Information Theory Based Quantification Of DTI Alterations In Cognitive Impairment

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Introduction: Diffusion tensor imaging (DTI) is generally considered a sensitive tool (1) for detecting subtle alterations in fiber bundles in various brain conditions, including Alzheimer's disease (AD). However, the best approach for maximizing DTI information is still a matter of intense debate, especially when it comes to quantifying the integrity of nerve fiber bundles. We explored the value of information theoretic measures, such as the Kullback-Leibler (KL) divergence , to quantify DTI variations along fibers as indices of fiber integrity. We predicted that the approach would capture decreased structures within fiber bundles in AD, providing complementary information to the conventional DTI measures, such as fractional anisotropy.

Theory: *Let* $\mathbf{x} = \{x_1, x_2 ... x_n\}$ be a chain of DTI values, such as FA, along locations in a fiber bundle. To determine fiber uniformity, we design a weight matrix $\mathbf{W}$ for similarity/dissimilarity between all values of **x**. **W** has the components $w_{ij} = \varepsilon / \left(|x_i - x_j| + \varepsilon \right)$, *where the scale* $\varepsilon > 0$ maps w_{ij} to the interval [1, 0]. Further, to quantify uniformity expressed in **W**, we compare the distribution of w_{ij} values to that of w_{ij}^{Random} from a chain of random values in **x**.

Figure 1: Weight Matrix Simulations

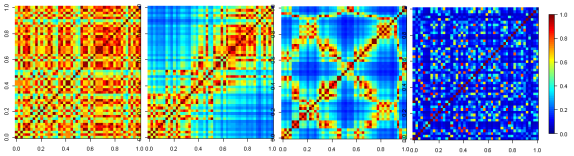


Figure 1 illustrates simulations of weight matrices for uniform, linearly growing, periodic and random values of **x** (from left to right) with some noise added. The information in each **W** is quantified using the symmetrized form of KL divergence and with the assumption that w_{ij} values derive from isotropic Gaussian distribution mixtures.

Methods: We tested the approach on DTI data from 29 AD patients (age: 65 ± 8; MMSE: 21 ± 6), 29 subjects with mild cognitive impairment (MCI, age: 71 ± 8; MMSE: 28 ± 2) , a precursor of AD, and 32 healthy controls (age: 65 ± 8; MMSE: 29 ± 1). All subjects had high-resolution MPRAGE and DTI (TR/TE = 6000/77ms; 2 ×2 ×3mm^3 with 40 continuous slices, 6 diffusion sensitizing directions, b = 800 s/mm^2, 4 averages, and 2-fold acceleration by parallel imaging) scans on a 4 Tesla (Bruker /Siemens) MRI system. Individual DTI images were corrected for eddy-currents, susceptibility distortions and aligned to the T1-weighted images. FA measures were obtained from continuous locations along the left and right descending cingulum fibers, which are usually impacted in AD. For comparison, we also obtained FA along the cortical spinal tract, which usually remains intact in AD. We used non-parametric Wilcoxon rank tests to determine the extent to which variations in **W** across subject groups were significantly different.

Results: Individual weight matrices **W** of FA along the cingulum (A) and cortico-spinal tract (B) fibers from a control, a MCI and an AD subject are shown in Figure 2. Each map depicts the similarity of FA measurements within the right (R), left (L) and across left and right fibers. This shows that the weight matrix of the cingulum has a distinctly different pattern for the AD patient than for the control and MCI subjects, whereas the corresponding patterns of the cortico-spinal tract are similar across the subjects. Figure 3 depicts the variations in weight matrices of the cingulum (left) and the cortical-spinal tract (CST, right) at the group level. The vertical axis in Figure 3 depicts increasing KL divergence from randomness (increasing uniformity). The weight matrix of the cingulum showed on average higher uniformity in AD patients than in control and MCI subjects ($p < 0.003$).

Figure 3: Experimental Weight Matrices

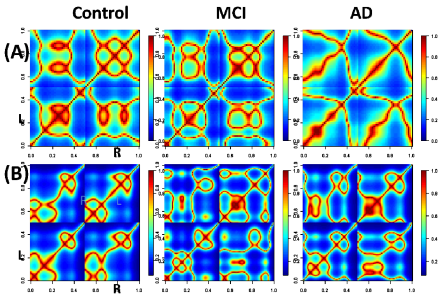
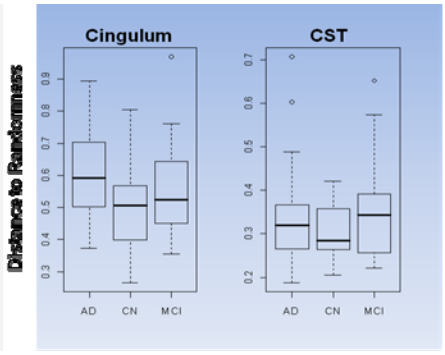


Figure 2: Divergence of Weight Matrices from Randomness



Conclusion: We developed a new approach for quantifying DTI measures of fiber uniformity based on use of information theoretic measures. The approach captured variations in FA features of the cingulum fiber bundle in controls, MCI and AD subjects. FA features along the cingulum indicated a change toward greater uniformity from normal to MCI to AD. The increase in uniformity indicated increasing breakdown of the white matter microstructure. Fiber uniformity may provide a more specific index of brain damage than measurements of absolute FA.

Reference:

1). Chua TC. Curr Opin Neurol. 2008 Feb;21(1):83-92