Concordant brain structural and diffusion changes in frontotemporal dementia with and without motor neuron disease

Y. Zhang[1,2], N. Schuff[1,2], M. Tartaglia[2], J. Laxamana[1,2], H. J. Rosen[2], M. Gorno-Tempini[2], B. L. Miller[2], and M. W. Weiner[1,3]

[1]Center for Imaging of Neurodegenerative Diseases, VA Medical Center, San Francisco, CA, United States, [2]University of California, San Francisco, San Francisco, CA, United States, [3]University California, San Francisco, CA, United States

Background: Frontotemporal dementia (FTD) and motor neuron disease (MND) are neurodegenerative conditions with overlapping clinical and neuropathological features. 10-15% of FTD patients develop features of MND (FTD/MND) and show a more rapid decline of both physical and cognitive abilities than FTD patients without MND. MRI studies have shown systematic patterns of brain atrophy in both FTD and FTD/MND relative to controls [1, 2]. However, direct comparisons between FTD and FTD/MND are rare and little is known about differences in brain morphology between these two conditions. We hypothesized that FTD and FTD/MND would differ in terms of both macroscopic brain atrophy, measured using structural MRI and microscopic tissue integrity measured using DTI. In this study specifically, we aimed to evaluate the differences in concordant variations of regional atrophy and mean diffusivity (MD) changes of gray (GM), and concordant variations of regional atrophy and fractional anisotropy (FA) changes of white matter (WM) between FTD and FTD/MND patients compared to controls and to each other.

Methods: Fifteen behavior variant FTD patients (mean age=60.9±5.7yrs, mean MMSE=24.9±4.5), 13 FTD/MND patients (mean age=62.6±9.9yrs, mean MMSE=25.1±3.6), and 24 healthy controls (CN, mean age=62.2±7.4yrs, mean MMSE=29.6±0.5) were included in the study. All subjects underwent MPRAGE (TR/TE/TI = 2300/3/950ms, 7° flip angle, 1 × 1 × 1mm^3 resolution) 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 distortion and aligned to the T1-weithged images. GM and WM segmentation and masking were performed using SPM8 (http://www.fil.ion.ucl.ac.uk/spm/). GM and WM probabilistic maps, GM mean diffusivity (MD) and WM fractional anisotropy (FA) maps were transformed into a common brain template space at 1.5 × 1.5 × 1.5mm^3 resolutions using DARTEL [3]. The spatially normalized images were then smoothed with an 8mm^3 FWHM Gaussian kernel. For each modality (i.e. GM volume, GM MD, WM volume and WM FA), group differences were tested voxel-by-voxel using a t-test between the paired groups, with age and sex as covariates and the significant level was set at family wise error corrected p=0.05. To evaluate differences in concordant variations of regional atrophy and diffusion, we used concordant analysis, in which the t-scores of each measure are compared using combining functions (i.e. the concordant atrophy and MD changes in GM, or the concordant atrophy and FA changes in WM), as described by Hayasaka et al [4] and implemented in SnPM. To determine if discoveries of concordance are above chance, we used non-parametric tests based on 1000 fold permutations of the subject labels. Results of the statistic significances were then superimposed on a common brain atlas for visualization.

Figure 1. Regional pattern of significantly concordant GM atrophy and MD increases in FTD vs. CN (row-1), FTD/MND vs. CN (row-2), and FTD/MND vs. FTD (row-3).

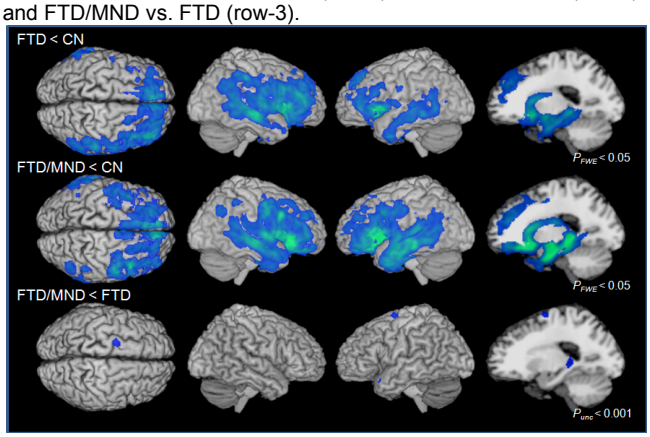
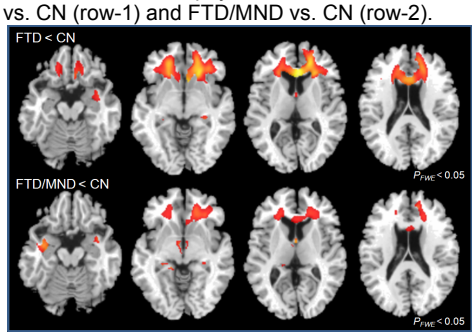


Figure 2. Regional pattern of significantly concordant WM atrophy and FA decreases in FTD vs. CN (row-1) and FTD/MND vs. CN (row-2).



Results: 1) Figure 1 shows regional patterns of concordant volume loss and MD increase of GM from group comparisons: a) Compared to CN, FTD showed both GM loss and increased MD, predominantly in the right frontal and temporal lobes. b) Compared to CN, FTD/MND showed a bilateral frontotemporal pattern of concordant GM abnormalities which was largely overlapping with the pattern of FTD vs. CN, but was more spread. c) FTD/MND had greater concordant GM loss and increased MD in the left ventral thalamus and the left motor cortex, in direct comparison with FTD. 2) Figure 2 shows the regional pattern of concordant WM atrophy and WM FA decrease from group comparisons: a) Compared to CN, FTD had strong concordant WM abnormalities in bilateral frontal and temporal WM regions. The frontal damage was more pronounced. b) Compared to CN, FTD/MND showed a pattern of WM abnormalities in both frontal and temporal regions but weaker than that in FTD vs. CN. c) No significant differences were found between FTD/MND and FTD with respect to the structural and diffusion changes in WM.

Conclusion: Neuropathological differences have been demonstrated in the type and distribution of pathological inclusions when comparing FTD/MND and the other FTD syndromes and this could be reflected in our results but further radiological-pathological studies will be needed.

Reference:

1. Rosen HJ, et al. Neurology. 2002;58:198-208. **2.** Chang JL, et al. Neurology. 2005;65:75-80. **3.** Ashburner J. Neuroimage. 2007;15;38:95-113. **4.** Hayasaka S. Neuroimage. 2006, 15;30:768-79.