

Supplementary Table 2. CES-D and medication adjusted differences in MRI measures in fatigue impact groups.

	Outcome	BPF (%ICV)	Log T2LV (mL)
fatigued (SF+1F) vs non-fatigued (RF+NF)	β (95% CI) p	-0.01 (-0.02 to 0.01) 0.338	0.54 (0.04 to 1.04) 0.033
SF vs NF	β (95% CI) p	-0.01 (-0.03 to 0.01) 0.182	0.85 (0.23 to 1.46) 0.008
1F vs NF	β (95% CI) p	-0.01 (-0.04 to 0.01) 0.192	0.72 (-0.03 to 1.46) 0.061
RF vs NF	β (95% CI) p	-0.01 (-0.03 to 0.00) 0.103	0.53 (0.02 to 1.04) 0.042
SF vs 1F	β (95% CI) p	0.00 (-0.02 to 0.03) 0.841	0.13 (-0.65 to 0.91) 0.741
SF vs RF	β (95% CI) p	0.00 (-0.02 to 0.02) 0.984	0.32 (-0.29 to 0.92) 0.302
1F vs RF	β (95% CI) p	0.00 (-0.03 to 0.02) 0.853	0.19 (-0.59 to 0.96) 0.634

The fatigue groups were compared using general linear models controlling for age, sex, disease duration, EDSS, medication, CES-D (and ICV in the analysis of log T2LV). According to the group allocation based on one MFIS assessment, the fatigued group corresponds to Sustained Fatigue (SF) and 1 time point Fatigue (1F) groups, while the Reversible (RF) and Never Fatigue (NF) groups are nested in the non-fatigued group. Abbreviations: Brain Parenchymal Fraction (BPF); Center for Epidemiologic Studies - Depression Scale (CES-D); confidence interval (CI); Expanded Disability Status Scale (EDSS); Intracranial Cavity Volume (ICV); logarithmic-transformed T2 lesion volume (log T2LV).