Is the Superficial White Matter Important in Alzheimer's Disease?

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Introduction: White matter abnormalities have been reliably shown in the large deep early myelinating fibers in Alzheimer's disease. However, the late myelinating white matter comprised of intracortical myelin, short-range association fibers and interstitial neurons, at the juncture of the neuropil, here called "superficial white matter", has not received much attention. The superficial white matter[2,3] shows high plasticity as well as high vulnerability[1], which makes it especially sensitive to the normal aging process[2]. In light of this, we hypothesized that it may be particularly susceptible to Alzheimer's disease processes. The purpose of this work is to determine if the superficial white matter is impaired in Alzheimer's disease patients compared to healthy controls.

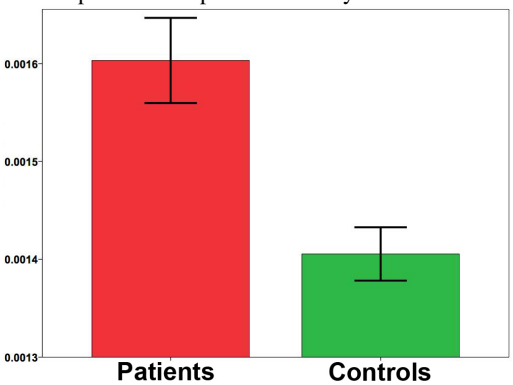

Figure 1. Graphs show the significant differences between whole brain Superficial White Matter Mean Diffusivity. The error bars represent the SEM. Mean units: 10−3 mm2/s.

Methods: Our data consisted of consisting of 91 subjects (44 AD patients (age: 71.02+5.84), 47 healthy controls (age: 69.23+4.4)) from our memory clinic in Rome, Italy. All MRI data were acquired on a 3T Allegra MRI system. 1) T1-weighted 3D images, with partitions acquired in the sagittal plane using a modified driven equilibrium Fourier transform sequence (TE/TR/TI: 2.4/7.92/910 ms, flip angle: 15°, 1 mm3 isotropic voxels); and 2) Three diffusion-weighted volumes were also acquired using SE echo-planar imaging (TE/TR: 89/8500 ms, bandwidth: 2126 Hz/voxel, matrix: 128 × 128, 80 axial slices, voxel size: 1.8 × 1.8 × 1.8 mm) with 30 isotropically distributed orientations for the diffusion sensitizing gradients at a b value of 1000 s/mm2 and 6 b = 0 images. The T1 and DTI data were processed to obtain the white matter (WM) surfaces using BrainSuite[5] (http://brainsuite.org). Mean diffusivity (MD) was computed from the diffusion tensor model and resampled at each vertex along the WM surface using ShapeTools[6] after registering to the BrainSuite WM atlas using Svreg[7]. MD was analyzed across the whole brain mean superficial white matter and with high spatial resolution with the General Linear Model (http://brainsuite.org/bss/) with sex and age included as covariates. P-values underwent FDR corrections.

Results: *Figure 1.* Patients had significantly ($p < 0.001$) increased whole brain superficial white matter MD. *Figure 2.* Patients had significantly increased superficial white matter MD in most areas of the brain that was most prominent in the temporal lobe.

Discussion: This study demonstrates large increases in superficial white matter MD across the brain in a pattern related to the described progression of Alzheimer's Disease[4]. This means that the superficial white matter, with its peculiar features (late myelinating fibers, short-range association fibers and interstitial neurons) is particular sensitive to the Alzheimer's disease neurodegenerative process.

Conclusion: The superficial white matter is uniquely complex in humans. Given the unique cellular makeup and its importance in neuronal synchrony, the superficial white matter likely plays an important role in Alzheimer's disease.

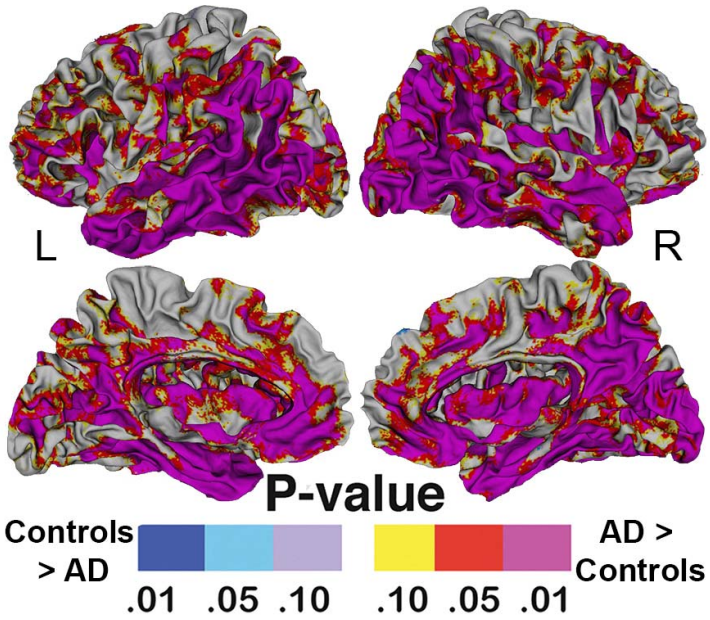

Figure 2. Probability maps showing FDR corrected effects of Alzheimer's disease on the superficial white matter MD, controlling for age and gender mapped at high-spatial resolution at thousands of homologous locations within the superficial white matter. The direction of effects are indicated by the color bar. Red indicates increased MD with disease.

References:

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