

## Commentary

# Role of Physical Activity and Exercise in Alleviating Cognitive Impairment in People With Epilepsy

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### ABSTRACT

Many persons with epilepsy (PWE) experience problems with a wide range of cognitive functions, including learning, memory, attention, and executive control. These deficits in cognition result in diminished quality of life for PWE and are related to many factors, including the etiology of their epilepsy, recurrent seizures, side effects of antiseizure medications, or a combination of these factors. Various treatments to ameliorate cognitive deficits experienced by PWE have been implemented, although noninvasive and nonpharmacologic strategies may be more appealing options due to their relatively low cost, reduced risk of side effects, and/or reduced potential interactions with antiseizure medications. Physical activity and exercise may improve cognition in PWE but have not been well researched in this respect. To date only 1 study has directly investigated the effects of exercise on cognition in PWE, and it showed improved performance on tests of attention and executive function. The goal of the present article was to examine how increased physical activity and exercise contributes to 3 strategies (reducing seizure frequency, reducing epileptiform discharges, and decreasing symptoms of depression) that have been described as having a positive impact on cognition in PWE, as well as highlight related findings in experimental models of epilepsy. There is a definite need for more randomized controlled trials to establish greater clinical evidence for the use of physical activity and exercise in ameliorating cognitive impairment in PWE. We also need to better understand the factors contributing to reduced physical activity in PWE, as well as ways to overcome such barriers. With the available research in the area of exercise in epilepsy showing positive results, and a supportive research climate encouraging PWE to engage in

greater physical activity overall, further investigations into the relationships between physical activity and cognition in epilepsy are warranted. (*Clin Ther.* 2017;■■■■-■■■) © 2017 Elsevier HS Journals, Inc. All rights reserved.

**Key words:** cognitive function, complementary therapy, epilepsy, physical activity, physical exercise, seizure.

### INTRODUCTION

Up to 3.4 million people in the United States (1.2% of the population) reportedly have active epilepsy.<sup>1</sup> Up to one half of the persons with epilepsy (PWE) experience and display cognitive impairment in one or more domains, including learning, memory, attention, and executive functioning,<sup>2-8</sup> with memory impairment being the most common.<sup>9,10</sup> These deficits are related to the etiology of their epilepsy, recurrent seizures, use of anticonvulsant agents, or a combination of these factors. All of these factors greatly contribute to poor quality of life in PWE and keep them from engaging in day-to-day activities and even gainful employment.<sup>11,12</sup> Thus, there is a significant need to ameliorate the cognitive deficits experienced by PWE.

Cognitive rehabilitation programs and psycho-education have been implemented to treat cognitive deficits in PWE<sup>13-15</sup>; however, the efficacy of these approaches remains unclear. A recent review by Farina et al<sup>14</sup> found limited evidence for the efficacy of cognitive rehabilitation in epilepsy, and it stressed

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the need for randomized controlled studies with larger sample sizes. Another review outlined various other strategies in addition to cognitive rehabilitation that may help ameliorate cognitive impairments in PWE.<sup>8</sup> These strategies include improving seizure control, minimizing adverse effects of anticonvulsant agents and of surgical resection, suppressing interictal epileptiform discharges (IEDs), treatment of depression, use of pharmacologic cognitive enhancing agents, and brain stimulation. Noninvasive and nonpharmacologic interventions may be viable options for and preferred by many PWE due to their relatively low cost, reduced risk of side effects, and/or reduced potential interactions with antiseizure medications.<sup>16</sup>

One possible strategy for improving cognition in PWE that has received little attention is increased physical activity and exercise. Only 1 small study to date has investigated the effects of exercise on cognition in PWE.<sup>17</sup> In the study, 10 children with benign epilepsy with centro-temporal spikes participated in 10 supervised exercise sessions and home-based exercises for 5 weeks. Compared with baseline, significant improvements in the Comprehensive Attention Test and the Children's Color Trails Test (executive function) were observed after completion of the exercise program, although there was no control group. All but 2 of the 10 children were seizure free, with rare seizures in the 2 children (ie, frequency <1 per year). Clinical symptoms including seizure frequency did not worsen, which shows that the exercise program in children was feasible. It is unclear if these results will generalize to adults with epilepsy, and randomized controlled trials are needed in both children and adults to test the efficacy of exercise interventions on improving cognitive functions.

The paucity of studies investigating exercise-induced changes in cognition in PWE represents a significant knowledge gap. Physical activity has been found to be beneficial for cognition throughout one's life span.<sup>18,19</sup> In addition to the known cardiovascular and physiologic health benefits of physical activity, it may have a protective effect against cognitive decline,<sup>20</sup> whereas physical inactivity is considered one of the modifiable risk factors for Alzheimer's disease.<sup>21</sup> The goal of the present article was to provide a better understanding of the role that physical activity may play in improving cognitive function in PWE. We first define physical activity

and appreciate what the typical state of physical activity level is for PWE, in addition to factors contributing to their current state. We then examine how increased physical and/or sports activity contributes to 3 strategies that have been described as having a positive impact on cognitive function in PWE, specifically improving seizure control, reduction of IEDs, and decreasing symptoms of depression.<sup>8</sup> Also highlighted are related findings in animal models of epilepsy concerning exercise and cognitive functions. We then discuss potential barriers to research and the next steps in examining the effects of physical activity and exercise on cognitive functions in PWE.

## PHYSICAL ACTIVITY AND PHYSICAL FITNESS IN PWE

Physical activity is defined as a "bodily movement produced by skeletal muscles that requires energy expenditure"<sup>22</sup> and physical exercise as "a subcategory of physical activity that is planned, structured, repetitive, and purposeful in the sense that the improvement or maintenance of one or more components of physical fitness is the objective."<sup>23</sup> Physical activity is often assessed by using standardized questionnaires, including the Physical Activity portion of the Health Behaviour in School-Aged Children study,<sup>24</sup> the International Physical Activity Questionnaire,<sup>25</sup> and a series of questions on the California Health Interview Survey specific to regular, moderate, or vigorous exercise.<sup>26</sup> Physical activity levels can then be quantified by using an index representing the average daily energy expenditure that is expressed in kilocalories per kilogram of body weight per day; average energy expenditure of <1.5 kcal/kg/d is considered to be physically inactive.<sup>27</sup> Frequency, duration, and the metabolic equivalent of task value of an activity for each session can also be used to quantify levels of physical activity. For example, 1 study compared those with and without epilepsy in their monthly frequency of physical activity during leisure of >15 minutes.<sup>28</sup>

Studies suggest that PWE do not engage in regular physical activity.<sup>29–33</sup> A large population study of 400,055 Canadian individuals found that physical inactivity was associated with epilepsy compared with the general population.<sup>27</sup> PWE report being involved in less leisure time physical activity and exercise as they would like.<sup>34</sup> They also participate less frequently

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