information. Considering the growing evidence in the literature about the positive effects of exercise for both seizure control and improvement of quality of life of individuals with epilepsy, it seems reasonable to include programs of exercise as a complementary non-pharmacological treatment of epilepsy.

QUESTIONS:

- 1) What is the role of physiotherapy in the management of children with epilepsy?
- 2) What is the effect of epilepsy on health related quality of life of children?
- 3) What is the knowledge of health professionals on the role of physiotherapy in the management of children with epilepsy?

PROJECT OBJECTIVES

- To investigate the role of Physiotherapy in the management of children with epilepsy.
- To assess the health related quality of life in children with epilepsy.
- To review effective modalities and exercises used in the management of children with epilepsy.
- To provide handbook on the role of Physiotherapy in epilepsy.

Research Design: Review of Articles.

PROJECT OUTCOME.

Literature was searched on the effective modalities and exercises used by physical therapists (PTs) in the physiotherapy intervention in the management of children with epilepsy. Then a handbook was provided that will be distributed to our medical colleagues in different settings.

CHAPTER TWO

The word "epilepsy" comes from the Greek word epi meaning "upon, at, close upon", and the Greek word Leptos meaning "seizure". From those roots we have the Old French word epilepsie, and Latin word epilepsia and the Greek words epilepsia and epilepsies. Epileptic seizures and epilepsy syndromes should be classified according to the description of seizure, the seizure type, the epilepsy syndrome and the aetiology. The seizure type(s) and epilepsy syndrome, etiology, and comorbidity should be determined, because failure to classify the epilepsy syndrome correctly can lead to inappropriate treatment and persistence of seizures. Children and young people with epilepsy and/or their family/carers should be given information about their seizure type(s) and epilepsy syndrome, and the likely prognosis(NICE Clinical Guideline,2012)

Prevalence:

Epilepsy is a common neurological disorder in childhood. Seizures and epilepsy affect infants and children more than any other age group (NICE CKS, 2014). Epilepsy is about twice as common in children as in adults (about 700 per 100,000 in children under the age of 16 years compared to 330 per 100,000 in adults).The incidence of status epilepticus in developed countries is between 17 and 23/100,000 with a higher incidence in younger children(Neville, Chin and Scott, 2007). There is an increased risk of seizures in children of parents with epilepsy. The probability that a child will be affected is generally low but will depend on the family history (NICE Clinical Guideline, 2012).

There are twice as many people with epilepsy in developing nations than industrialized countries. Unfortunately, over 60% of people in poorer nations do not receive proper medical care for epilepsy, researchers from the University of Oxford reported in the journal *The Lancet*(2013). The authors added that the burden of epilepsy in developing countries is "under-acknowledged by health agencies", even though treatments for the disorder are very cost-effective. However, the burden of epilepsy in these regions is at least double that found in high-income countries, and sadly, adequate facilities for diagnosis, treatment and ongoing management of epilepsy are virtually non-existent in many of the world's poorest regions. Many people with epilepsy or their families do not even know that they have a disorder that can be controlled with biomedical treatment, so it is vitally important that awareness is raised and medical care improved in these regions."

They further explained that Epilepsy and life expectancy indicated premature death is 11 times more common among people with epilepsy compared to the rest of the population. The authors added that the risk is even greater if a person with epilepsy also has a mental illness.

Causes of Seizures in Children:

Though seizures have many known causes for most children, and some cause remains idiopathic. In many of these cases, there is some family history of seizures. The remaining causes include infections such as meningitis, developmental problems such as cerebral palsy, head trauma, and many other less common causes. About one fourth of the children who are thought to have seizures are actually found to have some other disorder after a complete evaluation. These other disorders include fainting, breath-holding spells, night terrors, pavor nocturnes, migraines, and psychiatric disturbances (Frank, 2015).

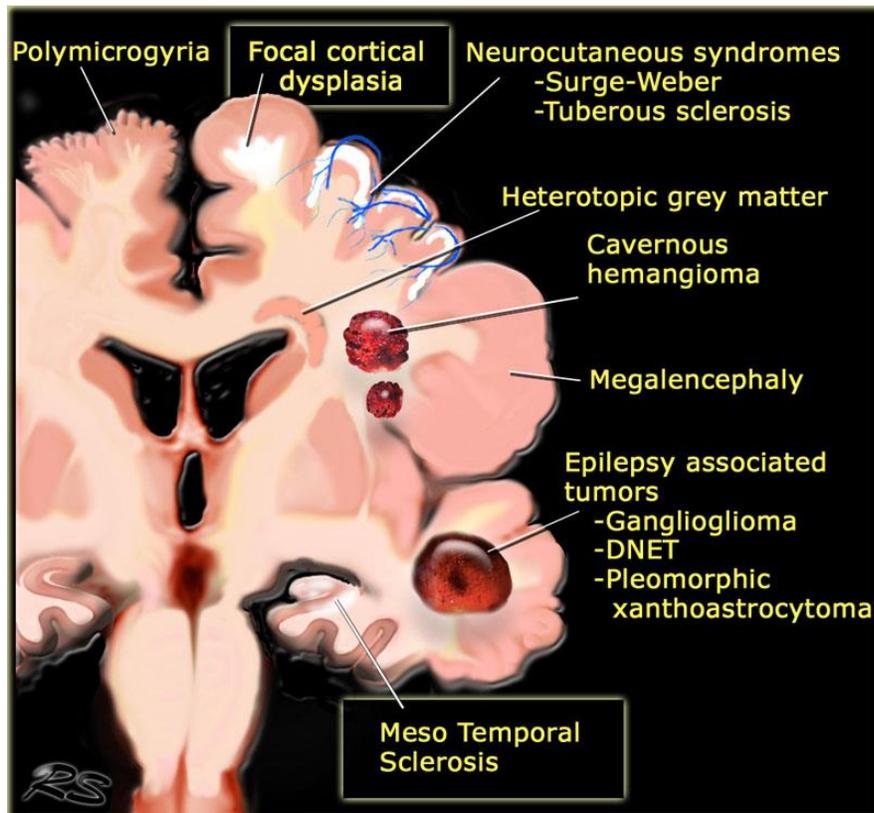
The most common type of seizure in children is the febrile seizure, which occurs when an infection associated with a high fever develops. Other reasons for seizures are these:

- * Infections
- * Metabolic disorders
- * Drugs
- * Medications
- * Poisons
- * Disordered blood vessels
- * Bleeding inside the brain

Many yet undiscovered problems (Frank,2015).

Woermann and Vollmar (2009), summarizes in the illustration below the most common causes of seizures in patients with medically uncontrollable epilepsy. Some of these lesions are readily identifiable. Meso temporal sclerosis and focal cortical dysplasia are the most common causes

and can only be depicted with a dedicated protocol. It also summarizes epileptogenic lesions that are detected in patients with uncontrollable seizures. Mesial temporal sclerosis is the most common cause of intractable epilepsy. In medication refractory epilepsy the most common location of the epileptogenic lesion is *temporal lobe* (60%), frontal lobe (20%) and parietal lobe (10%), periventricular (5%) and cipital(5%).



Trigger factors

- Watching television and lack of sleep are two common triggers.
- It has been shown that observing the set with one eye covered prevents the occurrence of these seizures (Woermann & Vollmar ,2009)

Clinical Presentation:

When a child or young person presents with a seizure, a thorough physical examination should be performed, including cardiac, neurological and mental state. An assessment of development is important for children presenting with a seizure (NICE Clinical Guideline 2012).

Presenting features in children are identical to those in adults. However, these subtypes are more common, or occur exclusively, in childhood:

- **Typical absences** ('petit mal' seizures): petit mal epilepsy is manifest by frequent (as many as 100 times per day or more) episodes of brief staring spells (lasting seconds at a time):
 - Onset in childhood; attacks continuing into adult life are rare.
 - A typical absence attack lasts only a few seconds. The onset and termination are abrupt. The child ceases what he or she is doing, stares, looks a little pale and may flutter the eyelids.
 - Sometimes more extensive bodily movements occur (such as dropping the head forwards) and there may be a few clonic movements of the arms.
 - The interruption of the normal stream of consciousness is very brief and the child may be unaware of the attacks, as indeed may be the parents for some time after onset, assuming that the child is just day-dreaming.
 - About one third of all children with petit mal will have one or more tonic-clonic convulsions.
- **Infantile spasms:**
 - Occur in infants aged 4-8 months.
 - Consist of clusters of myoclonic spasms that occur when waking up.
- **Dravet's syndrome.**
 - Dravet's syndrome includes severe myoclonic epilepsy of infancy with the onset of recurrent febrile and/or afebrile hemiclonic or generalised seizures, or status epilepticus, in a previously healthy infant.
 - Multiple seizure types develop which are generally resistant to AEDs. There is also developmental arrest or regression.
 - Onset up to 15 months of age may occur.
 - Mortality may be up to 15% by age 20 years (NICE Clinical Guideline 2012).

- **Lennox-Gastaut syndrome.**
- **Juvenile myoclonic epilepsy:**
 - Occurs in the teen years.
 - Early morning sudden myoclonic jerks, especially of the arms and shoulders.
 - Often later develop generalised tonic-clonic (GTC) seizures.
 - May be inherited as autosomal dominant (Catarino, et al; 2011).

- **Panayiotopoulos syndrome:**
 - Panayiotopoulos syndrome is a common multifocal autonomic childhood epileptic disorder.
 - Affects otherwise normal children with onset at around 3-6 years.
 - Seizures are often prolonged, with predominantly autonomic symptoms and mainly ictal vomiting.

- Electroencephalogram (EEG) shows shifting and/or multiple foci, often with occipital dominance.
- Often confused with occipital epilepsy and acute non-epileptic disorders - eg, encephalitis, syncope, cyclical vomiting or atypical migraine.
- Benign Rolandic epilepsy:
 - Also known as benign focal epilepsy.
 - It occurs in children aged 4-10 years and is more common in boys.
 - Nocturnal seizures that are characterised by facial twitching and aphasia.
 - Some children with benign Rolandic epilepsy may also have GTC seizures.
- Benign childhood epilepsy with centrotemporal spikes:
 - Some older children may have focal or generalised seizures.
 - The interictal EEG is characterised by large spike discharges over the Rolandic area of one hemisphere.
 - Is not associated with any structural lesion and has an excellent prognosis (Michael, Tsatsou & Ferrie, 2010).

Types of seizures

There are three types of diagnoses a doctor might make when treating a patient with epilepsy:

Idiopathic - this means there is no apparent cause.

Cryptogenic - this means the doctor thinks there is most probably a cause, but cannot pinpoint it.

Symptomatic - this means that the doctor knows what the cause is.

There are three descriptions of seizures, depending on what part of the brain the epileptic activity started:

Partial seizure;

A partial seizure means the epileptic activity took place in just part of the patient's brain.

There are two types of partial seizure:

Simple Partial Seizure - the patient is conscious during the seizure. In most cases the patient is also aware of his/her surroundings, even though the seizure is in progress.

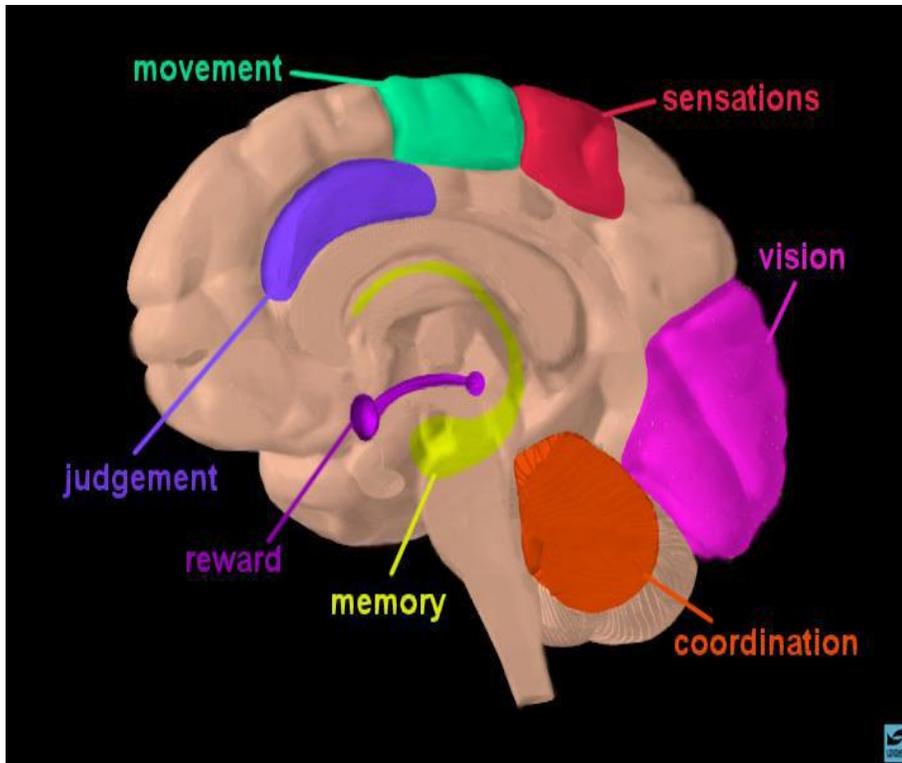
Complex Partial Seizure - the patient's consciousness is impaired. The patient will generally not remember the seizure, and if he/she does, the recollection of it will be vague.

Generalized Seizure

A generalized seizure occurs when both halves of the brain have epileptic activity. The patient's consciousness is lost while the seizure is in progress.

Secondary Generalized Seizure

A secondary generalized seizure occurs when the epileptic activity starts as a partial seizure, but then spreads to both halves of the brain. As this development happens, the patient loses consciousness.



In generalized seizures, both hemispheres are widely involved from the outset. Manifestations of the seizure are determined by the cortical site at which the seizure arises. Present in 40% of all epileptic.

PATHOPHYSIOLOGY OF SEIZURE

Ananya (2013) stated that seizure is the clinical manifestation of epilepsy. This occurs basically due to excessive firing of the neurons and fast spread of these impulses over the brain. Thus there are two phenomenons in the pathophysiology of a seizure:-

- hyper-excitability of a neuron
- hyper synchronization

Hyper synchronization means that a hyper-excitabile neuron leads to excessive excitability of a large group of surrounding neurons. This means that when a large electrical impulse is generated in one part of the brain from a focus of tissues millions of neurons in the brain fire excessively in addition bringing on a seizure

Mechanism of seizure formation

- Excitation of a group of nerves. This is caused by inward currents of Na, Ca and involvement of excitatory neurotransmitters like Glutamate and Aspartate.
- Too little inhibition.

- Epileptogenesis and hyperexcitability and hypersynchronization of neurons that facilitates spread. There has to be abnormal synchronization – a property of a population of neurons to discharge together independently. Alone, a hyperexcitable neuron cannot generate a seizure (Ananya, 2013).

Quality of life in children with epilepsy.

In the year 2000, Christianson and co workers stated that Epilepsy is a chronic medical condition with so many co-morbid features. It has been observed that children with epilepsy (CWE) have a compromised quality of life (QOL). Epilepsy can significantly affect the quality of life (QOL) not only because of its chronicity need for regular medications and their side effects, but also due to prejudices and social conventions that still surround it.

The traditional medical goal in the management of epilepsy has focused almost exclusively on seizure control with minimal or no adverse medication effect (Christianson et.al ., 2000), whereas the importance of assessing QOL has been ignored. This is particularly true for Indian children, where the QOL is probably affected by the social stigma associated with the disease. Studies from India on children with epilepsy (CWE) (Malhi & Singhi,2005; (Datta et.al.,2006) and a notable study of Thomsa and co workers in adults with epilepsy and have shown a relatively compromised QOL. Overall QOL was affected more in older children as compared to younger age group in the study of Devinsky *et al.*(1999) Emotional, social and behavioral domains were affected more in older age group. This may be due to the fact that older children are more likely to perceive a greater negative impact on life and general health and have more negative attitude toward epilepsy. Language and memory were also found to be affected in the older age group. Rochelle Caplan *et al.*(2009) reported that older epileptic children had more language impairment and a wider range of linguistic defects.

Malhi and Singhi (2005) Correlates the Quality of life of children living in rural area and found a significant difference as compared to QOL of those in urban area. Behavioral and social domains were more significantly affected in rural areas. This may be due to the additive effect of lack of access to medical facility, illiteracy and more negative attitude and stigma present in rural community.

Treatment and drugs.

Doctors generally commence with treating epilepsy with medication. Whether or not this doesn't work, they may propose surgical procedures or another type of treatment.

Medication

the majority with epilepsy can become seizure-free which has a single anti-epileptic drug. Others can limit how often and power with their seizures. Sudden expenses your children with medication-controlled epilepsy can eventually stop medications and live a seizure-free life. Many adults may possibly also discontinue medication after Two or more years without seizures. Determining the top medication and dosage could possibly be complex. Your doctor likely will first dictate one particular drug at the relatively low dosage and may also increase the dosage gradually until your seizures are controlled. (Avinash,2012).

Surgery

Surgeries are most commonly done when tests show your seizures originate in a very well-defined area of your brain which does not interfere with vital functions like speech, language or hearing. Of such types of surgeries, surgeon removes the area inside brain that's creating the seizures.

Should your seizures originate really part of your brain that could not be removed, a medical expert may recommend a few other sort of surgery in which surgeons make a compilation of cuts with your brain. These cuts are created to prevent seizures from spreading with aspects of the brain.

Although a number of people continue to might need some medication to help you prevent seizures after successful surgery, you might be able to take fewer drugs losing dosages. In a number of cases, surgery for epilepsy could cause complications such as permanently will be cognitive abilities. Talk to your surgeon about his experience, success rates and complication rates when using procedure you're considering (Avinash,2012).

PHYSIOTHERAPY MANAGEMENT.

Exercise and Epilepsy

According to Abdallah (2015), exercise improves fitness, energy and mood and relieves stress. Improving overall health and wellbeing in this way can help reduce seizures and the impact of epilepsy for some people. It can also help people feel more in control of their health. Exercise releases 'feel good' hormones into the brain, helps to keep your muscles active, reduces fat levels in the body and increases oxygen flow to your brain. It can also increase your bone density which can help to prevent osteoporosis (where bones become fragile and are more likely to break).

He further explained that research in the USA has shown that people with epilepsy exercise less than those without epilepsy. A study in Norway of women with uncontrolled epilepsy showed that regular sessions of aerobic exercise (for example running, walking, swimming, cycling) for 60 minutes, twice a week, for 15 weeks resulted in a significant reduction in the number of seizures they had. They also had fewer muscle pains, sleep problems and fatigue, and had lower cholesterol and better oxygen flow around the body. Some specific diseases that are linked to a lack of exercise, poor diet and being overweight include cardiovascular disease (which can lead to heart attacks and strokes), type 2 diabetes, hypertension (high blood pressure), osteoporosis and certain cancers. A lack of exercise can also be linked to increases in depression and anxiety. Studies shown that people with epilepsy are at an increased risk of developing most of these conditions, so being active and maintaining a healthy diet can help your overall health.

Thapar, Kerr and Harold (2009) explained that Patients with epilepsy frequently experience psychiatric comorbidities, especially depression and anxiety disorders. These conditions have a negative impact on quality of life and share common pathogenic mechanisms. A broad range of evidence has demonstrated that abnormalities of neurotransmitter systems such as serotonin,

noradrenaline, dopamine, glutamate, and GABA are found in mood disorders and epilepsy. Physical exercise can modulate several neurotransmitter systems (Blomstrand, Perrett, Parry-Billings & Newsholme,1989; F. Chaouloff,1989; and Dunn, Reigle, Youngstedt, Armstrong & Dishman,1996) and, therefore, act positively on these conditions. For example, a regular exercise program increases serotonin, noradrenaline, dopamine synthesis and release, up-regulates neurotrophins, reduces stress and, therefore, decreases hypothalamic–pituitary–adrenal activity and adrenal glucocorticoids(Park, Chan, . Li, *et al* ,2005), which consequently, may reduce seizure susceptibility and epilepsy comorbidities.

According to Roth, Goode, Williams and . Faught (1994) ; Eriksen, Ellertsen, Gronningsaeter, *et al.*(1994) in studies with epileptic patients have demonstrated that active subjects have significantly lower levels of depression than inactive subjects . Factors such as ability to work, social functioning, family stability, stigma, and adjustment to seizures significantly affect the quality of life of people with epilepsy and are commonly related to depression and anxiety disorders (Devinsky,2004; Kellett, Smith, & Chadwick,1997).

Following this, regular physical exercise has received considerable attention as a mechanism for enhancing resistance to the negative effects of psychosocial stress in a healthy adult population(Scully, Kremer , Meade, Graham, & Dudgeon,1998). Indeed, single sessions of moderate aerobic exercise can provide acute mood benefits(Roth, , *et al.*1989) and exercise programs reduce depression (Griest, et al.1979).

Aydin, Serdaroglu, Okuyaz, Bideci and Gucuyener (2005) explained another comorbidity which has been poorly examined in epilepsy is obesity. During patient management, there is a great risk of weight gain with some antiepileptic medications. An elegant study conducted by Daniels and collaborators(2009) demonstrated that children with newly diagnosed, untreated epilepsy had a higher body mass index than healthy children.

From the few studies that have been evaluated supervised exercise programs for people with epilepsy, encouraging findings were found. Some studies demonstrated no increase in seizure frequency after 4 weeks or 12 weeks of a physical exercise program (Nakken, BJORHOLT, Johannessen, Loyning,& Lind,1990) . Further, in the 12-week study, there was increased quality of life in the exercise group compared to the control group (McAuley, Long, Heise, et al.2001). Women with intractable epilepsy exhibited a decrease in number of seizures during the exercise period.

Person with epilepsy may not feel like doing exercise if you are tired due to seizures or because of the side effects of your medication. However, even gentle exercise can actually boost energy levels. Some people with epilepsy may worry about doing in exercise in case they hurt themselves during a seizure. In fact, research shows that although seizures can happen during exercise, the positive effects of exercise may help to reduce seizures for some people with epilepsy. Exercise can be to start with a short, regular session of activity that feels manageable and that becomes part of your daily routine. Some ideas to help to start and keep going with exercise include the following.

- Stretch to warm up (see below). It is important to warm up and stretch before and after energetic activity. Stretching warms your muscles and helps prevent strain and aching. Doing a stretching routine every day can also help you develop a habit of exercising that is easier to maintain. Stretching can also help relieve stress because it releases tension from your muscles, making you feel more relaxed.
- Walk around the block or even around your house regularly, and gradually increase the distance.
- Do exercise to music that you enjoy.
- Drink water, diluted fruit juice or squash while exercising, to help replace the fluids and body salts you lose.
- Do not exercise straight after a meal (Abdallah,2015).

Team sports, or group activities such as walking or gardening groups, can also be a good way of increasing self-confidence, make new friends and help with any feelings of isolation. Most sports, including contact sports like football, hockey, basketball and rugby, have not shown to increase the chance of someone having a seizure, but contact sports may come with an increased risk of head injuries, which could affect epilepsy for some people. Protective sports headgear helps to reduce this risk, and there are team sports that are not likely to risk head injuries. (Abdallah,2015).

Vagus nerve stimulation.

This therapy involves your personal computer called a vagus nerve stimulator that's implanted from the skin of your chest to be a heart pacemaker. Wires over the stimulator are wrapped during the entire vagus nerve in your neck. The battery-powered device delivers short bursts of electricity on the brain over the vagus nerve. It isn't really clear how this inhibits seizures, the device can reduce seizures by 20 to Forty percent and completely control seizures inside 5 % of people. Most of the people still require anti-epileptic medication. Unwanted side effects of vagus nerve stimulation include hoarseness, throat pain, coughing, deficiency of breath, tingling and muscle pain (Avinash, 2012).

CONCLUSION

Although people with epilepsy are increasingly involved in physical or sport activities, there is still limited information about the effect of exercise programs or “physical training” in humans. Exercise programs comprise regular exercise, and for effective results, one must have sustained adherence to the training. Factors such as difficulties in arranging transportation, dependence on family, cognitive impairments, low motivation, and fear of having a seizure during exercise contribute to reduced exercise adherence and therefore, to the difficulties in conducting research on this topic.

Translating findings from the laboratory bench is crucial in treating epilepsy. The aim of investigating exercise and epilepsy from a translational science perspective is to transfer

knowledge published in the literature to the clinic. This review describes a considerable number of nonclinical studies that could contribute to our knowledge of beneficial effect of exercise on epilepsy. Eventhough the beneficial impact of exercise on epilepsy has been reported in human studies, our understanding of the mechanisms by which epilepsy is influenced by exercise is still limited. Data arising from laboratory benches can complement the limited information on physical and sport activities in humans. Nevertheless, the neuroprotective and antiepileptogenic actions of exercise illustrated above strengthen the role of exercise intervention as complementary non-pharmacological treatment of epilepsy. In this sense, we should emphasize that people with epilepsy should include exercise as a complementary therapy not only for seizure control but also for non-seizure conditions such as physical health promotion and psychosocial adjustment and improvement in mental state. People with epilepsy should be encouraged to exercise and efforts should be made to remove any barriers to exercise. To reach these goals, support of health authorities, social workers, sport instructors, and campaigns to inform and stimulate patients to become more active are necessary.

REFERENCES:

Abdallah M.(2015). Exercise and epilepsy. Epilepsy society.

Acharya, M.M., Hattiangady, B. and Shetty A.,K.(2008) Progress in neuroprotective strategies for preventing epilepsy Prog Neurobiol, 84 pp. 363–404

Ananya, M. (2013). Epilepsy pathophysiology *Journal of News medical life science and medicine*.

Arida, R.M., Scorza, F.A., Scorza, C.A. and. Cavalheiro, E.A. (2009). Is physical activity beneficial for recovery in temporal lobe epilepsy? Evidences from animal studies. *Neurosci Biobehav Rev*, 33 pp. 422–431

Avinash Sainin (2012). medical surgican and physiotherapy management of epilepsy. Medicinehealth.

Aydin, K. , Serdaroglu,A., Okuyaz, C., Bideci, A. and Gucuyener, K. (2005). Serum insulin, leptin, and neuropeptide y levels in epileptic children treated with valproate. *J Child Neurol*, 20 (, pp. 848–851

Aydin, K., Serdaroglu,A., Okuyaz, C., Bideci,A. and Gucuyener,A. (2005). Serum insulin, leptin, and neuropeptide y levels in epileptic children treated with valproate. *J Child Neurol*.20 pp. 848–85

Barbara B.(2015). Medical and surgical treatment of epilepsy. Epilepsy foundation.

Blomstrand, E., Perrett, D. , Parry-Billings, M. and Newsholme, E.A. (1989). Effect of sustained exercise on plasma amino acid concentrations and on 5-hydroxytryptamine metabolism in six different brain regions in the rat. *Acta Physiol Scand*, 136 pp. 473–481

Caplan, R., Siddarth, P., Vona, P., Stahl, L., Bailey, C., Gurbani, S, et al. (2009). Languages in pediatric epilepsy. *Epilepsia*.50:2397–407. [PubMed]

Catarino ,C.B., Liu, J.Y., Liagkouras, I. et al. (2011). Dravet syndrome as epileptic encephalopathy: evidence from long-term course and Brain.134(Pt 10):2982-3010. Epub 2011 Jun 29. Available at : <http://www.ncbi.nlm.nih.gov/pubmed/21719429?dopt=Abstract>

Chaouloff, F. (1989). Physical exercise and brain monoamines: a review. *Acta Physiol Scand*, 137 pp. 1–13

Christianson, A.L., Zwane, M.E., Manga, P., Rosen, E., Venter, A. and Kromberg, J.G.(2000) Epilepsy in rural South Africa children-prevalence, associated disability and management. *S Afr Med J*.;90:262–6.

Crawford P.M. (2009). Managing epilepsy in women of childbearing age. *Drug Saf* ;32(4):293-307.

Daniels, Z.S. , Nick, T.G. , Liu, C. , Cassedy, A. and Glauser, T.A. (2009). Obesity is a common comorbidity for pediatric patients with untreated, newly diagnosed epilepsy. *Neurology*, 73 pp. 658–664

Datta, S.S., Premkumar, T.S., Fielding, S., Chandy, S., Kumar, S. et al.(2006). Impact of pediatric epilepsy of Indian Families: Influence of psychopathology and seizure variable. *J Epilepsy Behav.* 9:145–51.

Devinsky, O. (2004). Diagnosis and treatment of temporal lobe epilepsy. *Rev Neurol Dis*, 1 pp. 2–9

Devinsky, O., Westbrook, L., Cramer, J., Glassman, M., Perrine, K. and Camfield, C.(1999). Risk factors for poor health-related quality of life in adolescents with epilepsy. *Epilepsia*.;40:1715–20. [[PubMed](#)]
Diagnosis and management of epilepsy in adults(2015). Scottish Intercollegiate Guidelines Network - SIGN

Dunn, A.L. ., Reigle, T.G., Youngstedt, S.D., Armstrong, R.B. and Dishman, R.K. (1996). Brain norepinephrine and metabolites after treadmill training and wheel running in rats. *Med Sci Sports Exerc.*28 pp. 204–209

Epilepsia, 35 pp. 1256–1264

Eriksen, H.R., Ellertsen, B. H., Gronningsaeter, *et al.* (1994). Physical exercise in women with intractable epilepsy

Frank L.,C.(2015) seizure in children *Medicine Health*.

Griest, J.H. Klein, M.H., Eischens, R.R. *et al.* (1979). Running for treatment of depression *Comput Psychiatry*, 20 pp. 41–54

Kellett, M.W., Smith, D.F. and Chadwick,e. (1997). Quality of life after epilepsy surgery. *J Neurol Neurosurg Psychiatry*, 63 pp. 52–58

Malhi, P., Singhi, P.(2005). Correlates of Quality of life with epilepsy. *Indian J Pediatr.* 72:131–5. [[PubMed](#)]

Malhi. P. and Singhi. P.(2005). Correlates of Quality of life with epilepsy. *Indian J Pediatr.* 2005;72:131–5. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15758535>

McAuley, J.W., Long, L. Heise, J. *et al.* (2001). A prospective evaluation of the effects of a 12-week outpatient exercise program on clinical and behavioral outcomes in patients with epilepsy. *Epilepsy Behav*, 2 pp. 592–600

Michael, M., Tsatsou, K, and Ferrie, C.D. (2010). Panayiotopoulos syndrome: an important childhood autonomic epilepsy to be Brain Dev;32(1):4-9. Epub 2009 Apr 21. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19386455?dopt=Abstract>

Nakken, K.O., Bjorholt, P.G., . Johannessen, S.I ., Loyning, T. and Lind E. (1990). Effect of physical training on aerobic capacity, seizure occurrence, and serum level of antiepileptic drugs in adults with epilepsy. *Epilepsia*, 31 pp. 88–94

Neville B.G., Chin, R.F. and Scott, R.C.(2007) Childhood convulsive status epilepticus: epidemiology. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17784533?dopt>

NICE CKS,(2014) Epilepsy; (UK access only).

NICE Clinical Guideline (2012). Epilepsies: diagnosis and manageme. Available at: <https://www.nice.org.uk/guidance/cg137/chapter/introduction>

NICE Clinical Guideline (January 2012) Epilepsies: diagnosis and management.

NICE Quality Standard (2013). The epilepsies in adults.

Nordqvist and Christian.(2015) "Epilepsy: Causes, Symptoms and Treatments." Medical News Today. MediLexicon, Intl.

Nunes V.D., Sawyer L, Neilson J, et al; (2012) Diagnosis and management of the epilepsies in adults and children: summary of BMJ. Jan 26;344:e281.

Park, O. Chan, Q. Li, *et al.* (2005). Changes in basal hypothalamo-pituitary–adrenal activity during exercise training are centrally mediated. *Am J Physiol Regul Integr Comp Physiol*, 289 pp. R1360–R1371

Roth, D.L., Goode, K.T., Williams, V.L. and Faught, E. (1994). Physical exercise, stressful life experience, and depression in adults with epilepsy *Epilepsia*, 35 pp. 1248–1255

Roth, D.L., Wiebe, D.J., Fillingim, R.B. *et al.* (1989). Life events, fitness, hardiness, and health: a simultaneous analysis of proposed stress resistance effects *J Pers Soc Psychol*, 57 pp. 136–142

Schachter, S.C. (2008) Complementary and alternative medical therapies *Curr Opin Neurol*, 21, pp. 184–189

Scully, D., Kremer, J. , Meade, M.M., Graham, R. and Dudgeon, K. (1998). Physical exercise and psychological well-being: a critical review. *Br J Sports Med*. 32 pp. 111–120

Sirven, J.I. (2007). Alternative therapies for seizures: promises and dangers *Semin Neurol*, 27 pp. 325–330

Sirven, J.I., Drazkowski, J.F., Zimmerman, R.S., Bortz, J.J. Shulman, D.L. and Macleish, M. (2003), Complementary/alternative medicine for epilepsy in Arizona. *Neurology*, 61 pp. 576–577

Thapar, A., Kerr, M. and Harold, G. (2009). Stress, anxiety, depression, and epilepsy: investigating the relationship between psychological factors and seizures. *Epilepsy Behav*, 14 pp. 134–140

Thomas. S.V., Koshy S, Nair ,C.R. and Sarma, S.P.(2005). Frequent seizures and polytherapy can impair quality of life in persons with epilepsy. *Neurol India.*;53:46–50

Verrotti, A. , Basciani, F. , De Simone, M., Trotta, D.,Morgese, G. and Chiarelli, F. (2002). Insulin resistance in epileptic girls who gain weight after therapy with valproic acid. *J Child Neurol*, 17 pp. 265–268

Woermann, F.G.,and Vollmar, C.(2009). *Epilepsy behaviour* 15(1):40-9.