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EFFECTS OF PHYSICAL ACTIVITY ON BRAIN FUNCTION: MECHANISMS, ADAPTATIONS AND CLINICAL IMPLICATIONS

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ABSTRACT

The effects of physical activity on brain function, the mechanisms involved, adaptations, and clinical implications are topics of great importance given the increasingly common sedentary lifestyle. This paper explores these relationships, starting with the evolutionary aspects of brain development in the context of physical activity. It discusses a variety of forms of exercise, from intense exercise to daily NEAT (non-exercise activity thermogenesis). A key issue is neuroplasticity, which plays an important role in adaptation to external stimuli. The article identifies key neurotrophic factors, such as BDNF (brain-derived neurotrophic factor) and VEGF (vascular endothelial growth factor), which are regulated by physical activity and contribute to improved cognitive function and mental health. The paper demonstrates the multifaceted effects of physical activity on neuroplasticity and brain health.

KEYWORDS: brain, physical activity, brain plasticity, neuroplasticity, BDNF, VEGF

1. Brain evolution and physical activity

Physical activity has played a key role in the evolution of our species. Humans, like many other animal species, use physical activity to obtain food, reproduce, and avoid predators. Our ancestors' evolutionary success resulted from a positive feedback loop between increased physical activity on the one hand and brain and cognitive development on the other. Changing living conditions several million years ago forced humans to evolve away from the sedentary lifestyle typical of forest herbivores towards hunting and gathering (Bramble et al. 2004).

The emergence of bipedalism was a key moment. This position enabled humans to move upright quickly—thanks to this posture, running became a hunting strategy. Hunting, which is indirectly a physical activity, also forced the development of the brain in terms of the cognitive skills associated with navigating different environments, tracking game, and identifying edible plants. The increasing complexity of skills required the acquisition of more and more energy resources, resulting in a further increase in physical activity. Over millions of years, endurance running became the drive that stimulated brain development, while the increasing energy intensity of the organ necessitated greater activity (Hill i Polk 2019). Many modern neuroscience studies support these assumptions. Almost all types of brain plasticity as we know it, among them, changes in the strength of connections between neurons or the emergence of new neurons, are strongly stimulated by physical activity. Secreted substances such as neuronal and vascular growth factors, which promote brain development and health, play a key role in this process. Studies on athletes show that prolonged physical activity affects the brain's reward system, leading to the phenomenon of so-called runner's high, caused by the production of endogenous cannabinoids and opioids. Such biochemical mechanisms provide evidence that evolution equipped us with an ‘intrinsic need to run’ and that the benefits associated with physical activity were essential to our ancestors (Hill i Polk 2019) (Brellenthin et al. 2017).

However, it is worth mentioning that, from an evolutionary point of view, every adaptive strategy has limitations. This raises the question: why do so few people regularly engage in physical activity? The answer lies in the biological mechanisms of energy conservation. All living organisms strive to conserve energy. This is crucial for their survival and reproduction. When resources are readily available, our organism tends to reduce energy expenditure. Such energy-saving mechanisms are strongly rooted in evolutionary survival strategies. When the organism receives signals of satiety or abundance, the tendency to avoid physical activity will dominate the need for sport (Rybakowski 2019). Therefore, it is the state of energy deprivation that often motivates the urge to engage in physical activity. This mechanism not only applies to exercise but to the functioning of other organs as well. The relationship is also perfectly illustrated by the bone metabolism system; when the skeletal system is not required to be strong and resilient, the body may start to economise, leading to tissue degeneration and osteoporosis. Given the context of modern times, with overall less activity and the prevalence of sedentary lifestyles, it can be argued that physical inactivity also leads to physiological changes that limit brain plasticity (Rybakowski 2019) (Duclos et al. 2013).

When analysing the evolutionary changes that occurred in the Homo sapiens organism, it is also important to note the considerable differences between physical activity and intellectual activity. Intense mental exertion can act similarly to physical activity, but the potential to stimulate the production of plasticity regulators such as neurotrophins or vascular growth factors is much lower in the case of cognitive activity (Rybakowski 2019).

2.1 What is physical activity?

According to the literature, 'physical activity', 'physical fitness', and 'exercise' are different terms. However, they are often confused with each other and used interchangeably. Physical activity is defined as any body movement produced by skeletal muscles, resulting in an energy expenditure that can be measured in kilocalories. Physical activity daily can be subdivided into sporting activities, fitness activities, work activities, home activities, or other activities. Exercise, in turn, represents a subset of physical activity. Exercise is an activity that is structured, planned, and repetitive. The goal of exercise is to improve or maintain physical fitness (Caspersen et al. 1985) . An indicator depicting exercise intensity and mobility is the MET parameter. MET is defined as the metabolic equivalent and indicates the consumption of one kilocalorie of energy by one kilogram of body weight in one hour of rest (calories/ kilogram of body weight per hour). MET is the approximation of the actual values, as resting energy expenditure is influenced by parameters such as age, sex, and body weight. The MET value shows how many times more energy is used during exercise compared to energy expended at rest (Jetté et al. 1990) (Podgórska 2023).

2.2 Single session of physical activity

A single session of physical activity has a proven beneficial effect on mood, well-being as well as anxiety, and pain reduction. These relationships have been recognised as far back as antiquity, and have begun to be documented by numerous scientific studies since the 1980s. One of the key mechanisms responsible for the feelings associated with physical activity is the increased release of biogenic amines such as serotonin and dopamine. Studies indicate that physical activity affects the activation of the brain's reward system, and these responses are particularly noticeable in people who regularly participate in sports (Rybakowski 2019) (Wardle et al. 2018). In addition to serotonin and dopamine, the already mentioned endogenous opioids and cannabinoids, which are already produced during a single but prolonged physical activity, also play a role in improving mood (Wardle et al. 2018).

The aforementioned ‘runner's high’ is a specific sensation of positive energy during a long run. Detailed imaging studies using positron emission tomography (PET) have shown the opioidergic mechanisms associated with this state. The analysis revealed that, during a long run, a decrease in the availability of opioid receptors is observed in the brain, mainly in the frontal and limbic areas, which are crucial for emotion processing. The feeling of euphoria, measured after exercise, was inversely correlated with opioid binding. These studies support the theory of endogenous opioids' role in inducing a state of euphoria (or ‘high’) (Boecker et al. 2008).

2.3 NEAT – a movement that happens to us

NEAT is the thermogenesis of non-exercise physical activity, i.e., movement undertaken by the human body that is not planned training, or sleep. NEAT is the body's spontaneous physiological and metabolic response to movement (other than planned training) intending to generate heat. Activities such as shopping, cleaning, cooking, walking the dog, gesticulating, or taking the stairs instead of the lift can be classified as NEAT. The factors influencing a person's NEAT can be easily divided into biological factors, such as weight, gender, and body mass, and environmental factors, such as work or a place of residence. The influence of these factors together explains a considerable variation in human NEAT. Research shows that the benefits gained from planned workouts largely depend on how we spend the rest of the day. A sedentary lifestyle can largely nullify the benefits of regular scheduled training, which is why the NEAT index is important in everyday life. Spontaneous physical activity is an outgrowth of our lifestyles, and its caloric consumption can be as high as three-quarters of the calories burned during the day (Levine 2002).

3.1 Brain plasticity

Neuroplasticity is the brain's ability to adapt as a result of a variety of external stimuli and experiences. Neuroplasticity is also the brain's ability to regenerate in response to damage. This phenomenon is claimed to underlie the functioning of the nervous system and its ability to learn and remember. In the past, neuroplasticity was often seen as a repair mechanism to recover from brain damage, such as a stroke. Modern neuroscience demonstrates the widespread presence of plasticity in various brain structures, proving that it is a key process accompanying everyday experiences and lifelong learning (Kossut 2019).

When discussing neuroplasticity, it is important to mention synaptic plasticity, which refers to permanent changes in the strength of synaptic connections. Synaptic plasticity is classified into two main forms: Hebb's and homeostatic plasticity. Hebb's rule, formulated by Donald Hebb in 1949, states that activation of one presynaptic neuron influences the enhancement of the cell's postsynaptic response. Mechanisms underlying this phenomenon include long-term synaptic potentiation (LTP) and long-term synaptic depression (LTD) (Kossut 2019) (Kossut 2018).

One of the fundamental processes in memory trace formation is long-term synaptic potentiation (LTP). Induction, through intense neuronal stimulation, causes the presynaptic neuron to release glutamate. The neurotransmitter acts on AMPA and NMDA receptors, which allow Ca^{2+} to enter the neuron. This particular aspect is important because Ca^{2+} ions themselves function as activating factors for enzymes, for example, CaMKII kinase, to participate in the modification of synapses with the aim of increasing their efficiency. Such processes make synaptic connections more efficient, which has implications for neurogenesis and learning processes.

Long-term synaptic depression (LTD) is a process in which low stimulation frequency ultimately leads to the elimination of ineffective synaptic connections. The LTD mechanism is of the same importance as LTP, as it allows the elimination of redundant connections, which may be necessary to maintain the efficiency of neural networks (Kossut 2019) (Kossut 2018).

Synaptic plasticity leads to structural changes in neurons. A neuron that responds to changes in the strength of synapses can adjust its morphology. Such changes include adjustments in the shape of synapses and the number and size of dendritic spines. Structural modifications of synapses are very rapid, occurring within minutes following stimulation. One example would be the transformation of thin dendritic spines into mushroom-shaped spines, which is associated with memory processes (Kossut 2019) (Kossut 2018).

Homeostatic plasticity, on the other hand, refers to how neurons adjust their responses when reacting to prolonged stimulation or depression. This involves regulating the strength of all synapses on a given neuron sufficiently to maintain balance and responsiveness to stimuli. Homeostatic plasticity is analogous to the operation of a clutch in a car: these mechanisms must operate at all neural synapses to keep their interactions constant (Kossut 2019) (Turrigiano 2017).

Both developmental plasticity and learning are closely linked to neuroplasticity. The brain can adapt to new experiences, especially during developmental periods. The functional activity of neurons plays a key role in guiding the growth of axons and the formation of synaptic connections. During adolescence, the brain's capacity for plasticity decreases, which is related to the regulation of the gene expression that is responsible for the formation of synapses. Research shows that in adults, neuroplasticity is still present, but at a much less intense level. Learning and memory processes still take place, but they now require more commitment and repetition to maintain effective synaptic connections, which is why physical activity playing a role in neuroplasticity processes, affecting the structure and function of the brain, is so important. Studies indicate that regular exercise promotes neurogenesis, i.e., the formation of new neurons. An eminently important and susceptible area is the hippocampus, the structure responsible for learning and memory processes. During physical activity, a variety of neurotrophic factors such as brain-derived neurotrophic factor (BDNF), vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF-1), and nerve growth factor (NGF) are released to stimulate neuronal development and the formation of synapses. Physical activity also leads to improved circulation, increased blood flow to the brain, and reduced stress levels. This promotes a better environment for neuroplasticity processes to take place. Studies show that people who regularly participate in sports have an increased volume of grey cells in the areas responsible for memory and learn new skills more easily. Physical activity also improves cognitive function and may protect the brain from the effects of ageing (Kossut 2018) (Turrigiano 2017) (Di Liegro et al. 2015).

3.2 BDNF

Brain-derived neurotrophic factor (BDNF) is a key protein in our body. It plays an important role in brain health and function. In recent years, interest in BDNF has increased in the context of physical activity and its impact on cognitive function and ageing processes. Physical activity is one of the strongest determinants of BDNF levels in the body (Szuhany et al. 2015).

BDNF is present in the central and peripheral nervous systems. It is also found in muscle cells, adipose tissue, and endothelial cells. Peripheral BDNF molecules are mainly bound to platelets. The role of platelets is to store and release BDNF molecules. An important aspect of BDNF is its ability to cross the blood-brain barrier, thus proving a significant effect of this factor on brain function. BDNF is essential for neurogenesis, synaptic plasticity, and protection of neurons from damage (Yang et al. 2017) (Walsh et al. 2020).

Current research shows that physical activity has a direct effect on BDNF levels both in the blood and in the central nervous system. Acute episodes of physical activity, especially aerobic training, lead to significant increases in circulating BDNF levels. Meta-analyses indicate that long-term physical activity, mainly in the form of regular exercise, has a beneficial effect on cognitive function. These changes are likely the result of transient increases in BDNF that occur in response to regular exercise (Walsh et al. 2020).

There are no clear recommendations on the dosage of physical activity that leads to optimal increases in BDNF. The literature highlights the importance of exercise type, intensity, and duration. It has been established that activity exceeding 30 minutes results in a greater BDNF concentration increase (Dinoff et all. 2017).

Various mechanisms contribute to the BDNF level increasing in response to physical activity. One of the main factors is increased blood flow, both in the peripheral and cerebral circulatory systems. The release of platelet-bound BDNF is also an important mechanism. Platelet-bound BDNF is stored in the body and released in response to physical activity, further highlighting the role of systematic exercise in optimising BDNF levels (Walsh et al. 2020) (Brunelli et al. 2012).

BDNF also plays a key role in biological ageing processes in the brain. Studies show that BDNF can protect neurons from oxidative stress and prevent neuronal cell loss in degenerative processes. Regular physical activity, by stimulating BDNF production, may contribute to slowing age-related processes, including protection against cognitive disorders. This information allows us to conclude that regular physical exercise is essential for maintaining brain health and cognitive function, especially given the context of the ageing population (Walsh et al. 2020) (Hachem et al. 2015).

3.3 VEGF

VEGF, or vascular endothelial growth factor, plays a key role in vasculogenesis, i.e., forming new blood vessels. It is the major regulator of the cell differentiation process and the formation of branches from the existing vascular network, i.e., angiogenesis. VEGF induces endothelial cell permeability and stimulates their proliferation, a process essential for the normal development and function of the vascular system (Podgórska 2023).

VEGF expression begins at early developmental stages, and its action is crucial in both vasculogenesis, which is the formation of vessels from endothelial cell precursors, and angiogenesis, in which new vessels grow from existing ones. The regulators of VEGF signalling are the two primary receptors, VEGFR1 (Flt1) and VEGFR2 (Flk1). Their presence is essential for normal vascular development. High regulation of VEGF expression is important not only for embryonic development but also for maintaining vascular health in the adult body (Maharaj i D'Amore 2007) (Zachary i Gliki 2001).

In the context of physical activity's effect on VEGF, studies have shown that regular exercise can significantly increase levels of this factor in the brain. Physical exercise, especially at high intensity, increases lactate production in muscle, which may have a signaling role. Activation of the lactate receptor HCAR1, concentrated in cells surrounding the brain blood vessels, stimulates VEGF secretion and the process of angiogenesis. This finding is highly relevant as it demonstrates how physical activity supports brain function through the induction of VEGF production (Morland et al. 2017).

Angiogenesis, stimulated by VEGF, leads to increased capillary density in the brain, which is particularly important for maintaining cognitive health, especially in older people. Increased cerebral perfusion has been associated with improved cognitive function, and it may be a significant component in the prevention and treatment of dementia and neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. Each of these conditions is related to reduced metabolic capacity and reduced vascular density, leading to chronic cerebral hypoperfusion that contributes to cognitive decline (Morland et al. 2017) (Ferrara 2000).

In vitro and in vivo studies have demonstrated that VEGF not only promotes new vessel formation but also directly affects neurogenesis and synaptic function, suggesting an even deeper link between exercise and brain health. Regular physical activity is, therefore, a key factor for brain vascular health, supporting the regeneration and plasticity of the nervous system (Morland et al. 2017).

DISCUSSION

The presented scientific evidence demonstrates the positive impact of physical activity on brain function and even its indispensability in the proper functioning of the brain. The evolutionary context in which the development of neuroplasticity mechanisms is embedded highlights the relationship between physical activity and cognitive abilities. The variety of forms of activity, from single high-intensity exercise sessions to NEAT strategies, points to the need to include any form of movement in daily life to support brain health. In particular, attention has been given to the role of neurotrophins, such as BDNF and VEGF, which not only influence synaptic plasticity but also prevent brain damage and degeneration. In a clinical context, integrating physical activity programmes into neurological therapies may help improve patients' cognitive function and offer the chance to delay the onset of neurodegenerative diseases.

CONCLUSIONS

Physical activity is crucial for brain health. By promoting neuroplasticity and stimulating the production of neurotrophins, this becomes its key component. The work emphasises the importance of regular high-intensity activity and increasing daily NEAT activities to maintain optimal cognitive and mental function. Further research is needed in the future to understand better the mechanisms by which physical activity affects brain health and to develop effective therapeutic intervention strategies.

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