Brain Alternations in Alzheimer Disease and Frontotemporal Dementia: A Multimodal MRI Analysis

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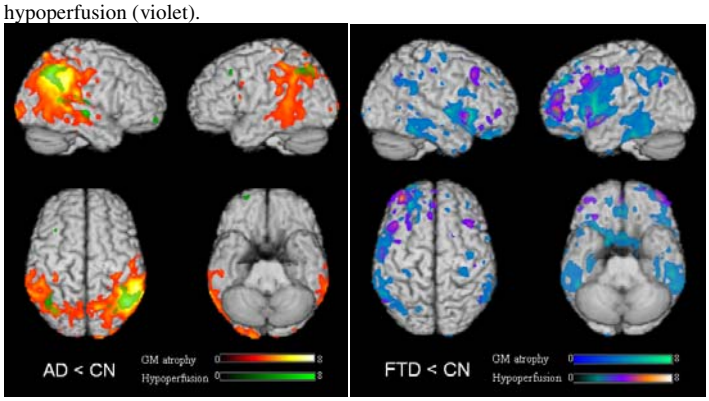
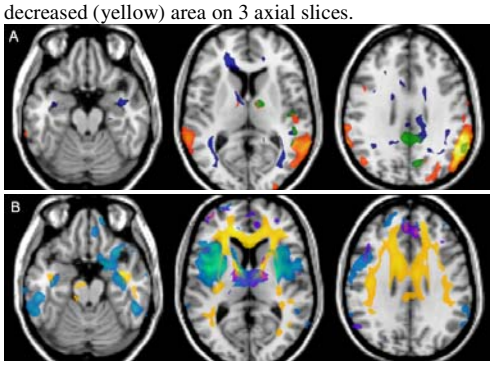
Background: Alzheimer's disease (AD) and frontotemporal dementia (FTD) can be difficult to differentiate because their clinical symptoms overlap. Previous structural MRI studies have generally shown prominent cortical atrophy[1] and arterial spin labeling (ASL) MRI studies have revealed cortical hypoperfusion[2] in both AD and FTD. More recently, diffusion tensor imaging (DTI) studies also found evidence of white matter degradation in AD and FTD[3]. However, most studies assessed structural, perfusion, and diffusion alterations separately. In this study, we report initial attempts to utilize structural, perfusion and diffusion information together toward a comprehensive analysis of multimodality MRI data. Specifically, we hypothesized that such an analysis will reveal that in AD the cortical damage exceeds the white matter damage whereas in FTD the amount of white matter degradation is greater and proportionate to the cortical damage.

Figure 1. Left, AD < CN: Overlaid GM atrophy (hot) and hypoperfusion (green) area on the rendered brain. Right, FTD < CN: Overlaid GM atrophy (cold) and hypoperfusion (violet).



Methods: This study involved 18 patients diagnosis with AD, 18 with FTD and 19 age- and gender matched cognitive normal (CN) subjects. All scans were preformed on a 4 Tesla (Bruker /Siemens) MRI system with an 8 channel head coil. MRI acquisition included T1-weighted imaging (MPRAGE TR/TE/TI = 2300/3/950ms, 7° flip angle, 1 × 1 × 1mm^3 resolution); Continuous ASL with TR/TE=5200/9ms, 1590ms post labeling delay, 5mm thick slices with 24% gaps, 3.75 × 3.75mm^2 in-plan resolution and oriented 10º up from PC-PC line; DTI with TR/TE = 6000/77ms; 2 × 2mm^2 in-plan 40 continuous slices each 3 mm thick, six diffusion sensitizing directions b = 800 s/mm^2, 4 averages, and two-fold acceleration by parallel imaging. Probabilistic segmentation maps of gray/white/CSF were generated from T1 weighted MRI; Partial volume corrected CBF images were created from ASL data, following our previous publications[4], and fractional anisotropy (FA) images of DTI were created by dtv-VolumeOne software[5]. All images were transformed into common brain template space using nonlinear transformation at 1 × 1 × 1mm^3 resolution by SPM2 (http://www.fil.ion.ucl.ac.uk/spm/). The spatially normalized images were then uniformly smoothed with an 8mm^3 FWHM Gaussian kernel. For each MRI modality, group effects were tested voxel-by-voxel using analysis of covariance with diagnosis as main effect, age and sex as covariates and a significant level of P<0.001. The t-maps from these tests were then superimposed on a brain template to assess simultaneously the patterns of structural, perfusion, and diffusion changes.

Figure 2. A. AD < CN: Overlaid GM atrophy (hot), hypoperfusion (green) and WM FA decreased (blue) area on 3 axial slices. **B.** FTD < CN: Overlaid GM atrophy (cold), hypoperfusion (violet) and WM FA decreased (yellow) area on 3 axial slices.



Results: 1) AD vs. CN: AD was associated with a) diffuse GM volume loss bilaterally in parietal and temporal regions, most pronounced in the left tempoparietal cortex; b) prominent hypoperfusion in bilateral parietal and left temporal regions, most pronounced in the left tempoparietal regions and posterior cingulate gyrus; c) lower FA values in temporal, parietal and frontal white matter regions (Figure1, 2A). **2) FTD vs. CN**: FTD was associated with a) GM loss predominantly in bilateral frontal and temporal regions, the loss also extended to bilateral parietal lobes; b) prominent hypoperfusion in bilateral frontal and temporal regions; c) significant FA reduction in vast frontal and temporal regions (Figure1, 2B). **3) FTD vs. AD**: Compared with AD, FTD patients showed significant GM loss in frontal and anterior temporal regions; significant hypoperfusion in the right frontal regions; and significant lower FA in frontal and anterior temporal regions, similarly to the VBM findings. **4) AD vs. FTD**: compared with FTD, AD patients had significant GM loss in the precuneus regions; significant hypoperfusion in the left temporal lobe and the cingulate gyrus; however, FA difference was not significant. **5) Extent of GM and WM involvement**: The volume of abnormal GM or WM regions relative to total GM or WM is listed in Table 1, separately for AD and FTD. This shows that FTD is associated with greater WM involvement and also higher GM involvement than AD.

Table 1. Ratios (percentage) of the involved voxels (p<0.001) divided by the tested voxels (total GM or WM).

	AD<CN	FTD<CN	AD<FTD	FTD<AD
GM volume loss (VBM)	6.7%	10.4%	0.2%	10.1%
GM hypoperfusion (ALS)	2.1%	1.1%	1.3%	0.5%
WM FA reduction (DTI)	5.0%	34.7%	0.0%	17.8%

Conclusion: The results support our hypothesis that AD is primarily associated with gray matter damage whereas FTD also involves prominent white matter degradation in addition to gray matter damage. These tissue specific patterns may shine a light on the differential pathologies underlying AD and FTD. They may also aid a differential diagnosis between the diseases and emphasize the benefit of multimodality MRI.

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Reference:

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