

# Characteristic Patterns of White Matter Disintegration in Frontotemporal Dementia and Alzheimer's Disease by DTI

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**Background:** While several diffusion MRI studies<sup>1,2</sup> reported patterns of white matter alternations in Alzheimer's disease (AD) and normal aging, little is known about white matter degradation in frontotemporal dementia (FTD)<sup>3</sup>, which has a different etiology than AD but sometimes difficult to differentially diagnosis because of overlapping symptoms with AD. In this cross-sectional study, we performed diffusion tensor imaging (DTI) and tractography based region of interest (ROI) as well as regionally unbiased voxel-wise analysis of Fractional Anisotropy (FA) in 13 AD patients, 12 FTD, and 13 age-matched controls (CN). The main objective was to determine if FTD is associated with a characteristic pattern of FA alterations with respect to normal aging and AD that may improve diagnosis of FTD.

**Methods:** DTI was performed on a 4 Tesla (Bruker /Siemens) MRI system, employing a spin-echo echo-planner sequence, with a factor 2 parallel imaging acceleration (GRAPPA): TR/TE = 6000/77ms; field of view 256cm x 224cm; 128 x 112 matrix; b = 0, 800 s/mm<sup>2</sup>, 6 directions, 2 x 2 mm<sup>2</sup> in-plane resolution; 40 continuous slices with no gap, each 3 mm thick; 4 averages were acquired per slice and diffusion weighted images. Using a tractography-guided ROI analysis<sup>4</sup>, we measured mean FA in anterior / posterior callosal fibers (ant.CC / post.CC), bilateral anterior / posterior cingulum (ant.Cg / post.Cg), temporal cingulum (temp.Cg), uncinate (Unc) fibers and corticospinal tracts (CST) (Figure1). Statistical significant difference was set at P<0.05 by ANOVA using FA regressed against group, age and gender effects.

Furthermore, we also performed voxel-wise analysis using SPM2 (<http://www.fil.ion.ucl.ac.uk/spm/>) by warping each FA image to a population based FA template for spatial normalization and then smoothing the data with a 6mm<sup>3</sup> FWHM Gaussian kernel. FA differences between groups were performed voxel-by-voxel using analysis of covariance with diagnosis as main effect and, age and gender as covariates. The significance level was set to an uncorrected P<0.001.

**Results:** 1) Tract-based analysis: Compared to controls, FTD patients had significantly lower FA values in ant.CC, bilateral ant.Cg, temp.Cg and Unc fibers, whereas AD patients had significant lower FA values in post.CC, bilateral post.Cg, temp.Cg, left ant.Cg and left Unc fibers. Compared to AD, FTD patients had significantly lower FA values in ant.CC and bilateral Unc fibers, whereas AD patients, when compared to FTD, had significantly lower FA values in post.CC (table1). 2) The voxel-wise analysis showed a similar pattern of reduced FA (Figure2), supporting the findings based on ROI analysis.

**Conclusions:** FTD is associated with a characteristic pattern of FA reductions in the frontal and temporal regions, whereas FA reductions in AD involved predominantly the parietal and temporal regions, which consistent with other studies on MRI<sup>5</sup>. These distinct FA patterns of FTD and AD may aid the differential diagnosis between these dementias.

## Reference:

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Figure1. Determination of fiber ROIs

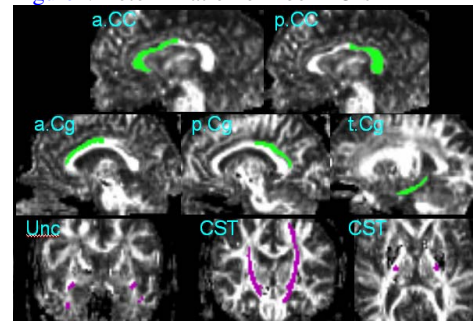


Table1. Group comparisons of FA in specific fiber tracts

Tracts	CN	FTD	AD	P			
	FA Mean (STD)			CN>FTD	CN>AD	AD>FTD	FTD>AD
ant.CC	0.54 (0.03)	0.45 (0.07)	0.50 (0.04)	<0.001	-	0.02	-
post.CC	0.65 (0.03)	0.63 (0.04)	0.59 (0.04)	-	0.001	-	0.05
L.ant.Cg	0.49 (0.04)	0.42 (0.06)	0.44 (0.04)	0.001	0.004	-	-
R.ant.Cg	0.40 (0.03)	0.37 (0.04)	0.38 (0.04)	0.02	-	-	-
L.post.Cg	0.48 (0.04)	0.45 (0.04)	0.44 (0.02)	-	0.01	-	-
R.post.Cg	0.43 (0.04)	0.42 (0.05)	0.40 (0.03)	-	0.03	-	-
L.temp.Cg	0.37 (0.03)	0.32 (0.03)	0.31 (0.03)	<0.001	<0.0001	-	-
R.temp.Cg	0.39 (0.03)	0.33 (0.05)	0.35 (0.05)	0.001	0.01	-	-
L.Unc	0.40 (0.03)	0.33 (0.04)	0.36 (0.03)	<0.0001	0.01	0.03	-
R.Unc	0.38 (0.04)	0.33 (0.05)	0.36 (0.04)	0.01	-	0.05	-
L.CST	0.52 (0.03)	0.52 (0.03)	0.53 (0.03)	-	-	-	-
R.CST	0.57 (0.02)	0.57 (0.04)	0.57 (0.02)	-	-	-	-

Figure2. 2D views of the whole brain findings by voxel-wise study: Left, significantly reduced FA in FTD, AD compared to control group. Right, significant group difference between FTD and AD.

