Exercise and the Prevention of Dementia

As the burden of age-related diseases increases, healthcare professionals look for ways not just to treat Alzheimer's disease (AD), but also to prevent cognitive impairment. Preliminary clinical trials suggest that regular exercise can improve cognition in as little as one month. They also indicate that people who exercise have lower rates of AD and other dementias and have slower rates of cognitive decline. This article discusses the relationship between physical activity and improved cognition and what might be recommended to patients pending more definitive exercise-prescription guidelines.

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Treatment of AD cannot return patients to their former selves, nor can it prevent the progression of the disease. At best, it alters the course of the disease, while generally slowing progression.[1] Given that treatment is still less than ideal, prevention is of utmost importance. Substantial evidence suggests that people who exercise lower their risk of dementia and that by exercising, people can improve their cognitive performance. This article discusses research that has investigated the association between physical activity and cognition and what might be suggested to patients in clinical practice.

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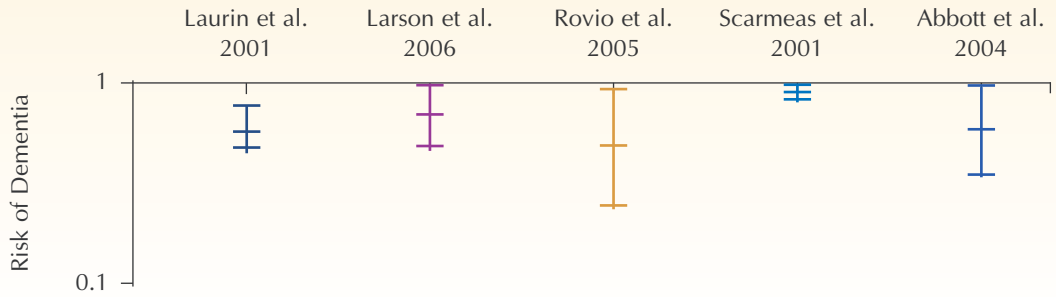
Lessons from Epidemiology

Even if some degree of cognitive decline is inevitable with aging, dementia does not appear to be. Some people avoid dementia despite extreme old age and even with a substantial burden of neuropathologic lesions associated with dementia.[2] A number of lifestyle factors, including education, leisure activity, and diet, are associated with a reduced risk of dementia. Research studies included patients from a variety of countries and age groups with different definitions of exercise, and concluded that people who exercise are at a lesser risk of developing dementia (Figure 1).[3]

Of note, it does not seem to matter whether people exercise at a young or old age. Most studies have been of older populations (at least 65 years) but have had only a short follow-up time (approximately 5 years). These studies found that those people who exercised had 10% to 45% less chance of being diagnosed with dementia at follow-up.[3] An important study from Finland examined the risk of late-life dementia in relation to mid-life physical activity.[4] People who exercised during their middle age had half the risk of developing dementia in old age, compared to those who did not exercise. The nature of the optimal timing of exercise as a preventive maneuver remains unresolved however, as those people who were active during their mid life might also be more physically active in late life. In general, it is reasonable to expect that a longer duration of exercise is better than a shorter one, even though the benefits of exercise can

Figure 1

Risk of Dementia in Exercisers Relative to Non-exercisers[3]



be realized at any point in the life span. Age should not be a contraindication to taking up an exercise program, other things being equal.

The association between exercise and the risk of dementia is stronger for AD than it is for vascular dementia. Why this is so remains unclear, although it might simply be associated with diagnostic preferences. Though neurodegenerative and cerebrovascular disease rarely occur in isolation, the number of people diagnosed with vascular dementia is substantially lower than the number diagnosed with AD in most studies. Though no major studies found a significant association between physical activity and vascular dementia, the point estimates for the risk of vascular dementia consistently suggest that people who are physically active have reduced risk. Alternatively, physical activity may affect the course of vascular dementia differently than the course of AD. In a study of lesser impaired states, people who were physically active had less risk of vascular cognitive impairment-no dementia (related to vascular dementia) but not of mild cognitive impairment (related to AD).[5] This suggests that physical activity might delay vascular dementia, whereas its impact on AD might be a reduction in severity.

In this regard, we might consider how to conceptualize the prevention of AD. In the treatment of the disease, we recognize that success can fall short of a cure.[1] In other words, successfully treated AD is not normal cognitive function. Similarly, successfully prevented AD might not be considered normal cognitive function—instead it might look more like mild cognitive impairment. This might explain why exercise appears to reduce the incidence of AD, but not that of mild cognitive impairment.

Of note, physical activity is associated with reduced rates of cognitive decline in people of all cognitive abilities.[6] Regardless of diagnostic status, those people who are physically active seem to have better cognitive function and slower cognitive decline than those who are sedentary.[7] If people who are physically active still experience cognitive decline but more slowly, then some cases of "prevented" dementia might present as mild cognitive impairment rather than normal cognition. Overall, people who are physically active have less risk of both cognitive impairment and dementia though it is unclear whether physical activity delays impairment or whether it can, in some cases, prevent cognitive impairment entirely.

An optimist's view proposes that if we could delay the onset of dementia by 2 years, then we could reduce the prevalence by as much as 25%, all things being equal.[8] Of course, all things are never equal and people who exercise might also be better educated, have better diet, and have less vascular risk. Even so, it appears that walking at an easy pace for at least 1.5 hours per week might be able to delay the onset of dementia by 1.5 years.[9] As evidence suggests that there exists a dose response with exercise,[3] then more frequent or more vigorous activity might further delay the onset and decrease the prevalence.

Clinical Trials

Despite the strength of the epidemiologic studies, it is difficult to confirm a true relationship because confounding factors can never be completely controlled outside an experimental design. Preliminary clinical trials confirm the benefits of exercise to cognition. Clinical trials in humans suggest that cognition can improve with exercise and animal models suggest possible mechanisms for this improvement.

Two recent meta-analyses analyzed clinical trials on the effect of physical activity on cognition. One study examined 18 controlled clinical trials of physical activity in high-functioning adults aged 55 to 80 years.[7] Another study examined the effects of physical activity in people aged 65 years and older who had cognitive impairment or dementia.[10] The results of both studies were remarkably similar, with overall effect sizes of 0.60 and 0.57 respectively. Effects are maximized in programs incorporating aerobic, strength, and flexibility training over aerobic training alone and in programs where exercise duration is between 31 and 45 minutes.[7] The largest cognitive effect seems to be on executive function[7] though most important to caregivers might be the improved behavioural symptoms and functional capacity associated with exercise (Table 1).[10] Notably, the effects of physical activity seem to be broader-ranging than the effects of cognitive training, which are very task-specific.[11]

Table 1

The Benefits Associated with Exercise

Exercise as Prevention

People who exercise have:

- Decreased risk of dementia
- Decreased risk of AD
- Slower cognitive decline

People with AD who exercise have:

- Slower cognitive decline
- Slower functional decline
- Less behavioural problems

The effects of exercise and fitness on brain structure and function are still speculative. Tentative conclusions from human interventions provide support that exercise alters the neural networks involved in attention and short-term memory.[11] Additionally, exercise training is associated with reduced brain atrophy, especially in the prefrontal, temporal, and parietal regions.[11] The mechanisms seem to be multi-faceted and may include improved cerebrovascular profusion, better cardiovascular health, improved neuroplasticity, and increased neurogenesis.

Vascular health alters not only the risk of vascular dementia but also of AD. In older people, cerebrovascular and neurodegenerative disease rarely occur in isolation. As little as one cerebral infarct can worsen the cognitive impairment seen with a given level of neurodegenerative pathology.[12] Dementia and atherosclerosis share many risk factors (hypertension, elevated cholesterol, diabetes)[13] and physical activity can alter these factors[14] as well as enhance angiogenesis.[15]

There is also increasing evidence that physical activity can affect neurodegeneration. In an animal model, rats that exercise have reduced levels of β-amyloid plaques, closely associated with AD. Furthermore, rats that participated in high levels of voluntary physical activity for as little as one week increased their levels of brain-derived neurotrophic factors (BDNF).[15] This could be particularly relevant for people with cognitive impairment whose BDNF levels are 50% to 75% lower than normal. In controlled environments, BDNF enhances synaptic transmission, long-term potentiation, and neurogenesis. In a similar fashion, rats that are physically active also have increased neuroplasticity, neurogenesis, and long-term potentiation, possibly related to higher levels of BDNF.[15]

The limited clinical trials available support the conclusions from observational studies that people who exercise have improved cognitive function. People who participate in exercise interventions as short as one month show improved cognitive performance, especially in executive function.[7] Mechanisms including modification of vascular health and increased neurogenesis

Table 2

Characteristics of Recommended Exercise

To Maximize Benefits:	To Maximize Safety and Adherence:
Type of exercise: • Variety of activities • Activities with social interaction **Intensity of activity:** • Gradually increase intensity • Pay attention to health status **Frequency of activity:** • As frequent as possible (5+ days/week) **Duration:** • At least 30 minutes/session	**Ability** • Consider fitness, functional ability and cognitive ability to minimize risk **Preference** • Choose preferred activities **Environment** • Choose a rich but safe environment • Consider what is available and appropriate to abilities

could be involved, as suggested in animal trials.

Other Benefits of Exercise

Though the relationship between exercise and cognitive impairment needs further investigation, there is incontrovertible evidence that exercise is associated with a range of health benefits. People who are physically active have lower rates of cardiovascular disease, diabetes, cancer, hypertension, obesity, depression, osteoporosis and premature death.[16] In addition, exercise is beneficial in the secondary prevention of cardiovascular disease, cancer, and diabetes.[16] The benefit seems to be dose-dependent where those who exercise the most have the least risk of various health outcomes.[16] Interestingly, the relationship with most health outcomes seems to be similar regardless of whether physical activity levels or physical fitness is considered.

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Recommendations to Patients

Physicians can greatly influence exercise behaviour. In one study, 40% of seniors who exercised started the program because of physician advice.[17] Recommendations to patients should be simple and easy to follow and need not take much time. The specific type of activity does not seem to matter, though it appears that an exercise program including a variety of activities and social engagement may offer the greatest reward. Aerobic activity is good but incorporating strength and flexibility training is even better.[11] In general, at least 30 minutes of physical activity, at least 3 times a week, at an intensity greater than walking, seems to decrease the risk of dementia.[6,7,18] Where there seems to be a dose response, more frequent and more intense activity may be more protective, though both should be increased gradually (Table 2).

Many people participate in low amounts of physical activity despite extensive information relating physical activity to health outcomes. Seniors cite safety issues, health problems, physical ailments, and concerns about self-efficacy as barriers to starting an exercise program.[17] With respect to safety, the most important issue to recognize is that there is more risk associated with being sedentary than being physically active. Not only are there health benefits to exercise,[16] but people who exercise are less likely to fall and less likely to injure themselves from falls.[19,20] To minimize safety concerns, the exercise program should be adapted to the individual's abilities and to the environment. The frequency and the intensity of the exercise program should be increased especially gradually in those with health problems. The choice in activity

should account for any physical impairment. For example, people who are limited can swim or can even "wheel" for exercise. For those with cognitive impairment, well-known activities may be easier to perform. It is always safer to exercise with a partner who can help if difficulty arises. Specifically for people with cognitive impairment, a partner can help realize when activities may be dangerous or when exhaustion is reached.

No one wants to look foolish. People who are inexperienced may be reluctant to start an exercise program because they do not want to appear amateurish. Personal trainers and exercise groups geared towards beginners can help relieve these concerns, by giving prospective exercisers the training and confidence to carry out training activities in front of others. There are many exercise programs geared towards prevention of health problems in seniors that may also be appropriate for people at risk of cognitive impairment. For example, there is some evidence to suggest that a cardiac rehabilitation program can also improve cognitive performance.[21]

Conclusions and Future Directions

Most studies that examined exercise and cognition are observational. However, there is preliminary evidence from clinical trials and animal studies to suggest that the relationship between physical activity and improved cognition is real. Given the many health benefits that arise from exercise, it is reasonable even now to recommend an exercise program as part of the treatment prescription for people with AD.

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