Location of Affected Pathways in MCI and AD Through FA Comparison

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Introduction

The objective of this study was to detect common areas of the brain where, compared to normals, there is greater reduction in fractional anisotropy (FA) in Alzheimer Disease (AD) verses mild cognitive impairment (MCI). After detection of these regions, the goal was to also demarcate pathways in the brain affected by the lower FA values. Pathway determination is made possible in one common space by the application of our unique DTI tractography normalization procedure.

Method

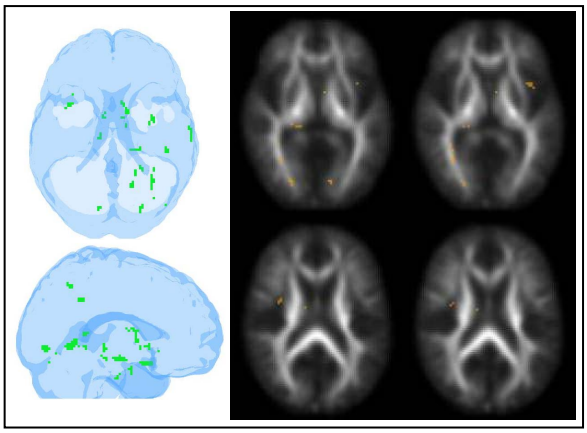

Fig. 1: (Left) ROIs (green) derived from common areas of FA reductions in MCI and AD relative to normals shown in a rendered normal brain. **(Right)** Few representative FA reduction areas displayed on the FA template.

The data used were acquired on a 3T GE scanner consisting of three different populations (10 normal control, 8 MCI, and 7 AD probable) as determined by neuropsychological testing. Multi-slice (2.04 x 2.04 x 4 mm voxel size, 4 mm thick slices no gap) data were acquired using 25 encoding gradient directions at b-values of 0 and 1000 sec/mm2 with an acquisition matrix of 128x128. Fractional anisotropy (FA) maps were calculated for each subject and used for the basis of normalization to a 10 subject FA template created for SPM.

The normalized FA maps of the three different populations were compared using two value T-score statistical analysis between normal control verses MCI; and normal control verses AD probable. Using $p>0.005$ and a voxel limit of 8, we used the intersection of the clusters from the two group analysis to provide ROIs of voxels where FA changes occurred in both MCI and AD probable in respect to normal. The mean FA value were calculated for each ROI in all three populations.

Additionally, streamline tractography incorporating tensor interpolation with 0.2 mm steps was conducted on anatomically equivalent seed points defined in individual subjects by inverse normalization using an SPM template, and individual tracts were warped back to the SPM template. The tracts for the normal population were then filtered using the ROIs yielded from the FA group analysis to obtain the fiber tract which lie on the ROIs.

Results and Discussion

FA comparisons between the ROIs show a general trend of lower FA values for AD probable as compared to MCI (18 out of 22 regions where FA is reduced both in AD and MCI when compared to normal). In addition, the ROIs contains tracts which connect regions involved in Alzheimer Disease including the Fornix, Medial Temporal, Parietal, Frontal, and Occipital regions.

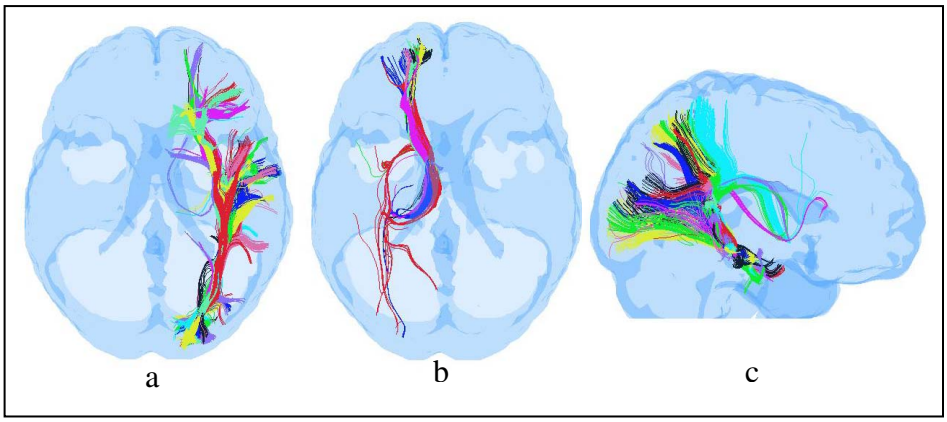

Fig. 2: Affected fiber tracts superimposed from all normal subjects, different color per subject (a) ROI #13 (highest degradation of FA from MCI to AD): Frontal-Occipital, Temporal-Occipital, and Fornix, (second highest FA degradation shows same pathways *ROI #8*). A few other biologically significant pathways are shown in (b) and (c). (b) ROI #16 Thalamic Radiations, (c) ROI #6 Parietal-Temporal, Temporal-Occipital.

DTI and white matter tractography interpretation is still an area of on-going research. Our method of group comparison to find ROIs of FA change and the subsequent filtering of normalized tractography to find the affected axonal pathways provides an objective isolation of fiber tracts which are affected by disease without *a priori* knowledge.

Table 1: Mean FA values of ROIs

ROI #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Normal	.55	.34	.19	.13	.12	.35	.33	.44	.29	.23	.13	.40	.43	.22	.15	.25	.26	.23	.12	.25	.45	.32
MCI	.43	.26	.10	.09	.08	.26	.23	.31	.19	.13	.08	.29	.32	.14	.10	.19	.21	.13	.07	.19	.35	.16
AD	.44	.23	.09	.07	.07	.22	.25	.27	.18	.12	.08	.28	.30	.14	.09	.17	.20	.12	.07	.17	.35	.19