

	Healthy Controls	Multiple Sclerosis		
	All N = 51	PPMS N = 28	SPMS N = 35	RRMS N = 56
Mean periventricular NAWM MTR gradient \pm SE				
-baseline (pu/band)	0.122 \pm 0.038	0.952 \pm 0.185	1.360 \pm 0.143	1.031 \pm 0.117
-annual change (pu/band/year)	-0.011 \pm 0.051	0.090 \pm 0.040	0.021 \pm 0.030	0.046 \pm 0.069
Mean NAWM MTR \pm SE				
-baseline (pu)	39.779 \pm 0.111	38.254 \pm 0.281	38.282 \pm 0.143	38.780 \pm 0.142
-annual change (pu/year)	-0.289 \pm 0.150	-0.231 \pm 0.107	-0.446 \pm 0.099	0.032 \pm 0.139
Mean NAWM volume \pm SE				
-baseline (cm ³)	460.091 \pm 6.665	415.386 \pm 10.490	383.094 \pm 7.337	413.295 \pm 7.477
-annual change (cm ³ /year)	-4.671 \pm 3.973	-1.248 \pm 0.442	-1.314 \pm 0.541	-0.611 \pm 0.515
Mean cortical GM MTR gradient \pm SE				
-baseline (pu)	-2.860 \pm 0.051	-3.214 \pm 0.103	-3.328 \pm 0.101	-3.072 \pm 0.058
-annual change (pu/band/year)	0.090 \pm 0.146	-0.018 \pm 0.039	0.037 \pm 0.009	0.047 \pm 0.070
Mean cortical GM MTR \pm SE				
-baseline (pu)	32.183 \pm 0.093	30.998 \pm 0.206	30.556 \pm 0.154	31.509 \pm 0.140
-annual change (pu/year)	-0.071 \pm 0.239	-0.238 \pm 0.090	-0.346 \pm 0.097	-0.145 \pm 0.148
Mean CGM volume \pm SE				
-baseline (cm ³)	612.545 \pm 7.463	570.030 \pm 12.886	534.389 \pm 8.917	570.364 \pm 8.241
-annual change (cm ³ /year)	-5.490 \pm 5.393	-3.427 \pm 1.071	-1.363 \pm 0.888	-2.668 \pm 0.741

Mean brain parenchymal fraction \pm SE				
-baseline	0.761 \pm 0.001	0.738 \pm 0.004	0.726 \pm 0.003	0.743 \pm 0.002
-annual change	0.001 \pm 0.001	-0.001 \pm 0.001	-0.001 \pm 0.001	-0.001 \pm 0.000
Mean T2 lesion number \pm SE				
-baseline	N/A	41.1 \pm 5.8	43.2 \pm 4.1	42.6 \pm 4.1
-annual change	N/A	-3.3 \pm 1.3	-2 \pm 1.5	0.3 \pm 0.8

eTable 2: *Imaging outcomes at baseline and annualised changes during follow-up in healthy controls, people with primary progressive multiple sclerosis (PPMS) and people with secondary progressive multiple sclerosis (SPMS). BPF=brain parenchymal fraction. GM=grey matter. NAWM=normal appearing white matter. SE=standard error. MTR is expressed as percentage units (pu).*

The NAWM periventricular gradient was significantly shallower (less abnormal) in healthy controls (0.122 \pm 0.038 pu/band) compared to those with RRMS (1.031 \pm 0.117 pu/band, $p < 0.0001$). This persisted when the model was additionally adjusted for mean NAWM MTR ($p = 0.002$) or when adjusted for BPF instead of NAWM volume ($p = 0.034$). The cortical gradient was significantly shallower (less abnormal) in healthy controls (-2.860 \pm 0.051 pu/band) compared to RRMS (-3.072 \pm 0.058 pu/band, $p = 0.030$). These differences lost significance when the model was additionally adjusted for mean cortical GM MTR ($p = 0.668$) or when the model covaried for BPF instead of cortical volume ($p = 0.975$).