Drew University

College of Liberal Arts

The Effects of Physical Activity on Cognitive Development in Adolescents

A Thesis in Neuroscience

by

Grace Crozier

Submitted in Partial Fulfillment of the Requirements for the Degree of Bachelor in Arts Specialized Honors in Neuroscience

May 2021

Abstract

Introduction: Numerous benefits of physical activity relating to cardiovascular health, sleep and mood have been largely examined in the current scientific literature. However, a lesser understood relationship is that of physical activity and brain health. Brain health has typically been described as cognitive performance, but it can also be elaborated and include brain structure and brain function. Various brain structures have been shown to increase or decrease in size as a result of physical activity, as well as activity in those areas has been shown to either increase or decrease. Research regarding the impact of physical activity on brain structure and brain function is already largely understood, however, the resulting changes in cognition have yet to be explored extensively, specifically in adolescents.

Methods: PubMed, PsychINFO, and ERIC were used for the literature search. Search terms relating to "physical activity", "cognition", and "adolescent" were used in each database. The inclusion criteria as for which studies were reviewed included if it used an RCT study design, it included adolescents between the ages of 12 and 18, the population didn't have preexisting health conditions, and it examined the effects of various manipulations (frequency, intensity, duration, time of day, and time of cognitive testing) of physical activity on cognitive functions.

Results: A total of 13 RCT studies were reviewed. When looking at how the duration of physical activity affected cognition, it was shown that short durations were effective at improving attention, concentration, and inhibitory control, while memory didn't improve for either short or long durations. Single bouts of exercise were more effective at improving attention and inhibitory control, compared to increased frequencies of activity. No clear conclusions were

drawn from looking at the intensity of physical activity because different studies defined moderate- and high-intensity differently, limiting the ability to directly compare results. For participants that were tested immediately after engaging in physical activity, attention, concentration, and inhibitory control were improved immediately. However, memory didn't begin to show improvements until up to 48 hours after activity. And finally, one study looking at physical activity in the morning showed improvements in attention and concentration, but not memory. Studies that looked at physical activity in the middle of the day showed improvements in inhibitory control and executive function.

Discussion: When considering the mechanisms by which cognition improved as a result of physical activity, CBF and BDNF are two possibilities. CBF may be responsible for the immediate, short-lived improvements in attention and inhibitory control because it is delivering additional glucose and oxygen to the brain which aids in functioning. However, longer term effects relating to memory didn't improve immediately most likely because the brain needs to undergo structural changes, which would require greater expression of BDNF overtime. When considering why increased frequencies didn't improve cognitive functions as effectively as single bouts, the idea of energy depletion in which the body begins to utilize oxygen and glucose elsewhere in the body, is considered.

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1. Introduction

As new literature continues to emerge, the relationship between physical activity and brain health continues to become more prevalent, with specific regards to cognition. This is not only amongst researchers, but also the general public. Within this area of study, numerous researchers have worked to understand the effects of physical activity on cognitive functioning in aging individuals. These studies were primarily done with the goal of evaluating if physical activity could serve as a preventative measure for the normal cognitive decline that is experienced in aging. Looking towards the other end of the age spectrum, the effects of physical activity on cognition in adolescents has not been reviewed as extensively. Given this hole in the current literature, the primary goal of this work was to systematically review published primary literature regarding the effects of physical activity on cognitive functioning in adolescents between the ages of 12-18 years old. This review specifically examined multiple variations of how physical activity was manipulated, including frequency, intensity, duration, time of day, and the time in which physical activity was administered compared to when cognitive tests were taken.

Before discussing the effects of physical activity on cognitive functions in adolescents, this review will start by acknowledging some of the current organizations and health guidelines in place that aim to educate and promote overall physical health. One of the ways in which these organizations promote physical health is through educating the general public on the benefits of physical activity, including cardiovascular health, sleep, and mood, all of which will be explored in more detail. Additionally, some of the current trends relating to obesity and rates of physical activity in adolescents will be addressed. This will lead into a discussion regarding the relationship between brain health and physical activity. Within this, we'll attempt to define the term "brain health", while addressing the current lack of consensus amongst neuroscientists as to what constitutes a healthy brain. From this, we'll draw upon two components that make up brain health: brain structure and brain function. To understand the relationship between physical activity and brain health, the changes to brain structure and brain function as a result of physical activity will be evaluated extensively. Additionally, the current literature regarding the effects of physical activity on cognition in aging populations will be explored. From there, the rationale for the current systematic review will be discussed.

1.1 Current health organizations and guidelines

For many years now there has been an increase in understanding not just amongst medical professionals, but also within the general public, that physical activity provides numerous benefits for overall health. These benefits have become so prevalent that organizations, such as the World Health Organization (WHO), have dedicated experts who are responsible for evaluating and communicating with the public current developments in research and worldwide action plans to encourage achieving the highest level of health. Included in these communications are specific guidelines for physical activity in order to educate and promote the public of the importance of exercise.

More specifically, the WHO provides information related to the frequency, intensity, duration, type, and total amount of physical activity to prevent diseases related to being physically inactive. According to the global recommendations by WHO on physical activity for health, children between ages of 5-17 years should have at least 60 minutes of moderate to vigorous-intensity of physical activity everyday (World Health Organization, 2015). Furthermore, for both age brackets of 18-64 years and 65+ years the recommended amount is at least 150 minutes of moderate-intensity aerobic physical activity weekly, with the addition of strength training activities at least twice a week (World Health Organization, 2015).

When following these specific guidelines, a variety of benefits for overall health have been observed. Some of the more prevalent benefits in current research include cardiovascular health, sleep and mood disorders.

1.2 The effects of physical activity on cardiovascular health

The benefits of physical activity have been shown to be especially prevalent when looking at cardiovascular health (Villareal et al. 2017; Sigal et al. 2014; Ho et al. 2012). More specifically, increased physical activity has been shown to lower body weight and body mass index (BMI), which indicates an individual's body fat through calculations using body mass and height; at the same time, cardiorespiratory fitness was shown to increase (Sigal et al. 2014; Ho et al. 2012). One study in particular looked more specifically into different types of physical activity, including aerobic exercise and resistance exercise, and their effect on cardiovascular risk factors. Aerobic exercise generally consists of activities that utilize oxygen as a way to meet the energy needs of the exercise through aerobic metabolism; some of these activities can include walking, running, swimming, rowing, and biking. On the other hand, resistance training generally has the goal of improving strength and endurance, and therefore involves activities such as lifting weights. Overall, this study demonstrated that a combination of both aerobic and resistance training led to the largest decrease in weight, BMI, and fat percentage, and the largest increase in VO_2 max (Ho et al. 2012). VO_2 max refers to the maximum rate of oxygen your body utilizes and processes while exercising. The oxygen that we breathe in while exercising is used by our lungs to produce adenosine triphosphate (ATP), which serves as a major source of energy

throughout the entire body. Thus, by increasing the rate in which the body can process oxygen $(VO_2 max)$, this can then lead to greater production of ATP, and therefore increased energy for cells and body overall. This finding of increased $VO_2 max$ for the group that did both aerobic and resistance training was in comparison to a sedentary control group, aerobic exercise group, and resistance exercise group.

This finding was further supported in another study, which looked at the same comparisons of different types of physical activity (Villareal et al. 2017). Within this study, the combination group improved more on the physical performance test, which consisted of walking, going up and down stairs, picking up a penny, etc., and in VO₂ max. However, with regard to body composition, this study presented contradictory findings than those of Ho and colleagues. This study instead demonstrated that aerobic exercise resulted in the greatest decrease in body weight and lean mass, while resistance exercise resulted in the greatest decrease in fat mass (Villareal et al. 2017). Additionally, another study suggested that endurance training in particular has been seen as an effective measure to lower blood pressure (Fagard 2006).

These studies ultimately demonstrate that physical activity can provide benefits to overall cardiovascular health, but more specifically with respect to decreasing weight, BMI, blood pressure, fat mass, while also increasing lung capacity and heart volume, reflective in increased VO₂ max. This is crucial given that all of these factors, if not maintained at recommended values, can lead to health conditions such as hypertension, heart attack, stroke, coronary artery disease, etc. Not only do these studies demonstrate the general benefits, but they are also suggestive of different types of physical activity being more effective at producing these benefits, which may prove to be useful when considering different risk factors of individuals.

1.3 The effects of physical activity on sleep and mood

Not only can physical activity influence risk factors related to various cardiovascular health problems, but increased exercise has also been seen to improve sleep and mood in people who suffer from chronic insomnia (Hartescu et al. 2015; Reid et al. 2010). While previous studies have shown that high levels of activity can help reduce insomnia, one study aimed to demonstrate if minimal amounts of recommended physical activity were sufficient to improve sleep (Hartescu et al. 2015). The results of this study showed that a minimum of 150 minutes of exercise a week was sufficient in reducing insomnia severity. These findings are in line with the recommended amount made by the WHO of 150 minutes of exercise on a weekly basis. As a result of following this recommendation, it was shown that one of the benefits of maintaining exercise on a regular basis is improvements in sleep, specifically in those with insomnia. While this study examined individuals who specifically had insomnia, given that only about 22.1% of the population who report having difficulty sleeping actually meet the Diagnostic and Statistical Manual of Mental Disorder, 5th Edition (DSM-5) criteria for insomnia (Dopheide, 2020), it is also important to examine if these benefits are prevalent in individuals who have not been clinically diagnosed with insomnia.

One systematic review aimed to evaluate the effects of both acute and chronic resistance training on sleep quantity and sleep quality in healthy participants (Kovacevic et al. 2018). The results of this review showed that acute resistance training was not effective at improving sleep quantity. Additionally, the effects of acute resistance training on sleep quality was inconclusive because the studies the authors had reviewed had widely varied results with regard to the number of arousals during sleep and the time spent in various sleep stages. Contrary to this, when examining chronic resistance training, there was a small-to-moderate effect on the duration of sleep. This suggests that chronic resistance training is effective at improving sleep quantity with regard to the duration of sleep. Likewise, when looking at the effects of chronic resistance training on sleep quality, there was a moderate-to-large effect. Additionally, greater improvements in sleep quality were seen with greater intensities and frequencies of resistance training. Overall, this review points to how the effects of physical activity on sleep quantity and quality are not just limited to those who have insomnia, but rather healthy individuals can also benefit.

Additionally, from the study previously discussed, Hartescu and colleagues showed that there were significant reductions in depression and anxiety scores in those in the intervention group. The latter finding would be expected when evaluating the numerous studies that have evaluated the relationship between depression and anxiety and physical activity. From this area of study, a number of researchers have shown that increased physical activity can alleviate the severity of symptoms associated with depression and anxiety. One correlational study in particular assessed the odds of having moderate to severe symptoms of depression and anxiety based on whether individuals were generally active or sedentary in their behaviors (Belair et al. 2018). Researchers found that those considered to be "non-sedentary" were 1.38 times less likely to have symptoms of depression and 1.31 times less likely to have symptoms of anxiety compared to those considered to be sedentary. This finding ultimately demonstrates how being more active can be associated with less severe depression and anxiety-related symptoms. Because this is only a correlational study, it can not be concluded that exercise itself causes a decrease in these symptoms. But also, one could imagine the inverse relationship in which increased severity of depression and anxiety-related symptoms may actually make it more difficult for a person to engage in physical activity. Either way, it is important to note that while

the benefits of exercise on depression and anxiety are significant, they have not been shown to be more effective than traditional psychopharmaceuticals (Carek et al. 2011). So, while physical activity may be beneficial in managing mood disorders, including anxiety and depression, it should not be viewed as a sole treatment for more serious cases of these disorders.

While it may be more common for the general public to more readily recognize the cardiovascular benefits of physical activity, increased rates of sleep (Garland et al. 2018) and mood disorders (CDC 2020) demonstrate the importance of also understanding how physical activity can affect these areas of health. Overall, what these studies demonstrate are two additional facets of general health that can be improved by following the recommendations regarding the intensity, frequency, duration, and type of physical activity made by the WHO.

1.4 Current trends related to obesity and physical activity in adolescents

Understanding the benefits of exercise in relation to overall health is becoming increasingly more important given that sedentary behaviors tend to increase with age (Schwarzfischer et al. 2019). Within this long-term study, researchers looked at how the amount in time of different types of activity varied across a 5-year span in children aged 6, 8, and 11. The types of activity tracked were moderate-to-vigorous physical activity (MVPA), light physical activity (LPA), and sedentary behavior (SB). The results of this study indicate that total physical activity decreased by 75.3 minutes a day as children continued to age. More specifically, LPA decreased by 44.6 minutes a day, while MVPA decreased by 30.7 minutes. As would be expected as a consequence of this trend, sedentary behavior increased by 107 minutes a day from the age of 6 to the age of 11 (Schwarzfischer et al. 2019). What this demonstrates is that as children continue to age, the amount in which they are physically active decreases significantly, and

instead they become more sedentary in behavior. In this, the majority of children are no longer meeting the minimum requirement of 60 minutes of moderate to vigorous-intensity physical activity a day and therefore likely do not obtain the benefits of physical activity as previously discussed.

To go along with these findings, it is no surprise that the rates of obesity in the general population, but also specifically in adolescents, has drastically increased. This increase has been so significant that adolescent obesity is now considered to be an epidemic within the United States (Sanyaolu et al. 2019). Childhood obesity has been defined as having a BMI greater than or equal to the 95th percentile, whereas an individual is considered overweight if they have a BMI between the 85th and 95th percentile. As of 2019, 17% of children are considered obese. Obesity has been shown to have clear effects on physical health with respect to metabolic, cardiovascular, and orthopedic health (Sanyaolu et al. 2019). What this means is that in not partaking in a healthy amount of physical activity, such as that recommended by the WHO, adolescents become more at risk for cardiovascular health issues, including high blood pressure, diabetes, and high cholesterol. Thus, there is a critical public health need for encouraging adolescents to be more physically active, rather than partaking in more sedentary behaviors.

1.5 Physical activity and brain health

While the benefits of physical activity on overall health are largely understood by the general public, a lesser understood relationship is that of the effect of physical activity on brain health. To this day, there is still discrepancy amongst neurologists as to a precise definition of brain health. According to the Centers Diseases Control and Prevention (CDC), brain health can be described in terms of being able to perform cognitive functions, such as learning,

remembering and using language (CDC 2011). While also, brain health has been described in a more general concept of average cognitive performance across all people who are free of any diseases or disorders that would impede performance (Gorelick et al. 2017). These discrepancies demonstrate a lack of consensus as to what constitutes a healthy brain, therefore making it difficult to make clear recommendations for optimal brain health.

A publication from the American Heart Association/American Stroke Association established the idea that brain health consists of three domains: thinking, moving, and feeling (Gorelick et al. 2017). These domains are described as consisting of paying attention, receiving and interpreting sensory stimuli, learning and remembering, problems-solving, mobility, and regulating emotions. Also discussed in this publication is the relationship between cardiovascular health and brain health (Gorelick et al. 2017). Many age-related processes result in decreased functioning in systemic organs including liver, kidney, lungs, endocrine and immune systems. Decreases in these organs and systems consequently impact overall functioning of the brain (Gorelick et al. 2017). These negative effects on the brain can then in return cause harm to an individual's cardiovascular system. This is mainly due to the disruption in mechanisms that control heart, blood vessels, and metabolism. As a result, that individual becomes increasingly at risk of cardiac damage and hypertension (Gorelick et al. 2017). In evaluating this relationship, the authors of this study established 7 metrics in which brain health can be assessed. These metrics include non smoking status, physical activity, BMI, diet, blood pressure, cholesterol, and fasting blood glucose; specific thresholds for each metric have been set using current guidelines and recommendations. In establishing these metrics with regard to measuring brain health, this ultimately aids individuals in being able to partake in specific behaviors or lifestyle choices that

can intentionally promote better brain health. This becomes especially crucial for those who have known cardiovascular risks, such as high blood pressure, high cholesterol, obesity, etc.

While the previously discussed definitions of brain health focus heavily on cognitive aspects, another way in which neurologists can define brain health is by examining structural components and functional aspects of the brain itself. By structural components, this refers to the structural changes, such as an increase in volume of various parts of the brain. Functional aspects, on the other hand, refers to increases or decreases in relative activity within different parts of the brain when performing certain tasks. Examining the effects of physical activity on both of these facets can prove to be useful when trying to understand how physical activity can potentially improve overall brain health in an individual.

1.6 The effects of physical activity on brain structure

One component of brain health that researchers have explored is the impact that physical activity has on the structure and anatomy of the brain itself. Various brain regions and structures have been shown to be altered as a result of various manipulations of physical activity. One of the most prominent changes within the brain that has been researched is those related to the hippocampus. The hippocampus is located in the medial region of the temporal lobe in each of the brain hemispheres. This structure is deeply embedded in the temporal lobe, suggestive of its functional significance and need to protect this structure from damage. The function of the hippocampus is generally associated with the learning and memory because of its critical role in forming and consolidating long-term memories and spatial navigation. In investigating the relation between physical activity and the hippocampus, numerous alterations have been observed. The first of these includes an increase in overall volume of the structure (Erickson et

al. 2011). Within this commonly cited study, researchers looked at older adults who did not have dementia and examined the effects that aerobic exercise would have on hippocampal volume. They found that after a year of participating in aerobic exercise, hippocampal volume increased by 2.12% in the left hemisphere and 1.97% in the right hemisphere. Contrary to this, those in the stretching control group, after a time span of one year, showed an average 1.41% decrease in volume in both hippocampi. This finding was shown to have linear effects in that greater improvements in aerobic exercise resulted in greater increases to hippocampal volume. Understanding this relationship becomes especially critical when considering brain health in aging adults. This is largely because as an individual continues to age, hippocampal volume progressively continues decreasing, putting that individual more at risk of cognitive decline.

Looking closer at the results of this study, an additional finding in this study showed that one of the areas in particular that increases in volume with physical activity is the dentate gyrus. The dentate gyrus is a part of the hippocampus in which multiple types of sensory stimuli converge to form mental representations and memories. Furthermore, the dentate gyrus has been shown to exhibit neurogenesis, or the process in which new neurons are formed. This process is thought to be relatively exclusive to the dentate gyrus. Thus, given this structural function and understanding that increased physical activity results in increased volume of this particular area, numerous studies have shown that increased physical activity results in increase neuronal proliferation and survival of neurons in the hippocampus (Kronenberg et al. 2006, van Praag et al. 2005). One study, using a mouse model, was able to demonstrate that proliferation of progenitor cells that occurred as a result of running led to an increase in the number of more mature cells (Kronenberg et al. 2006). That is, as the mice continued to age, with increased exercise, including running on a wheel, the decline rate of proliferation that is typical with aging, was reduced. Thus, this enhanced proliferation and cell survival serves as a key factor in maintaining intact memories and the abilities to form new memories as an individual continues to age.

Another aspect that has been observed with regard to the relationship between hippocampus and physical activity is the amount of cerebral blood flow to the hippocampus. Cerebral blood flow serves as a primary mechanism of delivering blood, which contains oxygen and glucose, to the brain, both of which are crucial elements needed for brain function. Increasing this blood flow in the hippocampus specifically would therefore enhance the function of the hippocampus with relation to learning and memory, given that more nutrients are being delivered to this brain area. One study examined the effects of aerobic exercise on cerebral blood flow in children between 7-9 years old (Chaddock et al. 2016). The main finding demonstrated that higher aerobic exercise resulted in greater cerebral blood flow to the hippocampus specifically. This was shown to be especially true for the posterior hippocampus. What made this finding more intriguing was that this effect was independent of hippocampal volume. This is suggestive that the increase in cerebral blood flow is not a result of larger volume, but rather aerobic exercise was the cause. An additional study provided a more detailed exploration of the relationship between cerebral blood flow and physical activity (van der Kleij et al. 2018). This study looked specifically at older individuals with Alzheimer's disease. Participants were randomly assigned to either the intervention group, which consisted of 16 weeks of moderate-to-high intensity aerobic exercise, or to the control group. The results of this study were suggestive that short-term exercise interventions may not be sufficient enough in increasing cerebral blood flow. That is, partaking in moderate-to-vigorous exercise for only a few weeks

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will not be as successful in enhancing cerebral blood flow. This finding essentially demonstrates the importance of physical activity as a lifelong habit.

While the hippocampus is a major structure that has been shown to be impacted by the amount of exercise an individual partakes in, gray matter and white matter in the brain have also shown enhancements with increased activity. For starters, gray matter is largely composed of neuron somas, whereas white matter is composed of myelinated axons. Gray matter is generally found on the outside of the brain and is oftentimes referred to as cortex. Its function is related to processing information that comes from sensory organs or other areas of gray matter. Sensory input is directed by gray matter to various areas of the brain to be processed further and in return elicit a response to the initial sensory stimuli. Contrary to this, white matter is found deeper inside the brain. Its primary function is in relation to learning and communication within the brain. The long axons that make up white matter span throughout the brain and allow different regions to communicate with each other. When looking at adolescent brain development, one of the more prevalent changes that occurs within the brain is an increase of white matter density. (Blakemore 2012). Because white matter is largely associated with its role in mediating learning, the growth and development of this makes it a crucial component in developing and strengthening different cognitive functions. Additionally, as the density of white matter increases, the amount of gray matter decreases (Blakemore 2012). These changes are most commonly attributed to the hormonal changes, specifically testosterone and estradiol, that occur during adolescence (Goddings et al. 2019; Herting et al. 2014).

Studies that looked at how white matter and gray matter are impacted by increases in physical activity found that generally both increase in volume (Ruotsalainen et al. 2020; Boraxbekk et al. 2016; Colcombe et al. 2006). One study objectively measured physical activity with an accelerometer and white matter was captured through use of MRI (Ruotsalainen et al. 2020). Within this study, aerobic exercise was shown to be associated with more white matter tracts. These "tracts" are the way in which the myelinated axons that make up white matter travel throughout the brain and allow different regions to communicate with one another. Thus, by increasing the number of tracts, this allows for more widespread communication within the brain. Also, if one tract were to be damaged, communication and, as a result the neuronal response to stimuli, may not be as severely impacted because there are more alternative tracts as a result of increased physical activity. This idea was further supported in another study that looked at both white matter and gray matter volume (Colcombe et al. 2006). This study consisted of participants taking part in a 6-month intervention in which they were placed in either the experimental group, which consisted of aerobic training, or the control group, which consisted of toning and stretching exercises. Results showed that those who had participated in the aerobic exercise experimental group showed significant increase in gray matter volume after the 6-month intervention. These changes were most apparent in the frontal lobe, the area of the brain responsible for voluntary movements, language, and executive functions, including attention, organizing and planning, and regulating emotions. Similar to the previous study, there was an increase in white matter tracts, particularly around the corpus callosum. This finding is significant in that the corpus callosum is the structure in the brain that allows the two hemispheres to communicate. Without this structure, numerous functions would be at a deficit, including motor functions and some sensory input. This is because many of the stimuli that come in through the left side of the body or left visual field are processed on the right side of the brain, and vice versa for stimuli on the right side of the body. Without the ability to cross hemispheres

through the corpus callosum, these sensory inputs would not be able to reach the correct locations in order to be processed.

1.7 The effects of physical activity on brain function

While alterations in brain structures as a result of physical activity is one valuable component of what contributes to brain health, another component is the functional changes that occur within the brain as a result of activity. Functional refers to changes in levels of activation in particular areas in response to increased amounts of physical activity. A number of studies have observed such functional changes through use of fMRI imaging. These images work by detecting the change in blood oxygenation levels. Essentially, when areas of the brain are active, they show greater depletion of oxygen compared to areas that are less active; this is because more oxygen is being utilized to perform that task. This allows researchers to examine the functional changes that occur in response to engaging in certain activities and what structures of the brain are active when performing particular tasks. Using fMRI scans, researchers have been able to examine the functional changes that occur within the brain in specific structures as a result of physical activity.

Many studies that have utilized fMRI imaging to capture functional differences as a result of physical activity have focused on examining various types of memory, including working memory, episodic memory, and semantic memory. These studies primarily aimed to examine the changes in performance with regard to these types of memories and the correlating functional changes that were shown through fMRI imaging.

The first of these studies looked at the effects of physical activity on the neural processing of working memory (Chen et al. 2019). Working memory can be described as the

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ability to temporarily hold information while that information is being used for processing. One of the simplest examples that can be used to demonstrate working memory is a person's ability to retain what the first words of this sentence were by the time they get to the end in order to understand the message that was conveyed. One defining characteristic of working memory is its limited capacity, meaning that the brain can only hold on to so much information at once. Thus, a person with better functioning working memory will be able to retain more information within that short time frame. The brain regions that have been identified as being involved in working memory include the inferior frontal gyrus, anterior cingulate gyrus, hippocampus, and thalamus (Chen et al. 2019).

This first study that examined working memory consisted of 70 middle-aged adults who were separated into three different groups (Chen et al. 2019). The first was an open-skill group, which consisted of activities such as basketball, tennis, badminton, etc.; the second was a closed-skill group, which consisted of activities such as cycling, running, and swimming; the final group was an irregular exercise group. Of those in the closed- and open-skilled groups, participants engaged in activity at least 3 times a day, for 30 minutes each session, for a total of 3 months. Behavioral results with regards to working memory demonstrated that both the open-skilled and closed-skilled experimental groups exhibited greater improvements with regard to working memory, as compared to the irregular exercise group. This behavioral finding corresponded with greater activation in the left inferior frontal gyrus, left anterior cingulate gyrus, left thalamus, and right hippocampus within the open-skilled exercise group when looking at fMRI imaging results. As stated previously, all of these structures have been shown to be associated with working memory; therefore, it would make sense for working memory to

improve behaviorally as activity in these particular brain regions increase as a result of physical activity. These findings ultimately demonstrate, first, how physical activity improves cognitive functions such as working memory in older adults; but this study also demonstrates a mode-sensitive mechanism related to working memory. That is, specific exercises, such as those involving more executive aspects of working memory may have varying functional effects on different brain structures, as shown by this current study.

Two additional studies looked instead at the effects of physical activity on semantic memory (Won et al. 2018) and episodic memory (Friedl-Werner et al. 2020) and the corresponding brain activity using fMRI. Semantic memory is one of two types of explicit memory, the other being episodic memory. Semantic memory is often described as the general world knowledge and includes things like facts, concepts, or dates in history; contrary to this episodic memory consists of more personalized experiences that relate to an individual's life experiences, such as a particular birthday or graduation.

The first study examining the effects on semantic memory consisted of 32 older adults, between the ages of 55-85 years (Won et al. 2018). These participants were randomly divided into either the exercise or rest group. Those in the exercise group participated in a single acute bout of exercise, consisting of 30 minutes of moderate-intensity cycling. The fMRI captured brain activity while participants did the Famous Names Task (FMT), which was the task used to activate semantic memory by identifying and recognizing household names. From these images, four regions showed greater activation for those in the exercise group as compared to the rest group. These regions included: inferior temporal gyrus, middle temporal gyrus, fusiform gyrus, and middle frontal gyrus. This is suggestive of neural circuits involved in semantic memory being enhanced by physical activity, which as a result increases may improve semantic memory.

As previously stated, another study examined episodic memory, which is the other type of explicit memory relating to recollection of personal experiences. While the previous study consisted of older adults, this study was composed of 23 young men, some of whom underwent two months of bedrest, while others were in an exercise group that consisted of high-intensity jump training (Friedl-Werner et al. 2020). From this study, there was increased blood-oxygen-level-dependent (BOLD) signal to the left hippocampus and parahippocampal gyrus in the non-exercise group, while the training group showed less activity. This data differs greatly from what other researchers have shown, in that many other studies have demonstrated that those in the exercise group tend to have greater activity in particular brain regions. The explanation for this difference in data within the current study was particularly interesting. In previous studies, researchers had identified increased neuronal activity as a positive effect of exercise because increased activity likely explained the cognitive enhancements that were shown behaviorally on various cognitive tasks. However, researchers in this study proposed this decrease in activity to be a positive effect because it is suggestive of high neural efficiency in the training group. The neural efficiency hypothesis suggests that "smarter" individuals show lower brain activity than those considered to be "less smart" when performing the same cognitive task (Dunst et al. 2014). What this means is that those who have less activation essentially require less energy and biological resources to complete the same task, which can be useful in more vigorous tasks and energy conservation.

While the studies previously described focused primarily on the functional effects of physical activity on varying types of memory, many other studies have looked at other cognitive functions such as cognitive control (Chaddock-Heyman et al. 2013) and executive functions (Davis et al. 2011). The first study looked at children who either participated in the exercise group, consisting of about 75 minutes of moderate to vigorous physical activity, or the control wait-list group (Chaddock-Heyman et al. 2013). From this study it was first shown that the right anterior prefrontal cortex and the anterior cingulate cortex were associated with the cognitive control task, independently of if the participants were in the exercise or control group. Additionally, it was shown that those in the exercise group had decreased activation in the right anterior prefrontal cortex, suggestive of the neural efficiency hypothesis that was previously discussed. This ultimately demonstrates that physical activity again results in a reduction of activity, this time more specifically in the anterior prefrontal cortex and the anterior prefrontal cortex and the anterior prefrontal cortex has previously discussed. This ultimately demonstrates that physical activity again results in a reduction of activity, this time more specifically in the anterior prefrontal cortex and the anterior cingulate cortex.

An additional study looking at executive functions consisted of randomly assigning children to either one of two experimental groups, including the low dose (20 minutes/day) or the high dose (40 minutes/day), or the control group (Davis et al. 2011). Within this study, the exercise group demonstrated greater increase in activation in the bilateral prefrontal cortex and greater decrease in activation in the bilateral posterior parietal cortex. Both of these functional changes were shown to be associated with enhanced executive functions.

Overall, in using fMRI imaging, functional changes that occur as a result of physical activity have been evident in areas such as the left inferior frontal gyrus, left anterior cingulate gyrus, left thalamus, and right hippocampus (Chen et al. 2019); inferior temporal gyrus, middle

temporal gyrus, fusiform gyrus, and middle frontal gyrus (Won et al. 2018); and bilateral prefrontal cortex (Davis et al. 2011). These areas each have associated cognitive functions, such as working memory, semantic memory, and executive functions, which have also been shown to improve with physical activity. This is suggestive that with increasing activity, there is the potential for related cognitive functions to be enhanced. However, there is discrepancy within the current literature with regard to the neural efficiency hypothesis which suggests less activation within particular brain regions may be a result of needing less energy and resources in individuals with considerably higher cognitive capabilities. Two studies support this hypothesis in that they showed reduced activity in areas including the left hippocampus and parahippocampal gyrus (Friedl-Werner et al. 2020) and the right anterior prefrontal cortex (Chaddock-Heyman et al. 2013) as a result of physical activity. These studies are instead suggestive of the idea that less activation may actually reflect greater cognitive enhancement as a result of physical activity.

1.8 Physical activity and cognition in the aging brain

In considering the structural and functional changes that occur within the brain as a result of increased physical activity, one question researchers are left with is how then cognitive functions are influenced as a result of anatomical and functional alterations. As of recently, this area of study has been extremely prevalent when looking at older populations, typically consisting of individuals of 65+ years of age. This research initially exploded within the population in specific regards to the aging brain to see if physical activity could serve as a preventative measure against cognitive decline. Brain aging refers to this idea that as we continue to age the brain undergoes changes that can contribute to the cognitive deficits that healthy individuals commonly face. There are numerous physical changes that occur within the brain as we age. The most prominent change is the decrease in overall volume of the brain (Peters 2006). This means that the actual structures within the brain itself are shrinking. This shrinkage results in decreased activity within the brain because there are less synaptic formations throughout the structures. Synapses are the spaces between neurons in which neurochemical signals are released and transferred between neurons, allowing for cellular communication. Having more synapses allows for more connections within the brain, which can serve to increase the complexity and specificity of brain function. The commonly used term neuroplasticity refers to this idea that the synapses are able to change shape and function based on experiences and new information. This unique function of the brain is essentially what allows for learning and recall of memories. However, as the brain shrinks, a number of synapses are lost or there is a loss of synaptic plasticity, thus leading to impairments related to learning and memory.

These physiological changes that occur as a result of aging are ultimately thought to cause common cognitive deficits experienced by an average, healthy individual. These deficits include functions related to memory, thinking clearly, and learning (National Institute of Aging 2020). An important note to make here is that these changes within the brain increases the risk of more concerning neurodegenerative diseases within an individual, one of the most prevalent being dementia. While some degree of forgetfulness is normal with aging, dementia is a considerably more severe extensive loss of cognitive functions related to memory, thinking, and reasoning (National Institute of Aging 2020). Some of the more common symptoms are difficulties with language, visual perception, or paying attention. In some cases, these symptoms

can develop to the extent of inferring with daily activities and can result in individuals becoming dependent on others for tasks that they once did without trouble (e.g., running errands, driving, making appointments).

Given the concerns related to brain aging and the resulting decline of cognitive functions, extensive research has been done with regard to finding preventative measures; one of these measures consists of physical activity and its effects on reducing the cognitive deficits that come with aging. One study in particular examined cognitively healthy adults between the ages of 57-75 years old (Chapman et al. 2013). These participants were divided into either a physical training group or a wait-list control group. Those in the physical training group partook in aerobic exercise 3 times a week, with each session lasting an hour in total; this went on for a total of 12 weeks. The cognitive functions of interest in this study consisted of executive function, memory, and attention. The cognitive tests were administered for both groups prior to the start of the study, 6 weeks into the study, and when the study had concluded after 12 weeks. The results indicated that initially there were not significant differences in memory for the two groups. However, by the end, the physical training group had greater improvements in both immediate and delayed memory. This finding was further supported by additional studies that also showed participants who engaged in physical activity had more enhanced memory (Wheeler et al. 2020; Etnier et al. 2018). These studies serve as demonstrations of how physical activity can improve functions such as memory, which is one of the most common cognitive functions to face deficit with aging.

A longitudinal study done over the course of 6 months total aimed to understand the effects of physical activity on inhibitory control in older populations (Colcombe et al. 2004). This study consisted of participants between the ages of 58-77 years old. These participants were

divided into either the aerobic exercise group or the control group. The aerobic exercise group consisted of walking, while the control group participated in stretching. At the start of the study, the aerobic exercise group walked for about 10-15 minutes per session; this was gradually increased to 40-45 minutes over the course of the study. As previously mentioned, this study was focusing primarily on the cognitive function of inhibitory control. In this, the cognitive test that was utilized was a Flanker task. Within this task, participants were asked to respond to a central arrow that was surrounded by additional arrows pointing in different directions. This task requires participants to essentially cancel out the distracting arrows and instead focus just on the central arrow. Their performance of this task is therefore indicative of their inhibitory control. The results of this study showed that those in the aerobic exercise group had greater improvements in the Flanker task, suggesting that inhibitory control had improved with increased physical activity.

From these studies we see how physical activity can potentially act as a preventative measure against common cognitive deficits that are experienced as a result of normal aging. This includes memory, which is the most prevalent cognitive deficit that results from brain aging. Additional reviews have examined and summarized other studies that have suggested that physical activity can also result in improved attention, processing time, spatial memory, and executive functioning (Meijer et al. 2020; Cui et al. 2018; Erickson et al. 2012).

In considering the more extensive research already done on how physical activity affects the aging brain, there is still a need in the current literature to explore the effect of physical activity in the developing adolescent brain. That is, can engaging in increased amounts of physical activity improve the development of adolescents' brains with specific regard to cognitive functions.

1.9 Rationale for the current systematic review

While the literature regarding older populations and the impact physical activity has on cognitive functions as the brain ages has largely been reviewed by researchers, that of adolescents between the ages of 12-18 years old has yet to be reviewed extensively. Thus, the primary goal of this work was to systematically review published primary literature on the effects that physical activity has on cognitive functions in adolescents. A systematic review is a specific type of review that consists of evaluating previously published data relating to a specific question. This would differ from any experimental study in which researchers would collect data most commonly in a lab. Instead, a systematic review uses reproducible search methods to select relevant studies. These results then get analyzed and summarized in a way that presents novel information compared to what has already been published.

This review specifically examined multiple variations of how physical activity is manipulated, including the frequency, intensity, time in which physical activity was administered compared to when cognitive functions were tested, the time of day in which physical activity was administered, and the duration of a single bout of activity. The specific effects that were examined included cognitive functions, such as working memory, attention, and inhibitory control.

This review consisted of examining randomized control trial (RCT) study designs. By including only RCT study designs, this review aimed to identify the causal relationship between various manipulations of physical activity and brain development with regard to cognitive functions. RCT study designs consist of a study design in which participants are randomly assigned to either the control group or the various experimental groups. In having this randomization, it is expected that the only difference between the groups would be the variable that is being tested; in this case, this would mean the only difference between controls and experimental groups was the differences in physical activity. This ultimately allowed researchers to establish a causal relationship between physical activity and cognitive functions, meaning physical activity was responsible for the changes in cognitive functions.

In examining the current literature in this area of study, it was expected that as the amount, with regard to frequency and duration of a single bout, and intensity of physical activity increased, cognitive functions would be enhanced. Likewise, it was expected that for cognitive tests that were performed immediately after would show greater enhancement as compared to those performed days or weeks after activity.

2. Methods

As part of the preliminary stages of this project, previously published systematic reviews and meta analyses were reviewed. This preliminary review of the literature was done as a way to gain insight into what research, specifically what questions have already been addressed regarding the relationship between physical activity and general brain development. More specifically, this research served as a way to evaluate some of the research trends made by other authors with respect to databases searched, search terms, types of studies included, sample populations, and some of their general findings. In completing this review upon initial research, this information would ultimately influence and guide some of the research criteria for the current project. A total of 11 systematic reviews and 7 meta analyses were reviewed for reference. In completing this review of reviews, the following information was noted: the year of publication, the age group of participants, whether the review consisted of experimental or association study designs, the search terms used, the question being asked, the measures and manipulations, and the general conclusions of the review.

The majority of systematic reviews and meta analyses were done within the last five years, which ruled out replicating a previous study. This would have been done by using the same search methods with the goal of answering the same question with more recent data. Another noticeable trend was that previous research appeared to have a bimodal pattern with respect to population age; that is, many researchers either focused on children, typically between the ages of 5 and 12, or on elders, typically older than 65. This ultimately indicated that little research has yet been done on the ages in-between these populations, including adolescents between the ages of 12 and 18. Many of the reviews consisted of a combination of both association and experimental study designs, suggesting enough experimental research has been done within this area of study to only include experimental designs. Search terms were reviewed, and the most frequently used terms were used in the current study. One of the last trends observed in this preliminary research stage was many reviews focused on one of three manipulations of physical activity: frequency, intensity, or duration of activity.

From this process, it was concluded that there was limited research done on the relationship between physical activity and brain development in adolescents between the ages of 12 and 18. This directed the focus of the current study to this specific age population and reviewing the experimental research that has been done in this area.

2.1 Literature search

Following the review of reviews, during November 2020, a comprehensive search of the literature was done using three electronic databases (PubMed, PsychINFO, and ERIC). These databases were searched using the following terms: (1) "physical activity" or "exercise" or "sports" or "physical education" and (2) "cognition" or "cognitive performance" or "cognitive function" or "executive function" or "memory" or "learning" and (3) "adolescent" or "youth" or "teen".

2.2 Inclusion criteria

Studies were included if they met the following criteria: (1) it used an RCT study design; (2) it included adolescents between the ages of 12 and 18; (3) the population did not have preexisting health conditions (cognitive or mental illnesses and physical injuries); (4) it examined the effects of differing amounts of physical activity on cognitive functions (e.g., working memory, attention, inhibitory control, spatial memory); (5) it was published in English. Date criteria was not required for inclusion.

2.3 Data extraction

The following information was extracted from the included studies: (1) study characteristics (e.g., last name of first author, title, year of publication); (2) sample characteristics (e.g., age range and population size); (3) study design, including intervention and control groups

(e.g., type, frequency, intensity); and (4) outcome measures (e.g., type of cognitive assessment or physiological measurement, including EEG recordings and blood samples).

3. Results

3.1 Search results

To aid with the literature review portion of this project, the systematic review software, Covidence, was used by importing the search results from all three databases. The initial search retrieved a total of 372 studies, of which 4 duplicates were removed in the import process. A total of 320 studies were deemed irrelevant based on title and abstract for reasons including not meeting age criteria or wrong intervention and measurements. Upon reviewing full texts of the 48 remaining studies, 40 studies were excluded based on age criteria alone. This left a total of 8 studies that fit the inclusion criteria to be analyzed. Given how much this greatly limited analytical abilities, the age criterion was expanded from 13-18 years of age, to 12-18 years. This change was made based on the assumption that there wouldn't be drastic developmental differences between 12-year-olds and 13-year-olds. Because of this change in criteria, it was necessary to rescreen all studies to ensure studies previously excluded based on age criteria were reevaluated for inclusion.

The search methodology across the three databases did not change; therefore, the same initial 372 studies were screened, with the same 4 duplicates removed. After rescreening the remaining 368 studies based on title and abstract, no additional studies were deemed relevant. Studies that now fit the age criteria were not added to full text review as they had either an incorrect intervention or outcome measurements that were irrelevant. However, when

rescreening the same 48 studies based on full text, an additional 5 studies were included for now abiding by the age criteria. In total 13 studies were included based on full text review, as they met all inclusion criteria and were included in the current systematic review (Table 1).

3.2 Variations in the duration of physical activity

3.2.1 Short duration exercise bouts enhance attention, concentration, and inhibitory control, but not memory

Short duration of physical activity was defined as any time under 30 minutes of activity in a single day. A total of 7 studies were classified as examining short durations of physical activity in adolescents. Of these 7 studies, a total of 3 tested the effects of short duration of physical activity on selective attention (1, 9, 3). Overall, results indicated that short durations of physical activity, ranging from 8 minutes to 16 minutes, resulted in increased selective attention and concentration. Though this result is found to be statistically significant, the effect was shown to be small. One study in particular measured the effect of PA on selective attention for the following 48 hours (1). From this study, researchers found that for the initial 1-2 hours after a single 16-minute bout of physical activity, adolescents' selective attention increased by 17.39%, as compared to those in the control group who performed static stretching. However, this effect was only found to be significant for up to two hours post-activity. Another study made a distinction between 10 minutes of non-specific physical education (control) compared to 10 minutes of coordinative exercise (3). Although both groups show improvement, from this comparison, it was shown that coordinative exercise results in greater enhanced selective attention.

In addition to selective attention, memory has also been shown to improve with short durations of physical activity. A total of 3 studies looked at the effect short durations of physical activity have on memory (1, 12, 13). One study that looked just at memory in general found that single, short bouts of physical activity did not improve memory at any point in 48 hours post-activity (1). That is, those in both the control group that participated in static stretching and those in the experimental group that participated in C-HIIT activity did not exhibit significant differences in memory performance. In addition to this study, two other studies looked more specifically at working memory. From these studies it is shown that physical activity, ranging from 12-20 minutes, has a small effect on enhancing working memory; that is, working memory improves only slightly from exercise (12, 13). This was illustrated through a reduced reaction time in either the Sternberg task (13) or the Letter Digit Span task (12).

In conjunction with selective attention and working memory, inhibitory control has been shown to also improve as a result of physical activity. Of the 7 total studies that examined acute bouts of physical activity, only one study looked at the effect this activity would have on inhibitory control (8). From this study, results indicate that 20 minutes of physical activity increased inhibitory control in those in the exercise group compared to those in the control group. That is, as a result of activity, adolescents that were physically active had a lower reaction time while performing the Stroop test.

Overall, short durations of physical activity were shown to be effective in enhancing cognitive functions including attention, concentration, and inhibitory control. There were contradictory findings when considering memory in that one study did not find significant

enhancements to memory initially after engaging in physical activity, while another study demonstrated a small effect on working memory.

3.2.2 Long duration exercise bouts do not enhance attention, short-term memory, or inhibitory control

Long durations of physical activity were defined as any time that lasted longer than 30 minutes. A total of 6 studies were classified as examining long durations of physical activity in adolescents. Of these 6 studies, 3 studies tested the effects of physical activity, ranging from 40 minutes a day to 105 minutes a day, on attention. In comparing these studies, the effect was shown to be somewhat varied. One study demonstrated that 40 minutes of physical activity a day enhanced selective attention in adolescents (7). This was demonstrated by those in the intervention group making fewer errors in the Wisconsin Card Sorting Test (WCST), indicating improved attention. Another study looked at the total amount of time adolescents spent sitting during a school day and evaluated the effect that reducing this amount of time spent sitting would have on mental attention capacity (4). This study consisted of the control group, who spent 225 minutes sitting during the day, and a reduced sitting group, who spent 102 minutes sitting during the day. Within the reduced sitting group, time that would have normally been spent sitting, was replaced with light physical activity (LPA). From this study, results showed that mental attention capacity declined throughout the day in those in the control group but increased in those in the reduced sitting group. While this finding was not shown to be statistically significant, it had a medium effect size. On the other hand, a third study looked at how both selective attention and sustained attention were influenced by increased physical

activity (5). Within this study, students used desk bikes for 1 hour a day, 4 times a week. Selective attention was measured through use of the Stroop test, while sustained attention was measured through use of RCPT. Both of these functions, selective attention and sustained attention, were shown to have no significant effect between students who biked during lessons and those that did not.

In addition to examining the effects of physical activity on selective and sustained attention, Torbeyns and colleagues (#5) also looked at the effect on short-term memory. This was measured by the Rey Auditory Verbal Learning Test (RAVLT). From this, results indicate that long durations of exercise, consisting of using bike desks for 1 hour a day, do not enhance short-term memory, as there was no significant interaction or main effect found (5).

An additional study looked at the effects of long durations of physical activity on inhibitory or cognitive control (6). Within this study, a total of 16 schools were randomly assigned to either the intervention group, in which students participated in physical activity for 60 minutes a day, or to the control group. Inhibitory control was assessed using a modified version of the Eriksen flanker task. The results of this study showed no significant differences between the intervention and control groups with respect to accuracy and response time in the task.

Overall, the studies examining long durations of physical activity and its effects on cognition demonstrated no improvements with regard to short-term memory or inhibitory control, as these findings were not found to be statistically significant, although no effect size was reported for either. Looking at attention, these results appeared varied given that one study

showed enhancements, while two did not. However, in one study that did not show statistical significance, there was a medium effect size.

Additionally, in comparing short durations and long durations of physical activity, short durations were shown to be more effective in improving attention, concentration and inhibitory control, as these were reported to be statistically significant. Contrary to this, long durations did not improve these functions. Additionally, neither short durations or long durations were shown to be effective in improving various memory types, including working memory and short-term memory; although, there was a small effect on working memory.

3.3 Single bouts of activity improve attention and concentration, while increased frequency improves inhibitory control

A total of 3 studies looked at the effects of a single bout of physical activity (1, 10, 12). The first of these studies examined selective attention and concentration and reported a group and time interaction for both functions (1). This suggests that those in the exercise group, after a single bout of activity, showed greater improvements with regard to selective attention and concentration as compared to control participants. Additionally, another study examined inhibitory control and found that only those in the moderate-intense exercise group showed enhanced control after a single bout of activity (10); this was compared to those in the high-intensity exercise group and controls. Two studies looking at memory presented contradictory results (1, 12). One study demonstrated no interaction between group and time (12), suggesting that the exercise group did not improve with regard to working memory more

than controls. Contrary to this finding, another study showed significant improvements in memory in the exercise group, but not until a couple hours after exercise (1).

A total of 2 studies consisted of participants engaging in physical activity 2-3 times per week (9, 11). Of these studies, one showed a significant interaction between group and time with respect to metacognition, which included total executive time, total planning-solving time, and total move score (11). In this, the exercise group improved more on these functions compared to the control participants. Contrary to this, another study looking more generally at executive functions, including visual attention, speed of processing, speed scanning, and mental flexibility, found no significant differences between control groups and exercise groups (9). That is, the participants engaging in physical activity did not improve significantly better than those who did not.

A total of 5 studies consisted of participants engaging in physical activity 4-5 times per week (2, 5, 7, 8, 13). Of these studies, only two showed a significant group and time interaction (8, 13). One study looking at inhibitory control showed that the exercise group had greater enhancements to this function, compared to controls; a similar finding was shown in another study, but with regard to working memory (13). These two studies, however, were the only that showed the exercise groups performing significantly better than controls. In another study, there was a main effect on time with regard to selective attention and sustained attention, however, no group and time interaction (5). What this means is that all participants had better attention over time, but the exercise group did not improve any more than the controls. Additionally, from this study, there were no improvements overall in short-term memory (5). Two other studies looked more generally at cognitive performance and executive functions in examining processes such as

non-verbal and verbal abilities, abstract reasoning, spatial ability, verbal reasoning, and numerical ability (2, 7). From this study researchers found no significant differences between improvements in the exercise group compared to the control group.

Overall, single bouts of exercise were shown to be sufficient in enhancing functions such as selective attention and concentration. Contrary to this, increased frequencies in physical activity did not show improvements in attention. Both variations in frequencies demonstrated enhanced inhibitory control. Additionally, no clear conclusions can be made about memory, as different studies examined various types of memory (general memory, working memory, short-term memory), making direct comparison difficult. Also, across these different types of memory there were varied results seen for both single bouts and increased frequencies.

3.4 Intensity of physical activity

One of the questions we had asked was whether or not various intensities of physical activity would demonstrate different effects on cognitive functions. Upon reviewing the current dataset, there was no apparently clear way of answering this question. For starters, many of the researchers define light, medium, and high intensity differently, making direct comparisons difficult. On average, light intensity is defined as 40-54% maximal heart rate, medium as 55-69%, and high as anything greater than 70%. However, the majority of the current studies being reviewed only reported average heart rate in beats per minute (bpm). Because there is no direct conversion from heart rate in bpm to a percentage of maximal heart rate, it was not possible to reclassify the measurements from each study as the standards for light, medium, and high intensities.

Only one study looked at variations in intensities between two different experimental groups (2). The results of this study indicate that in the second experimental group, who engaged in high-intensity exercises, participants demonstrated a significant effect on what was referred to as "cognitive performance". Cognitive performance consisted of a questionnaire that evaluated non-verbal and verbal abilities, abstract reasoning, spatial ability, verbal reasoning, and numerical ability. Therefore, those that engaged in higher intensities of physical activity showed greater improvements in these abilities, compared to controls and those of the moderate-intensity experimental group.

Additionally, 3 other studies were classified as high intensity based on the reported maximal heart rate (1, 7, 9). These findings showed that high intensities improved concentration and attention (1). Contrary to this, the other two studies looked more broadly at executive functions and found little to no improvements with respect to executive functions in those exercising at high intensities (7,9). Overall, from these findings, no conclusions can be drawn from this because there is no variability between intensities to allow for comparisons.

3.5 Physical activity immediately improves attention and inhibitory control, but not memory

A subset of 7 studies explicitly identified the time difference between when physical activity was administered and when the cognitive testing took place. Of these 7 studies, only 2 studies took multiple tests of various time points (1, 10). It was shown that memory, selective attention, and concentration all had a main effect for testing time point (1), suggesting that across all participants there was improvement in these functions over time. More importantly, selective attention and concentration showed a group and time interaction, suggesting that those in the

exercise group showed greater improvements over time as compared to controls. To be more specific, selective attention was 17.39% higher in the experimental group immediately after activity (p=0.015, d=0.587) and concentration improved by 20.31% higher immediately after activity (p=0.059, d=0.416). However, this group difference was only significant for selective attention when tested immediately after engaging in activity and significant for concentration for up to 2 hours post-activity. Contrary to this, memory did not improve in the experimental group until 4 hours after engaging in physical activity and was sustained for up to 48 hours post-activity (1).

The second study took cognitive measurements immediately after, 30 minutes after, and 60 minutes after engaging in physical activity (10). This study looked specifically at the effects on inhibitory control and found that participants in the moderately-intense exercise group showed greater improvements through decreased reaction times than those in the control group. This effect was significant at all testing points; that is, moderate reductions in reaction time could still be observed up to 60 minutes after engaging in physical activity.

An additional 2 studies took cognitive measures the day after participants engaged in physical activity (8, 13). The first of these studies examined inhibitory control and found that, when testing the following day after engaging in activity, participants in the exercise group showed greater enhancement through decreased reaction time, but not through increased accuracy, as compared to the controls (8). The second study instead looked at working memory and found again that those in the exercise group showed greater enhancement through decreased reaction times with no improvements in accuracy, as compared to the controls (13). In this, both studies that tested cognitive functions, including inhibitory control and working memory, showed significant enhancements that lasted at least until the following day after engaging in activity.

A total of 3 studies tested cognitive functions only immediately after engaging in physical activity (3, 4, 12). Of these studies, two looked at attention (3, 4). The first of these studies showed that with regard to attention and concentration, all participants showed improvement over time, however, greater enhancement was seen in the exercise group (3). Contrary to this, the other study looking just at attention, showed that there were no significant group differences over time, meaning the exercise group did not improve significantly more than the controls (4). An additional study examined working memory immediately after engaging in activity and found no significant group differences over time, again meaning the exercise group did not improve any more than the controls (12).

Overall, cognitive functions including attention, concentration, and inhibitory control were all shown to improve immediately after engaging in physical activity. However, these results were no longer statistically significant after 2 hours, suggesting that these enhancements are rather short-lived. Contrary to this, studies looking at memory didn't show improvements until either a couple hours or an entire day after engaging in physical activity.

3.6 Time of day physical activity is administered has no clear impact on cognitive functions

Only one study looked at the effects of physical activity when administered first thing in the morning on cognitive functions (1). The results of this study showed no significant group differences between exercise and control groups with regard to memory, suggesting that when tested in the morning, participants in the exercise group did not perform better with respect to memory than control participants. However, there was a significant group and time interaction for selective attention and concentration. That is, participants who engaged in physical activity first thing in the morning demonstrated greater improvements with respect to attention and concentration, as compared to the control participants.

A total of 4 studies examined the effects of physical activity, when administered in the middle of the day, typically after lunch (8, 9, 12, 13). Of these studies, two showed a group and time interaction with regard to inhibitory control (8) and working memory (13). Within both of these studies, participants in the exercise group demonstrated greater improvement in inhibitory control or working memory through decreased reaction times, however, did not increase accuracy. Contrary to the latter study examining working memory, another study that also had participants engage in activity mid-day and measured working memory did not show a group and time interaction (12). This means the participants in the exercise group in this study did not improve significantly more than the control group, as was shown in a previous study. Additionally, a study looking at executive functions, consisting of visual attention, speed of process, and mental flexibility, participants in the cardiorespiratory exercise group showed greater enhancement of these function (9); this was compared to participants who engaged in a combination of cardiorespiratory exercises and body-weight resistance training and control participants.

Generally speaking, those that exercised first thing in the morning showed improvements with regards to selective attention and concentration, however, not memory. Additionally, for those that exercised in the middle of the day, inhibitory control and working memory improved. However, there are no clear overall conclusions that can be drawn from studies looking at different times of day in which adolescents partake in physical activity. Only one study examined the effects of exercising first thing in the morning, making it difficult to draw comparisons of exercising mid-day compared to the morning. Additionally, no two studies examined the same cognitive functions making direct comparisons between improvements unreasonable.

3.7 Variations in cognitive testing makes findings less robust

In examining the resulting effects of various manipulations of physical activity on cognitive functions in adolescents, it's important to note these findings should be taken cautiously because of the inconsistencies of cognitive tests. What is meant by this is that while numerous studies aimed to examine the same cognitive function, many used a variety of cognitive tests to do so. These variations not only make it more difficult to make direct comparisons between two studies that use two different methods of measuring cognition, but they also introduce the risk of measuring additional cognitive functions than the intended function. This would ultimately influence performance and not be truly reflective of how specific cognitive functions are changing as a result of physical activity.

The first of these consists of 3 studies that looked at selective attention, 2 of which used a d-2 test (1, 3) and the other used the Stroop test (5). All studies showed a main effect on time (1, 3, 5), suggesting that over time, across all three studies, all participants had significant changes in attention. However, only the studies using the d-2 test also showed a group and time interaction (1, 3). This interaction shows that, while all participants improved somewhat with regard to attention, the exercise groups showed greater improvements as compared to the controls. So, while studies that used the d-2 test to measure selective attention participants

demonstrated greater cognitive enhancements with regard to attention in the exercise groups compared to the control groups, another study that used the Stroop test did not have this same group and time interaction, meaning the experimental group did not improve more than the control group with regard to attention.

Additionally, two other studies both examining inhibitory control used two different cognitive tests for assessment. One study used the Flanker task (10), while another used the Stroop test (8). Despite using two different tests, both studies presented similar results; there was a group and time interaction in both studies, in that exercise groups showed greater improvements in inhibitory control over time This was demonstrated through decreased reaction times across participants in both studies, however accuracy did not improve across participants in either study.

Furthermore, in looking at working memory, one study used the LDS task (12), while another study used the Sternberg task to also examine working memory (13). These two tests demonstrate contradictory results in that for the study using the Sternberg task, a significant interaction between time and group was shown (13). This interaction was demonstrated through participants within the exercise group having shorter reaction times, which ultimately suggested enhanced working memory; this was compared to control participants who did not engage in physical activity. Meanwhile, the study using the LDS task to assess working memory demonstrated no significant interaction between group and test changes (12), suggesting those in the exercise group did not show significant improvements with regard to working memory compared to the control group. Therefore, the study using the Sternberg task showed participants improving with regard to working memory, while the LDS task did not.

4. Discussion

The goal of this work was to systematically review published primary literature regarding the effects that physical activity has on cognitive functions in adolescents between the ages of 12-18 years. More specifically, this review explored questions related to multiple variations of how physical activity is manipulated, including the frequency, intensity, time in which physical activity was administered compared to when cognitive functions were tested, the time of time in which physical activity was administered, and the duration of a single bout of activity. This was done by using precise search terminology and screening process of resulting studies. Specific criteria were used in the screening process, such as if it were an RCT study design, population age, and that there were no preexisting health conditions. The measures that were accounted for included cognitive functions such as working memory, short-term memory, attention, concentration, and inhibitory control.

4.1 General findings and recommendations

One variable that was examined in this review was short duration, which was defined as engaging in activity for less than 30 minutes, and long durations, which was defined as any amount of time greater than 30 minutes. When examining the effects of short durations of physical activity compared to longer durations, short durations were shown to be more effective in improving attention, concentration, and inhibitory control, as these were reported to be statistically significant. Contrary to this, long durations of activity did not improve these functions. Additionally, neither short durations nor long durations were shown to be effective in improving various memory types, including working memory and short-term memory; although, there was a small effect on working memory. Based on these findings, it would be recommended to engage in shorter durations, less than 30 minutes, as this amount of time was most effective for improving attention, concentration, and inhibitory control. Engaging in activity for any time greater than 30 minutes does not appear to be effective in improving these functions, therefore it wouldn't be recommended.

Looking next at variations in the frequency of physical activity, frequencies were categorized as single bouts, 2-3 times per week, or 4-5 times per week. From the reviewed studies, it was shown that single bouts of exercise were sufficient in enhancing functions such as selective attention and concentration. Contrary to this, increased frequencies of 4-5 times per week, did not significantly improve attention. Both degrees of frequency, low and high, demonstrated enhanced inhibitory control. Additionally, no clear conclusions can be made about memory, as different studies examined various types of memory (general, working memory, short-term memory), making direct comparisons of changes difficult. Also, across these different types of memory there were varied results seen for both single bouts and increased frequencies Therefore, from these findings, what ultimately can be recommended to engage in single bouts of exercise, as opposed to more frequent bouts, at improving attention, concentration, and inhibitory control. This recommendation contradicts what was initially predicted that higher frequencies of physical activity would result in greater enhancements in cognitive functions.

As previously discussed, evaluating the results related to various intensities was more difficult than intended. This was mainly because researchers don't use a standardized definition of low, medium, and high intensity, and therefore, what some studies indicated as medium intensity, other studies classified as high intensity. Additionally, when trying to reclassify studies according to standard intensity definitions, this was not possible because the majority of studies only reported the average heart rate in beats per minute (bpm), which cannot be converted into a maximal heart rate percentage. Ultimately this limited the ability to draw direct comparisons between studies and therefore reach a generalized conclusion and recommendation. From the studies that did look at physical activity of high intensity, it was shown that attention and concentration were enhanced; another study reported more generally of cognitive performance with respect to non-verbal and verbal abilities, abstract reasoning, spatial ability, verbal reasoning, and numerical ability and showed that these functions were also enhanced as a result of high intensity activities. However, these results ultimately cannot be taken in a conclusive manner and be interpreted as higher intensity exercises are more effective at improving cognition in adolescents because there was little variability in intensities being tested.

Another question that was asked when looking at these studies was what effect the time difference between when physical activity was administered and when cognitive tests took place. When tested immediately after engaging in physical activity, attention and concentration were shown to improve right after exercising. These improvements can be considered as short-lived, however, given that the effect was only shown to be statistically significant for up to two hours post-activity. Contrary to this, memory did not show immediate improvement, but did demonstrate improvements after a couple house or an entire day after engaging in physical activity. From these findings, it's reasonable to recommend partaking in some kind of physical activity immediately before performing a task in which attention and concentration are highly important. However, if trying to enhance more long-term related cognitive functions, such as

memory, then it is likely that a difference will not be seen immediately after exercising once, but rather it'll require a cumulation of engaging in physical activity.

Finally, in considering the time of day in which physical activity was administered, those that exercised first thing in the morning showed improvements with regard to selective attention and concentration, however, not memory. Additionally, for those that exercised in the middle of the day, inhibitory control and working memory improved. However, in reviewing these studies, only one of them examined the effects of exercising first thing in the morning, making it difficult to draw comparisons of exercising mid-day compared to the morning. Additionally, no two studies measured the same cognitive functions making direct comparisons between improvements unreasonable. Ultimately because of these limitations, no clear conclusion or recommendation can be made from these studies alone. That is, it remains unclear as to whether or not engaging in physical activity at particular times during the day is more effective for enhancing cognition.

4.2 Recognizing inconsistencies within current literature with regard to cognitive tests

As previously mentioned, there were numerous studies in this review that aimed to measure the same cognitive function, but used a variety of tests to do so. Within some of these cases, the various tests showed contradictory results. These variations not only make it more difficult to make direct comparisons between two studies that use two different methods of measuring cognition, but they also introduce the risk of measuring additional cognitive functions than the intended function. This ultimately makes the findings of these studies less robust. Examples in which two studies used different tests and produced varying changes in cognition can be explained by looking closer at what these tests consist of and the different functions that may be at play.

One such example of studies using different tests and producing different results consisted of two studies that used the d-2 test to measure selective attention (1, 3) and another study that used the Stroop test to measure selective attention (5). From this, studies that used the d-2 test to measure selective attention showed greater cognitive improvements compared to the study that used the Stroop test. The d-2 test consists of asking participants to indicate the letter "d" with two marks either above or below the letter. Surrounding the target letter are typically similar letters, such as "p" with two marks above or below or "d" with either one or three marks instead of two; these surrounding letters are meant to distract the participant from the target letter. This test measures selective attention in that participants must concentrate on and attend to one particular aspect of the task, while ignoring the distracting stimuli. In doing this, participants must focus and attend to only the letter "d" with the correct surrounding markings, while ignoring similar stimuli. By examining the accuracy of this test with respect to misidentified letters and missed target letters, researchers are able to capture an individual's selective attention abilities.

Contrary to this, the Stroop test consists of participants reviewing a list of words that appear in a different color than the color that they actually read. For example, the written word "red" would be printed in a yellow-colored text. In this, participants are asked to ignore the more automatic response of reading what the actual word is, but instead say the color in which the word is printed in. In doing this, selective attention is measured based on the ability to tune out what would be considered distractions, meaning what the word actually reads, and instead allocate the limited resource of attention on naming the color the word appears in. Depending on the speed and accuracy in which an individual is able to identify the color the word appears in, instead of reading the word, is thought to be a reliable indication of their selective attention abilities.

However, while both the d-2 test and the Stroop test were intended to measure selective attention in participants, the varying results may imply that other cognitive functions are being tested. It's reasonable to argue that the Stroop test may also be measuring inhibitory control. Inhibitory control refers to a suppression of behaviors and actions that are irrelevant to the overarching goal. This would relate to the Stroop test in that participants would need to inhibit their instinct to initially read what the word actually says. They would need to inhibit that behavioral response and instead only respond to the color in which the word is printed in. Given that this task may be assessing inhibitory control, the reason why there were contradictory results between the d-2 test results and the Stroop test results could be because the Stroop test is actually implying that inhibitory control may not have improved as a result of physical activity. In this, it becomes very difficult to draw conclusions from these three studies because of the inconsistency in cognitive tests used and the fact that those tests produce varying results.

Another example of numerous studies using different cognitive tests to assess the same cognitive function consists of one study that used the Letter Digit Span (LDS) task to assess working memory (12) and another used the Sternberg task (13). Within the LDS task participants listen to an audio recording of a randomized string of letters and numbers. Right after listening to this recording they are asked to write the numbers they heard in numerical order and the letters in alphabetical order. The randomized strings start smaller, consisting of only 2 items (such as q7),

and progress to 7 items (such as q73h8s). This test assesses working memory in that participants must actively retain the string that they had just heard and rearrange the items in the correct order without forgetting the proceeding items.

Contrary to this, the Sternberg task consists of participants being presented with a list of words to memorize. After presenting this list, the participants undergo what is referred to as a maintenance period in which they have to try and retain as many words on that list as possible. Once this maintenance period has passed, participants are then shown a variety of words, one at a time, and are asked to identify if the word being presented was on the initial list. In this participants engage in recognition in that they are simply asked to recognize the correct information. This is significantly easier than engaging in free recall, which refers to the ability to retrieve past information without the assistance of cues. The LDS task would be an example of engaging in free recall because participants are not provided with a list of letters and numbers that may be the correct response. Instead participants must use free recall each trial to reproduce the correct sequence of letters and numbers. In this, it may not be that working memory improved in those using the Sternberg task as a result of physical activity, but instead these results may be explained by the ease in recognizing something over using free recall to reproduce it. From this, we again see how using two different cognitive tests to examine the same cognitive function can result in contradictory results, which makes it unclear whether physical activity is improving this function or not.

Overall, these examples demonstrate a need for greater consistency within the literature with respect to the cognitive tests that are used to assess particular cognitive functions. In doing this, this would not only clear up the effect that physical activity is having on cognition, but it would also allow for direct comparisons between studies that use different variations of physical activity in their experimental groups.

4.3 Exploring mechanisms by which physical activity improves cognition4.3.1 Immediate, short-lived effects of physical activity

The results of this study demonstrated that some of the immediate effects of physical activity were enhancements in attention, concentration, and inhibitory control. These findings were repeatedly seen in single bouts of exercise, in shorter durations of activity, and when participants took the cognitive tests immediately after engaging in activity. Thus, these effects can be described as more immediate and short-lived because they take effect right after engaging in activity, but do not last that long once activity has ceased.

When exploring one way in which these immediate effects of physical activity on cognitive functioning are able to occur, one idea to consider is increases in cerebral blood flow (CBF). As previously discussed in this review, physical activity has been shown to increase cerebral blood flow to the brain (Chaddock et al. 2016). To quickly reiterate, cerebral blood flow serves as a primary mechanism of delivering blood, which contains oxygen and glucose, to the brain, both of which are crucial elements needed for brain function. Essentially, it is the CBF that is responsible for delivering nutrients (e.g., oxygen and glucose) that are necessary for the brain to function effectively. As presented in one study, glucose is a main source of energy for the brain (Mergenthaler et al. 2013). The metabolism of glucose helps maintain brain functioning with specific regard to signaling of neurons within the brain. This is because glucose provides the precursors that are necessary for neurotransmitter synthesis. Without neurotransmitter

synthesis, neurons would not be able to release their neurotransmitter, which is the chemical signal that carries messages representing our current experience. If neurotransmitters cannot be released onto the following neurons, neuronal communication cannot occur, and therefore the messages cannot be transmitted to various brain regions for further processing. This would greatly limit a host of functions, including those related to cognition. This information points largely to the importance of glucose for brain functioning and the significance of more glucose reaching the brain through CBF as a result of increased physical activity.

When considering this role of CBF, one logical explanation as to how attention, concentration, and inhibitory control were able to improve after engaging in such little physical activity could be related to the increased delivery of nutrients to the brain. In having more nutrients, especially glucose, reach the brain as a result of physical activity, this could allow for greater functional capabilities. This is likely because greater amounts of glucose in the brain result in greater production of precursors that are necessary for neurotransmitter synthesis. Increased synthesis then leads to greater release of neurotransmitters in neuronal signaling. This would contribute to more efficient communication between neurons that is necessary for cognitive functions such as attention, concentration, and inhibitory control, all of which were shown to improve with physical activity.

However, because these effects are only short-term, as shown by being ineffective after 2 hours post-activity, it's likely that after a certain period of time the body returns to its normal state and the CBF decreases to its baseline. This would therefore explain why these effects are not long-term, as the body likely cannot operate with constant increased amounts of cerebral blood flow.

4.3.2 Long-term effects of physical activity

In comparison to the short-lived cognitive changes regarding attention, concentration, and inhibitory control, one of the considerably long-term effects that was observed was memory. That is, in the majority of studies, memory did not show improvement until a significant amount of time after engaging in activity. It is likely that improvements in memory require more structural changes within the brain, which would require engaging in physical activity on a consistent basis over a longer period of time. This idea comes with understanding the mechanism in which memories are formed. Learning and forming new memories is a result of the properties of synapses. As previously mentioned, synapses are the spaces between neurons in which neurochemical signals are released and transferred between neurons, allowing for cellular communication. One of the key characteristics of synapses is that they change shape based on experiences and new incoming information. This change in shape, often referred to as neuroplasticity, is essentially representative of new information and therefore new memories that are formed. As we learn new information, new pathways in the brain form as physical changes occur at the synapses. These new pathways contribute to our retainment of the new information, and eventually to the memory that forms.

One of the ways in which various brain structures, and therefore the synapses within those structures, can change shape and size is through brain derived neurotrophic factor, or BDNF. BDNF is a type of protein that plays a role in the growth and maturation of neurons, which can increase the overall survival of neurons and therefore aid in brain growth (Miranda et al. 2019). This protein becomes especially crucial in adolescent brains, given that they are still in the process of developing and physically growing in size. BDNF is typically highly expressed in areas of the brain including the hippocampus, which plays a fundamental role in learning and memory, along with the amygdala, cerebellum, and cerebral cortex. BDNF is said to be involved in the neuronal plasticity that occurs from learning in that it increases the number, size, and complexity of dendritic spines. Dendritic spines are the part of a neuron in which incoming neuronal signals from preceding neurons dock onto the next neuron. This docking of neurotransmitters allows for transmission of signals between neurons. By increasing the number and size of spines, this ultimately serves to increase the number of available sites in which incoming neurotransmitters can bind to the neuron. Additionally, by increasing the complexity of the spines, this allows for higher processing of incoming stimuli and more varied responses to those stimuli. Overall, the role of BDNF suggests how greater expression of this protein can potentially lead to improved cognitive abilities with regard to learning and memory in particular. In understanding this role of BDNF in promoting physical synaptic changes in response to learning and forming new memories, many researchers have started investigating ways in which an individual can increase the expression of BDNF; one such way that has been reviewed is physical activity.

One study examining the effects of physical activity on the expression of BDNF within the brain used a mouse model (Sleiman et al. 2016). In this, mice were divided into either the control group or exercise group. The control group was not provided with a running wheel, while the exercise group was. It was importantly noted in the methods of this study that the researchers only measured voluntary wheel running in the exercise group of mice. This was because stress induced from handling of the mice has been shown in previous research to

decrease BDNF levels. Given this, if researchers had controlled the amount of wheel running by forcing the mice on the wheels, this would skew the actual effect of exercise on BDNF because there may be a decrease in BDNF as a result of stress. Researchers measured voluntary wheel-running for a total of 30 days, and tracked both distance and time. The results of this study showed that in the mice that had engaged in wheel-running, there was a greater increase in BDNF protein levels, as compared to the control mice. This increase in protein levels would result from greater expression of the BDNF gene. Additionally, this increase was found to be significant specifically in the hippocampus. This suggests that exercise can increase BDNF levels, particularly in the hippocampus, by promoting greater expression of the BDNF gene.

Given the results of this study, which demonstrate how physical activity can increase BDNF protein levels in the brain, it would be reasonable to think that physical activity can lead to changes in brain structure by way of increasing BDNF. This is, as previously discussed, given the role that BDNF plays with regard to changes of synapses that can occur from learning and forming new memories. However, as can be seen from the current review, memory did not improve until a significant amount of time after engaging in physical activity. This is likely because these structural changes resulting from increased BDNF would not happen immediately after engaging in activity. Instead, these physical changes would most likely occur gradually over a period of time. This would explain why memory was consistently shown to not improve, since the majority of the studies reviewed were not longitudinal studies. So, it could be possible that if these studies were to continue over a longer period of time, then memory would eventually show improvements as a result of physical activity because of the gradual structural changes that are occurring at the synapses as a result of greater expression of BDNF.

4.4 Possible explanations for hypotheses that were not supported

There were three primary hypotheses made at the beginning of this review that turned out to be incorrect in the end. It was hypothesized that as the duration, intensity, and frequency of physical activity increased, there would be greater improvements in cognitive functions, such as working memory, attention, and inhibitory control. It was assumed that in doing more of something that has been shown to be good for the brain, in this case exercising, then consequently there should be greater benefits. However, instead it was shown that shorter durations were more effective at improving attention, concentration, and inhibitory control, as compared to longer durations. Additionally, it was shown that increased frequencies of activity were not as effective at improving inhibitory control, attention, and concentration as single bouts of activity were. And finally, no clear conclusions could be drawn from increasing the intensity of activity given that there was not a standardized definition of low, medium, and high intensity, which made direct comparisons of results between studies nearly impossible.

One explanation that can account for why increased duration of physical activity did not further improve cognitive performance is in relation to this idea of energy depletion. As it was previously discussed, immediate effect of physical activity on cognitive functions can be explained by way of more CBF being delivered to the brain as a result of increased activity. In this, more oxygen and glucose are able to reach the brain, which then help cognitive functions. However, one idea to consider is the possibility that the body has a threshold for the amount of energy (in the form of glucose and oxygen) that can be delivered to the brain for cognitive functions, before the body starts utilizing energy elsewhere for physical demands of exercising. What this means is that after surpassing this threshold, the peripheral nervous system is using up more of the glucose and oxygen, putting the brain at an energy deficiency, hence why we don't see improvements in cognitive performance.

One study that suggested this mechanism is at play consisted of measuring blood glucose levels across the brain after varying durations of physical activity (Matsui et al. 2011). This study utilized rats as their model, who were trained to run on a treadmill for varying durations of 0, 30, 60, or 120 minutes. Post-activity, the rats were anaesthetized and blood glucose assays were done in order to measure glucose levels after engaging in activity. From these assays, it was shown that overall blood glucose levels were 45% lower in those in the exercise group compared to the sedentary group. Furthermore, those that engaged in physical activity for 120 minutes showed the greatest decrease in blood glucose, compared to the sedentary group, in addition to those that engaged in activity for 30 and 60 minutes. This was apparent in areas including the hippocampus and cortex, which have previously been discussed as having a role in attention and memory; this was in addition to decreased glucose in the hypothalamus, cerebellum, and brainstem. This suggests that prolonged exercise results in decreased levels of glucose to the brain, most likely because that glucose is needed elsewhere in the body to fuel the physical demands of exercising. This ultimately results in the brain having less energy, therefore making it less efficient in performing cognitive functions, such as inhibitory control and attention.

To connect this back to the findings of this review, short durations were more efficient in improving cognitive performance with relation to attention, concentration, and inhibitory control. In this, CBF is able to sufficiently provide the nutrients that support the brain function relating to inhibitory control and attention. However, after surpassing a certain threshold of duration of physical activity the brain goes into a state of energy depletion because the body is utilizing glucose as an energy source elsewhere. In this state, the brain no longer has the capacity to support the cognitive functions of inhibitory control and attention. Because of this, we instead see that these functions do not continue to improve with increased time in durations of physical activity.

While this study in particular only looked at varying the duration of physical activity and how that affected glucose levels in various brain regions, a similar explanation could be applied to why cognitive functions did not improve with increased intensities of activity. Exercising at greater intensities presumably uses increased amounts of energy in the same way that longer durations do. Because of this, it would be reasonable to expect to see similar decreased levels of glucose across the brain, possibly in similar brain regions as was shown in this study. This decrease in glucose as a result of increased intensity would potentially explain why cognitive functions did not improve, in that once again, the brain would not have enough energy, partly in the form of glucose, to perform adequately.

It is unlikely that this explanation of decreased glucose and energy deficiency also explains why increased frequencies did not improve cognitive functions, but rather single bouts of activity did. It's unlikely because one could imagine doing workouts for short durations, at moderate-intensity multiple times a week, which would go against what is recommended by the results of this review. However, given that the workouts would be short durations and not high-intensity and the fact that there's presumably sufficient rest between exercises, that individual wouldn't likely experience the same energy consumption and, therefore, energy deficits as someone working out for longer durations at high intensities.

4.5 Taking a holistic approach and addressing physical activity across the lifespan

From the results of this systematic review, individual recommendations have been made regarding the different manipulations of physical activity, including duration and frequency. However, in thinking further about these recommendations, it's reasonable to argue that they do not capture the full benefits and effects that physical activity can have on an individual. In considering this, it's first important to note that these individual recommendations previously made were based solely on the results from this review and were made with the intent of improving just cognition in adolescents. For example, the findings regarding the frequency of physical activity suggested that single bouts of exercise were more effective in improving cognitive functions, as opposed to greater frequencies; given this finding, it would be recommended to engage in infrequent, single bouts of exercise. However, while this may be what the findings from this review suggest, the benefits and enhancements in cognitive functioning that occurred were not shown to be long-lasting. That is, it may be great to engage in a single bout of exercise at moderate-intensity for no more than 30 minutes on the day of an exam or presentation for work, as these variables of physical activity were shown to improve concentration and attention. However, engaging in sporadic, single bouts of physical activity will most likely not provide longer lasting changes in, not just cognition, but also benefits in overall health.

As previously discussed in this work, physical activity has been shown to provide benefits relating to cardiovascular health, sleep, and mood. To reiterate, when considering cardiovascular health, physical activity has been shown to lower body weight and body mass index (BMI). However, it is highly unlikely that any of these effects would occur if an individual is not participating in physical activity on a regular basis. This ultimately has an impact when considering the rates of obesity, which were previously indicated. If individuals are not engaging in physical activity on a regular basis, and therefore their cardiovascular health does not benefit, then this does nothing for helping the current obesity epidemic in the U.S.

What we can take from this is that in order to get long, sustained effects from physical activity, both with regard to brain health and cognition, but also overall body health, participation in physical activity needs to be a consistency that occurs across the lifespan. Understanding the effects that physical activity can have on cognition in adolescents may demonstrate the importance of engaging and forming habits relating to health and wellness early in life. However, getting adolescents to exercise more frequently and regularly should just be the first step in adopting healthier lifestyle choices.

This becomes even more prevalent when revisiting how physical activity was shown to have many of the same effects in aging individuals, with specific regard to memory, inhibitory control, and attention. This suggests that physical activity can provide the same cognitive enhancements, possibly through the same mechanisms, independently of age. Therefore, making physical activity a habit earlier on in life may make these effects more robust as the mechanisms that lead to the changes in cognitive functioning have more time to develop and undergo change. This may also show to be effective in further preventing neurodegenerative diseases, such as dementia.

4.6 Areas to expand on in the current literature

It's fair to suggest that this area of research involving the effects of physical activity on cognitive functioning in adolescents as a whole needs further attention and development. While the research databases used in the current review were not exhaustive, by the end of the screening process there were only 13 remaining studies that met the inclusion criteria. This is also taking into account that the exclusion criteria was rather limited compared to the exclusion criteria used in other systematic reviews. Even though some conclusions were able to be drawn from these 13 studies, a much more expansive dataset is necessary in order to draw more robust and generalizable conclusions.

Not only is it important to have a more elaborate database to work with to make more generalizable conclusions, but as previously discussed in this review, physical activity has numerous health benefits related to overall health, not just brain health. Some of these benefits include lowering BMI, body weight, and improvements in cardiovascular health (Sigal et al. 2014; Ho et al. 2012). Targeting these health components is becoming increasingly crucial as obesity rates in adolescents specifically increase (Sanyaolu et al. 2019), as well as sedentary behavior continue to increase with age (Schwartzfischer et al. 2019). Increases in sedentary behavior only work to contribute to the downfall of overall health in adolescents. It's suggestive that in having more sufficient data to point to as to why physical activity is so crucial for health in adolescents, and in particular brain health, this may serve as a way to create programs that promote engaging in physical activity more frequently, which would begin to decrease obesity rates and sedentary behavior in adolescents.

Additionally, some of the most apparent limitations from reviewing these studies were the number of inconsistencies that are within even the existing literature. Two of the most prominent examples of this included the type of cognitive test used to measure cognitive performance for specific functions and how low, medium, and high intensity was defined across studies. These inconsistencies again made it difficult to draw definite conclusions from the result. Additionally, because direct comparisons within the data could not be made, mainly because a variety of cognitive tests were used, doing any sort of statistical analysis was not possible. This greatly limits the validity and does not capture the strength of the effect of each of these results. That is, coming out of this review, it is difficult to discern the extent to which physical activity improves cognitive functions, with specific regard to the frequency and time of day.

Overall, this area of study needs further development as a whole. Additionally, as these ideas and future studies continue to unfold, it is important to emphasize a need for consistencies across upcoming research. These consistencies will ultimately allow for a better understanding and therefore more concrete recommendations regarding the duration, frequency, and intensity of physical activity. These recommendations can then be referenced and used when making public health policies relating to the health of adolescents.

References

- Ardoy, D.N. Fernandez-Rodriguez, J.M., Jimenez-Pavon, D., Castillo, R., Ruiz, J.R., Ortega,
 F.B. (2014). A physical education trial improves adolescents' cognitive performance and academic achievement: the EDUFIT study. *Scand J Med Sci Sports, 24(1),* 52-61.
- Belair, M.A., Kohen, D.E., Kingsbury, M., Colman, I. (2018). Relationship between leisure time physical activity, sedentary behaviour and symptoms of depression and anxiety: evidence from a population-based sample of Canadian adolescents. *BMJ Open, 8(10).* doi:

10.1136/bmjopen-2017-021119

- Blakemore, S.J. (2012). Imaging brain development: the adolescent brain. *NeuroImage*, *61*, 397-406.
- Boraxbekk, C.J., Salami, A., Wahlin, A., Nyberg, L. (2016). Physical activity over a decade modifies age-related decline in perfusion, gray matter volume, and functional connectivity of the posterior default-mode network-a multimodal approach. *NeuroImage*, *131*, 133-141.
- Budde, H., Voelcker-Rehage, C., Pietradbyk-Kendziorra, S., Machado, S., Ribeiro, P., Arafat,
 A.M. (2010). Steroid hormones in the saliva of adolescents after different exercise
 intensities and their influence on working memory in a school setting. *Psychoneuroendocrinology*, *35(3)*, 382-391.
- Budde, H., Voelcker-Rehage, C., Pietradbyk-Kendziorra, S., Ribeiro, P., Tidow, G. (2008). Acute coordinative exercise improves attentional performance in adolescents. *Neurosci Lett*, 441(2), 219-223.
- Carek, P.J., Laibstain, S.E., Carek, S.M. (2011). Exercise for the treatment of depression and anxiety. *The International Journal of Psychiatry in Medicine*, *41(1)*, 15-28.

- Centers for Disease Control and Prevention. (2011). Promoting brain health. Retrieved from https://www.cdc.gov/aging/pdf/cognitive impairment/cogImp_genAud_final.pdf.
- Centers for Disease Control and Prevention. (2020). What is a healthy brain? New research explores perceptions of cognitive health among diverse older adults. *Healthy Aging,* Retrieved from <u>https://www.cdc.gov/aging/pdf/perceptions_of_cog_hlth_factsheet.pdf</u>.
- Chaddock-Heyman, L., Erickson, K.I., Voss, M.W., Knecht, A.M., Pontifex, M.B., Castelli,
 D.M., Hillman, C.H., Kramer, A.F. (2013). The effects of physical activity on functional
 MRI activation associated with cognitive control in children: a randomized controlled
 intervention. *Frontiers in Human Neuroscience*, *7*(*72*), 1-13.
- Chapman, S.B., Aslan, S., Spence, J.S., Defina, L.F., Keebler, M.W., Didehbani, N., Lu, H.
 (2013). Shorter term aerobic exercise improves brain, cognition, and cardiovascular fitness in aging. *Front Aging Neurosci.*, *5*(75), doi: 10.3389/fnagi.2013.00075.
- Chen, F.T., Chen, S.R., Chu, I.H., Liu, J.H., Chang, Y.K. (2017). Multicomponent exercise intervention and metacognition in obese preadolescents: a randomized controlled study. J Sport Exerc Psychol, 39(4), 302-312.
- Chen, F.T., Chen, Y.P., Chneider, S., Kao, S.C., Hunage, C.M., Chang, Y.K. (2019). Effects of exercise modes on neural processing of working memory in late middle-aged adults: an fMRI study. *Frontiers in Aging Neuroscience*, *11(224)*, doi: 10.3389/fnagi.2019.00224.
- Chen, S.R., Tseng, C.L., Kuo, S.Y., Chang, Y.K. (2016). Effects of physical activity intervention on autonomic and executive functions in obest young adolescents: a randomized controlled trial. *Health Psychol*, 35(10), 1120-1125.

Colcombe, S.J., Erickson, K.I., Scarf, P.E., Kim, J.S. Prakash, R., McAuley, E., Elavsky, S.,

Marquez, D.X., Hi, L., Kramer, A.F. (2006). Aerobic exercise training increases brain volume in aging humans. *Journal of Gerontology*, *61A(11)*, 1166-1170.

- Colcombe, S.J., Kramer, A.F., Erickson, K.I., Scalf, P., McAuley, E., Cohen, N.J., Webb, A., Jerome, G.J., Marquez, D.X., Elavsky. (2004). Cardiovascular fitness, cortical plasticity, and aging. *Proc Natl Acad Sci U S A*, 101(9), 3316-3321.
- Costigan, S.A., Eather, N., Plotnikoff, R.C., Hillman, C.H., Lubans, D.R. (2016). High-intensity interval training for cognitive and mental health in adolescents. *Med Sci Sports Exerc*, 48(10), 1985-1993.
- Cui, M.Y., Lin, Y., Sheng, J.Y., Zhang, X., Cui, R.J. (2018). Exercise intervention associated with cognitive improvement in Alzheimer's disease. *Neural Plasticity*, <u>https://doi.org/10.1155/2018/9234105</u>
- Davis, C.L., Tomporowski, P.D., McDowell, J.E., Austin, B.P., Miller, P.H., Yanasak, N.E.,
 Allison, J.D., Naglieri, J.A. (2011). Exercise improves executive function and
 achievement and alters brain activation in overweight children: a randomized controlled
 trial. *Health Psychol*, 30(1), 91-98.
- Dopheide, J.A. (2020). Insomnia overview: epidemiology, pathophysiology, diagnosis and monitoring, and nonpharmacologic therapy. *Am J Mang Care, 26*, 76-84.
- Dunst, B., Benedek, M., Jauk, E., Bergner, S., Koschutnig, K., Sommer, M., Ischebeck, A., Spinath, B., Arendasy, M., Buher, M., Freudenthaler, H., Neubauer, A.C. (2014). Neural efficiency as a function of task demands. *Intelligence*, 42(100), 22-30.

Erickson, K.I., Voss, M.W., Prakash, R.S., Basak, C., Szabo, A., Chaddock, L., Kim, J.S., Heo,

S., Alves, H., White, S.M., Wojcicki, T.R., Mailey, E., Vieira, V.J., Martin, S.A., Pence, B.D., Woods, J.A., McAuley, E., Kramer, A.F. (2011). Exercise training increases size of hippocampus and improves memory. *Proc Natl Acad Sci U S A*, *108(7)*, 3017-3022.

- Erickson, K.I., Weinstein, A.M., Lopez, O.L. (2012). Physical activity, brain plasticity, and Alzhiemer's disease. *Archives of Medical Research*, *43*, 615-621.
- Etnier, J.L., Karper, W.B., Labban, J.D., Piepmeier, A.T., Shih, C.H., Dudley, W.N., Henrich,
 V.C., Wideman, L. (2018). The physical activity and Alzheimer's disease (PAAD) study:
 cognitive outcomes. *Ann Behav Med*, *52(2)*, 175-185.
- Fagard, R.H. (2006). Exercise is good for your blood pressure: effects of endurance training and resistance training. *Clinical and Experimental Pharmacology and Physiology, 33(9)*.
- Friedl-Werner, A., Brauns, K., Gunga, H.C., Kuhn, S., Stahn, A.C. (2020). Exercise-induced changes in brain activity during memory encoding and retrieval after long-term bed rest. *NeuroImage*, 223
- Garland, S.N., Rowe, H., Repa, L.M., Fowler, K., Zhou, E.S., Grandner, M.A. (2018). A decade's difference: 10-year change in insomnia symptom prevalence in Canada depends on sociodemographics and health status. *Sleep Health*, 4(2), 160-165.
- Goddings, A.L., Beltz, A., Peper, J.S., Crone, E.A., Braams, B.R. (2019). Understanding the role of puberty in structural and functional development of the adolescent brain. *Journal of Research on Adolescence*, 29(1)
- Gorelick, P.B., Furie, K.L., Iadecola, C., Smith, E.E., Waddy, S.P., Lloyd-Jones, D.M., Bae, H.J.,
 Bauman, M.A., Dichgans, M., Duncan, P.W., Girgus, M., Howard, V.J., Lazar, R.M.,
 Seshadri, S., Testai, F.D., van Gaal, S., Yaffe, K., Wasiak, H., Zerna, C. (2017). Defining
 optimal brain health in adults. *Stroke, 48(10),* 284-303.

- Hartescu, I., Morgan, K., Stevinson, C.D. (2015). Increased physical activity improves sleep and mood outcomes in inactive people with insomnia: a randomized controlled trial. *J Sleep Res.*, 24(5), 526-534.
- Herting, M.M., Gautam, P., Spielberg, J.M., Kan, E., Dahl, R.E., Sowell, E.R. (2014). The role of testosterone and estradiol in brain volume changes across adolescence: a longitudinal structural MRI study. *Human Brain Mapping*, 35, 5633-5645.
- Ho, S.S., Dhaliwal, S.S., Hills, A.P., Pal, S. (2012). The effect of 12 weeks of aerobic, resistance or combination exercise training on cardiovascular risk factors in the overweight and obese in a randomized trial. *BMC Public Health*, 12(704).
- Kovacevic, A., Mavros, Y., Heisz, J.J., Fiatarone Singh, M.A. (2018). The effect of resistance exercise on sleep: a systematic review of randomized controlled trials. *Sleep Medicine Reviews*, 39, 52-68.
- Kronenberg, G., Bick-Sander, A., Bunk, E., Wolf, C., Ehninger, D., Kempermann, G. (2006).
 Physical exercise prevents age-related decline in precursor cell activity in the mouse dentate gyrus. *Neurobiol Aging*, *27(10)*, 1505-1513.
- Ludyga, S., Gerber, M., Kamijo, K., Brand, S., Puhse, U. (2018). The effects of a school-based exercise program on neurophysiological indices of working memory operations in adolescents. *J Sci Med Sport*, 21(8), 833-838.
- Ludyga, S., Kochli, S., Puhse, U., Gerber, M., Hanssen, H. (2019a). Effects of a school-based physical activity program on retinal microcirculation and cognitive function in adolescents. *J Sci Med Sport*, 22(6), 672-676.

Ludyga, S., Puhse, U., Lucchi, S., Marti, J., Gerber, M. (2019b). Immediate and sustained effects

of intermittent exercise on inhibitory control and task-related heart rate variability in adolescents. *J Sci Med Sport, 22(1),* 96-100.

- Matsui, T., Soya, S., Okamoto, M., Ichitani, Y., Kawanaka, K., Soya, H. (2011). Brain glycogen decreases during prolonged exercise. *J Physiol*, *589(13)*, 3383-3393.
- Meijer, A., Konigs, M., Vermeulen, G.T., Visscher, C., Bosker, R.J., Hartman, E., Oosterlaan, J. (2020). The effects of physical activity on brain structure and neurophysiological functioning in children: a systematic review and meta-analysis. *Developmental Cognitive Neuroscience*, 45, <u>https://doi.org/10.1016/j.dcn.2020.100828</u>.
- Mergenthaler, P., Lindauer, U., Dienel, G.A., Meisel, A. (2013). Sugar for the brain: the role of glucose in physiological and pathological brain function. *Trends Neurosci*, 36(10), 587-597.
- Mezcua-Hidalgo, A., Ruiz, Riza, A., Suarez-Manzano, S., Martinez-Lopez, E.J. (2019). 48-hour effects of monitored cooperative high-intensity interval training on adolescent cognitive functioning. *Percept Mot Skills, 126(2),* 202-222.
- Miranda, M., Morici, J.F., Zanoni, M.B., Bekinschtein, P. (2019). Brain-derived neurotrophic factor: a key molecule for memory in the healthy and the pathological brain. *Front. Cell. Neurosci.*, https://doi.org/10.3389/fn- cel.2019.00363.
- National Institute of Aging. (2020) Cognitive Health and Older Adults. *Cognitive Health*, Retrieved from https://www.nia.nih.gov/health/cognitive-health-and-older-adults.
- Penning, A., Okely, A.D., Trost, S.G., Salmon, J., Cliff, D.P., Batterham, M., Howard, S., Parrish, A.M. (2017). Acute effects of reducing sitting time in adolescents: a randomized cross-over study. *BMC Public Health*, 17(1), 657.
- Peters, R. (2006). Ageing and the brain. Postgrad Med J., 82(964), 84-88.

- Reid, K.J., Baron, K.G., Lu, B., Naylor, E., Wolfe, L., Zee, P.C. (2010). Aerobic exercise improves self-reported sleep and quality of life in older adults with insomnia. *Sleep Med.*, *11(9)*, 934-940.
- Ruotsalainen, I., Gorbach, T., Perkola, J., Renvall, V., Syvaoja, H.J., Tammelin, T.H., Karvanen, J., Parvianinen, T. (2020). Physical activity, aerobic fitness, and brain white matter: their role for executive function in adolescence. *Developmental Cognitive Neuroscience, 42,* <u>https://doi.org/10.1016/j.dcn.2020.100765</u>.
- Sanylaolu, A., Okorie, C., Qi, X., Locke, J., Rehman, S. (2019). Childhood and adolescent obesity in the United States: a public health concern. *Glob Pediatr Health*, *6*, doi: 10.1177/2333794X19891305.
- Schwarzfischer, P., Gruszfeld, D., Stolarczyk, A., Ferre, N., Escribano, J., Rousseasux, D., Moretti, M., Mariani, B., Verduci, E., Koletzko, B., Grote, V. (2019). Physical activity and sedentary behavior from 6 to 11 years. *Pediatrics*, 143(1), doi: <u>https://doi.org/10.1542/peds.2018-0994</u>
- Sigal, R.J., Alberga, A.S., Goldfield, G.S., Prud-homme, D., Hadjiyannakis, S., Gougeon, R.,
 Phillips, P., Tulloch, H., Malcolm, J., Doucette, S., Wells, G.A., Ma, J., Kenny, G.P.
 (2014). Effects of aerobic training, resistance training, or both on percentage body fat and cardiometabolic risk markers in obese adolescents: the healthy eating aerobic and resistance training in youth randomized clinical trial. *JAMA Pediatr.*, *168(11)*, 1006-1014.
- Sleiman, S.F., Henry, J., Al-Haddad, R., Hayek, L.E., Haidar, E.A., Stringer, T., Ulja, D., Karuppagounder, S.S., Holson, E.B., Ratan, R.R., Ninan, I., Chao, M.V. (2016). Exercise promotes the expression of brain derived neurotrophic factor (BDNF) through the action of the ketone body β-hydroxybutyrate. *eLife*, *5*. doi: 10.7554/eLife.15092.

- Tarp, J., Domazet, S.L., Froberg, K., Hillman, C.H., Andersen, L.B., Bugge, A. (2016). Effectiveness of a school-based physical activity intervention on cognitive performance in Danish adolescents: LCoMotion-learning cognition and motion- a cluster randomized controlled trial. *PLoS One, 11(6)*.
- Torbeyns, T., de Geus, B., Bailey, S., Decroix, L., Van Cutsem, J., De Pauw, K., Meesusen, R.
 (2017). Bike desks in the classroom: energy expenditure, physical health, cognitive performance, brain functioning, and academic performance. *J Phys Act Health*, 14(6), 429-439.
- Van der Kleij, L.A., Petersen, E.T., Siebner, H.R., Hendrikse, J., Frederisken, K.S., Sobol, N.A., Haseelbalch, S.G., Garde, E. (2018). The effect of physical exercise on cerebral blood flow in Alzheimer's disease. *Neuroimage Clin.*, 20, 650-654.
- Van Praag, H., Shubert, T., Zhao, C., Gage, F.H. (2005). Exercise enhances learning and hippocampal neurogenesis in aged mice. *Journal of Neuroscience*, 25(38), 8680-8685.
- Villareal, D.T., Aguirre, L., Gurney, A.B., Waters, D.L., Sinacore, D.R., Colombo, E., Armamento-Villareal, R., Qualls, C. (2017). Aerobic or resistance exercise, or both, in dieting obese older adults. *N Engl J Med*, *376(20)*, 1943-1955.
- Wheeler, M.J., Green, D.J., Ellis, K.A., Cerin, E., Heinonen, I., Naylor, L.H., Larsen, R.,
 Wennberg, P., Boraxbekk, C.J., Lewis, J., Eikelis, N., Lautenschlager, N.T., Kingwell,
 B.A., Lambert, G., Owen, N., Dunstan, D.W. (2020). Distinct effects of acute exercise
 and breaks in sitting on working memory and executive function in older adults: a
 three-arm, randomised cross-over trial to evaluate the effects of exercise with and without
 breaks in sitting on cognition. *Br J Sports Med.*, *54(13)*, 776-781.

Won, J., Alfini, A.J., Weiss, L.R., Michelson, C.S., Callow, D.D., Ranadive, S.M., Gentili, R.J.,

Smith, J.C. (2019). Semantic memory activation after acute exercise in healthy older adults. *Journal of International Neuropsychological Society*, *25*, 557-568.

World Health Organization. (2015). Global recommendations on physical activity for health.

Retrieved from

https://www.euro.who.int/ data/assets/pdf_file/0005/288041/WHO-Fact-Sheet-PA-2015.pdf.

Appendix

Table 1

Summary of RCTs included in current systematic review

ID	Lead Author	Year	Population	Manipulations of	Measures	Overall
			Age	РА		Findings
1	Mezcua-Hidalgo	2019	12-16	Control (static stretching) Experimental (16 minutes of C-HIIT)	Memory, selective attention, concentration	Selective attention and concentration improved more in exercise group immediately after; memory did not improve in exercise group until 4 hours after activity
2	Ardoy	2014	12-14	Control (55 min, 2x/week) Experimental 1 (55 min, 4x/week) Experimental 2 (55 min, 4x/week, increased intensity)	Academic achievement, cognitive performance	No significant differences between control and experimental 1; experimental 2 improved significantly more
3	Budde	2008	13-16	Control (normal sport lesson)	Attention, concentration	Experimental group improved performance

				Experimental (coordinative exercises)		more than control group
4	Penning	2017	12-15	Amount of time spent sitting was manipulated Control ("typical" amount of time – 65% of day spent sitting) Experimental (reduced sitting – 50% less time spent sitting)	Mental attention capacity	Experimental group improved more than control; not found statistically significant
5	Torbeyns	2017	13-15	Control (no cycling desk) Experimental (cycling desk for four class hours)	Short-term memory, selective attention, sustained attention, academic performance	Attention improved over time, but exercise group did not improve more than control; no improvement s in short-term memory
6	Tarp	2016	12-14	Control Experimental (60 min of activity/day)	Cognitive control, academic performance	No significant differences between exercise group and control group

7	Chen	2016	12-15	Wait-list control group Experimental (physical activity program – moderate intensity exercises 4x/week, 40 min sessions, 3 months total)	Executive function	No significant differences between the two groups
8	Ludyga	2019	12-15	Wait-list control group Experimental (20 min, 5x/week, 8 weeks, aerobic and coordinative exercises of moderate intensity)	Inhibitory control	Reaction time decreased more in exercise group; no differences in accuracy between groups
9	Costigan	2016	14-16	Control Experimental (HIIT, AEP group and RAP group, 8-10 min, 3x/week, 8 weeks total)	Executive functions (visual attention, speed scanning, speed of processing, and mental flexibility)	No significant differences between exercise groups and control group
10	Ludyga	2019	12-15	Control (physically-inactiv e) Experimental 1 (high-intense intermittent exercise – 60 sec of each exercise) Experimental 2 (moderately-intens e intermittent	Inhibitory control	Moderately-i ntense exercise group had significant improvement s up to 1 hour after activity; no effects were seen in high-intense

				exercise – 30 sec of each exercise)		exercise or control group
11	Chen	2017	13-16	Control (read textbooks or did homework) Experimental (20-30 min, 3x/week, 12 weeks total)	Metacognition (planning, strategy, procedural knowledge, declarative knowledge)	Experimental group improved more than control group
12	Budde	2010	15-16	Control (remained sedentary) Experimental 1 (12 min running at 50-65% max) Experimental 2 (12 min running at 70-85% max)	Working memory	No significant differences between exercise groups and control group
13	Ludyga	2018	12-15	Wait-list control group Experimental (aerobic and coordinative exercises, 20 min, 5x/week, 8 weeks total)	Working memory	Experimental group improved more than control group