Mapping the Distribution of Local Cross-term Gradients Using DTI in Patients with Alzheimer¡¯s Disease

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Introduction: Diffusion tensor (DT) MRI involves the application of external diffusion-sensitizing magnetic field gradients along different orientations to obtain diffusion anisotropy. In addition to the external gradients, there may be local susceptibility-induced background gradients, related to intrinsic magnetic properties of brain tissue, such as local iron concentration (1). For example, paramagnetic iron-containing amyloid plaques in Alzheimer disease (AD) (2) may induce local background gradients, interfering with diffusion measurements in the brain (3,4,5). The objective of our study was to map the distribution of local cross-term gradients between the external and internal gradients in patients with AD, mild cognitive impairment (MCI), a group at increased risk for AD, and cognitive normal (CN) subjects using DTI. Specifically, we tested whether AD and MCI have higher cross-term gradients than CN, presumably reflecting differences in brain iron across the groups.

Methods and Materials: Two DT-MRI sets with positive and negative polarities of diffusion-sensitizing gradients were obtained in 15 AD and18 MCI patients and 16 CN controls, applying in six diffusion-encoding directions with four b-values of 0, 160, 360, 640 sec/ mm^2. Cross-term b-values (bc) were computed voxel-by-voxel separately for AD, MCI, and CN subjects according to $bc = 1/D \cdot \sqrt{S_n/S_p}$, where S_p and S_n are the signals acquired with positive (p) and negative (n) polarities of diffusion-sensitizing gradients, respectively. D is derived from the Trace map obtained by geometric mean of $\sqrt{S_p \cdot S_n}$. The bc maps were compared across three groups for each b value by ANOVA tests in SPM2 with the significant level of p-value=0.0001 without adjusting for multiple comparisons. Furthermore, bc maps were compared among four b values by ANOVA within-subject model in using SPM2 at the significance level of corrected FWE p=0.00000000005 for each subject group, respectively.

Results: Comparing bc maps among three subject groups for each b value: We found bc values were increased in AD patients compared to MCI or CN. Figure 1a shows representative sections of one of the significantly different regions in right middle temporal gyrus white matter comparing MCI to AD patients (AD>MCI) based on b=640. Figure 1b shows representative sections of one of the significantly different regions in right temporal sub-gyral gray matter comparing CN to AD (AD>CN) also based on b=640. In addition, we didn't find any significant different between MCI and CN subjects for all b-values.

Comparing bc maps among four b values for each group: We found bc values increased proportionately with increasing b-values, as expected. Figure 2 shows representative sections of significant differences compared bc maps between b=160 and b=0 (b0<b160) (Fig 2A) and compared bc maps between b=640 and b=0 (b0<b640) (Fig 2B) in AD patients.

Discussions and Conclusions: The finding of regional differences in bc maps between AD and MCI or CN subjects is consistent with our hypothesis that AD is associated with more brain iron, inducing local susceptibility variations. In addition, the effect increases with increasing strength of the external magnetic field gradients, as we expected. Therefore, high b-value may be increased in sensitivity to map bc. Finally, the strength of a local background gradient G_b can be calculated based on the equation of $b_c = -\gamma^2\delta^3(a_1 G_d \cdot G_b + a_2 G_i \cdot G_b)$, where G_d, G_i, and G_b are the gradient strengths of external diffusion-sensitizing, imaging, and background gradients, respectively. The coefficients of a_1 and a_2 are constants related to integration of gradients over time. This method may provide a new approach for quantification of brain iron and may separate diffusion abnormalities in AD from tissue degeneration or iron-depositions.

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Fig.1. Results of bc-map comparisons between AD and MCI or CN using b=640(p=0.0001, NONE).

a. AD >MCI b. AD>CN

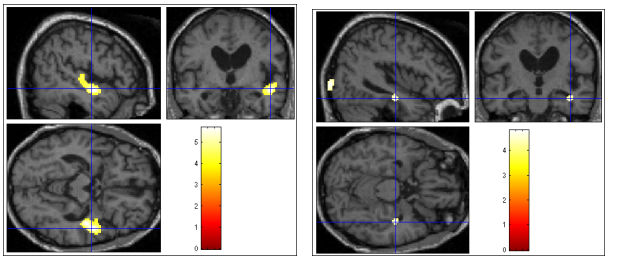
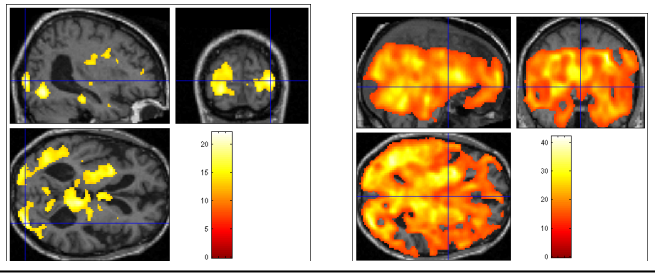


Fig.2. Results of bc-map comparisons between b=0 and b=160 or b=640 within AD subjects (p=0.00000000005, FEW).

a. b0<b160 b. b0<b640



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