**Supplementary Materials**

**Predicting Progression in Parkinson's Disease Using Baseline and 1-Year Change Measures**

**Supplement to Assessments Section**

Tremor and PIGD score calculations: as previously described (reference 10), a tremor score was generated, as the mean of MDS-UPDRS items 2.10, 3.15 (right and left separately), 3.16 (right and left separately), 3.17 (each body region separately), and item 3.18. A PIGD score was generated as the mean of MDS-UPDRS items 2.12, 2.13, 3.10, 3.11, and 3.12.

OFF/ON testing in PPMI: As previously described (reference 11), OFF medication state in PPMI as more than 6 hours post–last dose of DT. ON state is MDS-UPDRS score approximately 1 hour after the last dose of DT. Examination only in the ON state occurs for participants treated with other PD medications besides levodopa or dopamine agonists, such as monoamine oxidase inhibitors and amantadine.

**Supplement to Statistical Analysis Section**

The optimal longitudinal model (linear vs nonlinear time and covariance structure) for each outcome was determined using Akaike information criterion (AIC). Non-linear trends were modeled by inserting time as a categorical variable. First, the optimal covariance structure for each mean structure was found. Using the selected covariance structure, the model fit between non-linear and linear models was compared. The optimal model structure for all change in MDS-UPDRS outcomes, and percent change in mean striatum was a linear time model with a random intercept and slope and an unstructured covariance structure. The optimal model fit for percent change in mean putamen was a linear time model with a random intercept and an unstructured covariance structure. All models adjusted for the baseline value of the respective outcome.

**Supplementary Table 1. AIC Values for Models Treating Time as a Linear & Categorical (Non-Linear) Variable**

|  |  |  |
| --- | --- | --- |
| **Outcome** | **Model** | **AIC** |
| Change in MDS-UPDRS Part III Score Off | Linear Effects | 11666.1 |
| Categorical Effects | 11855.3 |
| Change in MDS-UPDRS Part III Score On | Linear Effects | 14296.8 |
| Categorical Effects | 14542.7 |
| Change in MDS-UPDRS Total Score Off | Linear Effects | 12883.9 |
| Categorical Effects | 13131.7 |
| Change in MDS-UPDRS Total Score On | Linear Effects | 15653.7 |
| Categorical Effects | 15992.2 |
| % Change in Mean Putamen DAT | Linear Effects | 8807.7 |
| Categorical Effects | 8809.4 |
| % Change in Mean Striatal DAT | Linear Effects | 8256.3 |
| Categorical Effects | 8268.2 |
| Change in MoCA | Linear Effects | 7292.9 |
| Categorical Effects | 7406.7 |

**Supplementary Table 2**. Pseudo-univariate and multivariate relationships of all potential baseline predictors to key outcomes in mixed models. All multivariate models adjusted for baseline age, gender, baseline disease duration, as well as baseline of the outcome variable (depicted below the dotted line)\*. CV, cross-validation.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Baseline Predictor Models** |  | **Baseline Backwards Selection Final Model** |  |
| **Outcome** | **Predictor** | **Pseudo-UnivariateEffect Estimate** |  | **Pseudo-univariate CV Selections** | **Multivariate Effect Estimate** | **Multivariate** | **Multivariate CV Selections** |
| (95% CI) | p-value | N (%) | (95% CI) | p-value | N (%) |
| **MDS-UPDRS Total Score Off - Change from Baseline**       | abeta | -0.0035 (-0.0062, -0.0008) | 0.0102 | 777 (77.70%) | -0.0031 (-0.0058, -0.0005) | 0.0217 | 286 (28.60%) |
| Age | 0.0703 (-0.0176, 0.1583) | 0.1170 | 420 (42.00%) | NS [0.0438 [-0.0496, 0.1371)] | NS [0.3576] |  |
| a-syn | -0.0013 (-0.0026, -0.0001) | 0.0418 | 586 (58.60%) | NS | NS | 93 (9.30%) |
| BMI | 0.1663 (-0.0164, 0.3490) | 0.0744 | 491 (49.10%) | NS | NS | 8 (0.80%) |
| Clinical Site (US) | 1.3103 (-0.9846, 3.6052) | 0.2628 | 258 (25.80%) | \* | \* | 8 (0.80%) |
| ESS | -0.1126 (-0.3657, 0.1405) | 0.3828 | 187 (18.70%) | \* | \* | 6 (0.60%) |
| GDS | 0.1774 (-0.1827, 0.5375) | 0.3338 | 242 (24.20%) | \* | \* | 12 (1.20%) |
| Gender (Male) | 2.4710 (0.7000, 4.2419) | 0.0063 | 804 (80.40%) | 1.9042 (0.0550, 3.7535) | 0.0436 |  |
| HY (HY = 1) | 0.4147 (-1.5579, 2.3873) | 0.6800 | 96 (9.60%) | \* | \* | 14 (1.40%) |
| Mean Striatum | -2.8628 (-5.0818, -0.6438) | 0.0115 | 774 (77.40%) | -2.5317 (-4.8456, -0.2179) | 0.0320 | 161 (16.10%) |
| MoCA | -0.3288 (-0.6919, 0.0342) | 0.0758 | 480 (48.00%) | NS | NS | 0 (0%) |
| MODSEADL | -0.1035 (-0.2676, 0.0606) | 0.2162 | 290 (29.00%) | \* | \* | 2 (0.20%) |
| p-tau | -0.0325 (-0.1989, 0.1339) | 0.7014 | 79 (7.90%) | \* | \* | 41 (4.10%) |
| PIGD Score | -2.6909 (-7.0477, 1.6658) | 0.2258 | 343 (34.30%) | \* | \* | 24 (2.40%) |
| RBDSQ | 0.1870 (-0.1406, 0.5146) | 0.2628 | 248 (24.80%) | \* | \* | 5 (0.50%) |
| SBP | -0.0445 (-0.1103, 0.0213) | 0.1850 | 315 (31.50%) | -0.0779 (-0.1468, -0.0090) | 0.0267 | 1 (0.10%) |
| SCOPA-AUT | 0.1521 (0.0022, 0.3021) | 0.0467 | 578 (57.80%) | 0.1413 (-0.0174, 0.3000) | 0.0809 | 12 (1.20%) |
| STAI | -0.0220 (-0.0701, 0.0260) | 0.3680 | 190 (19.00%) | \* | \* | 8 (0.80%) |
| t-tau | -0.0071 (-0.0221, 0.0079) | 0.3549 | 196 (19.60%) | \* | \* | 30 (3.00%) |
| Tremor Score | -0.7227 (-3.4978, 2.0524) | 0.6094 | 103 (10.30%) | \* | \* | 8 (0.80%) |
| UPSIT |  | 0.0231 |  | NS | NS |  |
|  | UPSIT (Hyposmia) | -1.3548 (-4.3740, 1.6644) |  | 657 (65.70%) |  |  | 107 (10.70%) |
|  | UPSIT (Anosmia) | 1.1790 (-1.9744, 4.3324) |  |  |  |  |  |
|  | Baseline Duration |  |  |  | 0.1596 (0.0204, 0.2988) | 0.0246 |  |
|  | Baseline UPDRS Tot Off |  |  |  | -0.1345 (-0.2097, -0.0593) | 0.0005 |  |
| **MDS-UPDRS Total Score On - Change from Baseline**       | abeta | -0.0030 (-0.0056, -0.0003) | 0.0280 | 657 (65.70%) | -0.0028 (-0.0054, -0.0001) | 0.0407 | 75 (7.50%) |
| Age | 0.0702 (-0.0171, 0.1574) | 0.1150 | 401 (40.10%) | NS [0.0354 (-0.0585, 0.1293)] | NS [0.4596] |  |
| a-syn | -0.00128 (-0.00254, -0.00001) | 0.0481 | 572 (57.20%) | NS | NS | 93 (9.30%) |
| BMI | 0.1064 (-0.0751, 0.2878) | 0.2503 | 270 (27.00%) | \* | \* | 14 (1.40%) |
| Clinical Site (US) | 1.1314 (-1.0920, 3.3548) | 0.3183 | 250 (25.00%) | \* | \* | 15 (1.50%) |
| ESS | -0.1255 (-0.3775, 0.1266) | 0.3290 | 220 (22.00%) | \* | \* | 6 (0.60%) |
| GDS | 0.1825 (-0.1748, 0.5398) | 0.3165 | 269 (26.90%) | \* | \* | 13 (1.30%) |
| Gender (Male) | 2.1592 (0.3992, 3.9191) | 0.0162 | 725 (72.50%) | 1.6797 (-0.1650, 3.5244) | 0.0743 |  |
| HY (HY = 1) | 0.2263 (-1.7404, 2.1929) | 0.8214 | 94 (9.40%) | \* | \* | 27 (2.70%) |
| Mean Striatum | -2.0453 (-4.2259, 0.1352) | 0.0660 | 511 (51.10%) | NS | NS | 0 (0%) |
| MoCA | -0.3836 (-0.7439, -0.0233) | 0.0370 | 621 (62.10%) | -0.3482 (-0.7439, 0.0474) | 0.0844 | 14 (1.40%) |
| MODSEADL | -0.0715 (-0.2356, 0.0927) | 0.3931 | 165 (16.50%) | \* | \* | 3 (0.30%) |
| p-tau | -0.0429 (-0.2074, 0.1216) | 0.6090 | 113 (11.30%) | \* | \* | 40 (4.00%) |
| PIGD Score | -2.6408 (-6.9570, 1.6754) | 0.2302 | 331 (33.10%) | \* | \* | 13 (1.30%) |
| RBDSQ | 0.2229 (-0.1010, 0.5467) | 0.1773 | 347 (34.70%) | NS | NS | 2 (0.20%) |
| SBP | -0.0356 (-0.1019, 0.0307) | 0.2918 | 227 (22.70%) | \* | \* | 1 (0.10%) |
| SCOPA-AUT | 0.1396 (-0.0117, 0.2909) | 0.0705 | 514 (51.40%) | 0.1487 (-0.0105, 0.3079) | 0.0671 | 7 (0.70%) |
| STAI | -0.0209 (-0.0687, 0.0270) | 0.3925 | 152 (15.20%) | \* | \* | 6 (0.60%) |
| t-tau | -0.0059 (-0.0207, 0.0089) | 0.4370 | 168 (16.80%) | \* | \* | 31 (3.10%) |
| Tremor Score | -1.2634 (-4.0437, 1.5168) | 0.3728 | 180 (18.00%) | \* | \* | 1 (0.10%) |
| UPSIT |  | 0.0379 | 591 (59.10%) | NS | NS | 49 (4.90%) |
| UPSIT (Hyposmia) | -0.2285 (-3.1993, 2.7422) |  |  |  |  |  |
| UPSIT (Anosmia) | 2.1034 (-1.0028, 5.2096) |  |  |  |  |  |
| Baseline Duration |  |  |  | 0.0980 (-0.0414, 0.2374) | 0.1681 |  |
| Baseline UPDRS Tot On |  |  |  | -0.1990 (-0.2721, -0.1260) | <0.0001 |  |
| **MDS-UPDRS Part III Score Off - Change from Baseline**       | abeta | -0.0021 (-0.0040, -0.0002) | 0.0278 | 656 (65.60%) | -0.0021 (-0.0039, -0.0002) | 0.0284 | 109 (10.90%) |
| Age | 0.0436 (-0.0184, 0.1057) | 0.1680 | 346 (34.60%) | NS [0.0306 (-0.0339, 0.0951)] | NS [0.3522] |  |
| a-syn | -0.0007 (-0.0016, 0.0002) | 0.1191 | 430 (43.00%) | NS | NS | 11 (1.10%) |
| BMI | 0.0350 (-0.0942, 0.1641) | 0.5953 | 154 (15.40%) | \* | \* | 42 (4.20%) |
| Clinical Site (US) | 2.0422 (0.4481, 3.6364) | 0.0121 | 736 (73.60%) | 1.1952 (0.2462, 3.5841) | 0.0246 | 254 (25.40%) |
| ESS | -0.1108 (-0.2855, 0.0639) | 0.2134 | 292 (29.20%) | \* | \* | 3 (0.30%) |
| GDS | -0.0308 (-0.2753, 0.2136) | 0.8046 | 95 (9.50%) | \* | \* | 20 (2.00%) |
| Gender (Male) | 0.8969 (-0.3577, 2.1515) | 0.1610 | 347 (34.70%) | NS [0.6142 (0.6671, 1.8955)] | NS [0.3471] |  |
| HY (HY = 1) | -1.0725 (-2.5206, 0.3757) | 0.1464 | 358 (35.80%) | NS | NS | 0 (0%) |
| Mean Striatum | -1.8003 (3.3585, -0.2422) | 0.0236 | 674 (67.40%) | -1.6005 (-3.1793, -0.0218) | 0.0469 | 72 (7.20%) |
| MoCA | -0.1538 (-0.4106, 0.1029) | 0.2400 | 267 (26.70%) | \* | \* | 6 (0.60%) |
| MODSEADL | -0.1204 (-0.2290, -0.0118) | 0.0299 | 625 (62.50%) | NS | NS | 68 (6.80%) |
| p-tau | -0.0221 (-0.1395, 0.0954) | 0.7124 | 59 (5.90%) | \* | \* | 12 (1.20%) |
| PIGD Score | -0.3681 (-3.2093, 2.4731) | 0.7993 | 157 (15.70%) | \* | \* | 64 (6.40%) |
| RBDSQ | 0.0027 (-0.2208, 0.2262) | 0.9810 | 53 (5.30%) | \* | \* | 15 (1.50%) |
| SBP | -0.0165 (-0.0626, 0.0297) | 0.4836 | 110 (11.00%) | \* | \* | 2 (0.20%) |
| SCOPA-AUT | 0.0940 (-0.0032, 0.1912) | 0.0580 | 550 (55.00%) | NS | NS | 16 (1.60%) |
| STAI | -0.0235 (-0.0563, 0.0093) | 0.1604 | 341 (34.10%) | NS | NS | 3 (0.30%) |
| t-tau | -0.0027 (-0.0133, 0.0079) | 0.6199 | 86 (8.60%) | \* | \* | 12 (1.20%) |
| Tremor Score | 0.9381 (-1.0772, 2.9534) | 0.3612 | 190 (19.00%) | \* | \* | 11 (1.10%) |
| UPSIT |  | 0.3080 | 235 (23.50%) | \* | \* | 7 (0.70%) |
| UPSIT (Hyposmia) | 0.1747 (-1.9715, 2.3209) |  |  |  |  |  |
| UPSIT (Anosmia) | 1.1258 (-1.1170, 3.3686) |  |  |  |  |  |
| Baseline Duration |  |  |  | 0.1377 (0.0405, 0.2349) | 0.0055 |  |
| Baseline UPDRS III Off |  |  |  | -0.1849 (-0.2567, -0.1131) | <0.0001 |  |
| **MDS-UPDRS Part III Score On - Change from Baseline**       | abeta | -0.0018 (-0.0037, 0.0001)) | 0.0629 | 512 (51.20%) | -0.0019 (-0.0038, -0.0001) | 0.0417 | 8 (0.80%) |
| Age | 0.0319 (-0.0302, 0.0939) | 0.3138 | 224 (22.40%) | \* [0.0320 (-0.0323, 0.0963)] | \* [0.3288] |  |
| a-syn | -0.0007 (-0.0016, 0.0002) | 0.1053 | 438 (43.80%) | NS | NS | 15 (1.50%) |
| BMI | 0.0248 (-0.1037, 0.1533) | 0.7052 | 139 (13.90%) | \* | \* | 47 (4.70%) |
| Clinical Site (US) | 1.9321 (0.3793, 3.4848) | 0.0148 | 704 (70.40%) | 1.9541 (0.3446, 3.5636) | 0.0174 | 209 (20.90%) |
| ESS | -0.1465 (-0.3214, 0.0284) | 0.1005 | 439 (43.90%) | -0.1572 (-0.3351, 0.0207) | 0.0833 | 5 (0.50%) |
| GDS | -0.0309 (-0.2751, 0.2133) | 0.8042 | 128 (12.80%) | \* | \* | 54 (5.40%) |
| Gender (Male) | 0.9623 (-0.2899, 2.2146) | 0.1319 | 384 (38.40%) | NS [0.7485 (-0.5336, 2.0306)] | NS [0.2522] |  |
| HY (HY = 1) | -0.8419 (-2.2934, 0.6096) | 0.2554 | 243 (24.30%) | \* | \* | 1 (0.10%) |
| Mean Striatum | -0.8990 (-2.4458, 0.6477) | 0.2544 | 260 (26.00%) | \* | \* | 3 (0.30%) |
| MoCA | -0.2205 (-0.4774, 0.0363) | 0.0923 | 447 (44.70%) | NS | NS | 3 (0.30%) |
| MODSEADL | -0.0820 (-0.1914, 0.0274) | 0.1418 | 282 (37.30%) | NS | NS | 0 (0%) |
| p-tau | -0.0442 (-0.1616, 0.0733) | 0.4611 | 124 (12.40%) | \* | \* | 6 (0.60%) |
| PIGD Score | -1.4680 (-4.2889, 1.3528) | 0.3074 | 251 (25.10%) | \* | \* | 22 (2.20%) |
| RBDSQ | 0.0004 (-0.2225, 0.2233) | 0.9970 | 55 (5.50%) | \* | \* | 11 (1.10%) |
| SBP | -0.0027 (-0.0495, 0.0440) | 0.9087 | 55 (5.50%) | \* | \* | 12 (1.20%) |
| SCOPA-AUT | 0.0610 (-0.0382, 0.1603) | 0.2281 | 238 (23.80%) | \* | \* | 0 (0%) |
| STAI | -0.0318 (-0.0645, 0.0010) | 0.0576 | 528 (52.80%) | NS | NS | 32 (3.20%) |
| t-tau | -0.0039 (-0.0145, 0.0067) | 0.4726 | 138 (13.80%) | \* | \* | 9 (0.90%) |
| Tremor Score | 0.2344 (-1.7997, 2.2686) | 0.8211 | 56 (5.60%) | \* | \* | 21 (2.10%) |
| UPSIT |  | 0.2298 | 288 (28.80%) | \* | \* | 11 (1.10%) |
| UPSIT (Hyposmia) | 0.9171 (-1.2029, 3.0372) |  |  |  |  |  |
| UPSIT (Anosmia) | 1.7453 (-0.4735, 3.9642) |  |  |  |  |  |
| Baseline Duration |  |  |  | 0.1239 (0.0252, 0.2227) | 0.0140 |  |
| Baseline UPDRS III On |  |  |  | -0.2497 (-0.3199, -0.1795) | <0.0001 |  |
| **Mean Putamen - % Change from Baseline**       | abeta | 0.0060 (0.0005, 0.0116) | 0.0339 | 675 (67.50%) | 0.0055 (-0.0001, 0.0111) | 0.0526 | 127 (12.70%) |
| Age | -0.0892 (-0.2735, 0.0951) | 0.3424 | 259 (25.90%) | \* [-0.1052 (-0.2983, 0.0878)] | \* [0.2847] |  |
| a-syn | 0.0018 (-0.0010, 0.0045) | 0.2020 | 318 (31.80%) | \* | \* | 5 (0.50%) |
| BMI | -0.1643 (-0.5459, 0.2173) | 0.3980 | 220 (22.00%) | \* | \* | 14 (1.40%) |
| Clinical Site (US) | 2.7520 (-1.9649, 7.4689) | 0.2524 | 274 (27.40%) | \* | \* | 2 (0.20%) |
| ESS | -0.4840 (-1.0132, 0.0453) | 0.0730 | 466 (46.60%) | NS | NS | 2 (0.20%) |
| GDS | -0.2271 (-0.9408, 0.4865) | 0.5322 | 185 (18.50%) | \* | \* | 8 (0.80%) |
| Gender (Male) | 1.0072 (-2.7172, 4.7317) | 0.5956 | 125 (12.50%) | \* [1.9656 (-1.9023, 5.8335)] | \* [0.3186] |  |
| HY (HY = 1) | 2.3358 (-1.3313, 6.0029) | 0.2115 | 314 (31.40%) | \* | \* | 3 (0.30%) |
| Mean Putamen | -15.7191 (-22.0544, -9.3838) | <0.0001 | 992 (99.20%) | -17.1848 (-23.6240, -10.7457) | <0.0001 | 978 (97.80%) |
| MoCA | 0.0555 (-0.7111, 0.8221) | 0.8870 | 71 (7.10%) | \* | \* | 19 (1.90%) |
| MODSEADL | 0.2015 (-0.1061, 0.5091) | 0.1988 | 277 (27.70%) | NS | NS | 3 (0.30%) |
| p-tau | 0.1671 (-0.1953, 0.5295) | 0.3656 | 215 (21.50%) | \* | \* | 26 (2.60%) |
| PIGD Score | -2.3506 (-10.3081, 5.6070) | 0.5621 | 192 (19.20%) | \* | \* | 48 (4.80%) |
| RBDSQ | -0.9601 (-1.6256, -0.2946) | 0.0048 | 833 (83.30%) | -1.0837 (-1.7730, -0.3945) | 0.0021 | 560 (56.00%) |
| SBP | 0.0891 (-0.0485, 0.2268) | 0.2040 | 259 (25.90%) | \* | \* | 0 (0%) |
| SCOPA-AUT | -0.1534 (-0.4520, 0.1452) | 0.3135 | 328 (32.80%) | \* | \* | 29 (2.90%) |
| STAI | -0.0342 (-0.1312, 0.0627) | 0.4881 | 271 (27.10%) | \* | \* | 29 (2.90%) |
| t-tau | 0.0137 (-0.0191, 0.0465) | 0.4125 | 207 (20.70%) | \* | \* | 36 (3.60%) |
| Tremor Score | 2.6902 (-2.8959, 8.2762) | 0.3447 | 229 (22.90%) | \* | \* | 0 (0%) |
| UPSIT |  | 0.2316 | 373 (37.30%) | \* | \* | 40 (4.00%) |
| UPSIT (Hyposmia) | 2.9512 (-3.3957, 9.2982) |  |  |  |  |  |
| UPSIT (Anosmia) | -0.2143 (-6.8186, 6.3899) |  |  |  |  |  |
| Baseline Duration |  |  |  | 0.0858 (-0.1971, 0.3686) | 0.5517 |  |
| **Mean Striatum - % Change from Baseline**       | abeta | 0.0045 (0.0003, 0.0088) | 0.0360 | 614 (61.40%) | 0.0039 (-0.0003, 0.0081) | 0.0708 | 98 (9.80%) |
| Age | -0.0925 (-0.2329, 0.0480) | 0.1960 | 304 (30.40%) | NS [-0.1038 (-0.2499, 0.0423)] | NS [0.1630] |  |
| a-syn | 0.0010 (-0.0011, 0.0031) | 0.3575 | 203 (20.30%) | \* | \* | 5 (0.50%) |
| BMI | -0.0315 (-0.3089, 0.2458) | 0.8231 | 86 (8.60%) | \* | \* | 23 (2.30%) |
| Clinical Site (US) | 0.8462 (-2.7074, 4.3998) | 0.6396 | 149 (14.90%) | \* | \* | 36 (3.60%) |
| ESS | -0.1990 (-0.6012, 0.2032) | 0.3308 | 214 (21.40%) | \* | \* | 5 (0.50%) |
| GDS | -0.3795 (-0.9135, 0.1545) | 0.1629 | 329 (32.90%) | NS | NS | 13 (1.30%) |
| Gender (Male) | -0.0264 (-2.8404, 2.7876) | 0.9853 | 81 (8.10%) | \* [0.8985 (-1.9990, 3.7959)] | \* [0.5420] |  |
| HY (HY = 1) | 1.8940 (-0.8534, 4.6414) | 0.1758 | 334 (33.40%) | NS | NS | 5 (0.50%) |
| Mean Striatum | -5.2263 (-8.7353, -1.7174) | 0.0036 | 674 (67.40%) | -6.2020 (-9.7532, -2.6508) | 0.0007 | 654 (65.40%) |
| MoCA | -0.1489 (-0.7256, 0.4278) | 0.6117 | 95 (9.50%) | \* | \* | 7 (0.70%) |
| MODSEADL | 0.2744 (0.0451, 0.5038) | 0.0192 | 687 (68.70%) | 0.2417 (0.0037, 0.4797) | 0.0466 | 95 (9.50%) |
| p-tau | 0.1045 (-0.1661, 0.3751) | 0.4475 | 208 (20.80%) | \* | \* | 18 (1.80%) |
| PIGD Score | -3.1364 (-9.1145, 2.8417) | 0.3026 | 312 (31.20%) | \* | \* | 57 (5.70%) |
| RBDSQ | -0.9296 (-1.4272, -0.4321) | 0.0003 | 958 (95.80%) | -1.0030 (-1.5268, -0.4793) | 0.0002 | 853 (85.30%) |
| SBP | 0.0959 (-0.0083, 0.2002) | 0.0711 | 488 (48.80%) | 0.1154 (0.0074, 0.2235) | 0.0364 | 35 (3.50%) |
| SCOPA-AUT | -0.1796 (-0.3985, 0.0393) | 0.1075 | 485 (48.50%) | NS | NS | 48 (4.80%) |
| STAI | -0.0252 (-0.0981, 0.0478) | 0.4978 | 288 (28.80%) | \* | \* | 35 (3.50%) |
| t-tau | 0.0087 (-0.0160, 0.0334) | 0.4904 | 196 (19.60%) | \* | \* | 39 (3.90%) |
| Tremor Score | 2.0497 (-2.1528, 6.2523) | 0.3378 | 220 (22.00%) | \* | \* | 2 (0.20%) |
| UPSIT |  | 0.2199 | 400 (40.00%) | \* | \* | 37 (3.70%) |
| UPSIT (Hyposmia) | 2.0668 (-2.7102, 6.8438) |  |  |  |  |  |
| UPSIT (Anosmia) | -0.4112 (-5.3757, 4.5532) |  |  |  |  |  |
| Baseline Duration |  |  |  | 0.0442 (-0.1683, 0.2568) | 0.6824 |  |

\*variables depicted below the dotted line are those forced into the model regardless of their p-value

**Supplementary Table 3**. Univariate and multivariate relationships of all potential baseline and 1-year-change predictors to key outcomes in mixed models. All multivariate models adjusted for baseline age, gender, baseline disease duration, as well as baseline of the outcome variable(depicted below the dotted line). In addition, baseline variables found to be significantly associated with the outcome (see supplementary table 1 and table 3) were also included in the model\*. Selection percentages for mean putamen and mean striatum are reported out of the iterations with model convergence. CV, cross-validation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **STP Predictor Models** |  | **STP Backwards Selection Final Model** |  |
| **Outcome** | **Predictor** | **Effect Estimate** |  | **Pseudo-Univariate CV Selections** | **Effect Estimate** |  | **Multivariate CV Selections** |
| (95% CI) | p-value | N (%) | (95% CI) | p-value | N (%) |
| **MDS-UPDRS Total Score Off - Change from Baseline** | a-syn | -0.0001 (-0.0038, 0.0036) | 0.9447 | 135 (13.50%) | \* | \* | 52 (5.20%) |
| BMI | -0.4240 (-1.3076, 0.4596) | 0.3457 | 271 (27.10%) | \* | \* | 52 (5.20%) |
| ESS | 0.3753 (-0.0571, 0.8077) | 0.0886 | 453 (45.30%) | NS | NS | 1 (0.10%) |
| MDS-UPDRS Total Score Off | 0.5403 (0.4228, 0.6578) | < 0.0001 | 1000 (100%) | 0.5403 (0.4228, 0.6578) | < 0.0001 | 999 (99.90%) |
| Mean Striatum | -5.8551 (-14.0603, 2.3501) | 0.1612 | 325 (32.50%) | NS | NS | 6 (0.60%) |
| MODSEADL | -0.1456 (-0.3666, 0.0754) | 0.1957 | 322 (32.20%) | NS | NS | 194 (19.40%) |
| PIGD Score | 13.7955 (8.7532, 18.8378) | < 0.0001 | 989 (98.90%) | NS | NS | 125 (12.50%) |
| SCOPA-AUT | 0.5398 (0.1953, 0.8843) | 0.0022 | 880 (88.00%) | NS | NS | 47 (4.70%) |
| Tremor Score | 8.7921 (3.3900, 14.1942) | 0.0015 | 875 (87.50%) | NS | NS | 74 (7.40%) |
|  | Baseline Abeta |  |  |  | -0.0027 (-0.0066, 0.0012) | 0.1725 |  |
|  | Baseline Age |  |  |  | 0.0213 (-0.1163, 0.1589) | 0.7605 |  |
|  | Gender (Male) |  |  |  | 3.0895 (0.3104, 5.8687) | 0.0295 |  |
|  | Baseline disease duration |  |  |  | 0.3506 (0.1457, 0.5554) | 0.0009 |  |
|  | Baseline MDS-UPDRS Total Score Off |  |  |  | -0.1986 (-0.3149, -0.0822) | 0.0009 |  |
|  | Baseline Mean Striatum |  |  |  | 0.1031 (-3.4696, 3.6758) | 0.9547 |  |
|  | Baseline SBP |  |  |  | -0.0225 (-0.1205, 0.0754) | 0.6509 |  |
|  | Baseline Scopa |  |  |  | 0.1244 (-0.1095, 0.3582) | 0.2960 |  |
| **MDS-UPDRS Total Score On - Change from Baseline**       | a-syn | -0.0022 (-0.0058, 0.0014) | 0.2238 | 313 (31.30%) | \* | \* | 8 (0.80%) |
| BMI | -0.2217 (-1.0999, 0.6565) | 0.6200 | 172 (17.20%) | \* | \* | 18 (1.80%) |
| ESS | 0.4344 (0.0177, 0.8511) | 0.0411 | 574 (57.40%) | NS | NS | 9 (0.90%) |
| MDS-UPDRS Total Score On | 0.5217 (0.4214, 0.6221) | < 0.0001 | 1000 (100%) | 0.4985 (0.3953, 0.6018) | < 0.0001 | 999 (99.90%) |
| Mean Striatum | -4.8251 (-12.0051, 2.3548) | 0.1872 | 318 (31.80%) | NS | NS | 4 (0.40%) |
| MODSEADL | -0.0775 (-0.2917, 0.1366) | 0.4770 | 188 (18.80%) | \* | \* | 159 (15.90%) |
| PIGD Score | 11.4838 (6.3234, 16.6443) | < 0.0001 | 974 (97.40%) | NS | NS | 59 (5.90%) |
| SCOPA-AUT | 0.7130 (0.3974, 1.0285) | < 0.0001 | 978 (97.80%) | 0.3629 (0.0623, 0.6636) | 0.0181 | 344 (34.40%) |
| Tremor Score | 8.6491 (3.4112, 13.8869) | 0.0013 | 874 (87.40%) | NS | NS | 137 (13.70%) |
|  | Baseline Abeta |  |  |  | -0.0039 (-0.0077, -0.0002) | 0.0414 |  |
|  | Baseline Age |  |  |  | 0.0478 (-0.0866, 0.1823) | 0.4848 |  |
|  | Gender (Male) |  |  |  | 4.0093 (1.3736, 6.6451) | 0.0030 |  |
|  | Baseline Disease Duration |  |  |  | 0.2087 (0.0075, 0.4098) | 0.0421 |  |
|  | Baseline MDS-UPDRS Total Score On |  |  |  | -0.2384 (-0.3492, -0.1276) | < 0.0001 |  |
|  | Baseline MoCA |  |  |  | -0.0822 (-0.6537, 0.4892) | 0.7774 |  |
|  | Baseline Scopa |  |  |  | 0.3266 (0.0766, 0.5767) | 0.0106 |  |
| **MDS-UPDRS Part III Score Off - Change from Baseline**       | a-syn | 0.0001 (-0.0024, 0.0026) | 0.9219 | 92 (9.20%) | \* | \* | 39 (3.90%) |
| BMI | -0.5705 (-1.1535, 0.0125) | 0.0551 | 487 (48.70%) | -0.5612 (-1.1287, 0.0063) | 0.0526 | 21 (2.10%) |
| ESS | 0.1592 (-0.1322, 0.4505) | 0.2832 | 231 (23.10%) | \* | \* | 3 (0.30%) |
| MDS-UPDRS Part III Score Off | 0.5443 (0.4324, 0.6562) | < 0.0001 | 1000 (100%) | 0.5155 (0.3875, 0.6436) | < 0.0001 | 1000 (100.00%) |
| Mean Striatum | -1.7207 (-7.2708, 3.8294) | 0.5422 | 138 (13.80%) | \* | \* | 14 (1.40%) |
| MODSEADL | -0.0826 (-0.2317, 0.0665) | 0.2767 | 234 (23.40%) | \* | \* | 160 (16.00%) |
| PIGD Score | 8.7090 (5.2699, 12.1481) | < 0.0001 | 981 (98.10%) | 3.4132 (-0.0565, 6.8829) | 0.0538 | 206 (20.60%) |
| SCOPA-AUT | 0.1094 (-0.1085, 0.3273) | 0.3240 | 198 (19.80%) | \* | \* | 8 (0.80%) |
| Tremor Score | 6.6023 (2.9899, 10.2146) | 0.0004 | 931 (93.10%) | NS | NS | 57 (5.70%) |
|  | Baseline abeta |  |  |  | -0.0018 (-0.0045, 0.0009) | 0.1971 |  |
|  | Baseline Age |  |  |  | 0.0066 (-0.0870, 0.1002) | 0.8896 |  |
|  | Clinical Site (US) |  |  |  | 1.8213 (-1.0536, 4.6962) | 0.2134 |  |
|  | Baseline Disease Duration |  |  |  | 0.1558 (0.0152, 0.2965) | 0.0301 |  |
|  | Gender (Male) |  |  |  | 1.7635 (-0.1740, 3.7009) | 0.0743 |  |
|  | Baseline MDS-UPDRS Part III Score Off |  |  |  | -0.1690 (-0.2823, -0.0557) | 0.0036 |  |
|  | Baseline Mean Striatum |  |  |  | 0.2018 (-2.2333, 2.6370) | 0.8705 |  |
| **MDS-UPDRS Part III Score On - Change from Baseline**       | a-syn | -0.0013 (-0.0038, 0.0013) | 0.3275 | 240 (24.00%) | \* | \* | 8 (0.80%) |
| BMI | -0.4668 (-1.0665, 0.1329) | 0.1267 | 411 (41.10%) | NS | NS | 16 (1.60%) |
| ESS | 0.1578 (-0.1457, 0.4612) | 0.3075 | 210 (21.00%) | \* | \* | 3 (0.30%) |
| MDS-UPDRS Part III Score On | 0.5132 (0.4149, 0.6115) | <0.0001 | 1000 (100%) | 0.5132 (0.4149, 0.6115) | <0.0001 | 1000 (100.00%) |
| Mean Striatum | -0.7738 (-5.7476, 4.2001) | 0.7599 | 97 (9.70%) | \* | \* | 13 (1.30%) |
| MODSEADL | 0.0156 (-0.1329, 0.1642) | 0.8363 | 94 (9.40%) | \* | \* | 27 (2.70%) |
| PIGD Score | 5.8192 (2.1699, 9.4685) | 0.0019 | 833 (83.30%) | NS | NS | 41 (4.10%) |
| SCOPA-AUT | 0.1718 (-0.0417, 0.3852) | 0.1144 | 421 (42.1%) | NS | NS | 6 (0.60%) |
| Tremor Score | 5.7443 (2.0657, 9.4229) | 0.0023 | 846 (84.60%) | NS | NS | 146 (14.60%) |
|  | Baseline abeta |  |  |  | -0.0025 (-0.0051, 0.0001) | 0.0633 |  |
|  | Baseline Age |  |  |  | 0.0608 (-0.0294, 0.1511) | 0.1859 |  |
|  | Clinical Site (US) |  |  |  | 2.1511 (-0.1819, 4.4841) | 0.0706 |  |
|  | Baseline Disease Duration |  |  |  | 0.0959 (-0.0433, 0.2351) | 0.1764 |  |
|  | Baseline ESS |  |  |  | 0.0975 (-0.1640, 0.3589) | 0.4641 |  |
|  | Gender (Male) |  |  |  | 2.1375 (0.3268, 3.9482) | 0.0208 |  |
|  | Baseline MDS-UPDRS Part III Score On |  |  |  | -0.2610 (-0.3659, -0.1562) | <0.0001 |  |
| **Mean Putamen - % Change from Baseline**       | a-syn | 0.0007 (-0.0049, 0.0064) | 0.7976 | 13 (1.39%)\* | \* | \* | 1 (0.11%)\* |
| BMI | 1.0462 (-0.2473, 2.3397) | 0.1125 | 255 (26.07%)\* | NS | NS | 4 (0.42%)\* |
| ESS | -0.3707 (-0.9910, 0.2495) | 0.2403 | 150 (15.29%)\* | \* | \* | 0 (0%)\* |
| Mean Putamen | 65.3565 (51.7328, 78.9803) | <0.0001 | 977 (100%)\* | 65.3565 (51.7328, 78.9803) | <0.0001 | 947 (100%)\* |
| MODSEADL | 0.1195 (-0.2106, 0.4497) | 0.4765 | 41 (4.19%)\* | \* | \* | 1 (0.11%)\* |
| PIGD Score | 4.0421 (-4.9224, 13.0066) | 0.3752 | 116 (12.05%)\* | \* | \* | 0 (0%)\* |
| SCOPA-AUT | -0.1674 (-0.6377, 0.3030) | 0.4842 | 94 (9.58%)\* | \* | \* | 8 (0.84%)\* |
| Tremor Score | 3.8611 (-4.5071, 12.2294) | 0.3642 | 65 (6.74%)\* | \* | \* | 0 (0%)\* |
|  | Baseline abeta |  |  |  | 0.0026 (-0.0031, 0.0083) | 0.3648 |  |
|  | Baseline Age |  |  |  | 0.0726 (-0.1272, 0.2724) | 0.4749 |  |
|  | Baseline Disease Duration |  |  |  | 0.2063 (-0.0795, 0.4921) | 0.1564 |  |
|  | Gender (Male) |  |  |  | 0.3810 (-3.5834, 4.3453) | 0.8500 |  |
|  | Baseline Mean Putamen |  |  |  | -4.0574 (-3.9405, 12.0554) | 0.3187 |  |
|  | Baseline RBDSQ |  |  |  | -0.8478 (-1.5740, -0.1216) | 0.0223 |  |
| **Mean Striatum - % Change from Baseline**       | a-syn | 0.0032 (-0.0022, 0.0085) | 0.2055 | 99 (10.54%) | \* | \* | 0 (0%) |
| BMI | 0.6979 (-0.4675, 1.8634) | 0.2117 | 197 (20.14%) | \* | \* | 2 (0.21%) |
| ESS | -0.2556 (-0.8134, 0.3022) | 0.3314 | 96 (9.81%) | \* | \* | 0 (0%) |
| Mean Striatum | 44.9234 (35.1309, 54.7160) | <0.0001 | 971 (100%) | 45.9181 (35.9935, 55.8427) | <0.0001 | 934 (100%) |
| MODSEADL | 0.1472 (-0.1835, 0.4778) | 0.3403 | 88 (9.00%) | \* | \* | 0 (0%) |
| PIGD Score | 3.7638 (-4.4192, 11.9467) | 0.3253 | 136 (14.09%) | \* | \* | 0 (0%) |
| SCOPA-AUT | -0.3456 (-0.7662, 0.0751) | 0.0971 | 344 (35.17%) | -0.3251 (-0.6948, 0.0446) | 0.0786 | 10 (1.07%) |
| Tremor Score | 1.2758 (-6.5618, 9.1135) | 0.7212 | 30 (3.12%) | \* | \* | 1 (0.11%) |
|  | Baseline abeta |  |  |  | 0.0029 (-0.0023, 0.0080) | 0.2407 |  |
|  | Baseline Age |  |  |  | 0.0212 (-0.1560, 0.1984) | 0.7950 |  |
|  | Baseline Disease Duration |  |  |  | 0.1466 (-0.1075, 0.4007) | 0.2277 |  |
|  | Gender (Male) |  |  |  | -0.0081 (-3.5220, 3.5059) | 0.9960 |  |
|  | Baseline Mean Striatum |  |  |  | 7.2315 (2.2679, 12.1951) | 0.0088 |  |
|  | Baseline MODSEADL |  |  |  | 0.1733 (-0.1194, 0.4659) | 0.2165 |  |
|  | Baseline RBDSQ |  |  |  | -0.6229 (-1.2910, 0.0452) | 0.0645 |  |
|  | Baseline SBP |  |  |  | 0.0140 (-0.1195, 0.1476) | 0.8195 |  |