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How Exercise Impacts the Brain and Cognition

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Title: How Exercise Impacts the Brain and Cognition

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One Sentence Summary: A literature review looking at the relationships between exercise the brain and cognition.

Abstract:

Physical exercise has been shown to impact the brains composition and functionality. The changes that arise in the structure of brain, as result of engaging in physical exercise, give rise to cognitive changes. Structural changes are observed most notably in the prefrontal cortex and hippocampus. These changes are preceded by elevations in cerebral blood flow, and growth factors, resulting increased neuroplasticity and neurogenesis. Frequency, duration, intensity, and type of physical exercise can have differing effects on the brain. Moderate intensity aerobic exercise presents the most profound improvements in memory, and inhibitory control over time.

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Introduction

Physical exercise has the remarkable ability to alter our brains, both in structure, and in function. Structure and function within the brain have an intricate relationship. Through a complex and not well understood process, these neural structures give rise to cognition, or our psychological experiences and wellbeing. Exercise can reshape the structure and therefore function of the brain. It has been demonstrated that physical exercise has the ability to change neural connections in such a way that demonstrate a positive psychological effect[1]. The health of the brain is a broad topic and though there is an abundance of evidence suggesting exercise's direct role in the health of the brain, there are still many gaps. Research has focused on specific areas such as cognition, sense of wellbeing, disease preventions, mood, and addiction as well as physical changes as it relates to neuroplasticity and neurogenesis. It should be noted that psychological and biological implications are often studied as separate entities and this review will take a bidirectional approach, in that psychology modulates biology and biology modulates biology.

This paper will overview the mechanisms by which exercise influences brain and psychological health with a focus on the frontal cortex and hippocampus, the two areas of the brain that appear to be the most influenced by exercise. It will look at some of the general benefits of exercise and their probable causes. It is also important to define physical exercise and its criteria for each effect seen. In general, physical exercise increases heart rate and respiratory output, impacting the brains blood supply and oxygen usage. Adjusting these levels will influence processes in the brain. These adjustments can divert blood supply from one area of the brain to another increasing metabolic processes in some areas and inhibit processes in others.

Mechanisms currently thought to be responsible for changes in the brain resulting from physical exercise are increased blood flow therefore increased oxygen to the brain. Others include increases in Brain Derived Neurotrophic Factor (BDNF) and Insulin Growth Factor(IGF), blood redistribution, as well as different neural firing patterns such as when inhibiting one's response to stop exercise when experiencing discomfort. There are also social factors promoting wellbeing, such as being a part of a team or achieving a personal or team goal.

There are general, brain-wide, structural improvements seen when exercising. These improvements result from general increased blood circulation and other previously mentioned factors, but many effects are best understood when looking at specific regions of the brain, or specific cortical connections and how these are shaped and molded by exercise. For example, the cortical volume of the hippocampus can increase during exercise overtime, improving memory and protecting against Alzheimer's Disease and depression[2-4]. Narrowing the view to one region of the brain, in this case the hippocampus, can be correlated with changes in disease risk and cognitive changes. The brain and cognition have a much more complex relationship than that but some regional specific alterations offer great insight into their link to cognitive manifestations and how exercise can enhance these processes.

One region of the brain that is greatly affected by exercise is the frontal and prefrontal cortex. Within the frontal cortex certain localized areas have been studied such as the Dorsal Lateral area of the Pre-frontal Cortex. The frontal cortex is responsible for many areas of cognition such as inhibitory control, decision making, regulating creativity and other higher level processes[5]. Much of the literature has focused on one specific area of the frontal cortex, such as the dorsal lateral prefrontal cortex (DLPFC), or sensory and motor cortexes. Others have focused on general activation or inhibition of the entire frontal cortex.

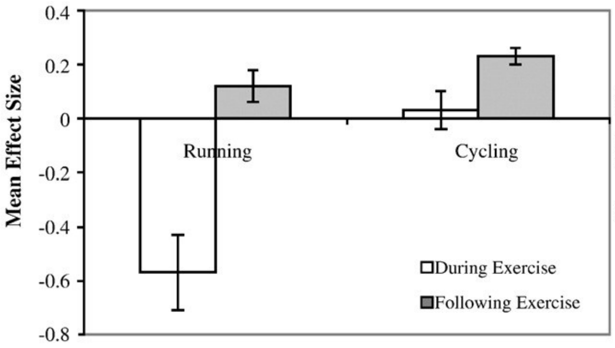
The structural changes overtime, and the immediate molecular alterations that occur in conjunction with physical exercise offer a physiological explanation about the robust psychological benefits that arise. It is widely known about the cardiorespiratory health benefits and disease prevention potential of physical exercise. It is only recently that investigation into the psychological relationship with exercise has started to be explored and already is showing promise as a profound tool to improve psychological health and wellbeing.

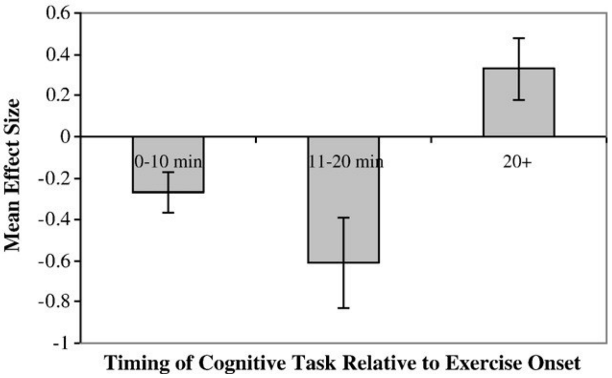
Frequency, Duration, Intensity, Type of Exercise

It is important to define some parameters as relates to studying the biological and psychological benefits of exercise. The first thing to note is that the type, intensity, duration, and frequency of physical exercise may offer different results in terms of health benefits and different magnitudes of these effects. Aerobic and anaerobic physical exercise offer different health benefits. Aerobic exercise allows the body to resynthesize ATP under adequate oxygen availability. Aerobic exercises include activities such as walking, jogging, swimming, or cycling.

The intensity of the session is in reference to the percentage of the maximum heart rate reached during activity or to the maximum oxygen consumption measured as VO_{2max}. VO_{2max} is a useful and frequently used measure of cardiorespiratory fitness. Higher cardiorespiratory fitness is associated with greater cognitive measures such as executive control, attention, and response speed and biological measures of hippocampus and prefrontal cortex volumes[6, 7]. Exercise intensity follows in an inverted U shape in reference to the cognitive benefits seen in acute bouts of exercise[6]. That is, moderate intensity exercise shows the most cognitive benefit compared to light or heavy intensities.

The effects of chronic exercise vary from the effects of acute exercise. Chronic exercise is the accumulation of multiple sessions of aerobic exercise over a period of time whereas acute exercise is a single session of activity and measurements can be taken before, during, and after the activity. Chronic aerobic exercise is a more potent neuro modulator, showing greater effects on functional neuroplasticity and cognition compared to acute bouts of aerobic exercise[8]. However, acute aerobic exercise does have a mild effect on cognitive function and increases mood and wellbeing, especially in major depressive disorder (MDD)[9]. Lambourne & Tomporowski reviewed studies that tested cognitive faculties during and after exercise, also comparing running versus cycling as the method of aerobic activity(see fig). Cognition is impaired during the actual bout of aerobic exercise(running) except for in the case of cycling. However, following the exercise there is a temporary increase in arousal which facilitates processing speed and enhances memory[10]. These findings are independent of physical fitness levels implying that everyone can benefit, at least temporarily from a single session of physical exercise.





Anaerobic exercise is short in duration and high in intensity depleting ATP from the muscles, converting to anaerobic metabolism. Exercises include things such resistance training, and sprinting. There are a limited number of studies of investigating the relationship between anaerobic exercise and brain health and most of focus is on older populations. However, there are recent findings that resistance training can improve executive functioning, more specifically reaction times and inhibitory control[11, 12].

Neuroplasticity

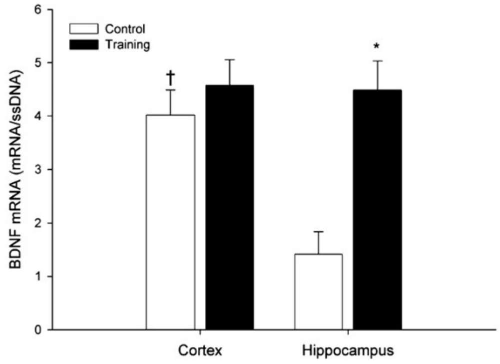
The nervous system has the capacity to reorganize itself in response to altered demands[7]. This ability of the nervous system to restructure itself is termed “neuroplasticity”. There are different levels involved in the process of neuroplasticity ranging from ion channels and synapses to behaviors. Behaviors can elicit structural changes in the brain. Learning a new language has been shown to increase gray matter volume of the hippocampus as well as the inferior frontal gyrus, left middle frontal gyrus, and superior temporal gyrus[13]. When engaging in addictive behaviors the frontal cortex and hippocampus are involved in the maintenance of these negative behaviors and rewire their circuits. The brain changes to make the addictive connections in the brain more salient[14]. It is altering the connectivity in the brain to generate strengthened or novel cortical pathways. This “rewiring” is one way to measure the structural changes that take place in the brain during or following exercise.

Neuroplasticity can give rise to cognitive changes as well as sensory and motor neuronal changes. Being physically active is a potent activator of neuroplastic changes in the brain. Exercise can promote angiogenesis, neurogenesis, and brain synaptogenesis[15]. This means that the act of physical exercise has the potential to physically reshape the brain. Human studies have demonstrated structural changes in brain volume such as increased gray matter volume in the frontal cortex and hippocampus[3, 16].

Our understanding of neuroplasticity and the utilization of neuroimaging techniques help provide a causal link between exercise and cognitive improvements. For example, there were functional brain changes in the frontal cortex of sedentary individuals after six months of an aerobic exercise intervention [16]. The changes in structure were correlated with improved cognitive performance tasks.

There are a few neurophysiological explanations as to why physical exercise can promote neuroplasticity. The first is the increased blood flow to several cortical regions of the brain. This can increase synthesis of neurotransmitters such as serotonin, noradrenalin, and acetylcholine which can alter neuronal structure from the synaptic level to major cortical pathways[17]. These neurochemical changes can be associated with the feeling of wellbeing and control one experiences when exercising.

Another cause of plasticity in the brain has been shown to be the result of an increase in synthesis and release of brain derived neurotrophic factor or BDNF [18]. BDNF is a protein that promotes neuronal survival, differentiation, and neuronal growth[19]. BDNF enhances synaptic connectivity and transmission by altering morphology on the post synaptic neuron[20].Increased levels of BDNF during and after exercise enhances neuroplasticity and is thought be responsible for some of the cognitive enhancements seen when exercising, such as improved memory and learning[21]. It has been shown that BDNF levels decline with age and is reduced in the elderly with several neurodegenerative diseases such as mild cognitive impairment, Parkinson’s disease, dementia, and Alzheimer’s disease[22]. Exercise is thought to be a neuroprotective factor against many of these diseases, in one way, by increasing BDNF serum levels. There are limitations when studying BDNF. Only peripheral levels of BDNF have been measured in humans during exercise. Mice studies, however, were able to measure increased levels of BDNF mRNA in the brain of trained mice versus untrained mice[23,



24] . Almost 75% of BDNF is synthesized in the brain which suggests that the brain is the main site of production for circulating BDNF as it is able to cross the blood brain barrier [23]. Insulin Growth Factor 1 (IGF-1) is another neurotrophin involved in promoting neurogenesis, neuronal differentiation and survival. It also can enhance BDNF function[25]. Exercising at high intensities can show an increase in IGF-1 levels by up to 15% compared to before exercising. Improvements in executive function were found to be positively correlated with post exercise IGF-1 increases[26].

Cerebral Blood Flow

Cerebral blood flow changes during exercise is a variable that cannot be ignored. Altering the amount of blood and ultimately oxygen supply to the brain are implicated in the process of neuroplasticity and neurotransmitter production. It also may be responsible for some functional, cognitive changes observed during exercise. The body has a limited blood supply and when engaging in physical activity, major muscle groups are recruiting much of the oxygen requirements.

Functional near-infrared spectroscopy (fNIRS) can be used to measure cortical oxygenated hemoglobin (O_2Hb) and deoxygenated hemoglobin (dHb) levels in the superficial cortexes of the brain during exercise. It has been found that when engaging in exercise at 60% of maximal heartrate increases prefrontal cortex O_2Hb levels but when exercise intensity is high, O_2Hb levels actually decline[27]. Although there is some inconsistency in this trend. One study found a steady increase in PFC blood flow even when in engaging in 84% of maximal heart rate and maximal VO_2 peak[28]. Other measures are being explored such as measuring carotid artery blood velocity, EEG, SPECT, and PET. There are consistencies in the fact that there are changes to different areas of cerebral blood flow during exercise. Notable increases in blood flow are consistently seen in the motor cortex, as well as changes in PFC. Other areas such as brainstem nuclei, hypothalamus, the sensory thalamus, white matter in the cerebellum and corpus callosum have all been reported to have altered blood flow during exercise[5]. Increases in the total blood volume of the hippocampus is associated with neurogenesis and angiogenesis that takes place in the dentate gyrus[29].There are also inconsistencies in whether overall CBF increases or if it is just a regional redistribution of blood. The inconsistencies may be attributed to the measurement tools used in the study. CBF is associated with local cerebral glucose utilization. Increased blood flow indicates increases in function and activation and furthermore glucose utilization or metabolism.

The areas of the brain receiving the greatest amount blood flow are considered to be utilizing the most energy and therefore have increased activity, meaning other areas of the brain are inhibited or inactive. One hypothesis is that the areas of the brain not directly associated with executing the physical activity are inhibited and only the essential areas are activated. This is more relevant at high intensities as blood distribution is localized to the areas in more immediate need[5].

Cognition

Morphological changes of the brain alter neural circuits and ultimately functional outcomes, arising in the form of cognition modifications. Some of the cognitive benefits seen as a result of physical exercise are improved memory, attentional processes, executive-control processes, academic achievement, and prevention of cognitive decline. These cognitive benefits arise from the structural changes that occur during physical exercise such as increased brain volumes or elevated neurotrophins[9]. Thus, linking structure and function.

Memory is one cognitive faculty that frequently improves when one engages in physical exercise. The hippocampus is responsible for memory consolidation and therefore learning and also plays a role in overall mood and cognition. Increasing levels of BDNF and IGF-1 through exercise stimulates neurogenesis in the dentate nucleus of the hippocampus which can explain the effects on memory[2, 25]. It is shown that hippocampal volume is greater in those who are physically fit. Acute and long-term aerobic exercise may have different effects on memory. Acute bouts of moderate intensity aerobic exercise have been shown to improve long-term and may prime the brain for learning whereas long term exercise may play more of a neuroprotective role[30].

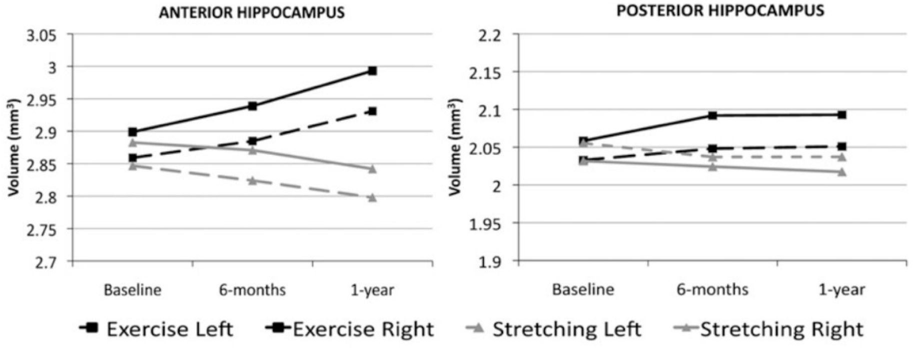


Figure 1. The exercise group showed a selective increase in the anterior hippocampus and no change in the posterior hippocampus.

The hippocampus loses volume into late adulthood. As a result, memory declines and the risk for dementia is more prevalent. Erickson et al showed that aerobic exercise can increase the volume of the hippocampus in elderly individuals by 2%. This correlates to 1-2 years of age-related hippocampal volume loss, indicating physical exercise as a method of prevention of age-related cognitive decline. They compared an aerobic exercise group consisting of 1 year, three sessions per week of moderate aerobic exercise to a control group consisting of only stretching.

MRI scans found that the aerobic exercise group displayed increases in the anterior portion of the hippocampus and had improved spatial memory tasks compared to the control. The anterior hippocampus includes the dentate gyrus, the site of cell proliferation which explains the increase in anterior hippocampal volume as opposed to posterior or (see fig.).

One cognitive faculty that surprisingly is underrepresented in the literature is that of attention. However, there are consistent finding in reference to exercise-induced increases in performance on attention tasks such as the Flanker and Go/No-go tasks which are measures of attention allocation and execution[31]. Also, higher fitness levels are associated with improved performance on these tasks compared to lower fitness levels. 6 months of aerobic training versus the control group, consisting of stretching and toning procedures, showed similar results[32].

Depression, Anxiety, Addiction and Wellbeing.

It has been demonstrated that exercise can improve psychological well-being in people of any age and overall quality of life[33]. Areas correlated with well-being include higher levels of self-efficacy, tasks goal orientation, and perceived competence in children who engage in physical exercise[34]. In adults it has been demonstrated that physical exercise improves mood and self-concept [9]. Together these areas contribute to an increase sense of wellbeing. Though an abstract and subjective concept, improved wellbeing may serve as the foundation for combating, or at least offering a nonpharmaceutical adjunction for mental health disorders.

It is thought that these positive effects of well-being are the result of increased cerebral blood flow and maximal oxygen consumption, as well as increased serum concentrations of endocannabinoid receptors[9]. Improved neural metabolism can help regulate neurotransmitters production.

Physical activity has also been shown to be an effective treatment in disorders such as anxiety, depression, and addiction. Aerobic exercise in particular has shown promise in alleviating symptoms of depression and anxiety. Individuals with Major Depressive Disorder showed significant improvement in depressive symptoms after a 16 aerobic exercise training[35].In general, people who regularly exercise are less depressed and anxious than individuals who do not and this is true for most types and durations of physical activity[36].

BDNF may play a role in linking physical activity to its efficacy as a treatment option for these mood disorders[17]. It has been shown that exercise directly increases serum levels of BDNF and correlated with reduced depressive symptoms. In terms of utilizing exercise for treatment it is important to adjust the type and duration of exercise based on the patient. Aerobic and anaerobic forms of exercise both have a beneficial effect on depression and anxiety[36]. Exact duration and intensities of both are still being studied.

Major Depressive Disorder also presents higher than normal levels of oxidative stress and exercise has been shown to reduce oxidative stress in MDD patients and correlates with a decrease in depressive symptoms[37].

Using exercise as a treatment for addiction has shown promise also. There is evidence showing that physical exercise can reduce cravings to addictive substances and behaviors such as nicotine, alcohol, and gambling and also can improve impulse control[38]. This is true for most unhealthy behaviors and is closely linked to the prefrontal cortex activity.

Not only does exercise directly improve symptoms of depressions, anxiety, and addiction, but in many ways can indirectly benefit individuals suffering from these disorders. Exercise can improve confidence and self-image which may supplement the direct physiological benefits.

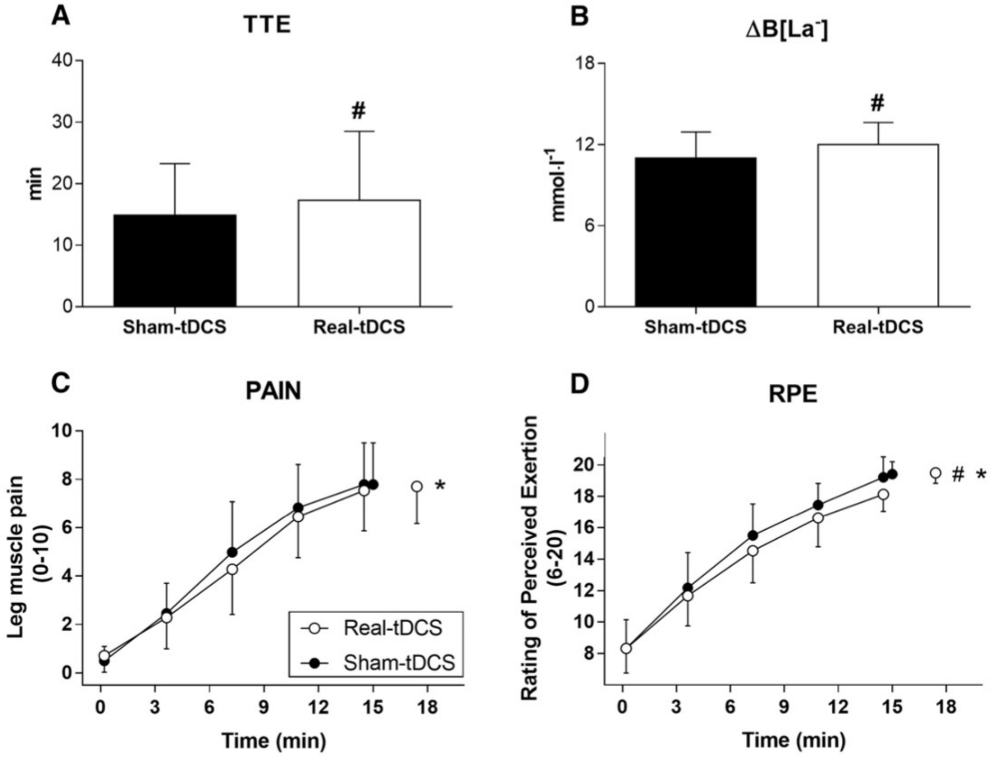
Improved social connections cannot be overlooked either. Joining a gym, club, or team brings along with it a sense of common purpose and community which are beneficial to mental health.

The Prefrontal Cortex

The prefrontal cortex is the most recently evolved area of the brain and is involved in a lot of the processes that make us human[39]. The prefrontal cortex is involved in inhibitory control, decision making, working memory, problem solving, addictive behavior, and emotion regulation [40] [39]. Together these are termed executive functioning. Simple reflexes and automatic behaviors are not dependent on the prefrontal cortex. These innate or automatic behaviors are essential to survival. They control the control the drive to keep us alive and reproduce. These are termed “bottom up” behaviors, as they originate in lower, more primitive areas of the brain and are seen across species. As humans evolved, the size of the prefrontal cortex increased in mass and so did complex behaviors associate with it. When the bottom up impulses are not regulated by top down processes, self-regulation is impaired. This is due to a failure in the prefrontal cortex or a strong bottom up stimulus as seen in addictive behaviors. When the addictive behavior is queued from a stimulus associated with that behavior, the impulse can be strong enough to override the self-regulation from the prefrontal cortex[40]. The prefrontal cortex works in a top down matter to synthesize, integrate, and inhibit neural activity. This is done through higher order of thought and planning.

An effective metric of prefrontal cortex activity is measuring inhibitory control. The classic experimental design to measure inhibitory control is the Stroop Test [41]. The Stroop test is designed to elicit inhibitory by selectively attending to one attribute of a stimulus. Typically, this is done by showing the word of a color displayed in either the correct color of the word displayed or a different color than the word displayed. For example, inhibitory control is utilized when quickly reading the word “RED” displayed in a green color. This shows the ability to select a weak, task-relevant response, when stronger irrelevant stimulus is present. When the prefrontal cortex is impaired, performance on this is test suffers[42]. In particular the dorsal lateral pre-frontal cortex area of the brain is important in inhibitory control and is the focus of a lot of research.

Regulatory control, more specifically, inhibitory control is highly involved in regulating strenuous exercise. Inhibitory control is applied during exercise to reduce unpleasant sensations along with exercising. As such, people with greater inhibitory control are able to engage longer in unpleasant physical activity. It was shown that professional cyclists have greater inhibitory control capacity and display greater tolerance to mental fatigue. Professional cyclist, more specifically, have better performance on Stroop tests than recreational cyclists[43]. Both the prefrontal cortex, and the motor cortex are engaged and connected when executing physically demanding exercise. Manipulating the activity of the prefrontal cortex through transcranial direct current stimulation has been shown to improve performance on cognitive and inhibitory tests, such as the Stroop test[44].A recent study looked at transcranial direct stimulation (tDCS) of the left dorsolateral prefrontal cortex(L-DLPFC) and its effect on not only on the Stroop task but on its effect on endurance tasks[45]. Inhibitory control is hypothesized to



be important in regulating, or suppressing the unpleasant feelings associated with strenuous exercise. Inhibitory control is a feature of cognitive self-control that is subject to fatigue if applied over long duration or during episodes of extreme effort. Depletion of self-control capacity leads to self-regulatory failure. Rest and training in self-control can replete these cognitive reserves[46]. By directly stimulating the L-DLPFC, the area of the prefrontal cortex involved in inhibitory control, The results were consistent with previous findings that tDCS improved performance on Stroop tests. However, they also found that participants were able to engage longer in physical activity as participants perceived their own exertion as being less than that of the control group who received no tDCS. Participants even had decreased heart rates during strenuous exercise after receiving the tDCS treatment(See Fig). In In connection with the inhibitory control hypothesis, participants perceived the effort and unpleasant feelings associated with strenuous exercise to be less after receiving the tDCS indicating that their self-control capacity was greater than the control and were able to self-regulate their behavior better[45].

Functional near-infrared spectroscopy methods found that moderate intensity, acute aerobic exercise enhances activation of the DLPFC and was associated with improved Stroop test results[47]. Which offers evidence of an interesting dynamic between the DLPFC and physical exercise. Moderate aerobic exercise transiently enhances the DLPFC. In turn, activation of the DLPFC is a neural substrate for inhibitory control, with stronger activation associated with increased levels of inhibitory control and the ability to sustain unpleasant feelings for a longer duration. The ability for acute exercise to enhance inhibitory control may be due to increased wakefulness, as fatigue is associated with decreased activation of the prefrontal cortex[47].

These findings emphasize the importance of top down processing when engaging in unpleasant tasks. Not only is the activity of the DLPFC elevated in individuals with greater inhibitory control, gray matter volume is also increased. Aerobic fitness and executive function are both positively correlated with increased gray matter in the PFC. More specifically, fitness levels are positively correlated with greater DLPFC volume of the PFC and executive functioning[48]. MRI studies have shown that long-term exercise can increase volume in the prefrontal cortex as well as the hippocampus and striatum[49].

There are also the transient effects of acute exercise on the prefrontal cortex that can last up to two hours after termination of physical activity[50]. This is consistent with studies showing transient increases in neurotransmitters, neurotrophins, neuromodulators, specifically BDNF and IGF-1. These effects also last up to two hours post physical activity[51]. Therefore, an accumulation of sessions of moderate intensity aerobic exercise will, over time, increase neurogenesis and angiogenesis in the prefrontal cortex, promoting greater executive control.

In contrast, fatigue or overtraining can result the inhibition of this top down control giving rise to impulsivity as inhibitory control is depleted[52]. This was found to be the accumulation of overtraining over a period of time (3 weeks).A single session of extreme exertion does not produce these effects. However, the biological causes have not been identified for this phenomenon.

Discussion

This review highlights how physical exercise has the ability to reshape the brain and alter cognitive faculties. At the molecular level, BDNF and IGF-1 increase the brains plasticity by inducing the generation of new neurons and increasing synaptic connectivity. Increased cardiac output and redistribution of blood during exercise increases metabolic processes in areas of the brain and proved other areas with increased resources for neurogenesis. These processes physically alter the size and connectivity of the brain leading to enhanced cognitive faculties such as improved memory, and inhibitory control.

Exercise is a neural protective factor against many diseases such as dementia, and Alzheimer's Disease. It also can alleviate symptoms of depression and addiction. It is a cheap, easily accessible treatment option for patients. Exercise is not only a means to improve cardiovascular health and manage weight, it also can improve mental health and neurological disorders and needs to be considered when discussing the health benefits of physical exercise. In order to effectively prescribe physical exercise as treatment option, proper protocols need to be set. As physical exercise and brain health is a relatively new field of study, there has been a wide range of protocols implemented. As discussed, there are differences between a single bout of exercise and exercising over a period of time. Having standardized measures of duration, frequency, intensity, and type of physical activity need to be set in order to identify the proper way to exercise based on desired outcomes. The literature has mostly focused on the elderly and on developing children. More needs to be explored about the differences and or similarities of outcomes between ages.

Exercise increases the volume of the PFC. These changes are correlated with greater executive control. Not only does activity in the DLPFC increase during exercise to inhibit unpleasant feelings and repress the desire to discontinue, it also accumulates volume over time. Therefore, physical exercise improves inhibitory control in two-fold manner. This may explain its role in repressing cravings in individuals suffering from addiction.

Our brains are always adapting and changing in response to the environment and time. The areas of the brain that are the most malleable, such as the PFC and the hippocampus, are the two areas that seem to benefit the most. Implementing an exercise regimen is a healthy to ensure that the brain is adapting in a positive fashion.

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