Metabolic Activity in Non-enhancing Lesions and Normal-Appearing White Matter of MS Patients

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Introduction

Relapsing-remitting (RR) MS activity, reflected by Gd-enhancing lesions accumulation, is ~10 times more frequent than clinical relapses (1). While T2 weighted imaging (T2WI) lacks pathological specificity and is insensitive to microscopic disease in the normal appearing white matter (NAWM) (1), other quantitative MR techniques have shown structural and metabolic differences amongst lesions, reflecting various pathological processes (2). Our goal was to study, with 3D ^{1}H-MRS, the metabolic characteristics of non-enhancing T1 hypo- and iso-intense lesions of RR MS patients to investigate whether: *(a)* concentrations are reduced compared to NAWM or normal white matter (NWM); and *(b)* their abnormal metabolic activity persists even without Gd-enhancement.

Methods

Nine patients [median disease duration 6.4 years and expanded disability status scale (EDSS) of 2.5] and 9 matched controls underwent MRI and 3D-^{1}HMRS at 1.5 T. Contiguous axial, sagittal and coronal T1W spin-echo (TE/TR=15/450 ms) and axial T2WI SE (TE_1/TE_2/TR=16/90/2500 ms) were obtained. Then, a 3D ^{1}H-MRS sequence (TE/TR =135/1600 ms) excited an 8 cm left-right (LR) ×10 cm anterior-posterior (AP) ×6 cm inferior-superior (IS) = 480 cm^3 VOI (*cf.* Fig. 1) and partitioned it into $8_{LR}\times10_{AP}\times8_{IS}$ = 640 voxels, 0.75 cm^3 each (3). Classification of T2WI hyperintense lesions was based on average intensity (AI) on the axial T1WI: Two SD or darker than the AI of the surrounding NAWM were defined as hypo-intense, otherwise iso-intense. Absolute NAA, Cr and Cho concentrations were obtained in 171 voxels: 66 in T2WI lesions (43 hypo, 23 1T iso-intense), 31 from NAWM; and 74 from analogous NWM in controls.

Results

NAA levels were significantly lower in hypo- than in iso-intense lesions, NAWM and NWM. Cho levels in iso-intense lesions were indistinguishable from NAWM (Fig. 2). Compared with NWM, NAA was significantly (14%) lower in iso-intense lesions, whereas Cr (24%) and Cho (20%) higher. That pattern (NAA 20% lower, Cr 15% and Cho 17% higher) was repeated on comparing NAWM with NWM.

Discussion

Non-enhancing lesions, now considered quiescent, undergo metabolic activity. Specifically, loss of NAA reflects axonal damage in all MS tissue types. Higher Cr and Cho levels probably indicate gliosis and attempted remyelination, in the iso-intense lesions and increased membrane turnover (*de-* and *re*-myelination) and/or increased cellularity (gliosis, inflammation) in NAWM.

References

1. Milller DH, *et al.* Brain 1998; 121:3-24.
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3. Gonen O, *et al.*Magn Reson Med. 1998; 39:34-40.

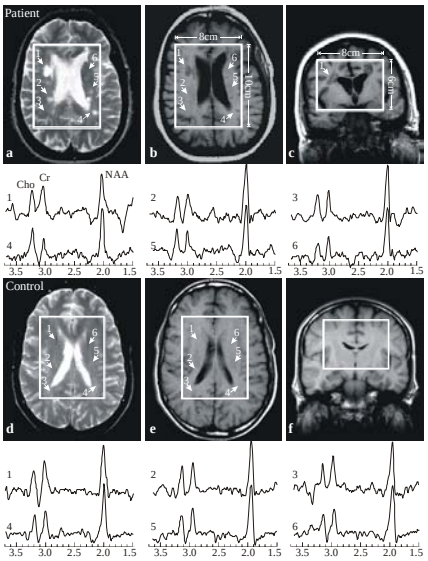

Fig. 1.. Axial T2W (**a**), axial and coronal T1WI (**b**-**c**) of a 26 yo. female MS patient, superimposed with the MRS VOI. Real part of the ^{1}H MR spectra from hypo- (arrows 1 & 4), iso- (arrows 2 & 5) intense lesions and two NAWM regions (arrows 3 & 6) are shown below the images on common intensity and chemical shift (*ppm*) scales.
d - f: Corresponding slices from a female control. Arrows indicate equivalent regions from where metabolite concentrations & Spectra were compared with **a** – **c**.

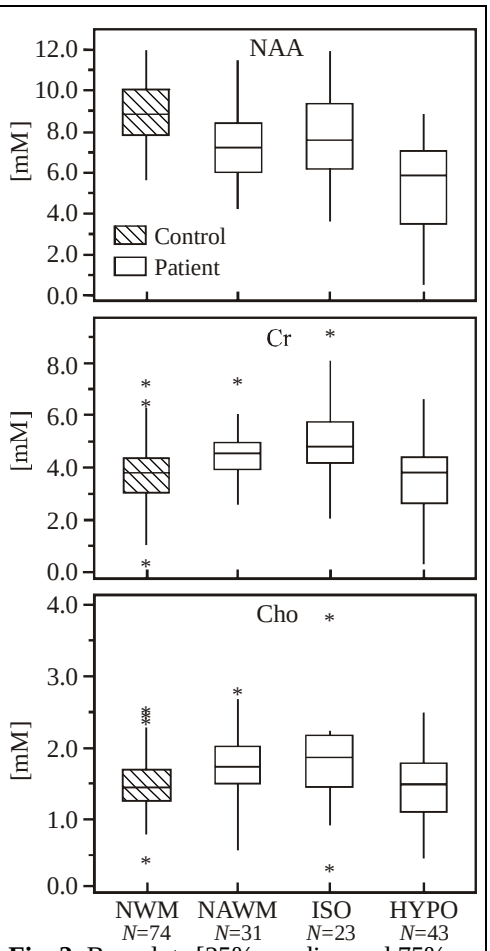

Fig. 2: Box plots [25%, median and 75% (box), ±95% (whiskers) and outliers (∗)] range of the of the metabolites' levels within the 4 tissue types in patients and controls. Note the lower median NAA in hypo-intense lesions and higher Cr and Cho in NAWM and iso-intense lesions.