Original Article

Sport and Physical Activity in Epilepsy

A Systematic Review

Franziska van den Bongard, Hajo M. Hamer, Robert Sassen, Claus Reinsberger

Summary

Background: For many years, people with epilepsy were advised not to engage in sports. In this systematic review, we investigated whether persons with epilepsy exercise less than the general population, and what effect physical activity has on epilepsy.

Methods: A literature search was carried out in PubMed and the Web of Science, and 14 269 studies were entered into the selection process. The selected studies were assessed for their methodological quality and accordingly assigned an evidence level.

Results: 42 studies were included in the review; 10 were classified as evidence level 3, 27 as evidence level 2–, 2 as evidence level 2+, and 3 as evidence level 1–. Persons with epilepsy are less physically active and less physically fit than the general population. Reduced physical activity is associated with a higher frequency of comorbidities and lower quality of life. Physical interventions can improve quality of life. In most cases, physical exercise did not increase seizure frequency.

Conclusion: There is no reason to forbid persons with epilepsy to participate in sports; they should, rather, be encouraged to do so. The decision on a particular type of sport should, however, be taken individually in each case.

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Epilepsy is a common neurological disorders with a lifetime prevalence of 7.6 per 1000 persons (e1). In addition to recurrent seizures, epilepsy is also associated with comorbidities such as cognitive and psychological problems, as well as social difficulties (e2). Despite the known positive effects of sports and physical activity on quality of life and general disease prevention (e3), patients with epilepsy have long been discouraged from participating in sports activities (e4). This recommendation is likely based on the fear that sporting activity may cause injuries, potentially induce seizures, and have a negative effect on disease course.

However, over the past few decades, studies have shown that sports-related injuries are not more common in these patients compared to the general population (e5). Therefore, the questions arise as to whether patients with epilepsy avoid sports and take less physical exercise than the general population on the basis of unverifiable rationales and prejudices (e6) and whether this leads to further disadvantages for this group.

In 2016, the International League Against Epilepsy (ILAE) published a consensus paper that recommends safe sports participation for patients with epilepsy (e7). It is unclear which positive effects of sports on actual disease activity these patients are being deprived of. Therefore, the aim of this systematic review is to answer the following questions:

- Are patients with epilepsy less physically active and less fit than the general population?
- What effect does physical activity have on comorbidities in epilepsy?
- What effect does physical activity have on the frequency of seizures?

Methods

The literature search was conducted on 31 January 2019, in the PubMed (Medline/PubMed Central) and Web of Science databases. The following search terms were used: (epilepsy OR “AED” OR seizure OR anti-epileptic OR epileptic) AND (exercise OR “physical activity” OR sport OR training OR “physical effort” OR “physical therapy”). Longitudinal and cross-sectional human studies, as well as case studies, were included. Diagnosed epilepsy and endpoints on

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Selection process: PRISMA flow diagram (e8)

PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses

physical activity of any form were used as additional inclusion criteria. With regard to activity habits, only controlled studies were included.

A total of 14 269 studies were found and included in the selection process, which is presented in the *Figure*. The studies were selected and evaluated by two independent reviewers (FvdB, CR).

Methodological quality assessment

Interventional studies were assessed according to the risk-of-bias principle (e9). Seven assessment categories were analyzed per study:

- Selection bias: generation of a randomization sequence
- Selection bias: blinding to allocation
- Performance bias: blinding of personnel and endpoints
- Detection bias: blinding of subjects
- Attrition bias: incomplete data
- Reporting bias: selective reporting
- Other bias.

The cross-sectional studies were assessed on the basis of the publication by Hammer et al. on the prevention of distorted results in observational studies (e10). Five assessment categories were analyzed per cross-sectional study:

- Selection bias

- Information bias
- Measurement errors
- Confounding
- Other bias.

The risk for each bias in both assessment instruments could be classified as high, unknown, or low. High and unknown risk were assigned one point and low risk no points, thereby achieving an overall score for each study. The higher the score, the worse the methodological quality. Case studies, epidemiological studies, and interview-based studies were not assessed for methodology. Methodological quality assessments were performed for 10 interventional studies and 25 cross-sectional studies.

Evidence levels

The included studies were assigned an evidence level (e11). Studies with a comparison group—i.e., with a healthy or diseased control group or with a sample divided into active and inactive, or with group observation over several time points—were classified as evidence level “2.” All studies without a comparison group in the cross-section were classified as level “3.”

Results

In all, 42 studies were included in the systematic review. These studies can be divided into seven groups:

- Case studies (n = 4)
- Interventional studies (n = 10)
- Epidemiological studies (n = 1)
- Survey-based studies (n = 12)
- Interview-based studies (n = 2)
- Combined cross-sectional studies (survey and physical tests) (n = 4)
- Studies on one-time physical effort (n = 9).

Altogether, 15 studies investigated physical activity in patients with epilepsy compared to healthy individuals. Of these, six evidence-level “2–” studies showed that individuals with epilepsy are less physically active (1–6). In addition, five studies (n = 4 evidence-level “2–” and n = 1 “2+”) reported lower physical fitness (in relation to various aspects such as VO₂max, blood pressure) compared to healthy controls (7–11). In contrast, the results of three other studies (evidence level “2–”) revealed no differences between groups in terms of physical activity (12–14). However, a further study (“2+”) found an association between physical fitness (activity) early in life and a reduced risk of epilepsy in later life (15).

In all, 17 studies investigated the effect of physical activity on comorbidities such as anxiety and depression, as well as quality of life. Ten of these studies (“2–” n = 8, “3” n = 2; survey-/interview-based studies, combined studies, studies on one-time physical effort) showed physical activity to have a positive effect (4, 9, 12, 14, 16–21). The results of six interventional studies (n = 2 evidence-level “1–”, n = 4 “2–”) revealed a similar picture. Only one evidence-level “2–” combined study found no association (e12).

TABLE 1

Results in detail of higher-quality studies (selected according to evidence levels)

Study	Evidence level	Statement
Lundgren et al. (2008) (26)	1–	<ul style="list-style-type: none"> • 5-Week yoga intervention (8 patients) and acceptance and commitment therapy (ACT) (10 patients) • Follow-up: seizure frequency: declined in all subjects • Pre-/post: seizure index*¹: declined in ACT ($p > 0.01$)/declined in yoga group ($p > 0.01$) • Pre-/post: quality of life: improved in ACT group in the WHOQOL-BREF*² ($p < 0.01$)/improved in yoga group in the SWLS*² ($p < 0.05$)
Sathyaprabha et al. (2008) (27)	1–	<ul style="list-style-type: none"> • 10-Week yoga intervention (18 patients) and exercise therapy (simple exercises) (16 patients) • Pre-/post: seizure frequency scores: improved in yoga group ($p = 0.001$) • Interaction effect group $\times$ time: seizure frequency ($p < 0.001$) (reduced in yoga group and increased in exercise therapy group)
McAuley et al. (2001) (30)	1–	<ul style="list-style-type: none"> • 12-Week combined training (cardiovascular and strength training) (14 patients) and a control group with no intervention (9 patients) • During intervention: seizure frequency: training group: $n = 10$ were and remained seizure-free; $n = 4$ with active epilepsy, of which $n = 2$ experienced no change, $n = 1$ an increase, $n = 1$ a decline/control group: $n = 6$ were and remained seizure-free; $n = 3$ with active epilepsy, of which $n = 1$ experienced no change, $n = 1$ an increase, $n = 1$ a decline • Pre-/post: quality of life: improved in training group (overall questionnaire score, domains: physical function [$p = 0.02$], self-perceived health [$p = 0.05$], energy/fatigue [$p = 0.02$], role limitation [positive trend])/improved in control group (domain: energy/fatigue [$p < 0.01$])
Fialho et al. (2017) (11)	2+	<ul style="list-style-type: none"> • One-time treadmill exercise (Bruce protocol), patient group ($n = 30$) and healthy control group ($n = 30$) • Control group: higher peak heart rate ($p = 0.002$), longer exercise duration ($p = 0.004$), higher metabolic equivalent during exercise ($p = 0.006$), greater distance covered ($p = 0.007$), higher end-exercise level ($p = 0.004$), higher Duke score ($p = 0.02$), higher rate pressure product ($p = 0.03$) • Chronotropic incompetence more prevalent in epilepsy group ($p < 0.001$)
Nyberg et al. (2013) (15)	2+	<ul style="list-style-type: none"> • Epidemiological study with 1 173 079 male conscripts aged 18 and over and follow-up of up to 40 years • 6796 (0.6%) developed epilepsy • Low and moderate cardiovascular fitness (at 18 years) were associated with an increased risk of developing epilepsy (hazard ratio: 1.79; 95% CI: [1.57; 2.03]*³ and hazard ratio: 1.36; 95% CI: [1.27; 1.45]*³) • Having one or more brothers with epilepsy doubles one's own risk of developing the disorder (fitness remained a significant predictor of developing epilepsy)

*¹ (Seizure frequency $\times$ seizure duration)

*² Survey instrument: World Health Organization Quality of Life instrument, short version (WHOQOL-BREF); Satisfaction with Life Scale (SWLS)

*³ Adjusted for calendar year, body mass index (BMI), region, test center, parental education; absolute values were not reported

CI, confidence interval

Altogether, 21 studies investigated the effect of physical activity or one-time exertion on seizure frequency. Two studies reported no seizures during a one-time physical activity (22, 23) (evidence level “2–”). In three studies, a reduction in epileptiform discharges during physical exercise testing was achieved (2, 24, 25) (“2–” $n = 1$; “3” $n = 2$). However, two of these studies found a rebound effect, with an increased number of discharges during the recovery phase compared to the resting phase (24, 25). Two interventional studies (“1–”) found a statistically significant reduction in seizures as a result of completing the exercise program in the epilepsy exercise groups ($p < 0.01$; $p < 0.001$) (26, 27). A survey-based study identified a statistically significant association between increased physical activity and a reduced number of seizures ($p < 0.05$) (“3”) (e13). One further study revealed a trend towards a correlation between a higher frequency of seizures and lower physical activity (“2–”) (5).

Three survey-based studies reported a heterogeneous picture in terms of the effect of physical activity on seizures, with sports triggering seizures in some patients and not in others (“2–” $n = 2$; “3” $n = 1$) (6, 8, 28). The effect of physical activity on seizure frequency was similarly inconsistent in four interventional studies (“1–” $n = 1$, “2–” $n = 3$) (29–32). In summary, a total of 49 patients (with focal and/or generalized epilepsy) took part in three of these studies (29–31). The frequency of seizures remained unchanged by the intervention in 12 subjects. Frequency during/after training diminished in 25 subjects and rose in 12. A further interventional study (“2–”) identified no change in seizure frequency in the exercise group following a Kempo karate program (33). Four case studies described only individuals in whom sports/physical activity induced seizures (“3”) (34–37). The *eResults* section provides the study results in greater detail. The results of studies with the highest level of evidence (“1–”

TABLE 2

Evidence level results

Evidence levels	Type of study	Studies
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with an extremely low risk of bias	
1+	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias	
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias	● Intervention: (26, 27, 30)
2++	High-quality systematic reviews of case-control studies or cohort studies	
2+	Well-conducted case-control studies or cohort studies with a low risk of confounding or bias and moderate probability that the relationship is causal	● Epidemiological study: (15) ● One-time physical effort: (11)
2-	Case-control studies or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal	● Surveys: (1, 3–6, 12, 13, 16, 17, 20) ● Combined cross-section: (8, 7, 21, e12) ● One-time physical activity: (2, 9, 10, 14, 22, 23) ● Interventions: (29, 31–33, 38, 39, 40)
3	Non-analytic studies, e.g., case reports, case series	● Surveys: (28, e13); interviews: (18, 19) ● One-time physical activity: (24, 25) ● Case studies: (34–37)
4	Expert opinion	

RCT, randomized controlled study

and “2+”) referred to in this review are additionally shown in *Table 1*.

Methodological quality assessment

The median number of points in the methodological quality assessment of the interventional studies is seven (= maximum possible number of points, highest risk).

The median number of points for the survey-based studies was four, for the combined cross-sectional studies it was 4.5, and for the studies on one-time physical activity it was four (maximum possible number of points, highest risk). The results are presented in detail in *eTables 1a and 1b*.

Evidence levels

Three of the 42 studies included are classified as evidence level “1–,” two as evidence level “2+,” 27 as evidence level “2–,” and 10 studies as evidence level “3” (*Table 2*).

Discussion

Overall, 11 of 15 studies found low levels of physical activity or fitness in individuals with epilepsy. Another study highlighted the significance of physical activity at an early age in the prevention of epilepsy. A link was identified by 16 of 17 studies between physical activity and comorbidities and/or quality of life in patients with epilepsy. The available studies on the effect of physical activity on seizure frequency are heterogeneous; however, in most cases, no increase in the number of seizures was seen.

Only five studies could be classified as evidence level “1–” and “2+.” However, one must bear in mind

that sports intervention studies are generally unable to achieve a “1+” evidence level due to their design.

The methodological quality of all studies included is overall low across all study types. The evaluability and quality of the studies is limited due to:

- Lack of information
- Lack of randomization
- Lack of control groups
- Lack of blinding
- Lack of consideration paid to inclusion factors
- Restrictions in the recruitment strategies.

A number of limitations arise as a result of poor patient accessibility as well as the peculiarity of this group. Comparability is overall limited, particularly in the case of studies on seizure frequency, due to the differing intervention programs, exercise intensities, and duration/frequency of the programs.

In addition, most studies amalgamated various syndromes and types of seizures, which needs to be viewed critically, particularly in terms of seizure frequency, since this can differ between syndromes. Therefore, reliability in terms of the effect of physical activity on seizure frequency remains limited. Results from animal models are clearer due to the number of studies and their comparable design: physical exercise reduced the number of recurrent seizures in the majority of animals (e14).

Potential mechanisms for a possible anticonvulsive effect include increased release of hippocampal brain-derived natriuretic factor (BDNF), increased neurogenesis in the cornu ammonis 1 (CA1) region of the hippocampus, and increased sprouting of mossy

fibers (e14). Without exception, all studies included in this investigation demonstrated a positive effect for physical activity on various aspects of comorbidity and quality of life. Despite their low methodological quality, the absence of a negative effect in these studies demonstrates the relevance of exercise in this context (studies with evidence levels 1–, 2–, 3).

The occurrence of isolated cases—as well as subjective reports made by patients—suggests that sports may induce seizures or worsen seizures in general. Potential pathophysiological mechanisms could be linked to, e.g., hyperventilation-induced hypercapnia or a rise in body temperature, although systematic investigations on this mechanism are still lacking.

When providing individual counseling on safety during sports activity, one can use clearance to drive a motor vehicle as an approximate guide. As in the assessment of fitness to drive, one should take the following factors into consideration when recommending a particular activity and intensity (for example, running or cycling) (e7):

- Type of sport
- Likelihood of a seizure
- Seizure triggers (for example, strenuous activity)
- Type and severity of seizures
- Usual timing of seizures
- Individual attitude.

In case of doubt, types of sport that carry no significant risk, such as team sports, dancing, and golf, can be recommended for all patients with epilepsy. An individual risk assessment should always be carried out for moderate-risk types of sport such as alpine skiing, gymnastics, and swimming, as well as high-risk sports such as climbing, motor sports, and surfing (e7). The same applies to cycling, since here—in contrast to driving motorized vehicles (including e-bikes)—neither a clear legal basis nor guidelines are available for guidance. With cycling, however, there is a significant risk of injury, given that the cyclist is exposed in a virtually unprotected manner; therefore, patients with epilepsy should only be allowed to return to cycling following a critical consideration of their status.

As a general rule, clearance to engage in sports in or on water in epilepsy requires special evaluation due to the risk of peri-ictal drowning. Here again, individual decisions need to be made on the basis of the described factors. Having said that, Ryan and Dowling showed that, of 482 deaths from drowning among patients with epilepsy, only 25 cases were directly related to seizures (e15). Nevertheless, caution is generally advised in water sports. Tools that may be helpful in the assessment of individual risk include additional investigations such as stress EEG, although there are currently no diagnostic data available to guide clinical decision making. In general, however, the overall risk of injury in patients with epilepsy does not appear to be higher compared to healthy individuals (e5, e15)—indeed, sports-related injuries occur less frequently in epilepsy patients (e5).

Key messages

- Only a handful of studies have investigated the effects of sports and physical activity on epilepsy. Although these are often of low methodological quality, the majority demonstrate positive or neutral, and only very rarely negative, effects.
- People with epilepsy should not be discouraged as a general rule from sports, but instead encouraged to be physically active.
- Advice on the possibilities of physical activity and sports should be provided on an individual basis for people with epilepsy, whereby the type and frequency of seizures, as well as the underlying syndrome, need to be taken into consideration. Clearance to drive a motorized vehicle may serve as first guidance.
- Sports and physical activity can enhance quality of life, reduce comorbidities, and potentially have a positive effect on seizure frequency.
- When choosing a suitable type of sport, one should not only take into consideration the clinical situation of the patient, but also the risk profile of the respective sport.

Conclusion

There is no rationale to support a general ban on sports for patients with epilepsy. As a general rule, an individual risk assessment should be performed for each particular case. However, it is possible to find a type of sport with a favorable risk profile for the vast majority of patients. In this context, epilepsy rehabilitation sports groups could also offer an entry point. Despite the scant number of studies to date and the heterogeneity of their results, there is rather evidence to support the assumption that sport activity does not lead to an increase in seizures, but—if it has any effect at all—results in a reduction in the number of seizures.

Conflict of interest statement

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► Supplementary material

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eRESULTS

Results in Detail

Physical activity in patients with epilepsy

Elliott et al. (1) showed, on the basis of a survey of 5506 individuals (epilepsy group [EG] $n = 97$, healthy control group [hCG] $n = 5409$) using the Ohio Behavioral Risk Factor Surveillance System, that 58.1% of patients with epilepsy and 76.1% of healthy controls had been physically active in the preceding months. Similarly, the investigation by Vancini et al. (2) showed the activity level in leisure time to be 14.8% higher in the hCG ($n = 19$) compared to the patient group ($n = 19$).

Computer-assisted interviews carried out as part of the Canadian Community Health Survey with 2555 patients with epilepsy and 400 055 controls revealed that 58.3% of patients and 49.7% of the general population were physically inactive (3).

A comparison between healthy individuals in the Norwegian population ($n = 2336$) and patients with epilepsy ($n = 204$) showed a significant difference, with a larger proportion of inactive individuals found in the EG ($p < 0.005$) (6).

Ogwumike et al. (4) surveyed 60 children with epilepsy and 60 healthy children. A comparison of their activity levels yielded a significant difference between groups (Chi² test, $p = 0.032$). The majority of children in both groups were moderately active (EG $n = 46$; hCG $n = 49$), whereas the percentage of less active children in the EG was higher ($n = 12$ versus $n = 4$) and the percentage of highly active children in this group was lower ($n = 2$ versus $n = 9$).

Wong et al. (5) surveyed 79 children with epilepsy, without motor or sensory impairments, as well as 99 healthy siblings and their parents. Children with epilepsy were less physically active in terms of general sports habits and group sports activities compared to their siblings.

Three survey-based studies that compared patients and healthy subjects ($n = 31$, $n = 31$ [12]; $n = 341$, $n = 53\ 210$ [13]; $n = 38$, $n = 20$ [14]) found no difference between groups in terms of activity habits.

Physical fitness was also lower in EGs compared to hCGs (7–9). The study conducted by Yerdelen et al. (10) found significant differences in terms of increased heart rate recovery (after 1 min $p = 0.001$, after 3 min $p = 0.027$) and lower maximum blood pressure ($p = 0.036$) between patient group and control group. In addition, Fialho et al. (2017) (11) found differences in reactions to a maximal treadmill test for the following parameters:

- Maximum heart rate
- Duration of exercise
- Metabolic equivalent (energy consumption)
- Distance covered on the treadmill
- Duke score (treadmill score to predict prognosis in coronary heart disease) (lower risk scores in the hCG) and
- Chronotropic incompetence (more frequent in the EG).

An epidemiological study conducted by Nyberg et al. (15) on 1 173 079 male conscripts over a follow-up period of 40 years yielded the observation that low and moderate cardiovascular fitness early in life (at age 18) could potentially be associated with epilepsy in later life (hazard ratio 1.79; 95% confidence interval [CI]: [1.57; 2.03]/adjusted for calendar year, body mass index, region, test center, parental education: hazard ratio: 1.36; 95% CI: [1.27; 1.45]/absolute values were not reported).

Comorbidities and physical activity

In a study conducted by Vancini et al. (9), 20 patients with temporal lobe epilepsy (TLE) and 20 control subjects underwent one-time maximal incremental testing. The authors reported a significant negative correlation ($p = 0.0460$, $r = -0.31$) between the domain tension/anxiety (significantly higher scores in the EG: $p = 0.0223$), profile of mood states evaluation, and maximum oxygen uptake (VO₂max) (significantly lower in the EG: $p = 0.0361$).

De Lima et al. (12) investigated 31 individuals with epilepsy (generalized tonic-clonic seizures [GTC] $n = 13$, focal aware seizures [FAS] $n = 10$, focal impaired awareness seizures [FIAS] $n = 8$) and 31 control subjects. Correlation analysis showed a significant association between the overall score in the Beck Depression Inventory (BDI) and physical

activity in leisure time ($p < 0.005$, $r = -0.35$), as well as between anxiety levels in the State-Trait Anxiety Inventory and activity in leisure time ($p < 0.015$, $r = -0.30$). There were no differences between the groups in terms of leisure activities. Significant differences between the groups, with higher scores in the EG in each case, were registered not only for the Beck Depression Inventory ($p = 0.02$), but also for state anxiety ($p = 0.01$) and anxiety level ($p = 0.02$) in the State-Trait Anxiety Inventory.

A comparison of active and inactive patients with epilepsy ($n = 178$) (TLE: $n = 105$, frontal lobe epilepsy = 13, occipital lobe epilepsy $n = 8$, parietal lobe epilepsy $n = 22$, generalized epilepsy [genEpi] $n = 30$) revealed that inactive individuals have higher levels of anxiety and are more susceptible to depression (17). Roth et al. (16) also reported an association between regular physical activity and BDI scores ($p < 0.01$, $r = -0.23$). A total of 133 patients with epilepsy ($n = 93 =$ inactive, $n = 40 =$ active) were investigated. Inactive patients had significantly higher BDI scores ($p = 0.01$). Furthermore, Volpato et al.'s results show that active compared to inactive patients have a higher quality of life ($p = 0.04$) (World Health Organization Quality of Life instrument [WHOQOL-BREF]) (14).

In two interview-based studies, four (19) and eleven (18) patients with epilepsy were interviewed. In summary, the statements made by the respondents show that sport enhances quality of life (19) and has a positive effect on physical and mental health (18).

Ogwumike et al. (4) demonstrated a significant correlation between activity levels and health-related quality of life in 60 children with and 60 children without epilepsy. This was determined in the EG for the areas physical function ($p = 0.001$, $r = 0.428$), social problems ($p = 0.002$, $r = 0.397$), and school performance ($p = 0.005$, $r = 0.359$). The overall scores for psychosocial health ($p = 0.002$, $r = 0.391$) and pediatric quality of life inventory (PedsQL) ($p = 0.001$, $r = 0.421$) were also recorded. The groups differed significantly in terms of activity levels ($p = 0.032$) and in five of six areas (not emotions) also in terms of health-related quality of life.

Whitney et al. (e12) found no association between the daily number of steps and the factors quality of life, enjoyment of physical activity, athletic skills, self esteem, depression, and stress in eight children with epilepsy and their parents (focal epilepsy [focEpi] $n = 5$, genEpi $n = 3$). On the basis of (unadjusted) linear regression, Hfele et al. (20) showed a significant negative association between physical activity and depression ($p = 0.046$), state of anxiety ($p = 0.014$), and trait of anxiety ($p = 0.015$), as well as a positive association with quality of life ($p < 0.001$) in 101 individuals with epilepsy. Rauchenzauner et al. (21) found a significant link between the 6-min walk test and mental wellbeing in children with epilepsy ($n = 48$) ($p = 0.014$, $r = 0.406$), but not in the hCG.

Contant et al. (33) held a Kempo karate program over 10 weeks with nine children with epilepsy (FAIS $n = 5$, GTC $n = 2$, absence epilepsy $n = 2$). Based on the parent questionnaire, a positive, but not significant, trend was seen in all health-related domains of the Quality of Life in Childhood Epilepsy questionnaire. Furthermore, the research group led by Eom et al. conducted two studies (38, 39), each with 10 children with benign epilepsy and centrotemporal spikes; the children took part in a program consisting of activities such as basketball, table tennis, and a parent-child dance, twice weekly over 5 weeks combined with home-based exercises (38), as well as in a further program once weekly over 5 weeks, followed by 30-week home-based exercises (39). Psychological functioning in the area of emotional and psychosocial adjustment were improved following the shorter intervention (38) and in neurocognitive function and quality of life following the longer intervention (39).

A 15-week exercise program (warm-up, aerobic dancing, cool down, stretching, strength training, and relaxation) with 15 women (dropout $n = 1$) (focEpi $n = 12$, genEpi $n = 3$) was unable to achieve a significant change in psychological/social difficulties, anxiety, depression, and locus of control. However, overall health complaints, as determined using the Ursin Health Inventory, were significantly reduced (ANOVA: $F = 9.61$, $df 2,24$, $p = 0.0008$) (29). In another study, 18 patients (GTC $n = 12$, myoclonic seizures $n = 3$, FAIS $n = 5$, absence seizures $n = 1$) were assigned to either Acceptance and Commitment Therapy (ACT, a form of psychotherapy) or a yoga intervention, with both groups receiving treatment over a 5-week period. Quality of life was measured using two questionnaires: the Satisfaction with Life Scale (SWLS) and WHOQOL-BREF. A significant improvement was seen following the intervention in quality of life in both groups as measured by one of the two quality-of-life instruments (ACT WHOQOL-BREF $p < 0.01$; yoga SWLS $p < 0.05$) (26). A 12-week intervention consisting of a combination of cardiovascular and strength training achieved an

improvement in mood and quality of life in a sample of 23 patients (GTC, FAIS, FAS; randomized to an exercise group [EG] and an exercise control group [eCG]) in the EG (30).

Seizure frequency

In a survey of 207 patients with epilepsy, 11% reported experiencing seizures in over 10% of the training sessions they took part in, while 36% reported better seizure control through regular exercise and 11% worse control. A total of 53% had never experienced activity-induced seizures (6). In another study, 36 of 136 surveyed patients with epilepsy reported that they had experienced seizures during sports (8), as did 56.3% of 193 respondents in another questionnaire-based study (28).

Four case studies described altogether 17 patients who experienced seizures during physical exertion (34–37). The seizures occurred during particular types of activity (running/walking $n = 5$; cycling $n = 6$; netball $n = 1$; line dancing $n = 1$; weightlifting $n = 1$; martial arts $n = 1$; swimming $n = 1$) or at certain intensities (strenuous $n = 8$; light $n = 1$). Respondents comprised children, adults, and senior citizens.

In two studies, no seizures occurred in 17 TLE patients (23) nor in 12 patients with juvenile myoclonic epilepsy (22) during and following one-time strenuous physical effort. In a further study, Vancini et al. (2) reported a drop in the number of epileptiform discharges during exertion (0.18 ± 0.10 discharges/min) and in the recovery phase (0.26 ± 0.12 /min) compared to measurements at rest (1.0 ± 0.5 /min) on average for all 19 TLE patients investigated. The number of discharges between resting and exertion fell by 82% and by 74% between resting and recovery. Nakken et al. (25) made similar findings in the context of exercise in children ($n = 26$) (symptomatic focEpi $n = 7$; rolandic epilepsy $n = 1$; cryptogenic focEpi $n = 8$; idiopathic genEpi $n = 9$; Lennox-Gastaut syndrome $n = 1$). None of the patients experienced seizures during the test. Focal epileptiform discharges decreased in 20 patients during exercise and a rebound increase was seen in 17 patients following exercise.

Esquivel et al. (24) performed a one-time physical exercise test in children with absence epilepsy ($n = 12$). Seizures occurred during rest ($n = 6$; average number of absences: 1.3/child for the whole group), during physical exercise ($n = 3$; number: 0.6/child), in the recovery phase ($n = 5$; number: 3.2/child), and in the hyperventilation phase ($n = 9$; number: 2.1/child). However, the children with a high number of seizures during the test also had a high frequency of daily seizures.

A survey of 79 children with epilepsy revealed a trend in terms of an association between a higher seizure frequency and lower physical activity (5). Denio et al. (e13) showed a significant association between higher physical activity and lower seizure frequency ($\text{Chi}^2 = 16.457$, $\text{df} = 3$, $p < 0.05$).

A total of seven interventional studies investigated the effect of exercise or sports on seizure frequency. A short-term ACT ($n = 10$; $p < 0.01$) or yoga intervention ($n = 8$; $p < 0.01$) significantly reduced the seizure index (seizure frequency $\times$ seizure duration). Due to pre-test differences, change scores were calculated, revealing a stronger change in the ACT group (26).

A yoga intervention ($n = 18$: genEpi $n = 3$, focEpi $n = 15$) also produced a significant reduction in seizures ($p < 0.001$; pre- = 7.2 ± 1.31 , post- = 5.7 ± 0.91). No change was observed in the eCG (sitting and simple physical exercises) ($n = 16$: genEpi $n = 3$, focEpi $n = 13$) (27).

During combined training with 14 women (dropout $n = 1$) (focEpi $n = 12$, genEpi $n = 3$), seven subjects experienced a total of 27 seizures during the 30 training sessions. The remaining seven subjects experienced no seizures. The majority of seizures occurred during aerobic dancing or cool down. A comparison of seizure frequency before and after the intervention revealed that the weekly frequency declined in 10 patients and rose in four. A median for seizures per week was calculated for 13 patients, with a decline from 2.9 (prior to the intervention) to 1.7 (during the intervention) (29).

A 10-week Kempo karate program with nine children with epilepsy (FAIS $n = 5$, GTC $n = 2$, absences $n = 2$) failed to affect seizure frequency (33).

Following a 12-week combined strength and endurance exercise program with 14 subjects (GCT FIAS, FAS) and an eCG ($n = 9$; GCT, FAIS, FAS), 10 patients in the exercise group, as well as six in the eCG, were and remained seizure-free. Of the four patients with active epilepsy in the exercise group (eCG $n = 4$), seizure frequency remained unchanged in two subjects (eCG $n = 2$), rose in one subject (eCG $n = 1$), and declined in the other subject (eCG $n = 1$). No subjects experienced seizures during exercise (30).

Kim et al. (2015) reported seizures in only 11 (FAIS n = 9, epileptic aura n = 1, myoclonic seizure development to GTC n = 1) of 350 patients while riding an exercise bike (minimum of 1 h training/day). Seven of the 11 subjects experienced one seizure while riding the exercise bike, two subjects experienced two seizures, and two subjects four seizures (32).

Another 4-week training program, consisting of a variety of activities such as, e.g., jogging, volleyball, and horse riding, was conducted with 21 epilepsy patients (genEPI n = 6, focEPI n = 15). Two thirds of patients had more seizures in the 4 inactive weeks during their stay at the epilepsy center, while a third had more seizures in the 4 weeks during training. The majority of seizures during the training phase occurred at rest. Of the 21 patients, 15 had no seizures during training. No predominance was observed for an epilepsy syndrome or type of seizure, nor was an association between the type of activity or pulse rate seen in the six subjects that experienced 2–30% of the seizures during the training period (31).

As part of another intervention, quantitative EEG changes were investigated in eight children with benign epilepsy and centrottemporal spikes before and after a 5-week intervention comprising basketball and table tennis, as well as a parent–child dance combined with home-based exercises. Increased cortical power in the right temporal regions for the alpha band were observed following the intervention (40).

eTABLE 1a

Methodological quality assessment of the interventional studies according to the risk-of-bias principle

Study (year)	Randomization (selection bias)	Allocation (selection bias)	Blinding of personnel (performance bias)	Blinding of subjects (detection bias)	Incomplete data (attrition bias)	Selective reporting (reporting bias)	Other bias	Overall score
Contant et al. (2008) (33)	High risk	High risk	Unclear risk	High risk	High risk	High risk	Unclear risk	7
Eom et al. (2014) (38)	High risk	High risk	Unclear risk	High risk	No risk	High risk	Unclear risk	6
Eom et al. (2016) (39)	High risk	High risk	Unclear risk	High risk	No risk	High risk	Unclear risk	6
Kim et al. (2015) (32)	High risk	High risk	Unclear risk	High risk	Unclear risk	Unclear risk	Unclear risk	7
Koirala et al. (2017) (40)	High risk	High risk	Unclear risk	High risk	Unclear risk	High risk	Unclear risk	7
Eriksen et al. (1994) (29)	High risk	High risk	Unclear risk	High risk	High risk	High risk	Unclear risk	6
Lundgren et al. (2008) (26)	No risk	Unclear risk	Unclear risk	High risk	Unclear risk	High risk	Unclear risk	6
McAuley et al. (2001) (30)	Unclear risk	Unclear risk	Unclear risk	High risk	High risk	High risk	Unclear risk	7
Nakken et al. (1990) (31)	High risk	High risk	Unclear risk	High risk	Unclear risk	High risk	Unclear risk	7
Sathyaprabha et al. (2008) (27)	High risk	High risk	Unclear risk	High risk	High risk	High risk	Unclear risk	7

Color coding:
 No risk = zero points
 Unclear risk = one point
 High risk = one point

eTABLE 1b

Methodological quality assessment of the survey-based studies, combined cross-sectional studies, and studies on one-time physical effort based on Hammer et al. (2009) (e10)

Study (year)	Selection bias	Information bias	Measurement errors	Confounding	Other bias	Overall score
Ablah et al. (2009) (28)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	5
de Lima et al. (2013) (12)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	4
Denio et al. (1989) (e13)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	5
Elliott et al. (2008) (1)	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	3
Gordon et al. (2010) (13)	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	3
Häfele et al. (2017) (20)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	4
Han et al. (2011) (17)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	4
Hinnell et al. (2010) (3)	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	3
Nakken (1999) (6)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	5
Ogwumike et al. (2016) (4)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	4
Roth et al. (1994) (16)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	4
Wong et al. (2006) (5)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	4
Jalava et al. (1997) (7)	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	5
Rauchenzauner et al. (2017) (21)	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	4
Steinhoff et al. (1996) (8)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	5
Whitney et al. (2013) (e12)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	4
Camilo et al. (2009) (23)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	4
de Lima et al. (2011) (22)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	4
Esquivel et al. (1991) (24)	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	4
Fialho et al. (2017) (11)	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	3
Nakken et al. (1997) (25)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	5
Vancini et al. (2010) (2)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	5
Vancini et al. (2015) (9)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	5
Volpato et al. (2017) (14)	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	4
Yerdelen et al. (2012) (10)	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	4

Color coding:
 No risk = zero points
 Unclear risk = one point
 High risk = one point