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

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Introduction: White matter (WM) abnormalities have been reliably shown in the large deep and early myelinating fibers in Alzheimer’s disease. However, the late myelinating WM comprised of intracortical myelin, short-range association fibers and interstitial neurons, at the juncture of the neuropil, here called “superficial WM”, has not received much attention. The superficial WM shows high plasticity as well as high vulnerability, which makes it especially sensitive to the normal aging process. 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 WM is impaired in Alzheimer’s disease patients compared to healthy controls.

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 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 WM surfaces using BrainSuite5 (http://brainsuite.org). Mean diffusivity (MD) was computed from the diffusion tensor model and resampled at each vertex along the WM surface using ShapeTools6 after registering to the BrainSuite WM atlas using Svcrg7. MD was analyzed across the whole brain mean superficial WM 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 WM MD. Figure 2. Superficial WM mean diffusivity values were averaged at each vertex point across the white matter surface separately for patients and controls. Figure 3. Patients had significantly increased superficial WM MD in most areas of the brain that was most prominent in the temporal lobe.

Discussion: This study demonstrates large increases in superficial WM MD across the brain in a pattern related to the described progression of Alzheimer’s disease. This means that the superficial WM, with its peculiar features (late myelinating fibers, short-range association fibers and interstitial neurons) is particularly sensitive to the Alzheimer’s disease neurodegenerative process. The superficial WM is uniquely complex in humans. Given the unique cellular makeup and its importance in neuronal synchrony, the superficial WM likely plays an important role in Alzheimer’s disease.

References: