

MRS shows glial increase but no neuro-axonal damage in MS NAWM

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Introduction

For several (semi)quantitative MR parameters, differences have been reported between the normal-appearing white matter (NAWM) in Multiple Sclerosis (MS) and healthy control white matter (WM). A decreased tNAA/tCr ratio has been measured using MRS, but studies on absolute concentrations have reported conflicting results, some showing decreased tNAA in MS NAWM, suggesting neuro-axonal damage [e.g., 1,2], while unchanged tNAA has also been observed [3,4].

Mean \pm SD Number of subjects / VOIs	PP 12 / 21	RR 40 / 74	SP 16 / 32	Combined MS group 68 / 127	Controls 24 / 45
SNR	8.2 \pm 1.5	8.5 \pm 1.5	8.4 \pm 1.8	8.4 \pm 1.6	8.4 \pm 1.6
FWHM (Hz)	3.2 \pm 0.3	3.3 \pm 0.5	3.3 \pm 0.4	3.3 \pm 0.4	3.2 \pm 0.5
Error estimate of tNAA (%)	4.4 \pm 0.7	4.2 \pm 0.6	4.3 \pm 0.7	4.2 \pm 0.6	4.2 \pm 0.7
VOI free water content (%)	3.8 \pm 4.2	4.6 \pm 4.4	3.3 \pm 2.4	4.1 \pm 4.0	3.3 \pm 4.1
tNAA	8.1 \pm 1.2	8.5 \pm 1.0	8.3 \pm 1.0	8.4 \pm 1.0	8.0 \pm 1.1
NAA	5.0 \pm 0.9	5.2 \pm 0.7	4.9 \pm 0.7	5.2 \pm 0.7	5.2 \pm 0.7
NAAG	3.0 \pm 0.7	3.3 \pm 0.7*	3.3 \pm 0.7*	3.3 \pm 0.7*	2.8 \pm 0.8
tCr	4.9 \pm 0.7*	5.1 \pm 0.6 *	5.2 \pm 0.8 *	5.1 \pm 0.7 *	4.4 \pm 0.7
Cho	1.44 \pm 0.23	1.46 \pm 0.20	1.51 \pm 0.19 *	1.47 \pm 0.20 *	1.37 \pm 0.20
Ins	4.1 \pm 0.9 *	4.3 \pm 0.9 *	4.7 \pm 1.4 *	4.4 \pm 1.1 *	3.3 \pm 0.6
tNAA/tCr	1.67 \pm 0.28 *	1.67 \pm 0.21 *	1.61 \pm 0.23 *	1.66 \pm 0.23 *	1.87 \pm 0.23

Table Absolute concentrations in mM. *: significant difference with controls.

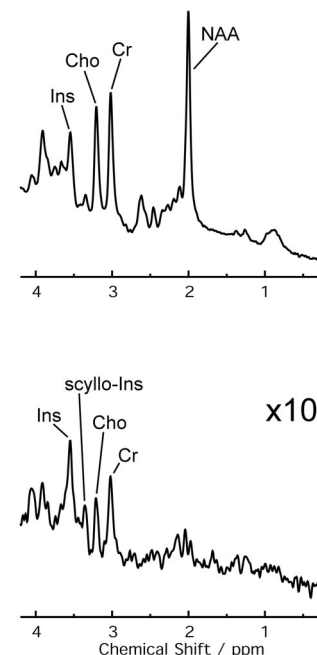


Figure Average MS spectrum (top) and subtraction spectrum showing difference with controls (bottom).

Methods

Quantitative single voxel STEAM (TR 6000/TE 20) at 1.5 T (Siemens Vision) was used to determine metabolite concentrations bilaterally in cerebral NAWM of 68 MS patients and in WM of 24 controls, avoiding lesions, grey matter and cerebrospinal fluid when positioning the 6.4 ml VOIs. Concentrations were quantified using LCModel [5] and compared between MS disease types (primary progressive [PP], relapsing-remitting [RR] and secondary progressive [SP]) and with controls, using analysis-of-variance.

Results and discussion

The reliability of the results is demonstrated by measures of spectral quality (SNR, FWHM and error estimate, see Table), which are the same for patients and controls. The concentration ratio tNAA/tCr was decreased in NAWM of all MS disease types compared to control WM. Remarkably, this decrease was entirely due to an increase of tCr in MS patients, which can also be recognized in the subtraction spectrum, see Figure. Together with a strong increase of myo-inositol (Ins), this suggests increased glial cell numbers. There was also a small increase of Cho. There was no difference in tNAA concentration between MS patients and controls. Of the two tNAA components, NAAG showed a small -but significant- elevation in MS patients, while the purely neuro-axonal NAA was unchanged. We conclude that there is no evidence for neuro-axonal damage in MS NAWM from this data. There were no differences between disease types, and there was no correlation with expanded disability status scale (EDSS) scores. Further studies should elucidate the mechanism underlying increased NAAG in MS NAWM.

References

1. Chard DT *et al.*, Brain 2002; 125: 2342-52.
2. Sarchielli P *et al.*, Brain 1999; 122: 513-21.
3. Helms G *et al.*, Magn Reson Med 2000; 43: 102-10.
4. Schubert F. *et al.*, MAGMA 2002; 14: 213-22.
5. Provencher SW, Magn Reson Med 1993; 30: 672-9.