**Estimating the evolution of disease in the Parkinson’s Progression Markers Initiative**

Samuel Iddia,b, Dan Lia, Paul S. Aisena, Michael S. Rafiia, Irene Litvand, Wesley K. Thompsonc, & Michael C. Donohuea\*

aAlzheimer’s Therapeutic Research Institute, University of Southern California, San Diego, USA

bDepartment of Statistics, University of Ghana, Legon-Accra, Ghana

cDepartment of Neurosciences, University of California, San Diego, USA

dDepartment of Family Medicine and Public Health, University of California, San Diego, USA

# \*Correspondence: [mdonohue@usc.edu](mailto:mdonohue@usc.edu)

**Supplementary Appendix**

**[ FIGUREA1.JPEG HERE]**

Figure A.1: Distribution of estimate of time shift, by disease status. **Abbreviations**: PD, Parkinson Disease; HC, Healthy Control.

**[ FIGUREA2.JPEG HERE]**

**Figure A.2**: Correlation between random slopes for pair of outcomes.

**Abbreviations**: PIGD, Posture Instability and Gait Difficulty; RBD, REM sleep behavior disorder; UPSIT, University of Pennsylvania Smell Identification Test; MOCA, Montreal Cognitive Assessment; HVLT, Hopkins Verbal Learning Test; GDS, Geriatric Depression Scale; SFT, Semantic Fluency Test; SCOPA, Scale for Outcomes in Parkinson’s; LINEORT, Line Orientation Test; UPDRS, Unified Parkinson Disease Rating Scale; STAI, State Trait Anxiety Index; PD, Parkinson Disease; HC, Healthy Control.

**[ FIGUREA3A.JPEG and FIGUREA3B.JPEG HERE]**

(a) For 17 outcomes (b) For 9 outcomes with UPDRS separated

**Figure A.3**: Population level predicted severity for female with mean age and median latent time of a healthy control. The legend is ordered by the age at which the predicted severity level for each outcome is 0.5 (sliced horizontally).

**Abbreviations**: PIGD, Posture Instability and Gait Difficulty; RBD, REM sleep behavior disorder; UPSIT, University of Pennsylvania Smell Identification Test; MOCA, Montreal Cognitive Assessment; HVLT, Hopkins Verbal Learning Test; GDS, Geriatric Depression Scale; SFT, Semantic Fluency Test; SCOPA, Scale for Outcomes in Parkinson’s; LINEORT, Line Orientation Test; UPDRS, Unified Parkinson Disease Rating Scale; STAI, State Trait Anxiety Index; PD, Parkinson Disease; HC, Healthy Control.

**[ FIGUREA4ALJPEG AND FIGUREA4B.JPEG HERE]**

(a) Female. (b) Male.

Figure A.4: Positional variance diagram of the central ordering. The x-axis is the event position.

**Abbreviations**: PIGD, Posture Instability and Gait Difficulty; RBD, REM sleep behavior disorder; UPSIT, University of Pennsylvania Smell Identification Test; MOCA, Montreal Cognitive Assessment; HVLT, Hopkins Verbal Learning Test; GDS, Geriatric Depression Scale; SFT, Semantic Fluency Test; SCOPA, Scale for Outcomes in Parkinson’s; LINEORT, Line Orientation Test; UPDRS, Unified Parkinson Disease Rating Scale; STAI, State Trait Anxiety Index; PD, Parkinson Disease; HC, Healthy Control.

**[ FIGUREA5.JPEG HERE]**

**Figure A.5**: Positional variance diagram of the central ordering

**Abbreviations**: PIGD, Posture Instability and Gait Difficulty; RBD, REM sleep behavior disorder; UPSIT, University of Pennsylvania Smell Identification Test; MOCA, Montreal Cognitive Assessment; HVLT, Hopkins Verbal Learning Test; GDS, Geriatric Depression Scale; SFT, Semantic Fluency Test; SCOPA, Scale for Outcomes in Parkinson’s; LINEORT, Line Orientation Test; UPDRS, Unified Parkinson Disease Rating Scale; STAI, State Trait Anxiety Index; PD, Parkinson Disease; HC, Healthy Control.

Table A. 1: Results of posterior estimates of parameters and corresponding 95% credible interval for all 17 outcomes from the Parkinson’s Progression Markers Initiative (PPMI).

|  |  |  |
| --- | --- | --- |
| Post. 95%  Parameter Mean Credible Interval | Post. 95%  Parameter Mean Credible Interval | Post. 95%  Parameter Mean Credible Interval |
| **CSF Abeta 42** | **MOCA** | **Tremor** |
| Intercept -0.099 (-0.586,0.405) | Intercept -1.871 (-2.304,-1.431) | Intercept -0.203 (-0.975,0.572) |
| Age 0.003 (-0.005,0.011) | Age 0.030 (0.023,0.036) | Age -0.009 (-0.021,0.002) |
| Female -0.073 (-0.234,0.076) | Female -0.284 (-0.427,-0.148) | Female -0.176 (-0.419,0.065) |
| Latent time, *γ*1 0.023 (0.015,0.032) | Latent time, *γ*8 0.945 (0.917,0.974) | Latent time, *γ*15 0.094 (0.071,0.114) |
| Error Variance, *σ*1 0.416 (0.387,0.448) | Error Variance, *σ*8 0.945 (0.917,0.974) | Error Variance, *σ*15 0.811 (0.796,0.827) |
| **CSF Alpha-synuclein** | **PIGD** | **UPDRS Total** |
| Intercept 0.813 (0.342,1.274) | Intercept -2.250 (-3.054,-1.4) | Intercept -0.524 (-0.985,-0.06) |
| Age -0.012 (-0.019,-0.004) | Age 0.016 (0.003,0.028) | Age 0.010 (0.003,0.017) |
| Female -0.151 (-0.309,0.007) | Female 0.076 (-0.164,0.328) | Female -0.047 (-0.188,0.098) |
| Latent time, *γ*2 0.034 (0.024,0.045) | Latent time, *γ*9 0.114 (0.085,0.139) | Latent time, *γ*16 0.073 (0.054,0.088) |
| Error Variance, *σ*2 0.424 (0.394,0.454) | Error Variance, *σ*9 1.156 (1.134,1.178) | Error Variance, *σ*16 0.349 (0.343,0.356) |
| **CSF p-Tau181P** | **REM Sleep** | **UPSIT** |
| Intercept 0.352 (-0.109,0.81) | Intercept 0.317 (-0.121,0.745) | Intercept -1.103 (-1.567,-0.642) |
| Age -0.005 (-0.013,0.002) | Age -0.006 (-0.013,0.001) | Age 0.019 (0.012,0.026) |
| Female 0.084 (-0.065,0.23) | Female -0.115 (-0.256,0.027) | Female -0.210 (-0.352,-0.067) |
| Latent time, *γ*3 0.025 (0.017,0.033) | Latent time, *γ*10 0.040 (0.03,0.05) | Latent time, *γ*17 0.043 (0.032,0.055) |
| Error Variance, *σ*3 0.717 (0.667,0.766) | Error Variance, *σ*10 0.584 (0.568,0.6) | Error Variance, *σ*17 0.218 (0.059,0.446) |
| **CSF Total tau** | **SBR Striatum** | **Heterogeneous parameters** |
| Intercept 1.773 (1.318,2.252) | Intercept -1.079 (-1.476,-0.681) | Intercept, *τ*0 5.002 (4.19,5.831) |
| Age -0.027 (-0.035,-0.02) | Age 0.018 (0.012,0.025) | Age, *τ*1 -0.001 (-0.012,0.009) |
| Female -0.223 (-0.374,-0.063) | Female -0.084 (-0.211,0.043) | Female,*τ*2 -0.063 (-0.287,0.159) |
| Latent time, *γ*4 0.036 (0.025,0.046) | Latent time, *γ*11 0.049 (0.035,0.061) |  |
| Error Variance, *σ*4 0.275 (0.255,0.295) | Error Variance, *σ*11 0.212 (0.2,0.224) |  |
| **GDSSHORT** | **SCOPA** | **Model comparison criteria** |
| Intercept -0.388 (-1.044,0.287) | Intercept -2.319 (-2.685,-1.933) | WAIC 117860.0 |
| Age -0.002 (-0.012,0.008) | Age 0.033 (0.027,0.039) | LOOIC 120166.7 |
| Female -0.097 (-0.302,0.115) | Female 0.504 (0.388,0.618) |  |
| Latent time, *γ*5 0.069 (0.051,0.084) | Latent time, *γ*12 0.038 (0.029,0.047) |  |
| Error Variance, *σ*5 1.116 (1.088,1.147) | Error Variance, *σ*12 0.469 (0.456,0.482) |  |
| **HVLT** | **SFT** |  |
| Intercept -1.157 (-1.488,-0.813) | Intercept -0.905 (-1.286,-0.536) |  |
| Age 0.021 (0.016,0.026) | Age 0.017 (0.011,0.023) |  |
| Female -0.335 (-0.446,-0.224) | Female -0.492 (-0.616,-0.368) |  |
| Latent time, *γ*6 0.022 (0.017,0.029) | Latent time, *γ*13 0.022 (0.016,0.029) |  |
| Error Variance, *σ*6 0.551 (0.534,0.568) | Error Variance, *σ*13 0.429 (0.417,0.443) |  |
| **LINEORNT** | **STAI** |  |
| Intercept -2.041 (-2.609,-1.493) | Intercept 0.701 (0.26,1.139) |  |
| Age 0.022 (0.014,0.03) | Age -0.012 (-0.018,-0.005) |  |
| Female 0.763 (0.592,0.932) | Female 0.136 (0.002,0.274) |  |
| Latent time, *γ*7 0.028 (0.019,0.038) | Latent time, *γ*14 0.044 (0.033,0.054) |  |
| Error Variance, *σ*7 1.185 (1.152,1.22) | Error Variance, *σ*14 0.594 (0.578,0.61) |  |