

SUPPLEMENTARY RESULTS:

In the following tables, the full results from the multivariate mixed-effects models of subcortical GM, thalamic, putaminal and T2 lesion volumes (T2LV) are presented. The dependent variable is the log-transformed volume fraction of interest (i.e. normalized to total intracranial volume), multiplied by 100. The independent variables included are the following (as well as their interactions with follow-up time):

Model 1:

- Time: follow-up time from baseline in years
- DMT category: (DMT-L: 0; DMT-H: 1)
- Race: (non-African-American: 0; African-American: 1)
- Sex: (Female: 0; Male: 1)
- Baseline age (centered at 40 years)
- Baseline disease duration (centered at 8 years)
- Baseline EDSS (centered at 2.5)

Model 2:

Model 1 PLUS:

- Baseline T2LV fraction (log-transformed and converted to Z-scores)
- T2LV annualized rate of change during follow-up (calculated as described in the Supplementary Statistical Methods and converted to Z-scores)

MODEL 1 RESULTS:

Subcortical GM	β	95% CI	P-value
Time	-0.7216	-0.9289 to -0.5142	<0.001
DMT category	-3.824	-8.399 to 0.7509	0.101
DMT category X Time	0.5599	0.1976 to 0.9222	0.002
Race	-3.7657	-11.6224 to 4.091	0.348
Race X Time	-0.2292	-0.7738 to 0.3154	0.409
Sex	-5.0633	-10.9682 to 0.8415	0.093
Sex X Time	-0.2414	-0.5724 to 0.0896	0.153
Baseline Age	-0.0512	-0.3451 to 0.2428	0.733
Baseline Age X Time	-0.0144	-0.0304 to 0.0016	0.078
Baseline Disease Duration	-0.4745	-0.849 to -0.0999	0.013
Baseline Disease Duration X Time	0.0278	0.0026 to 0.0529	0.03
Baseline EDSS	-0.751	-1.8756 to 0.3736	0.191
Baseline EDSS X Time	-0.0407	-0.178 to 0.0965	0.561
Intercept	-375.33	-378.86 to -371.80	<0.001

Thalamus	β	95% CI	P-value
Time	-0.712	-0.9538 to -0.4702	<0.001
DMT category	-5.5515	-11.6155 to 0.5125	0.073
DMT category X Time	0.6345	0.2093 to 1.0598	0.003
Race	-5.2354	-15.8098 to 5.339	0.332
Race X Time	-0.0737	-0.7175 to 0.5701	0.822
Sex	-7.7726	-15.7165 to 0.1713	0.055
Sex X Time	-0.2879	-0.674 to 0.0983	0.144
Baseline Age	0.0944	-0.3009 to 0.4896	0.64
Baseline Age X Time	-0.0109	-0.0295 to 0.0078	0.253
Baseline Disease Duration	-0.5939	-1.0892 to -0.0986	0.019
Baseline Disease Duration X Time	0.0257	-0.0037 to 0.055	0.086
Baseline EDSS	-0.9008	-2.3367 to 0.5351	0.219
Baseline EDSS X Time	-0.0339	-0.1951 to 0.1272	0.68
Intercept	-456.37	-461.11 to -451.63	<0.001

Putamen	β	95% CI	P-value
Time	-0.6621	-0.8159 to -0.5082	<0.001
DMT category	-0.0109	-5.2094 to 5.1876	0.997
DMT category X Time	0.4051	0.125 to 0.6852	0.005
Race	-1.5823	-9.7429 to 6.5783	0.704
Race X Time	-0.2913	-0.7293 to 0.1467	0.192
Sex	-2.104	-8.2448 to 4.0368	0.502
Sex X Time	-0.0793	-0.3242 to 0.1655	0.525
Baseline Age	0.0293	-0.2752 to 0.3339	0.85
Baseline Age X Time	-0.012	-0.0236 to -0.0003	0.044
Baseline Disease Duration	-0.2529	-0.6484 to 0.1426	0.21
Baseline Disease Duration X Time	0.0183	-0.0003 to 0.0368	0.054
Baseline EDSS	-1.3254	-2.5121 to -0.1387	0.029
Baseline EDSS X Time	0.0255	-0.0814 to 0.1325	0.64
Intercept	-508.84	-512.57 to -505.1	<0.001

T2 Lesion Volume	β	95% CI	P-value
Time	6.3669	2.7447 to 9.9892	0.001
DMT category	45.2084	0.8488 to 89.568	0.046
DMT category X Time	-5.5099	-11.8067 to 0.7869	0.086
Race	41.5522	-22.5125 to 105.6169	0.204
Race X Time	4.0265	-5.4333 to 13.4862	0.404
Sex	27.1444	-21.2881 to 75.5768	0.272
Sex X Time	-0.179	-5.9582 to 5.6003	0.952
Baseline Age	0.8176	-1.5815 to 3.2168	0.504
Baseline Age X Time	0.0421	-0.2362 to 0.3203	0.767
Baseline Disease Duration	3.4661	-0.0239 to 6.9561	0.052
Baseline Disease Duration X Time	-0.203	-0.641 to 0.2349	0.363
Baseline EDSS	-1.3694	-14.6849 to 11.946	0.84
Baseline EDSS X Time	0.126	-2.2648 to 2.5167	0.918
Intercept	-617.23	-647.05 to -587.41	<0.001

MODEL 2 RESULTS:

Subcortical GM	β	95% CI	P-value
Time	-0.6499	-0.8527 to -0.4471	<0.001
DMT category	-0.8898	-4.3962 to 2.6165	0.619
DMT category X Time	0.3798	0.0244 to 0.7352	0.036
Race	-0.3302	-6.7246 to 6.0641	0.919
Race X Time	-0.1397	-0.6674 to 0.388	0.604
Sex	-2.9008	-7.6779 to 1.8762	0.234
Sex X Time	-0.2497	-0.5619 to 0.0625	0.117
Baseline Age	0.0276	-0.21 to 0.2652	0.82
Baseline Age X Time	-0.0162	-0.0312 to -0.0011	0.035
Baseline Disease Duration	-0.2182	-0.5339 to 0.0974	0.175
Baseline Disease Duration X Time	0.0243	0.0005 to 0.0481	0.045
Baseline EDSS	-1.3214	-2.5317 to -0.1111	0.032
Baseline EDSS X Time	-0.0292	-0.1584 to 0.0999	0.657
Baseline T2LV	-7.7002	-10.0198 to -5.3806	<0.001
Baseline T2LV X Time	0.0452	-0.1165 to 0.2068	0.584
T2LV rate	-0.6513	-2.1907 to 0.8882	0.407
T2LV rate X Time	-0.1951	-0.3224 to -0.0679	0.003
Intercept	-377.6	-380.46 to -374.75	<0.001

Thalamus	β	95% CI	P-value
Time	-0.5987	-0.7983 to -0.399	<0.001
DMT category	-0.6615	-4.837 to 3.5139	0.756
DMT category X Time	0.3876	0.0281 to 0.7471	0.035
Race	0.344	-7.3255 to 8.0134	0.93
Race X Time	0.0172	-0.5298 to 0.5642	0.951
Sex	-4.2055	-9.936 to 1.525	0.15
Sex X Time	-0.277	-0.5851 to 0.0312	0.078
Baseline Age	0.2332	-0.0517 to 0.5182	0.109
Baseline Age X Time	-0.0125	-0.0272 to 0.0022	0.095
Baseline Disease Duration	-0.1587	-0.537 to 0.2196	0.411
Baseline Disease Duration X Time	0.0202	-0.0031 to 0.0436	0.09
Baseline EDSS	-2.1633	-3.6179 to -0.7088	0.004
Baseline EDSS X Time	-0.016	-0.1471 to 0.1151	0.811
Baseline T2LV	-12.0768	-14.8561 to -9.2974	<0.001
Baseline T2LV X Time	-0.0199	-0.1782 to 0.1385	0.806
T2LV rate	-1.056	-2.8782 to 0.7662	0.256
T2LV rate X Time	-0.3124	-0.4389 to -0.1859	<0.001
Intercept	-460.08	-463.51 to -456.66	<0.001

Putamen	β	95% CI	P-value
Time	-0.647	-0.8061 to -0.4879	<0.001
DMT category	1.0102	-3.8472 to 5.8676	0.684
DMT category X Time	0.3673	0.0739 to 0.6606	0.014
Race	1.0572	-6.5841 to 8.6984	0.786
Race X Time	-0.2029	-0.6521 to 0.2463	0.376
Sex	-1.1268	-6.8383 to 4.5846	0.699
Sex X Time	-0.0879	-0.3328 to 0.157	0.482
Baseline Age	0.0523	-0.2311 to 0.3356	0.718
Baseline Age X Time	-0.012	-0.0237 to -0.0003	0.044
Baseline Disease Duration	-0.182	-0.5677 to 0.2037	0.355
Baseline Disease Duration X Time	0.0158	-0.0029 to 0.0345	0.097
Baseline EDSS	-0.5207	-2.0063 to 0.9648	0.492
Baseline EDSS X Time	0.02	-0.0869 to 0.1269	0.714
Baseline T2LV	-5.6521	-8.4806 to -2.8237	<0.001
Baseline T2LV X Time	-0.0111	-0.1366 to 0.1144	0.863
T2LV rate	-2.4948	-4.419 to -0.5706	0.011
T2LV rate X Time	-0.0965	-0.1989 to 0.006	0.065
Intercept	-510.24	-513.75 to -506.73	<0.001