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The Gravity of Weight

A Body in Motion: Exercise and Cognition

The science behind the relationship of exercise to cognitive functioning

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The famous six-day bicycle race in Berlin's sport stadium, 1929.

Source: Alamy images, used with permission.
Photographer: Album

Following high school graduation, these boys seem without direction or ambition and have very limited opportunity for advancement. They spend many days sunbathing and diving into the old stone quarry. Only when they envision a highly competitive bicycle race against the perceived superior community of university students, do they become motivated. Significantly, our protagonist Dave is not only the most determined but also the smartest of his friends. And the more he excels competitively in his physical prowess, the more he can allow himself to aspire to greater cognitive challenges and higher education. Ultimately, he is the only one of his group who will matriculate at prestigious Indiana University.



Gustave Courbet's "The Stone Breakers," 1849. Apparently, this painting was destroyed by fire in 1945. The young men in "Breaking Away" were called "cutters" because their fathers had been stone cutters in their younger years.
Source: Wikimedia Commons/Public Domain

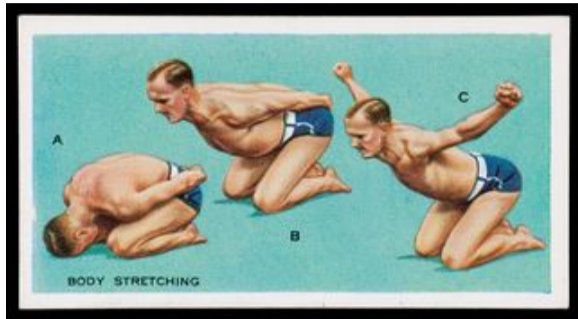


"Men in uniform doing physical exercise." Color lithograph. Researchers believe that all forms of exercise, including stretching, may benefit cognitive functioning.
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Physicians have known of the importance of physical activity, including walking, on health, at least since the time of Hippocrates and his treatise *Regimen*. (Book II, Precope, 1952) In general, *physical activity* is defined by the World Health Organization "as any bodily movement, produced by skeletal muscles, that requires energy expenditure; *exercise* is physical activity that is planned, structured, and repetitive for the purpose of conditioning parts of the body." (Frederiksen et al, *Journal of Alzheimer's Disease*, 2018)

Clinicians and researchers have become increasingly interested in studying the effects of non-pharmacological strategies, such as physical activity, on cognition as the population ages and medications have generally failed to prevent the onset and progression of the neurodegenerative diseases of the elderly. More than 200 diseases may cause dementia, which is the general term for these diseases that impair memory and judgment and ultimately the ability to function independently in the activities of daily living. (Pedersen and Saltin, *Scandinavian Journal of Medicine & Science in Sports*, 2015) Alzheimer's Disease is the most common of these and accounts

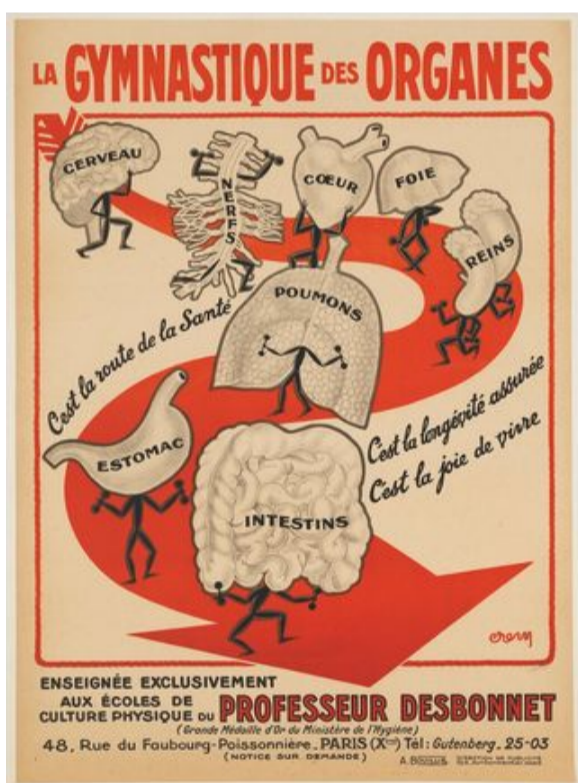
for from 60 to 80% of the cases of dementia. (Guure et al, *BioMed Research International*, 2017; Cass, *Current Sports Medicine Reports*, 2017) While old age is the strongest risk factor for developing dementia, it is not necessarily a natural consequence of aging. Statistically, about 3% of people between ages 65 and 74 develop dementia but almost half the population will develop some form of it after the age of 85. (Pedersen and Saltin, 2015) By the year 2025, the U.S. is projected to have about 7.1 million people living with dementia. (Guure et al, 2017) There are both *modifiable* (e.g. cardiovascular disease, obesity, smoking, diabetes, depression, social engagement, physical activity) and *non-modifiable* (e.g. family history, age, genetic mutations such as APOE-4) risk factors for the development of dementia. (Guure et al, 2017)



"Body Stretching." Ironically, this image was one in a series of color cigarette cards produced in 1939 by British American Tobacco to promote physical fitness through exercise.

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Mild cognitive impairment (MCI) is a syndrome in which there is a decline in cognitive functioning greater than expected for age and education but without interfering with daily life activities. About half of those who develop MCI will progress to Alzheimer's Disease within five years. (Cass, 2017) Typically, those with Alzheimer's Disease develop neurofibrillary tangles and plaques of beta-amyloid and a progressive loss of neurons in the hippocampus, an area crucial to memory, among other pathological changes. (Cass, 2017; Bernardo et al, *Brain Pathology*, 2016) There is speculation that these changes, at least in some forms of Alzheimer's (e.g. sporadic and late-onset), are related to a *dysregulation* of mitochondria, the powerhouse of the cell; since the brain uses about 20% of the body's oxygen, it is *highly dependent* on the production of energy by mitochondria. As a result of this early dysregulation and the accumulation of beta-amyloid and other substances, there is a disruption of axonal transport, depletion of ATP, and the synapse "starves." (Bernardo et al, 2016) Because some studies report decreased glucose metabolism and increased levels of oxidative stress in the brains of those with Alzheimer's, some researchers have hypothesized that Alzheimer's is a form of diabetes, i.e., type 3 diabetes. (Trigiani and Hamel, *Journal of Cerebral Blood Flow & Metabolism*, 2017) Though symptoms can vary, they often include a progressive cognitive decline, confusion, disorientation, apathy, agitation, anxiety, and depression. (Bernardo et al, 2016)



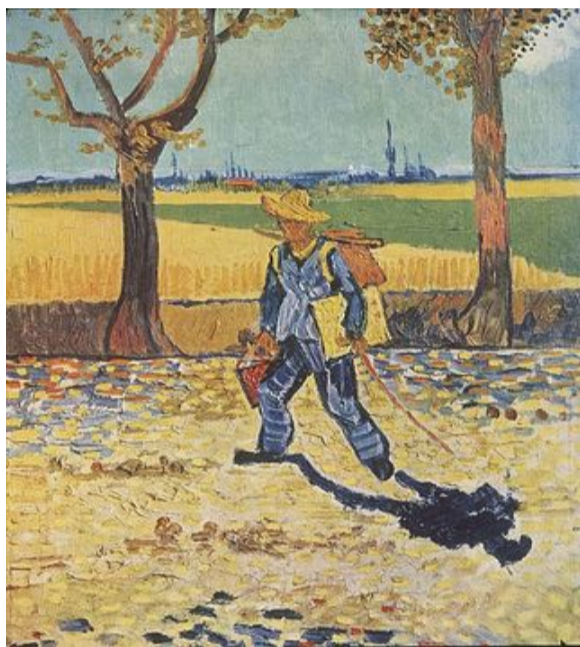
"Organs of the body performing gymnastic exercise." Edmond Desbonnet, early 20th century lithograph. Exercise potentially affects many organs of the body, but its health-inducing effects on the brain and the heart are particularly significant.

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Evaluating the effects of exercise on cognitive functioning, though, is complex, particularly when conducting meta-analyses or systematic reviews in which studies have different sampling techniques, lengths of observation, methods, definitions of exercise (e.g. type, amount, intensity), reports of compliance, and sample size. (Ross et al, *British Journal of Sports Medicine*, 2019) There is also the *implication* that a one-time measurement of physical activity reflects a stable pattern of behavior. (Cheng, *Current Psychiatry Reports*, 2016) Many studies suffer from poor methodological quality (Frederiksen et al, 2018) and even rely on inaccurate self-report questionnaires to assess physical activity. (Guure et al, 2017) Further, some researchers have found a bias or "blind spot" against evidence supporting exercise as a viable alternative to medications: "the changing landscape seems to increasingly favor drug interventions over strategies to modify lifestyle." (Naci and Ioannidis, *British Journal of Sports Medicine*, 2015)

Most studies, both human and animal, strongly support that exercise has a "neuro-protective" effect on cognition, and some researchers even consider exercise "vascular medicine." (Green and Smith, *Cold Spring Harbor Perspectives in Medicine*, 2018) Many questions remain, including the optimum dose and type of exercise (e.g. aerobic, anaerobic or combination) for maximum benefit. (Alkhadi, *Molecular Neurobiology*, 2018) And there are few studies that "allow firm conclusions" about the effect of exercise on those who already have the diagnosis of dementia. (Pedersen and Saltin, 2015)

Over 80% of the brain's gray matter have shown "significant modifications" related to exercise. (Batouli and Saba, *Behavioral Brain Research*, 2017) But it is an increase in actual cardio-respiratory fitness that may be "crucial." (Barnes and Corkery, *Brain Plasticity*, 2018) Theoretically, exercise can prevent dementia by its effect on increasing the volume of the hippocampus, possibly mediated by a brain-derived neurotrophic factor (BDNF). (People with dementia have low levels of BDNF) BDNF seems to be the key mediator of cognition as it is highly expressed in the hippocampus and cortex. (Kennedy et al, *Journal of Alzheimer's Disease*, 2017) Physical activity/exercise not only increases blood volume and enhances blood flow to the brain, but it improves respiratory function. It also can affect brain structures by the growth of new neurons, but assessing neurogenesis in humans is "fairly difficult," (Cass, 2017) and it is not clear how the formation of new neurons (neurogenesis) can be beneficial (though these may integrate into existing circuits.) Physical activity/exercise affects the brain's "synaptic architecture" by increasing dendritic spines, density, and length. (Alkhadi, 2018) In general, it stimulates growth factors such as BDNF and insulin-like growth factor, down-regulates oxidative stress and inflammatory responses, and reduce the brain's exposure to neurotoxic substances such as beta-amyloid and excessive glucose. (Cheng, *Current Psychiatry Reports*, 2016) As a result of all these mechanisms, it may improve attention, processing speed, and executive function. (Cass, 2017; Trigiani and Hamel, 2017)

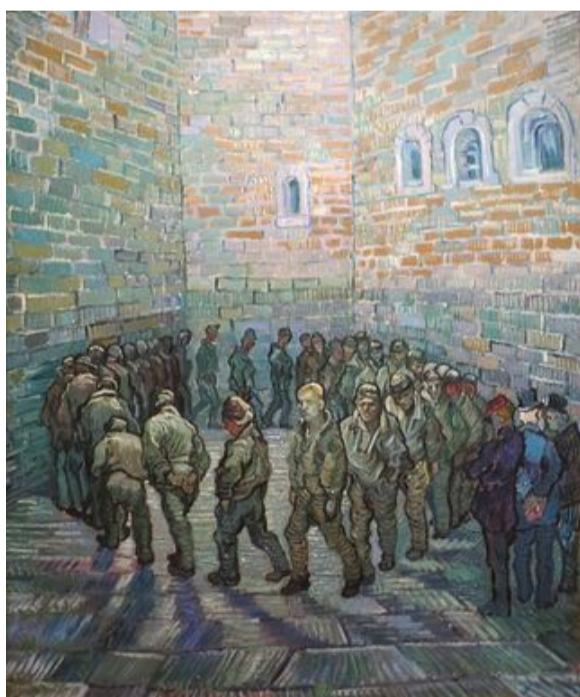


"A Painter on his Way to Work," by van Gogh, 1888. This painting, originally in the Kaiser-Friedrich-Museum in Germany, was destroyed by fire in 1945. Even walking may be beneficial for a healthy brain. Researchers still do not know exactly how much or at what intensity to recommend for exercise to be maximally beneficial.

Source: Wikimedia Commons/Public Domain

How do muscles, though, actually "communicate" with the brain? In recent years, researchers have found, first in mice and then in humans, a myokine (i.e, a substance released by the muscles) called cathepsin B that crosses the blood-brain barrier and increases with exercise and may be involved in mediating exercise-induced improvement in neurogenesis in the hippocampus. Researchers support the importance of exercise "through the lifespan" as a positive influence on neurogenesis, particularly in the hippocampus. (Pedersen, *Nature Reviews/ Endocrinology*, 2019)

There is, though, more need for standardization of measurement and a need to consider day-to-day variability in a subject. (Ross et al, 2019) And there is apparently considerable variability among individuals in their responses to exercise as measured by maximal oxygen uptake (VO_2 max); most exercise studies focus on group differences and ignore inter-individual cardio-respiratory fitness. Exercise must be tailored to the individual. Further, some people are genetically are more susceptible to the effects of exercise than others, just as some mice can be bred to be *high-responders* or *low-responders*. (Ross et al, 2019)



"Prisoners Exercising," or "The Round of the Prisoners," by van Gogh, 1890. Pushkin Museum, Moscow. Perhaps even prisoners, under these terrible conditions, may derive some benefit from exercise.

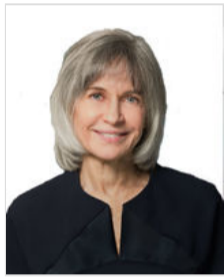
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Bottom line: Over 80% of the brain, and particularly the hippocampus that is so crucial for memory, seem to be modifiable by physical activity/exercise. Exercise can increase hippocampus volume, increase synaptic plasticity, increase blood flow to the brain, decrease age-related brain atrophy in many areas, and increase the synthesis and release of neurotrophins and growth factors. In other words, physical exercise offers protection against cognitive decline by inducing both neurochemical and structural changes within the brain. The volume, intensity, type, and duration required for these effects are still unknown. And it may not just be physical activity/exercise itself but an improvement in cardio-respiratory fitness that is necessary. Further, some people are more susceptible genetically to the effects of exercise. But like the adolescent boys of *Breaking Away*, it is probably never too early to start to increase physical activity/exercise, and it may never be too late. As Kierkegaard has said, "Health and salvation can only be found in motion."



The School of Public Health, one of the many beautiful stone buildings on the campus of Indiana University in Bloomington, where "Breaking Away" was filmed in the late 1970s. Source: Wikimedia Commons/Public Domain.

About the Author



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