



Review

Epilepsy and physical exercise

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ARTICLE INFO

Article history:

Received 29 June 2014

Received in revised form 24 September 2014

Accepted 26 September 2014

Keywords:

Epilepsy

Physical exercise

Risks

Benefits

Comorbidities

ABSTRACT

Epilepsy is one of the commonest neurologic diseases and has always been associated with stigma. In the interest of safety, the activities of persons with epilepsy (PWE) are often restricted. In keeping with this, physical exercise has often been discouraged. The precise nature of a person's seizures (or whether seizures were provoked or unprovoked) may not have been considered. Although there has been a change in attitude over the last few decades, the exact role of exercise in inducing seizures or aggravating epilepsy still remains a matter of discussion among experts in the field. Based mainly on retrospective, but also on prospective, population and animal-based research, the hypothesis that physical exercise is prejudicial has been slowly replaced by the realization that physical exercise might actually be beneficial for PWE. The benefits are related to improvement of physical and mental health parameters and social integration and reduction in markers of stress, epileptiform activity and the number of seizures.

Nowadays, the general consensus is that there should be no restrictions to the practice of physical exercise in people with controlled epilepsy, except for scuba diving, skydiving and other sports at heights. Whilst broader restrictions apply for patients with uncontrolled epilepsy, individual risk assessments taking into account the seizure types, frequency, patterns or triggers may allow PWE to enjoy a wide range of physical activities.

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1. Introduction

The practice of physical exercise by persons with epilepsy (PWE) has been a matter of debate for health professionals dealing with this disease, and of concern for the patients themselves and families and caregivers. A question frequently asked is if exercise could result in an increase of the seizures. As physicians themselves were unable to properly counsel PWE, they have been discouraged from participating in physical activities or sports. PWE must deal with many social and cultural stigmas, so that restricting physical activity contributes to further limitations to a normal and healthy life.

Some surveys performed in the last decade showed that PWE perceive their health as poor and exercise less than the population without epilepsy.^{1–3} Additionally, a sample of 176 PWE followed for a mean of 35 years presented a significantly poorer physical fitness than matched controls, even if they had a feeling of good personal health.⁴ Guidelines to physical activity issued by medical

organizations are scarce and general, although there appears to be a recent shift toward encouraging rather than restricting participation. Finally, articles in neuroscience or even in epilepsy journals are mainly based on small groups and sometimes they fail to provide adequate and updated information to those in charge of taking care of this population.

This article presents and discusses some of the main issues related to physical exercise and epilepsy aiming to provide recent information to enable guidance of PWE on this subject.

2. General aspects of epilepsy

Currently, epilepsy is defined as a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by neurobiological, cognitive, psychological, and social consequences of this condition.⁵ The non-clinical part of this definition should be kept in mind. Stigma has been described as “a distinguishing mark of disgrace” or “an attribute that is deeply discrediting”, and PWE still carry the burden of psychosocial stigmatization, in both developed and developing countries.⁶ These may include lower income, poorer quality of life, low rates of marriage and of employment, and, for children, lower school

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attendance and poor performance, among many others.^{6–8} Another important issue is the comorbid conditions, of which psychiatric and behavioral problems are the most frequent (2–60%).⁷ In addition, approximately 40% of children and adolescents suffer from cognitive delay, speech/language disabilities or other specific learning disabilities, either due to the primary disease causing epilepsy or to the associated treatment.

Despite these handicaps, more and more PWE all over the world are choosing to carry out physical activity or practice sport. It should also be remembered that children have compulsory physical education in school and therefore limiting them to practice sports will reduce their self-esteem and social integration.

3. Does physical activity worsen epilepsy?

Discouraging physical activity in PWE has been the norm until the mid seventies. The American Medical Association (AMA), in 1968, recommended restricting the activity of PWE for fear of injury or of inducing seizure activity.⁹ Due to raised controversy, AMA, in 1974, permitted the participation in contact sports if “to do so is considered a major ameliorating factor in the patient’s adjustment to school, associates, and the seizure disorder”.¹⁰

It is of importance to distinguish between those PWE exercising as part of a healthy lifestyle from those who make sport their profession. The number and the intensity of eventual seizure precipitating factors involved in both situations vary and this must be taken into account when counseling.

3.1. Precipitating factors

Potentially, many seizure precipitating factors exist in relation to physical exercise, fatigue, stress, repeated head injury during contact sports, excessive aerobic exercise, hyperventilation, changes in the metabolism of antiepileptic drugs (AEDs), and ionic/metabolic disturbances.^{8,11,12} In general, seizures seem to rarely be triggered by physical activity. In a study encompassing 400 PWE, only two were able to identify physical activity as a precipitant.¹³ No link has been established between post exercise fatigue and increased seizure frequency.⁸ Stress has been identified as a seizure trigger in a considerable number of patients, suggesting that intense athletic activity may increase seizures.^{8,11,13} In addition, physical stress and neurosteroids appear to be linked in epilepsy. In response to stress induced by physical exercise, it has been demonstrated, both in human and animal models, that the activation of the hypothalamic–pituitary–adrenal axis affects adrenal steroids and neurosteroids and increases the seizure susceptibility.¹³ However, the same stress may also activate hypothalamic corticotrophin-releasing hormone, which in turn stimulates deoxycorticosterone production in the adrenal gland. Increased levels of allotetrahydrodeoxycorticosterone synthesized in the liver and brain by circulating deoxycorticosterone activates GABA_A receptors in certain brain regions, with decreased seizure susceptibility.¹³ Further studies are needed to elucidate the exact role of the physical stress in the control of seizures.

It is well known that hyperventilation at rest triggers absence seizures; therefore one might assume that the same would apply during exercise. However during exercise, hyperventilation is a physiological response to an increased metabolic demand, a compensatory response to prevent hypercapnia. On the other hand, resting hyperventilation leads to hypocapnia and vasoconstriction. Furthermore, exercise-induced hyperventilation, as an adaptive reaction to acidosis, may even produce suppression of interictal abnormalities.^{11,12} Therefore, hyperventilation during exercise appears to deter seizure onset.

Exercise is thought to increase liver-enzyme metabolism and so could also increase the metabolism of several AEDs, particularly the “old generation” ones.¹⁴ Greater drug clearance and competition for protein (albumin) binding sites are factors that may account for a decrease in their serum levels.¹¹ A prospective study on the effect of physical training on serum levels of AEDs, however, failed to show any correspondent decrease or abnormality of the metabolism rate.¹⁵ Another study showed only slight variations in serum levels, especially for phenytoin (small decrease) and valproic acid and phenobarbital (small increase) between the exercise and pre-exercise periods, not statistically relevant and with no repercussion on seizure frequency, as it was a small sample conclusions must be drawn with caution.¹⁴ Despite this contradictory evidence, we would only recommend checking serum levels of AEDs in PWE practicing sports when clinically indicated.

Finally, hypoxia (mainly altitude-related), hyperhydration, hyperthermia, hypoglycemia and hyponatremia are all disturbances linked to physical activity and known to trigger seizures, although, at least some of them, may correspond to acute symptomatic seizures.¹² There are no studies showing a link between these metabolic disturbances and the increase of true epileptic seizures, nor that PWE are more susceptible to them than athletes without epilepsy.⁸ However, it is also true that robust studies have not yet been carried out.

3.2. Influence of the type of physical exercise

There is no evidence in literature that minor head trauma exacerbates seizures, implying that contact sports are not harmful for PWE.^{11,16} Only a few cases of seizures occurring during football have been identified, perhaps wrongly attributed to excessive physical activity, although one report has linked seizures to blows to the head and most of the head injuries suffered during physical exercise are so mild that it is highly unlikely that they induce epilepsy.^{11,16}

Although aerobic exercise has been reported to trigger seizures, this has not had a significant impact because patients themselves are soon able to recognize the association and avoid the activity if necessary.^{11,17} A small study submitted patients with temporal lobe epilepsy to maximal/exhaustive exercise and showed that none experienced seizures during or after exercise.¹⁸ Interictal epileptiform activities usually remain unchanged or even decrease during or immediately after exercise, even in those patients with exercise-related seizures.¹⁵ There are other clinical and animal reports pointing to the benefit of aerobic exercise in reducing seizure frequency.^{14,19,21,22} This reduction both in number of seizures and epileptiform discharges during exercise (aerobic and anaerobic) is thought to be due, among other factors, to a mental activation that suppresses the epileptiform activity.²³

A Norwegian study was devised to compare the exercise habits in a sample of 204 outpatients with epilepsy (better controlled epilepsy than inpatients) with those of age and sex matched controls in the general population, and to study physical exercise as a seizure precipitant and the risk of sustaining seizure-related injuries while exercising.²⁴ PWE with any neurologic impairment or disability were excluded. In accordance with the general impression, the proportion of individuals not exercising was significantly higher in the patient group. Of those who did exercise, the pattern of exercise was similar to the controls. About half of the patients had never experienced seizures while exercising. Among those who did experience seizures, about 10% claimed to experience them in more than 10% of the training sessions, but only 2% of these had “genuine” exercise-induced seizures (arbitrarily defined as having seizures in more than 50% of the training sessions). In addition, structural epilepsies (with no preferential localization) predominated in the group prone to have

exercise-induced seizures, the majority complex partial seizures with or without secondary generalization. Most of these seizures occurred during strenuous exercise (ball games, jogging and hiking), nevertheless this may be due to the fact that these are the most popular sports in Norway. Hence, for the majority of the patients, physical activity had no adverse effects, and a considerable proportion (36%) claimed to experience better epilepsy control with regular exercise. However, it must be kept in mind that the conclusions were based on a self-reported questionnaire and the answers may not reflect the patients true activities and experiences.

Therefore, it seems that aerobic exercise can be recommended, for the majority of PWE, if each individuals experience and limitations are taken in account.

4. Risks associated with physical exercise

The main concerns regarding epilepsy and physical exercise are the induction of seizures and injuries secondary to them during physical activity.²⁵

Based on prospective and retrospective studies, it is considered that persons with epilepsy have a higher risk of injuries.²⁶ These can be of various types, the most common being minor head injuries generally derived from a seizure; minor head injuries themselves do not provoke epilepsy. In the previously mentioned Norwegian study of the 45% who reported injuries associated with seizures during exercise most (94%) had minor injuries (mainly soft tissue injuries). In a prospective study by Nakken and Lossius,²⁷ with 62 PWE with severe therapy-resistant epilepsy, only 1.2% of seizures provoked injuries, the most common being head trauma, submersion injuries, burns and fractures, the last also assumed to be a consequence of mineralization loss secondary to certain AEDs (in particular cytochrome p450 inducers).²⁶ Although these studies did not specifically address injuries occurring during physical exercise, they concluded that PWE should not be forbidden from participating in sports simply to avoid possible injuries, and should instead be stimulated to do so.²⁶

Téllez-Zenteno et al.²⁸ performed a population based study comparing the occurrence of injuries severe enough to interfere in normal activities in adolescents and adults with epilepsy and the general population and the situations where these occurred. There was no statistical difference between the number of injuries reported in both groups and the only difference found was that among the general population the injuries occurred more during sports activities compared to PWE. For both groups most injuries occurred at home, and for PWE commercial areas followed it. So in this study the idea that PWE are at higher risk of injuries during sports seen in many studies that are based on more restricted epilepsy populations was not confirmed.²⁸

It goes without saying that the risk of seizures and associated injuries is rather elevated in patients with uncontrolled epilepsy with primarily or secondarily generalized seizures and high seizure frequency as well as in those with multi-handicaps and mental retardation.²⁶ In these cases, there is a higher risk of having a seizure during either normal daily activities or physical exercise, however as concluded in most studies the most common type of injury related to seizures are soft-tissue injuries.²⁶ Some factors preclude a lower risk of injuries during activities as seizures that occur mainly at night and those with previous aura.²⁶

The type of seizures is also important when recommending physical exercise and the risks associated with it. Some types of seizures preclude a higher risk of injury than others. Namely generalized tonic-clonic and atonic seizures that can induce unprotected falls. In the case of seizures with disturbance of consciousness (absence and complex partial seizures) the patient loses awareness of the surroundings and might be at the risk of

losing balance or being hit by a ball or other sports participants. Simple partial seizures are the ones less likely to induce injury due to the retained consciousness and brief duration.¹¹

5. Factors that influence physical exercise adherence

In a selected group of in-patients with uncontrolled epilepsy although access to sports facilities was not a problem the great majority lead a sedentary lifestyle and the reasons given for that were lack of interest in physical exercise, fatigue resulting from medication, fear of seizures/injuries, lack of instructors and lack of drivers license. However the authors consider that this group may not be representative of the general PWE population.³⁰

In a small Canadian study which compared the sedentary and sports activities between children/teens with epilepsy (cognitively normal) and their siblings without epilepsy (similar ages) based on parental and children/teens applied qualitative questionnaires a statistically significant difference between teens (not children) with epilepsy and their siblings was found, having the first a lesser amount of time spent in total sports and in group sports activities. Only a trend was found concerning higher seizure frequency (at least one seizure every three months) and decreased total participation in sports. The teens (with epilepsy) lesser activity did not seem to correlate with parental restrictions but rather to lack of interest or laziness. No differences were found between physical activity levels between children with epilepsy regarding presence of generalized tonic-clonic seizures in the preceding year or the etiology of epilepsy.³¹

Another study,³² based on a self-report questionnaire, tried to determine the adherence to exercise in an adult, cognitively normal cohort of PWE and to find out the barriers to exercise. Seventy-eight percent of the participants (total of 193) reported having some kind of physical activity, mainly walking. However, due to the frequency, duration and intensity the majority did not qualify as having an active life style. A small percentage (15%) thought of increased seizures in relation to exercise. The barriers to exercise determined, beyond the ones also present in the general population (lack of motivation, time), were personal safety concerns (19%), fear of seizures (19%) and access to facilities (18%). Worth mentioning was also the fact that most of the participants were unemployed or retired and had lower incomes which might influence adherence to more structured physical activities.

A third study³³ also using questionnaires but additionally a clinical evaluation selected 136 outpatients and compared their habits and views about exercise with controls. This study differed from the previous in the number of subjects but also in the fact that more than half of them had controlled epilepsy. The results showed that both groups thought that sports were positive and suitable for PWE but only 25% of the patients in comparison to 42% of the controls performed sports regularly, and surprisingly most of the patients preferred swimming and bicycling. The most frequent reason for inactivity was the disease itself, however in a more recent study the disease was considered as physically limiting by only two percent of the patients but 68% of these subjects had discontinued AEDs and were seizure free.⁴ Although no patient had been advised against the practice of sports by teachers or sports instructors and only six had been forbidden of exercising by their doctors or relatives. However 41% of the patients feared having a seizure during sports and 40% were afraid of seizure related injuries. Worth noticing was the fact that around 45% of the patients had never talked with their doctors about the practice of sports and recommendations.³³ Arida et al.³⁴ studied the exercise habits of Brazilian patients and found similar results. For 84% (of 100 patients) no seizures had occurred during physical activities, and 85% did not believe that exercise precipitated seizures.

However, 45% were afraid of having seizures during exercise and making fools out of themselves, 15% were not allowed by their physicians to engage in physical activities, and relatives or friends discouraged it in 14%. Most of the patients preferred engaging in individual physical activities.

A Canadian study that assessed the exercise habits of individuals 12–39 years old found that there was no difference between PWE and persons without epilepsy in the monthly leisure exercise frequency. However, the exercise profiles did differ, walking being the most common among PWE.³⁵

6. Recommendations regarding sports participation for PWE

In 1997, and for the last time, the ILAE Commission Report³⁶ changed its previous policy on exercise and children with epilepsy. It was considered difficult to determine guidelines regarding exercise for all children with epilepsy, therefore risks and benefits would have to be weighed separately in each case. Nevertheless, it was deliberated that most of these children should only have restrictions if they had poorly controlled epilepsy, in the first 2–3 months after a first untreated seizure, and during the first months after AEDs were initiated or discontinued. Sports like scuba diving and skydiving were the only ones that should be avoided, and others such as horseback riding, motor sports, and sports performed at heights were permitted with caution, considering the potential risk to the patients themselves and to others. In general, we believe that the restrictions and assessments proposed for children can be extrapolated for older PWE.

The American Academy of Pediatrics (AAP) published a policy statement in 2008, reviewing previous statements, in which it deliberated that children with certain medical conditions should have limitations in sporting activities. For children with epilepsy with controlled seizures there were no limitations and for those with poorly controlled seizures an individual assessment should be made in order to protect them from self-injury or injury to others.³⁷

7. Higher risk sports

Throughout the literature, sports that involve motor vehicles, heights (including sky diving) and scuba diving due to their known associated risks are not advised for people with epilepsy.⁸ The legal considerations in each country concerning driving also have to be taken into account in relation to motor sports.

Recommendations to avoid water sports are due to the associated risk of drowning during a seizure. The conclusions of the studies on this subject vary owing to different populations and different methodologies of analysis. The determined risk of drowning ranges from that of the general population to around 4 times or higher in different studies. Diekema et al.³⁸ underwent a population-based cohort study that analyzed epilepsy as a risk factor for submersion and drowning death among children. Based on 336 non-intentional submersion incidents they found that children with epilepsy (CWE) had a relative risk of 13.9 for submersion and 13.8 for drowning compared to non-epileptic children. Bathtubs were the first and swimming pools the second most common site of submersion. No difference between the two groups was found for other bodies of water and the risk was always higher for CWE five years of age or older. According to this study, and removing the CWE with additional handicap, the risk of submersion and drowning of CWE was approximately 10-fold, especially in older children and when there was no direct supervision of CWE even in supervised pools. They consider that their data supports the conclusion that CWE can swim safely with constant supervision, because although submersion accidents occur in a greater proportion, death and major injuries can be

prevented.³⁸ The recommendation remains that swimming should take place in supervised facilities, in which supervisors are informed that the swimmer has epilepsy and supervise PWE constantly, so that in the event of submersion accident prompt cardio resuscitation intervention is possible.^{24,25,39,40}

In 2008 a meta-analysis on the risk of drowning in PWE was published. According to the 51 cohorts analyzed, death by drowning constituted 5% of all deaths in the studies and the calculated standardized mortality ratio was 18.7, the ratio was higher for PWE with learning disabilities, people in institutions for epilepsy and after temporal lobe excision. Based on their data they considered that they showed that PWE had a 15–19 fold increased risk of death due to drowning compared with the general population, being this risk lower in children, probably because they are more supervised. However this meta-analysis evaluates articles that approach the general causes of death in PWE and not exclusively deaths due to drowning occurring during water physical activities, so it is not possible to transport these observations to the practice of sports. Nevertheless one assumption is useful, the fact that PWE should be under direct supervision when bathing or swimming because in these cases death is avoidable when the necessary precautions are taken.⁴¹

Arida et al.¹² considered that activities to be avoided in people with epilepsy were scuba diving, motor racing, various sports at heights (parachuting, high-altitude climbing, gliding, hand gliding) and aviation. Also, when deciding whether or not to practice sports the crucial factor was the balance between its potential risks and benefits to each patient, because generalizations in this group of patients are difficult to create.

In 2007, a review on the contraindication of scuba diving⁴² focused on the possible physiological alterations that could occur in this setting (decompression sickness, oxygen toxicity, nitrogen narcosis), and on the possible risk to the patient and the diving buddy (who could suffer from decompression sickness in the need of rapid ascent). It concluded that, although the risk of death associated with diving was greater in these individuals, if they were seizure free for a minimum of 4 years, the risk of having a seizure while diving was minimal. However, this was an empirical conclusion with no substantial studies backing it up. Notwithstanding, taking into account the possible sedative effect of some antiepileptic medication, people who report having sedation, as a side effect should not dive because it could increase the possibility of nitrogen narcosis. Thus, it remains an individual decision, and the physician should explain the possible risks even if the patient is seizure free for four years or more, as there always remains the possibility of having a seizure. In general, scuba diving is still contraindicated by epilepsy and sports committees/associations. For example, according to the diving medical committee of the United Kingdom Sports, a person with epilepsy is permitted to dive when he reaches a period of five years seizure free and without medication; if the seizures are during the night only, a three-year period is required.⁴³

Besides the risk of seizures during sports in persons with diagnosed epilepsy, there is also the question whether certain sports associated injuries can induce epilepsy. In the case of boxing, studies of amateur boxers demonstrated that head concussions were minor and did not result in neurophysiologic or clinical signs of epilepsy. A sports practitioner can have a convulsive convulsion as a result of a minor concussion but this is a limited event in time and does not provoke epilepsy.¹¹

8. Does physical activity benefit epilepsy?

Over the years, many basic and clinical investigations have been developed to study the benefits of physical activity on epilepsy. These investigations encompass the influence of physical activity

in preventing and controlling epilepsy and reducing comorbidities directly linked to this pathology.

8.1. The role in epilepsy prevention

Positive results have been found in basic research about physical activity as a primary prevention to the development of epilepsy. Exercise can reduce brain cell loss or neuronal damage secondary to brain insults in animal studies.²⁰ One study about physical exercise during post-natal brain development in rats showed that when they were submitted to daily exercise for forty days they presented a delayed onset and a reduced intensity of pilocarpine-induced motor symptoms during midlife.⁴⁴ The kindling model of epilepsy induced by repeated administration of a subconvulsive stimulus into a limbic structure has been frequently used in animal studies of physical exercise.¹² The effect of acute and chronic physical exercise was evaluated on the development of amygdala kindling, showing that more stimulus were necessary to provoke seizures in rats submitted to exercise than controls.¹² Neurotransmitters play an important role here as they are influenced by exercise. Noradrenaline appears to be increased in rats submitted to physical training, it has an inhibitory effect on the development of kindling, and its depletion facilitates the propagation of epileptiform activity of hippocampal kindling.¹²

The possible preventive effects of exercise on epilepsy in humans are still uncertain. There is only one study in a Swedish population-based cohort of 6796 individuals followed through a period of 40 years examining this issue.⁴⁷ It was observed that subjects who presented low cardiovascular fitness at the age of 18 had an increased risk of being diagnosed with epilepsy later in life, and this association remained after adjusting for several potential confounders. However, other variables that could influence this association were not analyzed, and the sample was only made up of males. Despite its limitations, the study suggests that physical exercise at an early age may have a protective effect on the later development of epilepsy by building neural reserves, but more epidemiologic and prospective studies are needed to confirm this hypothesis.

8.2. The influence in seizure induction and control

The pilocarpine model of epilepsy is an experimental model in rats of temporal lobe epilepsy in humans. Rats with pilocarpine-induced epilepsy submitted to a physical training program presented a lower frequency of spontaneous seizures than controls.^{19,20,46,48,49} A very low probability of exercise-induced seizures was found and no sudden death occurred while exercising. Even strength training (climbing series with progressively heavier load) improved seizure frequency.⁵⁰ Other animal models of epilepsy (penicillin, pentylenetetrazol, kainic acid) have shown similar positive results.^{51–53} Although these studies reveal important data, they cannot be translated readily to humans.

PWE who practice regularly physical exercise tend to report fewer seizures than inactive ones.²⁵ Nevertheless, clinical investigation presents several limitations, such as lack of appropriate controls and the presence of potential confounders, like compliance to physical exercise and to AEDs therapy.⁴⁸ Some human researches have been more successful than others. Nakken et al.¹⁴ studied twenty-one patients with uncontrolled epilepsy submitted to aerobic physical exercise for four weeks, and no difference between seizure frequency two weeks before, during, or two weeks after the exercise program was found. Hence, physical activity seemed not to represent an important seizure-inducing factor, a fact also demonstrated in a randomized controlled study with twenty-three patients during a twelve week aerobic exercise program.⁵⁴ Another study with fifteen women with

pharmacologically intractable epilepsy submitted to aerobic activity for fifteen weeks presented a decrease in seizure frequency during the exercise period.⁵⁵ In addition to aerobic exercise, the effect of maximal physical effort was also studied. In a sample of sixteen patients with temporal lobe epilepsy, no one presented seizures after an exhaustive physical exercise.¹⁸ Similar findings were observed in nineteen PWE submitted to a cardiopulmonary exercise test where a decrease in the number of epileptiform discharges was seen between the rest and the exercise state and between the rest and recovery state.⁵⁶ A related study in juvenile myoclonic epilepsy found a significant reduction in the number of epileptiform discharges during recovery state compared with the resting one.⁵⁷

In general, and according to Arida et al. in a recent review of antiepileptogenic and neuroprotective effects of exercise in clinical and experimental models of epilepsy, physical activity seems not to be a seizure-inducing factor but indeed provide benefit as a complementary therapy for epilepsy.^{20,21}

8.3. The effect in epilepsy comorbidities

The effect of physical exercise in reducing comorbidities related to epilepsy is not as controversial. Nevertheless, we have to keep in mind that these comorbidities are interconnected to each other.

Mental health disorders are more frequently found in PWE than in general population, and they include psychoses, mood and personality disorders, and behavioral problems.^{58–60} A higher prevalence of suicidal ideation in PWE was reported as well.⁵⁹ Within the psychiatric comorbidities in PWE, depression seems to be the most frequent one, but other psychological problems such as anxiety and stress are also frequently reported.^{58,61–63} Mental health disorders in epilepsy result from the interplay of neurobiologic, iatrogenic (AEDs or epilepsy surgery effects) and psychosocial mechanisms.⁶⁴ In a neurobiologic view, it is known that both epilepsy and mood disorders share dysfunctions in neurotransmitter systems (serotonin, noradrenaline, dopamine, glutamate and GABA), which might contribute to their coexistence and bidirectional relationship.^{22,65,66} It seems important to manage these disorders in addition to seizure management when treating PWE.^{64,65} Research on physically healthy adults has consistently shown an emotional well being associated to a regular exercise program.²⁵ The therapeutic effect of exercise training on depression in PWE has been studied with promising results. Some explanations for that consist in the increase and regulation of neurotransmitter systems involved in depression physiopathology and other comorbidities improvement that can influence depression.²² PWE who practice exercise present lower levels of depression independently of other factors like age, gender, seizure frequency or stressful life experience.^{25,55,60} Nakken et al.¹⁴ recorded a beneficial effect in mental state, self-esteem and social integration after four weeks of intensive physical training program. Eriksen et al. showed that women with intractable epilepsy exposed to exercise (aerobic dancing with strength training and stretching) for fifteen weeks did not present significant changes in anxiety and depression scales. However, there was a significant reduction in overall health complaints, like fatigue and sleep problems.⁵⁵ A randomized controlled study for twelve weeks documented an improvement in the exercise arm for mood, self-esteem and quality of life measured by self-administered questionnaires.⁵⁴ Depression seems to mediate the relationship between stress and anxiety and to change seizure frequency.⁶⁵ There is evidence that people having regular physical activity cope better with stressful situations, thus minimizing the seizures induced by psychological stress.¹³ Hence, it seems important to propose a regular and appropriate program of exercise to PWE in order to avoid or treat depression associated with epilepsy.

Studies of mental health disorders in PWE can be confounded by multiple factors, like AEDs therapy, psychosocial, familial, socioeconomic and intellectual effects.⁶⁷

Obesity is another common comorbidity found in PWE associated to low self-confidence and that can be improved with physical training.^{1–3,68,69} Animal and human studies showed that animals and PWE present a higher body mass index than healthy ones.^{34,69} Overweight is frequently associated to AEDs and sedentary because of the fear of exercise induce-seizures.^{22,32,70} Generalized epilepsy, idiopathic syndrome and family history of epilepsy seem to represent some factors associated with obesity in these patients.⁶⁸ Like in healthy people, PWE can benefit of weight and body fat reduction with physical training, as well as risk factors reduction for diabetes, hypertension, obesity and coronary heart disease.^{12,14,71}

Vitamin D metabolism is another factor affected by AEDs leading to a reduced bone density.^{22,72,73} Indeed, PWE present a bigger predisposition to fractures than the general population.^{58,74} The exact mechanisms by which AEDs affect bone architecture are not fully understood.⁷² A bone mineral density screening as well as an osteoprotective behavior is being promoted in PWE through an individual basis.⁷⁵ Nutritional supplementation, diet and physical exercise are some of the methods to prevent osteoporosis. In the general population, it is well known that physical activity induces osteoprotection. Indeed, it will increase bone growth in width and mineral content in girls and female adolescents, but also in postmenopausal women, carried out in volumes and at intensities seen in athletes, with a great hormonal influence and accompanied by adequate caloric and calcium intakes.^{22,76,77} The main sports associated to this issue are those that involve running and jumping (like soccer, basketball, volleyball, tennis, running, weight lifting, gymnastic).⁷⁶ In PWE, experimental data about exercise to prevent and treat bone loss are still lacking.²² Nevertheless, it is recommended to patients of all ages as a bone health protector.

In summary, even though the role of physical activity in preventing and controlling epilepsy and its comorbidities is not always clear, exercise programs should be encouraged as a complementary therapy for PWE due to its proven benefits.

9. Recommendations

Some online sites counseling PWE provide recommendations regarding different sport activities, and most are quite liberal in the

sports recommended. Especially for PWE with controlled epilepsy, however, there is still some conflicting opinions regarding more controversial physical activities, like sky diving, scuba diving, water skiing, climbing, hand gliding, or boxing and other contact sports.

Most consider that water sports should always be performed under a trained supervisor, with a lifejacket, and that swimming should be done in supervised pools.⁷⁸

Some consider that restrictions for persons with complex partial or tonic-clonic seizures are needed even when preceded by warnings for sports like skydiving and scuba diving. A more radical position is the one not recommending it in general for PWE because they are life-threatening in case of a seizure occurrence.^{79–83} While some do not limit participation, others do not recommend or counsel caution for the practice of combat sports like boxing or martial arts that may involve blows to the head. Nevertheless, as seen in the literature from studies with boxers and other sports that might involve concussions, most of these are mild and do not preclude the development of epilepsy nor do they aggravate a preexisting epilepsy.^{79–83} Taking into account the articles reviewed, there seems to be currently a general consensus that sports and physical activity, excluding scuba diving, skydiving and solo hand gliding, should be encouraged to all PWE with controlled epilepsy (seizure free for more than one year). For higher risk sports like climbing, cycling, horseback-riding, water sports and swimming, snorkeling, among others, PWE should practice them with a friend/relative, or under close surveillance of someone who knows that the person has epilepsy and how to deal with the occurrence of a seizure. For those not well controlled, limitations should be applied according to the seizure type and the particular sport or physical activity to be performed, always after discussing the risks, benefits and sports possibilities, and the need for suitable protective equipment with the assistant physician and with the sports professional.

The practice of sports is still an individual choice and decision because no guidelines are available according to each particular frequency or type of seizures and AEDs intake. However, those that continue having seizures only at night, or always preceded by an aura allowing the activity arrest should have less limitations than those with myoclonic, atonic, absence, complex partial or tonic-clonic seizures. Rice and the Council of Sports Medicine and Fitness³⁷ elaborated guidance for clinicians, including those who

Table 1
Sport recommendations.^{8,11,36,37,84}

Swimming and water sports	Always swim in supervised pools with direct supervision of trained professionals (cardiopulmonary resuscitation training) that are aware of the condition of the sports practitioner. Do not swim in unsupervised open waters. Always wear a life-vest when in a boat, when water-skiing or any other similar sport (sports not to be undertaken alone), avoid these sports in uncontrolled epilepsy. Scuba diving is generally not recommended.
Sports at heights	Hand-gliding, parachuting, sky-diving are not recommended; horseback-riding permitted if under supervision as therapy; the risk for certain sports (bicycling, gymnastics at parallel bars or involving acrobatic activities, rock climbing) should be assessed for those with controlled epilepsy ^a and the recommendation is to perform them with the necessary safety equipment and not alone. For cycling avoidance of busy roads is also recommended.
Motor sports	Not recommended for those with uncontrolled epilepsy. No formal restrictions if epilepsy is controlled ^a and according to the driving regulations of each country, however the safety of others and not only of the PWE should be accounted for.
Shooting sports	Not recommended for those with uncontrolled epilepsy.
Contact sports	For PWE with controlled epilepsy the type of seizures and type of weapon should be evaluated. Not recommended for those with uncontrolled epilepsy.
Aerobic sports (e.g.: running, basketball, stationary bike, aerobics, gymnastics not involving heights)	Generally recommended with the exception of boxing, a sport for which no general consensus has been reached on whether it is harmful or not to PWE. No restrictions with the use of appropriate safety equipment when advised.

^a Controlled epilepsy means seizure absence for more than one year.

treat CWE, and they do not recommend special precautions for those with controlled epilepsy. For the ones with uncontrolled seizures, an individual assessment for collision, contact or limited-contact sports, and avoidance of archery, swimming, weightlifting, power lifting, strength training and sports involving heights are recommended.

For PWE there are general recommendations for each type of sports (Table 1), which should be useful when assessing individual patients.

10. Conclusions

People with chronic diseases including epilepsy, should be encouraged to exercise, as should the general population. The mental and physical advantages of regular exercise are regarded as highly beneficial to a group that is normally sedentary, overweight and with higher rates of depression. Sports medicine professionals should have an understanding of epilepsy syndromes, types of seizures, medications, what to do when a seizure occurs during sports practice, the effect of physical exercise on seizures, and when restrictions are applied to the practice of sports.

However, literature on this subject is still scarce and most of the studies presented in this review were based on a small number of patients. Furthermore, a good proportion of the data collected and analyzed was based on questionnaires constructed by the authors with qualitative measurements and relying only on patients or relative's reports, though without clinical confirmation or based on clinical reports collected retrospectively. Therefore, other, more robust, controlled, randomized studies on epilepsy and physical exercise are deemed in order to provide basis for physicians to give informed counseling on this subject.

General physicians, neurologists and pediatricians should support the practice of regular physical exercise and inform patients and caregivers about the benefits associated with physical activity and the necessary precautions, like protective gear. For handicapped patients, better access to exercise facilities and an appropriate exercise program ought to be provided. An effort should be made to reduce the stigma associated with epilepsy, so that quality of life of people with epilepsy can continue improving.

Conflict of interests

None of the authors has any conflict of interest to disclose.

Acknowledgements

The authors want to thank Dr. Mrinali Honavar for her technical assistance in writing the manuscript.

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