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# Effects of physical activity on cognition and psychosocial functioning in pediatric epilepsy: A systematic review

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ABSTRACT

Pediatric patients with epilepsy often have psychosocial and cognitive difficulties. Physical activity has emerged as a lifestyle modification that may reduce seizure burden, enhance brain plasticity, and improve cognitive and psychosocial comorbidities. We systematically reviewed published studies examining the effect of physical activity on cognitive and psychosocial function in children and adolescents with epilepsy. Studies were identified with PubMed and Emory Library databases. Eleven studies met inclusion criteria. Six of 10 studies related to psychosocial outcomes showed benefits of physical activity in children and adolescents with epilepsy, including improvements in internalizing symptoms, relationships, self-esteem, and psychological well-being, but four of the 10 studies showed no psychosocial benefits. Of the six studies evaluating cognitive outcomes, all six indicated that physical activity was associated with cognitive improvements in pediatric epilepsy, including areas of attention, processing speed, executive function, and memory. Our review was limited by the paucity of published studies on this topic, and the use of different measurement tools limited our ability to make direct comparisons between studies. Additional studies that compare pediatric epilepsy populations to non-epilepsy control groups are needed to better understand how physical activity affects seizure control and epilepsy-related comorbidities.

## 1. Introduction

Around 1 % of the United States (US) population has epilepsy [1], including 470,000 children and 3 million adults. Rates of epilepsy increase in rural areas and underdeveloped countries [2,3], where access to healthcare is reduced and resources to treat epilepsy and its comorbidities are limited. In the US, pediatric epilepsy has been associated with higher levels of psychological comorbidity, specifically those related to anxiety and depression, than is seen in children and adolescents without epilepsy [4]. Similarly, pediatric patients with epilepsy have a higher likelihood of experiencing cognitive deficits, including intellectual disability and attention-deficit/hyperactivity disorder (ADHD) [4–6].

Currently, antiseizure medication (ASM) is the first-line treatment for managing seizures associated with epilepsy [7]. However, ASMs may have significant adverse effects, including cognitive disturbances (e.g., learning and memory, attention, word-finding), behavioral changes (e.g., irritability, aggression), headaches, nausea, dizziness, sleep disturbances (e.g., initiation, maintenance), and fatigue [8–10]. For patients whose seizures are not well managed with ASMs, surgical intervention, vagus nerve stimulator placement, and diet modifications may be effective in reducing seizure burden [7]. Despite advancements, the search continues for epilepsy interventions that improve seizure burden and treat cognitive and emotional comorbidities with minimal to no adverse effects. Further, availability of ASMs and surgical treatments for epilepsy may not be available in rural areas and underdeveloped

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countries [2].

Physical activity (used interchangeably with "exercise") has been shown to benefit emotional wellbeing and cognition, including depression, anxiety, self-esteem, and ADHD in multiple pediatric clinical populations [11–13], and is neither costly nor limited depending on location. However, the benefit of physical activity on epilepsy has been a controversial topic stemming from the 1960s when the American Medical Association discouraged exercise in individuals with epilepsy due to fear it would exacerbate seizure activity [14]. Despite concerns, multiple studies have found that individuals with epilepsy should not be denied the ability to engage in physical activity [15]. In fact, results from studies across the lifespan suggest physical activity may be an effective form of treatment in the reduction of mood symptoms and improvement in quality of life in individuals of all ages with epilepsy [16,17].

Physical activity has been associated with enhanced brain plasticity and neurogenesis in human [18,19] and animal models [20,21], suggesting physical activity and exercise are potentially modifiable targets for intervention to reduce seizure burden, promote brain plasticity, and improve cognition and mental health symptoms. For example, one study found that engaging in a moderately intense aerobic exercise program resulted in increased hippocampal volume associated with improved spatial memory in elderly adults [19]. Additionally, studies examining exercise in people with epilepsy across the lifespan suggested it was associated with improvement in mental health and social relationships, [22–27] reduction of seizures [23–27], and reduction of biomarkers of stress and inflammation [23,24]. However, none of these studies focused exclusively on pediatric patients with epilepsy or quality of life-related outcomes (i.e. cognitive and emotional wellbeing). This topic is particularly important for pediatric epilepsy because there are currently few interventions aimed at improving brain plasticity and promoting neuropsychological and psychosocial development in this population. Further, children stand to benefit the most from physical activity interventions because they could result in long-term healthy habits.

Overall, published research suggests a beneficial effect of physical activity on epilepsy comorbidities, but studies vary widely in their age ranges and methods. Moreover, there remains a limited understanding regarding the effects of physical activity on the developing brain of pediatric epilepsy patients. With this in mind, we provide a systematic review of available studies examining the effects of physical activity on cognitive and psychosocial function in pediatric patients with epilepsy.

## 2. Methods

This study was designed and carried out following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for reports [28]. PubMed and Emory Library were used to conduct the search. Emory Library encompasses multiple databases, including Scopus, Web of Science, Academic Search Complete, JSTOR, Springer Link, Wiley Online Library, APA PsycArticles, and ProQuest, among others.

The keywords [physical OR activity OR exercise] AND [epilepsy OR seizure] AND [mood OR emotion OR psychological OR mental health OR cognition] were utilized. Selection criteria for this review included: (1) a full report published in a peer-reviewed journal, (2) available in English, (3) participants were human pediatric populations, (4) participants had epilepsy or a seizure disorder, (5) participants engaged in a type of exercise or physical activity (including non-interventional studies), and (6) findings on mood or cognition were available. After duplicates were removed, all abstracts were reviewed. Articles' full text was reviewed if their abstracts indicated they clearly met inclusion criteria, or if their abstracts were unclear whether inclusion criteria were met. Screening for articles was performed independently by three researchers to identify and confirm articles used. The lead author (DA) made the final decision on which articles were included. The terms "exercise" and "physical activity" were used interchangeably throughout the studies in this review, and some utilized those terms when speaking of specific sports programs (e.g., karate). In the remainder of our review, the term "physical activity" is used to describe both terms.

Following the selection of articles to be included in our review, each experimental study was evaluated using the class of evidence (CoE), a ranking system for assessing the quality of interventional studies [29]. According to this ranking system, *Level I* refers to a study that exhibits the strongest evidence, whereas *Level IV* refers to the weakest evidence and includes all studies that lack control groups (see Table 1 for specific CoE guidelines). Next, the class of recommendation (COR) and level of evidence (LOE) rating systems [30] were used to rank the overall strength of physical activity as a treatment for cognitive and psychosocial function in pediatric patients with epilepsy based on studies included in our review. COR ranking includes Class I (strongest evidence for a treatment's effectiveness), Class II (equivocal evidence), Class IIa (available evidence supports efficacy), Class IIb (more evidence is needed), and Class III (treatment is ineffective). LOE ranking ranges from A to C with A indicating existence of evidence from numerous randomized controlled trials (RCT) or meta-analyses, B indicating existence of evidence from at least one RCT or large non-randomized studies, and C, which indicates agreement among experts in the field and/or existence of less rigorously designed studies with small sample sizes [30].

## 3. Results

Our search on PubMed and Emory Library yielded 132 papers published in English in the past 30 years (between January 1993 and October 2023). Of these papers, 50 duplicates were removed. The remaining 82 abstracts were reviewed from which 49 were removed because they did not include exercise/physical activity, and 13 were removed because participants were not human or were not pediatric populations. The full text of the remaining 20 articles was reviewed either because all inclusion criteria were met or because the abstract was unclear whether criteria were met. Of these, five were removed because they did not include exercise/physical activity and four were removed because they did not include a pediatric population. Only 11 studies remained that met inclusion criteria for this systematic review. The databases, search strategies, and included studies are displayed in Fig. 1.

A detailed analysis of these studies showed that seven (64 %) were pre-test/post-test experimental studies [31–37], including one RCT [32]. There were also four (36 %) cross-sectional studies [38–41]. The seven experimental studies reviewed included data from 206 individuals, ranging from eight [31] to 122 [32] participants. The cross-sectional studies ranged from eight [41] to 1,189 [38] participants with ages ranging from six to 17 years of age. Studies were from six countries: Canada [32,33,41], South Korea [31,34,35], United States [36,38], Austria [39], Turkey [40], and China [37].

Of the 11 studies included, 10 of them (91 %) included outcome measures related to psychosocial functioning (all except [31]) (Table 2), and six of them (55 %) included outcome measures related to cognition or academic performance [31,34–36,38,39] (Table 2). Three studies involved walking as the physical activity and instructed participants to electronically monitor/track (via pedometer or smart phone) their walking and improve their daily step count [32,33,41]. Four studies developed long-term supervised programs led by an instructor that featured sport-based activities such as karate, basketball, or soccer [31,34–36].

We evaluated each of the seven experimental studies included in our review using the CoE ranking system [29]. Results indicated six of the studies were Level IV (lowest level of evidence; none included a control group) [31,33–37], and one was Level II [32]. The latter study did not meet Level I criteria due to a decline in participant responses at the final follow-up point (<85 %). Regarding COR [30], the reviewed studies were equivocal regarding support for physical activity as a treatment for psychosocial function in pediatric patients with epilepsy (Class II

**Table 1**
Class of Evidence (CoE) guidelines.

| Common Sources of Bias When Critically Appraising a Study [29] |
|---|
| 1. Patient selection and allocation of treatment |
| 2. Intention-to-treat analysis |
| 3. Blind or independent assessment for important outcomes |
| 4. Co-interventions applied equally to study groups |
| 5. Patient follow-up rate of less than 85 % |
| 6. Adequate sample size |
| 7. Controlling for possible confounding |

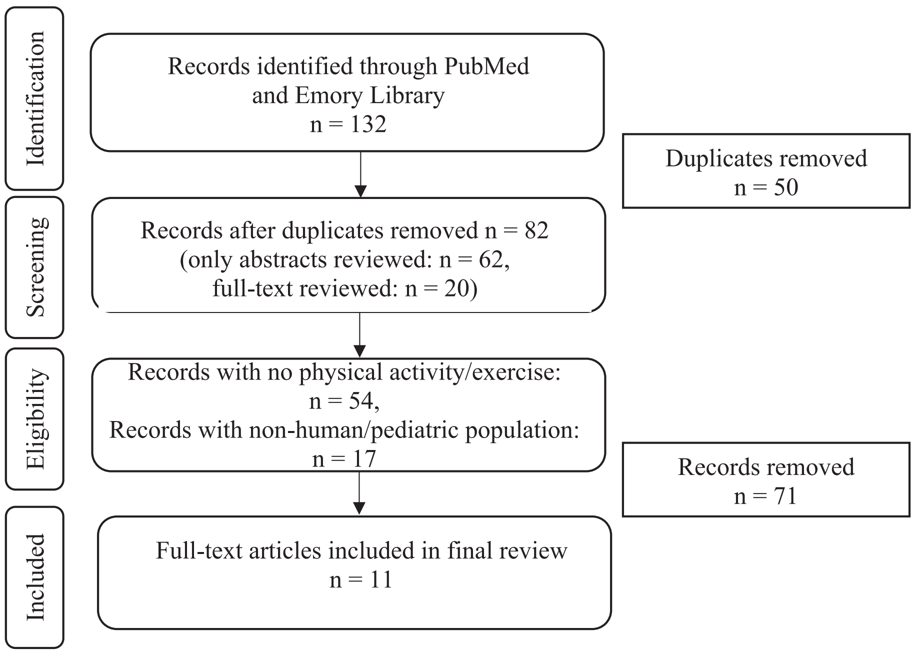


**Fig. 1.** PRISMA diagram displaying studies identified during literature search and screening process.

recommendation [equivocal evidence]), LOE C (agreement among experts in the field/existence of less rigorously designed studies with small sample sizes). In contrast, the use of physical activity to improve cognitive problems in pediatric patients with epilepsy was promising but needs more evidence to establish its efficacy (Class IIb [more evidence is needed]), LOE C (agreement among experts in the field/existence of less rigorously designed studies with small sample sizes). Additional information about each study is presented in Table 2.

### 3.1. Cognition

Three studies using standardized neuropsychological assessment revealed improvements when comparing children's' performance between pre- and post-physical activity intervention in areas of attention, processing speed, and executive functioning [31,34,35]. Questionnaire-based measures indicated an improvement in memory and better school performance associated with physical activity in children and adolescents with epilepsy [36,39], but not in their language, attention/concentration, or other cognitive performances between pre- and post-intervention [36]. Further, Brown and Ronen [38] found that children and adolescents with active epilepsy (i.e., those with an epilepsy diagnosis taking ASMs and/or those who had one or more seizure in the previous year) who engaged in higher levels of physical activity were more likely to be diagnosed with ADHD. On the other hand, children with inactive epilepsy (e.g., those with an epilepsy diagnosis who were currently not taking ASMs and had not had a seizure in the previous year) who engaged in higher levels of physical activity were less likely to also have an ADHD diagnosis.

### 3.2. Psychosocial functioning

Physical activity studies associated with psychosocial benefits in our review involved either a team-based approach (i.e., participation in formal sports team/group karate class) or an intensive supervised treatment protocol and included improvements in internalizing symptomatology, social difficulties, and overall well-being [34,35,37]. The one study that employed subjective reports of functioning using semi-structured interviews found that physical activity increased psychological well-being and confidence in children and adolescents with epilepsy [33]. Similarly, Rauchenzauner et al. [39] found that youth with epilepsy who had a higher level of physical fitness worried less about the future. In another study, Brown and Ronen [38] found that higher engagement in physical activity in children and adolescents with either active or inactive epilepsy was linked to lower levels of depressive symptoms, while physical activity was linked to higher odds of anxiety in children with inactive epilepsy.

In contrast, some studies found no significant differences in emotional wellbeing after physical-activity intervention. Specifically, there were no significant differences related to depression in three studies [32,36,41], anxiety in one study [36], self-esteem in two studies [36,41] overall psychological well-being in one study [41], and quality of life in three studies [32,40,41] for youth with epilepsy. In fact, the only randomized controlled trial (RCT) in the current review [32] found no significant differences between the intervention and control groups in depression or quality of life over a one-year period aimed at increasing walking activity, but the participants did not differ in their physical activity levels at the end of the intervention. Further, many

**Table 2**
Psychosocial and cognitive findings from reviewed studies, arranged alphabetically by first authors' last name.

| Author, year | Study Population | Class of Evidence (CoE) | Study Design and Intervention | Exercise and Outcome Measures | Conclusions |
|---|---|---|---|---|---|
| Brown et al., 2019 [32] | N=122 (58 boys and 62 girls, 2 missing), ages 8 to 14 years | CoE: Level II: patient follow-up rate < 85 % | Longitudinal multisite randomizedcontrolled trial; 15-minute physical activity counseling sessions, instructed to increase average step count by 10 % weekly and track with provided pedometer. | Fitbit® Ultra Wireless Activity Tracker (replaced by the Fitbit® One Wireless Activity Tracker), 25-item Childhood Epilepsy Quality of Life scale (CHEQOL) [47], KidScreen-27 [48], Children's Depression Inventory — Short (CDI-S) [49] | Psychosocial: Counseling program was unsuccessful in increasing physical activity levels, and there were no significant differences in depression or quality of life over the one-year period. |
| Brown and Ronen, 2021 [38] | N=1,189 (with active and inactive epilepsy), ages 6 to 17 years | N/A | Multivariate logistic regression analyses on cross-sectional data. | National Survey of Children's Health [50] | Psychosocial: In those with active epilepsy, engagement in physical activity was associated with lower odds of depressive symptoms and higher likelihood of being diagnosed with conduct disorders and ADHD. In those with inactive epilepsy, physical activity engagement and participation in sports were linked to higher odds of anxiety, lower odds of depression, and lower levels of conduct disorder and ADHD diagnoses.<br><br>Cognitive: In those with inactive epilepsy, physical activity engagement and participation in sports were linked to lower levels of ADHD diagnoses |
| Conant et al., 2008 [36] | N=9 (2 boys and 7 girls), ages 8 to 16 years | CoE: Level IV: no control group, small sample size | Quasi-experimental study; 10-week, 1 h/week karate program. | Parental Stress Index Short Form, Third Edition [51]; Quality of Life in Childhood Epilepsy inventory (QOLCE) [52]; Piers–Harris Children's Self-Concept Scale 1 (PH-1) [53] | Psychosocial: No significant differences in depression, anxiety, self-esteem between pre- and post-intervention.<br><br>Cognitive: There was significant improvement in memory, but not language, attention/concentration, or other cognitive domains. |
| Eom et al., 2014 [34] | N=10 (4 boys and 6 girls), ages 8 to 12 years | CoE: Level IV: no control group, small sample size | Quasi-experimental pilot study; 10, three-hour supervised multisport exercise sessions and home-based exercises for five weeks. | The Wechsler Intelligence Scales for Children—Third Edition [54], Comprehensive Attention test [55], Children's Depression Inventory [56], Revised Children's Manifest Anxiety Scale [57], and Quality of Life in Childhood Epilepsy (K-QOLCE) questionnaire [58] | Psychosocial: Significant improvements in internalizing behavior problems, social problems, and overall well-being (mood).<br><br>Cognitive: Significant improvements in attention, executive function. |
| Eom et al., 2016 [35] | N=10 (4 boys and 6 girls), ages 8 to 12 years | CoE: Level IV: no control group, small sample size | Quasi-experimental 35-week supervised and home-based multisport exercise program. | Wechsler Intelligence Scales for Children—Third Edition (Digit Span and Matching subtests) [54], Comprehensive Attention Test [55], Children's Color Trails Test [59], Korea–Child Behavior Checklist [60], K-QOLCE [58], two satisfaction surveys | Psychosocial: Significant improvements in social and behavioral problems, and internalizing behavior problems were observed after intervention.<br><br>Cognitive: Significant improvements in attention, processing speed, executive function |
| Koirala et al., 2017 [31] | N=8 (3 boys and 5 girls), ages 8 to 12 years | CoE: Level IV: no control group, small sample size | Quasi-experimental study using EEG-based analysis of neurological changes in epilepsy patients before and after three-hour exercise sessions twice a week, and regular home-based resistance exercises for five weeks. | EEG recording, Comprehensive Attention Test [55], Children's Color Trails Test [59] | Cognitive: Significant positive correlation between the effect of physical activity on brain functional connectivity and neuropsychological test scores of attention and executive function. |
| Rauchenzauner et al., 2017 [39] | N=107 (46 boys and 61 girls), ages 7 to 14 years | N/A | Cross-sectional cohort study. | 6-minute walk test, standardized background and history questionnaire, Kinder Lebensqualität Fragebogen (Questionnaire for Measuring Health Related Quality of Life in Children and Adolescents—revised version [KINDL-R]) [61,62] | Psychosocial: There was a statistically significant association between the walk test and mental wellbeing in children with epilepsy. Patients with a higher level of physical fitness reported to have better performance in school and less worry about the future. |

(*continued on next page*)

**Table 2** (*continued*)

| Author, year | Study Population | Class of Evidence (CoE) | Study Design and Intervention | Exercise and Outcome Measures | Conclusions |
|---|---|---|---|---|---|
| | | | | | Academic: Patients with a higher level of physical fitness reported to have better performance in school. |
| Sırtbaş et al., 2021 [40] | *N*=41 (24 boys and 17 girls), ages 6 to 12 years | N/A | Cross-sectional, non-interventional study evaluating physical fitness, activity, and health-related quality of life in children with epilepsy and non-epilepsy matched peers. | Fitnessgram Test Battery, flamingo balance test, 6-minute walk test, Pediatric Quality of Life Inventory 4.0 [63] | Psychosocial: Both parent and self-report of psychosocial functioning showed children with epilepsy had significantly poorer psychosocial functioning than controls. However, there was no significant correlation between physical activity or fitness and quality of life in children with epilepsy, nor controls. |
| Whitney et al., 2013 [41] | *N*=8 (4 boys and 4 girls), ages 8 to 14 years | N/A | Prospective non-interventional pilot study; children instructed to wear a pedometer for seven days and keep a log of total daily steps, activities performed, and time the pedometer was worn. | Measurement of physical activity via pedometer, KidScreen-27 questionnaire [48], the Children's Self Adequacy and Predilection in Physical Activity (CSAPPA) [64], Harter's Self-Perception Scale [65], Childhood Depression Inventory [49,66], Parental Stress Index [51,67] | Psychosocial: No relationship was found between daily step count and overall quality of life, psychological well-being, social and peer relationships, self-adequacy, self-worth, or depression. |
| Willis et al., 2018 [33] | *N*=11, ages 8 to 14 years | CoE: Level IV: no control group, small sample size | Personal coaching via phone to help increase step count. | Semi-structured interviews, pedometer | Psychosocial: Per the interviews, physical activity had subjective positive effects including increase in psychological well-being and confidence, as well as a decrease in seizure activity. |
| Zhang et al., 2020 [37] | *N*=36 (23 boys and 13 girls), ages 11 to 17 years | CoE: Level IV: no control group, small sample size | Quasi-experimental study; home-based, moderate-intensity aerobic exercises for 30 min/day, 5 days/week for 6 months and a low glycemic diet. | Children's Depression Inventory (CDI) [49,66] Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-55) [68] | Psychosocial: Significant improvement in quality of life, reduction in depression symptoms, and reduction in self-reported seizure frequency. |

*Note*: In our study, the term "quasi-experimental" is defined as experimental research that lacks a control group and/or random selection/assignment [69]. The term "N/A" means not applicable as these were not experimental studies.

participants were near their country's age-based average step count at the study's outset. Another explanation for lack of success in this study and those like it is the lack of accountability for participants in increasing their level of physical activity (e.g., only required to track daily activity).

### 3.3. Seizure burden

Two studies found that physical activity decreased perceived and self-reported [33,37] seizure frequency or epileptic activity among children and adolescents. None of the researchers stated that physical activity posed inherent risks to this patient population, and instead, some studies highlighted the detrimental effects of insufficient participation in physical activity among pediatric patients with epilepsy [32,40].

## 4. Discussion

Results from our literature review showed that physical activity may lead to improvements in cognitive and psychosocial function in pediatric patients with epilepsy, including attention, processing speed, executive function, depression, and anxiety, as well as quality of life. These findings are consistent with prior studies examining positive effects of physical activity in individuals with epilepsy [17,26,27,42–44,8]. However, not all reviewed studies found a beneficial association between physical activity and psychosocial function [32,36,40,41], and the efficacy regarding the benefit of physical activity on cognitive function is not yet fully established. These results emphasize the need for rigorously designed studies, including more RCTs. Fortunately, results from our review do not support physical activity-related risks for pediatric patients with epilepsy, consistent with results from adult research in this area [45]. In fact, available results suggest physical activity may reduce seizure burden [33,37]. These findings underscore the need to address and overcome misconceptions that result in barriers to physical activity in pediatric epilepsy patients. Further, physical activity started in childhood could result in lifelong benefits.

While our review highlights how physical activity may benefit both cognitive and emotional well-being in pediatric epilepsy patients, no studies have investigated the complex interplay among these constructs. Cognitive and emotional symptoms may have a reciprocal relationship in which cognitive difficulties lead to stress that increases emotional problems (e.g., depression, anxiety), and emotional problems, in turn, affect cognitive functions (e.g., reduce attention span and processing speed), all of which is exacerbated by seizures and medication in patients with epilepsy (Fig. 2). Thus, more research is required to understand mechanisms of effect and change through which physical activity may beneficially influence both emotional and cognitive functioning. Further, although physical activity is a potentially modifiable factor influencing brain plasticity [46] and cognitive functioning during neurodevelopment in pediatric patients, more research is necessary to understand this relationship (e.g., type, intensity, duration of physical activity; optimal neurodevelopmental stages, etc.).

### 4.1. Strengths and limitations

Limitations of our review include the paucity of available research on physical activity within pediatric epilepsy. Among existing studies, only one was an RCT. Remaining studies were either quasi-experimental or

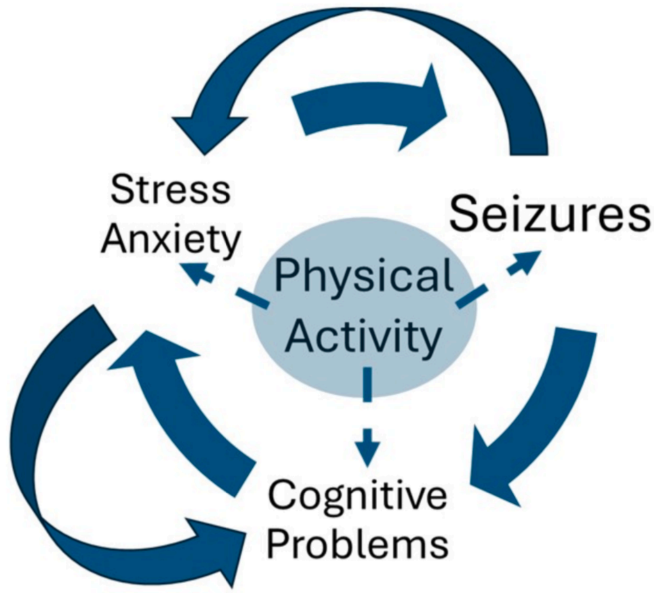


**Fig. 2.** Depiction of the complex relation among seizures and emotional and cognitive problems in pediatric patients with epilepsy and the beneficial influence physical activity may have on them.

non-interventional and most had relatively small sample sizes. For these reasons and differences in study methodology, a meta-analysis was not possible. These limitations restrict generalizability of current findings.

## 5. Conclusions

Emerging research examining the influence of physical activity on pediatric epilepsy and its cognitive and psychosocial comorbidities is limited and few published studies are rigorously designed, and available studies vary in their methodology, making comparisons challenging. Multiple studies suggest a beneficial relation between physical activity and cognition in this population; however, findings regarding the benefit of physical activity on psychosocial function are equivocal. Similarly, there is some support for physical activity-induced reduction in seizures but the mechanisms behind this are not well understood.

## Ethical statement

This study was performed in line with the principles of the Declaration of Helsinki.

## CRediT authorship contribution statement

**Demy Alfonso:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Investigation, Formal analysis, Data curation, Conceptualization. **Alyssa Ailion:** Writing – review & editing, Supervision, Conceptualization. **Nicole Semaan:** Writing – review & editing, Writing – original draft, Data curation. **Evie Davalbhakta:** Writing – review & editing, Writing – original draft, Data curation. **Donald J. Bearden:** Writing – review & editing, Supervision, Project administration, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References

[1] Centers for Disease Control and Prevention (CDC) (2020, September 30). Epilepsy Fast Facts. Retrieved October 20, 2023, from https://www.cdc.gov/epilepsy/about/fast-facts.htm#:~:text=Active%20Epilepsy&text=This%20is%20about%203.4%20million,million%20adults%20and%20470%2C000%20children.&text=According%20to%20the%20latest%20estimates,17%20years%20have%20active%20epilepsy.&text=Think%20of%20a%20school%20with,of%20them%20could%20have%20epilepsy.

[2] Espinosa-Jovel C, Toledano R, Aledo-Serrano Á, García-Morales I, Gil-Nagel A. Epidemiological profile of epilepsy in low income populations. Seizure 2018 Mar;1(56):67–72. https://doi.org/10.1016/j.seizure.2018.02.002.

[3] Camfield P, Camfield C. Incidence, prevalence and aetiology of seizures and epilepsy in children. Epileptic Disord. 2015 Jun;17(2):117–23. https://doi.org/10.1684/epd.2015.0736.

[4] Dagar A, Falcone T. Psychiatric comorbidities in pediatric epilepsy. Curr. Psychiatry Rep. 2020 Dec;22:1. https://doi.org/10.1007/s11920-020-01195-8.

[5] Nickels KC, Zaccariello MJ, Hamiwka LD, Wirrell EC. Cognitive and neurodevelopmental comorbidities in paediatric epilepsy. Nat. Rev. Neurol. 2016 Aug;12(8):465–76. https://doi.org/10.1038/nrneurol.2016.98.

[6] Oh A, Thurman DJ, Kim H. Comorbidities and risk factors associated with newly diagnosed epilepsy in the US pediatric population. Epilepsy Behav. 2017 Oct;1(75):230–6. https://doi.org/10.1016/j.yebeh.2017.07.040.

[7] Perucca P, Scheffer IE, Kiley M. The management of epilepsy in children and adults. Med. J. Aust. 2018 Mar;208(5):226–33. https://doi.org/10.5694/mja17.00951.

[8] Akyüz E, Köklü B, Ozenen C, Arulsamy A, Shaikh MF. Elucidating the potential side effects of current anti-seizure drugs for epilepsy. Current neuropharmacology. 2021 Nov 11;19(11):1865. https://doi.org/10.2174%2F1570159X19666210826125341.

[9] Hakami T. Neuropharmacology of antiseizure drugs. Neuropsychopharmacol. Rep. 2021 Sep;41(3):336–51. https://doi.org/10.1002/npr2.12196.

[10] Tsvere M, Chiweshe MK, Mutanana N. General side effects and challenges associated with anti-epilepsy medication: A review of related literature. Afr. J. Primary Health Care Family Med. 2020 Jan 1;12(1):1–5. https://doi.org/10.4102/phcfm.v12i1.2162.

[11] Dale LP, Vanderloo L, Moore S, Faulkner G. Physical activity and depression, anxiety, and self-esteem in children and youth: An umbrella systematic review. Ment. Health Phys. Act. 2019 Mar;1(16):66–79. https://doi.org/10.1016/j.mhpa.2018.12.001.

[12] Ng QX, Ho CY, Chan HW, Yong BZ, Yeo WS. Managing childhood and adolescent attention-deficit/hyperactivity disorder (ADHD) with exercise: A systematic review. Complement. Ther. Med. 2017 Oct;1(34):123–8. https://doi.org/10.1016/j.ctim.2017.08.018.

[13] Suarez-Manzano S, Ruiz-Ariza A, De La Torre-Cruz M, Martinez-Lopez EJ. Acute and chronic effect of physical activity on cognition and behaviour in young people with ADHD: A systematic review of intervention studies. Res. Dev. Disabil. 2018 Jun;1(77):12–23. https://doi.org/10.1016/j.ridd.2018.03.015.

[14] Pimentel J, Tojal R, Morgado J. Epilepsy and physical exercise. Seizure 2015 Feb;1(25):87–94. https://doi.org/10.1016/j.seizure.2014.09.015.

[15] Capovilla G, Kaufman KR, Perucca E, Moshe SL, Arida RM. Epilepsy, seizures, physical exercise, and sports: a report from the ILAE Task Force on Sports and Epilepsy. Epilepsia 2016 Jan;57(1):6–12. https://doi.org/10.1111/epi.13261.

[16] Arida RM, de Almeida AC, Cavalheiro EA, Scorza FA. Experimental and clinical findings from physical exercise as complementary therapy for epilepsy. Epilepsy Behav. 2013 Mar 1;26(3):273–8. https://doi.org/10.1016/j.yebeh.2012.07.025.

[17] Duñabeitia I, Bidaurrazaga-Letona I, Diz JC, Colon-Leira S, García-Fresneda A, Ayán C. Effects of physical exercise in people with epilepsy: A systematic review and meta-analysis. Epilepsy Behav. 2022;137:108959. https://doi.org/10.1016/j.yebeh.2022.108959.

[18] Chang H, Kim K, Jung YJ, Kato M. Effects of acute high-intensity resistance exercise on cognitive function and oxygenation in prefrontal cortex. J. Exercise Nutr. Biochem. 2017 Jun 6;21(2):1. https://doi.org/10.20463%2Fjenb.2017.0012.

[19] Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, et al. Exercise training increases size of hippocampus and improves memory. PNAS 2011;108:3017–22. https://doi.org/10.1073/pnas.1015950108.

[20] Sun J, Sun J, Ming GL, Song H. Epigenetic regulation of neurogenesis in the adult mammalian brain. Eur. J. Neurosci. 2011 Mar;33(6):1087–93. https://doi.org/10.1111/j.1460-9568.2011.07607.x.

[21] van Praag H, Shubert T, Zhao C, Gage FH. Exercise enhances learning and hippocampal neurogenesis in aged mice. J. Neurosci. 2005;25:8680–5. https://doi.org/10.1523/JNEUROSCI.1731-05.2005.

[22] Bhatt G, Gupta N, Manwadkar S, Mehendale P, Kothary K. Impact of Physical activity on Epilepsy: A Review. Pakistan Heart J. 2023 Oct 13;56(3):728–37.

[23] Cavalcante BR, Improta-Caria AC, de Melo VH, De Sousa RA. Exercise-linked consequences on epilepsy. Epilepsy Behav. 2021 Aug;1(121):108079. https://doi.org/10.1016/j.yebeh.2021.108079.

[24] Carrizosa-Moog J, Ladino LD, Benjumea-Cuartas V, Orozco-Hernández JP, Castrillón-Velilla DM, Rizvi S, et al. Epilepsy, physical activity and sports: a narrative review. Can. J. Neurol. Sci. 2018 Nov;45(6):624–32.

[25] Johnson EC, Helen Cross J, Reilly C. Physical activity in people with epilepsy: A systematic review. Epilepsia 2020 Jun;61(6):1062–81. https://doi.org/10.1111/epi.16517.

[26] Arida RM, Teixeria-Machado L. Physical exercise for children and adolescents with epilepsy: What have we learned? *Seizure: European.* J. Epilepsy 2023;111:1–8. https://doi.org/10.1016/j.seizure.2023.07.005.

[27] Häfele CA, Rombaldi AJ, Feter N, Häfele V, Gervini BL, Domingues MR, et al. Effects of an exercise program on health of people with epilepsy: A randomized clinical trial. Epilepsy Behav. 2021;117:107904. https://doi.org/10.1016/j.yebeh.2021.107904.
[28] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Int. J. Surg. 2021;88:105906. https://doi.org/10.1016/j.ijsu.2021.105906.
[29] Dettori J. Class or level of evidence: epidemiologic basis. Evidence-Based Spine-Care J. 2012 Aug;3(03):9–12.
[30] Priebe HJ. Perioperative use of beta-blockers. F1000 Med. Rep. 2009;1.
[31] Koirala GR, Lee D, Eom S, Kim NY, Kim HD. Altered brain functional connectivity induced by physical exercise may improve neuropsychological functions in patients with benign epilepsy. Epilepsy Behav. 2017 Nov;1(76):126–32. https://doi.org/10.1016/j.yebeh.2017.06.021.
[32] Brown DM, Mahlberg N, Pohl D, Timmons BW, Bray SR, Streiner DL, et al. Can behavioral strategies increase physical activity and influence depressive symptoms and quality of life among children with epilepsy? Results of a randomized controlled trial. Epilepsy Behav. 2019 May;1(94):158–66. https://doi.org/10.1016/j.yebeh.2019.03.011.
[33] Willis J, Hophing L, Mahlberg N, Ronen GM. Youth with epilepsy: Their insight into participating in enhanced physical activity study. Epilepsy & Behavior. 2018 Dec 1;89:63-9. Epilepsy & Behavior, 89, 63-69. https://doi.org/10.1016/j.yebeh.2018.10.011.
[34] Eom S, Lee MK, Park JH, Jeon JY, Kang HC, Lee JS, et al. The impact of an exercise therapy on psychosocial health of children with benign epilepsy: a pilot study. Epilepsy Behav. 2014 Aug;1(37):151–6. https://doi.org/10.1016/j.yebeh.2014.06.017.
[35] Eom S, Lee MK, Park JH, Lee D, Kang HC, Lee JS, et al. The impact of a 35-week long-term exercise therapy on psychosocial health of children with benign epilepsy. J. Child Neurol. 2016 Jul;31(8):985–90. https://doi.org/10.1177/0883073816634859.
[36] Conant KD, Morgan AK, Muzykewicz D, Clark DC, Thiele EA. A karate program for improving self-concept and quality of life in childhood epilepsy: Results of a pilot study. Epilepsy Behav. 2008 Jan 1;12(1):61–5. https://doi.org/10.1016/j.yebeh.2007.08.011.
[37] Zhang H, Yu L, Li H, Liu Y. Effect of low glycaemic diet and structured exercise on quality of life and psychosocial functions in children with epilepsy. 0300060519893855 J. Int. Med. Res. 2020 Oct;48(4). https://doi.org/10.1177/0300060519893855.
[38] Brown DM, Ronen GM. Associations between 24-hour movement guideline adherence and mental health disorders among young people with active and inactive epilepsy. Epilepsy Behav. 2021 Dec;1(125):108386. https://doi.org/10.1016/j.yebeh.2021.108386.
[39] Rauchenzauner M, Hagn C, Walch R, Baumann M, Haberlandt E, Frühwirth M, et al. Quality of life and fitness in children and adolescents with epilepsy (EpiFit). Neuropediatrics 2017 Jun;48(03):161–5. https://doi.org/10.1055/s-0037-1599236.
[40] Sırtbaş G, Yalnızoğlu D, Livanelioğlu A. Comparison of physical fitness, activity, and quality of life of the children with epilepsy and their peers without epilepsy. Epilepsy Res. 2021 Dec;1(178):106795. https://doi.org/10.1016/j.eplepsyres.2021.106795.
[41] Whitney R, Bhan H, Persadie N, Streiner D, Bray S, Timmons B, et al. Feasibility of pedometer use to assess physical activity and its relationship with quality of life in children with epilepsy: a pilot study. Pediatr. Neurol. 2013 Nov 1;49(5):370–3. https://doi.org/10.1016/j.pediatrneurol.2013.06.002.
[42] Arida RM. Physical exercise and seizure activity. Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease 2021;1867(1):165979. https://doi.org/10.1016/j.bbadis.2020.165979.
[43] Feter N, Alt R, Häfele CA, da Silva MC, Rombaldi AJ. Effect of combined physical training on cognitive function in people with epilepsy: results from a randomized controlled trial. Epilepsia 2020;61(8):1649–58.
[44] de Fatima Svierkovski L, Miki Stein A, Cavazzotto T, Carolina Paludo A. The Benefits of Physical Activity in Children and Adolescents with Epilepsy: A Systematic Review. J. Pediatr. Epilepsy 2021;10(03):097–103. https://doi.org/10.1055/s-0041-1725991.
[45] van den Bogard F, Hamer HM, Sassen R, Reinsberger C. Sport and Physical Activity in Epilepsy. Deutsches Arzteblatt Int. 2020. https://doi.org/10.3238/arztebl.2020.0001.
[46] Bidzan-Bluma I, Lipowska M. Physical activity and cognitive functioning of children: a systematic review. Int. J. Environ. Res. Public Health 2018;15(4):800. https://doi.org/10.3390/ijerph15040800.
[47] Ronen GM, Streiner DL, Rosenbaum P, Canadian Pediatric Epilepsy Network. Health-related quality of life in children with epilepsy: development and validation of self-report and parent proxy measures. Epilepsia. 2003 Apr;44(4):598-612. https://doi.org/10.1046/j.1528-1157.2003.46302.x.
[48] Ravens-Sieberer U, Auquier P, Erhart M, Gosch A, Rajmil L, Bruil J, et al. The KIDSCREEN-27 quality of life measure for children and adolescents: psychometric results from a cross-cultural survey in 13 European countries. Qual. Life Res. 2007 Oct;16:1347–56. https://doi.org/10.1007/s11136-007-9240-2.
[49] Smucker MR, Craighead WE, Craighead LW, Green BJ. Normative and reliability data for the Children's Depression Inventory. J. Abnorm. Child Psychol. 1986 Mar;14:25–39.
[50] Blumberg SJ. Design and operation of the National Survey of Children's Health, 2003.
[51] Abidin RR. Parenting stress index: Professional manual. Psychol. Assess. Resour. 1995.
[52] Goodwin SW, Ferro MA, Speechley KN. Development and assessment of the Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-16). Epilepsia 2018 Mar;59(3):668–78. https://doi.org/10.1111/epi.14008.
[53] Piers EV. Piers-Harris children's self-concept scale. Los Angeles: Western Psychological Services; 1984.
[54] Wechsler D. Wechsler Intelligence Scale for Children Third Edition manual (WISC-III). San Antonio, TX The Psychological Corporation.
[55] Yoo K, Lee JS, Kang SH, Park EH, Jung JS, Kim BN, Son JW, Park TW, Kim BS, Lee YS. Standardization of the comprehensive attention test for the Korean children and adolescents. Journal of the Korean Academy of Child and Adolescent. Psychiatry 2009;20(2):68–75.
[56] Cho SC, Lee YS. Development of the Korean form of the Kovacs' Children's Depression Inventory. J. Korean Neuropsychiatr. Assoc. 1990;29(4):943–56.
[57] Reynolds C, Richmond BO. Revised children's manifest anxiety scale. Psychol. Assess. 1985.
[58] Lim K, Kang HC, Kim HD. Validation of a Korean version of the quality of life in childhood epilepsy questionnaire (K-QOLCE). J. Korean Epilepsy Society 2002:32–44.
[59] Llorente AM, Voigt RG, Williams J, Frailey JK, Satz P, D'Elia LF. Children's Color Trails Test 1 & 2: test–retest reliability and factorial validity. Clin. Neuropsychol. 2009 May 1;23(4):645–60. https://doi.org/10.1080/13854040802427795.
[60] Oh K, Lee H, Hong K, Ha E. Korean version of child behavior checklist (K-CBCL). Seoul: Chung Ang Aptitude Publishing Co.; 1997.
[61] Bullinger M, Brütt AL, Erhart M, Ravens-Sieberer U, BELLA Study Group. Psychometric properties of the KINDL-R questionnaire: results of the BELLA study. Eur. Child Adolesc. Psychiatry 2008 Dec;17:125–32.
[62] Ravens-Sieberer U, Bullinger M. Questionnaire for measuring healthrelated quality of life in children and adolescents. Revised Version. Recuperado de: http://kindl.org/cms/wpcontent/uploads/2009/11/ManEnglish.pdf. 2000.
[63] Varni JW, Seid M, Rode CA. The PedsQL™: measurement model for the pediatric quality of life inventory. Med. Care 1999 Feb;1:126–39.
[64] Hay JA. Adequacy in and predilection for physical activity in children. Clin. J. Sport Med. 1992 Jul 1;2(3):192–201.
[65] Harter S. The perceived competence scale for children. Child Dev. 1982 Feb;1:87–97.
[66] Knight D, Hensley VR, Waters B. Validation of the Children's Depression Scale and the Children's Depression Inventory in a prepubertal sample. J. Child Psychol. Psychiatry 1988 Nov;29(6):853–63. https://doi.org/10.1111/j.1469-7610.1988.tb00758.x.
[67] Loyd BH, Abidin RR. Revision of the parenting stress index. J. Pediatr. Psychol. 1985 Jun 1;10(2):169–77. https://doi.org/10.1093/jpepsy/10.2.169.
[68] Conway L, Widjaja E, Smith ML, Speechley KN, Ferro MA. Validating the shortened Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-55) in a sample of children with drug-resistant epilepsy. Epilepsia 2017 Apr;58(4):646–56. https://doi.org/10.1111/epi.13697.
[69] Abraham I, MacDonald K. Quasi-experimental research. Encyclopedia Of Nursing Research. Springer Publishing Company. 2011.