Role of Aerobic Fitness and Aging on Cerebral White Matter Integrity

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ABSTRACT: Neuroimaging research suggests that cerebral white matter (WM) integrity, as reflected in fractional anisotropy (FA) via diffusion tensor imaging (DTI), is decreased in older adults, especially in the prefrontal regions of the brain. Behavioral investigations of cognitive functioning suggest that some aspects of cognition may be better preserved in older adults who possess higher levels of aerobic fitness. There are only a few studies, however, investigating potential mechanisms for the improvements in aerobic fitness. Our study suggests that greater aerobic fitness may be related to greater WM integrity in select brain regions.

KEYWORDS: aging; aerobic fitness; exercise; white matter integrity; older adults

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Ann. N.Y. Acad. Sci. 1097: 171–174 (2007). © 2007 New York Academy of Sciences.
doi: 10.1196/annals.1379.022

INTRODUCTION

Executive functioning and the cortical volume of corresponding prefrontal brain regions have been shown to decline with aging. Although there is an emerging body of evidence suggesting that higher aerobic fitness (VO_2 max, maximal amount of oxygen consumed) may be related to improved executive functioning in older adults, there is a paucity of human-derived data regarding the potential mechanisms linking aerobic fitness to the functional anatomy of the brain.[1] Previous studies suggest that there is an age-related decline in cerebral white matter (WM) integrity, thus individual differences in aerobic fitness may be associated with differing levels of WM integrity, which may in turn have implications for preserved cognitive function. Diffusion tensor imaging can provide detailed delineation of WM pathways based on rates of microscopic water diffusion. A higher degree of WM integrity is reflected in a greater degree of fractional anisotropy (FA) of diffusion. Prior research has shown an age-related decline in FA, particularly in the prefrontal regions.[2] Therefore, the purpose of this study was to determine if individual differences in aerobic fitness would be associated with variations in WM integrity, independently of age and gender. Our hypothesis was that higher aerobic fitness would be positively associated with greater WM integrity (higher FA) in the prefrontal (executive function) areas of the brain (i.e., genu, pericallosal frontal).

METHODS

This research was approved by Duke University Health System's Institutional Review Board. Twenty-eight healthy subjects (13 younger adults, 24 ± 3 years; 15 older adults, 69.6 ± 4.7 years) consented to participate. None were depressed or neurologically impaired (BDI Score: 2.4 ± 2.3; MMSE Score: 29.6 ± 0.06).

Aerobic Fitness Estimation

Because exercise testing was not available, aerobic fitness was calculated from a nonexercise aerobic fitness regression equation using gender, age, body mass index (BMI), and a physical activity rating score (PAS) as predictors for estimated maximal oxygen consumption (VO_2 max in mL/kg/min). This equation was validated in a study sample of 2,009 men and women (18–70 years of age) at the Cooper Aerobic Clinic ($r = 0.78$; $P < 0.01$, SE = 5.6 mL/kg/min).[3] The PAS questionnaire required the subjects to rank their average level of physical activity/exercise on a 0–7 rating scale with a ranking of "0" representing little or no physical activity/exercise and a ranking of "7" representing running more than 10 miles a week or participating in 3 or more hours of heavy exercise weekly. Subjects were probed regarding the exact nature of their daily physical activity/exercise routine (mode, frequency, duration, and intensity of effort) by the telephone interviewer. The VO_2 max estimation formula was: $VO_2max\ (mL/kg/min) \approx 56.363 - (0.381 * age) + (1.951 * PAS) - (0.754 * BMI) + (gender * 10.987)$, where: PAS = physical activity rating score (0–7 scale); BMI = weight (kg) ÷ [height (m)]^2, and gender: 0 = women; 1 = men.

Diffusion Tensor Imaging (DTI)

Magnetic resonance imaging was conducted at 4T with 30 contiguous near-axial slices parallel to the AC–PC, 3.8 mm thick; TR = 30,000; per slice, diffusion measured in six directions ($b = 1{,}000$ sec/mm^2) plus one image with no diffusion weighting ($b = 0$); five signal averages. Diffusion tensor eigenvalues were calculated from custom MATLAB scripts. Structural imaging consisted of 3D fast IRP SPGR sequence, 60 contiguous slices, parallel to AC–PC, 1.9 mm thick. For each subject, seven regions of interest were drawn on the diffusion tensor images on a slice-by-slice basis using the high-resolution SPGR images as a reference.

RESULTS AND CONCLUSIONS

Analyses of aerobic fitness yielded significant, independent effects of age group ($t = -9.46$; $P < 0.0001$) and gender ($t = -5.88$; $P < 0.0001$), representing higher levels of fitness for younger adults and males, respectively. After covarying for age and gender, significant ($P < 0.05$) positive correlations remained between aerobic fitness and FA in two regions, the uncinate fasciculus (UNC) and the cingulum (CIN). Regression analyses revealed that the unique contribution of aerobic fitness to the FA variance was 15% for the UNC and 13% for the CIN. Although these preliminary findings suggest that increased aerobic fitness may be associated with greater WM integrity in select regions of the brain, independently of age and gender, the hypothesis that aerobic fitness is significantly related to specific prefrontal regions of the brain is not supported. These results should be viewed with caution due to potential influence of outliers and limitations with estimating VO_2max. Future research needs larger sample sizes and direct VO_2 assessments.

ACKNOWLEDGEMENT

This research was funded in part by NIH Grants RO1 AG11622 and T32 AG000029.

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