

Acute Effects of Exercise on Brain Function

Introduction

It is well known that physical exercise has beneficial effects on brain health and function (Hillman, Erickson, & Kramer, 2008). The chronic effects of exercise training indicate that exercise can have protective effects on white-matter integrity (Johnson, Kim, Clasey, Bailey, & Gold, 2012), cognition (Hötting & Röder, 2013), and memory (Roig, Nordbrandt, Geertsen, & Nielsen, 2013). Acute exercise has also been shown to elicit improvements in mental health including cognition (Chang et al., 2014), motor function (Roig, Skriver, Lundbye-Jensen, Kiens, & Nielsen, 2012; Skriver et al., 2014), memory (Pesce, Crova, Cereatti, Casella, & Bellucci, 2009), and others (Chen, Yan, Yin, Pan, & Chang, 2014). Exercise has been used as a clinical intervention for many neurological and cerebrovascular diseases including stroke (Austin, Ploughman, Glynn, & Corbett, 2014), Parkinson's disease (Tambosco, Percebois-Macadré, Rapin, Nicomette-Bardel, & Boyer, 2014), and Alzheimer's disease (Pérez & Cancela Carral, 2008). Exercise is an attractive treatment because it is low-cost and has virtually no detrimental side-effects (aside from disease-limiting conditions). Exercise has shown improvements in clinical populations as well as normal, healthy populations for a variety of aspects of brain health. Improvements have been quantified by changes in cerebral blood flow (CBF) during and following acute exercise as well as changes in motor function and cognition following acute exercise. Knowledge on potential mechanisms is limited, but researchers are examining certain processes including neurogenesis and angiogenesis, and exploring biomarker roles in improving brain function.

This review will provide an updated report on the current status of research on the effects of acute exercise on cognitive and motor function, focusing on several areas in particular: the

effects of acute exercise as potential treatments for cerebrovascular disease; changes in exercise-induced cerebral blood flow (CBF); the effects of exercise on cognition and motor function; and, finally, potential mechanisms such as neurogenesis and angiogenesis.

Cerebrovascular Diseases

There is a limited body of research that has examined the effects of acute exercise on patients who have sustained a brain injury or a degenerative condition. This is, however, a nascent research area, and experimentation is difficult due to conditions limiting these populations from exercising. One study showed that in patients with chronic stroke, 20 minutes of acute weight-supported treadmill walking (at 70% Heart Rate Reserve [HRR]) improved skilled movement in the hemiplegic upper extremity, but cognitive performance did not change (Ploughman, McCarthy, Bossé, Sullivan, & Corbett, 2008). These researchers concluded that exercise can improve skilled movement following acute exercise that is unrelated to visuomotor processing and attention. Cognition was assessed with a series of common tests including Trail Making Tests Parts A and B, Symbol Digit Substitution Test, and the Paced Auditory Serial Addition Test. The Action Research Arm Test (ARAT) was utilized to measure hemiplegic upper-extremity motor skill. With populations with neurodegenerative disease, where there is commonly a wide range of severity, it is important to note that those able to participate in exercise studies may not be the most representative of the population. In this particular study, 51 stroke patients were excluded (out of 72) for various reasons, of which some included the inability to walk and lack of hand movement. Perhaps these more severe cases have more room for improvement, and may show different results on cognitive tests. Further research must be done for acute exercise in stroke patients in order to make conclusions.

In a rat study, the effects of acute exercise in mice with an induced ischemic stroke were tested and biomarker values were obtained to measure the potential for brain remodeling (Ploughman et al., 2007). Mice were separated into a motorized (forced) wheel running group and a voluntary running group. The motorized running group exercised at a higher intensity and for a longer duration, eliciting a greater increase in BDNF than the other group. However, the voluntary running group also saw significant increases in BDNF that were sustained for longer period, i.e., up to two hours following a bout of acute wheel running. For clinical applications, because the motorized group also experienced stress-related increases in corticosterone and down regulation of pCREB, shorter, frequent bouts of exercise are suggested over prolonged, higher intensity exercise in stroke populations.

It is evident that in populations where physical capabilities limit the amount of exercise participants can perform, different prescriptions must be made in order to elicit beneficial effects. However, it is important to note that even with limited ability to exercise, similar findings occur. One major benefit that exercise has on brain health can be examined by changes in cerebral blood flow.

Changes in Cerebral Blood Flow

When examining motor function with brain imaging, functional magnetic resonance imaging (fMRI) is a great tool use for measuring changes in cerebral blood flow (CBF). CBF is quantified by a signal produced when a brain region responds to stimuli. (This signal is known as the blood oxygen level dependent [BOLD] response.) This signal in fMRI is indicative of oxygen consumption by brain tissue, and can be made visible during fMRI processing. When looking at motor function, brain areas of particular interest include the motor cortex, premotor cortex, somatosensory cortex, and other cortical areas. Finger tapping is an excellent tool that

elicits localized brain activation and a significant increase in motor-related BOLD response (Olman, Pickett, Schallmo, & Kimberley, 2012). It typically involves having a participant tap a response button at a particular rhythm (2-3 Hz) for a period of about 20-60 seconds. Examining the brain regions activated by this task is important to examine neuromotor health.

Certain groups have used fMRI following acute exercise in order to examine the resultant changes in CBF (Smith, Paulson, Cook, Verber, & Tian, 2010). 30 minutes of moderate intensity acute exercise elicited a significant increase in CBF in the motor cortex during a subsequent simple motor task. Finger-tapping and acute exercise (likely independently) elicited an increase in CBF to the motor cortex during the subsequent motor task. However, cerebral blood flow is still just an estimate of neuronal activation. Study designs must be examined closely to make certain that findings are a result of the desired performance on the task, not simply an exercise-induced increase in global CBF. If CBF is increased and neuronal demand is similar to that at resting, an increase in oxygenated hemoglobin to certain brain areas (i.e., the motor cortex during a finger-tapping task) may suggest lower neuronal activation. It is often unclear if increased perfusion reflects increased neuronal activation.

Another fMRI study demonstrated a significant increase in CBF in sensorimotor areas of the brain following a 20-minute, moderate intensity bout of acute cycling exercise (Rajab et al., 2014). These areas included the pre and/or postcentral gyri, secondary somatosensory area, and thalamus. It is interesting to note that these CBF changes occurred without any sort of motor task. These findings suggest that CBF in motor areas can be increased independently by acute exercise, regardless of the presence of a motor task.

Using cerebral blood flow as a measure of brain health is commonly used, and is an excellent indicator of brain vascularization and its ability to provide oxygen to functioning areas.

Although it is an indirect measure of neuronal activity, it is highly correlated to the functioning brain. Exercise elicits changes in cerebral blood flow which may yield or explain certain changes in motor and cognitive function.

Changes in Motor Function and Cognition

Motor function and cognition are two significant indicators of overall brain health and function. One bout of acute exercise has been demonstrated to significantly improve motor memory (Roig et al., 2012). When twenty minutes of intense aerobic exercise (intensity measured by maintenance of a minimum blood lactate level) was performed immediately before practicing a visuo-motor accuracy-tracking task, these participants saw a significantly greater retention of this skill both 24-hours and seven days after the control group. A group that exercised immediately after practicing this task showed even more significant motor task retention than both other groups (rest and pre-practice) seven days later. Aside from motor memory tasks, reaction time is a very sensitive measure of cognitive and motor function.

Electromyography (EMG), a very accurate tool to measure the health and functionality of muscles and their connected motor neurons, is one of the best ways to measure motor function through reaction time. One study led by Ozyemisci-Taskiran used EMG to examine the premotor fraction of reaction time, i.e., the period between the stimulus onset and the onset of the response signal (Botwinick & Thompson, 1966) following a 20-minute bout of acute cycling (Ozyemisci-Taskiran, Gunendi, Bolukbasi, & Beyazova, 2008). The task involved squeezing a ball immediately upon receiving an electrical stimulus. They found that there was a significant reduction in reaction time in the exercise group, but for the group who performed the task twice 20 minutes apart, no significant reduction was reported. It is important to note that the control group also performed the task 20-minutes apart to eliminate a “practice effect.” Another group

using EMG examined reaction time following an auditory stimulus (Audiffren, Tomporowski, & Zagrodnik, 2008). In this study, reaction time was examined during and following exercise, and there was a significant reduction in time to respond to the stimuli during the exercise, immediately following exercise, but no difference in reaction time more than 15 minutes after exercise cessation. This indicates that motor processes were enhanced with exercise during and immediately after exercise, but not for long afterwards. An important aspect of this study was that it was performed within participants. Every participant performed both a rest session and an exercise session on separate days, in a randomized, counterbalanced order. This style of experiment eliminates any group difference interactions in results.

The evidence suggesting exercise-induced increases in motor function, motor memory, and cognitive and executive function is quite strong and consistent. This finding is repeated frequently in the literature, and regardless of what measuring tools were used, it is quite difficult to track down an exact causal relationship. In order to determine what particular pathway causes exercise to elicit such changes in brain blood flow and functions, several studies explore the potential mechanisms of these changes.

Neurogenesis, Angiogenesis and Other Potential Mechanisms

Mechanistic studies are immensely important to cognitive motor neuroscience; however, major limitations exist in human mechanism studies. Techniques such as fMRI are non-invasive, have high spatial resolution (usually 2-3mm) with relatively high temporal resolution (about 2 seconds), yet noise is a huge detrimental factor for fMRI data acquisition. An ideal fMRI study has no movement from the participant, and therefore prolonged exercise whilst in an fMRI scanner is not feasible.

Aside from neuroimaging studies, some groups have looked at potential biomarkers having an influence on enhanced brain function. Acute exercise increased levels of lactate, vascular endothelial growth factor (VEGF), dopamine, norepinephrine (NE), epinephrine, brain derived neurotrophic factor (BDNF), and insulin-like growth factor (IGF-1) (Skriver et al., 2014). The exercise group compared to the rest group showed significantly better motor skill retention 24 hours and seven days following practice of a newly learned motor skill. Higher concentrations of BDNF correlated with better skill retention 1 hour and seven days after practice. Higher NE correlated with significantly better skill retention at seven days. Also, lactate levels were significantly correlated with skill retention at 1 hour, 24 hours, and seven days following practice. It is important to note that peripheral BDNF levels and motor performance has not been convincingly shown to have a strong correlation. However, as the brain commonly uses lactate as an energy supply, and peripheral lactate can in fact be shuttled across the blood-brain barrier, this finding suggests quite strongly a potential mechanism for enhanced motor memory.

Conclusion

Exercise as a non-pharmacological treatment has quite interesting implications. Its potential benefits in treating Alzheimer's disease and stroke provide relevance to its low-cost and simple administration. Although exercise prescriptions for these conditions differ from prescriptions assigned to healthy populations in order to improve overall health or other brain health facets, it is important that research is done in order to determine how much should be performed and how it is beneficial to clinical populations. Studies must be done in order to determine a safe exercise prescription as well as to determine what benefits can be realized in clinical populations. Methods of determining changes in brain health and functions have also

been discussed. Cerebral blood flow and the BOLD response are very important for imaging methods in examining changes in neuronal activation and oxygen consumption. With imaging techniques such as fMRI, examining CBF in the brain has led to some important findings.

Increases in CBF in the motor cortex have been shown as a result of a task as well as following exercise unrelated to a simple motor task being performed. Such findings support increases in motor, cognitive, and executive functions.

Some of the most convincing evidence that exercise can improve brain function in motor areas is the increases in cognition, motor function and reaction time, and motor memory. Consistent findings exist that one single bout of exercise enhances many measures of cognitive and motor function. What is needed in this area is the duration and mode of exercise that elicits the most significant benefit if it is to be prescribed to anyone. Understanding why exactly a certain type, intensity, or duration of exercise is most beneficial is one of the most difficult questions to answer. What mechanisms are involved in enhancing brain function? It is a common notion that neurogenesis must follow angiogenesis; that new brain tissue must have an oxygen supply to go along with it in order to arise. Some studies have examined this notion but not many have reached thorough conclusions. Evidence of brain-derived and plasticity-enhancing molecules have been examined like BDNF and VEGF, and exercise has been shown to increase these molecules. Though there have been findings that examine these as potential mechanisms for brain health and function, many more studies must be conducted in humans. Animal studies are important for this sort of thing, but it is very hard to certainly determine that this can be applied to the human brain.

Overall, there has been significant evidence supporting the benefits of exercise on brain function, particularly in cognitive and motor function. Though not fully decisive, there are some important implications as a potential non-pharmacological intervention in cognitive health.

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