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Exercise as Medicine to Prevent Cognitive Decline and Dementia:

Is it Worth the Sweat?

What Is Already Known

The U.S. Department of Health and Human Services recommends that all adults get at least 150 minutes of moderate-intensity exercise or 75 minutes of vigorous-intensity exercise, or an equivalent combination, per week to maintain overall health and function and reduce the risk of a number of chronic diseases. It has also become clear that high-intensity aerobic exercise improves not just the function of the body but also function of the brain. Based on research to date, the potential benefits of physical exercise on cognitive health cannot be overstated. The World Health Organization included physical activity as a top priority in its recent review of 12 non-pharmacological interventions with the potential to reduce the risk of cognitive decline and dementia.

Background and Evidence Base

More than two decades of research in both animal and human studies strongly supports a relationship between aerobic exercise and beneficial effects on the brain. A 2017 review summarized findings from the human and animal literature on the positive effects of physical exercise on the brain and highlighted the vascular links underlying those benefits. The review reported that exercise was associated with increased neurorepair, increased clearance of hyperphosphorylated tau, improved glucose metabolism, reduced inflammation, reduced β-amyloid plaques in the brain, and reduced oxidative stress. Observational studies in humans report that aerobic exercise results in improved cognitive function and a reduced risk of cognitive decline and Alzheimer's disease, and it has positive effects on brain volume and Alzheimer's disease biomarkers. Findings from randomized controlled trials are less consistent, but preliminary evidence suggests that aerobic exercise results in positive effects on cognition, brain structure and function, and Alzheimer's disease biomarkers.

A 2018 meta-analysis of 19 studies (17 of which were randomized controlled trials) involving a total of 1,145 older adults concluded that exercise improves cognition among individuals with mild cognitive impairment. There was a 1.3-fold higher effect when the analysis examined only the effects of aerobic exercise (excluding light physical activity).

A hallmark study in 2006 showed that, among cognitively normal older adults, six months of high-intensity aerobic exercise increased volumes in parts of the brain associated with executive function. This study provided the inspiration to examine exercise as a potential therapeutic intervention in adults with mild cognitive impairment. The Piedmont Aging, Cognition, and Exercise (PACE) study is one such randomized controlled trial. The intervention included six months of aerobic exercise compared with a control group that received six months of stretching and balance activities. Participants completed glucose tolerance tests, 400-meter walk tests, lumbar puncture (for evaluations of Alzheimer's disease biomarkers in cerebrospinal fluid), magnetic resonance imaging of the brain (to evaluate brain volumes and blood flow), and various standardized cognitive assessments. The results indicated that, compared with baseline levels, participants in the aerobic exercise group experienced significant improvement in executive function, while participants in the stretching group experienced a significant decline in this cognitive ability. (In essence, because only cognitively impaired individuals were enrolled in the trial, the control group's decline in cognitive ability indicates the stretching and balance activities had no effect). Additionally, aerobic exercise was shown to increase overall blood flow in the brain and in regions associated with executive function that included the right and left prefrontal, right and left posterior parietal, and right and left cingulate cortices.

The potential therapeutic effects of aerobic activity among individuals with Alzheimer's-type dementia have also been examined. The Alzheimer's Disease Exercise Program Trial (ADEPT) tested the effects of a six-month intervention of aerobic exercise in adults with early-stage Alzheimer's dementia, with stretching used as the control intervention. Cognitive, functional, cardiorespiratory fitness, and brain imaging outcomes were evaluated. Results showed that the six-month program of aerobic exercise was associated with a modest gain in functional ability. Secondary analyses revealed that improvements in cardiorespiratory fitness over time were positively correlated with improved memory performance and increased bilateral hippocampal volume.

Despite the generally positive research findings that exercise improves cognitive function in both healthy adults

and adults with varying stages of cognitive decline, results are not always consistent. This inconsistency is likely related to differences in study design, such as the use of supervised versus unsupervised home-based exercise interventions, and differences in the intensity, frequency, and overall duration of interventions. Health-restoring effects of exercise take time; trials with interventions lasting less than six months rarely show cognitive benefits. Longer trials more commonly show benefits on executive function, but those with interventions lasting less than 12 months rarely show benefits on memory. Thus, interventions need to be of an appropriate intensity and an appropriate duration for individuals to experience benefits.

Additional challenges with respect to recommendations arise because many trials have historically enrolled cohorts that are not demographically representative of the overall population. Existing trials are more likely to have greater diversity, include more appropriate representation in their recruited cohorts, and ensure sustainability within the community if the trial results are positive. For example, in the Exercise in Adults with Mild Memory Problems (EXERT) study, nearly 20% of the recruited 300-person sample represents communities of color, and the intervention is delivered in the community at YMCAs under the supervision of study-certified YMCA trainers.

Implications for Public Health

The growing evidence for a relationship between physical activity and long-term preservation of cognitive function supports the need to promote community exercise participation. In addition, it is important to implement and assess new avenues for exercise participation in diverse communities and across all age groups, which will serve to strengthen the message that greater physical activity and exercise is a helpful pathway for reducing the burden of cognitive impairment and dementia in society. However, the success of intervention strategies depends on access and sustainability of delivery within the community.

Discussion

Public health interventions need to provide ongoing support (coaching) to enable participants to continue exercising at appropriate levels of intensity for an appropriate period of time so that they can experience the full therapeutic benefit. This support is especially important for older adults who are not regular exercisers before starting an exercise program, and for older adults with mild cognitive impairment who consequently face daily challenges. Without support, this type of an intervention that is designed to protect cognitive function in older adults will not likely succeed. Because research studies have funding and project duration limits and thus cannot provide ongoing support for interventions shown to be successful, there is a need for sustainable community-based programs that can be delivered by the community, using community-based infrastructure and resources. Health care providers should promote "exercise as medicine" to their patients and should provide appropriate referrals to evidence-based community programs that can properly and effectively assist and support individuals.

There is increasing evidence that physical exercise, and aerobic training in particular, has favorable effects on multiple health outcomes, including reduced risk against cognitive decline and possibly the development of Alzheimer's disease. Although the success of intervention strategies will depend on the ultimate sustainability of their delivery within the community, it is clear that all adults should be encouraged to talk to their health care providers about participating in vigorous aerobic activity in line with Department of Health and Human Services guidelines.

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