Imaging for White Matter Alterations After an Exercise Intervention: A DTI Study in MCI and Normal Controls

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Introduction: Despite the known neurotrophic and cognitive benefits of exercise in healthy older adults, little is known about the effects of exercise training on brain function in those with early signs of Alzheimer's disease (AD) [1]. Several studies have suggested the effects of exercise interventions to improve cognitive function in mild cognitive impairment (MCI) patients [2~4], yet it remains unclear if exercise training alters the cerebral white matter (WM) structure associated with the functional activations during memory retrieval [4]. A diffusion tensor imaging (DTI) study was performed to investigate the longitudinal alterations of fractional anisotropy (FA) measurements in human brains following a walking exercise intervention in both MCI patients and normal controls. The primary goal of this study is to test the hypothesis that an exercise intervention can enhance the WM integrity in relatively short period of time for both MCI and controls, and to identify the differences between the two groups in terms of the magnitude and spatial pattern of the exercise induced WM alterations.

Methods: Mild cognitive impairment (MCI) patients (N=15, age=80±6 years, female=9) and normal controls (N=17, age=77±7 years, female=14), matched in education years, participated in a 12-week exercise intervention consisting of supervised treadmill walking (30 min/day, 4 days/wk) at a moderate intensity (60-70% HRR). Before and after the intervention, participants completed a famous name discrimination task during fMRI and a neuropsychological battery, and a graded submaximal exercise stress test (VO_{2peak}), and underwent MRI scans using a GE Signa Excite 3T MR system. Each MRI session included T1-weighted anatomical imaging (1x1x1 mm), BOLD functional MRI (4x4x4 mm), and DTI (2x2x3 mm, b=1000 s/mm^2) scans. DTI data were pre-processed off-line to estimate the FA index in each imaging voxel, and the Track-Based Spatial Statistics (TBSS) toolbox [5] was used to spatially normalize the DTI images across the subjects, and up-sampled the images to 1x1x1 mm resolution. A general linear model and a two-way ANOVA program in AFNI [6] were used for voxel-based statistics in the normalized space.

Results: Significant gains in cardiorespiratory fitness (10% increase in VO_{2peak}) occurred in both MCI patients and healthy controls ($p<.01$) as a result of the exercise intervention. Within-subject ANOVA indicated that, as shown in Fig.1, FA measurements showed significant longitudinal reductions ($p<0.05$, uncorrected) in WM following the exercise interventions for both control and MCI groups. In comparison, greater post-exercise FA reductions were shown in the MCI group, as indicated by the much larger cluster sizes under the same significance level, although the regional patterns were quite different between the two groups. In Fig.2, a voxel-based group analysis using general linear model (where the factors of age and gender were regressed out) indicated that these FA reductions were widely spread in multiple major regions in cerebral WM, and the MCI group shows overwhelmingly more significant ($p<0.05$, uncorrected) FA reductions following the exercise interventions.

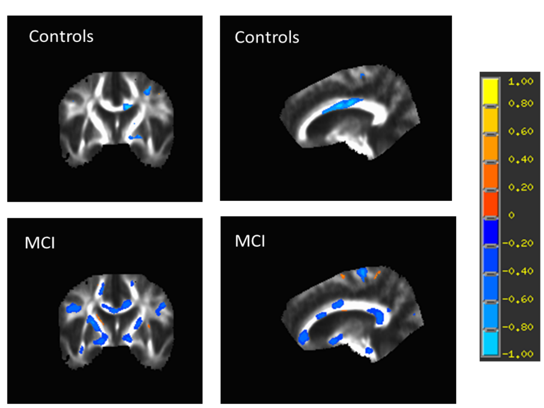

Fig.1: FA alterations in controls and MCI groups.

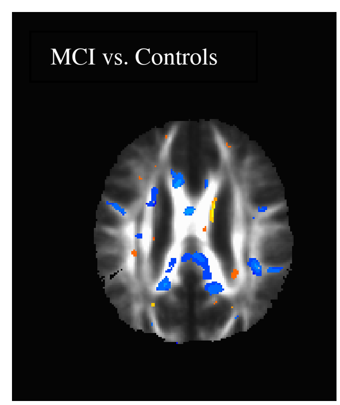

Fig.2: MCI vs. Control on FA reductions

Conclusion and Discussion: In contrast to our original hypothesis, the DTI data have shown longitudinal FA reductions following a 12-week moderate intensity walking exercise intervention in both MCI patients and normal control groups. The contribution of aging-related FA reductions has been excluded based on the fact that the period of interventions is relatively short, and that there is a small improvement in memory and cognition in our behavioral and fMRI tests. Therefore, our data suggest that there must be an uninvestigated mechanism to explain the systematic FA reductions during the exercise interventions. Moreover, this mechanism should be stronger than the potential FA increases introduced by the WM integrity enhancements as a result of the exercise. Thus we revise our hypothesis, such that the longitudinal FA reductions may reflect effects of increased tissue blood volume and/or flow, rather than the integrity degradation in WM. Further study using ASL techniques are on the way to reveal the histological mechanism of the longitudinal FA changes.

References

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