1H-MRS AND WATER PROTON T1 INVESTIGATIONS OF NEW LESIONS IN RELAPSE REMITTING MULTIPLE SCLEROSIS

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Introduction

Multiple Sclerosis (MS) is an autoimmune disease in which the central nervous system is attacked, leading to areas of demyelination and axonal loss in the brain and spinal cord, often seen as lesions on MR images. Relapse-remitting MS (RRMS) is the most common subtype of MS, characterized by attacks interspersed between remittance periods during which symptoms completely or partially disappear [1]. Currently, relapses are unpredictable and the mechanism behind the formation of new lesions is not well understood. Proton Magnetic Resonance Spectroscopy (^{1}H-MRS) allows quantification of brain metabolites and changes are observed in some metabolites in RRMS [2]. We used ^{1}H-MRS along with water proton T_1 measurements to investigate the time-course of chemical changes in new lesions.

Materials and Methods

Subjects Twenty subjects with RRMS (15F/5M; median EDSS = 2.5; mean age = 40yrs; mean disease duration = 8.5yrs) were volunteers for this study. Each subject had a corresponding age and gender matched control.

MR Examinations MRI and ^{1}H-MRS examinations were performed on a Philips 3T Achieva MR Scanner. T_1 images were obtained from an inversion recovery prepared sequence (5 T_1's from 150 to 3000ms, TR/TE = 6.4/3.1ms, matrix size = 256x256). The multi-voxel ^{1}H-MRS experiment consisted of a PRESS sequence (TR/TE =1000/35ms, 5 slices, 132 voxels per slice, voxel size = 10 x 10 x 5mm). The MS subjects were scanned at month 0, 1, 2, 3, 4, 5, 6. The controls were scanned at month 0 and month 6.

Analysis Analysis of ^{1}H-MRS data was performed using LCModel [3]. Water-scaling was used, referencing the metabolite signal to the water signal for n-acetyl-aspartate (NAA and NAAG), Creatine (Cre), and Choline (GPC and PCh). Regions of interest (ROI) were selected on the TI=750ms image from the T_1 experiment to correspond to the placements of the voxels from the ^{1}H-MRS study, and the mean water proton T_1 was calculated for each ROI. Metabolite and water proton T_1 values for lesion, NAWM and NWM were compared using the student-t test.

Results

Out of the 20 RRMS subjects, 6 had one or more new lesions appear enhancing on a T_1 weighted image at some point during the the study that were also in the volume covered by the ^{1}H-MRS examination. In total there were 37 voxels in which a lesion appeared at some time during study. Values for the absolute concentrations of NAA, Cre and Cho in these voxels were shifted relative to the time of first appearance of the lesion and averaged, with month 0 (Fig. 1-3) corresponding to the month when the lesion first appeared and similarly for water proton T_1 values (Fig. 4). Also shown are the mean metabolite concentrations and mean water proton T_1 values from 145 voxels of normal appearing white matter (NAWM) in RRMS subjects and from 325 voxels of normal white matter (NWM) in controls. Figure 1 shows a difference between NAA in lesion and NAWM. The NAA concentration in lesion is significantly different ($p < 0.03$) from the mean NAA for voxels of NAWM beginning at month -2. Creatine (Fig. 2) appears to be relatively constant and similar in lesion and NAWM. Choline (Fig. 3) in lesion is significantly different ($p < 0.02$) from NAWM in months -5, -4 and -3, after which the differences are not significant. For mean T_1 (Fig. 4) there is a significant difference ($p < 0.045$) seen between mean water proton T_1 in lesion and the mean for NAWM at all time points.

Discussion

All MR measures from NAWM and NWM were stable over time, indicating the robustness of the data. The similarity between NAWM and NWM, seen in Fig. 1-4, is in agreement with Tourbach *et al*. [4] and is possibly a reflection of the MS subject's relatively low disability and relapsing-remitting condition. The decrease in NAA concentration at the appearance of the lesion is expected [4]. The significant changes differences seen between Choline in lesion and NAWM may be due to noise. The means for months -5, -4 and -3 have n = 3, 4, and 7 respectively, much fewer than other time points. The elevated water proton T_1 is also expected [5]. However, this is the first time it has been seen prior to the lesion being visible on conventional imaging and this, along with the significant changes in NAA starting 2 months before, could potentially indicate changes in white matter before first appearance.

Figure 1 N-Acetyl-Aspartate

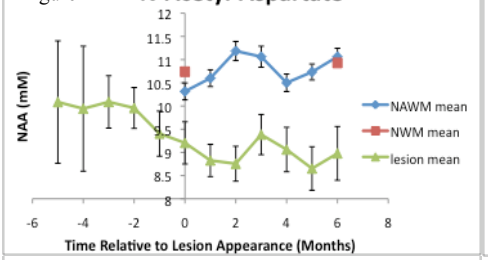


Figure 2 Creatine

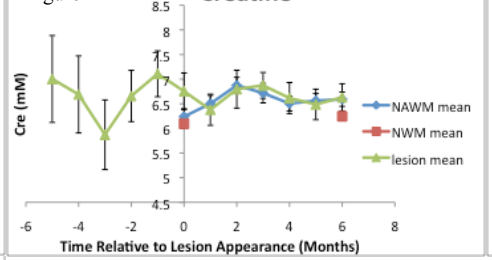


Figure 3 Choline

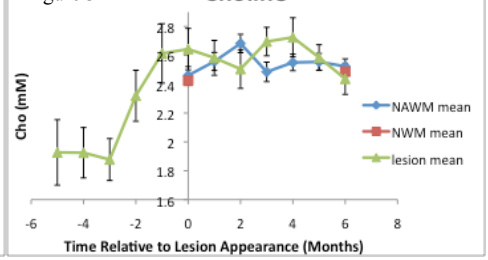
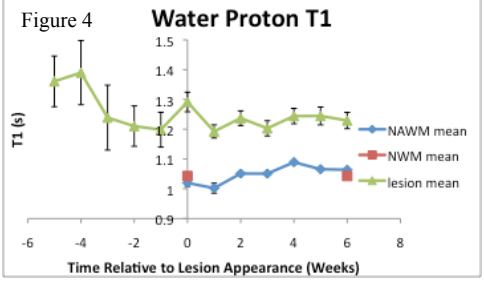


Figure 4 Water Proton T1



Average absolute concentration of metabolites (Figures 1-3) and water proton T_1 values (Fig. 4) for the same volume in NAWM, NWM and Lesion shifted relative to first appearance of lesion. Month 0 corresponds to the first appearance of enhancing lesion on a T_2 weighted image. Error-bars are standard error.

References

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