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REVIEW ARTICLE (META-ANALYSIS)

Effect of Exercise on Depressive Symptoms in Adults With Neurologic Disorders: A Systematic Review and Meta-Analysis

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Abstract

Objectives: To review and quantify the effect of exercise on depression in adults with neurologic disorders.

Data Sources: CINAHL, Cochrane Register of Controlled Clinical Trials, EMBASE, ERIC, MEDLINE, PsycINFO, PubMed, and SPORTDiscus were searched, with the last search performed in May 2014.

Study Selection: Included were randomized controlled trials conducted in adults with a diagnosed neurologic disorder that compared an exercise intervention group with a control group and used depression as an outcome measure.

Data Extraction: Depression data were extracted independently by 2 authors. Methodological quality was assessed independently by 2 authors.

Data Synthesis: Forty-three full-length articles were reviewed, and 26 trials met our inclusion criteria. These trials represented 1324 participants with 7 different neurologic disorders: Alzheimer disease (n=4 trials), migraine (n=1), multiple sclerosis (n=13), Parkinson disease (n=2), spinal cord injury (n=1), stroke (n=2), and traumatic brain injury (n=3). Data measuring depression were extracted and effect sizes were computed for 23 trials. Results from a meta-analysis yielded an overall effect size of .28 (SE=.07; 95% confidence interval, .15−.41; P=.00) favoring a reduction in depression outcomes after an exercise intervention compared with the control condition. Of note, interventions that met physical activity guidelines yielded an overall effect of .38 compared with .19 for studies that did not meet physical activity guidelines.

Conclusions: This review provides evidence that exercise, particularly when meeting physical activity guidelines, can improve depressive symptoms in adults with neurologic disorders.

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Depression and depressive symptoms are common in the general population of adults, and are particularly common in adults with neurologic disorders (ie, diseases or disorders of the nervous system). The lifetime prevalence of major depressive disorder in the United States population is 19.1%, and the rate is even higher among adults with neurologic disorders. For example, the lifetime prevalence for depression is approximately 50% in both multiple sclerosis[1] (MS) and Alzheimer disease[2,3] (AD). Studies of depressive symptoms report higher scores on depressive outcomes in populations with neurologic disorders than in the general population. For example, 1 community-based study[4] compared depressive symptoms based on the Beck Depression Inventory (BDI) among persons with Parkinson disease and 2 age-matched control groups, one composed of healthy older adults and one composed of older adults with diabetes mellitus. The mean score on the BDI was 12.8 among participants with Parkinson disease, 7.9 in participants with diabetes, and 5.9 among healthy older adult controls. In a large web-based survey[5] of depression in 4178 people with MS, the mean Hospital Anxiety and Depression Scale score was 7.6, whereas the mean score in a United Kingdom population reference group was only 3.7.

Depression and its symptoms may be associated with various adverse consequences in persons with neurologic disorders. Such consequences include loss of independence and even mortality. For example, depression has been associated with a higher rate of premature mortality in patients with AD.[2] In patients with recent spinal cord injury (SCI) undergoing rehabilitation, depression has been associated with fewer functional improvements, decreased mobility, and decreased functional independence.[6,7] Persons with migraine and comorbid depression experience decreased quality of life and restriction of activities.[8,9] Depression has been

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associated with decreased functional recovery poststroke.[10] Depression further has been associated with poor treatment compliance in people with MS.[11]

Pharmacologic treatment for depression in populations with neurologic disorders yields conflicting results. Antidepressant medications have improved depressive symptoms and other outcomes in persons with stroke.[10] By comparison, 1 review[11] of pharmacologic treatment of depression in MS reported a lack of consistent evidence for improvement of depression after drug treatment. One large-scale, double-blind trial[12] compared the effects of 2 different antidepressant medications (sertraline, mirtazapine) on depressive outcomes in clinically depressed persons with AD, and reported no clinical effectiveness of the drugs compared with a placebo. Other forms of treatment such as cognitive behavioral therapy (CBT) have similarly produced equivocal results in several populations. For example, 1 meta-analysis[13] of depression treatment methods after SCI reported positive reactions to CBT, but the included trials lacked the methodological rigor necessary to attribute depression improvement to CBT. One systematic review[14] of both pharmacologic and psychosocial treatment of depression after traumatic brain injury (TBI) concluded that there is insufficient evidence regarding the effects of antidepressant medication and psychotherapeutic methods. Interestingly, in patients with migraine, antidepressants have been used successfully not only for treatment of comorbid depression but in migraine prophylaxis as well.[15] Adverse effects of antidepressant medication are commonly reported, especially in the MS and AD populations.[11,13]

Exercise is defined as any planned, repetitive bodily movement done with the goal of increasing fitness, and is an effective behavioral approach for reducing depressive symptoms and treating major depressive disorder in otherwise healthy adults.[16,17] When comparing exercise with a control group, 1 meta-analysis[16] of 23 trials yielded an effect size (ES) of −.82 in favor of exercise reducing depressive symptoms. Another meta-analysis[17] of 17 trials with clinically depressed participants reported that the exercise groups had a 1-SD reduction in depression scores compared with control groups. There is additional evidence that exercise training is comparable with antidepressant medication (sertraline) in its effects on depression and depressive symptomology.[18] Similarly, a Cochrane review[16] of the effects of exercise training on depression reported no differential improvement in depressive symptoms for those receiving exercise and those receiving CBT.

List of abbreviations:

AD	**Alzheimer disease**
BDI	**Beck Depression Inventory**
CBT	**cognitive behavioral therapy**
CI	**confidence interval**
ES	**effect size**
MADRS	**Montgomery-Åsberg Depression Rating Scale**
MS	**multiple sclerosis**
PAG	**physical activity guideline**
PEDro	**Physiotherapy Evidence Database**
RCT	**randomized controlled trial**
RPE	**rating of perceived exertion**
SCI	**spinal cord injury**
TBI	**traumatic brain injury**
$\dot{V}o_2max$	**maximal oxygen consumption**

Multiple exercise intervention trials conducted in populations of adults with neurologic disorders have measured depressive symptoms as an outcome. These trials, unfortunately, yield conflicting results even when considering populations with the same neurologic disorder. For example, 2 separate 4-month trials conducted among participants with AD yielded ESs of −.06[19] and .39.[20] Both of these interventions consisted of walking and a comprehensive set of strength, balance, and flexibility exercises. There is similar variability in ESs for trials conducted among participants with diagnosed MS.[21,22]

We undertook a systematic review and meta-analysis of exercise training and depression in adults with neurologic disorders based on the evidence for improvement of depression and depressive symptoms after exercise interventions in the general population, and the conflicting evidence of its effects on depression in adults with neurologic disorders. This systematic review and meta-analysis serves to determine the efficacy of exercise interventions for improving depressive outcomes in persons with various neurologic disorders. We further provide information about the safety of exercise training in neurologic disorders based on reported adverse events, and the differences in efficacy of interventions that met or did not meet the *2008 Physical Activity Guidelines for Americans*.[23]

Methods

Search strategy

We followed protocol outlined by the Meta-analysis of Observational Studies in Epidemiology[24] and the procedure outlined by McDonnell et al[25] in a review of aerobic exercise and cognitive function in the same population. We searched the following databases, with no date limits: CINAHL, Cochrane Register of Controlled Clinical Trials, EMBASE, ERIC, MEDLINE, PsycINFO, PubMed, and SPORTDiscus. The key terms searched involved several possible acronyms for neurologic conditions (eg, nervous system diseases, autoimmune diseases of the nervous system) and several possible acronyms for exercise/physical activity (eg, exercise, physical fitness, resistance training). Although our aim was to include exercise interventions only (as opposed to physical activity interventions), we used "physical activity" as a search term so as not to miss any trials that may have included physical activity as a keyword. We further focused on exercise for consistency in comparison with other meta-analyses in adults[16,26] and persons with MS.[21,22] "Depression" or "depressive symptoms" were not used as search words so as to avoid potentially excluding any eligible studies that did not use depression as a key term if it was not a primary outcome measure of the study. See appendix 1 for an example of the search terms.

After initial searches, PubMed was searched again with each condition name (ie, Parkinson disease, multiple sclerosis, migraine, etc) as a medical subject heading (MeSH term) with a combination of exercise-related MeSH terms in order to find any other studies that were not included in the first search. Reference lists of the studies that fit the inclusion criteria were also searched for any additional studies.

After preliminary searching, irrelevant studies based on title and abstract were initially removed, as well as studies with no mention of measuring depression. Remaining articles were reviewed to identify the articles that met our inclusion criteria. The last search was performed in May 2014.