

Correlating Magnetization Transfer (MT) with Single Voxel Protons (1H) Magnetic Resonance Spectroscopy (MRS) in Multiple Sclerosis (MS)

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Introduction

The pathologic heterogeneity of MS lesions is not well characterized using conventional Magnetic Resonance Imaging (MRI). More specific information can be obtained by other techniques: T1 weighted MRI, Gadolinium-enhanced MRI, diffusion weighted MRI, MTR and MRS. In this study we made use of MTR and MRS to study normal appearing white matter (NAWM) and lesions in MS.

Methods

A total of 31 MS patients with EDSS score ranging from 1 to 8.5 (mean=4.0) and a mean age of 37 years old (18-69 years) were examined using a 1.5 T Signa Horizon equipment (GE, Medical Systems). The MRI examination included axial 5mm thick proton density weighted (TE=30ms and TR=2500ms) spin-echo images with and without application of an off-resonance (offset=1600 Hz) saturation prepulse. The Point Resolved Spectroscopy (PRESS) technique was chosen to obtain spectra with two different echo times TE=30 and 135 ms and a repetition time (TR) of 2s. The number of scans (NS) was varied from 96 to 160 depending on voxel size and 8 step phase cycling was used. The MRS voxel was placed either in a region involving MS lesions or Normal Appearing White Matter (NAWM). The size of the voxel was varied from 3 to 8 cm³, depending on the size and location of the lesion.

Spectroscopy raw data were transferred to a workstation (Sun, Mountain View, Calif) and processed using a software package provided by the manufacturer (SAGE, GE, Medical Systems). The free induction decays (FIDs) were apodized with a line broadening of 3Hz, zero filled to 4096 points, Fourier transformed, and an automatic zero-order phase correction was applied. The resulting spectra were fitted to a sum of Lorentzian lines in the range from 1.8 to 4.5 ppm using a Marquardt-fit. For quantification of the metabolites: N-Acetylaspartate (NAA), Choline (Cho) and myo-Inositol (mI), relative to Creatine (Cr), we considered only peak intensities, given the difficulty to determine the real linewidth of strong overlapping peaks. NAA/Cr and Cho/Cr were measured from the spectrum with TE=135ms and mI/Cr from short echo time spectrum.

The MTR is defined as (M0-MT)/M0, where MT and M0 are the respective intensities read from the images obtained with and without application of the saturating prepulse. Knowing the size and location of the MRS voxel the MTR was then calculated by placing a region of interest (ROI) of the same dimensions in the respective axial images and determining M0 and MT. Depending on the height of the voxel the MTR had to be calculated by averaging the MTR measured from 1 to 3 slices.

Correlation between spectroscopy and MTR data was evaluated by applying the Pearson correlation test.

Results

Comparing to NAWM we found in lesions lower mean values for NAA/Cr and higher mean values for Cho/Cr and mI/Cr. The mean MTR found in lesions was also lower than in NAWM. By comparing the spectroscopy data with the MTR values we found a positive correlation for NAA/Cr and MTR ($r=0.5203$, $p<0.001$) and a negative correlation for mI/Cr and MTR ($r=-0.4837$, $p=0.002$). No correlation was found between Cho/Cr and MTR.

Discussion

In this study we combined MTR and MRS techniques to study lesions and NAWM in MS patients. We correlated the findings of both techniques, in order to understand better the MRS results.

MTR values observed in NAWM voxels ranged from 24.0 to 31.7. As the MTR was calculated for the entire MRS voxel this large variation of MTR could be due to different amounts of contamination of the NAWM MRS voxel with surrounding grey matter or CSF. It was particularly difficult to place the MRS voxel exclusively on NAWM in patients presenting advanced stage of atrophy. It has also been shown [1] that NAWM in MS patients is lower than in healthy controls white matter, which was considered an indication of microscopic alterations

in MS. Small decreases of MTR can be already caused by edema, but larger decreases are associated with demyelination and axonal loss [1]. Given the heterogeneity of MS lesions we expected the MTR variation in the lesions group to be large, as it was found (20.2-29.7%). Actually the lesions themselves presented lower MTR values (9-25%), but due to partial volume effects in the MRS voxel, the lesion values were averaged with MTR of surrounding tissue.

NAA is considered a neuronal marker [2]. Hence its decrease in MS lesions is to be understood as neuronal damage. Previous studies trying to correlate MTR data to NAA/Cr have produced conflicting results [3-5]. Our results confirm the positive correlation between NAA/Cr and MTR, both reflecting demyelination and axonal loss. In addition we found a significant negative correlation between mI/Cr and MTR. mI increase has been explained as a consequence of gliosis, and in some cases has been related to myelin breakdown products [2]. Therefore the increase observed in mI/Cr with MTR decrease can be related to myelin degradation followed by gliosis. The absence of correlation between Cho/Cr and MTR, indicates that Cho/Cr changes observed in MS lesions might be better related to reversible alterations, such as inflammation.

References

- [1] V. Dousset, R. I. Grossman, K. N. Ramer, et al., Experimental allergic encephalomyelitis and multiple sclerosis: lesion characterization with magnetization transfer imaging. *Radiology* 182, 483-491 (1992).
- [2] B. D. Ross, A Biochemistry Primer for Neuroradiologists. ASNR-Advanced Imaging Symposium 13-27 (2000).
- [3] H. Kimura, R. I. Grossman, R. E. Lenkinski, F. Gonzalez-Scarano, Proton MR spectroscopy and magnetization transfer ratio in multiple sclerosis: correlative findings of active versus irreversible plaque disease. *AJNR Am J Neuroradiol* 17, 1539-1547 (1996).
- [4] J. F. Hiehle, R. E. Lenkinski, R. I. Grossman, et al. Correlation of spectroscopy and magnetization transfer imaging in the evaluation of demyelinating lesions and normal appearing white matter in multiple sclerosis. *Magn Reson Med* 32, 285-293 (1994).
- [5] G. B. Pike, N. Stefano, S. Narayanan, et al. Combined magnetization transfer and proton spectroscopic imaging in the assessment of pathologic brain lesions in multiple sclerosis. *AJNR Am J Neuroradiol* 20, 829-837 (1999).