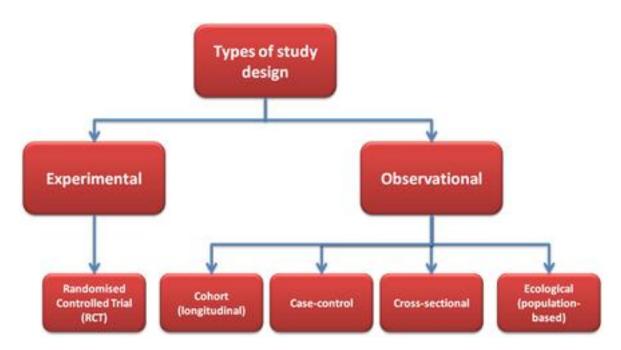
Adjourning Alzheimer's

Exercise (Day 67)

Many people are interested in the role of **exercise** in Alzheimer's. Sticking to an exercise program is more difficult than taking a medication. Moreover, exercise confers similarly modest benefits on cognition. However, unlike medications, the evidence suggests that exercise might slightly impact the Alzheimer's pathological process.

First, we must distinguish aerobic from resistance exercise. **Aerobic exercise** may be loosely defined as any activity that builds endurance by producing a sustained elevation in a person's heart rate and body oxygen uptake; examples of aerobic exercise include walking, cycling on an exercise bike, and raking leaves in the backyard. **Resistance exercise** may be defined as any activity that builds strength, often using weights or a person's own body weight, to fatigue a person's muscles; examples include squatting, lifting barbells, and moving furniture around the house.

Many **observational studies** show that people who undergo more aerobic or resistance exercise in mid-life develop less Alzheimer's later in life. However, although observational studies can tell us that more exercise is associated with less Alzheimer's, they cannot tell us whether the exercise "caused" the decrease in Alzheimer's - to do that, we need well-designed randomized controlled studies. If done correctly, **randomized controlled studies** can prove that one event "caused" another to occur.

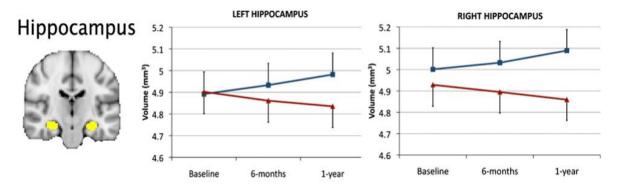


There are two types of scientific studies. Observational studies show associations, but cannot show whether one event "caused" another to occur. Randomized controlled studies can.

Several randomized controlled studies have examined the **effects of exercise on brain structure and function in humans**. Most of them pertain to aerobic exercise; let's go through some of the more prominent of these studies.

In 2006, a randomized controlled study examined **aerobic exercise versus stretching in 59 cognitively normal elderly people**. The aerobic exercise regime consisted of three 60-minute exercise sessions per week for 6 months. By the end of the study, there was a slight increase in cerebral cortex volume in the aerobic exercise group compared to the stretching group.

A later 2010 randomized controlled study examined aerobic exercise versus stretching in 120 cognitively normal elderly people. The aerobic exercise regime consisted of three 40-minute exercise sessions per week for 1 year. By the end of the study, there was a 2% increase in hippocampal volume in the aerobic exercise group, whereas there was a 1.4% decrease in volume in the stretching group.



Erickson and colleagues showed that after 1 year, the aerobic exercise group had a 2% increase in hippocampal volume, whereas the stretching group showed a 1.4% decrease in volume.

These two studies show that aerobic exercise may produce small but sure increases in size in the hippocampus and cerebral cortex, the two brain regions most afflicted in Alzheimer's. However, it is important to realize that both studies were done in cognitively normal elderly people, none of whom actually had cognitive impairment or Alzheimer's. Let's look at a couple more studies.

In 2008, a randomized controlled study examined aerobic exercise versus usual care in 170 elderly people with memory problems, but not dementia. The home-based aerobic exercise regime consisted of three 50-minute exercise sessions per week for 1 year. By the end of the study, there was a 1.3-point improvement on an 85-point cognitive scale, translating to a 1.5% improvement in cognition, in the aerobic exercise group compared to usual care.

Later, a 2011 randomized controlled study examined walking versus usual care in 21 nursing home residents with advanced Alzheimer's. The walking program consisted of four 30-minute walking sessions per week for 6 months. By the end of the study, there was only a 13% decline in mini-mental

state exam cognitive scores in the walking group, compared to a much higher 47% decline in scores in the usual care group.



Regular walking may benefit cognition, even in severe Alzheimer's.

These latter two studies show that aerobic exercise may produce small but sure gains in cognition for people with cognitive impairment. The 2011 study was small in numbers, but impressive in that it showed that a walking program alone may slow down cognitive decline - even in people with severe Alzheimer's.

There are other pros and cons to exercise worth considering before embarking on an exercise regime. In addition to the potential cognitive benefits, **potential pros** include a reduction in osteoporosis and bone fracture risk, a reduction in age-related muscle loss, and beneficial effects on mood disorders such as depression and anxiety. Obviously, the **potential cons** of exercise are an increased chance of injury or falls while exercising, and the extra physical strain may unmask an existing heart problem, sometimes even in the form of a heart attack. However, if a person is careful and uses a certified trainer to start things off, the chances of having an adverse event are rather small.

Let's sum up. Exercise may modestly increase hippocampal and cerebral cortex volumes in cognitively normal elderly people, and it may modestly improve cognition in cognitively impaired elderly people, including people with Alzheimer's. The potential increases in brain volume and cognition are **small**, on the order of 1-2% after 1 year, but given that neuron loss in Alzheimer's produces hippocampal and cerebral cortex atrophy, it is tempting to conclude that exercise **might impact the Alzheimer's pathological process** by slowing down neuron loss and brain atrophy. However, we need more randomized controlled studies on the effects of exercise in people with Alzheimer's before this can be definitively stated.

A regular exercise program is somewhat difficult to stick to, but exercise can **take you part-way to the edge**, the place where you challenge yourself. Exercise may help you reclaim some of your epigenetic power; it may awaken the anti-Alzheimer's genes that already exist within you, the ones we want to unleash against the pathological process. However, we must not overplay the benefits of exercise, for they are small. Let's keep looking!

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References

- (1) Ahlskog et al. 2011. Physical Exercise as a Preventive or Disease-Modifying Treatment of Dementia and Brain Aging. Mayo Clin Proc 86(9), 876-884.
- (2) Erickson et al. 2010. Exercise training increases size of hippocampus and improves memory. PNAS 108(7), 3017-3022.
- (3) Colcome 2006. Aerobic Exercise Training Increases Brain Volume in Aging Humans. J Gerontol 61A(11), 1166-1170.
- (4) Lautenschlager et al. 2008. Effect of Physical Activity on Cognitive Function in Older Adults at Risk for Alzheimer Disease: A Randomized Trial. JAMA 300(9), 10287-1038.
- (5) Venturelli et al. 2011. Six-Month Walking Program Changes Cognitive and ADL Performance in Patients With Alzheimer. Am J Alzheimers Dis Other Demen 26(5), 381-388.