Supplementary Table 1. Inter-rater and intra-rater reliability derived from repeated analysis of 10 multiple sclerosis cases.

		difference (D)	STD (D)	D/average	95% CI (D)	95% LOA	ICC	95% CI (ICC)
Intra-Rater	FA	0.013	0.040	2.1%	(-0.016, 0.041)	(-0.065, 0.091)	0.96	(0.91, 1.01)
	MD (μm^2/ms)	0.011	0.085	1.3%	(-0.050, 0.071)	(-0.156, 0.178)	0.96	(0.91, 1.01)
	$\lambda_{\parallel}$ (μm^2/ms)	0.033	0.096	2.4%	(-0.036, 0.010)	(-0.155, 0.222)	0.95	(0.89, 1.01)
	$\lambda_{\perp}$ (μm^2/ms)	-0.030	0.076	0.6%	(-0.057, 0.051)	(-0.152, 0.146)	0.96	(0.92, 1.00)
Inter-Rater	FA	0.025	0.040	4.1%	(-0.004, 0.053)	(-0.054, 0.103)	0.95	(0.88, 1.01)
	MD (μm^2/ms)	-0.039	0.095	4.7%	(-0.106, 0.029)	(-0.224, 0.148)	0.94	(0.87, 1.01)
	$\lambda_{\parallel}$ (μm^2/ms)	-0.028	0.094	2.0%	(-0.095, 0.039)	(-0.212, 0.155)	0.96	(0.91, 1.01)
	$\lambda_{\perp}$ (μm^2/ms)	-0.049	0.085	9.4%	(-0.110, 0.012)	(-0.216, 0.118)	0.94	(0.86. 1.01)

Abbreviations: FA, fractional anisotropy. MD, mean diffusivity. $\lambda_{\parallel}$, parallel diffusivity. $\lambda_{\perp}$, perpendicular diffusivity. STD, standard deviation. CI, confidence interval. LOA, limits of agreement. ICC, intra- or inter-class correlation coefficient.

Supplementary Table 2. DTI indices in the optic nerves.

	prior optic neuritis	# individuals (# analyzed nerves)	FA	MD (μm^2/ms)	$\lambda_{\parallel}$ (μm^2/ms)	$\lambda_{\perp}$ (μm^2/ms)
all MS	±	104 (197)	0.58±0.15	1.03±0.31	1.71±0.34	0.69±0.31
	-	96 (158)	0.58±0.15	1.03±0.31	1.69±0.33	0.69±0.32
	+	32 (35)	0.58±0.13	1.06±0.30	1.78±0.36	0.71±0.28
RRMS	±	63 (120)	0.60±0.16	1.02±0.33	1.71±0.35	0.67±0.33
	-	57 (91)	0.60±0.16	1.03±0.34	1.71±0.35	0.69±0.35
	+	25 (27)	0.60±0.13	1.00±0.28	1.72±0.33	0.65±0.28
SPMS	±	23 (42)	0.52±0.13	1.09±0.28	1.76±0.35	0.77±0.26
	-	21 (33)	0.52±0.14	1.05±0.27	1.70±0.32	0.74±0.27
	+	6 (7)	0.51±0.08	1.27±0.29	2.01±0.44	0.91±0.23
PPMS	±	18 (35)	0.57±0.13	1.01±0.26	1.66±0.27	0.67±0.26
healthy volunteers	N/A	15 (29)	0.63±0.11	1.00±0.41	1.71±0.56	0.66±0.36

Summary statistics (mean±standard deviation) are derived from all data and account for multiple observations per participant (i.e., right and left optic nerves). *Abbreviations*: MS, multiple sclerosis; RRMS, relapsing-remitting MS; SPMS, secondary progressive MS; PPMS, primary progressive MS. FA, fractional anisotropy. MD, mean diffusivity. $\lambda_{\parallel}$, parallel diffusivity. $\lambda_{\perp}$, perpendicular diffusivity. N/A, not applicable.

Supplementary Table 3. Partial correlation of visual acuity measurements with DTI indices and peripapillary retinal nerve fiber layer thickness.

		FA			$\lambda_{\perp}$		
		±	-	+	±	-	+
100% acuity	PRNFL	0.20 (<0.001)	0.11 (<0.001)	0.29 (<0.001)	0.20 (<0.001)	0.11 (<0.001)	0.29 (<0.001)
	DTI	0.08 (<0.001)	0.03 (0.02)	0.29 (0.001)	0.04 (0.01)	0.01 (0.08)	0.15 (0.03)
	PRNFL + DTI	0.21 (<0.001, 0.05)	0.10 (<0.001, 0.33)	0.33 (<0.001, 0.01)	0.19 (<0.001, 0.26)	0.10 (<0.001, 0.74)	0.31 (<0.001, 0.03)
2.5% acuity	PRNFL	0.26 (<0.001)	0.22 (<0.001)	0.15 (<0.001)	0.26 (<0.001)	0.22 (<0.001)	0.15 (<0.001)
	DTI	0.04 (0.01)	0.02 (0.04)	0.13 (0.02)	0.03 (0.03)	0.01 (0.21)	0.12 (0.04)
	PRNFL + DTI	0.26 (<0.001, 0.63)	0.22 (<0.001, 0.92)	0.20 (0.002, 0.08)	0.26 (<0.001, 0.99)	0.23 (<0.001, 0.53)	0.18 (0.001, 0.46)
1.25% acuity	PRNFL	0.16 (<0.001)	0.15 (<0.001)	0.09 (0.01)	0.16 (<0.001)	0.15 (<0.001)	0.09 (0.01)
	DTI	0.01 (0.05)	0.02 (0.11)	0.01 (0.69)	0.01 (0.05)	0.01 (0.09)	0.005 (0.81)
	PRNFL + DTI	0.16 (<0.001, 0.90)	0.15 (<0.001, 0.75)	0.09 (0.01, 0.51)	0.16 (<0.001, 0.91)	0.15 (<0.001, 0.99)	0.09 (0.01, 0.44)

Fractional variance (R^2) of visual acuity scores explained by peripapillary retinal nerve fiber layer (PRNFL) thickness and DIT indices. Each row corresponds to a different mixed-effects regression model, where the fixed-effect variables are: (1) PRNFL thickness alone; (2) one of the four DTI indices alone; or (3) PRNFL thickness plus one of the four DTI indices, taken together. Numbers in parentheses represent the p-values for the fixed-effects components in each model. Prior optic neuritis status is denoted: ±, all optic nerves; -, no prior optic neuritis; +, prior optic neuritis. *Abbreviations*: FA, fractional anisotropy. $\lambda_{\perp}$, perpendicular diffusivity.