

## Supplementary data

Supplementary Table 1 Baseline Advanced MRI metrics

Variable	MS Patients	Healthy Controls
Mean Whole Brain NAWM AD, $\times 10^{-3}\text{mm}^2/\text{s}$	1.17 (0.02)	1.16 (0.02)
Mean Whole Brain NAWM RD*, $\times 10^{-3}\text{mm}^2/\text{s}$	0.62 (0.03)	0.59 (0.02)
Mean Whole Brain NAWM MD*, $\times 10^{-3}\text{mm}^2/\text{s}$	0.8 (0.02)	0.78 (0.02)
Mean Whole Brain NAWM FA*	0.39 (0.02)	0.41 (0.01)
Mean OR NAWM AD, $\times 10^{-3}\text{mm}^2/\text{s}$	1.23 (0.04)	1.24 (0.02)
Mean OR NAWM RD*, $\times 10^{-3}\text{mm}^2/\text{s}$	0.61 (0.04)	0.56 (0.02)
Mean OR NAWM MD*, $\times 10^{-3}\text{mm}^2/\text{s}$	0.82 (0.03)	0.79 (0.01)
Mean OR NAWM FA*	0.43 (0.03)	0.48 (0.02)
Mean Whole Brain Chronic lesion AD, $\times 10^{-3}\text{mm}^2/\text{s}$	1.47 (0.11)	
Mean Whole Brain Chronic lesion RD, $\times 10^{-3}\text{mm}^2/\text{s}$	0.88 (0.12)	
Mean Whole Brain Chronic lesion MD, $\times 10^{-3}\text{mm}^2/\text{s}$	1.08 (0.11)	
Mean Whole Brain Chronic lesion FA	0.34 (0.04)	
Mean OR Chronic lesion AD, $\times 10^{-3}\text{mm}^2/\text{s}$	1.56 (0.10)	
Mean OR Chronic lesion RD, $\times 10^{-3}\text{mm}^2/\text{s}$	0.87 (0.09)	
Mean OR Chronic lesion MD, $\times 10^{-3}\text{mm}^2/\text{s}$	1.10 (0.08)	
Mean OR Chronic lesion FA	0.38 (0.04)	

\*Statistically significant between patient and controls ( $P < 0.002$ ), independent-samples T test. NAWM: Normal Appearing White Matter, AD: Axial Diffusivity, RD: Radial Diffusivity, MD: Mean diffusivity, FA: Fractional Anisotropy, OR: Optic Radiation

Supplementary Table 2 Longitudinal measurements

Variable	MS Patients				Healthy Controls			
	1	2	3	4	1	2	3	4
Time Points								
Mean EDSS (SD)	2.88 (1.40)	2.51 (1.29)	2.21 (1.62)	2.24 (1.53)				
Mean MARS (SD)	1.63 (0.20)	1.69 (0.19)	1.70 (0.21)	1.70 (0.21)	1.76 (0.12)	1.81 (0.07)	1.82 (0.07)	1.80 (0.08)
Mean RNFL thickness (SD) [mm]	84.2 (9.96)	83.72 (9.67)	84.33 (10.19)	85.04 (9.80)	91.77 (8.08)	91.58 (8.67)	91.75 (8.72)	90.70 (8.45)
Mean RNFL thickness (SD) [mm], ON eyes	78.23 (11.17)	80.49 (11.03)	78.95 (10.35)	80.52 (10.89)				
Mean RNFL thickness (SD) [mm], non-ON eyes	91.78 (8.19)	91.64 (8.79)	91.87 (8.83)	90.70 (8.45)				
Mean mfVEP Latency (SD) [ms]	162.94 (15.31)	161.45 (15.06)	161.26 (15.12)	161.18 (15.5)	150.14 (6.27)	149.94 (6.36)	149.97 (6.51)	150.56 (5.69)
Mean mfVEP Latency (SD) [ms], ON eyes	167.92 (15.57)	167.38 (15.55)	167.62 (15.70)	166.92 (16.01)				
Mean mfVEP Latency (SD) [ms], non-ON eyes	150.14 (6.36)	149.97 (6.45)	149.97 (6.41)	150.63 (5.76)				
Mean OR normalized lesional AD	1.28 (0.11)	1.28 (0.12)	1.30 (0.12)	1.32 (0.12)				
Mean OR normalized lesional RD	1.41 (0.15)	1.41 (0.16)	1.42 (0.17)	1.44 (0.16)				
Mean OR normalized lesional MD	1.34 (0.12)	1.35 (0.12)	1.36 (0.12)	1.38 (0.12)				
Mean OR normalized lesional FA	0.89 (0.11)	0.90 (0.12)	0.91 (0.13)	0.91 (0.12)				