

Therapeutic Effects of Exercise on Cognitive Function

There is considerable anecdotal evidence that physical fitness plays an important role in the preservation of cognitive and brain function throughout the life span. The Greek philosopher Plato emphasized the importance of maintaining an active lifestyle for balancing mind and body, and numerous health-related websites now recommend physical activity for enhancing and prolonging brain health, but is the anecdotal evidence of the importance of physical fitness on mental health built on a sound scientific foundation, or is it a fabricated remedy based on an association that has no causal basis? Over the past several decades, a wealth of evidence has helped to confirm the anecdotal evidence that remaining physically active and fit is associated with better mood and lower risk of experiencing cognitive dysfunction. Because of this, physical exercise has emerged as a promising method for the prevention and treatment of neurological and psychiatric conditions, as well as the enhancement of normal cognitive function. In this issue of the *Journal of the American Geriatrics Society*, two separate articles have added to the scientific literature on the importance of physical activity on cognitive performance in late adulthood. Before describing the significance of these two new studies and the questions they pursued, I will first provide a brief historical context for their research questions.

In the 1970s, it was reported that physically active older adults outperformed their more-sedentary peers on a variety of cognitive tasks.¹ Since then, randomized controlled trials have demonstrated that moderate-intensity exercise for several months improves cognitive function in late adulthood.² Meta-analyses have confirmed these effects and demonstrate that the most robust effects of exercise appear to be on measures of memory, processing speed, and executive function.^{3,4} Prospective studies have also confirmed these associations such that participation in greater amounts of physical activity in midlife reduces the risk of developing cognitive dysfunction in late life.⁵ More recently, neuroimaging methods have found that higher fitness levels and greater amounts of activity and exercise are related to greater gray matter volume, greater white matter integrity, higher cerebral blood flow, and more-efficient task-evoked activation.⁶ Although the molecular mechanisms by which exercise influences brain and cognitive function remain poorly understood in humans, years of animal research has discovered that exercise has myriad effects on the brain, including greater cell proliferation, production of new capillary beds, changes in expression and secretion of neurotransmitters and neurotrophic factors,

and lower amyloid burden, among many others.⁷ It is likely that the neuroimaging outcomes described above depend on some or all of these molecular mechanisms.

Despite this wealth of knowledge about the potent effects of exercise on brain health, many questions remain unanswered. For example, we still have a poor understanding of the dose-response effects of physical activity on cognitive performance. That is, how much (duration) and at what level (intensity) is necessary and sufficient for improving brain health? Answering this question is critical for the widespread prescription of physical activity for enhancing cognitive function or preventing decline and the adoption of the most effective and appropriate physical activity protocols for scientific purposes. In this issue, Kerr et al.⁸ addressed this question using an objective physical activity monitoring device in 215 older adults (mean age 83) residing in seven retirement communities in San Diego. After dividing activity levels into three categories: low-light, high-light, and moderate to vigorous physical activity (MVPA), they found that only MVPA was associated with better performance on the Trail Making Test after correction for demographic information and other categories of physical activity, although high-light levels of activity were also significantly predictive of better performance on the Trail Making Test, albeit only after correction for demographic variables and not after correction for low-light activity. In psychometric terms, they state the importance of MVPA on cognitive function: “assuming that, on average, 72 seconds were required to complete Trails B-minus-A test, results from the adjusted model indicate that older adults who regularly participated in 30 minutes of MVPA required only 61 seconds to complete that cognition test (15% faster time).” These results highlight the importance of moderate levels of activity for cognitive function, and executive function more specifically, in late life, but the interpretation of these results is limited in two main ways. First, because the sample came from retirement communities in San Diego, the participants might be different from community-dwelling older adults in other parts of the country that have more seasonal variation and greater (or fewer) options for participation in physical activity. Second, the cross-sectional design limits the ability to draw conclusions about whether different doses of physical activity cause differential, or parametric, improvements in cognitive performance. Despite these limitations, Kerr et al. provide compelling cross-sectional results emphasizing the importance of MVPA over lighter forms of activity and links to better cognitive function.

In addition to questions concerning the most-appropriate dose of physical activity that could influence cognitive

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function, there are other similarly important questions that are being asked about which populations could benefit from a physical activity intervention⁹ and how to combine physical activity with other behaviors to enhance cognitive function more effectively.¹⁰ For example, a healthy diet may magnify the effects of physical activity on cognitive function, whereas an unhealthy diet may mitigate, or reduce, the efficacy of physical activity on cognitive function. Unfortunately, these potential moderators of physical activity are poorly understood and infrequently studied.¹⁰ Similarly, most prior studies have examined the links between physical activity and brain function in individuals without cognitive impairment. Fewer studies have examined the effect of a physical activity intervention in individuals with signs of cognitive impairment or dementia. Physical activity may enhance cognitive function only during a “critical period” before significant brain atrophy or disease has progressed. This would suggest that individuals with cognitive impairment might benefit less than individuals without cognitive impairment. Alternatively, if physical activity is effective at enhancing cognitive function in those with cognitive impairment, it could be a therapy to help relieve symptoms or improve function in those experiencing memory problems.

In an innovative study published in this issue, Andrade and colleagues examined whether a multimodal intervention using a combination of cognitive stimulation and physical activity would influence cognitive function in a sample of 30 adults with Alzheimer’s disease.¹¹ They found that 16 weeks of a multimodal intervention improved performance on executive functioning tasks, dual tasks, and metrics of physical functioning. This study illustrates the importance of combining physical activity with a cognitively stimulating atmosphere to elicit significant benefits to cognitive function in an impaired sample. Although Andrade and colleagues present provocative results, there are several limitations of their study that preclude more-widespread applications. For example, although the intervention combined physical activity with cognitive stimulation, no groups received just physical activity or cognitive stimulation, so it is impossible to determine whether cognitive stimulation, physical activity, or the combination of treatments were driving the effects. Second, the lack of an active control group makes the Hawthorne effect difficult to eliminate. Third, a sample of 30 adults with Alzheimer’s disease is a respectable number, but future studies with larger sample sizes will be needed to replicate and extend these effects. Nonetheless, Andrade and colleagues suggest that the brain retains its capacity even in the face of Alzheimer’s disease and that only 16 weeks of a modest intervention was effective at improving cognitive function. Similar interventions are desperately needed to clarify the extent of the improvements, the pathways, and the factors that may magnify or attenuate the effects.

The publications by Kerr et al.⁸ and Andrade et al.¹¹ provide incremental and significant contributions to our understanding of the conditions and approaches that could influence cognitive function in individuals with and without dementia. Physical activity may not be a magic bullet for preventing cognitive decline, but if it is effective at improving some domains of cognitive function, delaying the onset of disease, improving physical function, and elevating mood, then it should be considered a propitious method of enhancing cognitive function in healthy and impaired populations. Until the pharmaceutical industry develops a drug that is effective at preventing cognitive decline, a good pair of walking shoes or a swim in the pool may be the best medicine for enhancing cognitive performance.

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