

**On-line Table 1: Brain regions and DTI measures of healthy control participants, patients with RRMS, and patients with PMS**

|                                         | MD ( $\times 10^{-3}$ ) |                  |                  | P Value | FA               |                  |                  | P Value |
|-----------------------------------------|-------------------------|------------------|------------------|---------|------------------|------------------|------------------|---------|
|                                         | HC (n = 110)            | RRMS (n = 210)   | PMS (n = 75)     |         | HC (n = 110)     | RRMS (n = 210)   | PMS (n = 75)     |         |
| NABT, mean (SD) and median              | 1.00 (0.07) 0.99        | 1.01 (0.09) 1.00 | 1.06 (0.12) 1.04 | .006    | 0.26 (0.01) 0.26 | 0.25 (0.02) 0.25 | 0.24 (0.02) 0.24 | <.001   |
| NAWM, mean (SD) and median              | 0.90 (0.06) 0.89        | 0.91 (0.08) 0.89 | 0.95 (0.11) 0.92 | .003    | 0.36 (0.03) 0.36 | 0.33 (0.03) 0.33 | 0.31 (0.04) 0.31 | <.001   |
| NAGM, mean (SD) and median              | 1.12 (0.08) 1.11        | 1.14 (0.01) 1.14 | 1.18 (0.13) 1.17 | .009    | 0.17 (0.01) 0.17 | 0.16 (0.01) 0.16 | 0.16 (0.01) 0.15 | .002    |
| Subcortical deep gray matter structures |                         |                  |                  |         |                  |                  |                  |         |
| Total SDGM, mean (SD) and median        | 1.01 (0.15) 1.00        | 1.10 (0.15) 1.07 | 1.18 (0.17) 1.15 | <.001   | 0.26 (0.03) 0.27 | 0.26 (0.02) 0.26 | 0.26 (0.02) 0.26 | .054    |
| Caudate, mean (SD) and median           | 1.21 (0.28) 1.12        | 1.33 (0.33) 1.26 | 1.51 (0.42) 1.41 | <.001   | 0.20 (0.03) 0.20 | 0.19 (0.04) 0.19 | 0.19 (0.04) 0.18 | .306    |
| Putamen, mean (SD) and median           | 0.82 (0.08) 0.82        | 0.83 (0.07) 0.82 | 0.83 (0.05) 0.82 | .439    | 0.27 (0.04) 0.27 | 0.27 (0.03) 0.27 | 0.28 (0.03) 0.28 | .025    |
| Globus pallidus, mean (SD) and median   | 0.79 (0.12) 0.81        | 0.82 (0.08) 0.81 | 0.83 (0.07) 0.81 | .053    | 0.40 (0.08) 0.41 | 0.40 (0.06) 0.39 | 0.42 (0.07) 0.41 | .331    |
| Thalamus, mean (SD) and median          | 1.07 (0.17) 1.04        | 1.17 (0.21) 1.12 | 1.29 (0.30) 1.26 | <.001   | 0.30 (0.02) 0.30 | 0.29 (0.03) 0.29 | 0.28 (0.04) 0.28 | .002    |
| Hippocampus, mean (SD) and median       | 1.09 (0.29) 1.14        | 1.23 (0.21) 1.21 | 1.27 (0.20) 1.21 | <.001   | 0.22 (0.07) 0.22 | 0.20 (0.04) 0.20 | 0.20 (0.05) 0.20 | .047    |
| Amygdala, mean (SD) and median          | 1.05 (0.33) 1.07        | 1.11 (0.23) 1.09 | 1.16 (0.27) 1.10 | .045    | 0.19 (0.06) 0.20 | 0.19 (0.04) 0.19 | 0.20 (0.03) 0.20 | .497    |
| Nucleus accumbens, mean (SD) and median | 0.89 (0.21) 0.90        | 0.94 (0.16) 0.91 | 0.99 (0.16) 0.93 | .003    | 0.19 (0.04) 0.20 | 0.21 (0.04) 0.20 | 0.22 (0.04) 0.21 | .006    |

**Note:**—FA indicates fractional anisotropy; HC, healthy control participants; MD, mean diffusivity; NABT, normal-appearing brain tissue; NAGM, normal-appearing gray matter; NAWM, normal-appearing white matter; PMS, progressive MS; RRMS, relapsing-remitting MS; SD, standard deviation; SDGM, subcortical deep gray matter structures. Groups were compared using the ANOVA test or Kruskal-Wallis. All P values were corrected for multiple comparisons using Benjamini-Hochberg correction.

**On-line Table 2: Brain regions and DTI measures of healthy control participants, patients with RRMS, and patients with PMS**

|                                         | AD ( $\times 10^{-3}$ ) |                  |                  | P Value | RD ( $\times 10^{-3}$ ) |                  |                  | P Value |
|-----------------------------------------|-------------------------|------------------|------------------|---------|-------------------------|------------------|------------------|---------|
|                                         | HC (n = 110)            | RRMS (n = 210)   | PMS (n = 75)     |         | HC (n = 110)            | RRMS (n = 210)   | PMS (n = 75)     |         |
| NABT, mean (SD) and median              | 1.26 (0.06) 1.25        | 1.26 (0.10) 1.26 | 1.29 (0.12) 1.28 | .060    | 0.88 (0.07) 0.87        | 0.89 (0.09) 0.88 | 0.94 (0.12) 0.92 | .001    |
| NAWM, mean (SD) and median              | 1.25 (0.05) 1.24        | 1.23 (0.09) 1.24 | 1.26 (0.11) 1.25 | .097    | 0.73 (0.07) 0.72        | 0.75 (0.09) 0.73 | 0.80 (0.11) 0.77 | <.001   |
| NAGM, mean (SD) and median              | 1.29 (0.09) 1.28        | 1.30 (0.12) 1.31 | 1.35 (0.14) 1.35 | .011    | 1.04 (0.08) 1.03        | 1.05 (0.10) 1.05 | 1.08 (0.13) 1.09 | .007    |
| Subcortical deep gray matter structures |                         |                  |                  |         |                         |                  |                  |         |
| Total SDGM, mean (SD) and median        | 1.29 (0.18) 1.27        | 1.37 (0.18) 1.34 | 1.47 (0.20) 1.44 | <.001   | 0.88 (0.14) 0.86        | 0.96 (0.13) 0.94 | 1.03 (0.16) 1.00 | <.001   |
| Caudate, mean (SD) and median           | 1.43 (0.30) 1.34        | 1.57 (0.36) 1.49 | 1.78 (0.45) 1.65 | <.001   | 1.09 (0.27) 1.02        | 1.22 (0.32) 1.15 | 1.38 (0.40) 1.28 | <.001   |
| Putamen, mean (SD) and median           | 1.06 (0.11) 1.07        | 1.07 (0.10) 1.07 | 1.09 (0.07) 1.08 | .183    | 0.69 (0.08) 0.70        | 0.70 (0.06) 0.70 | 0.70 (0.04) 0.69 | .526    |
| Globus pallidus, mean (SD) and median   | 1.16 (0.17) 1.18        | 1.19 (0.12) 1.18 | 1.23 (0.12) 1.22 | .011    | 0.61 (0.10) 0.63        | 0.63 (0.07) 0.63 | 0.63 (0.08) 0.62 | .202    |
| Thalamus, mean (SD) and median          | 1.38 (0.19) 1.34        | 1.48 (0.24) 1.43 | 1.62 (0.33) 1.56 | <.001   | 0.91 (0.16) 0.89        | 1.01 (0.20) 0.97 | 1.13 (0.29) 1.07 | <.001   |
| Hippocampus, mean (SD) and median       | 1.35 (0.35) 1.43        | 1.49 (0.23) 1.47 | 1.53 (0.22) 1.48 | <.001   | 0.96 (0.27) 1.02        | 1.10 (0.20) 1.08 | 1.13 (0.20) 1.08 | <.001   |
| Amygdala, mean (SD) and median          | 1.27 (0.40) 1.29        | 1.33 (0.27) 1.31 | 1.40 (0.31) 1.36 | .045    | 0.94 (0.30) 0.96        | 0.99 (0.22) 0.97 | 1.04 (0.26) 1.00 | .045    |
| Nucleus accumbens, mean (SD) and median | 1.07 (0.25) 1.08        | 1.13 (0.19) 1.10 | 1.21 (0.20) 1.14 | <.001   | 0.80 (0.19) 0.81        | 0.84 (0.15) 0.81 | 0.88 (0.14) 0.83 | .008    |

**Note:**—AD indicates axial diffusivity; HC, healthy control participants; NABT, normal-appearing brain tissue; NAGM, normal-appearing gray matter; NABT, normal-appearing gray matter; NAWM, normal-appearing white matter; PMS, progressive MS; RD, radial diffusivity; RRMS, relapsing-remitting MS; SD, standard deviation; SDGM, subcortical deep gray matter structures. Groups were compared using the ANOVA test or Kruskal-Wallis. All P values were corrected for multiple comparisons using Benjamini-Hochberg correction.