Graphical Review

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The Principles of Exercise Prescription for Brain Health in Aging

Jennifer J. Heisz and Emma E. Waddington

ABSTRACT

Alzheimer's disease and related dementias are among the world's greatest health challenges. As the population ages, global dementia rates are rising, and with no imminent cure, there is an urgent need for interventions that reduce the risk of dementia in healthy older adults. Exercise is a promising intervention; however, exercise prescriptions for optimizing brain health are lacking. This may undermine the perceived clinical utility of exercise and pose a barrier that prevents practitioners from prescribing exercise for brain health in primary care settings. This graphical review briefly summarizes the prominent neural changes in healthy aging versus Alzheimer's disease that exercise counteracts and provides evidence-informed principles for prescribing exercise to improve cognition as a reference point for formulating personalizable prescriptions.

Keywords: aging, cognition, dementia, exercise, FITT, prescription

INTRODUCTION

Alzheimer's disease and related dementias can be debilitating health conditions causing individuals to lose their ability to communicate, recognize family members, and adequately care for themselves. Currently, over 55 million people have dementia worldwide, and without an effective intervention, that number is projected to double every 20 yr to affect over 150 million people by 2050 (1). With no imminent cure, interventions are urgently needed to reduce dementia risk in healthy older adults. Exercise is a promising intervention (Fig. 1); however, exercise prescriptions for improving cognition do not exist. The goal of this graphical review is to briefly summarize the evidence and present principles for prescribing exercises that support brain health in aging.

Aging is accompanied by a gradual decline in memory and hippocampal neurogenesis, both of which are common and expected (Fig. 2). The loss of memory is caused by atrophy of the hippocampus, a key brain region involved in learning and memory. For individuals with Alzheimer's disease, the rate of hippocampal atrophy is 2.5 times faster than in healthy aging resulting in more rapid and ultimately debilitating cognitive decline that eventually interferes with daily living. In the absence of a cure, interventions that mitigate cognitive decline are critical.

Physical inactivity has been identified as the greatest modifiable risk factor for dementia prevention and can contribute to dementia risk as much as genetics (2). Individuals with lower aerobic fitness in midlife have a 1.92-fold increased risk of developing dementia later in life (3). This may not be surprising given that the health of the brain is intimately connected to the health of the body. When the body is not sufficiently active for good health, metabolic complications emerge, increasing one's risk of dementia (4). For example, hypertension caused by a sedentary lifestyle damages the blood vessels that feed the brain, causing small vessel disease and impairing cognition (5). Therefore, exercise interventions that are planned, structured, and repetitive to improve or maintain fitness represent an essential strategy for improving brain health (6). Indeed, exercise interventions that involve regular walking or jogging increase cardiovascular fitness, hippocampal blood volume, and memory, and it may never be too late to start (7) (Fig. 1). For example, sedentary older adults between 55 and 80 yr old who began walking three times per week for a year experienced improvements in memory in addition to a 2% increase in hippocampal volume (8). Older adults who began participating in a resistance training or Tai Chi intervention also experienced improvements in cognition and substantive neural changes in different brain regions, including the frontal lobe, suggesting the potential for greater cognitive benefits when engaging in a variety of different types of exercises (9,10).

EXERCISE FACILITATES MUSCLE-TO-BRAIN SIGNALING

Although consistent exercise protects the brain from neurodegeneration via multiple interacting pathways that enhance cerebral profusion, reduce inflammation, and clear amyloid plaques, exercise also benefits cognition directly by promoting neuroplasticity (11). In animal models, voluntary wheel running induced the proliferation of newborn brain cells in the dentate gyrus of the hippocampus, which improves memory across the life span, even in

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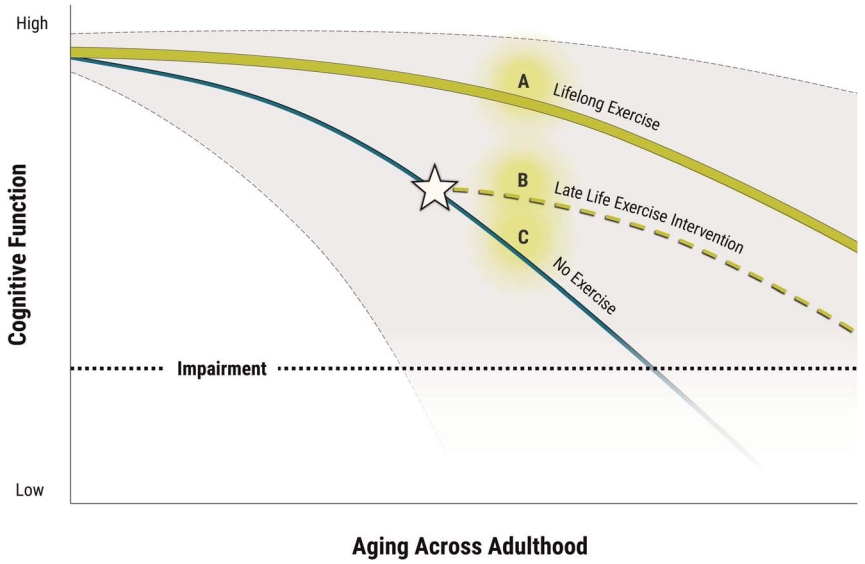


Figure 1. Hypothetical aging trajectories illustrate the protective effects of exercise on cognitive function, either by engaging in lifelong exercise or by engaging in exercise as an intervention later in life.

older animals (12). A key mediating factor is brain-derived neurotrophic factor (BDNF), which plays a major role in neuroplasticity, especially in the hippocampus where concentrations are critically reduced in the brains of Alzheimer's patients, yet drastically increased immediately after an acute bout of exercise (13,14). Emerging evidence suggests that muscle-derived signaling molecules, or myokines, activate BDNF in the brain. For example, the myokine l-lactate moves through the bloodstream and crosses the blood–brain barrier to the hippocampus where it activates BDNF (15) (Fig. 3). Importantly, l-lactate is abundantly excreted by contracting muscles during moderate-to-vigorous exercise, which may be why higher-intensity exercises increase BDNF and memory more than lower-intensity exercises (16,17). Of course, l-lactate is not the only myokine; there are multiple other pathways implicated in muscle-to-brain signaling, suggesting a rich network of communication (18).

THE PRINCIPLES FOR PRESCRIBING EXERCISE TO IMPROVE COGNITION

A personalizable approach to exercise prescription for brain health in aging is preferable given individual differences in response to exercise and heterogeneous health statuses among older adults. That said, practitioners can use evidence-informed principles to develop personalizable prescriptions. The principles for prescribing exercise to improve cognition in aging are summarized hereinafter and in Figure 4 using the FITT framework to specify frequency, intensity, time, and type (19,20):

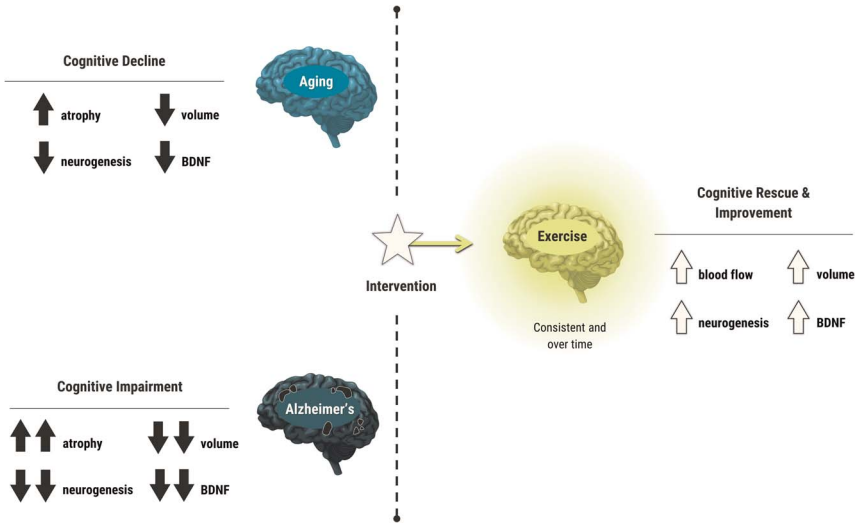


Figure 2. Neural changes in the hippocampus are associated with cognitive changes in aging and Alzheimer's disease. Engaging in exercise throughout life or engaging in exercise as an intervention later in life provides protective effects for cognition. BDNF, brain-derived neurotrophic factor.

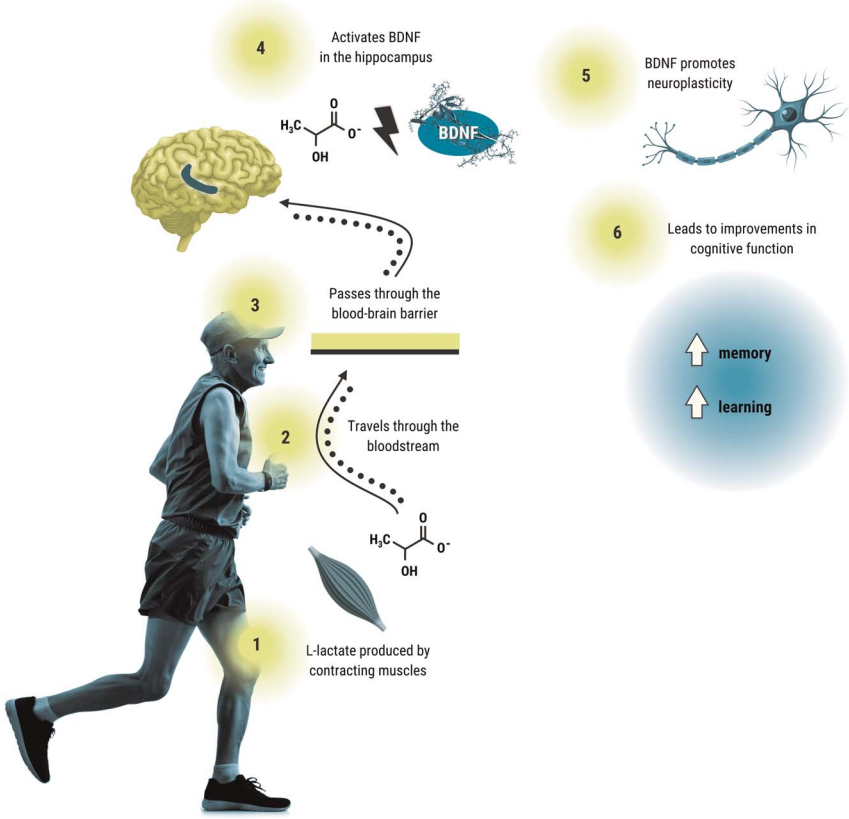


Figure 3. An example of muscle-to-brain crosstalk depicting the physiological and cognitive effects of vigorous exercise on the brain as mediated by the l-lactate and brain-derived neurotrophic factor (BDNF) pathways.

Frequency: As often as feasible
Intensity: Moderate-to-vigorous
Time:

A. Some movement is better than no movement
B. Weekly dose for clinically relevant cognitive improvements
   - Minimum:
     - 70 min of moderate exercise, or
     - 35 min of vigorous exercise
   - Optimal:
     - 140 min of moderate exercise, or
     - 75 min of vigorous exercise

Type:

- Aerobic: walking, swimming, cycling, hiking, etc.
- Resistance: strength training with bodyweight, resistance bands, weights, etc.
- Multicomponent: programs combining balance, resistance, and aerobic exercise
- Tai Chi or yoga

There is a remarkable similarity between these principles and the American College of Sports Medicine's (ACSM's) physical activity guidelines for general health (21). First, the intensity suggested in ACSM's physical activity guidelines is the same as is recommended for improving cognition, emphasizing the importance of moderate-to-vigorous exercise to facilitate muscle-to-brain signaling. The talk test can be used to gauge exercise intensity based on the ability to carry on a conversation (22). During moderate-intensity exercise, it is easy to carry on a steady conversation, whereas during vigorous-intensity exercise, only a few words can be uttered.

Furthermore, similar types of activities benefit cognition and general health. Specifically, evidence suggests that older adults should engage in aerobic and resistance exercises alongside balance-enhancing exercises like Tai Chi to reduce their risk of falls and help them feel safer while exercising (20). For additional brain health benefits, older adults are encouraged to engage in activities they enjoy while also trying new exercise modalities that simultaneously challenge the mind and body. Pairing exercise with a cognitively challenging task impacts the brain in synergistic ways, increasing neuroplasticity more than either activity alone (23). Walking and jogging while navigating through unfamiliar terrain, as is done in orienteering, is one way to make aerobic exercise more cognitively challenging (24). Evidence also points to the importance of exercising in socially supportive environments to help increase motivation and adherence while combating loneliness—a common chronic stressor for older adults associated with BDNF deficits, accelerated hippocampal atrophy, and cognitive decline (25,26).

A notable difference between ACSM's physical activity guidelines and exercise principles for cognition is that the latter are more flexible concerning time and frequency. Notably, there is no minimum threshold for the amount of exercise performed, meaning that some exercise is better than no exercise. Frequent movement breaks that interrupt prolonged sitting reduce the risk of dementia associated with sedentary behavior (4). The minimum and optimal

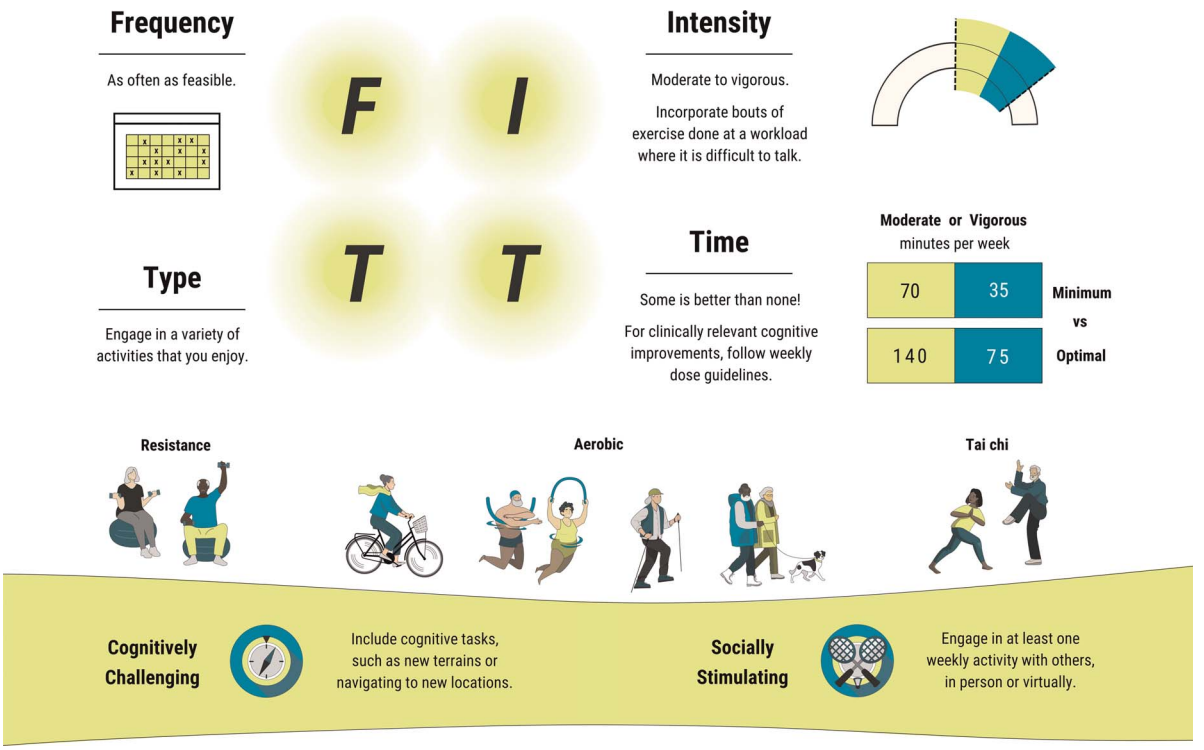


Figure 4. The principles for prescribing exercise to improve cognition in older adults.

duration of weekly exercise for aerobic and resistance exercises can be personalized to suit the individual's abilities and lifestyle. For example, weekly amounts could be divided into ~25–45 min of moderate exercise 3 d·wk^{-1} or ~20–35 min of vigorous exercise 2 d·wk^{-1} (19). Building flexibility into the principles for prescribing exercise is important because it allows for customizable programming that can be easily adapted to improve the feasibility and enjoyment of the exercises over the long term, because when using exercise for dementia, prevention consistency is key.

CONCLUSION

Engaging in consistent exercise elicits a multitude of brain health benefits that increase BDNF and neuroplasticity to support cognition in older adults. These evidence-informed exercise principles for cognition in aging include the optimal frequency, intensity, time, and type and represent an important starting point for the formulation of personalizable exercise prescriptions to help prevent dementia and keep the growing aging population healthier longer.

CONFLICTS OF INTEREST AND SOURCES OF FUNDING

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