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Abstract Title: Serum-Neurofilament light chain levels in secondary progressive multiple sclerosis are associated with grey matter destruction characterized by relaxation rates

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Introduction:
In multiple sclerosis (MS) patients the association of serum Neurofilament light chain (sNfl) values with grey matter (GM) pathology, namely atrophy, is well known. However, the underlying mechanisms leading to GM changes in different MS disease courses have not been established. Quantitative magnetic resonance imaging (MRI) parameters like relaxation rates provide biophysical measures of the microstructural tissue changes.

Objectives/Aims:
To analyze the association of relaxation rates of GM with sNfl in secondary progressive (SPMS) and relapsing (RMS) MS.

Methods:
RMS(n=20), SPMS(n=27) patients and Control subjects (CS, n=24) received quantitative synthetic MRI using a multiecho acquisition of saturation recovery pulse sequence on a 1.5 Tesla scanner to quantify relaxation rates (R1 and R2) and for GM segmentation. In patients, sNfl measurement using the Simoa HD-X analyzer by Quanterix was performed.

Results:
sNfl in RMS (mean=33.1 pg/ml ±24.3) and SPMS (mean=32.5 pg/ml ±29.3) showed no significant group difference. GM fraction (%of intracranial volume) was significantly ($p<0.001$) lower in RMS(mean=45.9±2.5) and SPMS(mean=45.2±3.9) compared to CS(mean=50.2±2.0). R1 and R2 in GM(sec^{-1}) were significantly ($p<0.001$) decreased in RMS(R1 mean=0.77±0.03/ R2 mean=10.3±0.3) and SPMS(R1 mean=0.78±0.02/ R2 mean=10.3±0.3) compared to HC(R1 mean=0.8±0.02/ R2 mean=10.7±0.2). In SPMS, sNfl correlated with R1($r=-0.46, p<0.016$) and R2($r=-0.43, p<0.025$) in GM, but not in RMS.

Conclusion:
While the extent of GM atrophy and reduction of GM relaxation rates were equally pronounced in both SPMS and RMS, no significant difference was found between SPMS and RMS with respect to sNfl. The exclusive association of sNfl with R1 and R2 in GM in SPMS implies that GM damage in SPMS corresponds to axonal degeneration, whereas in RMS several factors coming together may influence GM pathology. This suggests that the sNfL levels in RMS and SPMS are based on different forms of tissue affection and therefore have to be evaluated in the context of disease course.

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