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# Exercise, Brain Plasticity, and Brain-derived Neurotrophic Factors



by Kyle R. Hill

*Physical exercise influences neurobiological processes and cognitive abilities. For example, it increases the expression of brain-derived neurotrophic factor (BDNF), a protein responsible for maintaining synaptic connections as well as neuronal development, growth, and survival. The increase of BDNF promotes brain plasticity and has been shown to aid recovery from brain injuries, as well as to improve cognitive function in older adults. Recent studies with well-exercised rats showed strong, positive correlations between BDNF levels, cognitive performance in maze tasks, and recovery from fluid-percussion injuries to the hippocampus. Currently researchers are focusing on whether exercise prevents neurodegenerative diseases such as Alzheimer's and Parkinson's.*



It is commonly known that exercise benefits physiological health, such as decreased risk of obesity, diabetes, heart disease, and cancer (Bouchard, Shephard, & Stephens, 1994). Recently, research has demonstrated neurobiological effects of exercise and a wide range of benefits to cognitive and emotional health, including improved long- and short-term memory and learning (Bekinschtein et al., 2008; Liu et al., 2009), remission of the symptoms of depression (Lawlor & Hopker, 2001), improved executive-control processes (Colcombe & Kramer, 2003), increased cognitive function in elderly persons with dementia (Laurin, Verreault, Lindsay, MacPherson, & Rockwood, 2009), and remission of the symptoms of Parkinson's disease (Smith & Zigmond, 2003). These benefits are related to the effects of exercise on brain-growth factors, specifically, brain-derived neurotrophic factor (BDNF; Dishman et al., 2006). BDNF promotes neuronal growth and regulation, and synaptic function, all of which affect brain plasticity (Huang & Reichardt, 2001). Brain plasticity is essential for cognitive abilities, especially after middle age, when the risk of Alzheimer's disease and dementia increases (Cotman & Berchtold, 2002). Human and nonhuman research on the relationship between exercise, BDNF, and brain plasticity has implications for the preventive treatment of individuals at risk for neurodegenerative diseases, as well for the maintenance of cognitive ability across the lifespan (Colcombe & Kramer, 2003; Laurin et al., 2009). This review will examine the role of BDNF in promoting brain plasticity, the role of exercise in the upregulation of BDNF, and the implications of these roles for improving learning, memory, and executive processes in older adults.

## **BDNF and Neuroplasticity**

BDNF is part of a family of proteins called neurotrophins (NT), which regulate cell death, facilitate neuronal development, and modify

synaptic transmission and connectivity (Huang & Reichardt, 2001; Schinder & Poo, 2000). Though NTs are primarily active during embryonic development (Thoenen, 1995), they, and especially BDNF, also operate in adult brain structures (Liu et al., 2009).

BDNF is released from both presynaptic and postsynaptic sites and binds with tropomyocin-receptor-kinase (Trk) receptors. In mammals, Trk receptors are vital for normal cell function and are the central receptors for BDNF (Huang, & Reichardt, 2003). On a presynaptic level, the binding of BDNF facilitates the release of neurotransmitters, particularly glutamate. On a postsynaptic level, the binding of BDNF leads to activation of N-methyl-D-aspartate (NMDA) receptors (Yamada, Mizuno, & Nabeshima, 2002), which are glutamate receptors and the primary receptors involved in long-term potentiation (LTP). As neuronal activity is repeated, the action of BDNF is enhanced in the synapse, which enhances synaptic transmission and connectivity (Schinder & Poo, 2000). Thus BDNF plays a notable role in brain plasticity.

Brain plasticity refers to the brain's capability to be modified through repeated neuronal activity. It is supported by the action of BDNF (Bekinschtein et al., 2008; Smith, & Zigmond, 2003). The neurotrophin hypothesis of synaptic plasticity (Schinder & Poo, 2000) asserts that exercise increases the expression of BDNF, thereby promoting brain plasticity.

### **Exercise Promotes BDNF Expression**

Exercise leads to the upregulation (increase in expression) of BDNF. The first study to demonstrate that exercise can increase BDNF expression measured levels of BDNF in rat brains following 0 (control), 2, 4, or 7 nights of access to a running wheel (Neeper, Góaucomez-pinilla, Choi, & Cotman 1995). To determine the degree to which running increased BDNF levels, they compared the total distance run

by individual rats with their BDNF levels. There was a significant positive correlation between the two variables (2 nights,  $r = .967$ ; 4 nights,  $r = .95$ ; 7 nights,  $r = .89$ )

A similar study by Griesbach, Hovda, Molteni, Wu, and Gómez-pinilla (2004) measured BDNF levels in rats and compared the functional recovery of brain-injured rats that exercised (wheel-running) to that of rats that did not exercise. One group received a lateral fluid-percussion injury (FPI) to the hippocampus, replicating a traumatic brain injury. A second group received a sham injury. Subgroups were divided by acute exercise (0-6 days), delayed exercise (14-20 days), and no exercise following injury. All groups also were exposed to water-maze training. BDNF levels were assessed on day 7 or day 21. Rats in the delayed-exercise group had higher levels of BDNF than those in the acute-exercise group and the no-exercise group. BDNF levels positively correlated with the amount of exercise. Rats that received FPI and were in the delayed-exercise group performed significantly better in the water maze compared to FPI rats that didn't exercise. These findings suggest that exercise promotes upregulation of BDNF. However, because the acute-exercise group did not exhibit results similar to those observed in the delayed-exercise group, the study also implies there is latency to BDNF upregulation following traumatic brain injury.

### **Learning, Memory, and Executive Processes**

Animal models have been applied to exercise-related cognitive improvements in humans and the neurobiological etiology of cognitive decline in aged adults (Colcombe & Kramer, 2003; Dishman et al., 2006). Exercise increases BDNF upregulation in older adults and improves learning, memory, and executive functions. A meta-analysis by Colcombe and Kramer (2003) showed that processing speed, visuospatiality, working memory, and executive control increased an

average of 0.5 standard deviations in physically-active or exercised older adults compared to sedentary adults.

One theory of the cognitive benefits of exercise involves LTP in the hippocampus (Van Praag, Kempermann, & Gage, 1999). The hippocampus is predominantly involved with encoding new memories. As already mentioned, BDNF facilitates the release and binding of glutamate, which is the primary neurotransmitter involved in hippocampal LTP (Yamada et al., 2002). Furthermore, long-term memory and learning improve with exercise (Colcombe & Kramer, 2003; Cotman & Berchtold, 2002; Dishman et al., 2006; Van Praag, Christie, Sejnowski, & Gage, 1999), with implications for future research on the treatment of neurodegenerative diseases such as dementia and Alzheimer's.

## Conclusion

Exercising can be beneficial for physical and mental health. Exercise leads to the upregulation of BDNF, which promotes cognitive benefits, such as improved learning, memory, and executive processes. In adults, BDNF enhances LTP in the hippocampus. Future research with humans may reveal how exercise can become preventive for neurodegenerative diseases such as Alzheimer's.



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