Outline on Exercise and Brain Function

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Abstract

Exercise is seen to physically improve the health and function of the brain. This involves a variety of molecular and cellular mechanisms, including significant increases of beneficial neurotrophic factors like BDNF. In addition, neurogenesis in the hippocampus is also increased after exercise. Hippocampal vascular structures, like blood flow, are improved. Plasticity is also improved. Additional molecular mechanisms can contribute to alleviate symptoms of aging and more serious neuropathic diseases. Negative factors like inflammation and reactive oxygen species are mitigated.

For quite a while, people considered the mind and body separate. René Descartes himself proposed the idea of what is called the Cartesian dualism, that whatever happens to our body leaves our minds untouched. It was believed only the mind can truly affect itself, and thus was born "I think, therefore I am." More recent scientific advances proved quite the opposite. Our minds come from intricate neural connections in our brains. Both our bodies and outside influences affect the flow of messenger molecules in our brains analogously to the way our livers or muscles can be affected, to name a few. If anything, our minds could just be an extension of our body, rather than its own separate entity. For example, one of the best ways to improve our brain function is through exercise. While research is still discovering the complete effects of exercise on the brain, many molecular and cellular mechanisms have already been elucidated. Exercise is known to improve neural plasticity, increase neurotransmitter efficiency, expand neuron counts, and even prevent cognitive diseases.

One of the most significant findings of exercise on brain health was elucidated through neurotrophic factors. These molecules act as growth factors for brain cells, increasing cell growth, signaling, and neural wiring. Despite the importance of these factors for our brain, their expression depends on physical exercise. One of the most important neurotrophins is brain-derived neurotrophic factor (BDNF). This molecule can interact with synaptic development of dendrites and axons, allowing them to form specialized connections for specific neuron communication. In turn, better neural communication can aid in learning (Cohen-Cory et al., 2011). Improved learning can occur immediately after exercise. Human subjects were able to improve cognitive performances in learning new material after running on a treadmill. The increase in memory is correlated with BDNF concentration in the bloodstream that also spikes during exercise (Winter et al., 2007). It is also shown that consistent exercise can increase BDNF levels compared to sedentary behavior in rats (Berchtold et al., 2005). Conversely, blocking BDNF contributes to decreased synaptic efficacy and decreased vesicle proteins, both directly harming communication between neurons (Vaynman et al., 2006).

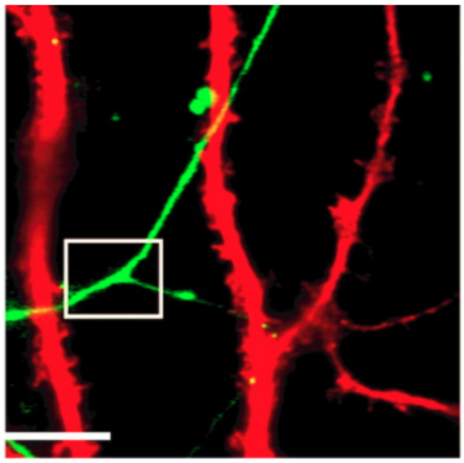

Figure 1A: Axon expressing BDNF-GFP (in green) superimposed with dendrites of second neuron, stained with MAP2 (in red) (Kohara, 2001).

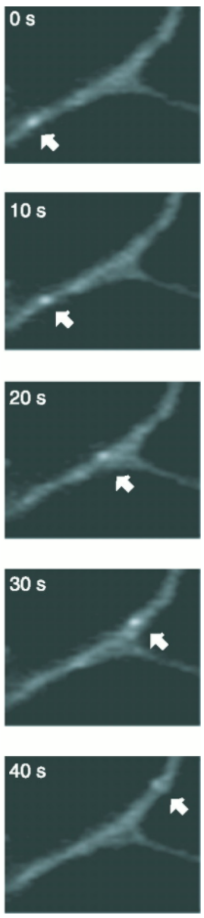

Figure 1B: Movement of BDNF-GFP in axon (Kohara, 2001).

(Other hormones, like the catecholamines dopamine, epinephrine, and norepinephrine were shown to increase through exercise. These hormones are thought to be associated with learning, as they increase signaling in the brain. It is also shown that increased levels of BDNF correlate with physical activity (Winter et al., 2007). There are also other neurotrophins with levels that increase with exercise. An example is IGF-1, which increases neuron counts in the hippocampus. (Trej et al., 2001). NMDA receptors, which are responsible for the health and function of neurons, also increase with exercise (Farmer et al., 2004). Other molecules include TNF-α and vascular endothelial growth factor (VEGF). Both these molecules improve vascular health, including blood vessel growth and differentiation throughout the body. TNF-α can also increase integrin protein production, which helps cells bind to extracellular structures. These activities can directly impact the vascular supply of nutrients in the brain (Ding et al., 2006). Because exercise can promote neurotrophic factors and hormones to signal in the brain, all of these effects can lead to a much healthier brain.

While the human brain's overall structure remains stable over adulthood, it can undergo slight changes for the better. Exercise can induce these modifications to physical structures. For example, exercise appears to promote neurogenesis, the creation of new neurons. While in most of the brain, the number of neurons stays the same throughout life, the number of neurons can increase in the hippocampus. Most of the newly generated neurons appear in the hippocampal dentate gyrus, a region highly responsible for learning and storing long-term memories (Cho et al., 2013). Higher rates of cell growth appeared in these regions for rats performing consistent treadmill exercise (Heo et al., 2014). Brain scans in animal studies have also shown improvement from exercise in vascular structures in the brain, like increased blood flow and permeability of the blood brain barrier (Yau et al., 2014). These are all correlated with supplying nutrients and cleansing factors to grow and protect neurons. Brain scans in mice have also confirmed greater growth in hippocampal areas after consistent exercise. Similarly, brain scans in humans have shown analogous changes in the hippocampus as well. The same human subjects were tested in cognitive trials like delayed recall, recognition, and source memory. Higher cognitive performance correlated significantly with more exercise (Peirera et al., 2007). Additionally, young neurons appear to contribute a greater learning potential. New neurons generate faster calcium and sodium concentration spikes, affecting action potentials and signal transduction to neighboring neurons. These neurons also change their behaviors more permanently to signals, compared to older neurons. (Schmidt-Hieber et al., 2004). These neurons are able to express greater responses to lower levels of signal as they mature, exhibiting long term potentiation. Older neurons are more resistant to these changes (Ge et al., 2007). Long term potentiation indicates increased plasticity, the ability to rewire neural circuits. Plasticity in the brain allows it to encode new information and boosts learning. Therefore, as consistent exercise increases new neurons, it ultimately leads to more plasticity to the brain and thus increased learning.

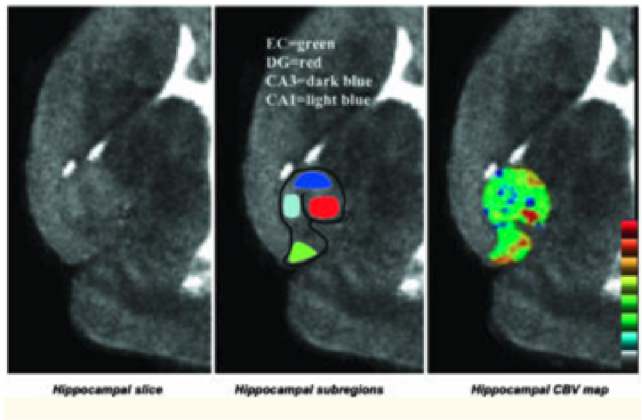

Figure 2A: Heat map showing neurogenesis activity in mice, based on cerebral blood volume (Peirera et al., 2007).

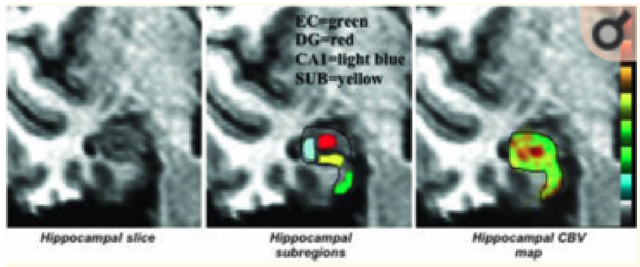

Figure 2B: Heat map showing neurogenesis activity in humans, based on cerebral blood volume (Peirera et al., 2007).

Exercise is associated with broader health effects as well. Even though neurological decline is correlated with aging, exercise has been shown to minimize and reverse these trends. For example, for older subjects, aerobic fitness has been associated with better performances on cognitive tasks, as well as retaining larger hippocampal sizes in the brain (Erickson et al., 2009). These trends also extend to symptoms of neurodegenerative diseases that tend to amplify in older age. For example, as exercise promotes neurogenesis in the hippocampus, it helps combat neuron loss in many diseases like Alzheimer's (Yau et al., 2014). Exercise is also seen to alleviate symptoms of diseases. In rats exhibiting symptoms of Parkinson's disease, consistent exercise appears to reduce short term memory damage (Cho et al., 2013). Similar findings are shown for rats exhibiting Alzheimer's symptoms, with exercise correlated with better performance in spatial learning (Heo et al., 2014). While exercise cannot cure neurodegenerative diseases, they can alleviate symptoms and improve quality of life for people with these diseases.

In addition to preventing neurodegenerative conditions, exercise also protects against physical damage to the brain. For example, exercise is shown to protect against stroke-like symptoms in the brain. In stroke, blood flow is deficient in the brain, which can cause swelling and cell death. In animal studies, these symptoms are reduced in animals who performed consistent exercise (Ding et al., 2006). Other physical damages to the brain come from reactive oxidative species (ROS), for example.

These are molecules that can originate as byproducts of metabolic reactions. However, ROS react inappropriately with other molecules in cells, stopping proper pathways for normal function. This can even affect signaling and cell survival. Exercise increases the amount of antioxidant enzymes in cells, protecting cellular function (Radak et al., 2016). In animal studies, the rat brain showed an increase in protease activity in cells in response to exercise. These proteases are responsible for breaking down proteins, including misfolded and damaged proteins that act as ROS (Ogonovsky et al., 2005). Exercise provides increased antioxidant protection, which protects the overall health and function of the brain.

Overall, exercise appears to play an overwhelmingly positive influence on the brain. Neurotrophins increase their function after exercise, promoting brain health and learning. Structures of the brain responsible for learning also change. Neurons increase their potential for efficient communication. Exercise also alleviates aging and neurodegenerative symptoms. Despite the knowledge already known about exercise, there is still much more to learn about its effects on the brain. Exercise also improves the rest of the body, in addition to the brain. Based on current knowledge of physical activity, consistent exercise would be a wise choice for improving quality of life.

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