Supplementary table S1. GEE model parameter estimates; including intermediates individually.

| Predictor | Model A | Model B | Model C | Model D |
|-----------|---------|---------|---------|---------|
|           | n/obs   | OR (95% CI) | p       | OR (95% CI) | p       | OR (95% CI) | p       | OR (95% CI) | p       |
| Cortical  | 74/146  | 0.99 (0.97, 1.00) | 0.086   | 0.99 (0.98, 1.01) | 0.28   | 0.99 (0.98, 1.00) | 0.075   | 0.99 (0.98, 1.01) | 0.39   |
| Subcortical | 74/147 | 0.88 (0.81, 0.96) | 0.003   | 0.91 (0.83, 1.00) | 0.044  | 0.88 (0.81, 0.96) | 0.005   | 0.91 (0.83, 0.99) | 0.035  |
| Thalamus  | 74/147  | 0.69 (0.52, 0.91) | 0.009   | 0.78 (0.57, 1.06) | 0.11   | 0.70 (0.53, 0.93) | 0.013   | 0.76 (0.57, 1.01) | 0.060  |
| Pallidus  | 74/147  | 0.24 (0.10, 0.61) | 0.03    | 0.35 (0.13, 0.95) | 0.040  | 0.26 (0.09, 0.71) | 0.009   | 0.34 (0.12, 1.02) | 0.053  |
| Putamen   | 74/147  | 0.61 (0.45, 0.83) | 0.002   | 0.69 (0.50, 0.96) | 0.027  | 0.62 (0.45, 0.86) | 0.004   | 0.66 (0.46, 0.94) | 0.021  |
| Caudate   | 74/147  | 0.68 (0.39, 1.18) | 0.17    | 0.80 (0.44, 1.43) | 0.45   | 0.69 (0.40, 1.20) | 0.19    | 0.84 (0.47, 1.50) | 0.55   |
| Hippocampus | 74/147 | 0.50 (0.32, 0.78) | 0.002   | 0.57 (0.37, 0.89) | 0.012  | 0.51 (0.33, 0.80) | 0.003   | 0.55 (0.35, 0.87) | 0.009  |

Legend: A = Adjusted for baseline covariates: center, sex, age and education; and time-varying MS course (using only observations that also have SDMT, FSS and EDSS). B = Adjusted for baseline covariates: center, sex, age and education; time-varying MS course; and time-varying SDMT. C = Adjusted for baseline covariates: center, sex, age and education; time-varying MS course; and time-varying FSS. D = Adjusted for baseline covariates: center, sex, age and education; time-varying MS course; and time-varying EDSS.