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[1]. 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 times/rates, provide biophysical measures of the microstructural tissue changes[2]. T1 relaxation is affected by axonal degeneration, such that the relaxation time increases and the relaxation rate ($R1=T1^{-1}$) decreases with disease progression and correlates with brain atrophy[3].

Objectives and 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[4]. In patients, sNfl measurement using the Simoa HD-X analyzer by Quanterix was performed. Group comparisons of brain measures and Nfl were performed by using univariate ANOVA in SPSS.

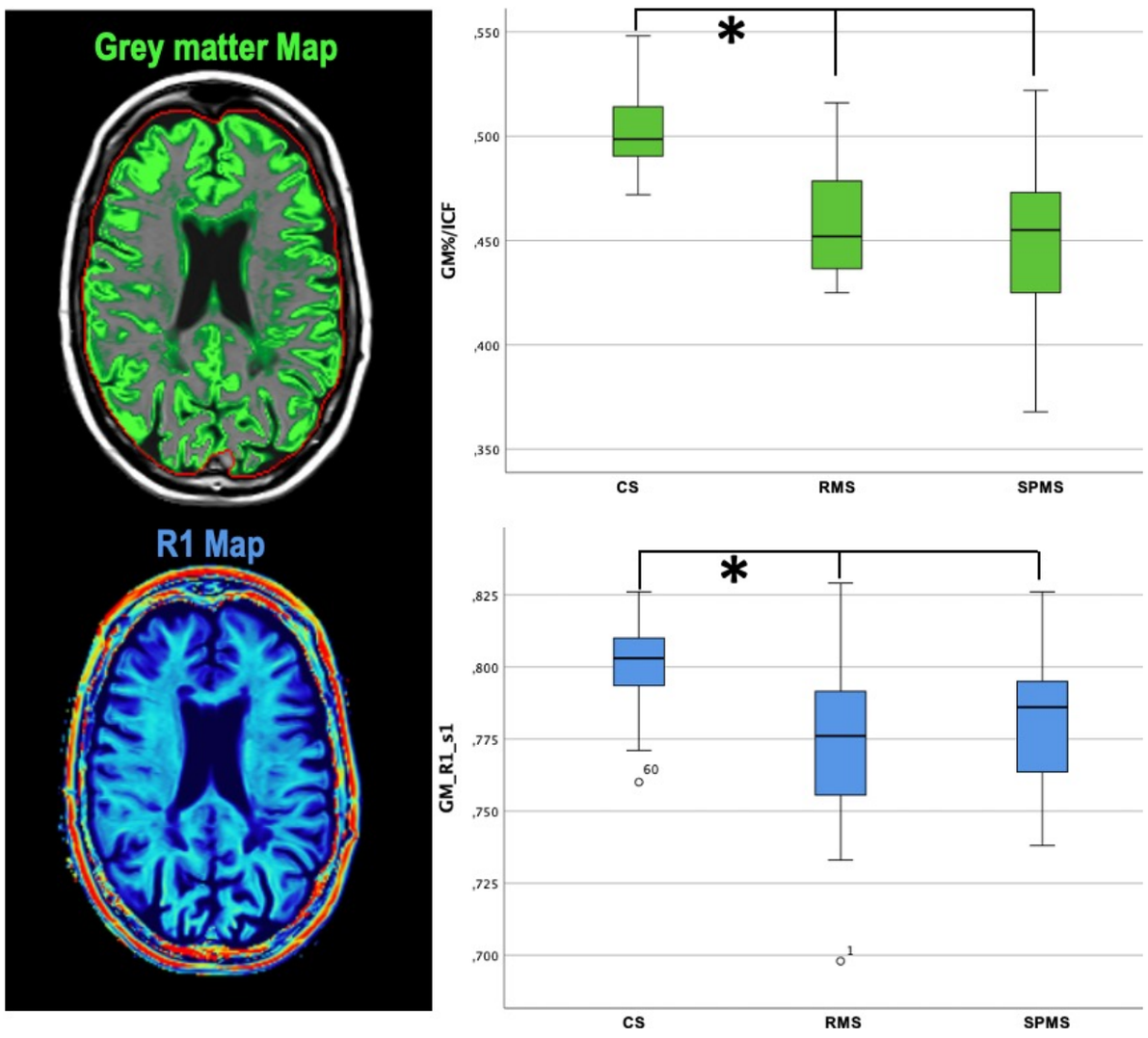

Figure 1. Boxplots depicting median proportion of GM%/ICV and GM-R1 in CS, RMS and SPMS patients. To the left of it, exemplary GM map and corresponding quantitative R1 map of a MS patient.

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 CS(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.

Table 1. Demographics and ANOVA-based group comparisons with *significant differences with a $p<0.05$ compared to CS.

	CS	RRMS	SPMS
N (%female)	24 (19)	20 (14)	27 (14)
Age (years, mean, +/-SD)	45.7 (7.69)	42.0 (13.1)	54.0 (10.2)*
Disease duration (years, mean, +/-SD)	-	12 (8.7)	22.2 (8.4) *
sNfl (pg/ml, SD)	-	33.1 (24.3)	32.5 (29.3)
GM (% ICV, mean, +/-SD)	50.2 (0.02)	45.9 (0.03) *	45.2 (0.04) *
GM R1 mean (sec^{-1}) +/- SD	0.80 (0.02)	0.77 (0.03) *	0.78 (0.02) *
GM R2 mean (sec^{-1}) +/- SD	10.7 (0.13)	10.3 (0.3) *	10.3 (0.3) *

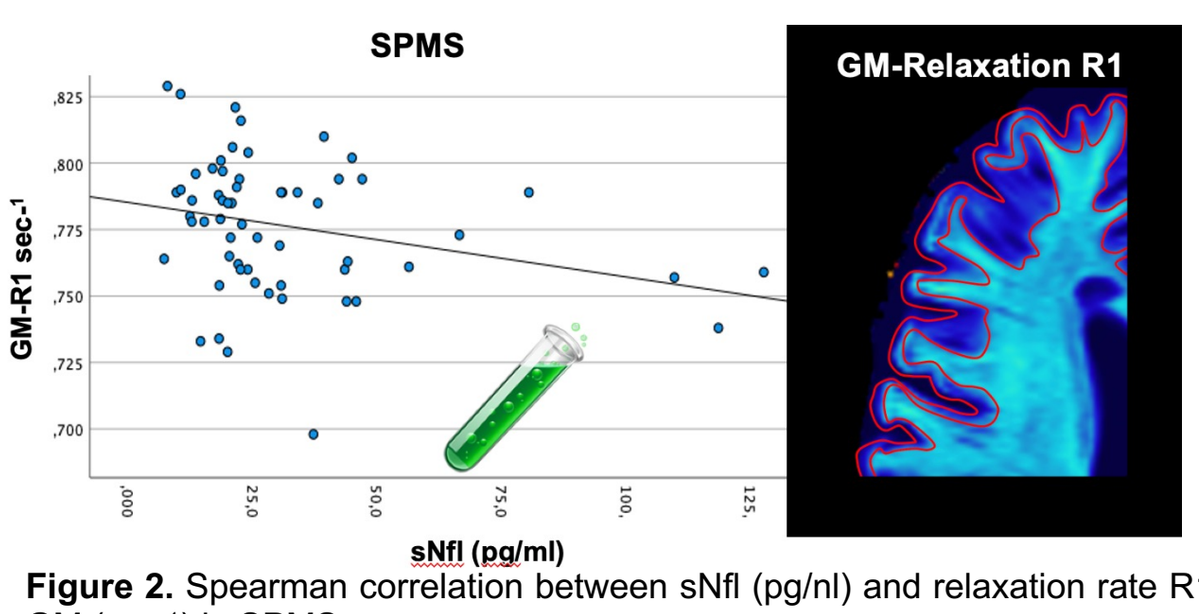

Figure 2. Spearman correlation between sNfl (pg/nl) and relaxation rate R1 of GM (sec^{-1}) in SPMS

Conclusions

- GM atrophy and reduction of GM relaxation rates were equally pronounced in SPMS and RMS
- no significant difference was found between SPMS and RMS with respect to sNfl
- **sNfl was associated with GM relaxation rates R1 and R2 only in SPMS**

→ GM damage in SPMS seems to correspond mainly to axonal degeneration, whereas in RMS multiple factors may influence GM pathology
→ 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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NiRiMS Neuroimaging Research in Multiple Sclerosis

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