Energy dysregulation is considered a key contributing factor to neuro-axonal loss in MS. Diffusion-weighted spectroscopy (DWS) measures in-vivo the diffusion properties of endogenous intracellular metabolites, including N-acetylaspartate (tNAA), a marker of neuro-axonal integrity, and Creatine-Phosphocreatine (tCr), which reflects the energy metabolism status in neuronal and glial cells. We employed DWS to explore the neuro-axonal damage and the ongoing energy dysregulation in the brain of patients with MS, and to investigate the clinical relevance of these processes.

Methods

- Twenty-five patients with MS (17 relapsing-remitting MS, 15 women, mean age=45.8 yrs±13) were scored on the Expanded Disability Status Scale (EDSS). All patients and a group of 18 age- and gender-matched healthy controls (HC) underwent a 3T MRI protocol, which included a cardiac-gated PRESS sequence equipped with diffusion gradients.
- Concentration and apparent diffusion coefficient (ADC) of tNAA and tCr were extracted from voxels localised in the normal-appearing white matter (NAWM) of the corona radiata and in the grey matter (GM) of the thalami (Figure 1).
- DWS-derived metrics were compared between patients and HC, and correlated with clinical scores in patients only, with multiple linear regressions, adjusted for age and gender (and normalized thalamic volumes, NTV, for GM-derived values).

Results

- There was a significant decrease in tNAA concentration in patients compared with controls (p=0.001).
- There was a significant decrease in tCr concentration in patients compared with controls (p=0.003 and p=0.01, respectively).
- Patients showed a significant decrease in ADC (tNAA) (p=0.016) and ADC (tCr) (p=0.02), which survived after adjustment for NTV (p=0.04).
- The mean GM ADC(tNAA) and ADC(tCr) inversely correlated with EDSS (p=0.03, B=-.46 and p=0.04, B=-.48, respectively) and TWT scores (ADC(tNAA): p=0.001, B=-0.68; ADC(tCr): p=0.009, B=-0.59)

CONCLUSIONS

- A reduced tCr diffusivity was found in the brain of patients with MS, which may reflect an ongoing energy dysregulation affecting neurons and/or glial cells in this disease.
- Two hypotheses may be proposed to explain this decrease in tCr diffusivity in MS: (i) an abnormal reduction of intercellular creatine transport; and/or (ii) an impaired function of the creatine kinase B, resulting in a pathological increase in the phosphocreatine/creatine ratio.
- DWS allows to capture the functional and potentially reversible mismatch between energy demand and supply that affects neurons in conditions of increased energy demand in MS, before the occurrence of neuro-axonal degeneration.