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Getting Physical: A Specific Boost for Cognition in Epilepsy?

Effect of Combined Physical Training on Cognitive Function in People With Epilepsy: Results From a Randomized Controlled Trial

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Objective: To examine the effect of 12-week exercise program on cognitive function in people with epilepsy. Methods: Twenty-one physically inactive patients were randomized into 2 groups: the exercise group (EG) or the control group. Exercise group performed 12 weeks of combined physical training. Control group was advised to maintain usual daily activities. Exercise group received a structured, individually supervised exercise program with two 60-minute sessions per week. Each session included warmup (5 minutes), aerobic (15-20 minutes at 14-17 on Borg scale), strength (2-3 sets, 10-15 repetitions), and 5-minute active stretches. Sociodemographic characteristics, clinical information, memory (Digit Span Test [DST]), executive function (Trail Making Test [TMT] A and B), Stroop Color and Word Test, a verbal fluency task, global cognitive function (Montreal Cognitive Assessment [MoCA]), anthropometric measurements (weight, height, and hip and waist circumferences), cardiorespiratory fitness (maximal oxygen consumption [$\dot{V}o_2max$]), and strength (dynamometer) were measured at baseline and after the 12-week intervention. Results: Exercise decreased time spent on TMT-A from baseline to postintervention (difference = −7.9 seconds, 95% CI = −14.5 to −1.3, $P = .023$). Exercise group improved total number of words on the verbal fluency task after intervention (difference = 8.1 words, 95% CI = 3.0-13.2, $P = .002$). Exercise group also improved the score on MoCA at 1.7 (95% CI = 0.1-3.3, $P = .043$) points. We observed a 22.4% (95% CI = 13.1-31.6, $P = .021$) improvement in executive function in EG. No effect of group, time, or group × time was observed on any other cognitive test. Changes in $\dot{V}o_2max$ were negatively associated with changes in performance on DST ($r = -0.445$, $P = .049$) and overall memory score ($r = -0.544$, $P = .042$). Significance: This randomized controlled trial provided the first evidence that combined physical training improves executive function in adults with epilepsy, showing main improvements in attention and language tasks. Physical exercise should be encouraged for people with epilepsy to reduce the burden on cognitive function associated with this disease.

Commentary

The never-ending desire to improve cognitive functioning has resulted in the development of what has now become a multibillion-dollar industry. Although the search continues for effective pharmacological treatments of cognitive impairment in patients with diagnosed neurological disorders, a number of other industries have arisen, marketing products directly to the general public, in the form of dietary supplements, computerized training apps, and other electronic devices aimed at improving cognitive functioning in normal functioning adults. The demand for these products has accelerated in recent years with many consumers looking for quick-fixes despite the fact that the available scientific evidence from studies performed on both patients and healthy samples indicates that less costly modifications to lifestyle, including increased physical exercise, adoption of a healthy diet, and increased sleep have the potential to be more effective for improving cognition in the long run.[1]

It is well known that cognitive impairment is a core feature of epilepsy with marked effects on quality of life.[2] As a result, any effective method for improving cognitive functioning in patients with epilepsy would certainly be welcomed with open arms. To date, there has been a lack of controlled clinical trials assessing treatments for cognitive impairment in patients with epilepsy. Results from the limited studies performed thus far on available drugs or other interventions have shown very little in terms of a positive therapeutic effect.[3]

Turning to lifestyle factors, there is evidence that patients with epilepsy have lower levels of health status and lower rates of health-related behaviors than the general population,[4] which has been shown to translate into reduced levels of brain health and cognitive functioning.[5] Given the known link between

health and cognition, it appears that the time has now come to determine whether or not prescribed increases in physical and other health-related behaviors can be effective in alleviating cognitive impairment in patients with epilepsy.

In the study by Feter and colleagues,[6] they randomly assigned 21 patients with epilepsy to 1 of 2 groups, consisting of an exercise group (EG), who completed a 12-week program of combined exercise training or a control group (CG), who maintained their usual daily activities over the same time period. The exercise training intervention was individually supervised over two 60-minute sessions per week and included a combination of aerobic, strength, and stretching activities. Patients received interviews prior to group assignment and were administered a modest battery of cognitive tests (eg, Montreal Cognitive Assessment [MoCA] and Trail Making Test [TMT]) in addition to anthropomorphic (eg, weight and waist circumference) and fitness measurements (eg, maximal oxygen consumption and strength). All of the tests and measures were administered to both groups at baseline and were repeated after completion of the 12-week trial period.

The major findings were that patients in the EG demonstrated significant improvement in global cognition as compared to those from the CG, as evidenced by an improvement in the MoCA, and improved executive functioning, described as a selective improvement on the TMT, Part A (TMT A). The investigators also reported an increase in cardiorespiratory fitness associated with memory performance, as demonstrated through significant correlations with changes in select cognitive indices. The conclusion was that combined physical training improves cognition and executive functions in patients with epilepsy as compared to controls.

Although there no doubt that the results of small studies like this hold promise for the prospect of using exercise training to improve cognition in patients with epilepsy, there are a number of issues with the methods and analysis from this particular study, which will likely restrict the generalizability and replicability of the findings. Much of this is related to the limitations of the cognitive test battery and its effects on the reported specificity of the findings. The improvement in executive functioning reported in this study is based on a mean decrease of 7.9 seconds on TMT A. Although this was a significant group finding, it is known that individual patients require a decrease of more than 14 seconds to achieve significant improvement in that particular test,[7] making it doubtful that any single patient from the EG exceeded the threshold required to document an improvement in executive functioning. Additionally, the reported positive finding regarding the fitness variable and memory change is based on one significant correlation coefficient observed within a table of 27 correlation values, raising questions about the reliability of that finding, given the possibility of a Type I statistical error.

The authors introduce a number of possible mechanisms, including neurotrophic factors and changes in brain connectivity, as possible explanations for their reported findings. However, it is noted that the study did not include any assessment of mood or quality of life, which are 2 factors have been shown in other exercise intervention studies to be affected to a larger degree than cognition.[8] It will be important to learn, through future investigations, whether the positive effects of exercise in patients with epilepsy reflect the influence of a unique underlying brain factor or whether the positive influence is simply the result of a general positive effect on subjective well-being, similar to what is experienced in many others who engage in regular exercise activities.

There is no doubt that we should be encouraging the use of low-cost approaches to decrease the burden of cognitive impairment and other comorbidities of epilepsy. However, it is important to have an accurate picture of how and why any of these approaches might provide effective treatments for cognition. A movement toward prescribing lifestyle interventions, such as combined exercise training, will have little downside and will likely lead to positive medical effects that extend beyond the treatment of epilepsy, while enabling us to move away from the use of many existing pharmacological and remediation strategies for treatment of cognitive impairments, which have proven, to date, to be both costly and ineffective. There are already indications that patients with epilepsy have been engaging in more physical activity, in addition to reducing negative health behaviors, such as smoking.[9] Let's hope that these trends continue with the result of an observable decrease in associated comorbidities, including cognitive dysfunction.

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