Serial proton MR spectroscopy of gray and white matter in relapsing-remitting multiple sclerosis
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TARGET AUDIENCE: Neurologists, multiple sclerosis researchers

PURPOSE: To characterize and follow the global gray and white matter (GM/WM) metabolism in early relapsing-remitting multiple sclerosis (RR MS) using proton magnetic resonance spectroscopic imaging (1H-MRSI).

PATIENTS AND METHODS: 29 patients (20 women) with clinically definite RR MS1 for less than 6 years, were recruited prospectively to be scanned semi-annually for 3 years (7 scans each). 10 age- and gender-matched (8 women) healthy volunteers were to be scanned annually (4 scans each). Post-hoc exclusion criterion was <5 scans for patients and <4 for controls.

Measurements were done at 3 T. MP-RAGE images were acquired for 1H-MRSI volume-of-interest (VOI) guidance and for tissue segmentation. Axial T2-weighted FLAIR images were acquired for lesion volumetry. The 10×8×4.5=360 cm3 1H-MRSI VOI (solid white lines) and field-of-view (dashed lines). The location of B is indicated on A by an arrowhead. CSI=chemical shift imaging.

RESULTS: 18 patients (13 women) and all controls met the enrollment criteria.

Cross-sectional: The average (over all time points) patients’ WM Cr, Cho and ml concentrations were higher than the controls’ (all p<0.01). Patients’ values were higher at all time points, by a range of 8-16% for Cr, 4-13% for Cho, and 7-17% for ml. In GM, there were no differences in average concentration values over all time points, but there were differences at single time points in 3 metabolites (Fig. 2, left panel). The patients’ average VOI T2 lesion load was 3.9±6.1 cm3 (median; 2.1 cm3).

Longitudinal: There were significant intra-cohort rates of change only for patients: (i) increasing WM Cr, Cho and NAA, decreasing GM Cho and ml (all p≤0.05); and (ii) increasing CSF and lesion volume and decreasing WMl (all p≤0.01). There were no significantly different inter-cohort (patients’ versus controls’) rates of change, but there was a trend for different CSFl rates (p=0.06). Finally, the rates of change in GM or WM metabolite levels did not correlate with the rates of change in CSFl, GMl, WMl, lesion volume, EDSS or relapses, with no trends observed.

DISCUSSION AND CONCLUSION: To our knowledge, the data here represents the most frequent 1H-MRS MS follow-up for the longest duration. In contrast to previous serial 1H-MRS, this study: (i) assessed metabolism of a large brain volume; (ii) accounted for partial volume effects; and (iii) investigated diffuse involvement. We found that WM glial abnormalities were larger in magnitude than the axonal and increased over time independently of conventional clinical or imaging metrics and despite treatment. In contrast, the axonal abnormalities showed partial recovery, suggesting that patients’ lower WM NAA levels represented a dysfunction, which may abate with treatment. Absence of widespread diffuse changes in GM suggests that injury there is minimal, focal, or heterogeneous between cortex and deep GM nuclei.

REFERENCES: