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Review

Epilepsy and physical exercise

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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.

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