White Matter Changes in AD Measured With Diffusion Tensor Imaging

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INTRODUCTION

Degeneration of brain white matter (WM) has received a great deal of attention with recent studies demonstrating that such changes are correlated with cognitive decline and may increase risk for the development of dementia. Recently, diffusion tensor MRI (DTI) has been employed to obtain regional measures of WM tissue microstructure, for better regional localization of pathologic changes. We used whole-brain DTI to examine the regional basis of alterations in brain WM in patients with Alzheimer's disease (AD) and adults with mild cognitive impairment (MCI).

METHODS

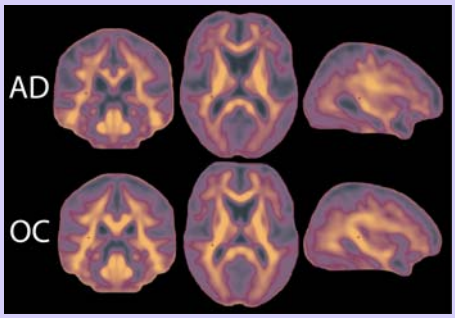
Participants:
We examined older non-demented adults (OA), patients with Alzheimer's disease (AD), and older adults with mild cognitive impairment (MCI). All patients were recruited through the MGH ADRC.

Demographics of OA, MCI, and AD

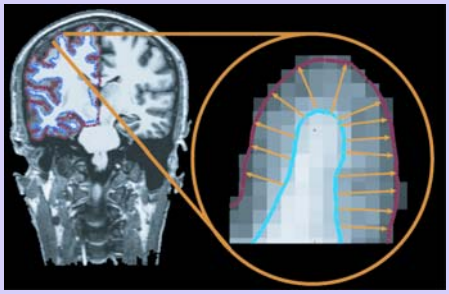
	n	Age	Sex	Years of Education	MMSE	CDR
OA	20	73.9	12M/8F	16.7	28.9	N/A
MCI	14	76.2	6M/8F	12.5	25.9	0.43
AD	13	76.6	8M/5F	15.7	20.0	1.15

Imaging:
All imaging was performed on a 1.5T Siemens Sonata scanner.

DTI:
Participants were imaged with whole-head, high-resolution diffusion tensor scans (2mm isotropic voxels). Fractional anisotropy (FA), a measure of white matter microstructure, was calculated as previously described (1). Group comparisons were performed with whole brain voxel-based t-tests and region of interest analyses.

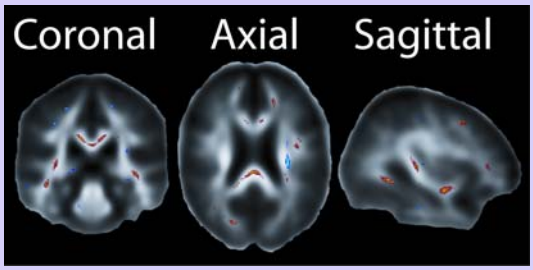


Cortical Thickness:
Participants were imaged with two T1-weighted MPRAGE scans. Cortical surface models for measures of cortical thicknes were created with a semi-automated procedure as previously described (2, 3). Thickness values were determined at each vertex by calculating the shortest distance from the gray/white border to the boundary of the cortex.



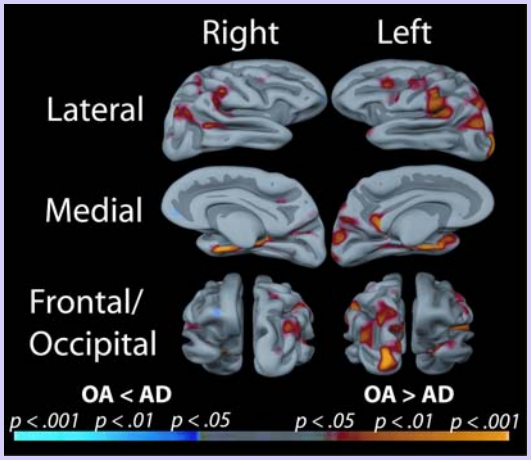
RESULTS

Reduced FA in AD compared to OA



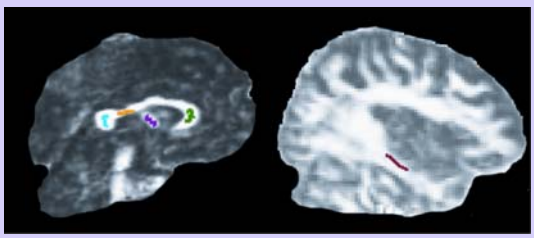
AD had significantly reduced FA in temporal white matter and in the splenium of the corpus callosum. Statistical reductions in FA are displayed in red-yellow in the coronal (left), axial (center), and sagittal (right) plane of a mean anisotropy map.

Cortical thinning in AD compared to OA

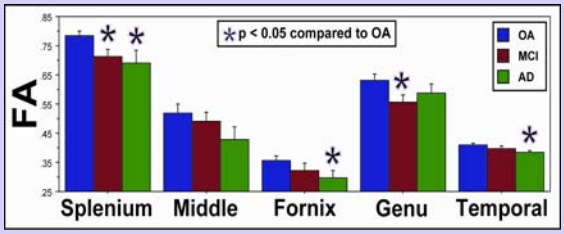


AD showed significant cortical thinning in parahippocampal cortex (likely corresponding to entorhinal cortex) and lateral parieto-occipital cortex with minor thinning in frontal cortex.

FA Region of Interest Analyses

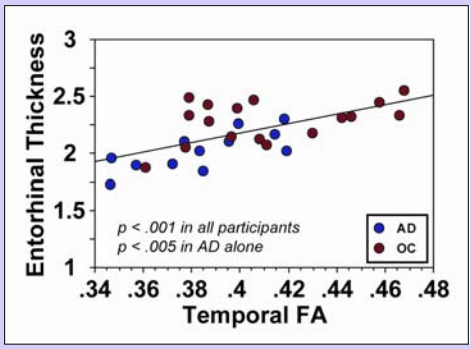


Regional measures were obtained from the splenium, middle, and genu of the corpus callosum and from the fornix and a portion of temporal white matter.



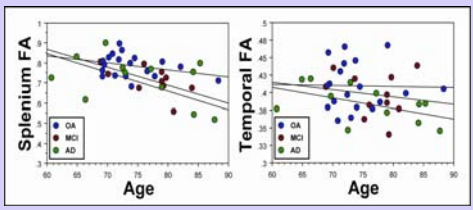
FA was statistically reduced in the splenium of the corpus callosum, the fornix, and temporal WM in AD, but not in the genu or middle of the callosum. FA was reduced in the splenium of the callosum in MCI.

Temporal FA correlates with parahippocampal cortical thickness



Temporal white matter FA was correlated with thickness of parahippocampal gray matter in all participants combined and in the AD participants alone. This correlation was not significant in OA alone.

FA correlates with age in AD/MCI but not OA



There was an age-related decline in FA in the splenium of the corpus callosum and in temporal white matter in AD but not OA. These regions also did not show an age-related decline in our prior study of normal aging, suggesting that AD results in abnormal age-related brain degeneration.

CONCLUSIONS

- AD results in alterations in WM that are most prominent in posterior regions of the temporal lobe and CC.
- These findings demonstrate that AD pathology differs from accelerated aging because our prior work demonstrated greatest age-related changes in anterior WM.
- Cortical degeneration was greatest in parahippocampal and lateral parieto-occipital cortex.
- FA was reduced in the splenium of the corpus callosum in MCI, suggesting that alterations in FA could be detected early in the process of AD brain degeneration.
- Thickness of parahippocampal cortex is related to temporal lobe white matter FA, suggesting a dependence of these processes.
- Future research will examine the clinical correlates of gray and white matter degeneration in AD.

REFERENCES

1. Pierpaoli C, Basser PJ., Magn Reson Med. 1996 Dec;36(6):893-906
2. Fischl Thickness
3. Salat Thickness.

ACKNOWLEDGEMENTS

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