HIGH-INTENSITY INTERVAL TRAINING’S EFFECT ON COGNITIVE FUNCTIONS

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ABSTRACT

HIIT has been known to improve cognitive function. In addition to its effect on the hippocampal area. After HIIT training, BDNF levels also increase in the spinal cord, cerebellum and several cortical areas through increasing levels of Insulin-like Growth Factor-1 (IGF-1). In neurons, BDNF is present not only in the cytoplasm, but also near the dendritic spines, which influences their development. BDNF stimulates the process of neuroplasticity, which is manifested in neurogenesis, stimulation of the plasticity of serotoninergic, dopaminergic, cholinergic or noradrenergic neurons, dendritogenesis, and synaptogenesis. Moreover, BDNF facilitates the growth and survival of neurons and microglial cells. It also participates in cell differentiation, potentiation of signal transmission, induction, and maintenance of long-term potentiation of the synapse enhancement. Because of these properties, BDNF enhances cognition and takes part in emotional processes, spatial orientation and learning, as well as body coordination. Evidence suggests that IGF-1 is a major determinant of the effect of physical exercise on BDNF levels and thus on cognition more generally. There is an upregulation of Fndc5 gene expression in skeletal muscle and an increase in irisin after prolonged resistance training in rats and humans following HIIT training. When hippocampal Fndc5 was upregulated during exercise, BDNF and other neuroprotective genes were also activated in the rat hippocampus. Exercise-induced adult hippocampal neurogenesis is associated with increased Fndc5 and BDNF genes thus enhancing cognition. Then, stroke is associated with neuroinflammation that affects the processes of neuroplasticity in the lesion core, penumbra and small areas such as the spinal cord.

INTRODUCTION

Physical activity and exercise are effective ways to improve physiological adaptation including the cardiovascular and musculoskeletal systems and brain function. Research shows that exercise improves various markers of cardiovascular and skeletal muscle adaptation (Hawley et al., 2014; Ploutz-Snyder et al., 2014). In addition, it also improves the central nervous system (CNS) such as adult hippocampal neurogenesis (AHN), which is related to spatial learning and memory functions that depend on the hippocampus. This evidence suggests that exercise can increase synapse transmission and plasticity (Lee et al., 2018).

Rapid technological advances have an impact on changing individual lifestyles to a sedentary lifestyle. A sedentary lifestyle is a habit of individuals who are less or lazy to do physical activity. According to the World Health Organization (WHO), lack of physical activity causes the death of around 3.2 million people each year. About 20% -30% of the causes of death are due to lack of physical activity. In addition, lack of physical activity can cause cognitive dysfunction. Cognitive
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is a process of the mind’s work that makes oneself aware of objects of thought or perception, covering all aspects of observation, thinking and memory. Cognitive consists of various functions, including orientation, language, attention, calculation, memory, construction and reasoning. Decline in cognitive function usually occurs slowly and indistinctly, generally it is difficult for sufferers to recognize it (Octaviani & Widodo, 2021).

Most people think that physical activity or exercise takes a long time. Therefore, unavailability of time or being busy is often the main reason for not getting enough exercise. Currently, a type of exercise that is more effective and efficient and does not require a long time has been developed, namely High-Intensity Interval Training (HIIT). HIIT is a new variation of aerobic exercise, which is an exercise program that combines high and low or moderate intensity at certain intervals. HIIT only takes about 20-30 minutes. Beyond its role in cardiorespiratory and muscular function, endurance training can also affect cognitive function. Higher-intensity workouts, such as HIIT, are emerging as alternatives that can improve heart and brain health. HIIT involves repeated short to long periods of high-intensity exercise interspersed with periods of active or passive recovery. HIIT training can improve attention, information processing speed, and implicit memory performance (Afzalpour et al., 2015; Hwang et al., 2011). According to Hugues et al (2021), endurance training can also improve cognitive function by stimulating synapse plasticity, neurogenesis and angiogenesis through upregulation of neurotrophin levels (de Assis & de Almondes, 2017).

Recent evidence points to a potential role for HIIT by measuring molecular circulating markers of neuroplasticity that may improve cognitive function. HIIT induced robust improvements in aerobic parameters, as well as upregulation of neuroplasticity markers in the hippocampus and cortex. However, the relationship between neuroplasticity and cognitive outcomes after HIIT has yet to be determined in preclinical and clinical studies, thus explaining why exercise guidelines for brain health remain unclear. The central mediator of neural plasticity, brain-derived neurotrophic factor (BDNF) has been studied extensively for its role in the formation and maintenance of synapses, and the ability of the central nervous system (CNS) to regenerate and adapt to damage. Higher levels of BDNF are associated with better cognitive states in healthy subjects and also with neurological disorders (de Assis & de Almondes, 2017).

In elderly patients, reduced blood BDNF has been recognized as a biological marker of deficits in memory and cognitive processes. Several studies suggest that the aging brain maintains a certain plasticity which can also be stimulated and corrected by physical activity. However, there is also evidence that there is atrophic process of brain structure with age. It has been shown that in persons over 55 years of age without dementia, hippocampal atrophy ranges from 1-2%, prefrontal cortex, caudate nucleus, and cerebellum 0.5-2%/yr, while the primary motor and sensorimotor stratum regions remain unchanged (Murawska-Ciałowicz, Wiatr, et al., 2021).

As a physiological regulator of BDNF production (de Assis & de Almondes, 2017), HIIT has been proven as an alternative strategy for the therapy and treatment of patients with neurological disorders including impaired cognitive function. The effects of HIIT are widely
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recognized in brain function. However, the molecular mechanisms underlying how HIIT exerts its effects on cognitive function are unclear.

Based on the explanation, the researchers thought that it was important to delve into the effects of HIIT on cognitive function. The researchers then decided to discover the HIIT effect on cognitive function in hopes for contributing to a wider range of knowledge for HIIT implementation, whether in general or specific context.

METHODS

The method of writing this article was a literature review by generating data from journals and references related to High-Intensity Interval Training, HIIT, and cognitive functions. The search for literature used sources such as ScienceDirect, Google Scholar, Emerald Insight, Springer Link, Proquest, EBSCO Host, Clinical Key, JSTOR, Cambridge Core, and PubMed. The data then analyzed by using inclusion and exclusion criteria, sorted into specific categories, and breaking down the most important points of each article.

RESULTS AND DISCUSSION

Effects of High Intensity Interval Training (HIIT) on Cognitive Function

Neurobiological Mechanisms

Physical exercise causes an increase in cerebral vascularity, protein and neurotransmitters, an increase in insult resistance, an increase in neurogenesis, synapse metabolism, angiogenesis, neuronal survival, and an increase in overall brain volume. More specifically, BDNF plays an active role in mediating the effects of HIIT on cognition. Animal studies have shown an increase in hippocampal BDNF after HIIT training which is very significant given the central role of the hippocampus in learning and memory and its decline in many degenerative diseases including Alzheimer's. This effect has been found to persist for at least several weeks, and therefore could potentially play an important role in HIIT-induced neural plasticity. In addition to its effect on the hippocampal area, after exercise HIIT BDNF levels also increase in the spinal cord, cerebellum and several cortical areas, this is likely through increased levels of Insulin-like Growth Factor-1 (IGF-1), a growth factor involved in neurodevelopment. Evidence suggests that IGF-1 may be a major determinant of the effect of physical exercise on BDNF levels and thus on cognition more generally (Budde & Wegner, 2018).

The increase in BDNF levels in cortical areas is consistent with a documented effect of exercise on serum BDNF (sBDNF). Several studies have found that exercise induces an increase in sBDNF levels (Schmolesky et al., 2013), usually within a few hours and the magnitude of the increase depends on the intensity of the exercise. In addition to exercise it is also possible to control harmful factors such as stress. Corticosteroids or stress hormones have deleterious effects on BDNF concentrations and, if maintained, lead to neuronal degradation and dendritic atrophy. HIIT training prevents these detrimental effects by blocking the downregulation of BDNF, particularly in the hippocampus. Further evidence of the effect of exercise is at the level of monoamine neurotransmitters (dopamine, epinephrine, norepinephrine) and tryptamine neurotransmitters.
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(serotonin, melatonin) which could be responsible for some of the benefits usually observed after physical exercise (Budde & Wegner, 2018).

Figure 1. Effects of HIIT and Cognitive Training on Neuroplasticity and Learning/Memory Performance in Animals (Hugues et al., 2021)

Several potential molecular factors that might mediate the effects of HIIT on neuroplasticity and cognitive enhancement processes. First, skeletal muscles are able to communicate with other organs such as the brain through many substances released during exercise (Murawska-Ciałowicz, de Assis, et al., 2021). Among other substances, lactate is released by active muscles during a HIIT session. Increased blood lactate concentration correlates with upregulation of serum BDNF levels, motor cortex excitability and motor learning in healthy humans (Al-Qahtani et al., 2018). This was found in mice whose lactate comes from active muscles can enter into neurons through its receptor (MCT2) to stimulate BDNF through the SIRT1 pathway. Upregulation of hippocampal and cortical BDNF expression as well as high-affinity tropomyosin receptor kinase B (TrkB) are known for the processes of neurogenesis, neuronal survival and synaptic plasticity as well as for inducing long-term potentiation (LTP). Increased hippocampal LTP is often associated with improved memory. Similarly, higher BDNF and/or VEGF (neurogenesis and angiogenesis) expression may improve memory performance in healthy mice after repeated injections of lactate to mimic high-intensity exercise. Moreover, blockade of MCT expression in in vitro experiments reduced lactate transfer to astrocytes and neurons and impaired long-term memory in rats. Lactate infusion at rest can increase circulating BDNF in humans (Hugues et al., 2021).

Recent evidence suggests a potential role in neuroplasticity after HIIT in humans and animals from the endurance exercise-induced myokine, fibronectin type III domain-containing 5 (FNDC5). Bostrom et al. (2012), have observed upregulation of Fndc5 gene expression in skeletal muscle and increased irisin after prolonged resistance exercise in mice and humans. It has been postulated that irisin alone may be able to cross the blood-brain barrier (BBB) to induce changes in gene expression, or irisin can induce factor x which can induce changes in gene expression. When hippocampal Fndc5 was upregulated during exercise, BDNF and other neuroprotective genes were
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also activated in the rat hippocampus. Exercise-induced adult hippocampal neurogenesis is associated with an increase in both the Fndc5 and Bdnf genes thus enhancing cognition in a mouse model of Alzheimer's disease. Thus, stroke is associated with intense neuroinflammation that affects neuroplasticity processes within the lesion core, penumbra and small areas such as the spinal cord. HIIT may be able to reduce pro-inflammatory cytokines in parallel with microglia activation (M2 phenotype) in rats with cerebral ischemia as well as the neurotrophil-lymphocyte ratio in patients with multiple sclerosis (Hugues et al., 2021).

**Figure 2.** Effects of HIIT on BDNF Synthesis in the Brain (Jiménez-Maldonado et al., 2018)

HIIT affects the synthesis of BDNF in the brain. In Figure 2; (A) HIIT increased mitochondrial activity as well as ROS concentrations in neurons. ROS induce higher transcription and Creb-Bdnf signaling. (B) HIIT causes greater concentration of Ca$^{2+}$ in neurons. This condition enhances CaMKII activity and MAPK/ERK/MSK signaling to activate Creb-Bdnf transcription and neuronal plasticity. In addition, intracellular calcium can enhance ROS generation in neurons. Once synthesized, ROS can activate Creb-Bdnf transcription. (C) HIIT increases the concentration of systemic blood lactate, and consequently increases NMDA receptor activity to increase intracellular Ca$^{2+}$ concentrations in neurons. The ions activate CaMKII activity and MAPK/ERK/MSK signaling to induce Creb-Bdnf transcription and neuronal plasticity (Jimenez-Maldonado et al., 2018).
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Figure 3. Potential Intracellular Signaling Mechanisms Involved in HIIT-induced mitochondrial biogenesis (Lee et al., 2018)

The molecular mechanisms underlying the metabolic adaptation of skeletal muscle to HIIT have recently been investigated. A significant breakthrough in unraveling the cellular events that trigger mitochondrial biogenesis was the discovery of the peroxisome proliferator-activated receptor-γ coactivator (PGC-1α), a coactivator that can be inducible to regulate the coordinated expression of mitochondrial proteins encoded in the nuclear and mitochondrial genomes (Lee et al., 2018).

In skeletal muscle, PGC-1α acts as a master regulator of mitochondrial biogenesis that responds to neuromuscular input and strong contractile activity. A single bout of endurance training induces a rapid and sustained increase in the PGC-1α gene and protein in skeletal muscle (Ward et al., 2015), whereas the muscle-specific overexpression of PGC-1α results in a large increase in functional mitochondria, an increase in whole-body VO₂max, switching from carbohydrate to fat fuel during submaximal exercise, and increased endurance performance. AMPK and p38 MAPK are two important signaling cascades that are integrated into the regulation of PGC-1α and lead to regulation of mitochondrial biogenesis. AMPK and p38 MAPK phosphorylate and activate the expression of PGC-1α, which is known as a regulator of PGC-1α. In addition, it also increases the PGC-1α protein by binding to and activating the CREB site on the PGC-1 promoter (Lee et al., 2018).

Evidence indicates that exercise intensity is a key factor influencing PGC-1α activation in human skeletal muscle. Recent observations place PGC-1α as a major role in regulating many oxidative adaptations to exercise. In this case, acute HIIT increased PGC-1α mRNA after exercise. Similar to endurance training, acute HIIT can activate PGC-1α by increasing nuclear translocation. The increase in nuclear PGC-1α after low-volume HIIT coincided with increased mRNA expression of several mitochondrial genes, suggesting that mitochondrial adaptation programs are involved with this short intensity exercise (Lee et al., 2018).

Study on Animal Models

HIIT is a high-intensity, low-volume workout. Regarding exercise intensity, evidence in healthy animals has shown that BDNF synthesis in the brain is higher in high-intensity training
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animals compared to low-intensity training and sedentary animals. On research Jiménez-Maldonado et al. (2018), using the continuous training protocol, the training time is similar in both models (low and high intensity training, 30 minutes/session) which means that the HIIT characteristics are not achieved.

Evidence points to a long-term effect of HIIT on BDNF synthesis in animals. Thirty sessions of HIIT significantly increased levels of BDNF (protein) in the brain compared to the continuous training protocol and the control group. According to Jiménez-Maldonado et al. (2018), stated that HIIT increases the concentration of hydrogen peroxide (H₂O₂) and Tumor Necrosis Factor Alpha (TNF-α) in the brain where these molecules can activate the synthesis of BDNF or CREB which are transcription factors that positively regulate the synthesis of BDNF. In the study by Freitas et al. (2018), 36 HIIT sessions increased BDNF levels in the hippocampal region of healthy rats and reduced hippocampal oxidative damage.

Studies on Human Models

There is evidence that there is an effect of a single HIIT session on BDNF. For example, one session of supramaximal HIIT increases serum BDNF levels, which suggests increased BDNF secretion from platelets that is not related to brain secretion. Marquez et al. (2015), found that HIIT was a stronger stimulus to increase systemic (serum) BDNF compared to MICT. The exercise modality used in the study (cycle-ergometer) does not cause muscle damage. Therefore, higher levels of BDNF are not due to activation of platelets to increase BDNF secretion, but physical exercise itself is sufficiently stimulating to cause higher levels of circulating BDNF. Thus, higher serum BDNF levels after HIIT result from greater BDNF synthesis in the brain. On research Jiménez-Maldonado et al. (2018), discussed that single bout HIIT induces higher levels of H₂O₂ and TNF-α in the brain. These molecules activate peroxisome proliferator-activated receptor-γ coactivator (PGC-1α) signaling to enhance neuronal BDNF synthesis. Similarly, a single HIIT session significantly increased peripheral plasma BDNF levels immediately after exercise. However, after the 60-minute HIIT session ended, BDNF concentrations returned to baseline. Given that plasma BDNF levels reflect BDNF secretion from the brain, the data reflect the influence of HIIT on BDNF in the brain. Jiménez-Maldonado et al. (2018), stated that brain hypoxia caused by HIIT was the main factor explaining these results.

CONCLUSION

Cognitive function is a complex function in the human brain that involves aspects of memory, both short-term memory and long-term memory, attention, planning and reasoning functions as well as strategic functions in someone's thinking. Cognitive function also involves cognitive aspects of a person, such as language and vocabulary.

As age decreases, it will be followed by physiological, psychological and biological decline in a person and accompanied by a decrease in cognitive function, which can cause disturbances in cognitive function. Impaired cognitive function is a disorder of the main function of the brain in the form of disturbances in orientation, attention, concentration, memory (memory), and language,
as well as impaired intellectual function will be seen by disturbances in arithmetic, language, semantic memory (words), and problem solving.

HIIT is one way to suppress the decline in cognitive function. Regular exercise can increase the formation of new brain cells and prevent damage to cells in the nerves. Regular exercise can help in increasing blood flow to the brain, thus increasing the intake of nutrients in the brain where it can ensure strong perfusion of brain tissue. The direct effect that occurs in a person's brain is in the form of maintenance of nerve structure and can increase the expansion of nerve fibers in the brain and in the capillaries in the brain.

**REFERENCE**


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Journal of Cardiopulmonary Rehabilitation and Prevention, 31(6).
https://doi.org/10.1097/HCR.0b013e31822f16cb


