Arq Neuropsiquiatr 2009;67(4):1007-1012

EVALUATION OF INTENSE PHYSICAL EFFORT IN SUBJECTS WITH TEMPORAL LOBE EPILEPSY

Fabio Camilo[1], Fúlvio Alexandre Scorza[2], Marly de Albuquerque[1], Rodrigo Luiz Vancini[3], Esper Abrão Cavalheiro[2], Ricardo Mario Arida[3]

Abstract – People with epilepsy have been discouraged from participating in physical activity due to the fear that it will exacerbate seizures. Although the beneficial effect of aerobic exercise in people with epilepsy, little objective evidence regarding the intensity of exercise has been reported. We investigated the effect of incremental physical exercise to exhaustion in people with epilepsy. Seventeen persons with temporal lobe epilepsy and twenty one control healthy subjects participated in this study. Both groups were submitted to echocolordoppler and electrocardiogram at rest and during physical effort. None of patients reported seizures during physical effort or in the recovery period of ergometric test. Both groups presented physiological heart rate and blood pressure responses during the different stages of the ergometric test. Only few patients presented electrocardiography or echocardiography alterations at rest or during effort. In conclusion, this work suggests that physical effort to exhaustion is not a seizure-induced component.

KEY WORDS: epilepsy, exercise, ergometric test, seizure, patient, maximal physical effort.

Avaliação do esforço físico intenso em indivíduos com epilepsia do lobo temporal

Resumo – Pessoas com epilepsia têm sido desencorajadas a participar de atividades físicas por medo que o exercício físico possa exacerbar as crises epilépticas. Apesar dos efeitos benéficos do exercício físico aeróbico em pessoas com epilepsia, informações em relação à intensidade do exercício têm sido pouco estudadas. Neste estudo, investigamos o efeito do exercício físico incremental até a exaustão (teste ergométrico) em pessoas com epilepsia. Dezessete pessoas com epilepsia do lobo temporal e vinte e um indivíduos saudáveis (controles) participaram do estudo. Os dois grupos foram submetidos a ecocardiograma e eletrocardiograma em repouso e durante o esforço físico. Nenhum indivíduo com epilepsia apresentou crises durante o esforço físico ou no período de recuperação do teste ergométrico. Ambos os grupos apresentaram respostas fisiológicas da frequência cardíaca e pressão arterial durante os diferentes estágios do teste de esforço. Somente algumas pessoas com epilepsia apresentaram alterações ecocardiográficas e eletrocardiográficas em repouso ou durante o esforço. Em conclusão, este estudo sugere que o esforço físico exaustivo parece não ser um componente indutor de crises epilépticas.

PALAVRAS-CHAVE: epilepsia, exercício, teste ergométrico, crises epiléticas, paciente, esforço físico máximo.

For many years, the question whether people with epilepsy should participate in a regular physical activity or sport recreation has been the source of strong controversy. Exercise is well known to improve health and quality of life in the general population and this is true for those with epilepsy as well. Overprotection, understimulation, low self-esteem, isolation, depression, and anxiety may create barriers to an active lifestyle[1]. People with epilepsy most often cite emotional difficulties, such as depression from underemployment, undereducation, and social isolation[2]. Single sessions of moderate aerobic exercise can provide acute mood benefits[3] and exercise programs reduce depression[4]. In spite of these facts, people with epilepsy are rather cautioned of sport activities and even

[1]Núcleo de Pesquisas Tecnológicas, Universidade de Mogi das Cruzes, Mogi das Cruzes SP, Brazil; [2]Disciplina de Neurologia Experimental, Universidade Federal de São Paulo/Escola Paulista de Medicina (UNIFESP/EPM), São Paulo SP, Brazil; [3]Departamento de Fisiologia, Universidade Federal de São Paulo/Escola Paulista de Medicina (UNIFESP/EPM), São Paulo SP, Brazil.

Research supported by FAPESP, CNPq, CAPES and CinAPCe (Brazil).

Received 30 March 2009. Accepted 6 August 2009.

Dr. Ricardo Mario Arida – Rua Botucatu 862 / Ed. Ciências Biomédicas / 5º andar - 04023-900 São Paulo SP Brasil. E-mail: arida.nexp@epm.br

physical exercises. This is based on a wrong but common belief that the physical activity exacerbates seizure disorders. Seizures during exercise occurred in six of 21 patients in the study of Bjorholt et al.[5] in four of 15 patients, mainly during aerobics in another study[6] and no seizures in Steinhoff et al study[7]. To this point, several human[6,8,9] and animal studies[10,11] have reported reduced number of seizures after a physical training program.

Exercise-induced seizures are rare despite the fact that most patients exercise to some degree. In many patients, exercise may offer moderate protection against seizures[12] and EEG studies have shown that epileptiform activity is often reduced during physical exertion[13]. Only in a small part of patients, an increase in interictal discharges is seen during or after exercise[13]. Another important point to be addressed is that although seizures do not occur frequently during low and moderate exercise, such as aerobic physical activities, some reports have also shown rare or no seizures during maximal physical effort[9,14]. These findings are quite interesting because among studies which evaluate the effect of physical exercise on epilepsy, most use questionnaires or standardized tests of physical endurance[1,7]. Thus, among the several factors to be considered when prescribing physical activities to people with epilepsy, such as recommendations for specific sports, seizure control, intensity and duration of exercise, intensity of effort is a subject not well explored. This is understandable because aerobic activities are preferentially recommended due their effects on the cardiorespiratory system and several other factors involved in quality of life.

Here, we investigated the effect of maximal physical effort, i.e., exercise to exhaustion in people with epilepsy.

METHOD

The study was approved by the Human Research Ethic Committee and all subjects signed an informed consent. Adult outpatients with temporal lobe epilepsy recruited from a Neurological Clinic (ITAPETI) – São Paulo, Brazil, were invited to participate as study subjects during a routine visit to the outpatient clinic. The study involved 17 persons with documented temporal lobe epilepsy (TLE) (5 man and 12 women, age ranging between 23 and 70 years, mean age=39.6±13.0 years). The control group (CTL) was constituted of 21 healthy subjects (12 men and 9 women, age ranging between 20 and 73 years, mean age=51.8±14.4 years).

Both groups were submitted to echocolordoppler (Atl Ultramark 9, New York) exam at rest and electrocardiogram at rest and during physical effort. The electrocardiogram test during exercise (ergometric test – ET) consisted of an incremental test to exhaustion (Ellestad protocol) (Imbramed, KT-4000 model, Brazil). All tests were realized in the morning, at room temperature around 20°C a 23°C.

All patients were treated with antiepileptic drugs (AED) and with at least one type of medication at the time of participation. Carbamazepine (29.4%) was the most common AED (Table 1). Seizure frequency during the last year is presented in Table 2. None of them presented any physical disability which could have contributed to patient's ability to participate in physical activities. Regarding their physical activity habits, patients were asked if they took part in any physical activity, for how long they have been engaged in this activity, how often and if they had any seizure during exercise. Therefore, patients were classified

Table 1. AED administration in TLE group (monotherapy and polytherapy).

	Mean dosage (mg)	Patients total	Patients %
CBZ	1060±260.8	5	29.4
OXC	1050	1	5.9
TPM	200	1	5.9
PHT	250	1	5.9
CBZ + CNZ	(933.3±305.5) and (0.58±0.29)	3	17.6
CBZ + CLB	(1200) and (15)	2	11.8
CBZ + NZP	(600) and (20)	1	5.9
OXC + CLB	(1050±212.1) and (15±7.1)	2	11.8
Without medication	–	1	5.9

CBZ: carbamazepine; OXC: oxcarbazepine; TPM: topiramate; PHT: phenytoin; CNZ: clonazepam; CLB: clobazam; NZP: nitrazepam.

Table 2. Seizure frequency among patients with TLE.

Number of patients	Weekly seizures	Monthly seizures	Controlled seizures	Epilepsy surgery
17 (100%)	1 (5.88)	4 (23.53)	12 (70.59)	5 (29.41)

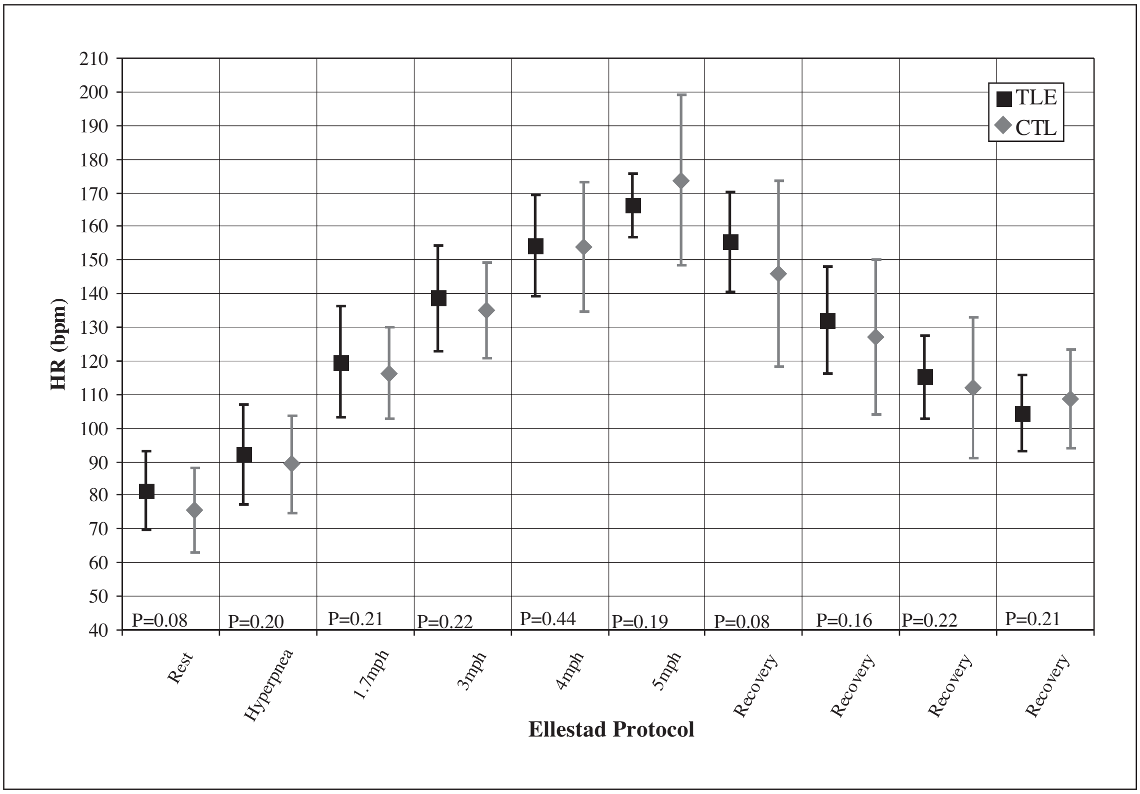

Fig 1. Heart rate (HR) responses during the different stages of the ergometric test. TLE: temporal lobe epilepsy group; CTL: control group. Data are expressed in mean ± SD.

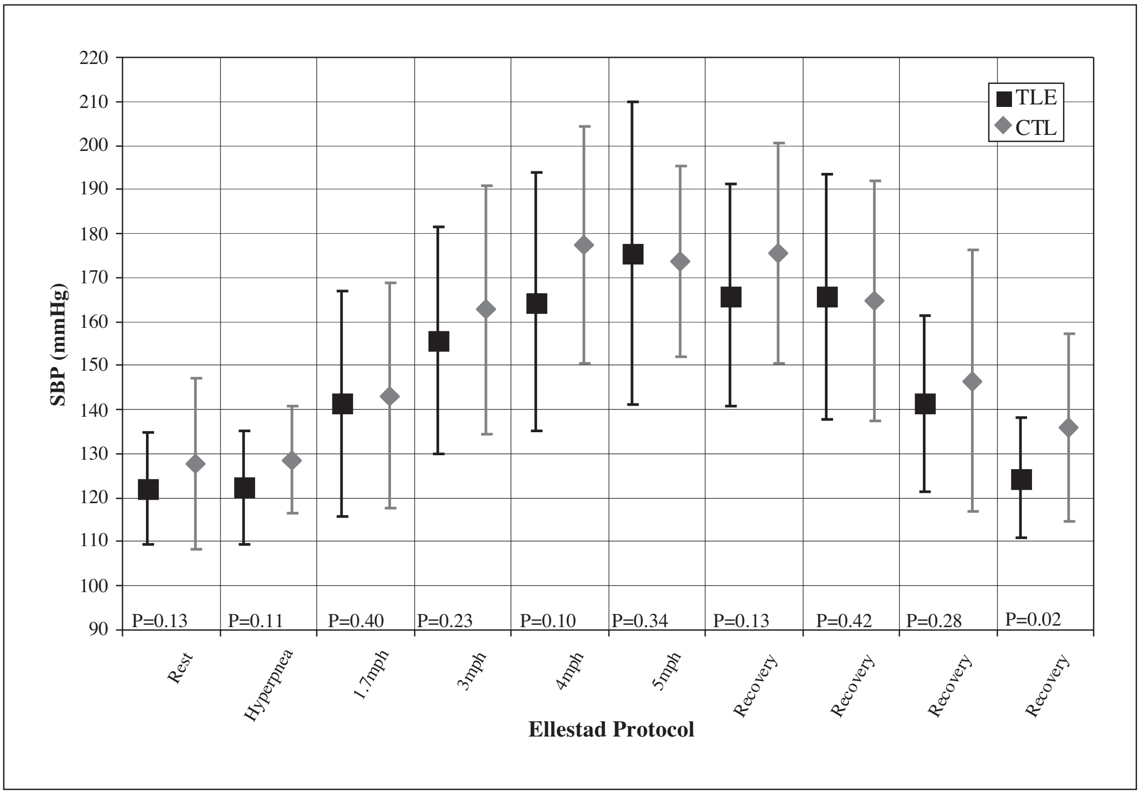

Fig 2. Systolic blood pressure (SBP) responses during the different stages of the ergometric test. TLE: temporal lobe epilepsy group; CTL: control group. Data are expressed in mean ± SD.

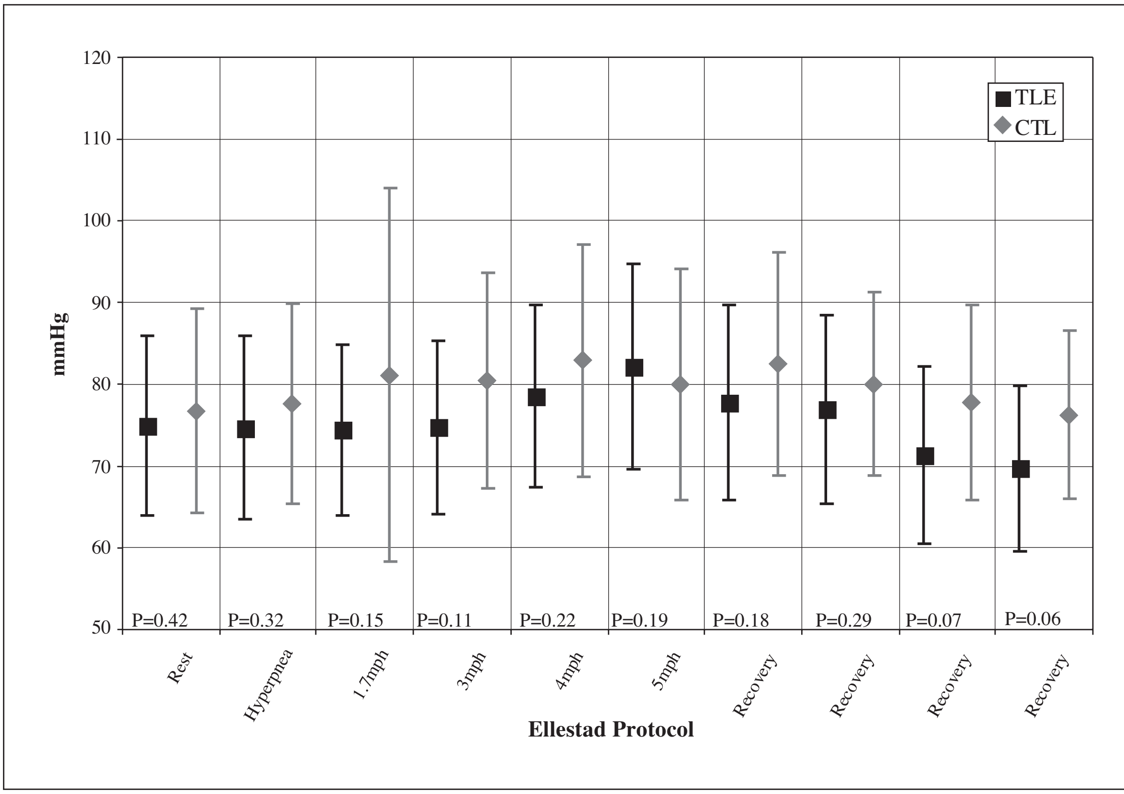

Fig 3. Diastolic blood pressure responses during the different stages of the ergometric test. TLE: temporal lobe epilepsy group; CTL: control group. Data are expressed in mean ± SD.

as physically active, non-active or sedentary according to the guidelines of the American College of Sports Medicine[15]. Active subjects were those who exercised at least three times a week for a minimum of 20 min at an adequate intensity; inadequately active patients exercised less than that and sedentary patients did not exercise at all.

Statistical analysis was carried out using the chi-square (χ^2) for HR responses. Student's t test was used to analyze the SBP and DBP responses. Values were considered significant for $p<0.05$. The results of echocardiographic from TLE group were presented in relative numbers (percent) without comparison between the groups.

RESULTS

Behavioral analysis

In this study, three TLE patients were considered as physically active (16.7 %) and fifteen patients as sedentary (83.3%). The sport activities more frequently practiced by the active patients were walking (20%), soccer (12%), bicycling (7%) and gymnastics (5%). None of patients reported seizures during physical effort or in the recovery period of ET. Patients were maintained in the cardiologic clinic for at least one hour after test termination to check eventual seizure occurrence during the later recovery period. No seizures were observed during this interval. Thus, the day after ergometric test, patients were questioned about any symptoms induced by the physical effort by a phone call and none of them presented seizures.

Heart rate (HR) and blood pressure (BP) changes

The mean time of ET was 7.4±1.6 min for the TLE group and 6.7±0.2 min for the control group. All individuals reached the maximal predicted HR for their age in the ET. Both groups presented physiological HR and BP responses during the different stages of the ET (Figs 1, 2 and 3). No significant differences of HR, systolic and diastolic BP were observed among groups during the stages of ET.

Electrocardiography and echocardiography analysis

The ECG at rest revealed alteration of ventricular repolarization in two (11%) patients, conduction disturbance in right bundle branch in one patient (5.6%) and sinus bradycardia in another patient (5.6%). Subjects of both groups did not present ST abnormalities during the ET. Thus, no patient presented arrhythmia during physical effort. Few anatomic alterations were observed in the TLE and CTL groups such as mitral valve prolapse or mitral insufficiency and concentric left ventricular hypertrophy.

DISCUSSION

This is one of the few studies specifically addressing the effect of exhaustive physical effort in people with epilepsy. Although studies aimed to investigate the relationship between physical exercise and epilepsy applied an ergometric test to evaluate physical fitness activities among people with epilepsy[6,9,14] their main purpose was not focused to the consequences of maximal physical effort in people with epilepsy. In our work, the sample of TLE patients analyzed did not present seizure after maximal/exhaustive physical exercise.

Historically, several recommendations had cautioned people with epilepsy to different sports or physical activities[16-20]. However, experts had felt that exercise, in general, did not affect seizure frequency and might, in fact, be protective against seizures. Actually, the main recommendation for people with epilepsy is concerned to aerobic physical activity[1,6,9,12,14,19]. Nevertheless, one question that has not been clarified is whether physical activities requiring intense, exhaustive, prolonged or maximal effort could precipitate seizures. To this point, we performed a maximal/exhaustive physical exercise to explore this subject.

The main exercise recommendation for general health is the aerobic exercise. It is well documented that this type of exercise provides positive effects on maximal aerobic and work capacity, body weight, self-steem[21], improved mood, life quality[3] and reduction in symptoms of anxiety and depression[22]. However, there are several sports activities which include anaerobic and aerobic components such as soccer, basketball, volleyball, etc. The motor development of children depends of number of stimulus, and in this sense, it is important to children experience different physical activities. Thus, collective sports can provide a better social integration to people with epilepsy. In this line, it is important to clarify whether anaerobic physical activities can be beneficial or harmful to persons with epilepsy.

Some physiological parameters could explain the possible protective effect of anaerobic exercise. Brief exercise to exhaustion has been shown to have a normalizing effect on EEG[23,24]. Gotze et al.[23] suggested that reduced epileptogenic EEG activity during exercise may be caused by an increase in GABA concentration as a consequence of metabolic acidosis. Enzymes controlling brain GABA-concentrations appear to be influenced by pH changes. Acidosis increases and alkalosis decreases GABA concentration[23]. In the hippocampal slice in vitro, acidification of the extracellular space to pH 6.7 terminated seizure-like burst firing facilitated by low-magnesium in the artificial CSF. The attenuation of epileptiform activity began within minutes of lowering pH[25]. Brief, intensive physical activity increases serum lactate content and causes metabolic acidosis. Reduction in pH reduces cortical irritability in animals; possibly the antiepileptic effect of ketogenic diet in humans results from the same mechanism[23]. Furthermore, contracting muscles produce lactic acid when anaerobic metabolism participates in the production of energy, and this leads to a reduction of the plasma pH value (metabolic acidosis)[26]. It is also important to emphasize that in animal studies, no seizures were observed during the maximum oxygen uptake test (anaerobic exercise)[9]. These animals were tested to their exhaustion limit, and none had seizures during this intensive effort.

The cardiovascular parameters analyzed in TLE patients did not demonstrate important changes during effort until exhaustion. Although this study was not focuses to seek hemodynamic alterations, we have to point out the importance of cardiovascular dysregulation in patients with TLE[27,28]. Patients with epilepsy are at increased risk of sudden unexpected death[29,30]. One possible contributory reason for this could be an altered autonomic heart function in epilepsy patients[31]. Heart-rate variability is a widely used parameter for assessment of autonomic cardiac regulation. Patients with epilepsy appear to have an altered autonomic control of the heart, with a reduction of heart-rate variability[27]. Nevertheless, the sample is small to make reliable conclusions.

Although this was a randomized, controlled intervention study, it is not without limitations. This includes a relatively small sample size. Additional studies on larger groups may reveal impacts, not demonstrated in this study. Another potential limitation of this study is that the sample includes patients with different seizure frequencies or seizure-free. Overall, this work indicates that physical effort to exhaustion seems not to be a critical factor to induce seizure. In this line, further information of exercise modalities requiring intensive effort for people with epilepsy is necessary.

REFERENCES

1. Jalava M, Sillanpaa M. Physical activity, health-related fitness, and health experience in adults with childhood-onset epilepsy: a controlled study. Epilepsia 1997;38:424-429.
2. Roth DL, Wiebe DJ, Fillingim RB, et al. Life events, fitness, hardiness, and health: a simultaneous analysis of proposed stress resistance effects. J Pers Soc Psychol 1989;57:136–142.
3. Folkins CH, Sime WE. Physical fitness training and mental health. Am Psychol 1981;36:373-389.
4. Martinsen EW, Medhus A, Sandvik L. Effects of aerobic exercise on depression: a controlled study. Br Med J 1985;291:109.
5. Bjorholt PG, Nakken KO, Rohme K, et al. Leisure time habits and physical fitness in adults with epilepsy. Epilepsia 1990;31:83-87.
6. Eriksen HR, Ellertsen B, Gronningsaeter H, et al. Physical exercise in women with intractable epilepsy. Epilepsy 1994;35:1256-1264.
7. Steinhoff BJ, Neusüss K, Thegeder H, et al. Leisure time activity and physical fitness in patients with epilepsy. Epilepsia 1996;37:1221-1227.
8. Denio LS, Drake ME, Pakalnis A. The effect of exercise on seizure frequency. J Med 1989;20:171-176.
9. Nakken KO, Bjorholt PG, Johannessen SI, et al. Effect of physical training on aerobic capacity, seizure occurrence, and serum level of antiepileptic drugs in adults with epilepsy. Epilepsia 1990;31:88-94.
10. Arida RM, Cavalheiro EA, Silva AC, et al. Physical activity and epilepsy: proven and predicted benefits. Sports Med 2008;38:607-615.

11. Arida RM, Scorza FA, Scorza CA, Cavalheiro EA. Is physical activity beneficial for recovery in temporal lobe epilepsy? Evidences from animal studies. Neurosci Biobehav Rev 2009;33:422-431.
12. Nakken KO. Physical exercise in outpatients with epilepsy. Epilepsia 1999;40:643-651.
13. Nakken KO, Loyning A, Loyning T, et al. Does physical exercise influence the occurrence of epileptiform EEG discharges in children? Epilepsia 1997;38:279-284.
14. McAuley JW, Long L, Heise J, et al. A Prospective Evaluation of the effects of a 12-week outpatient exercise program on clinical and behavioral outcomes in patients with epilepsy. Epilepsy Behav 2001;2: 592-600.
15. American College of Sports Medicine (ACSM) position stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness in healthy adults. Med Sci Sports Exerc 1990;22:265-274.
16. American Medical Association Committee on the Medical Aspects of Sports: Convulsive disorders and participation in sports and physical education. JAMA 1968;206:1291.
17. American Medical Association Committee on the Medical Aspects of Sports: Epileptics and contact sports. JAMA 1974;229:820-882.
18. American Academy of Pediatrics Committee on Children with Handicaps: The epileptic child and competitive school athletics. Pediatrics 1968;42:700-702.
19. American Academy of Pediatrics Committee on Children with Handicaps and Committee on Sports Medicine. Sports and the child with epilepsy. Pediatrics 1983;72:884-885.
20. Commission of Pediatrics of the International League Against Epilepsy: Restrictions for children with epilepsy. Epilepsia 1997;38:54-56.
21. DeBusk RF, Stenestrand U, Sheehan M, et al. Training effects of long versus short bouts of exercise in healthy subjects. Am J Cardiol 1990;65:1010-1013.
22. Martinsen EW, Medhus A, Sandvik L. Effects of aerobic exercise on depression: a controlled study. Br Med J 1985;291:109.
23. Gotze W, Kubicki ST, Munter M, et al. Effect of physical exercise on seizure threshold. Dis Nerv Syst 1967;28:664-667.
24. Horyd W, Gryziak J, Niedzielska K, Zielinski JJ. Exercise effect on seizure discharges in epileptics. Neurol Neurochir Pol 1981;6:545-52.
25. Velisek L, Dreier JP, Stanton PK, Heinemann U, Moshe SL. Lowering of extracellular pH suppresses low-Mg(2+)-induces seizures in combined entorhinal cortex-hippocampal slices. Exp Brain Res 1994;101:44-552.
26. Wasserman K, Wipp B, Koyal S, et al. Anaerobic threshold and respiratory gas exchange during exercise. J Appl Physiol 1973;35:236-243.
27. Tomson T, Ericson M, Ihrman C, et al. Heart rate variability in patients with epilepsy. Epilepsy Res 1998;30:77-83.
28. Ansakorpi H, Korpelainen JT, Tanskanen P, et al. Cardiovascular regulation and hippocampal sclerosis. Epilepsia 2004;45:933-939.
29. Tomson T, Walczak T, Sillanpaa M, et al. Sudden unexpected death in epilepsy: a review of incidence and risk factors. Epilepsia 2005;46:54-61.
30. Scorza FA, Colugnati DB, Pansani AP, et al. Preventing tomorrow's sudden cardiac death in epilepsy today: what should physicians know about this? Clinics 2008;63:389-394.
31. Nei M, Ho RT, Abou-Khalil BW, et al. EEG and ECG in sudden unexplained death in epilepsy. Epilepsia 2004;45:338-345.