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Narrative Review

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The Preventive Effect of Exercise on Epileptic Seizures: A Narrative Review

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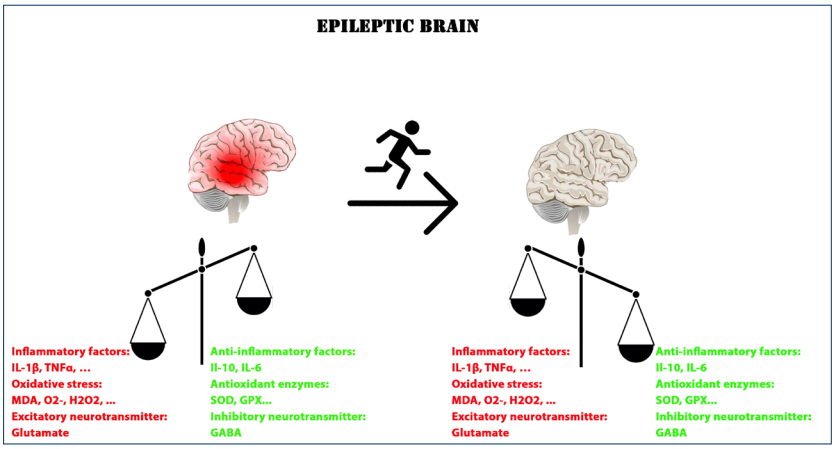
Abstract

Introduction: Epilepsy is a common neurological disease that leads to seizures and has been associated with cognitive, psychological, social, and neurobiological consequences. Exercise training is extensively addressed as a non-pharmacological intervention to reduce seizure susceptibility. Here, we review possible mechanisms of exercise training to reduce epileptic seizures.

Methods: The literature search was conducted in the Google Scholar, PubMed (Medline/PubMed Central), and Web of Science databases. The keywords "physical activity" OR "exercise" AND "epilepsy" OR "seizure" were searched in the title, abstract, or index term fields.



Results: Exercise training can improve quality of life, depression, anxiety, cognitive dysfunction, and memory loss, increase social engagement, and reduce the incidence of epileptic seizures by decreasing inflammation (IL-1β and TNF-α), oxidative stress (MDA, $O2^{-}$, and H_2O_2), and neurotransmitter (GABA and glutamate) modulation. However, regular exercise can have beneficial effects on health-related physical fitness factors such as cardiovascular fitness and body composition.

Conclusion: Regular physical exercise is an excellent complementary therapy that can be used in the treatment of epileptic seizures.

Keywords: Epilepsy, Seizures, Narrative review, Exercise

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Introduction

Epilepsy is one of the most common neurological diseases, affecting nearly 50 million people worldwide. It is the third most common neurological disease after stroke and dementia. The International League Against Epilepsy (ILAE) defines epilepsy as a "disorder of the brain characterized by recurrent epileptic seizures," and an epileptic seizure is defined as a "transient occurrence of symptoms induced by abnormal, excessive, or synchronous neuronal activity in the brain" (1). Various factors are involved in the occurrence of seizures, such as inflammation, genetic inheritance, oxidative stress, trauma, channelopathies, etc. Epilepsy is also associated with numerous psychiatric factors such as stress, anxiety, and depression, which can significantly impact quality of life (2). Although many people with epilepsy (PWE) benefit from antiepileptic drugs (AEDs), one-third of patients continue to have seizures, a condition known as drug-resistant epilepsy (DRE)(3), so they need complementary forms of therapy. In recent decades, attention has been drawn to the association between exercise and epileptogenesis, and many studies have investigated the relationship between exercise and physical activity and the improvement of the signs of epilepsy (4). Although

data have shown low levels of PA in people with epilepsy, and they usually have been prohibited from engaging in exercise for different reasons, including the fear of worsening the seizure, growing evidence continuously points to the positive effect of exercise on epilepsy (5). Exercise can induce improvement in the pathogenesis of the disease by exerting its effect through various factors, including neurotransmitters (6, 7), inflammation (8), oxidative stress (9), and improvement in the mental status (10). In this study, we aim to explore some physiological mechanisms by which exercise affects epileptogenesis.

Methods

We performed a narrative review to assess the effects of exercise on people with epilepsy and the mechanisms involved. The literature search was conducted in the Google Scholar, PubMed (Medline/PubMed Central), and Web of Science databases. The keywords used were "physical activity" OR "exercise" OR "training" AND "epilepsy" OR "seizure" OR "epileptiform discharge" in the title, abstract, or index term fields. No restriction was placed on the year of publication for the reports included. The search included both medical subject headings and text words for literature on exercise and epilepsy. We included reviews, case reports, case series, cohorts, clinical trials, meta-analyses, original articles, and book chapters.

Results

Inflammation and seizure

The body's immune system refers to the mechanisms and responses that maintain homeostasis. It removes the exogenous materials that enter the body and also abnormal endogenous materials like waste products or injured cells (11). Today, inflammation is known to be the cause of many diseases like cancer, ischemic heart disease, and cerebrovascular (12). The bulk of evidence supports the role and effectiveness of proinflammatory mediators in the brain in epileptogenesis, and research has shown that anti-inflammatory drugs can decrease and improve epilepsy symptoms (13-16). In the animal model of epilepsy, increased seizures have been reported to accompany increased inflammatory responses. These responses include increases in tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β) in microglia and astrocytes (17). Researchers have claimed that the increases in IL-1β and TNF-α are probably part of the cellular cascade that leads to the occurrence of hyperexcitability and generalized convulsions (18). Many studies have reported the excitatory effects of IL-1β; indeed, this factor exerts its effects by reducing the inhibitory action of GABA (19) and by inhibiting glutamate reuptake while enhancing glutamate production by astrocytes (20). These effects are mediated, in part, by increased Ca^{2+} influx through NMDA receptor activation (21). IL-1β can affect neural hyperexcitability, excitotoxicity, and, finally, neural death and damage in different ways. It can increase calcium influx by affecting N-methyl-D-aspartate (NMDA) receptors (21) as well as inhibiting glutamate reuptake by astrocytes, which may induce seizure-like activity in the brain (22, 23). IL-1β can phosphorylate the NR2A/B subunits of NMDA, and activation of this pathway increases the NMDA-induced Ca^{2+} influx (24).

On the other hand, injection of MNDA antagonists blocks the effects of IL-1β on the prolongation of seizure activity (25). To investigate these effects of IL-1β, Viviani et al. (2003) examined its influence on NMDA-mediated Ca^{2+} influx and the phosphorylation of the NR2A and NR2B subunits of the NMDA receptor. Their findings demonstrated that increasing concentrations of IL-1β significantly enhanced NMDA-induced neuronal death. The findings of the study revealed that increases of IL-1β, which occur in various pathologies of the brain and CNS, can result in the enhancement of NMDA receptor function and, consequently, an increase in Ca2 + influx, leading to hyperexcitability and neural injuries. On the other hand, injection of MNDA antagonists blocks the effects of IL-1β on the prolongation of seizure activity (21). The increase of glutamate that occurs during seizures results in an increase in the activity of NMDA receptors and hyperactivity of microglia. Activation of microglia can cause the production of inflammatory cytokines such as IL-1β and TNFα. Simultaneously, activation of microglia and increased levels of inflammatory cytokines can result in blood-brain barrier (BBB) dysfunction and disturbance of excitatory/inhibitory balance in the brain and finally induce epileptogenesis (20). It can be said that inflammation is both the cause of epilepsy and its consequence. The high mobility group box 1 protein (HMGB1) is released in response to internal factors like stimulation of neurons, microglia, or immune cells via inflammatory factors or oxidative stress, or in response to external stimuli such as tumors, trauma, and brain dysplasia (26). After release, HMGB1 binds to its receptor, TLR4, and creates the TLR4/HMGB1 complex. This complex sends its signals via myeloid differentiation primary response 88 (MyD88). It leads to the translocation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) into the nuclei and induces transcription of inflammatory factors (27). In the same way, IL-1β also binds to its receptor, IL-1R, and forms the IL-1R1/IL-1β complex, then recruits some intracellular factors, including TRAF6, MyD88, and IL-1R-associated kinase that activate some signaling pathways like NF-κB, eventually, augmenting the inflammation (28). IL-1R1/IL-1β and HMGB1/TLR4 pathways converge at the NF-κB, and this transcription factor leads to the production of inflammatory factors such as COX2, TNFα, and IL-1β (29). IL-1R1/IL-1β and HMGB1/TLR4 are two key upstream pathways in generating inflammatory responses. Studies have shown that these two pathways have an essential role in epileptogenesis induced by neuroimmune response to inflammation, and they participate in neuroinflammatory responses to brain damage after epilepsy (30).

On the other hand, seizures cause the production and aggravation of inflammation. For example, by injection

of lipopolysaccharide, which leads to TLR4 activation, seizures are reinforced, and this reinforcement itself induces more production of HMGB1 from astrocytes, resulting in the formation of a positive feedback loop (31). Also, HMGB1, like IL-1β, induces epileptogenesis by affecting NMDA and consequently increasing Ca^{2+} influx (32).

Oxidative stress and seizure

Oxidative stress refers to the accumulation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) because of dysfunction of mitochondria. Under physiologic conditions, the function of RNS/ROS is well-regulated, and they conduct actions such as apoptosis, autophagy, cell division, and chemical signaling in the body (33). Although it has not been fully determined if OS and mitochondrial dysfunction are the cause of seizure or its effect, many studies have shown that enzymatic actions related to OS result in dysfunction of mitochondria and accumulation of RNS/ROS, and the effects of mitochondrial dysfunction and OS on neuronal excitability, neural damage, and the apoptosis induced by seizures have been proven. On the other hand, epileptic seizures lead to mitochondrial dysfunction, which forms a vicious circle (34-37). As previously discussed, epilepsy leads to a reduction of antioxidant agents and a simultaneous increase in oxidative agents like NO, which is an indicator of responses to OS. OS is a risk factor in epilepsy. On the other hand, according to studies, exercise is a potential feature to reduce OS. So, it seems that there are some promising possibilities to alleviate epilepsy using exercise via reducing oxidative stress, which will be discussed in the next section.

Neurotransmitter and seizure

Alterations in neurotransmitter levels in epilepsy have been shown in numerous studies. There is some evidence to support the idea that exercise can result in improvement in behavior, mood, quality of life, and frequency of seizures through causing changes in neurotransmitter levels (7, 10, 38). For example, it has been proven that exercise can increase serotonin, endorphin, and norepinephrine, which are associated with mood and happiness (39, 40). In epilepsy, some neurotransmitter levels change. For example, research has shown the reduction of BDNF after seizure (41). The positive effects of exercise, such as reduction in seizure frequency and inhibition of memory and cognitive function loss, can likely be attributed to increased levels of BDNF and IGF-1, along with the activation of their associated signaling pathways, such as MEK and mTOR, as they are involved in cell growth, proliferation, differentiation, and survival (7). It has been observed that, during exercise, the intake of carbohydrates and lactate is increased by the brain. It seems that this increase, to some extent, is for GABA and glutamate synthesis, so exercise can cause an increase in GABA levels (42) and prevent GABAergic neuron loss (43). Another mechanism by which exercise can increase GABA and decrease the number of seizures may be acidosis. Indeed, reduction of pH can exert antiepileptogenic effects by increasing the concentration of GABA (44). It has been suggested that melatonin can influence epilepsy through different pathways. To investigate this hypothesis, Lima et al. (2005) conducted a study on epileptic rats subjected to pinealectomy. The results showed that pinealectomy facilitated epileptogenesis, and interestingly, this facilitation was reversed by injection of melatonin(45). It has also been observed that melatonin receptors, M1 and M2, experience a significant increase after 17 days of treatment with valproic acid (46). It was shown that adding melatonin to valproic acid results in better outcomes (47). It seems that melatonin can apply its antiepileptic effects by increasing GABA levels, reducing glutamate, and inhibiting nitric oxide (48). The reduced basal level of melatonin and an increase in it after seizures have been reported in epileptic people. Overall, research has shown a reduction in the intensity, time, and frequency of seizures by using melatonin in epileptic condition(47, 49). These data are representative of the antiepileptic features of melatonin. Norepinephrine (NE), the metabolite of dopamine, seems to have a modulatory role in epilepsy and seizure occurrence. Damage to the NE neurons of the locus coeruleus leads to a permanent status of epilepticus in the limbic system (50). Increased levels of dopamine were reported in a study on epileptic rats, suggesting that this elevation may represent a compensatory response to seizures (51). After the occurrence of a seizure, norepinephrine increases incrementally as a consequence of the sympathetic nervous system and causes vasoconstriction and enhancement of GABAergic activity, creating an inhibitory environment(52). Interestingly, chronically increased levels of NE can have epileptogenetic features. High levels of NE in circulation can pass through the blood-brain barrier (BBB) and, by inducing vasoconstriction, lead to brain ischemia and increase epileptic activity (53, 54).

Exercise training: types of exercise

Aerobic training

It has been demonstrated that aerobic training could be beneficial for a large number of human chronic diseases. The effects of aerobic training on epilepsy have also been examined in much research, all of which shows its beneficial effects on epilepsy (See Table 1). Hrncic et al. (2014) demonstrated that 30 days of aerobic exercise in male Wistar rats reduced seizure frequency, which coincided with an increase in antioxidant enzymes (9). In the same work, two months of aerobic treadmill exercise, totaling 40 sessions, reduced seizure frequency and increased antioxidant capacity (55). Swimming exercise can also modulate oxidative stress, as demonstrated in Kim et al.'s (2013) work. Six weeks of swimming exercise induced changes in catalase and superoxide dismutase enzyme activity and reduced seizure frequency (56). In the same work, they demonstrated that low-intensity exercise combined with ascorbic acid could modulate

Table 1. Studies on physical exercise and epilepsy in humans and animals

Type of training	N Participants	Procedure and protocol	Results
Aerobic exercise			
Swimming (62)	48 male Wistar rats	6 weeks of swimming, 4 days/week, and each session lasted 60 minutes	Decrease in the frequency and intensity of seizures, and side effects and doses of sodium valproate
Aerobic training (59)	117 participants	Regular aerobic exercise, 150 min/week	Nonsignificant improvement in seizure frequency and quality of life
Aerobic training (58)	42 participants, aged 11 to 17	5 days/week cycling, walking, or jogging for 30 minutes in combination with a ketogenic diet, for a total duration of 6 months	Improvement of seizure frequency, quality of life, and depression
Aerobic training(60)	50 male Wistar rats	Treadmill exercise 5 days/week for 4 weeks, and each session's duration was 30 min	Reduction of seizure intensity, increase in latency period, GABA levels, and improvement of excitatory/inhibitory balance of the brain
Aerobic training(41)	40 male Wistar rats	4 weeks of progressive treadmill training, each session comprising 5 minutes warm-up and 25 minutes main exercise	Enhancement of the decreased level of BDNF and decrease of the increased level of TrkB to basal levels
Aerobic training(9)	56 male Wistar rats	Treadmill exercises for 30 consecutive days, 1 session per day, each session lasting 30 minutes.	Decrease in seizure frequency and increase in latency period, increase in the antioxidant enzymes catalase and superoxide dismutase, and decrease in malondialdehyde
Aerobic training (55)	18 male Mongolian gerbils	Two months of treadmill exercise, 5 sessions per week, each session 20–8 minutes.	Reduction in intensity and frequency of seizures, along with changes in the levels of antioxidant enzymes
Aerobic training (16)	54 male Wistar rats	Two weeks of moderate intensity treadmill exercise in combination with prednisolone, each session 30 minutes	Decrease in the severity of seizures, increase in the latency period, simultaneous decrease in proinflammatory factors, such as TNF and IL-1, and increase in anti-inflammatory factors, such as IL-10
Swimming (56)	22 male mice	6 weeks of swimming in combination with resveratrol. Training was 5 days/week, each session lasting 60 minutes	Reduction in the number of seizures due to changes in catalase and superoxide dismutase levels
Swimming (57)	44 male mice	Low intensity swimming in combination with ascorbic acid. Swimming was performed for 8 weeks, 3 times a week, and each session's duration was 30 minutes.	Reduction in seizure activity due to alteration in antioxidant enzymes, such as SOD and GTx
Resistance exercise			
Resistance training(38)	70 male Wistar rats	Strength training 5 days/week for 4 weeks. Exercises included climbing the ladder with weights tied to the tail in a progressive manner, the weights ranging from 50% to 100% of body weight. Each training session consisted of 8 consecutive rounds of climbing the ladder and a 1-minute rest between rounds.	Reduction of seizure frequency
Resistance training(7)	20 male Wistar rats	Strength training 5 days/week for 4 weeks. Exercises include climbing the ladder with weights tied to the tail in a progressive manner, the weights weighing 50%, 75%, 90%, and 100% of body weight. Each training session consisted of 8 consecutive rounds of climbing the ladder and a 1-minute rest between rounds.	Reduction in seizure frequency and memory decline, restoration of IGF-1 and BDNF to baseline levels
Combined exercise			
Combined training (63)	18 participants, aged 18 to 60	12 weeks of progressive aerobic and resistance training twice a week	Reduction of seizure frequency, improvement in quality of life, stress, anxiety, quality of sleep, and physical fitness
Combined training(64)	21 participants, between 18 and 60 years old	12 weeks of combined training 2 days/week, each session comprising 5 min warm-up, 15–20 minutes aerobic training, resistance training including 2–3 sets of each exercise with 10–15 repetitions and 5 minutes cooldown, with a total duration of 60 minutes	Enhancement of cognitive and executive function and physical fitness
Combined training(65)	23 participants, between 16 and 60 years old	12 weeks of training twice a week, each session lasting 60 minutes, including warm-up, aerobic training with 60% VO_{2max}, 1 set, and 10 repetitions with 70% 1RM for each resistance exercise	Improvement of mood, quality of life, and physical fitness. There were no effects on serum drug levels and seizure frequency.
Combined training(66)	15 women	15 weeks of combined training 2 days/week, each session comprising aerobic dance, resistance training, and stretching with a total duration of 1 hour	Improvement of seizure frequency, muscle spasms, sleep disorders, and fatigue
Combined training(67)	10 children between 8 and 12 years old	5 weeks of training 2 days/week, each session including two 90-minute parts comprising activities such as football, basketball, ping-pong, badminton, and/or dance. They had been taught to perform body weight exercises like pull-ups, push-ups, etc., for 15 minutes every day at home	Enhancement of neurocognitive, mental, and motor function, quality of life, and social problems
Combined training(68)	16 participants between 18 and 55 years old	18 weeks of exercise for 3 times/week, each session lasting 1 hour, comprising 5 minutes warm-up, progressive cycling from 15 minutes to 30 minutes at 65– 80% HRR, and progressive resistance training, 3 sets for each exercise and 8–12 repetitions	Improvement in overall physical fitness, verbal memory, mood, learning, and cognition

oxidative stress, alleviating both the frequency and intensity of seizures (57). Numerous human studies have shown the positive effects of exercise training on epilepsy. For example, Zhang et al. (2020) demonstrated that a combination of a low-glycemic diet and aerobic exercise (cycling, jogging, or walking) for 24 weeks, performed five times per week, improved seizure frequency, quality of life, and depression in PWEs aged 11 to 17 years (58). In contrast, Kumar et al. (2022) found that 150 minutes per week of aerobic training did not

have a significant effect on seizure frequency or quality of life (59). Bayat et al. (2018) investigated the effects of treadmill exercise on neurotransmitters in epileptic rats. They found that four weeks of aerobic training modulated GABA and its receptors, GAD67 and GAD65. This modulation coincided with a reduction in seizure frequency and intensity, suggesting a potential link to an improved inhibitory/excitatory balance of neurons (60). Exercise may exert beneficial effects on epilepsy through modulation of BDNF. Almeida et al. (2018) showed that aerobic training reversed the decrease in BDNF levels observed in epileptic rats (41). Ogunsuyi et al. (2023) further demonstrated that treadmill exercise can also ameliorate and improve the therapeutic effects of curcumin in epileptic rats. They found a significant reduction in seizure frequency and ROS levels, along with an elevation of BDNF mRNA expression in the brains of rats treated with a combination of curcumin therapy and treadmill exercise (61). Aerobic training can also modulate seizure frequency by influencing inflammatory factors. Lima Rosa et al. (2022) demonstrated that two weeks of moderate-intensity treadmill exercise combined with prednisolone reduced proinflammatory factors like IL-1β and TNF-α while simultaneously increasing the anti-inflammatory factor IL-10. This coincided with a reduction in seizure severity and an increased seizure latency period (16).

Resistance exercise

Limited data exist on the effects of resistance training in epilepsy. Research has primarily been conducted in animal models (See Table 1). Pena et al. (2012) demonstrated that resistance training in rats, performed five days per week for four weeks, resulted in a reduction in seizure frequency (38). In another study, the reduction in seizure frequency following resistance exercise was accompanied by a return of BDNF and IGF-1 levels to baseline (7). Lima Rosa et al. (2024) demonstrated that resistance exercise was safe for epileptic rats, as it did not increase the risk of epileptogenic condition (69).

Combined exercise

Numerous studies have investigated the effects of combined training on epileptic symptoms (See Table1). For example, an 18-week combined exercise program, consisting of 15 to 30 minutes of progressive cycling and 30 minutes of resistance exercise, three times per week, improved cognition, verbal memory, and mood, in addition to overall physical health (68). Additionally, data revealed that combined training improved quality of life, alleviated stress and anxiety, and reduced seizure frequency (63). It seems that combined training can also enhance executive and cognitive function in PWEs (64). There have been concerns that, due to metabolic changes, exercise might influence the effectiveness of AEDs. However, Macauky et al. (1994) demonstrated that 12 weeks of combined exercise did not affect serum levels of AEDs or seizure frequency in patients with epilepsy (65). A combination of resistance and stretch training is beneficial for women with epilepsy, reducing muscle spasms, fatigue, sleep disorders, and seizure frequency (66). Eom et al. (2014) further demonstrated the potential benefits of combined exercise, finding that a 5-week program improved social problems, motor function, cognitive function, and mental health in children with epilepsy. This suggests that combined exercise may positively influence social life in PWE (67).

Can exercise trigger seizures?

People with epilepsy have historically been discouraged from engaging in physical activity due to concerns about potential seizure triggers. However, numerous studies have demonstrated the safety and benefits of exercise for individuals with epilepsy. While factors like hyperventilation, hyponatremia, hypoglycemia, and hyperthermia can trigger seizures, these risks can be mitigated through proper exercise planning and monitoring (70). Despite these concerns, studies have shown that exercise can reduce epileptic discharges. For example, research has demonstrated a decrease in EEG epileptic discharges during exercise (71). Additionally, another study found that epileptic activity remained unchanged or even decreased during or immediately after exercise (72). In a study involving 400 people with epilepsy, only two individuals attributed their seizures to exercise (73). In a study of 204 epileptic patients, half experienced no seizures during exercise. Over 10% reported seizures during more than 10% of exercise sessions, while only 2% experienced seizures during more than 50% of sessions (74). A case study of a woman in her 40s with drug-resistant epilepsy demonstrated the potential benefits of high-intensity exercise (CrossFit). After six months of training, three days per week, the patient experienced a 33% reduction in seizures, dropping from 23 to 16 seizures. Notably, no seizures occurred during or within the first five minutes of recovery after exercise (75). In a research work including 18 sessions of combined training three days a week, all participants completed all sessions with no adverse effects (68). Exercise in children with epilepsy is also safe, as shown in a study that included exercise both at the gym and at home, demonstrating that it is a safe complementary therapy with no detrimental effects for these patients (67). Another concern with exercise training is its impact on serum levels of drugs. To investigate these effects, 23 participants with an age range of 16 to 60 were recruited to conduct combined training for 12 weeks, three days per week. Measuring serum levels of drugs (carbamazepine, phenytoin, and valproate) revealed that exercise has no meaningful effects on drug concentration (65).

Can exercise reduce the possibility of epilepsy later in life?

Another good point to ask is whether exercise in the early years of life can reduce the susceptibility to epilepsy later in life? To examine this hypothesis, Arida et al. conducted a

meta-analysis including 15 studies, and they revealed that previous exercise training can reduce the susceptibility to seizure and the development of epilepsy in animal model(76). To survey the effects of preconditioning with aerobic training, rats at the age of 21 postnatal days were submitted to exercise from 60 postnatal days. After this period, epilepsy was induced by pilocarpine. They observed that pilocarpine-induced symptoms of epilepsy were lower in the exercise group. They claimed that exercise in early stages of life may exert neuroprotection against neurologic diseases in the future (77).

Discussion

As previously discussed, frequent studies have been conducted on the association between physical activity and neurological disorders, but an optimal method remains elusive. Research involving 21 participants aged 18 to 60 demonstrated that three months of combined training could enhance cognitive and executive functions, physical fitness factors, and improve performance on language and attention tasks(64). In another study, 15 women underwent combined training comprising aerobic dance and resistance exercise. After completing the training period, they observed improvements in the number of seizures, muscle spasms, sleep disorders, and fatigue (66). Additionally, 12 weeks of combined training significantly improved quality of life, mood, and physical fitness factors without any adverse effects on serum drug concentration (65). Physical exercise, as previously discussed, has benefits for children with epilepsy. One study revealed that aerobic training combined with a ketogenic diet in children aged 11 to 17 years could reduce seizure frequency and depressive symptoms, as well as enhance quality of life (58). Five weeks of supervised physical exercise combined with daily home-based exercise led to enhanced neurocognitive function, including visual, auditory, and attentional skills, increased social function, improved behavioral problems, and boosted self-esteem (67). In contrast, Kumar et al. (2022) showed that 150 minutes/week of physical activity had no effects on seizure frequency or quality of life in PWEs (12). Based on recent research by Alexander et al. (2024), the ACSM's guidelines for health, which recommend 150 minutes/week of physical activity, appear to have limitations for PWEs. This is evidenced by the low completion rate in studies, with only two out of ten participants completing the exercise program. One possible reason for this high dropout rate may be related to the presence of comorbid mental health conditions in individuals with DRE (78). Overall, it appears that aerobic training, resistance training, or their combination can exert positive effects on epilepsy and seizures. However, based on research, combined training appears to offer advantages over the other two methods in terms of practicality and participant adherence.

Conclusion

In conclusion, according to the data and results of research, it seems that despite fears of increased seizure activity during exercise, physical activity is not only harmless but also beneficial and can be considered a complementary non-pharmacological therapy for this population. Based on this review, different types of exercise can exert their effects on the epileptic brain in different ways. Overall, we can say that resistance exercise may influence neurotransmitters and neurotrophic factors like BDNF, while aerobic exercise may alleviate epilepsy symptoms by affecting oxidative stress and increasing antioxidant capacity by increasing antioxidant enzymes like SOD, CAT, and GPx. Aerobic exercise can also reduce inflammatory factors like TNFα and IL-1β and modulate the balance of excitatory/inhibitory neurotransmitters. It has been frequently demonstrated that exercise leads to delay in seizure onset and reduces seizure frequency and intensity. Participation in sports and physical activity exerts positive therapeutic and psychological effects on people with epilepsy, increasing self-esteem, social engagement, and overall long-term health. In addition to ameliorating the treatment of epilepsy, it can be a preventive tool, as it has been shown to reduce the susceptibility to the occurrence of epilepsy.

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Authors' Contribution

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Competing Interests

The authors declare that they do not have any conflict of interest.

Data availability statement

All necessary data will be available from the corresponding author upon reasonable request.

Ethical Approval

All study protocols have been approved by the Ethics Committee of the Faculty of Sport Sciences and Health, University of Tehran, Tehran, Iran.

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