The association between retinal nerve fibre layer thickness and N-acetyl aspartate levels in multiple sclerosis brain normal-appearing white matter: a longitudinal study using magnetic resonance spectroscopy and optical coherence tomography


BACKGROUND AND PURPOSE
N-acetyl aspartate (NAA) assessed using proton magnetic resonance spectroscopy ((1)H MRS) has a high pathological specificity for axonal density. Retinal nerve fibre layer thickness (RNFLT) measured by using optical coherence tomography is increasingly used as a surrogate marker of neurodegeneration in multiple sclerosis (MS). Our aim was to investigate the relation between RNFLT and NAA/creatine in brain normal-appearing white matter (NAWM), their dynamics over time and the association with clinical outcome measures in relapsing MS. T2 WM lesions served as control tissue.

METHODS
Forty-three MS patients underwent standardized neurological examination including the Expanded Disability Status Scale (EDSS), Multiple Sclerosis Functional Composite (MSFC) score, optical coherence tomography and magnetic resonance imaging including (1)H MRS at baseline and after 1 year.

RESULTS
At baseline, NAA/creatine level was lower in T2 WM lesions than in NAWM (1.64 ± 0.16 vs. 1.88 ± 0.24, P < 0.001). Lowest levels were found in secondary progressive MS (SPMS). Mean RNFLT was higher in clinically isolated syndrome than in the combined group of relapsing-remitting MS and SPMS (99.8 ± 12.3 μm vs. 92.4 ± 12.8 μm, P = 0.038). In all patients, mean RNFLT decreased by 1.4% during follow-up. At baseline, MSFC z-scores correlated with NAA/creatine levels both in NAWM (r = 0.42; P = 0.008) and T2 WM lesions (r = 0.52, P = 0.004). NAWM NAA/creatine variation correlated with the RNFLT change over 1 year (ρ = 0.43, P = 0.046).

CONCLUSIONS
N-acetyl aspartate/creatine level reduction correlated with RNFLT thinning over 1 year in an EDSS stable MS cohort suggesting that these techniques might be
sensitive to detect subclinical disease progression.

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