Investigation of the evolution of focal lesions and microscopic tissue changes in multiple sclerosis: sodium (^{23}Na) MRI studies

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Background: Conventional magnetic resonance imaging (MRI) is currently the most applied biomarker in multiple sclerosis (MS). For a long time it has been one aim to increase its sensitivity and specificity in order to improve the understanding of the pathophysiology in MS both in the development of focal lesions and the estimation of microscopic tissue damage. Recent studies using sodium (^{23}Na) imaging suggested that increased total sodium concentrations (TSC) are a sensitive measure and may reflect neuroaxonal damage.

Objective: To detect and quantify different degrees of disease-related tissue changes i) in the evolution of focal lesions ii) the microstructure outside macroscopically visible lesions using a multiparametric MRI protocol.

Methods: We performed ^{23}Na, ^{1}H and diffusion MRI in 14 healthy controls (HC), 18 patients with a clinically isolated syndrome (CIS), 47 patients with early relapsing-remitting multiple sclerosis (RRMS, < 5 years disease duration), 20 patients with advanced RRMS and 10 patients with secondary progressive multiple sclerosis (SPMS). We also investigated patients with new acute lesions serially.

Results: Normal appearing grey and white matter (GM, WM) TSC were significantly higher in advanced RRMS (GM: 46.7 ± 3.1 mM, WM: 40.5 ± 2.7 mM) and SPMS (GM: 52.5 ± 5.4, WM: 46.2 ± 5.0) vs. HC (GM: 40.1 ± 3.3, WM: 34.9 ± 2.4), CIS (GM: 41.5 ± 2.7, WM: 35.6 ± 2.2) and early RRMS (GM: 43.8 ± 2.5, WM: 38.1 ± 2.6). Total brain volume (TBV) and grey matter volume (GMV) and white matter (WMV) was significantly lower in advanced RRMS (TBV: 1396 ± 68 ml; GMV: 706 ± 44 ml; WMV: 690 ± 34 ml) and SPMS (TBV: 1352 ± 69; GMV: 684 ± 38; WMV: 668 ± 37) vs. HC (TBV: 1477 ± 52; GMV: 744 ± 28; WMV: 732 ± 37), CIS (TBV: 1472 ± 67, GMV: 748 ± 41; WMV: 724 ± 34) and early RRMS (TBV: 1454 ± 56; GMV: 748 ± 35; WMV: 706 ± 33). Apparent diffusion coefficients of the NAWM were significantly higher in SPMS (0.79 ± 0.07 x 10^{-3} mm/s^2) vs. HC (0.66 ± 0.04), CIS (0.71 ± 0.04) and early RRMS (0.72 ± 0.06, $p < 0.05$). Strong correlations between MRI parameters and EDSS were observed for TBV and TSC of the NAGM and NAWM.

Conclusion:

Sodium MRI is highly sensitive to pathological tissue changes in MS detecting increased sodium in focal lesions and in the NAWM and NAGM. *Focal lesions:* The highest sodium signal was seen Gd-enhancing lesions and also near normal sodium signal can be seen in very early lesions with a reduced ADC. *NAWM and NAGM:* Sodium increase, loss of TBV, GMV, WMV and increased diffusion were already present in patients with CIS and progress in later stages of MS and SPMS. The loss of TBV, GMV, WMV and increase of TSC in NAGM and NAWM showed strong correlation with EDSS suggesting that these parameters are highly sensitive to irreversible tissue damage.

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