

Tables

Table 1. Demographic, clinical and MRI characteristics.

	MS (n=112)	AQP4+ NMOSD (n=99)	AQP4- NMOSD (n=28)	MOGAD (n=28)	HC (n=48)
Clinical characteristic					
Sex, female ratio, No. (%)	77 (69) ^d	88 (89) ^{ac}	20 (71)	21 (75)	32 (67)
Age (median [IQR], year)	33 (25,40.5) ^{ad}	44 (30,56) ^b	39.5 (29.5,54.5)	36 (24,42)	36 (25,56)
Disease duration (median [IQR], month)	35 (12,83)	18 (5,60)	17 (7,46)	12 (4,57)	NA
EDSS (median [IQR])	3 (2,3.5) ^d	4 (3,5.5) ^{bc}	2.5 (1,4)	3 (2,3.5)	NA
Monophasic, No. (%)	30 (32) (n=94)	30 (33) (n=90)	7 (29) (n=24)	12 (44) (n=27)	NA
Number of relapses (median [IQR])	3 (1,3) (n=94)	2 (1,4) (n=90)	2 (1,3) (n=24)	2 (1,3) (n=27)	NA
Treatment, No. (%)					
No treatment	42 (37.50) ^d	25 (25.25)	11 (39.29)	10 (35.71)	NA
Glucocorticoid	8 (7.14)	3 (3.03)	1 (3.57)	2 (7.14)	NA
Immunosuppressor ¹	9 (8.04) (4/3/1/1)	23 (23.23) (13/10/0/0)	5 (17.86) (3/1/0/0)	4 (14.29) (4/0/0/0)	NA
Disease modifying therapy ²	53 (47.32) (10/30/8/3/2)	48 (48.48) (1/0/47/0/0)	11 (39.29) (0/0/11/0/0)	12 (42.86) (0/0/12/0/0)	NA
Cognitive assessment					
MMSE (median [IQR])	29 (28,30) (n=80)	29 (28,30) (n=67)	29 (27,29) (n=18)	29 (26,30) (n=23)	29 (29,30) (n=29)
MoCA (median [IQR])	27 (26,29) (n=79) ^b	26 (23,28) (n=66) ^a	26 (22,27) (n=18) ^a	26 (23,28.5) (n=22) ^a	29 (27,30) (n=29)
SDMT (median [IQR])	50 (40,56) (n=69)	43 (31,52) (n=54) ^a	51 (45,58) (n=14)	44 (30,53) (n=19) ^a	59 (50,65) (n=29)
CVLT (median [IQR])	91 (71,116) (n=71)	96 (77,105) (n=65)	87 (72,110) (n=18)	93 (69,109) (n=20)	104 (90,128) (n=29)
BVLT (median [IQR])	49 (36,56) (n=70)	45 (36,56) (n=58)	35 (20,51) (n=16) ^a	44 (33,52) (n=20)	50 (42,56) (n=24)

PASAT (median [IQR])	45 (36,50) (n=76)	41 (30,48) (n=55)	39 (27,54) (n=16)	42 (30,50) (n=22)	NA
NODDI metrics					
NAWM-NDI (median [IQR])	0.58 (0.55,0.60) ^{acd}	0.59 (0.57,0.60) ^a	0.60 (0.58,0.61)	0.59 (0.58,0.61)	0.60 (0.59,0.61)
NAWM-ODI (median [IQR])	0.28 (0.28,0.29)	0.28 (0.27,0.29)	0.28 (0.27,0.29)	0.28 (0.27,0.28)	0.28 (0.27,0.29)
NAWM-ISOVF (median [IQR])	0.084 (0.072,0.102)	0.083 (0.074,0.096)	0.085 (0.078,0.098)	0.091 (0.078,0.098)	0.085 (0.075,0.097)
WMH-NDI (median [IQR])	0.38 (0.34,0.40) (n=112) ^{acd}	0.40 (0.38,0.42)(n=80) ^a	0.42 (0.39,0.43)(n=24)	0.39 (0.38,0.43)(n=24) ^a	0.43 (0.42,0.45) (n=13)
WMH-ODI (median [IQR])	0.27 (0.25,0.29) (n=112) ^{abcd}	0.31 (0.29,0.34)(n=80)	0.32 (0.30,0.35)(n=24)	0.32 (0.29,0.35)(n=24)	0.33 (0.29,0.36) (n=13)
WMH-ISOVF (median [IQR])	0.24 (0.19,0.27) (n=112) ^{abcd}	0.31 (0.28,0.36)(n=80)	0.31 (0.28,0.35)(n=24)	0.29 (0.26,0.36)(n=24)	0.32 (0.28,0.38) (n=13)
Tissue volume					
WMH volume (median [IQR], ml)	11.99 (5.66,25.85)(n=112) ^{abcd}	2.95 (1.80,5.51)(n=80)	2.20 (1.49,3.12)(n=24)	3.35 (1.89,8.78)(n=24)	1.71 (0.96,2.16) (n=13)
TIV (median [IQR], ml)	1254 (1185,1409) ^d	1229 (1157,1299) ^a	1285 (1185,1365)	1271 (1216,1356)	1311 (1191,1427)
WMV (median [IQR], ml)	368 (346,390) ^{acd}	391 (370,408)	385 (364,415)	379 (360,400)	392 (370,412)
GMV (mean [SD], ml)	600 (554,625) ^a	612 (576,639) ^a	614 (596,644)	615 (545,633) ^a	639 (619,658)

Note: Clinical variables including number of relapses and cognitive score were only available in a subset, of which the available case number was also presented. IQR, interquartile range; MS, multiple sclerosis; AQP4+ NMOSD, aquaporin 4 seropositive neuromyelitis optica spectrum disorders; AQP4- NMOSD, aquaporin 4 seronegative neuromyelitis optica spectrum disorders; MOGAD, myelin oligodendrocyte glycoprotein antibody associated disease; HC, healthy control; EDSS, expanded disability status scale; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; SDMT, Symbol Digit Modalities Test; CVLT, California Verbal Learning Test; BVLTL, Brief Visuospatial Memory Test; PASAT, Paced Auditory Serial Addition Test; NDI, Neurite density index; ODI, orientation dispersion index; ISOVF, isotropic volume fraction; NAWM, normal-appearing white matter; WMH, white matter hyperintensity; WMV, white matter volume; GMV, grey matter

volume; TIV, total intracranial volume. WMV and GMV were age, sex and TIV adjusted. NAWM-NDI, NAWM-ODI and NAWM-ISOVF were age and sex adjusted.

^a indicates statistically significant difference compared to HC;

^b indicates statistically significant difference compared to MOGAD;

^c indicates statistically significant difference compared to AQP4- NMOSD;

^d indicates statistically significant difference compared to AQP4+ NMOSD;

¹ immunosuppressors include mycophenolate mofetil/azathioprine/ciclosporin/leflunomide;

² disease modifying therapies include β interferons/teriflunomide/rituximab/fingolimod/siponimod;

Statistical significance with two-sided $p < 0.05$.

Table 2. Estimated MRI metric in first periventricular ring (Intercept) and periventricular abnormality gradient (Slope) using LMM.

	MS	AQP4+ NMOSD	AQP4- NMOSD	MOGAD	HC
Normalized NAWM-NDI					
Intercept, 95%CI	-2.57 (-3.06,-2.06)*abcd	-1.09 (-1.45,-0.73)*	-0.27 (-0.85,0.31)	-1.14 (-2.08,-0.21)*	-0.034 (-0.46,0.39)
Slope, 95%CI	0.11 (0.086,0.14)*abcd	0.027 (-0.0049,0.050)	0.0050 (-0.029,0.039)	0.026 (-0.010,0.062)	0.011 (-0.017,0.039)
Normalized NAWM-ODI					
Intercept, 95%CI	0.13 (-0.14,0.39)abcd	-0.76 (-0.99,-0.52)*	-0.92 (-1.40,-0.44)*	-0.80 (-1.27,-0.34)*	-1.06 (-1.41,-0.71)*
Slope, 95%CI	-0.11 (-0.14,-0.076)*acd	-0.038 (-0.071,0.0056)	-0.0088 (-0.063,0.045)	-0.036 (-0.092,0.020)	-0.005 (-0.043,0.033)
Normalized NAWM-ISOVF					
Intercept, 95%CI	-2.47 (-2.78,-2.16)*abcd	-0.94 (-1.22,-0.66)*	-0.74 (-1.26,-0.21)*	-1.03 (-1.52,-0.55)*	-1.03 (-1.53,-0.52)*
Slope, 95%CI	0.20 (0.16,0.23)*abcd	0.028 (0.0012,0.055)	0.033 (-0.026,0.092)	0.050 (-0.0013,0.113)	0.043 (-0.0050,0.092)
Normalized WMH-NDI					
Intercept, 95%CI	-6.25 (-6.72,-5.79)*	-5.75 (-6.24,-5.25)*	-4.96 (-5.66,-4.26)*	-5.87 (-6.82,-4.92)*	-5.15 (-5.88,-4.41)*
Slope, 95%CI	-0.74 (-0.80,-0.69)*	-0.75 (-0.80,-0.69)*	-0.77 (-0.93,-0.61)*	-0.62 (-0.79,-0.46)*	-0.70 (-0.79,-0.61)*
Normalized WMH-ODI					
Intercept, 95%CI	-3.37 (-3.71,-3.04)*	-4.29 (-4.91,-3.68)*b	-3.38 (-4.33,-2.42)*	-2.18 (-3.53,-0.83)*	-4.02 (-5.09,-2.94)*
Slope, 95%CI	-0.11 (-0.15,-0.066)*	-0.092 (-0.17,-0.018)*	-0.15 (-0.26,-0.041)*	-0.057 (-0.16,0.042)	-0.082 (-0.21,0.045)
Normalized WMH-ISOVF					
Intercept, 95%CI	-0.36 (-0.79,0.065)abcd	3.36 (2.57,4.15)*	3.36 (2.12,4.61)*	4.30 (1.79,6.81)*	3.51 (2.33,4.69)*
Slope, 95%CI	-0.39 (-0.43,-0.36)*cd	-0.62 (-0.69,-0.55)*b	-0.68 (-0.78,-0.58)*b	-0.40 (-0.67,-0.13)*	-0.55 (-0.63,-0.46)*
WMH Volume					
Intercept, 95%CI	0.53 (0.34,0.72)*ad	0.19 (0.086,0.29)*	0.10 (0.014,0.20)*	0.38 (0.025,0.74)*	0.13 (0.049,0.22)*
Slope, 95%CI	-0.063 (-0.085,-0.041)*acd	-0.019 (-0.031,-0.0075)*	-0.0094 (-0.020,0.0014)	-0.036 (-0.070,-0.0031)*	-0.013 (-0.023,-0.0029)*

Note: Data was presented with average values and 95% CIs. LMM, linear mixed model; MS, multiple sclerosis; AQP4+ NMOSD, aquaporin 4 seropositive neuromyelitis optica spectrum disorders; AQP4- NMOSD, aquaporin 4 seronegative neuromyelitis optica spectrum disorders; MOGAD, myelin oligodendrocyte glycoprotein antibody associated disease; HC, healthy control; NDI, Neurite density index; ODI, orientation dispersion index; ISOVF, isotropic volume fraction; NAWM, normal-appearing white matter; WMH, white matter hyperintensity; CI, confidence interval.

*indicates statistically significance using one-sample t-test;

^a indicates statistically significant difference compared to HC;

^b indicates statistically significant difference compared to MOGAD;

^c indicates statistically significant difference compared to AQP4- NMOSD;

^d indicates statistically significant difference compared to AQP4+ NMOSD;

Statistical significance with two-sided $p < 0.05$.