Investigation of White-Matter Aging by Quantitative MRI and MRS

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Introduction. Cerebral white matter (WM) undergoes a variety of degenerative changes with normal aging [1,2]. At least in certain brain regions and during certain segments of adult age span such changes seem to be more prominent than cortical changes [3, 4]. Parametric MRI methods provide quantitative markers to study such changes. The magnetization-transfer ratio (MTR) is a sensitive identifier of underlying structural changes in the brain [5]. Besides the MTR, diffusion-tensor imaging (DTI) and proton magnetic resonance spectroscopy (MRS) were used in the current work to elucidate age-related WM changes and their microstructural correlate.

Methods. Whole-head (44 axial slices), high-resolution MT and DT images and single-voxel ^{1}H spectra were acquired in 12 healthy young volunteers (25 ± 5 y) as well as in 10 elderly, neurologically healthy adults (65 ± 5 y). All experiments were performed at 3 T (Siemens Magnetom Trio) using an 8-channel array head coil. MTRs were computed from spoiled gradient-echo sequences (α 30°; *TR* 750 ms; *TE* 10 ms; 0.9×0.9×3.0 mm^2) with and without pulsed off-resonance saturation of the bound water (offset 1950 Hz, bandwidth 375 Hz). Mean water diffusivity (trace) and fractional anisotropy (FA) were obtained with diffusion-weighted spin-echo EPI (*TR* 8100 ms; *TE* 120 ms; 1.7×1.7×3.0 mm^2; 2 acq.) with *b*-factors of 0 and 1000 s/mm^2 (24 directions). A three-dimensional T_1-weighted MPRAGE scan was used for fully automated segmentation. After calculating MTR, trace, and FA maps for each subject, corresponding histograms were distinguished for the WM compartment only (exclusively of microangiopathic lesions in the elderly subjects) and compared among groups. PRESS spectra (*TR* 5 s, *TE* 30 ms, 128 acq.) were recorded from a 3-mL voxel in the fronto-parietal WM. Absolute metabolite concentrations were estimated using LCModel and the unsuppressed water signal as a concentration reference.

Results. The histogram analysis demonstrated significant age-related changes in MTR-, DTI-, and MRS-derived measures (Fig. 1, Tab. 1). Mean values and peak heights of MTR and trace histograms were significantly lower in the elderly population, whereas the FA peak height was significantly higher. Peak widths were not significantly different among groups in all measures. Significant metabolic differences among both groups included reduced NAA and increased Ins and, as a trend below significance, increased tCh in the elderlies.

Figure 1. Group-averaged FA histograms.

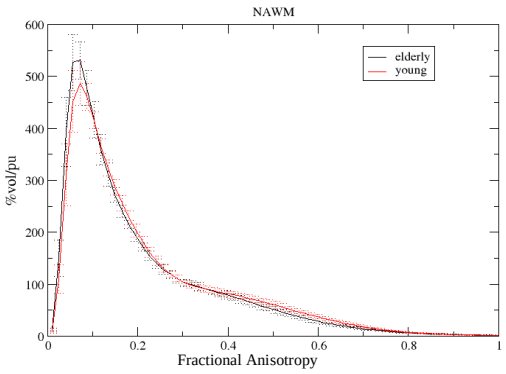

Table 1. WM metabolite concentrations (mmol/L).

Metabolite	Young	Elderly
N-acetylaspartate (NAA)	7.92 ± 0.58	7.20 ± 0.28**
N-acetylaspartylglutamate	1.54 ± 0.71	1.32 ± 0.32
GABA	1.18 ± 0.60	0.94 ± 0.33
Total choline (tCh)	1.67 ± 0.35	1.90 ± 0.27*
Total creatine	5.73 ± 0.56	5.99 ± 0.48
Glutamate	5.75 ± 0.75	5.51 ± 0.76
Glutamine	1.90 ± 0.86	2.15 ± 1.02
Myo-inositol (Ins)	3.49 ± 0.52	4.13 ± 0.58**
Lactate	0.87 ± 0.36	0.91 ± 0.39

* P < 0.1; ** P < 0.005.

Discussion. The different MTR, trace, and FA values in the two age groups suggest microscopic WM changes consistent with an increasing distance between myelinated fibers with advancing age. These results are consistent with earlier studies demonstrating the vulnerability of WM. MTRs have already been shown to be essential in the study of specific disorders of aging. Our results indicate that parameters derived from DTI provide additional important information to improve our understanding of the gross WM microstructural changes in the aging brain. This picture derived from MRI is finally supported by MRS: Decreased NAA indicates age-related axonal damage while increased Ins (and tentatively tCh) might point to subtle cell membrane breakdown or gliosis.

References. [1] Y. Tang et al., *Neurobiol. Aging* 1997; 18: 609-15. [2] L. Bronge, *Acta Radiol. Suppl.* 2002; 428: 1-32. [3] C.R.G. Guttmann et al., *Neurology* 1998; 50: 972-8. [4] D.H. Salat et al., *Arch. Neurol.* 1999; 56: 338-44. [5] Y.L. Ge et al., *Am. J. Neuroradiol.* 2002; 23: 1334-41.