Brain Metabolism in Primary Progressive Multiple Sclerosis:A Three-Dimensional Proton MR Spectroscopy Study at 3T

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Background: A minority of MS patients (10-15%) are diagnosed with PPMS, a subtype in which the disability progresses from disease onset and the pathology has been found to involve more axonal degeneration and less inflammation than the more common relapsing-remitting (RR) MS (1). MRI markers of disease progression that are useful in RRMS cannot be used to monitor PPMS because of the slower rate of new lesion formation, lower lesion burden, and diminished enhancement of lesions; thus, new disease markers are needed. ^{1}H-MRS has been used to characterize MS pathology and may provide such markers (2). Our goal was to use 3D ^{1}H-MRS to determine the absolute concentrations of metabolites in the normal-appearing white matter of PPMS in order to investigate metabolic abnormalities and define possible surrogate markers of disease.

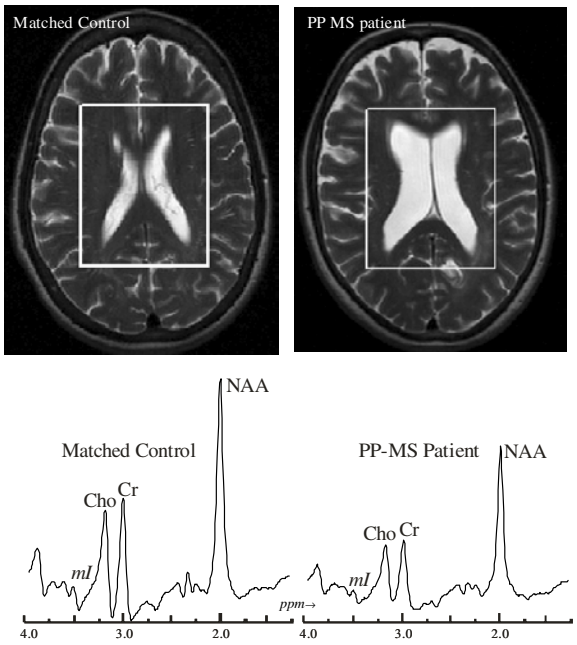

Fig.1. Axial T2W MRI of a 53 yo female PPMS patient (*left*) and a 54 yo female control (*right*), with the $8_{LR}\times10_{AP}\times3_{IS}$ = 240 cm^3 MRS VOI superimposed (white outline), with corresponding summed spectra below. Decreased NAA, Cho, and Cr peaks are visible.

Methods: Eight patients (median disease duration of 3 years and median expanded disability status scale (EDSS) of 4) and 8 age-matched controls underwent MRI and 3D-^{1}HMRS at 3 T. MPRAGE T1W (TR/TE, 2000/2.6) and dual echo images (TR, 5500; TE, 12/99) were obtained. Then, a 3D ^{1}H-MRS sequence (TE/TR =44/1600 ms) excited an image-guided 8 cm left-right (LR) × 10 cm anterior-posterior (AP) × 3 cm inferior-superior (IS) = 240 cm^3 VOI and partitioned it into $16_{LR}\times16_{AP}\times4_{IS}$ = 1024 voxels, $1.0_{LR}\times 1.0_{AP}\times 0.75_{IS}$ cm^3 each. Absolute NAA, Cr, Cho, and Myo concentrations were obtained by summing all voxels in each VOI, dividing by the VOI tissue volume obtained from MRI segmentation, and comparing the signal to that of a phantom of 11.0 mM NAA in water. A Mann-Whitney test was used for statistical comparisons between patients and controls.

Results: NAA levels were significantly lower (16.9%) in patients than in controls (p = 0.027). Cho and Cr levels were each lower than controls (12.5% and 12%, respectively) but did not reach statistical significance. No statistically significant difference in *mI* levels was found

Conclusion: Significantly decreased levels of NAA found in NAWM of PPMS patients reflect the axonal degeneration found to a greater extent in PPMS pathology than in other types of MS. Slightly decreased Cho and Cr levels, in contrast to the elevated levels found in RRMS (3), and unchanged *mI* levels, may be due to the lesser extent of inflammation and the lack of remyelination in PPMS; however, these findings are inconsistent with previous findings of increased gliosis in PPMS(4). 3D ^{1}H-MRS provides a promising surrogate marker for detecting and monitoring axonal degeneration in MS.

References

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	Control	PPMS
NAA (mmol)	9.80 ± 1.20	8.15 ± 2.23
Cr (mmol)	5.60 ± 0.67	4.91 ± 1.27
Cho (mmol)	1.50 ± 0.16	1.32 ± 0.34
mI (mmol)	4.20 ± 0.59	4.24 ± 1.44

Table 1: Mean ± SD metabolite concentrations from patients and controls