Voxelwise DTI and FLAIR Correlation Analysis for Characterization of White Matter Degeneration

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Introduction

White matter (WM) degeneration associated with aging, dementia, or vascular diseases have been investigated by MRI using either fluid attenuated inversion recovery (FLAIR) [1-3] or diffusion tensor imaging (DTI) [4-6], but the value of using both together characterizing WM lesions (WML) has not been thoroughly investigated [7]. In particular, information about the relationship between DTI and FLAIR measurements of lesions might be clinically relevant to better staging the pathology of lesions. The goals of this study were 1) to determine the relationship between DTI measures and lesion severity as measured using FLAIR and 2) to produce a generate profile of correlations between DTI and FLAIR based lesion measures on a voxel-wise basis for the human brain. Both *in vivo* and simulated data were used to investigate the DTI and FLAIR measurements of WML.

Methods

In Vivo Data: Cognitive normal elderly subjects, N=33 (Female=19), Age=71±10 yrs, MMSE = 27.6±3.3, were scanned on 4T MRI. Scan protocol included DTI (EPI: TR/TE=6s/77ms, voxel=2x2x3mm, GRAPPA=2, directions=6 at b=800s/mm^2), FLAIR (TR/TE/TI= 5s/355/2030s), and T1 MPRAGE images. The tract-based spatial statistics (TBSS) technique [8] was used for DTI processing and non-parametric statistics. Aligned DTI data were up-sampled to 1x1x1mm and normalized into a T1 template in the Talairach space. The WML maps were extracted from intensity corrected FLAIR images using a graph cuts algorithm [9]. The T1 template was used again to normalize the WML maps. DTI-FLAIR correlations were performed voxelwise across all subjects in the normalized space. A linear regression algorithm [10] was applied to estimate and remove the age and gender related effects on a voxel-wise basis.

Simulations: A 2-compartment model [11] was used to simulate the WM degeneration process. Relaxation times at 4T of normal WM (T1/T2=1043/65ms) and pure CSF (T1/T2=4500/120ms) were assumed for the 2 compartments, whereas the diffusion tensors were diag (0.95, 0.35, 0.35)x10^{-3} and diag (2.3, 2.3, 2.3)x10^{-3} mm^2/s, respectively. Varying the volume fraction f=0~1of the 2 compartments represents the degenerative progress from the normal WM to pure CSF. The FAIR and DTI signals were simulated by taking actual imaging parameters, and the noises level estimated from the raw data. A WM degeneration phantom with 10 different WML zones for f=0~1 were simulated, and the DTI-FLAIR correlations were estimated in each WML zone for N=20 independent trials.

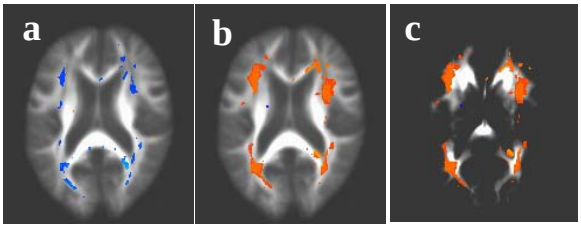

Fig 1: Correlations between (a:FA, b/c:MD)and WML

Results

In Vivo Data: In Fig.1, significant correlations ($p<0.001$) between WML volume and decreased FA (a) or increased MD (b) are illustrated as blue or red clusters superimposed on the mean FA map for the same axial slice. MD exhibits similar distributed yet stronger correlations to the WML. In (c), the MD-WML correlation is alternatively overlaid on the mean WML intensity maps at the identical slice. No significant correlations between DTI and WML were detected in the anterior pariventricular and the corpus callosum areas, where the WML intensities are usually high in FLAIR.

Simulations: In Fig.2, bars in the top row represent the simulated FLAIR intensity as a function of WML severity ranging from f = 0 (normal WM) to 1 (pure CSF). The corresponding correlation coefficients between the FLAIR signal to the FA or MD are plotted in the middle or bottom row, respectively. A consistency was found between the simulated and the *in vivo* data, in that both FA and MD demonstrated weak correlations with WML at severity of f = 0.7 where the FLAIR intensity reached the maximum.

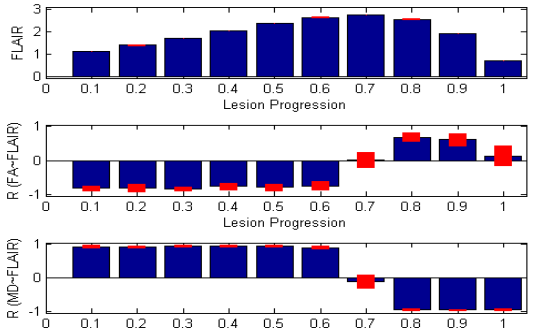

Fig.2: Simulations on WM degeneration phantom

Discussions

Our data show that the correlation between DTI and FLAIR measures of WML follow a characteristic pattern in human brain as lesion severity increases, starting as a positive correlation (MD) for mild lesions before correlations disappear at the peak of FLAIR intensity and then reversing sign as severity further increases. These correlations are found in brain regions, which partially agree with the mean WML distribution but do not overlap on the hyperintensities in the anterior pariventricular or corpus callosum. The relatively weaker correlations for FA are due to its higher sensitivity to the noise, especially to the end of f =1. Because of the intrinsic differences, DTI and WML together should achieve better specificity for characterization of WM degeneration than each measure alone.

References

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