

## **Donuts, Exercise, and the Neuroplasticity-Molecule BDNF**

**By Teresa Straub**

### **BDNF and the Brain**

Every single morning for the last five years you take a morning run then enjoy a cup of coffee with a donut before you start your day. You figure something about your routine helps you think better. You attribute the benefit to the crisp air and the sugar rush. But what if there is something deeper happening in your brain to super-charge the cognitive function? Exercise and diet affect levels of a protein in the brain, called Brain-Derived Neurotrophic Factor (BDNF), associated with neuronal development and survival in the brain (Jones, 1994). This protein is made in nerve cells (neurons), then released out of the neuron to affect other neurons close by. On the outside of neuron cells there are receptors that molecules can bind to and cause activity in the cell. The BDNF can bind to at least two types of receptors on other brain cells (Fundin, 1997; Nakagawara, 1994). When it binds to those receptors on the outside of the neuron, it triggers chemical pathways inside the neuronal cell to increase survival of that neuron and increase neuroplasticity – the connections between neurons (Glass, 1991). BDNF has two prominent roles: cell development and cell survival (Wu, Hongtao, et al., 2008). BDNF is a protein cells release to support and guide the development of new brain cells, a process called neurogenesis. BDNF promotes brain development through the growth and differentiation of new cells (Cheng, 2003). Brain development occurs as new cells mature into neurons and establish connections with other neurons. These connections are important for communication between cells, which is how the brain

carries out functions like thinking, memory, and desires. BDNF also encourages the growth and supports survival of existing neurons as they create new connections to other neurons (Dijkhuizen, 2005; Aguado, 2003). Among many other effects, BDNF activates excitatory (NMDA) receptors through phosphorylation which bind the brain's excitatory neurotransmitter, glutamate, and causes brain activity involved with learning and memory (Lin, 1998). BDNF expression mediates many pathways within neurons to improve cognitive function, including learning and memory. BDNF protein expression has been shown to be influenced by diet and exercise.

### **Diet and BDNF**

Broccoli has caused innumerable toddler tantrums and Brussels sprouts may still not be your favorite. However, vegetables may have been the secret to the academic performance of that kid in your high school who always got perfect grades. Studies are showing that a nutrient-rich, wholesome diet may improve neuronal plasticity and learning. One such study was a randomized clinical trial in Spain using the Mediterranean diet (MeDiet). The study assigned 243 participants to three years of one of three dietary interventions: control (low-fat) diet, MeDiet supplemented with virgin olive oil (MeDiet + VOO), or MeDiet supplemented with nuts (MeDiet + Nuts) (Sánchez-Villegas, 2011). After three years, the participants assigned to the MeDiet + nuts had significantly higher BDNF levels while overall higher levels of BDNF were observed in participants assigned to one of the two MeDiets. This study shows how important nutrient-dense, whole foods are for healthy brain function supported by BDNF.

What specifically about the Mediterranean diet is so powerful to increase BDNF levels? One element could be the Omega-3 fatty acids. Researchers have found that Omega-3 supports neurons making new connections to other neurons and regulates what proteins are made in the cell, which includes BDNF protein (Hashimoto et al., 2002). One study took this farther to investigate the effects of Omega-3 on BDNF-related changes after a traumatic brain injury (TBI) (Wu, 2004). Rats ate normal diets or diets supplemented with omega-3 fatty acids for four weeks then underwent a TBI. The rats eating normal diets had decreased levels of BDNF after the TBI while the rats supplemented with omega-3 had normal levels of BDNF and did not demonstrate the learning disability other rats suffered after the TBI. This suggests that omega-3 fatty acids can support neuronal health, especially offering protection against TBI-related neuron impairment. Together these studies suggest a Mediterranean diet high in Omega-3 fatty acids may be the secret to increasing your levels of BDNF, thereby improving neuronal plasticity.

What if the Mediterranean diet is not your thing: is there room for your morning donut, afternoon bag of potato chips, and nightly ice cream amongst the vegetables in your diet? One study performed by researchers at the UCLA Brain Injury Research Center suggests high fat, high sugar foods may drag down your cognitive performance by impairing brain plasticity. Maybe that morning donut you eat after your run is not helping you think better! The study finds a high fat, refined sugar diet reduces BDNF, neuronal plasticity, and learning in rats (Molteni, 2002). High levels of BDNF correlate with better performance on spatial memory tasks in rats, demonstrating how important BDNF is to cognitive function. The levels of

BDNF can vary with diet, as this study shows. After two months on a high fat, refined sugar diet similar to industrialized western diets, rats showed significant reduction in BDNF levels and poor spatial learning performance. After six months, the BDNF protein levels were dramatically reduced in the hippocampus – the memory center of the brain. The rats were kept on the diet up to twenty-four months at which time their BDNF mRNA values – the model for making the BDNF protein – were the lowest. This study demonstrates that the typical American diet high in fat and sugar can decrease levels of BDNF, which regulates neuronal plasticity and function, ultimately affecting learning and memory.

These results were confirmed by another study, this one was performed on mice in Korea, which suggests a diet high in saturated fat decreases BDNF and therefore impairs new neuron growth (Park, 2010). After seven weeks on a high fat diet, levels of BDNF in mice were reduced and neurogenesis was impaired. These results agree with what is known about the role of BDNF in supporting the generation and differentiation of new neuron cells. If levels of BDNF are low, this should affect the cells that BDNF supports, which is what the studies suggest. Maybe your Korean grandmother had it right when she told you to eat your fish and vegetables. Was she this smart because of the BDNF increased by her fish and vegetables or from all the exercise walking to the market and carrying the produce home?

## **Exercise and BDNF**

As a common saying goes, “No pain, no gain.” As research progresses, a more common quip associated with exercise may become, “No pain, no brain.”

Neuroscience research is drawing the connections between exercise and the benefits specific to the brain via an increase in BDNF protein levels. One such research study occurred on a group of young, sedentary male university students (Griffin, 2011). The students participated in a game where they matched faces with names. The task was repeated after half of the students exerted strenuously for 30 minutes on an exercise bike. The group that exercised performed significantly better than the group that did not exercise when the memory task was repeated. Analysis of the participants’ blood during the study showed elevated levels of BDNF in the participants who exercised before performing the task and no change in the levels of BDNF in the other participants. This suggests not only that exercise improves brain function, but specifically improves memory and recall with an increase in availability of BDNF.

Exercising increases BDNF proteins, which support healthy cognitive function, but how long do the effects last? A study used mice to assess the prolonged effects of exercise on cognitive performance (Berchtold, 2010). A group of mice were tested for memory by putting them in a water maze and having them swim to a platform. Each time they do this should be faster since they remember where the platform is located. They were tested one week after exercise, two weeks after exercise, or after three weeks of consecutive exercise. The best memory occurred immediately after exercise and the fastest acquisition occurred one week after

exercise. The highest levels of BDNF occurred immediately after exercise, and slowly returned to baseline by weeks three and four after exercise. Although this study was performed on mice, it implies that the beneficial effects of exercise on BDNF levels, and therefore on cognitive function, continue after exercise. The effects of exercise on neurogenesis and neuron survival are strongest immediately after exercise and gradually decrease over several weeks. If you want to improve cognitive function, go through a little exercise pain to gain your brain.

Exercise has been shown to increase BDNF levels while high fat diets have shown to decrease BDNF levels. Perhaps the morning runs – and not the donuts – are the beneficial part of your morning routine on your cognitive function. Could the effects neutralize each other so you can eat as many donuts as you want without risking a decrease in the levels of BDNF as long as you exercise? This is essentially the question one group of researchers at UCLA Brain Injury Research Center set out to answer (Molteni, 2004). They fed mice a high fat diet for two months and some of the mice had access to a running wheel while the other mice were sedentary. They found that the mice with access to exercise did not have reduced levels of BDNF like the sedentary mice, and they had better memory and learning. This demonstrates that lifestyle factors can influence cognitive function and neuroplasticity. However, one logistical question still remains: how far do you have to run to counter the effect of a donut on your BDNF levels?

## References

- Aguado, Fernando, et al. "BDNF regulates spontaneous correlated activity at early developmental stages by increasing synaptogenesis and expression of the K<sup>+</sup>/Cl<sup>-</sup>-co-transporter KCC2." *Development* 130.7 (2003): 1267-1280.
- Berchtold, Nicole C., Nicholas Castello, and Carl W. Cotman. "Exercise and time-dependent benefits to learning and memory." *Neuroscience* 167.3 (2010): 588-597.
- Cheng, Aiwu, et al. "Nitric oxide acts in a positive feedback loop with BDNF to regulate neural progenitor cell proliferation and differentiation in the mammalian brain." *Developmental biology* 258.2 (2003): 319-333.
- Dijkhuizen, Paul A., and Anirvan Ghosh. "BDNF regulates primary dendrite formation in cortical neurons via the PI3-kinase and MAP kinase signaling pathways." *Journal of neurobiology* 62.2 (2005): 278-288.
- Fundin, B. T., et al. "Differential dependency of cutaneous mechanoreceptors on neurotrophins, trk receptors, and P75 LNGFR." *Developmental biology* 190.1 (1997): 94-116.
- Glass, David J., et al. "Trkl3 mediates BDNF/NT-3-dependent survival and proliferation in fibroblasts lacking the low affinity NGF receptor." *Cell* 66.2 (1991): 405-413.
- Griffin, Eadaoin W., et al. "Aerobic exercise improves hippocampal function and increases BDNF in the serum of young adult males." *Physiology & behavior* 104.5 (2011): 934-941.
- Hashimoto, M., Hossain, S., Shimada, T., et al. (2002). Docosahexaenoic acid provides protection from impairment of learning ability in Alzheimer's disease model rats. *J. Neurochem.* **81**, 1084–1091.
- Jones, Kevin R., et al. "Targeted disruption of the BDNF gene perturbs brain and sensory neuron development but not motor neuron development." *Cell* 76.6 (1994): 989-999.
- Lin, Siang-Yo, et al. "BDNF acutely increases tyrosine phosphorylation of the NMDA receptor subunit 2B in cortical and hippocampal postsynaptic densities." *Molecular brain research* 55.1 (1998): 20-27.
- Molteni, R., et al. "Exercise reverses the harmful effects of consumption of a high-fat diet on synaptic and behavioral plasticity associated to the action of brain-derived neurotrophic factor." *Neuroscience* 123.2 (2004): 429-440.

- Molteni, Raffaella, et al. "A high-fat, refined sugar diet reduces hippocampal brain-derived neurotrophic factor, neuronal plasticity, and learning." *Neuroscience* 112.4 (2002): 803-814.
- Nakagawara, Akira, et al. "Expression and function of TRK-B and BDNF in human neuroblastomas." *Molecular and cellular biology* 14.1 (1994): 759-767.
- Park, Hee Ra, et al. "A high-fat diet impairs neurogenesis: involvement of lipid peroxidation and brain-derived neurotrophic factor." *Neuroscience letters* 482.3 (2010): 235-239.
- Reynolds, Gretchen. "How Exercise Benefits the Brain." *New York Times* (2011).
- Sánchez-Villegas, Almudena, et al. "The effect of the Mediterranean diet on plasma brain-derived neurotrophic factor (BDNF) levels: the PREDIMED-NAVARRA randomized trial." *Nutritional neuroscience* 14.5 (2011): 195-201.
- Wu, Aiguo, Zhe Ying, and Fernando Gomez-Pinilla. "Dietary omega-3 fatty acids normalize BDNF levels, reduce oxidative damage, and counteract learning disability after traumatic brain injury in rats." *Journal of neurotrauma* 21.10 (2004): 1457-1467.
- Wu, Hongtao, et al. "Simvastatin-mediated upregulation of VEGF and BDNF, activation of the PI3K/Akt pathway, and increase of neurogenesis are associated with therapeutic improvement after traumatic brain injury." *Journal of neurotrauma* 25.2 (2008): 130-139.