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Exercise, Cognition, and the Adolescent Brain

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Abstract

Few adolescents engage in the recommended levels of physical activity, and daily exercise levels tend to drastically decrease throughout adolescence. Beyond physical health benefits, regular exercise may also have important implications for the teenage brain and cognitive and academic capabilities. The current paper reviews a number of studies showing that regular patterns of exercise and physical activity relate to academic performance, cognitive function, brain structure, and brain activity in adolescents. We also discuss how additional intervention studies that examine a wide range of neurological and cognitive outcomes are necessary, as well as characterize the type, frequency, and dose of exercise and identify individual differences that contribute to how exercise may benefit the teen brain.

1 Introduction

Regular, or chronic, exercise is that which is planned, structured, and repetitive physical activities that aim to improve and maintain physical fitness (Caspersen *et al.*, 1985). The World Health Organization has suggested the daily recommendation for children and adolescents (ages 5 to 17 years) should include 60 minutes of moderate-to-vigorous intensity physical activity. As such, insufficient physical activity in adolescents is a severe problem worldwide, with 81% of adolescents between the ages of 11 and 17 years old, not fulfilling these daily recommendations (2015). In the United States, the numbers are similar to global rates, with less than 3 in 10 high school students participating in regular physical activity (CDC, 2017). Interestingly, these low physical activity levels appear with age from childhood and into adolescence, with sharp decreases typically seen between 9 and 15 years of age (Cairney *et al.*, 2014; Dumith *et al.*, 2011; Nader *et al.*, 2008; Troiano *et al.*, 2008). Multiple factors have been linked to these decreases, including interactions in social-cognitive variables, such as self-efficacy, perceived parental and friend support, and neighborhood environment (Dishman *et al.*, 2017), as well as biological maturity (Sherar *et al.*, 2010). Regardless of the reason(s), more active children and adolescents tend to remain more active as adults (Malina, 2001), and are more likely to have better health as a result (Sacker and Cable, 2006), suggesting that physical activity levels during the adolescent years may be especially important in building a foundation for later health.

Within the larger realm of physical activity, aerobic exercise seems to be especially important. Aerobic exercises are defined as those that can stimulate the heart in order to

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increase the amount of oxygenated blood sent to working muscles and cells (Armstrong and Welsman, 2007). Aerobic-based activities, including swimming, running, brisk walking and cycling, lead to improved oxygen transport to the body's cells. Aerobic exercise has the known benefits of reducing risk of cardiovascular disease (Janssen and Leblanc, 2010), type 2 diabetes (Stanford and Goodyear, 2014), and specific types of cancers (Ashcraft *et al.*, 2016). Moreover, aerobic exercise has also been extensively linked to positive neurological and cognitive outcomes in children and older adults (Chaddock *et al.*, 2011; Cotman and Berchtold, 2002; Hillman *et al.*, 2008). Animal studies also show that running affects the brain by increasing cell proliferation, survival, and differentiation of neurons (Cotman and Engesser-Cesar, 2002). Aerobic exercise in animals has also been found to increase trophic factors (e.g., brain-derived neurotrophic factor (BDNF)) that affect cell birth and brain development, as well as enhance neural transmission and improve learning and memory (Binder and Scharfman, 2004; Park and Poo, 2013). While initial evidence suggests exercise may be good for the brain at various ages, an adolescent's brain may respond differently to exercise, as compared to older or younger individuals, because the teenage brain is in the midst of extensive growth. That is, in addition to changes in physical activity behaviors, adolescence is also a time of dramatic brain maturation (Giedd *et al.*, 2009; Spear, 2013), including an increase in cell connections and subsequent communication. Thus, the malleable adolescent brain is thought to be especially susceptible to various modifiable lifestyle factors, such as physical activity and aerobic exercise. Secondly, exercise may have different effects on the brain, based on the differential developmental processes that occur in childhood versus adolescence (and even adulthood). For example, a meta-analysis has shown age to moderate the effect sizes seen between exercise and cognition, with larger effect sizes for younger individuals, as compared to older adults and the elderly (Etnier *et al.*, 1997; O'Connor *et al.*, 2015). Lastly, given rapid development of the teenage brain, the influence of exercise on the brain during this critical time may serve as a foundational period for future neural and cognitive outcomes. For these reasons, understanding the plausible neurocognitive benefits of exercise and physical activity during adolescence is likely to have vital implications in our efforts to help motivate more active lifestyles in teenagers, as well as to ensure that exercise is vigorous enough to promote healthy neurocognitive structure and function well into adulthood.

In the current paper, we summarize studies that have examined these associations between chronic or habitual exercise and (1) cognitive-related behaviors as well as (2) brain structure and function in adolescents. We first begin by reviewing how exercise is commonly measured in these studies. Next, we highlight recent findings of how exercise relates to academic achievement and cognition, as well as highlight the few existing studies on exercise and brain structure and function in adolescents. Lastly, we discuss remaining challenges and future directions for understanding the impact of exercise on the teenage brain.

2. Measuring physical activity and exercise

Exercise is typically measured in adolescents by self-report, accelerometers, and/or fitness testing (Shiely and MacDonncha, 2009). Validated self-report methods, such as questionnaires, are often used to determine the type and intensity of exercise and to estimate physical activity for a given period of time (i.e., day, week, month, year)(Sallis and Saelens, 2000). This method is financially advantageous and is not burdensome for participants. However, the results are subjective, which has led to self-reported physical activity levels that are both underestimated and overestimated in adolescents (Grasten *et al.*, 2012). This issue of reporting may be especially problematic for young adolescents, who may be unable to reliably recall or accurately estimate time spent participating in physical activities. This results in self-report questionnaires often being poor predictors of objective calculations of aerobic fitness in adolescents (Morrow and Freedson, 1994). More objective measurements include accelerometers to assess physical activity levels (usually in number of activity counts per minute) over a given period of time (i.e., 7 to 10 days), or having the adolescent complete aerobic fitness testing using a maximal oxygen uptake (VO2 peak or VO2 max) or shuttle–run protocol. VO2 measurements provide an estimate of cardiorespiratory fitness by assessing the maximal oxygen consumption during exercise (Armstrong, 2008). A VO2 max test usually includes having subjects work until exhaustion on a treadmill that incrementally increases in speed and incline every few minutes. Alternatively, a stationary cycle ergometer can be used with incremental increases in resistance. The shuttle-run protocol can also be used to estimate VO2max equivalents, and typically involves continuously running between two lines (usually 20 or 30 meters apart) in sync with prerecorded beeping sounds, with the time between beeps decreasing each minute. VO2 estimates are considered the single best criterion to estimate aerobic fitness since peak oxygen uptake is positively associated with the burden of aerobic physical activity (Armstrong and Welsman, 2007). The distance achieved during a timed shuttle-run test has also been shown to relate to VO2 estimates of aerobic fitness (Ahler *et al.*, 2012; Andersen *et al.*, 2008). These objective measurements are more burdensome as compared to questionnaires, as they require special equipment, more time to collect, and can be inconvenient or uncomfortable for the participant. Furthermore, while accelerometers are able to capture minutes of moderate-to-vigorous physical activity, these devices do not characterize the type of activity (aerobic or non-aerobic). In addition, daily patterns of physical activity only moderately relates to aerobic fitness in youth (Dencker and Andersen, 2011). Thus, given that each method has its own strengths and weaknesses, studies have often included more than one measurement, in order to better characterize the associations between exercise and neurocognitive outcomes.

3. Academic achievement and cognition

Most studies have discovered a positive association between physical activity and school performance and cognition among adolescents (Esteban-Cornejo *et al.*, 2015). For example, physical activity levels have been found to positively relate to measurements of academic performance, such as reading and mathematic achievement in adolescents (Sibley and Etnier, 2003). In a large-scaled self-report study in Minnesota, middle and high school physical activity and sports team participation predicted higher grade point averages (Fox *et al.*, 2010); with similar relationships also found among high school students in Hong Kong (Lindner, 1999; Lindner, 2002), Iceland (Sigfusdottir *et al.*, 2007), and Australia (Dwyer *et al.*, 2001). A more recent study also found that self-report of higher physical activity outside of school (reported via a 3 day recall) significantly related to observed academic grades (Coe *et al.*, 2006).

Beyond academic grades, a growing number of studies have begun to link aerobic exercise with more discrete cognitive abilities. Executive functions are a set of goal directed processes, including attention, planning, problem-solving, working memory, and inhibitory control (Diamond, 2013). These types of cognitive processes are important for academic achievement (Best *et al.*, 2011) and imperative for later success in career attainment and other major aspects of adulthood (Diamond and Ling, 2016). A study of 6th and 7th graders in Denmark, known as The Learning, Cognition, and Motion study, found that aerobic fitness was associated with faster reaction times and better inhibitory control on a flanker task, which requires an individual to suppress responses under congruent, incongruent, and neutral stimulus conditions (Huang *et al.*, 2015). In another large sample of 15 year olds, aerobic fitness, but not daily patterns of moderate-to-vigorous physical activity, were found to relate to faster reaction times and accuracy on a stop-signal attention and inhibitory control task; although this relationship did not replicate in a separate group of adolescents with a different stop signal delay length (Pindus *et al.*, 2015). Similarly, an additional study found aerobic fitness was associated with visual working memory on the Wechsler Memory Scale in obese and non-obese individuals ages 15-21 years old (Ross *et al.*, 2015). Two more recent adolescent studies examined cognitive abilities in regular exercisers versus matched controls. The first study found aerobic fitness to positively relate to spatial learning in older adolescent boys (ages 15 to 18 years), with more aerobically-fit teenage boys learning a virtual spatial task (virtual Morris Water Maze) faster than their less aerobically-fit peers (Herting and Nagel, 2012). The second study found that regular exercising males and females (average age of 16 years old) also performed better on a spatial associative learning task, as well as an inhibition test (Stroop color word task) and cognitive flexibility (Wisconsin Card Sorting Task) task (Lee *et al.*, 2014). In addition, this study found an interaction between neurotrophic levels (i.e., BDNF and vascular endothelial growth factor (VEGF)) and exercise on spatial associative learning and cognitive flexibility performance. Interestingly, regular exercise was linked with better spatial learning in both of these studies, whereas no group differences were seen in spatial memory performance in either study sample of adolescents (Herting and Nagel, 2012; Lee *et al.*, 2014).

In addition to cross-sectional studies, a few experimental studies have been conducted on adolescents. A four-month physical education intervention in a sample of 70 adolescents (ages 12 to 14) examined how ‘dose’ and type of exercise influenced a range of cognitive skills, such as verbal and non-verbal abilities, abstract reasoning, and spatial and numerical ability (Ardoy *et al.*, 2014). The results showed that individuals who were assigned physical education that involved high intensity activities (heart rate above 120 beats per minute) for four days per week showed cognitive performance improvements in all domains as compared to adolescents who completed either two days or four days of physical education per week but without any high intensity activities as part of their curriculum. However, another 20-week randomized intervention study in 12 to 14 year olds, involving 60 minutes of physical activity during school, physical activity homework and encouragement of cycling to/from school, did not find significant improvements in inhibitory control on a flanker task (Tarp *et al.*, 2016). It is feasible the difference between these studies is a difference in the inclusion of high intensity exercise; although it is also important to note that for the latter study, accelerometers in a subset of students suggest that there may have been poor adherence to the intervention protocol altogether (Tarp *et al.*, 2016).

While additional experimental studies in adolescents are needed, the existing findings suggest that regular engagement of physical activity, especially high intensity or aerobic in nature, may benefit academic performance and various cognitive processes, including reaction times, inhibition, and learning.

4. Brain structure and function

To date, a series of Magnetic Resonance Imaging (MRI) techniques have been used to assess regular aerobic exercise and brain structure. Structural MRI allows for various brain characteristics, including cortical thickness, cortical surface area, and cortical and subcortical volumes, to be quantified. Furthermore, diffusion MRI can be implemented to assess white matter microstructure. Using a cross-sectional design, we utilized these MRI approaches to examine brain structure and white matter microstructure in regular exercisers versus lean matched control adolescents, ages 15 to 18 years old. Greater aerobic fitness (as measured by VO2) related to larger hippocampal volumes (Herting and Nagel, 2012) as well as larger rostral middle frontal volumes (Herting *et al.*, 2016). In addition, a positive relationship was seen between aerobic fitness and bilateral lingual gyrus surface area, although this relationship did not exist for individuals with the less active form of the BDNF genotype (Met/Val and Met/Met)(Herting *et al.*, 2016). Using diffusion MRI in this same sample of adolescent males, we also found that those with higher aerobic fitness had lower fractional anisotropy (FA) values in the white matter pathway important for motor behavior, known as the corticospinal tract, as well as a larger number of white matter streamlines in the corticospinal tract and a pathway that carries fibers to the prefrontal cortex (Herting *et al.*, 2014). In another study, including 15 to 21 year olds, aerobic fitness was found to relate to larger orbital frontal cortex volumes in 63 obese and 43 non-obese individuals (Ross *et al.*, 2015). While these findings to date are based on small cross-sectional samples, similar relationships between exercise and these brain regions have been seen in studies spanning other age groups (Chaddock *et al.*, 2011; Hillman *et al.*, 2008; Lopez-Vicente *et al.*, 2017; Whiteman *et al.*, 2016). For example, similar hippocampal findings have been seen in studies of preadolescent children (9-10 years old)(Chaddock *et al.*, 2010) and older adults over 55 years old (Colcombe *et al.*, 2003; Colcombe *et al.*, 2006). Moreover, a more recent study reported a positive relationship between aerobic fitness and entorhinal cortex and the lingual gyrus in young adults (18 to 30 year-olds); suggesting similarities of associations between aerobic fitness and brain structure in older adolescents and young adults (Whiteman *et al.*, 2016). Overall, the results of these existing studies suggest that higher aerobic fitness correlates with distinct cortical, subcortical, and white matter structural connectivity profiles in older adolescents.

While a number of these aforementioned structural MRI studies have also linked brain structure to cognitive performance (Chaddock *et al.*, 2010; Chaddock *et al.*, 2012a; Herting and Nagel, 2012; Whiteman *et al.*, 2016), brain function can also be derived from the Blood-Oxygenated-Level-Dependent (BOLD) signal using functional MRI (fMRI) or measuring brain waves via electroencephalogram (EEG). In the previously mentioned sample of 15 to

18 year-old adolescent males, we also examined brain activity in regular exercisers versus lean matched controls during an associative learning fMRI task (Herting and Nagel, 2013). Specifically, teens were presented randomly paired words and told they would be tested on these word pairs later. Using an event-related design, brain activity was recorded during each word pair and brain images were later sorted into categories based on if that particular individual subsequently remembered or forgot that word pair. When comparing brain activity from successful and unsuccessful learning trials, the hippocampus of lower-fit adolescents was significantly more active than higher-fit adolescents, despite equivalent task performance (Herting and Nagel, 2013). These data suggest that exercise may influence how the brain encodes new memories and that lower-fit teens may need to utilize additional brain resources to learn something new. Furthermore, a set of EEG studies examined brain waves during an attention and inhibition task (Erikson Flanker Task) in fit and unfit adolescents (ages 13-14 years old), both at rest and after an acute bout of exercise (Hogan *et al.*, 2013; Hogan *et al.*, 2015; Stroth *et al.*, 2009). The higher-fit adolescents displayed event-related brain potentials (ERPs) that suggested greater task preparation before stimulus onset and enhanced response monitoring after target onset (Stroth *et al.*, 2009). In addition, in the resting condition, less-fit teens were also found to demonstrate more errors during the inhibition portion of the task, showed greater brain wave coherency while inhibiting a response (Hogan *et al.*, 2013) and higher EEG entropy post-stimulus in the left frontal hemisphere as compared to the more-fit group (Hogan *et al.*, 2015). The authors conclude that these data may suggest unfit teens possess poor efficiency in utilizing their neurocognitive and attentional resources to meet task demands (Hogan *et al.*, 2013; Hogan *et al.*, 2015).

Although studies examining exercise and brain function in adolescents remain scant in the literature, both fMRI or EEG methods suggests that having a more physically active lifestyle in adolescence may be linked with greater brain efficacy when performing goal directed tasks, such as inhibitory control or learning associations.

5. Remaining questions and future directions

While the initial findings from these studies seem promising, more research is needed in order to replicate findings and enhance our understanding of how aerobic exercise regimens can directly influence adolescent brain development and subsequent cognition. First, longitudinal and intervention studies that target adolescents are necessary. A number of exercise intervention studies, including FITKids (University of Illinois-Urbana; 7-9 year olds) (Hillman *et al.*, 2014), the ActiveBrains project (University of Granada; 8-11 year olds) (Cadenas-Sanchez *et al.*, 2016) and the Fuel Learning through Exercise (FLEX) study (Tufts University; 3rd to 5th graders) (Wright *et al.*, 2016) have been established to better understand the effects (rather than just the associations) of exercise on brain and cognition in children. Despite adolescent intervention studies on academic performance, to our knowledge LCoMotion is the only randomized controlled teen study to objectively measure physical exercise and cognition (Tarp *et al.*, 2016). Furthermore, while the FITKids study and ActiveBrains project includes brain imaging, no study to our knowledge has examined exercise interventions on cognitively related brain outcomes in teens. Thus, to date, only a snapshot exists on how aerobic fitness and physical activity influence the developing teen brain. Future adolescent intervention studies should aim to also examine the plausible widespread effects of aerobic exercise on different types of cognition (e.g. learning, working memory, inhibition, attention, decision-making etc.). Moreover, adolescent studies will not only bridge the age gap in experimental studies, but may also provide insight as to whether the effects of exercise on the brain are additive to those seen in childhood, and/or long-lasting, spanning into adulthood and old age. In fact, preliminary research has found that aerobic fitness level and larger hippocampal volumes in 9-10 year olds predicts spatial short-term memory performance one year later, as these children approach early adolescence (Chaddock *et al.*, 2012b). Although these data remain difficult to interpret because baseline memory was not assessed (Chaddock *et al.*, 2012b), these initial findings do suggest that benefits of exercise on cognition might persist. Additional research is necessary to further identify the exact type(s) of neurobehavioral changes that endure and for exactly how long.

Another existing challenge in this field is elucidating the dose-response relationships between exercise (e.g. frequency, duration) and brain and neurocognitive outcomes in adolescents. Future studies need to resolve how often and for how long adolescents need to exercise to have measurable effects on the brain and cognition. Recent findings also highlight that while aerobic exercise may be vital for neurological changes, non-aerobic exercise, including sports skill, may exert its own influence on the brain and behavior (Cassilhas *et al.*, 2012; Kobilo *et al.*, 2011; Marchetti *et al.*, 2015). This raises the question if there are also unique, additive, and/or exponential effects of aerobic and non-aerobic exercise on the teenage brain. Studies should consider randomized control trials that include aerobic and non-aerobic physical activity training both separately, as well as combined, in order to more fully address this question. In addition, when assessing sports participation, special attention is needed to quantify and minimize mild traumatic brain injury that can occur in sports as a potential confounder in both brain and cognitive outcomes related to exercise in adolescents (Kimbler *et al.*, 2011).

Beyond prescribed studies on type, frequency, and duration of exercise training, future studies need to consider what additional factors may contribute to individual differences in how the adolescent brain responds to exercise. That is, a number of genetic and environmental factors may not only influence an individual's exercise training potential, but also their gained brain-behavior benefits from physical activity. For example, in addition to the previously mentioned influence of BDNF levels and BDNF genotype on brain and behavior outcomes (Herting *et al.*, 2014; Lee *et al.*, 2014; Whiteman *et al.*, 2014), the maximal heritability estimate for the trainability of VO2 max has been found to be approximately 47% (Bouchard *et al.*, 1999), suggesting genes may contribute to both aerobic fitness capabilities as well as one's observed benefits. From the environmental perspective, chemicals and particulate matter in our everyday lives, such as air pollution, has been shown to impair cardiopulmonary development across childhood and adolescence (i.e. increasing risk for asthma). Moreover, a few studies also suggest that air pollution exposure during physical activity may diminish some of the benefits typically seen following exercise (Bos *et al.*, 2014; Bos *et al.*, 2011). Beyond these factors, individual differences in how aerobic exercise relates to neurocognitive function can be more or less confounded by obesity-related factors. Obesity has been related to impairments in cognition and neurological structure and function (Roberts *et al.*, 2010; Ross *et al.*, 2015; Wang *et al.*, 2016). Future studies that include overweight and obese individuals will need to tackle how to disentangle the effects of “fit” versus “fat” on the developing adolescent brain and cognitive functions. Some studies have tried to reduce this confound by including only lean adolescents (Herting and Nagel, 2012) or minimizing the proportion of overweight teens in their study (Tarp *et al.*, 2016). However, given that both fitness and fatness may change during an exercise intervention, future studies may aim to include both lean and obese individuals in order to help decipher if the neurocognitive changes are related to cardiovascular or other physical fitness components or due to changes in fat or metabolism that also occur with regular exercise. Either way, based on the current evidence between physical activity, body fat, cognitive function and academic achievement, it is likely that exercise may benefit adolescents in both physical (i.e. fitness and fatness) and cognitive (i.e. learning and academic performance) aspects of their daily lives (Donnelly and Lambourne, 2011; Ortega *et al.*, 2013).

6. Conclusion

Overall, relationships between regular exercise, brain structure and function, and cognition exist during adolescence. Although more research is needed, these studies suggest aerobic exercise and physical fitness may be important factors for the developing teen brain. Moving forward, it is vital to further understand to what extent aerobic exercise may help each teen maximize their own cognitive capabilities. Given the existing data, it is clear that helping adolescents dedicate more of their time to exercise, especially high intensity or aerobic activities, may not only better their physical health, but also positively influence the way their brain is structured and how it functions.

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