DTI Studies in Patients with Alzheimer¡¯s Disease, Mild Cognitive Impairment, and Cognitive Normal with Minimizing Contributions of Background Gradients

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Introduction

Diffusion tensor (DT) MRI, which is sensitive to the directionality of random motion of water, involves the application of external diffusion-sensitizing magnetic field gradients along different orientations to obtain diffusion anisotropy. In addition to the diffusion-sensitizing gradients, local magnetic field variations, also termed background gradients, can be induced by the magnetic properties of brain tissues that may affect diffusion measurements (1,2). For example, in Alzheimer disease (AD) the formation of paramagnetic iron-containing amyloid plaques (3) interfere with diffusion-encoding gradients, affecting the evaluation of the molecular mobility (2) and the precision of diffusion measurements in brain (4). Several methods have been proposed to compensate for background gradients (5,6,7) in DT-MRI studies. The objectives of our study, were first to determine the effects of background gradients on diffusion measurements, and second to compare fractional anisotropy (FA) and mean diffusivity (MD, tensor trace) maps among patients with AD, mild cognitive impairment (MCI, a potentially transitional stage from normal aging to AD), and cognitively normal (CN)subjects with and without minimization of background gradients. This approach may be useful for studying brain alterations in AD and normal aging.

Methods and Materials

Two DT-MRI sets with positive and negative polarities of diffusion-sensitizing gradients were obtained in 16 AD patients, 18 mild cognitive impairment (MCI) patients and 16 cognitive normal (CN) controls acquired with inversion-prepared magnetization to suppress cerebrospinal fluid (CSF) on a 1.5T MRI system. A double refocusing spin-echo acquisition with a single shot EPI sequence was employed to minimize artifacts due to eddy-currents. In addition, diffusion gradients were applied in six-encoding directions with five b-values of 0, 160, 360, 640, and 1000sec/ mm^2. Separate Trace and FA maps were obtained for DT-MRI data acquired with diffusion gradients of either positive or negative polarity. Furthermore, maps of the geometric mean (gmTrace/gmFA) value of DTI were also computed to minimize scalar effects of background gradients, where the geometric mean is defined as $\sqrt{S_{pos} * S_{neg}}$ and S_{pos} and S_{neg} are the signals acquired with positive (pos) and negative (neg) gradient polarities, respectively. FA and Trace maps between positive (posTrace/posFA) and negative (negTrace/negFA) gradient polarities were compared across all subjects voxel-by-vxoel using T-tests within the framework of SPM. Effects of group on FA and Trace maps were performed by 1-way analysis of variance (ANOVA).

Results

Comparing DTI indexes between two polarities of diffusion-sensitizing gradients: Comparisons between posTrace and negTrace or posFA and negFA in AD, MCI, and CN subjects respectively by using the paired T-test without adjustments for multiple comparisons revealed significant differences in Trace maps in all three groups (p=0.00001). Figure 1 shows representative slices of the result. In contrast to Trace maps, FA maps showed significant differences only in AD and MCI patients, but not in CN subjects (p=0.00001, data not shown).

Comparing DTI indexes between three groups of subjects: We compared gmFA or gmTrace maps among AD, MCI, and CN subjects with geometric mean data by using 1-way ANOVA test at the significance level of p=0.0005 without adjustment for multiple comparisons. Compared to MCI and CN subjects, AD patients had increased gmFA in left occipital guneus, right frontal postcentral gyrus, left inferior frontal gyrus(fig2.a), and left insula and decreased gmFA in left extra nuclear . Comparing MCI with AD patients, we also found increased gmTrace in right middle temporal gyrus, left limbic parahippocampal gyrus(fig2.b), right temporal angular gyrus and left parietal supramarginal gyrus (AD>MCI). Moreover, comparing CN with AD subjects (AD>CN), there is increased gmTrace in left limbic parahippocampal gyrus and right middle temporal gyrus could be observed.

Fig.1. The results of performing paired T-test.

a. AD (Trace) b. MCI (Trace)

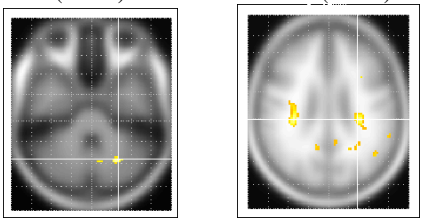
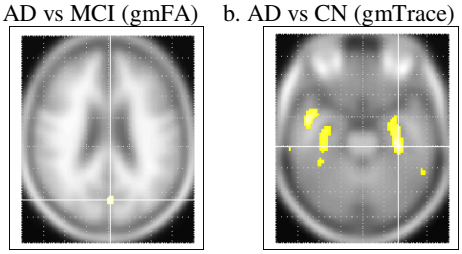


Fig.2. The results of performing ANOVA.

a. AD vs MCI (gmFA) b. AD vs CN (gmTrace)



Discussions and Conclusions

Our data demonstrate that presence of background gradients can influence local diffusion measurements. This suggests that DTI studies should include computation of the geometric average of the diffusion tensor to minimize the effects of background gradients or alternatively to identify contributions from background gradients (5). Moreover, our findings indicate that presence of AD pathology can also modulate background gradients. In particular, our finding that background gradients differed between AD and MCI or controls but not between MCI and controls is interesting. Under the assumption that amyloid plaques induce measurable background gradients, the result may reflect plaque pathology in AD. Using DTI together with amyloid PET imaging (8) may help to unravel the relationship between amyloid plaques and DTI background gradients. In conclusion, background gradients need to be considered when interpreting DTI data in AD.

Acknowledgement: This research was supported by the Program of Kyung Hee University for the Young Researcher of Medical Science in 2008 (20081229) and the grant of the Korean Health 21 R&D Project, Ministry of Health & Welfare, Republic of Korea (A062284).

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