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Effects of exercise on sleep in patients with epilepsy: A systematic review

Christina Mueller [a,*], Ashley Thomas [a], Amy W. Amara [b], Jennifer DeWolfe [a], S. Justin Thomas [c]

[a] University of Alabama at Birmingham, Department of Neurology, 1720 University Blvd, Birmingham, AL 35233, USA
[b] University of Colorado Anschutz Medical Campus, Fitzsimons Building, 13001 East 17th Place, Aurora, CO 80045, USA
[c] University of Alabama at Birmingham, Department of Psychiatry and Behavioral Neurobiology, 1720 University Blvd, Birmingham, AL, 35233, USA

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ABSTRACT

Exercise interventions in epilepsy have been shown to improve seizure frequency, physical capacity, quality of life, mood, and cognitive functioning. However, the effectiveness of exercise in improving sleep in epilepsy is less clear. The purpose of this report is to identify the published literature regarding exercise interventions in people with epilepsy to determine 1) what proportion of published clinical trials assess sleep as an outcome, and 2) what benefits of exercise interventions on sleep have been observed. We searched the PubMed, PsycINFO, and SCOPUS electronic databases using the search terms “epilepsy AND [exercise OR physical activity]” and identified 23 articles reporting on 18 unique clinical trials. Nine studies were conducted in adults, five in children, and four in adults and children with active seizures, controlled seizures, or both. Exercise modalities included aerobic exercise, strength training, walking, and yoga, among others, and some also included educational and motivational components. Exercise effects on sleep were tested in four studies, two of which only included indirect measures of sleep- and rest-related fatigue, with mixed results. Of the two reports assessing sleep directly, one reported marginal non-significant improvements in subjective sleep quality and no improvements in objective sleep quality in children after twelve weeks of walking, and the other reported no benefits in subjective sleep quality after twelve weeks of combined aerobic, strength, and flexibility training in adults. Given the health benefits of sleep and detrimental effects of sleep deprivation in epilepsy, epilepsy researchers need to assess the effects of exercise interventions on sleep.

1. Introduction

Exercise benefits overall health and can be protective in multiple health conditions, including cardiovascular disease [1,2], diabetes [3–5], and mental health [6–8]. Unfortunately, people with epilepsy engage in less physical activity than the general population [9–11], with barriers including lack of time, transportation issues, concerns about accidents, injuries, and fear of triggering seizures [12,13]. Contributing to this sedentary lifestyle is a lack of knowledge and education about the real risks and benefits of exercise for people with epilepsy, and the historical practice of advising people with epilepsy to refrain from exercising. Some animal and human studies demonstrated seizure-triggering effects in a small number of individuals during or after strenuous exercise [14–20]. Often, such effects were limited to single case reports and based on subjective patient reports. Other investigations have focused on determining the risk of accidents and injuries to patients and bystanders when people with epilepsy engage in sports-related activities such as swimming or operating sports equipment [21,22]. Despite these concerns, most recent studies show that exercise does not considerably increase the risk of accidents and injuries, and exercise-induced seizures are relatively rare [23–25]. The International League Against Epilepsy (ILAE) has released guidelines that unequivocally support regular exercise for people with epilepsy, with modifications needed in a small number of circumstances, notably those that could increase risks to bystanders or the patient [26].

Any risks inherent in physical activity must also be weighed against the potential benefits of engaging in regular exercise [23]. Exercise has been shown to improve physical and mental health in people with epilepsy. For example, six months of moderate-intensity home-based aerobic exercise combined with low glycemic diet improved self-reported seizure frequency, quality of life, and depressive symptoms in children with refractory epilepsy in an uncontrolled clinical trial [27]. Interestingly, as little as six weeks of combined endurance and resistance training has been shown to alter functional connectivity in widespread

* Corresponding author at: at: 1719 6th Ave S, CIRC 312, Birmingham, AL 35233, USA.
E-mail addresses: cm1@uab.edu (C. Mueller), aethomas@uabmc.edu (A. Thomas), AMY.AMARA@cuanschutz.edu (A.W. Amara), jdewolfe@uabmc.edu (J. DeWolfe), sjthoma@uabmc.edu (S.J. Thomas).

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brain regions, along with improvements in physical strength, cognitive functioning, and mood [28]. Studies also generally support the feasibility of exercise interventions in both children [29] and adults [30,31] with epilepsy. Clinical trials testing the benefits of exercise on seizure frequency, physical fitness, and cognitive functioning in people with epilepsy are underway, and could further help determine the types and intensity of exercise that offer maximum benefits while maintaining safety.

In the general population, exercise improves sleep disorders, including insomnia and obstructive sleep apnea [32], and it might reasonably have similar effects in people with epilepsy. Sleep disorders, including insomnia and obstructive sleep apnea, are approximately twice as common in people with epilepsy than in the general population [33], and experts have recommended careful co-management [34]. Relationships between sleep and epilepsy are reciprocal, whereby the presence of epilepsy and seizure occurrence affect sleep architecture and circadian rhythmicity, and sleep affects epileptic activity in the brain [35]. Decreased total sleep time, increased wake after sleep onset, and decreased rapid eye movement (REM) sleep are commonly observed sleep abnormalities in people with epilepsy, and are associated with epileptic activity [36–40]. Studies have shown that acute and chronic sleep deprivation can lower the seizure threshold [36,41–44] and chronic sleep deprivation negatively impacts quality of life and cognitive functioning in people with epilepsy [45]. Obstructive sleep apnea also increases seizure activity, particularly in older patients and those with late-onset epilepsy. Furthermore, anti-seizure medications used to treat epilepsy can negatively affect sleep by altering normal sleep architecture [46,47], although it is notable that seizure control is associated with a prevalence of sleep complaints comparable to that of the general population [48]. Effects of anti-seizure medications on sleep also vary across medications. There are medications that may improve sleep in some patients (e.g. eslicarbazepine acetate, lacosamide, and perampanel), some that have been shown to worsen sleep (e.g. clonazepam, felbamate, lamotrigine, oxcarbazepine, and phenobarbital), while others do not appear to impact sleep (e.g. cannabidiol, carbamazepine, and levetiracetam) [47].

Less is known about how exercise affects sleep in people with epilepsy. This review aimed to identify the published literature regarding exercise interventions in people with epilepsy to determine 1) what proportion of published clinical trials assess sleep as an outcome, and 2) what benefits of exercise interventions on sleep have been observed. This review also aimed to encourage the wider adoption of sleep assessments in clinical exercise trials with epilepsy patients.

2. Material and methods

We present a systematic review of exercise interventions in patients with epilepsy, with a particular focus on determining the effects of exercise on sleep outcomes in this patient population. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the review was registered on the International Prospective Register of Systematic Reviews (PROSPERO; CRD42023445175).

2.1. Search strategy

We searched all entries in the PubMed, PsycINFO, and SCOPUS electronic databases from inception until August 30, 2023 for intervention studies in epilepsy. We used the following search terms and Boolean operators: epilepsy AND [exercise OR physical activity].

2.2. Eligibility and study selection

Only studies in the English language reporting original data were included, while reviews and *meta*-analyses of previously published trials were excluded. Randomized controlled trials (RCTs), comparative studies, and single-group studies (without a control condition) were included as long as the intervention involved prescribing some type of physical exercise and was conducted in patients with epilepsy. Observational studies relating physical activity levels to other outcomes but that did not prescribe an exercise intervention were excluded. In a first step, all articles meeting search criteria from the three databases were imported into EndNote (version 20.6; Clarivate), and duplicates were removed. Titles and abstracts of the remaining studies were screened for eligibility. In the final step, full-text articles of included studies were obtained and used to determine final eligibility. Disagreements regarding eligibility were resolved through team discussions.

3. Results

3.1. Characteristics of included studies

A flowchart of the search and screening process is shown in Fig. 1. The search yielded 1,646 entries in PubMed, 1,664 entries in PsycINFO, and 2,093 entries in SCOPUS. After removal of duplicates, 4,322 unique publications were left. Of these, 299 non-English language articles were removed. Titles and abstract of the remaining 4,023 were screened, and 30 full-text articles were further screened. Of these, six studies were excluded due to presenting only observational (non-intervention) data, and one was excluded due to not prescribing exercise. We identified 23 articles from 18 unique interventional studies in patients with epilepsy that met all inclusion criteria.

Table 1 shows the characteristics of the included articles. Among the 18 unique included studies, nine (9) were conducted exclusively in adults, five (5) in children, and four (4) in adults and children. The greatest number of studies were conducted in the United States and India (n = 3 each), followed by Canada, Germany, Sweden, and Norway (n = 2 each), with one study each from South Korea, Brazil, Poland, and China. Nine studies exclusively enrolled patients with active/treatment-refractory epilepsy, six (6) enrolled both seizure-free and refractory epilepsy, two (2) focused exclusively on seizure-free populations, and one (1) was conducted in children with benign epilepsy with centrotemporal spikes.

The most frequently prescribed type of exercise was a combination of cardiovascular/aerobic and strength/resistance training (seven studies), which in some studies also incorporated flexibility/stretching exercises. Several studies adjusted the exercise intensity depending on each participant's current level of fitness (see Table 1). Of the 18 studies reported by 23 articles, four (4) exclusively used cardiovascular/aerobic training without a strength component. Two studies (three publications) from Canada assessed the effects of daily walking [49–51], one study each tested yoga [52] and balance training [53], and two studies did not report enough detail to determine the type of exercise or used different modalities for each participant [31,54]. Finally, one study tested yoga against "simple exercise" training [55], so both intervention arms could be considered exercise interventions for the purposes of this review. Several studies also incorporated educational or motivational components such as phone calls in their protocol to increase adherence. Notably, Zhang et al. [27] combined exercise with a low glycemic diet, and Seyer et al. [54] included exercise as one component of a multidisciplinary program that also included modules on cognitive rehabilitation, therapeutic counseling, educational sessions, mindfulness, and legal counseling. For these studies, it is not possible to determine the effects of exercise alone on seizure outcomes.

We identified eleven (11) controlled trials and seven (7) uncontrolled studies. A majority were conducted with small sample sizes. Of the controlled trials, only three included more than 20 participants in the intervention arm. Samples sizes tended to be larger in uncontrolled studies, ranging from one participant to over one thousand, though the majority still included fewer than 20 participants.

Control conditions included baseline, no-intervention, and waitlist conditions (where some participants receive the study intervention only

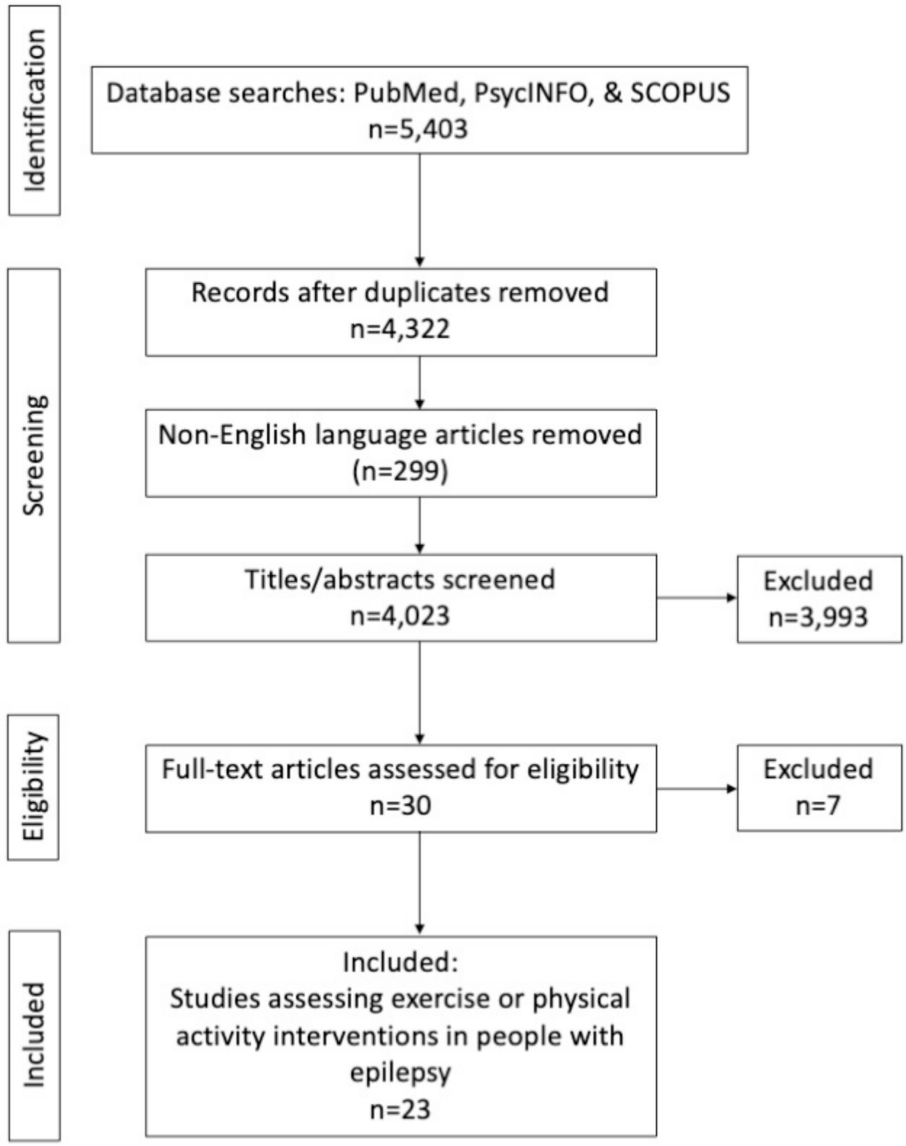

Fig. 1. Database search, screening, and eligibility determinations for the systematic review.

after the data analysis period ends, effectively acting as a no-intervention control group), maintenance of usual physical activity, standard medical care, relaxation, Acceptance and Commitment Therapy, and education. In one study, yoga was compared to another exercise condition.

3.2. Study outcomes and benefits

Quality of life, depression, and seizure frequency were the most frequently assessed outcomes. Some studies also assessed treatment compliance, morphometric data (e.g., body weight, body mass index), cognitive functioning, and metabolic markers. Improvements in seizure frequency, physical capacity/strength, quality of life, mood, and cognitive functioning were the most common benefits noted. Seizure frequency decreased in five studies after trials ranging from ten weeks to twelve months, two of which tested yoga [52,55], two of which tested combined aerobic, strength, and stretch training [56,57], and one of which combined aerobic exercise with a low glycemic diet [27]. Nine studies [28–31,58–62] specifically mentioned that the tested exercise intervention was feasible, and only one reported limited feasibility [63]. Although the exercise interventions were generally deemed safe, one study reported that half of participants (7 out of 14) experienced seizures during exercise [56].

3.3. Exercise effects on sleep

Six (6) out of the 23 published articles measured various sleep outcomes, and 17 did not. The two articles by Vooturi et al. [30,63] reported average sleep duration at baseline but did not assess the effects of the exercise intervention on sleep as an outcome. Two studies [56,60] did not assess sleep directly but included sleep and rest-related fatigue outcomes in their studies. Of these, a case study of four children with brain tumor diagnoses, one of which with a diagnosis of epilepsy, reported that 30–90 min of home-based exercise per week improved general and cognitive fatigue, but worsened sleep and rest-related fatigue over time [60]. It is notable that these results occurred in the context of a progressive cancer diagnosis that is typically associated with increasing levels of fatigue over time. Given that only one participant was diagnosed with epilepsy, the results also need to be interpreted with caution. In the other study, Eriksen et al. [56] administered the Ursin Health Inventory (UHI), which assesses subjective somatic and psychological problems over a 30-day period and includes a sleep-fatigue

Table 1
Characteristics of included studies.

Author, year, title	Design	Exercise type	Intervention duration & intensity	Comparison	Type of epilepsy	Sample size (completers)	Age range	Outcomes	Findings	Assessed sleep?	Sleep-related findings
Åkerlund et al., 2021. [59]	RCT	cardiovascular exercise	30 min/day, 5 days a week for 6 months	relaxation	focal drug-resistant epilepsy	exercise, 12; relaxation 10	16–65	SFQ, anxiety, depression, health status rating, aerobic capacity (VO_2 max), self-efficacy for exercise, level of physical activity, adverse events	exercise increased aerobic capacity (VO_2 max) and physical activity	no	
Allendorfer et al., 2019. [28]	waitlist-controlled pilot study; sequential assignment to groups with option to switch assignment depending on availability	combined endurance and resistance exercise	3 1hr sessions/ week over 6 weeks	no exercise (waitlist)	active or controlled idiopathic generalized epilepsy and temporal lobe epilepsy	exercise, 9; control, 8	18–55	physical fitness (VO_2 max), physical strength, verbal memory, changes in memory brain networks (functional MRI), QOL, habitual physical activity, mood	exercise increased strength, improved mood, increased verbal learning and recognition memory, decreased resting-state functional connectivity (rsFC) in paracingulate with anterior cingulate, increased rsFC for cerebellum, thalamus, posterior cingulate, and bilateral inferior parietal lobule	no	
Beller et al., 2023.[71]	single-group case study	combined strength, endurance, coordination, body awareness, and mobility training; mainly home-based with additional inpatient and outpatient visits	1 30–90 min session/week	–	epilepsy secondary to brain tumor	4 (1 with epilepsy)	7–13	Feasibility/ adherence, fatigue, physical strength, adverse events	73 % (SD = 9) adherence; exercise worsened general and cognitive fatigue, improved sleep/rest fatigue, worsened health-related QOL, brought no change in muscular endurance/leg strength, decreased grip strength; no adverse events	yes, sleep/rest-related fatigue	increased sleep/rest-related fatigue over time
Brown et al., 2019.[49]	RCT	walking; participants received scheduled motivational phone calls for six months to support reaching a daily step goal	daily goal of 12,000 steps for 12 months	no motivational intervention	active epilepsy (at least one seizure in the last year)	exercise, 56; control, 59	8–14	physical activity, depression, QOL, health-related QOL	intervention had no effects on any outcomes	no	
Do et al., 2020.[72]	single-group	walking (individualized weekly plan aimed at increasing daily steps by 3 % each week, with a target to increase daily steps by 25 % over the intervention period)	varied activity; 12 weeks; one exercise counseling session per week	–	active epilepsy (at least one seizure in the last year)	22	8–14	physical activity, sleep efficiency, total time asleep, sleep habits, QOL, fatigue, depression, anxiety	Changes in physical activity were not associated with changes in sleep outcomes when accounting for age, sex, and baseline epilepsy severity. Subjective sleep quality marginally improved with the intervention.	yes; sleep efficiency and subjective sleep quality (Children's Sleep Habits Questionnaire)	marginal improvements in subjective sleep quality
Dustin et al., 2019.[31]	single-group	individualized activity goals (e.g., daily step count, weight loss, BP reduction);	varied activity; 12 weeks; one educational session followed by	–	any (seizure-free and refractory)	24	18+	Self-Efficacy and Outcome Expectations, depression, QOL,	exercise improved depression	no	

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Table 1 (*continued*)

Author, year, title	Design	Exercise type	Intervention duration & intensity	Comparison	Type of epilepsy	Sample size (completers)	Age range	Outcomes	Findings	Assessed sleep?	Sleep-related findings
		encouraged to increase exercise level by at least 50 %	weekly phone calls					SFQ, physical activity, BMI			
Eom et al., 2016.[58]	single-group	supervised sessions (basketball, soccer, table tennis, badminton, jump rope, line dancing); home-based resistance activities (e.g., sit-ups, push-ups) plus 30 min of aerobic exercise; also encouraged to walk more than 7000 steps per day; four follow-up meetings involving hiking, bowling, and education sessions	2 3hr sessions/ week over 5 weeks, then 30 weeks of home-based exercises	–	BECS	10	8–12	feasibility, physical fitness, EEG, SFQ, psychomotor speed, attention, working memory, executive function, behavioral problems, QOL, study satisfaction	exercise improved psychomotor speed, sustained attention, divided attention, inhibition-disinhibition, internalizing behavior problems, general health, and QOL; satisfaction was high	no	
Eom et al., 2014.[29]	single-group pilot study	supervised sessions (basketball, soccer, table tennis, badminton, jump rope, line dancing); home-based resistance activities (e.g., sit-ups, push-ups) plus aerobic exercise	2 3hr sessions/ week over 5 weeks, plus 15–20 min home-based exercises	–	BECS; generalized and focal	10	8–12	feasibility, physical fitness, EEG, SFQ, psychomotor speed, attention, working memory, executive function, depression, anxiety, behavioral problems, QOL	100 % completion rate; exercise improved physical fitness, attention, psychomotor speed, inhibition–disinhibition, internalizing behavioral problems, social problems, mood-related QOL	no	
Eriksen et al., 1994.[56]	single-group	aerobic dancing with strength training and stretching	2 1hr sessions/ week over 15 weeks, individually adapted intensity	–	drug-refractory (at least one seizure/month during 12 precending months); temporal lobe epilepsy, n = 12; frontal lobe epilepsy, n = 1; generalized epilepsy, n = 3	14	18–46	SFQ, plasma triglycerides, cholesterol ratio, sodium, and potassium, blood lactate, physical fitness (VO_2 max), exhaustion, BP, resting HR, HR during VO_2 max, forced vital capacity, forced expiratory volume after 1 s, psychological and social problems, anxiety, depression, locus of control, subjective somatic and psychological problems	exercise decreased SFQ, increased VO_2 max, reduced cholesterol and cholesterol/ high-density lipoprotein cholesterol ratio, reduced overall health complaints, improved muscle pain, improved sleep-fatigue, reduced seizure severity, improved mood, increased mastery	yes, sleep-fatigue subscale of UHI	Improved sleep-fatigue
Feter et al., 2020.[61]	RCT	combined physical training (warmup,	2 1hr sessions/ week over 12 weeks	maintain usual daily activities	any (seizure-free and refractory)	exercise, 10; control, 10	18–60	Memory, executive function, verbal fluency, global	exercise improved psychomotor speed, verbal fluency, global cognitive	no	

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Table 1 (*continued*)

Author, year, title	Design	Exercise type	Intervention duration & intensity	Comparison	Type of epilepsy	Sample size (completers)	Age range	Outcomes	Findings	Assessed sleep?	Sleep-related findings
		aerobic, strength, stretches)						cognitive function, weight, height, hip and waist circumference, cardiorespiratory fitness (VO_2 max), grip strength	functioning, and executive functioning		
Häfele et al., 2021.[73]	RCT	combined physical training (warmup, aerobic, strength, stretches)	2 1hr sessions/ week over 12 weeks	maintain usual daily activities	any (seizure-free and refractory)	exercise, 10; control, 10	18–60	SFQ, QOL, depression, anxiety, side effects, stress, sleep quality (Pittsburgh Sleep Quality Index, PSQI), weight, height, hip and waist circumference, cardiorespiratory fitness (VO_2 max), grip strength, BP, HR	exercise reduced SFQ, improved QOL, stress levels, and physical fitness	yes; sleep quality (PSQI)	no effects on sleep
Koirala et al., 2017.[74]	single-group	supervised sessions varied (soccer, basketball, jump rope, dance); home-based resistance activities (e.g., sit-ups, push-ups) plus aerobic exercise	2 3hr sessions/ week over 5 weeks, plus regular 15–20 min home-based exercises	–	BECS; generalized and focal	8	8–12	functional connectivity on resting-state EEG (cortical current source density, CSD), attention, executive functioning	exercise increased CSD power in alpha band in right temporal region; significant correlations between functional connectivity and attention and executive functioning	no	
Kumar et al., 2022.[62]	RCT	moderate-intense aerobic activity (e. g., walking, hiking, jogging, running, biking)	150 min/week	standard medical care	generalized or focal epilepsy, SFQ up to four seizures/ month	exercise, 58; control, 59	18–65	QOL, physical activity, energy consumption, daily step count, body weight, BMI, SFQ, stigma	exercise improved energy/ fatigue domain of QOL	no	
Lundgren et al., 2008. [52]	RCT	yoga (deep breathing, physical postures, meditation)	12 h total therapy time over 12 months	ACT	drug-refractory	yoga, 8; ACT, 10	18–55	seizure index (SFQ x seizure duration), QOL	exercise improved seizure index and QOL	no	
McAuley et al., 2001. [75]	RCT	cardiovascular, strength, and flexibility training; duration and intensity were individualized	3 1hr sessions/ week over 12 weeks	continue current level of activity	any (seizure-free and refractory), BTC, simple partial, and complex partial	exercise, 14; control, 9	16–60	QOL, mood, physical self-concept, self-esteem, seizure activity, ASM concentration	exercise improved overall, physical, and energy/-fatigue-related QOL, physical self-concept and vigor, and total mood disturbance	no	
Nakken et al., 1990.[76]	single-group crossover (controlled)	aerobics, swimming, jogging, hiking, volley ball, horseback riding, table tennis, bicycling, rowing	3–5 45-min sessions/day, 6 days/week, over 4 weeks	no exercise (two weeks pre-intervention and two weeks post-intervention baseline)	drug-refractory; generalized, partial, symptomatic or idiopathic	21	18–39	SFQ, aerobic capacity (VO_2 max), BP, ECG, vital capacity, forced expiratory volume, body weight, body fat, serum ASM level, psychological and social functioning (instructor-reported)	exercise increased aerobic capacity, reduced weight (men only), improved mental state, increased sociability	no	

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Table 1 (*continued*)

Author, year, title	Design	Exercise type	Intervention duration & intensity	Comparison	Type of epilepsy	Sample size (completers)	Age range	Outcomes	Findings	Assessed sleep?	Sleep-related findings
Sathyaprabha et al., 2008. [55]	controlled trial (alternate assignment)	exercise (quiet sitting, simple physical exercise)	1hr/day for 10 weeks	yoga	drug-refractory (>2 seizures/month for 2 years; failed 2 ASM); generalized or partial	exercise, 16; yoga, 18	15–55	autonomic dysfunction, BP, HR	yoga decreased autonomic dysfunction, improved BP, SFQ; no benefits in exercise group	no	
Seyer et al., 2018.[54]	single-group	multidisciplinary program consisting of cognitive rehabilitation, physical fitness and motor coordination exercises, therapeutic counseling to improve disease coping, educational sessions, mindfulness training, and legal advice	1.5 hr/day across all modules for an average of 11 inpatient days	–	any	1,339	14–87	compliance, affect/mood, activity, communication, mobility/physical fitness, fine motor skills, autonomy/independence from assistance (observer-rated)	intervention improved compliance, activity, affect, and total impairment	no	
Szczygieł-Pilut et al., 2020. [77]	single-group crossover (controlled)	physiotherapy focused on balance training	2 30-min sessions/week over one month	baseline/no intervention (two months wait pre-intervention)	generalized epilepsy of unknown etiology, controlled with ASM	10	18–65 years	QOL	physiotherapy improved QOL in domains of physical functioning, physical limitations, pain, vitality, social functioning, mental health, emotional functioning, and total QOL	no	
Vooturi et al., 2020.[78]	RCT	moderate-intensity home-based aerobic (cardiovascular, endurance, flexibility) exercise at 60 % target heart rate	4 45-min sessions/week over 12 weeks	education only, continue existing exercise programs	controlled (seizure-free for two years, on ASM)	exercise, 48; control, 42	18–60	weight, BMI, abdominal, waist, and hip circumference, physical capacity, QOL, metabolic markers	exercise reduced weight and improved physical capacity and physical QOL	sleep duration reported only at baseline	
Vooturi et al., 2023.[30]	single-group	moderate-intensity home-based aerobic (cardiovascular, endurance, flexibility) exercise at 60 % target heart rate	5 45-min sessions/week over 12 weeks	–	controlled (seizure-free for two years, on ASM)	116	18–60	Adherence, barriers	26.7 % adherence; fear of seizures and lack of family support were barriers to exercising	sleep duration reported only at baseline	
Willis et al., 2018.[51]	single-group (part of larger multicenter RCT)	walking; participants received scheduled motivational phone calls for six months to support reaching a daily step goal	daily goal of 12,000 steps for 12 months	no motivational intervention	active (at least one seizure in the last year)	11 (intervention arm)	8–14	perceived impact of physical activity, facilitators and barriers to exercise, health domains	walking was associated with benefits in all health domains, improved attitude, confidence, insight into activity, and parent factors	no	
Zhang et al., 2020.[27]	single-group	moderate-intensity home-based aerobic exercise (walking,	5 30-min sessions/week over 6 months	–	drug-refractory	36	11–17	SFQ, QOL, depression	exercise reduced SFQ, improved overall quality of life and depression	no	

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Table 1 (*continued*)

Author, year, title	Design	Exercise type	Intervention duration & intensity	Comparison	Type of epilepsy	Sample size (completers)	Age range	Outcomes	Findings	Assessed sleep?	Sleep-related findings
		jogging, cycling), plus low glycaemic diet									

ACT = Acceptance and Commitment Therapy; ASM = anti-seizure medication; BECS = benign epilepsy with centrotemporal spikes; BMI = body mass index; BP = blood pressure; BTC = bilateral tonic-clonic; EEG = electroencephalography; HR = heart rate; QOL = quality of life; RCT = randomized controlled trial; SFQ = seizure frequency; UHI = Ursin Health Inventory.

subscale. In their single-group study of 14 adults with pharmacologically intractable epilepsy, 15 weeks of aerobic exercise improved sleep-fatigue on the UHI. Two studies assessed sleep outcomes directly. Do et al. [50] conducted an uncontrolled trial that measured both objective sleep duration and efficiency using a pedometer and subjective sleep quality using the Children's Sleep Habits Questionnaire (CSHQ). They reported marginal but not significant improvements in subjective sleep quality after a 12-week walking-based intervention in 22 children with active epilepsy between the ages of 8 and 14. Sleep efficiency was not affected by the intervention. Finally, Häfele et al. [57] measured subjective sleep quality using the Pittsburgh Sleep Quality Index (PSQI) within a randomized controlled trial comparing 12 weeks of combined aerobic, strength, and flexibility training with a control group maintaining usual level of activity. The study found that the intervention did not improve sleep quality in a mixed group of ten adults with controlled and refractory epilepsy who were randomized to the active intervention.

4. Discussion

The aim of this systematic review was to identify the published literature regarding exercise interventions in people with epilepsy to determine 1) what proportion of published clinical trials assess sleep as an outcome, and 2) what benefits of exercise interventions on sleep have been observed. We found that only 6 out of 23 included publications assessed sleep. Most studies only used self-report questionnaires that typically relied on one item or one facet of sleep (e.g., sleep quality or sleep duration) and/or only assessed sleep pre-intervention. Because we only found two studies that assessed sleep pre- and post-intervention, there are insufficient data to determine the impact of exercise on sleep in people with epilepsy, and we offer several suggestions for future trial design below.

Notably, one study reported marginal improvements in subjective sleep quality in children with epilepsy [50], while another study reported no improvements in subjective sleep quality in adults with epilepsy, although different questionnaires were used to assess subjective sleep quality and this could explain the discrepant findings [57]. The lack of an effect of exercise on sleep could be due to a variety of factors, including being underpowered to determine an effect (studies would likely not have been powered for sleep as a mediator/moderator or outcome) [60], heterogeneity of the sample to include epilepsy phenotypes where sleep disorders are less impactful, inclusion of participants without a sleep concern at baseline assessment producing a floor effect [50], or lack of rigorous assessment of sleep examining multiple domains. In particular, participants in Do et al.'s study were active at baseline and displayed normal sleeping patterns, which could have limited potential exercise-related impacts on their sleep [50]. A related study design issue is the fact that many of the published clinical trials did not include a control group. Only one of the studies that measured post-interventional sleep outcomes was an RCT, and the sample size in the exercise group was small ($n = 10$). Thus, future studies should also consider adding control arms and random assignment to groups, as this would strengthen the quality of evidence regarding exercise effects on sleep.

In addition to the assessment of sleep disorders (i.e., insomnia symptom severity), studies should consider examining multiple dimensions of sleep (e.g., duration, timing, quality) and the use of both objective and subjective measures. Beyond a focus on disordered sleep or sleep deficiencies (e.g., short sleep duration), sleep health is an outcome of increasing interest that incorporates multiple dimensions of sleep. For example, the RU-SATED questionnaire assesses sleep health by measuring sleep regularity, subjective satisfaction, appropriate timing, adequate duration, high sleep efficiency, and sustained alertness during the day [64]. Subjective and objective measures of sleep are often discordant and viewed as separate constructs. Therefore, a rigorous assessment of sleep should consider both types of measures. The PSQI is a validated self-report questionnaire measuring subjective sleep quality over the past month, and includes seven dimensions: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medications, and daytime dysfunction. It has good test–retest reliability and could be a suitable measure of exercise-related changes in subjective sleep quality [65].

Actigraphy is a popular method for complementing retrospective self-report questionnaires and sleep diaries. Actigraphy is a non-invasive technique to measure a person's activity and rest cycles using an actigraph unit worn continuously over several days (usually on the wrist), such as a smartwatch. Actigraphy does not directly measure sleep; rather, it distinguishes between periods of sleep and wakefulness based on movement. Importantly, actigraphy can provide longitudinal data on sleep duration, fragmentation, timing, as well as light exposure. Actigraphy can also be used to assess circadian parameters. Thus, actigraphy could be a useful tool to objectively assess multiple dimensions of both sleep health and disordered sleep among individuals with epilepsy, but it may not necessarily be congruent with more subjective measures of sleep [66], and may not be feasible in all settings [67]. We also note that ethical considerations should be taken into account when using remote technology such as actigraphy to measure health outcomes in children [68].

Given the beneficial effects of exercise on sleep in other patient populations (e.g., neurodegenerative disorders) [69,70], future studies examining the effects of exercise on seizures are needed. Studies should include both subjective and objective measures of sleep over multiple time points and considering multiple dimensions of sleep during and after the intervention. To determine potential effects of circadian mechanisms, timing of exercise and sleep among people with epilepsy should also be considered.

Further, several of the published studies included in this review noted the importance of designing exercise options accessible to those with disabilities and comorbid neurological conditions (other than epilepsy), and the need for formal guidance and monitoring by health professionals. They also noted that the high cost of attending formal exercise programs could be prohibitive for many patients. The rise in popularity of home-based exercise programs in recent years has greatly reduced some of these barriers to participation, and we hope to see an increase in formal clinical trials testing these interventions in people with epilepsy.

5. Conclusions

In summary, while exercise interventions have been tested in people with epilepsy, few have incorporated measures of sleep. Future studies should incorporate assessments of multiple dimensions of sleep, including subjective and objective measures of duration, timing, and quality. Given the known benefits of exercise on sleep in the general population and the effects of sleep (i.e., disordered or deficient sleep) on lowering the seizure threshold, it is possible that sleep mediates the relationship between exercise and lowered seizure threshold in people with epilepsy.

Ethical statement

This study is a systematic review of published studies and did not involve collection of original data from animals or human participants. No ethical approvals were sought, and no informed consent was obtained.

CRediT authorship contribution statement

Christina Mueller: Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ashley Thomas:** Writing – review & editing. **Amy W. Amara:** Writing – review & editing. **Jennifer DeWolfe:** Writing – review & editing. **S. Justin Thomas:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Data curation, Conceptualization.

Declaration of competing interest

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