REVIEW ARTICLE

Epilepsy, Physical Activity and Sports: A Narrative Review

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ABSTRACT: People with epilepsy (PWE) are less physically active compared with the general population. Explanations include prejudice, overprotection, unawareness, stigma, fear of seizure induction and lack of knowledge of health professionals. At present, there is no consensus on the role of exercise in epilepsy. This paper reviews the current evidence surrounding the risks and benefits associated with physical activity (PA) in this group of patients. In the last decade, several publications indicate significant benefits in physiological and psychological health parameters, including mood and cognition, physical conditioning, social interaction, quality of life, as well as potential prevention of seizure presentation. Moreover, experimental studies suggest that PA provides mechanisms of neuronal protection, related to biochemical and structural changes including release of β-endorphins and steroids, which may exert an inhibitory effect on the occurrence of abnormal electrical activity. Epileptic discharges can decrease or disappear during exercise, which may translate into reduced seizure recurrence. In some patients, exercise may precipitate seizures. Available evidence suggests that PA should be encouraged in PWE in order to promote wellbeing and quality of life. There is a need for prospective randomized controlled studies that provide stronger clinical evidence before definitive recommendations can be made.

RÉSUMÉ: Épilepsie, activité physique et pratique de sports : une revue non systématique. Les individus atteints d'épilepsie font en moyenne moins d'activité physique que la population en général. Parmi les explications avancées, on peut évoquer le fait de nourrir des préjugés à l'égard de l'exercice, une volonté de surprotection, la méconnaissance, la honte, la peur de provoquer des convulsions et un manque de connaissances de la part des professionnels de la santé les traitant. Pour l'instant, il n'existe aucun consensus quant au rôle que peut jouer l'activité physique chez des patients atteints d'épilepsie. Cet article entend passer en revue les preuves actuelles portant sur les risques et les bénéfices associés à l'activité physique dans le cas de patients atteints d'épilepsie. Au cours des dernières décennies, plusieurs publications ont montré l'existence de bienfaits importants tant en ce qui regarde des paramètres de santé physiologique que des paramètres de santé mentale, ce qui inclut l'humeur et les fonctions cognitives, la condition physique, le maintien d'interactions sociales, la qualité de vie de même que la capacité potentielle à prévenir de nouvelles crises convulsives. Qui plus est, des études expérimentales ont suggéré que l'activité physique fournissait des mécanismes de protection neuronale liés à des modifications structurales et biochimiques, par exemple la production de béta-endorphines et de stéroïdes, qui pourraient exercer un effet inhibiteur sur le déclenchement d'une activité cérébrale électrique anormale. Les décharges épileptiques peuvent en effet diminuer ou disparaître pendant l'activité physique, ce qui pourrait se traduire par une réduction de la récurrence des crises convulsives. Chez un nombre réduit de patients, le fait d'être physiquement actif peut toutefois entraîner de telles crises. Cela dit, les données disponibles donnent à penser que l'activité physique devrait quand même être encouragée chez les individus atteints d'épilepsie, et ce, afin de promouvoir leur bien-être et leur qualité de vie. Avant d'émettre des recommandations définitives, nous avons toutefois encore besoin d'études prospectives contrôlées à répartition aléatoire qui reposeraient sur des données cliniques plus solides.

Key words: Barriers, Benefits, Complementary Medicine, Exercise, Physical training, Wellbeing

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Background

Epilepsy is a highly prevalent chronic neurological disease. Approximately 50 million people have epilepsy worldwide, with 80% residing in developing countries.[1] Epilepsy is commonly associated with somatic, cognitive and psychiatric comorbidities such as anxiety and depression, which negatively impact quality of life.[2]

Epileptic seizures are unpredictable and sometimes occur without aura, leading to a sense of loss of control with negative effects on self-esteem and often force patients to make significant lifestyle changes. Despite evidence to the contrary, patients and clinicians may suffer the false pretense that physical activity (PA) is injurious to wellbeing.[3] Several studies have demonstrated the benefits of PA with respect to improved quality of life, seizure control, mental health[4–6] and a reduction in the interictal epileptiform discharges (IEDs) as seen on the electroencephalogram (EEG).[4] These findings are encouraging and may support a role for PA as a complementary therapeutic strategy in the treatment of epilepsy.[7,8]

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Material and Methods

We performed a narrative review with the aim of providing a summary of the evidence surrounding risks and benefits of PA in people with epilepsy (PWE). The literature search was performed using Medline®, Embase®, Index Medicus®, Google Scholars, Current Contents and Cochrane databases for articles published from 1960 to July 2017. The search included both medical subject headings and text words for literature on PA and epilepsy. The following keywords were used: activity, activities, athletic, epilepsy, electroencephalogram, EEG, epileptiform discharge, exercise, fitness, game, health behaviors, leisure, leisure time, outdoor, recreational, physical activity, physical effort, physical training, quality of life, recreation, seizure, sports, wellness and wellbeing. We included reviews, original articles and book chapters. Experts were consulted about unpublished studies. Article bibliographies were screened to identify additional sources.

Titles and abstracts were reviewed for original articles regarding effects of PA and sports on epilepsy in animals, children and adults. We included case reports, case series, cohorts, clinical trials and meta-analysis, regardless of language or country of origin. Two authors (JCM, LDL) independently screened and reviewed all the documents.

Five questions were posed:

1) What is the current state of PA in PWE?
2) What are the clinical effects of PA in this population?
3) Does PA reduce the number of IEDs seen on EEG and impact seizure frequency?
4) Which mechanisms related to PA could explain improved seizure control?
5) Can PA adversely affect seizure control?

Results

A total of 167 articles were identified, and after titles and abstracts were reviewed, we excluded 101 documents. Among them, 66 full-text articles were reviewed, including original articles, clinical trials and meta-analysis (see Figure 1).

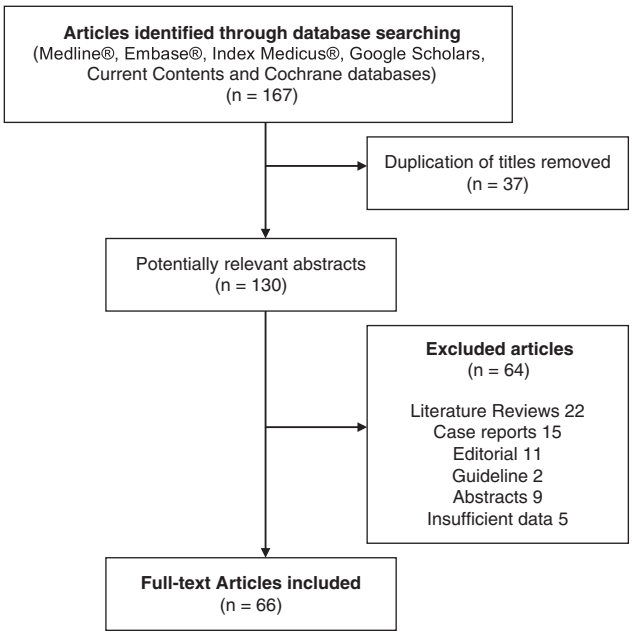

Figure 1: *Flowchart of the literature search.*

What is the Present State of PA in PWE?

The data on PA and sports in PWE are limited but tend to indicate lower levels of engagement compared with the general population. A survey conducted in Ohio, United States (US) revealed that while 47% of PWE were instructed to be more physically active versus 35% of controls, only 58% of PWE performed PA compared with 76% of controls.[9]

Similarly, a Norwegian study reported that sedentary lifestyle was more prevalent in PWE compared with controls (25% vs. 13%, $p < 0.05$).[10] Another study from the US Midwest documented that PWE performed low-intensity PA ≤3 times per week.[11] A German study demonstrated that controls were more likely to engage in sports on a regular basis (42% of controls vs. 25% of PWE) and less likely to state that they never played sports (15% of controls vs. 31% of PWE). The authors indicated that PWE were instructed to refrain from sports by teachers, instructors and even doctors.[12]

In their Brazilian study, *Arida* et al reported that 49% of the PWE did not perform PA on a regular basis. The reasons for this phenomenon included recommendations by relatives, friends and physicians, fear and embarrassment of having a seizure in public, lack of time or motivation, fatigue and absence of company, among others.[13] Identical results were seen in a Korean investigation which documented low PA participation owing to factors such as anxiety, polypharmacy and having experienced a seizure during exercise.[14]

A Canadian population-based study revealed that 60% of PWE reported being sedentary. Individuals with epilepsy had a higher likelihood of being physically inactive compared with the general population (odds ratio [OR]: 1.4, confidence interval [CI] 95% 1.1-1.7).[15] The 2010 US National Health Survey revealed that PWE were less likely to follow health guidelines concerning PA. For instance, when asked whether participants had walked at least 10 minutes in the past week, only 39% of PWE indicated they had versus 50% in the general population.[16]

Wong and Wirrell determined that adolescents with epilepsy were less likely to be involved in sports groups or engaged in PA and were more likely to be overweight and obese than siblings without the disease.[17] In Thailand, 38% of PWE surveyed did not perform PA on a regular basis.[18]

This trend may be reversible as evidenced by an epilepsy program which enrolled PWE in physical activities in Arizona and was able to achieve a reduction in activity-limited days.[19]

Some studies have failed to document differences in activity levels. In Finland, Jalava et al did not detect any significant difference between PWE and controls in terms of PA frequency. Nonetheless, 9% of PWE reported being physically inactive compared with 2% of controls. The same study found performance below expected levels in tests of muscle strength in people with a history of seizures.[20] Similar results were reported in another California-based study. However, in this study, PA was not addressed during routine medical consultation in the preceding year in 56% of appointments.[21] A Nova Scotia-based Canadian investigation did not relate any difference in PA levels but again revealed that PWE were less likely to participate in sports such as hockey or weight lifting and less likely to engage in PA at home.[22]

The preponderance of data would suggest that PWE are less active than their peers due to a variety of reasons such as

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Table 1: Studies on physical exercise and epilepsy

Country – Year	Study design	Patients *N*/ controls *N*	Results of exercise on epilepsy	Observations
Germany 1996[12]	Controlled study based on a questionnaire and standardized clinical tests of physical fitness	135/145	Controls participated in regular sports more frequently ($p = 0.005$). Aerobic endurance ($p < 0.001$), muscle strength ($p < 0.001$), and physical flexibility ($p < 0.001$) was better in the controls The BMI was significantly higher in PWE ($p = 0.03$)	Epilepsy might have a negative impact on PA frequency and physical fitness
Norway 1997[4]	Case series of children with drug-resistant partial and generalized epilepsy practicing exercise during video-EEG	26/0	During the exercise epileptiform discharges decreased in 20 of 26 children, five patients showed an atypical EEG response to PA with either unchanged or increased epileptiform activity	PA may reduce epileptiform discharges on EEG. EEG may be useful for prediction of PA-induced seizures
Finland 1997[20]	Population-based cohort of PWE monitored for a mean of 35 years	100/100	Muscle tests and physical fitness proved to be significantly poorer in PWE than in matched controls. Patients perceived their health status to be comparable with that of controls	Epilepsy might have a negative impact on physical fitness not perceived by the patients
Norway 1999[10]	Prospective population-controlled study	204/2336	Sedentary lifestyle was more common in the patient group ($p < 0.005$), 2% had exercise-induced (partial) seizures. 36% of patients claimed that regular PA contributed to better seizure control	Epilepsy might be linked to sedentary lifestyle. There is mild awareness of PA controlling seizures. There is a chance on exercise-induced seizures in partial epilepsy
US 2001[30]	Randomized, prospective, parallel and controlled study	14/9	The overall quality of life improved in the exercise group ($p < 0.031$), while the control group score did not change ($p = 0.943$)	Exercise is linked to improvement in quality of life. However, this was a study with a small sample size
Brazil 2003[13]	Questionnaire on physical and leisure time activities at an adult outpatient clinic	100/0	50% of patients engaged in PA, 29% were forbidden or cautioned by their physicians, friends or relatives against participation in sports, and 36% believed that PA has a positive influence on treatment	There is subjective awareness of PA controlling seizures. There are misconceptions restraining PA participation
Canada 2006[17]	Parent's questionnaire regarding sports activities	79/99	PWE participated less in sports activities than did controls. PWE is more likely to be overweight. Receiving polytherapy showed a significant negative correlation with sports participation	Epilepsy might be linked to sedentary lifestyle and overweight. Particular attention should be paid to patients with drug-resistant epilepsy
US 2008[9]	Ohio survey of the Centers for Disease Control and Prevention's yearly Behavioral Risk Factor Surveillance System	96/5410	PA was reported by only 58% of PWE compared with 76% of the population without epilepsy	Epilepsy might be linked to sedentary lifestyle
US 2008[21]	California Health Interview Survey in geographically stratified, random-digit-dialed, non-institutionalized people in California	604/42,410	PWE engaged in similar levels of regular, moderate or vigorous PA when compared with the non-epilepsy population	Possible Californian public policy and awareness favor participation of PWE in PA
US 2009[11]	Constructed e-mailed survey to 412 adult patients in Kansas	193/0	Lack of motivation, limited time and poor access to exercise facilities are an impediment to PA Fear of having a seizure, unemployment, and low household income are factors limiting exercise engagement in PWE	PA engagement of PWE needs a multifactorial approach trespassing the clinical perspective
US 2010[19]	Arizona-based, random-digit-dialed, telephone survey	125/9409	Regression models suggested that for individuals with active epilepsy, PA was associated with fewer activity-limited days	PA might have an impact in reducing labor absenteeism in PWE
Canada 2010[15]	2001–2005 Canadian Community Health Survey. Epilepsy, migraine and diabetes patients and general population	2555/397,500	In the logistic regression analysis, epilepsy was associated with physical inactivity in the past 12 months compared with the general population (OR 1.4, 95% CI 1.1-1.7)	Epilepsy might be linked to sedentary lifestyle
Brazil 2010[34]	Case–control study of physiological and EEG responses during a cardiopulmonary exercise test in patients with TLE	19/19	Lower aerobic fitness in PWE may be associated with their sedentary habits. A decrease in the number of epileptiform discharges was observed between the rest state and exercise	Epilepsy might be linked to sedentary lifestyle. PA may reduce epileptiform discharges
Canada 2010[22]	Health Survey with a cross-sectional, stratified cluster sample design	341/53,211	There was no difference in the monthly frequency of leisure PA of >15 min duration between those who did and did not have epilepsy	Possible Canadian public policy and awareness favor sports participation of PWE
South Korea 2011[14]	Questionnaire assessing PA and leisure time activities at an adult outpatient clinic	178/0	PWE who were on AED polytherapy (OR = 2.49, $p = 0.01$), had anxiety (OR = 3.25, $p = 0.02$) and previous seizure experiences during PA (OR = 2.84, $p = 0.01$) were more likely to be inactive	Treatment of anxiety, educational programs and being more effective in the approach of drug-resistant epilepsy could overcome barriers limiting participation in PA

Brazil 2011[35]	Case–control study: EEG analysis in patients with JME and healthy subjects at PA	12/12	JME group had a significantly lower VO2 at rest and resting metabolic rate. The number of epileptiform discharges in the JME group was significantly reduced during the recovery period compared with the resting state	PA may reduce EEG epileptiform discharges. Epilepsy might have a negative impact on physical fitness. Small sample size
Brazil 2013[29]	Prospective controlled study with questionnaires assessing PA, leisure time activities and mood disorders in adults	31/31	Linear regression analyses showed that low PA leisure level predicted 31% of depression levels and 26% of anxiety levels	Exercise may have a positive impact on depression and anxiety
Israel 2014[36]	Prospective controlled study	26/30	Children with generalized epilepsy showed a similar preference for participation in out-of-school activities, as did their healthy peers. Parents still afraid of children engaged in PA	Parents of children with controlled epilepsy should be encouraged to take part in PA taking into account child's preference
Italy 2014[37]	Consecutive patients at a tertiary care epilepsy clinic, prospective, open personal interview to identify seizure precipitants	104/0	Stress, sleep deprivation and fatigue were the most frequently reported precipitants	There was not an explicit remark on PA activity as a trigger factor for seizures
South Korea 2014[5]	Case series of children with BECTS assessing PA program, EEG, seizure frequency, psychological factors and quality of life assessment	10/10	Neurocognitive domains such as visual, auditory sustained and divided attention, psychomotor speed, as well as behavioral and social relations, mood-related wellbeing and quality of life improved after exercise therapy	PA may have a positive impact on neuropsychological factors. Small sample size
Canada 2015[38]	Nova Scotia Childhood Epilepsy population-based cohort. Injury inquiry	472/0	81 injuries. None of the accidents were the result of falls from bicycles and none occurred during sporting activities	PA and sports seem to be safe for PWE
Thailand 2015[18]	Random, university epilepsy clinic, interview and questionnaire	203/0	A total of 47% of the patients exercised at least three times per week, while 53% exercised two times or less a week	Epilepsy might be linked to sedentary lifestyle
US 2015[16]	Data from the 2010 cross-sectional National Health Interview Survey compared behavior	480/26,659	PWE were significantly less likely than adults without epilepsy to follow the recommended PA guidelines for Americans (35% vs. 46%) and to walk for at least 10 minutes during the 7 days before being surveyed (40% vs. 51%)	Epilepsy might be linked to sedentary lifestyle
UK 2016[39]	Narrative analysis – qualitative research	16/0	PA creates a positive effect on psychological and physical wellbeing. Prevention from PA per medical advice or recurrent seizures creates negative effects such as social isolation, anxiety, lack of confidence, frustration and anger	Treatment of anxiety, educational programs and being more effective in the approach of drug-resistant epilepsy could overcome barriers limiting participation in PA. Small sample size
Canada 2017[40]	A self-administered questionnaire, parent-child dyads. Validated HARCES parent scale and modified-HARCES completed by the child	21/0	Total HARCES scores showed no agreement between parent and child pairs with correlation of 0.2798 (*95% CI: 0.173–0.635*)	Youth with epilepsy face activity restrictions based on fear of perceived risk of injury. Education strategies are needed to overcome this barrier
Spain 2017[41]	Prospective controlled study with questionnaires assessing quality of life and daily habits	85/193	There was no difference in sports between the groups. PWE had a healthier lifestyle (lower BMI, lower alcohol consumption and a tendency toward smoking less)	Spanish public policy and awareness favor participation of PWE in PA
Brazil 2017[42]	Prospective study with questionnaires assessing quality of life, PA and stigma	67/0	Most PWE are sedentary and do not practice PA for fear of seizures. Clinical aspects of epilepsy negatively influence PA activity. Less PA is associated with depressive disorder, worse quality of life and higher perception of stigma	PA may have a positive impact on quality of life, emotional status and cultural stigma
Brazil 2017[43]	Prospective study with questionnaires assessing quality of life, emotional status, side effects and PA	101/0	PA was positively associated with quality of life ($p < 0.001$) and negatively associated with depression ($p = 0.046$), state of anxiety ($p = 0.014$), trait of anxiety ($p = 0.015$) and side effects of medications ($p = 0.01$)	PA may have a positive impact on quality of life and emotional status. Side effects may have a negative impact on exercise engagement
UK 2017[44]	Semi-structured interviews – qualitative research	11/0	PA motivators are: benefits on physical and mental health shown in an increase in mood, higher social interaction and perceived improvement in overall physical health. Barriers included a fear of injury, lack of social support and exercise-induced seizures. Adaptation techniques used were self-monitoring through the use of technology, reducing PA frequency and intensity level, and exercising at certain times of the day. Medical professionals requesting termination of some PA	Remarkable effects of PA. Exercise engagement of PWE needs a multifactorial and individual approach. Small sample size
Brazil 2018[45]	Descriptive observational study	101/0	65% were physically inactive	Epilepsy might be linked to sedentary lifestyle

AED = antiepileptic drug; BECTS = benign epilepsy with centro-temporal spikes; BMI = body mass index; HARCES = the Hague Restrictions in Childhood Epilepsy Scale; JME = juvenile myoclonic epilepsy; PA = physical activity; PWE = people with epilepsy.

prejudice, stigmatization, fear, shame, lack of knowledge or medical advice.

What are the Clinical Effects of PA in This Population?

Animal models confirm a positive effect of PA on mood and seizure control. In a murine model of depression, PA was correlated with a decrease in negative mood symptoms as well as a delay in the development of epilepsy.[23] This finding was associated with the production of galanin, a neuropeptide with antidepressant and anticonvulsive effects.[24]

PA and sports participation can have a positive impact on overall health status and quality of life of people living with chronic diseases such as depression,[25] arthritis,[26] asthma,[27] hypertension and diabetes.[28] People with epilepsy tend to be more sedentary than the general population, a finding associated with higher body mass index, minor physical resistance, low self-esteem, and increased likelihood of anxiety and depression. A Brazilian study documented that physical inactivity constitutes a risk factor for the development of depression and anxiety in PWE.[29]

In an Ohio-based study, a 12-week sports intervention program specifically designed for PWE generated enhanced quality of life scores in the PA group ($p < 0.031$) compared with controls ($p = 0.943$). Improvement was seen in variables such as self-image, vitality and emotional state.[30] Similarly, a study from the University of Alabama confirmed that adult PWE who practiced regular PA had lower levels of depression.[31] In a Korean study, it was also observed that a program of regular PA in children with benign epilepsy with centrotemporal spikes (BECTS) generated improvements in attention, psychomotor speed, impulse control, inhibition/disinhibition and problem-solving skills.[5] Overall, exercise seems to exert favorable effects on quality of life, neurocognitive domains and psychosocial function[32,33] (Table 1).

The pleiotropic effects of antiepileptic drugs (AEDs) must also be considered. Some AEDs such as carbamazepine, lamotrigine, oxcarbazepine, valproate and clobazam can positively impact mood, while others such as levetiracetam, zonisamide, perampanel and phenobarbital can do the opposite. Moreover, some AEDs are known to promote weight gain (i.e., valproic acid, carbamazepine, vigabatrin, gabapentin and phenobarbital), whereas others may be associated with weight loss (i.e., topiramate, zonisamide and felbamate).[46] Appropriate AED selection requires joint decision-making between patient and prescriber and a drug's side-effect profile should be discussed and fully considered before initiation.

Does PA Reduce the Number of IED Seen on EEG and Impact Seizure Frequency?

Electroencephalogram recordings in rats show IEDs decrease or disappearance during PA with returning of the interictal discharges at rest. One hypothesis for this finding is that increased vigilance and attention required in PA may reduce seizure frequency.[47] Basic research has shown that short-duration swimming exercise[48] and short-, moderate- and long-duration treadmill exercises[49] consistently decreased the frequency of penicillin-induced epileptiform activity in male Wistar rats. Likewise, a reduction in the number of clinical and electrographic seizures has been observed with both strengthening (i.e., weightlifting) and aerobic exercises.[50,51]

Findings in animal models may have direct observable clinical implications in humans. For instance, an analysis of video EEG recordings from 26 Norwegian children with epilepsy who attended an exercise program demonstrated a 25% decrease in IEDs in approximately 77% (20/26) of patients during exercise. IEDs increased in relation to baseline following cessation of exercise.[4] High-intensity exercise has been shown to reduce seizure occurrence and paroxysmal EEG activity in people with temporal lobe and juvenile myoclonic epilepsy.[34,35] Moreover, a population-based Swedish study demonstrated that low cardiovascular fitness status at 18 years of age correlated with an increased likelihood of developing epilepsy. The association remained even after controlling for several confounders such as family history, personal history of diabetes, stroke and traumatic head injury. The authors concluded that behaviors that increase cardiovascular fitness may act as positive disease-modifiers against the future development of epilepsy.[52]

Which Mechanisms Related to PA Could Explain Improved Seizure Control?

Data from animal studies would suggest that the putative neuroprotective effects of PA might be ascribed to various genetic, molecular, biochemical and structural changes.[23,47,51,53,54] The proposed mechanisms include:

1. Release of β-endorphins from the opioid system[55]
2. Release of steroids secondary to stress[56]
3. Increase in melatonin concentrations[57]
4. Increase of parvo albumin in affected cells after seizures. This molecule has been linked to antiepileptogenic effects, cytoprotection and prevention of neuronal death in the affected cells.[58]
5. CA1 cells hyperreactivity reduction and generation of structural changes within the hippocampus, which may have an inhibitory effect on the occurrence of abnormal electrical discharges.[58,59]

A study using a murine epileptogenic model by Arida et al[60] suggested that greater effort was needed to induce epileptogenesis in physical trained animals. The delay in seizure occurrence was attributed to the inhibitory effect of noradrenaline and GABA released during exercise.[27,61] Additionally, exercise resulted in decreased production of oxidants and free radicals.[50]

In a pentylenetetrazol murine model used to assess the effect of swimming on epileptogenesis after 6 weeks of practice, the exercise group had a greater latency to first seizure, shorter seizure duration, lower amplitude and frequency of IEDs, increased superoxide dismutase activity and non-protein sulfhydryl levels, and greater attenuation of oxidant production.[62]

Similarly, a Polish study that used a pilocarpine murine model of focal epilepsy determined that animals undergoing a PA program had a longer latency in the appearance of status epilepticus and demonstrated lower intensity and shorter seizure duration.[53] Possible hypotheses for these observations include increased angiogenesis resulting in decreased excitotoxicity,[63,64] release of neuroprotective trophic factors and expression of neuronal growth factors.[65,66]

Can PA Adversely Affect Seizure Control?

Sporadic case reports of PA-induced seizures should be weighed against the relatively numerous and well-established

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Table 2: Seizure induction by exercise

Author/ year	Country	Population (*N*)	Exercise-induced seizures/ EEG epileptiform discharge increasing definition	Patients with seizure induction	Clinical relevance
Ogunyemi 1988[67]	Canada	Three adults	Seizures triggered by exercise in patients with epilepsy diagnosis	Three patients with generalized epileptic seizures and epileptic discharges in the EEG during exercise (running) and normal EEG during resting wakefulness and sleep	In three PWE, there was seizure occurrence in the post exercise period
Simpson 1989[68]	United States	Three adults	Seizures exclusively triggered by exercise in patients without diagnosis of epilepsy	Three patients had convulsions while running. All of them debuted with seizures and were diagnosed with frontal cortex lesions	A seizure after high-intensity exercise might provide and early warning of the presence of an intracranial mass lesion
Bjørholt 1990[69]	Norway	44 adult inpatients with active epilepsy	Presence of a clinical seizure during or after the bicycle ergometer test	One patient (2%) had a single seizure immediately after the physical test	In 2% of PWE there was seizure occurrence in the post exercise period
Schmitt 1994[70]	Switzerland	Two children	Seizures triggered by exercise in patients with epilepsy diagnosis	Two patients with ataxia, developmental delay and epilepsy presented seizures and epileptic discharges in the EEG clearly induced by physical exercise	In two children with epilepsy appeared drug-resistant seizures associated to PA. Only the strict avoidance of physical exercise reduced seizure frequency
Eriksen 1994[71]	Norway	14 outpatient women with drug-resistant epilepsy	Presence of a clinical seizure during or after the aerobic dancing test	28% showed increase in the weekly seizure frequency and 72% showed decreased in the weekly seizure frequency During aerobic exercise, 50% subjects had seizures; the remaining 50% subjects had none. Most seizures occurred during aerobic dancing or during the cooling down period	In 28% of the women with drug-resistant epilepsy, exercise appeared to be a seizure precipitant
Nakken 1997[4]	Norway	26 inpatient children with difficult to treat epilepsy	> 30% increase in the EEG discharges during exercise or in the post exercise period	15% showed increase in the EEG discharges during exercise Two of the four had a further increase in the EEG discharges in the post exercise period. These four patients (15%) informed the authors in advance that they previously had experienced seizures during and/or immediately after exercise	In 15% of children with epilepsy there was an increase in the EEG discharges during or in the post exercise period. None of the patients suffered a seizure during or after the test
Nakken 1999[10]	Norway	204 adult outpatients with active epilepsy	Having seizures in >50% of the training sessions	2% had genuine exercise-induced seizures 10% of the patients were prone to have seizures while exercising 8% of patients frequently experienced seizures in the immediate post exercise period 10% experienced injuries in connection with physical exercise and seizures	In 10% of the PWE, exercise appeared to be a seizure precipitant, and this applied particularly to those with focal lesional epilepsy
Sturm 2002[72]	Australia	A 16 and a 28-year-old male patients	Having seizures in >80% of the training sessions	Two patients with TLE presented seizures and epileptic discharges in the EEG clearly induced by physical exercise Seizures occurred within 5-20 minutes of commencing activities such as running and playing soccer or tennis and were more likely if the exercise was strenuous	Almost all of the patients' seizures were triggered by PA, suggesting that this is a form of temporal lobe reflex epilepsy
Werz 2005[73]	United States	1 adult patient	Seizures exclusively triggered by exercise	This is a case of a young woman who had three episodes of generalized tonic-clonic seizures always associated with exercise. This case is unusual as no seizures were identified independent of exercise	Rarely, seizures may be limited exclusively to exercise and this may be documented by EEG recording during simultaneous cardiac exercise testing
Kamel 2014[74]	Australia	10 adult patients from a tertiary epilepsy care center	Seizures triggered by different types of exercise	This is a case series of 10 patients with TLE. Various forms of exercise were described among the patients including running, swimming, playing netball, dancing, cycling, weight lifting, and martial arts 90% of cases suffered left TLE	Although regular exercise should generally be encouraged in PWE, this is not the case once a clear exercise-related trigger has been identified
Collard 2017[44]	United Kingdom	11 adult patients	Qualitative study No quantitative data	Some of the participants reported exercise to be a trigger for their epilepsy. This was in connection with high-intensity exercise and overheating	The adaptations used and developed by the participants revealed that although certain aspects of exercise may trigger seizures for some, they felt continuing to exercise with adaptations was more beneficial to their overall mental health

PA = physical activity; PWE = people with epilepsy, TLE = temporal lobe epilepsy.

benefits of PA (Table 2). Based on scant data, up to 2-10% of PWE may have exercise-induced seizures (defined as seizures occurring in >50% of training sessions).[10,69] These case reports describe patients with both genetic generalized epilepsies[67,73] as well as symptomatic focal epilepsies[71] of frontal[68] and temporal lobe origin.[72,74]

A review of the limited literature on this subject would indicate that the occurrence of exercise-induced seizures is overall quite rare.[4,10] Of interest, PA-induced seizures have been mainly attributed to high-intensity exercise such as ball games, jogging, running and hiking. In addition, high altitude may also provoke seizures, due in part to hypoxia and hypocapnic hyperventilation.

Some patients are reported to present with a high frequency of seizures happening either often (>80% of the time) or exclusively occurring during PA. The authors surmise that these patients may have a form of temporal lobe reflex epilepsy[70,72,74] and that the temporal lobe might be uniquely more sensitive to the generation of exercise-induced IEDs compared with other cortical areas. In these cases, complex partial seizures might be most susceptible to activation during exercise.[75]

Arida et al[76] correlated the occurrence of PA-induced seizures with homeostatic alterations linked to general fatigue, psychic stress of competition, hypoxia, hypoglycemia, hyperhydration, hyponatremia and hyperthermia. It is known, for instance, that hyperventilation may frequently induce absence seizures and some focal seizures in patients at rest. It has been theorized that resting hyperventilation might trigger seizures due to respiratory alkalosis. However, this explanation is unlikely to be compelling in the case of exercise, which tends to result in metabolic acidosis.

Discussion

Epilepsy is associated with reduced sports participation and PA in PWE. Family, peers and educators may discourage PA due to the mistaken belief that epileptic seizures during exercise could lead to psychological and social stigma and adversely impact quality of life.[77,78] As PWE replace "outdoor" activities with "indoor" sedentary programs, physical exercise levels may further decline.[79]

Healthcare teams should extol the virtues of PA, which include: (1) better social integration, (2) improvement of depression and anxiety, (3) protection against osteopenia/osteoporosis, (4) enhanced sleep, (5) positive effects on quality of life and (6) possible reduction in seizure frequency.[76]

Education on the topic is essential and should extend to community, educators, patients and families. To achieve greater participation of PWE in sports, necessary infrastructure must be developed addressing issues such as accessibility, transportation and safety.[8]

The International League Against Epilepsy (ILAE) has proposed some recommendations concerning PA in children: in aquatic sports, one should weigh risks and benefits; in high-altitude sports such as rock climbing or tree climbing, it is noted that "regardless of whether the child has epilepsy, common sense prevails"; cycling, skating or skateboarding should be limited if there is inadequate seizure control or if epilepsy was recently diagnosed; on contact sports the ILAE states that mild traumatic head injury is unlikely to precipitate an epileptic seizure; finally, diving, parachuting and similar sports should be avoided.[80]

In 2016, the ILAE published a report that divided sports into low, moderate and high-risk categories. The level of risk should be considered along with variables such as type of sport, probability of seizures, type and severity of seizures, precipitating factors, diurnal variation, protective measures and patient risk tolerance. Ultimately, the report eschews blanket recommendations in favor of a patient-specific approach.[8] It is advised that high-performance athletes with epilepsy should inform coaches, training staff and sport committees about their pharmacotherapy to protect themselves from charges of doping.[81]

Rarely, exercise can have an activity on seizure occurrence,[67–74] and clinicians must be attuned to this possibility. In some cases, the possibility of a temporal reflex epilepsy must be considered, and clinicians should ask their patients whether specific activities lead to seizures. If a specific PA is identified as a trigger, it is advisable to record an EEG during this activity. Should such an activity be associated with the occurrence or increase in IEDs or result in seizure, avoidance may be prudent. Alternatively, the patient and clinician may also consider reducing frequency and intensity of the specific exercise, greater supervision during the activity and initiation of preventive antiepileptic therapy.

Conclusions

People with epilepsy are less physically active and less likely to be involved in sports than their peers. Data supporting the beneficial effects of PA on seizure control are insufficient. However, various positive effects on neuropsychological, emotional and quality of life measures have been documented. There is intriguing data to suggest that PA may reduce IED frequency and seizure occurrence, and thereby serve as a useful adjunctive therapy for the treatment of epilepsy. Stakeholders must be aware of various clinical, psychological and socio-economic barriers that limit PA in PWE. The benefits of PA should be analyzed as part of a holistic approach to patient health.

Statement of Authorship

Study concept and design: JCM, LDL. Literature review: DMCV, JPOH, VBC, LDL. Interpretation of data: JFTZ, JCM, LDL, SR. Drafting of manuscript and revisions: JFTZ, JCM, LDL, SR, VBC.

Disclosures

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