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White matter connectivity and aerobic fitness in male adolescents

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ABSTRACT

Exercise has been shown to have positive effects on the brain and behavior throughout various stages of the lifespan. However, little is known about the impact of exercise on neurodevelopment during the adolescent years, particularly with regard to white matter microstructure, as assessed by diffusion tensor imaging (DTI). Both tract-based spatial statistics (TBSS) and tractography-based along-tract statistics were utilized to examine the relationship between white matter microstructure and aerobic exercise in adolescent males, ages 15–18. Furthermore, we examined the data by both (1) grouping individuals based on aerobic fitness self-reports (high fit (HF) vs. low fit (LF)), and (2) using VO_2 peak as a continuous variable across the entire sample. Results showed that HF youth had an overall higher number of streamline counts compared to LF peers, which was driven by group differences in corticospinal tract (CST) and anterior corpus callosum (Fminor). In addition, VO_2 peak was negatively related to FA in the left CST. Together, these results suggest that aerobic fitness relates to white matter connectivity and microstructure in tracts carrying frontal and motor fibers during adolescence. Furthermore, the current study highlights the importance of considering the environmental factor of aerobic exercise when examining adolescent brain development.

Abbreviations: AD, axial diffusion; AF, arcuate fasciculus; ATR, anterior thalamic radiations; BMI, body mass index; CST, corticospinal tract; DTI, diffusion tensor imaging; DWI, diffusion-weighted images; FA, fractional anisotropy; FACT, fiber assignment by continuous tracking; FDR, false discovery rate; Fmajor, forceps major; Fminor, forceps minor; FSL, FMRIB Software Library; HF, high-fit; IFO, inferior fronto-occipital fasciculus; ILF, inferior longitudinal fasciculus; IQ, general intelligence; L, left; LF, low-fit; LME, linear mixed-effects; M, mean; MNI, Montreal Neurological Institute; PDS, Pubertal Development Scale; PLQ, Personal Lifestyle Questionnaire; R, right; RD, radial diffusion; ROI, region of interest; SE, standard error; SES, socioeconomic status; TE, echo time; TI, inversion time; TR, repetition time; UNC, uncinate fasciculus; VO_2 peak, peak aerobic uptake; YAAQ, Youth Adolescent Activity Questionnaire.

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1. Introduction

The adolescent brain undergoes significant changes (Giedd et al., 1996, 1999; Dahl, 2004; Casey et al., 2008), and this period of neurodevelopment may be particularly sensitive for environmental factors to impart their effects on brain and behavior (Andersen, 2003; Masten, 2004; Marco et al., 2011). Thus, it is important to identify environmental factors that may influence typical adolescent neurodevelopment. Aerobic exercise is defined as sustained activity that stimulates heart and lung function, resulting in improved bodily oxygen consumption, and includes a number of physical activities, such as running, walking, swimming, and cycling (Armstrong et al., 2007). Given the widespread epidemic of an increasing sedentary lifestyle for children and adolescents in Western countries, it has become of increasing interest to understand how aerobic exercise may influence not only the body but also the brain. In fact, aerobic exercise is an environmental factor that has been shown to substantially impact gray matter brain structure in children, adults, and elderly (for review see Hillman et al., 2008; van Praag, 2009). Furthermore, we have shown that aerobic exercise also relates to structure and function in the adolescent brain (Herting et al., 2012b, 2013). However, no study to date has assessed if aerobic fitness also relates to white matter microstructure during adolescence. White matter is primarily comprised of glial cells and myelinated neurons. Myelination leads to efficient neural transmission throughout the brain, and it is thought to contribute to enhanced processing speed and cognitive function seen to occur during childhood and adolescence (Casey et al., 2008). Thus, determining how exercise affects white matter connectivity may be particularly important for further understanding the developing adolescent brain.

In recent years, MRI advancements, such as diffusion tensor imaging (DTI), have allowed for in vivo assessment of white matter microstructure and connectivity in the human brain. DTI exploits characteristics of water diffusion in the brain to make inferences about white matter fiber microstructure (Basser, 1995). Primary metrics of DTI include fractional anisotropy (FA), radial diffusivity (RD), and axial diffusivity (AD). Together these variables characterize different components of water diffusion, including restricted, or anisotropic, diffusion (FA), diffusion along the primary eigenvector (AD), and diffusion perpendicular to the primary eigenvector (RD). These diffusion characteristics are thought to reflect different neurobiological components of white matter microstructure, with higher FA and AD, and/or lower RD values, likely representing increased axon caliber, myelination, and/or fiber organization in white matter pathways (Beaulieu, 2002; Alexander et al., 2007). Beyond quantifying diffusion patterns, DTI data can also be utilized to perform tractography, a three-dimensional modeling technique to estimate fiber tracts (Mori et al., 1999). This technique provides useful information by virtually separating different white matter tracts for each individual, and can be combined with basic DTI metrics (i.e., FA, RD, and AD) to provide individual volumes of interest for the assessment of white matter microstructure (Colby et al., 2012).

While no study has examined these relationships in youth, recent studies in healthy adults (≥21 years) and elderly samples (≥55 years) suggest aerobic exercise may influence white matter microstructural properties (Marks et al., 2011; Johnson et al., 2012; Voss et al., 2012; Tseng et al., 2013). However, one of the challenges facing aerobic exercise studies is accurately quantifying aerobic fitness in humans (Etnier et al., 2006; Armstrong et al., 2008). One approach is dichotomizing individuals into groups based on their history of aerobic training (frequency, type of exercise, etc.). However, self-reports of aerobic training can be biased by perception (Armstrong et al., 2008). Furthermore, an important factor in exercise training is the intensity with which the activity is performed. That is, aerobic quantity does not necessarily reflect aerobic intensity, and an increase in an individual's oxygen utilization of the body requires high intensity training (Midgley et al., 2006). In this regard, an individual's ability to utilize oxygen during exercise can be objectively measured by their body's maximum aerobic capacity, or VO_2 peak (Armstrong et al., 2007). To date, adult and elderly studies have utilized both approaches. Positive relationships have been detected between cardiovascular fitness (as indexed by VO_2) and FA in cingulum white matter (Marks et al., 2011), as well as in portions of the corpus callosum carrying premotor and prefrontal cortex fibers (Johnson et al., 2012). Similarly, using training experience as a dichotomous variable, a recent study showed higher FA in regions associated with motor function in previous Master athletes versus age-matched elderly controls (Tseng et al., 2013). However, Voss and colleagues (Voss et al., 2012) recently implemented an aerobic fitness intervention study to assess how aerobic exercise affects white matter microstructure. Interestingly, no significant differences were seen for FA, RD, or AD between groups, but greater improvements in aerobic fitness predicted larger increases in FA values in the prefrontal, parietal, and temporal cortex of a walking intervention group, but not a control (stretching) group (Voss et al., 2012). Together these findings reflect that exercise modality is not only important, but that the magnitude of fitness on white matter microstructure may matter.

Thus, the goal of the current study was to examine how aerobic fitness relates to white matter connectivity and microstructure in male youth, ages 15–18. To accomplish this, we employed DTI and assessed relationships between aerobic fitness and WM microstructure using tract-based spatial statistics and tractography-based along-tract statistics. Furthermore, given the aforementioned limitations in quantifying aerobic fitness (Etnier et al., 2006; Armstrong et al., 2008), we examined the data by both (1) grouping individuals based on aerobic exercise self-report (high fit (HF) vs. low fit (LF)), as well as (2) examining the relationship between VO_2 peak and white matter microstructure across the entire sample. Based on research in adults and elderly (Marks et al., 2011; Johnson et al., 2012; Voss et al., 2012), we hypothesized that HF youth would have higher FA (driven by lower RD) in white matter tracts carrying premotor and frontal cortical white matter fibers when compared to their LF peers. Based on Voss et al. (2012), we also hypothesized these relationships would be largely