Saraste M et al. Supplemental material

eTable 1. Results of the linear regression modelling exploring the association between serum NfL and TSPO-PET related, demographical and clinical parameters among brain DVR(high) patients (n = 19).

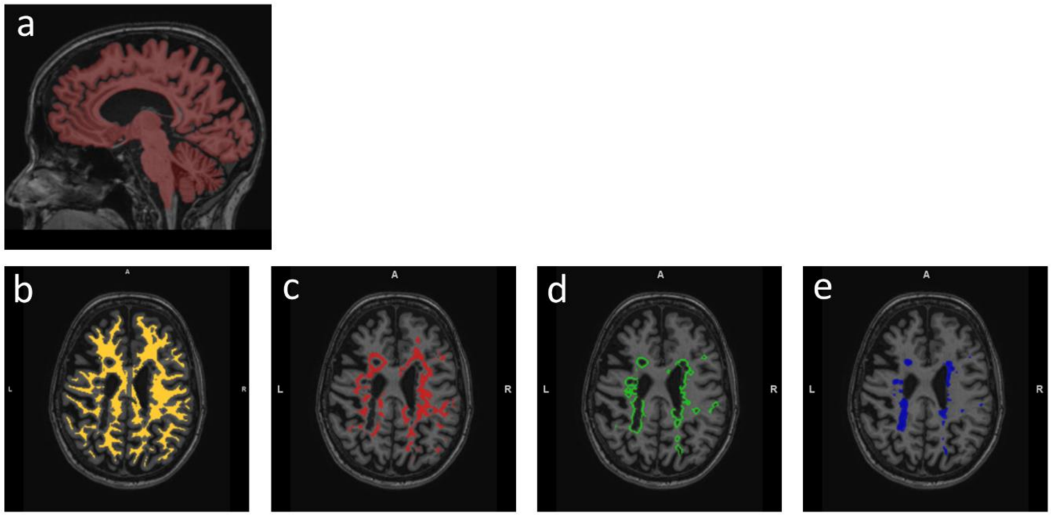
Univariate models					
Studied variable	**Estimate**	**95 % CI**	**Unadjusted p-value**	**FDR-corrected p-value**	**R-squared**
NAWM DVR	0.40	0.03 - 0.77	0.036	0.069	23 %
Perilesional NAWM DVR	0.48	0.14 - 0.83	**0.009**	0.039	34 %
Lesion rim DVR	0.49	0.15 - 0.83	**0.008**	0.039	35 %
T1 DVR	0.41	0.04 - 0.78	0.034	0.069	24 %
Number of rim-active lesions[a]	0.46	0.10 - 0.81	**0.008**	0.039	30 %
Number of overall-active lesions[a]	0.47	0.12 - 0.82	**0.011**	0.039	33 %
Volume of rim-active lesions[b]	0.50	0.17 - 0.84	**0.006**	0.039	37 %
Volume of overall-active lesions[b]	0.41	0.05 - 0.78	0.030	0.069	25 %
BMI	-0.43	-0.79 - -0.07	0.022	0.058	27 %
Annualized relapse rate	-0.14	-0.56 - 0.28	0.5	0.6	3 %
Time since last relapse	0.33	-0.06-0.72	0.092	0.15	16 %
EDSS	0.44	0.07 - 0.80	0.021	0.058	28 %
MSSS	0.24	-0.16 - 0.65	0.2	0.3	7 %
Disease duration	0.15	-0.27 - 0.57	0.5	0.6	3 %
Age	-0.20	-0.61 - 0.21	0.3	0.4	6 %
T1 lesion load	0.47	0.12 - 0.82	**0.011**	0.039	32 %
NAWM volume	-0.18	-0.60 - 0.23	0.4	0.5	5 %
Cortical GM volume	0.01	-0.42 - 0.43	1	1	0.006 %
DMT: Yes vs. No	-0.52	-1.14 - 0.09	0.091	0.15	16 %
Male vs. female	-0.05	-0.48 - 0.38	0.8	0.8	0.4 %
SPMS vs. RRMS	0.19	-0.36 - 0.75	0.5	0.6	3 %
Multivariate stepwise model					
Variables in the final model	**Estimate**	**95 % CI**	**p-value**		**R-squared**
Volume of rim-active lesions[b]	0.51	0.20 - 0.81	0.003		53 %
DMT: Yes vs. No	-0.53	-1.01 - 0.05	0.032		

The p-values of univariate models were corrected using false discovery rate (FDR) method for the number of investigated variables (n = 21). The significance of bolded p-values were sustained in FDR correction. The building of multivariate stepwise linear regression model started with a model without any predictors, and in each step the most suitable variable according to Bayesian information criterion was added to the model. All variables used in univariate models were considered. The p-values of final multivariate stepwise model were not corrected using FDR. ARR = annualized relapse rate between disease and study onset, BMI = body mass index, DMT = disease modifying treatment, DVR = distribution volume ratio (represents specific

binding of [^{11}C]PK11195), EDSS = expanded disability status scale, GM = grey matter, MSSS = multiple sclerosis status scale, NAWM = normal appearing white matter, RRMS = relapsing remitting multiple sclerosis, SPMS = secondary progressive multiple sclerosis

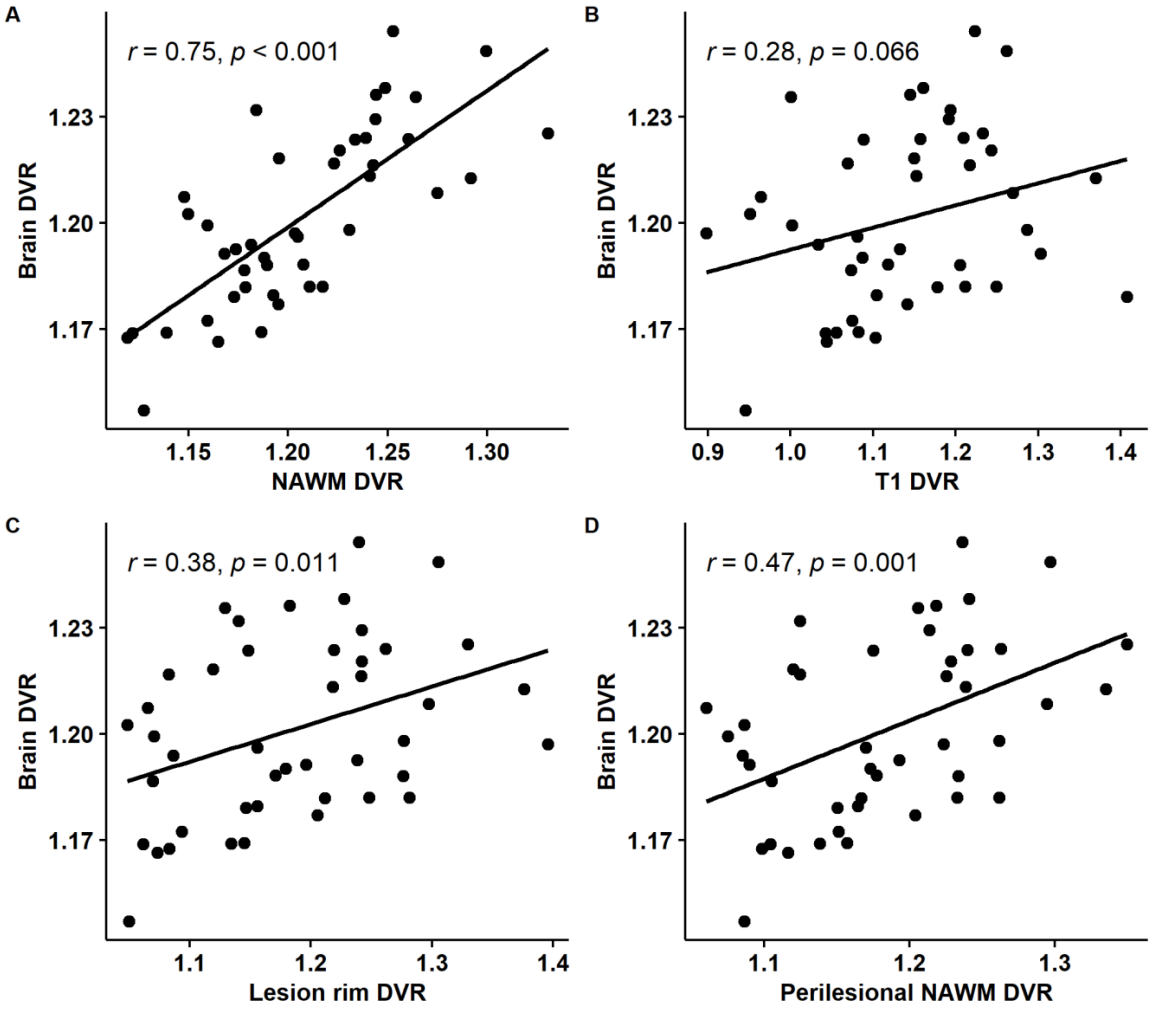
[a] Predictor added as log(number + 1) due to model assumptions [b] Predictor added as log(volume + 0.01) due to model assumptions

eFigure 1. Illustration of region of interests (ROI) used in the study

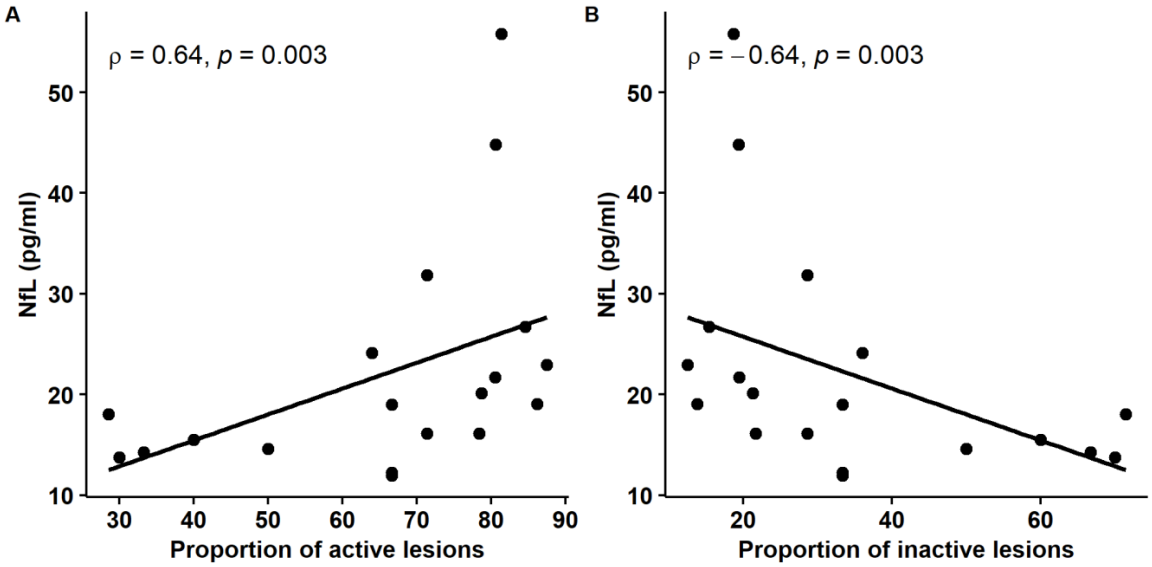


The 3 T MR-images are from an adult patient with RRMS. (a) Sagittal view of 3DT1 with overlaid brain ROI including cerebrum, cerebellum and brain stem. (b - e) Axial views of respective MRI with overlaid ROIs of normal appearing white matter (yellow, b), perilesional NAWM (red, c), lesion rim (green, d) and T1 hypo intense lesions (blue, e).

eFigure 2. Pearson correlation between brain DVR and DVRs in the other studied region of interests in the whole study cohort (n = 44).



eFigure 3. Spearman correlations between serum NfL and proportion of T1 hypointense lesions containing activated microglia (active lesions) and inactive lesions among MS patients having increased innate immune cell activation within the brain (n =19).



The separation of active and inactive lesions is based on the proportion of specific [^{11}C]PK11195 binding within the lesion rim and core. Increased serum NfL correlated with both a higher proportion of lesions containing activated microglia (A) and a lower proportion of inactive lesions (B).

eFigure 4. Spearman correlations between serum NfL and number and volume of T1 hypointense lesions containing activated microglia among MS patients having increased innate immune cell activation within the brain (n =19).