## Supplementary Table 1. Change in clinical characteristics among LRRK2 G2019S carriers with vs without baseline hyposmia

|                          | LRRK2 G2019S carriers: baseline hyposmia | LRRK2 G2019S carriers: no baseline hyposmia | p value |
|--------------------------|------------------------------------------|---------------------------------------------|---------|
|                          | Baseline (N = 20)                        | Year 1 (N = 20)                             | Year 2 (N = 13) | Baseline (N = 156) | Year 1 (N = 152) | Year 2 (N = 127) | Group × time effect |
| MDS-UPDRS total score    | 11.2 (11.3)                              | 11.4 (11.7)                                | 12.1 (14.7)     | 8.6 (6.9)          | 9.4 (7.9)        | 9.1 (8.5)        | 0.6752              |
| MDS-UPDRS Part I         | 5.0 (5.0)                                | 5.5 (5.8)                                  | 5.0 (5.6)       | 4.8 (3.7)          | 5.0 (3.9)        | 4.7 (3.9)        | 0.8862              |
| MDS-UPDRS Part II        | 2.3 (3.9)                                | 2.9 (5.4)                                  | 2.7 (4.1)       | 1.0 (1.9)          | 1.2 (2.2)        | 1.3 (2.4)        | 0.3978              |
| MDS-UPDRS Part III       | 4.7 (5.9)                                | 4.2 (3.9)                                  | 3.8 (5.3)       | 2.9 (3.8)          | 3.1 (4.1)        | 3.2 (4.9)        | 0.6363              |
| MOCA total score, mean (SD; range) | 26.9 (2.3; 22-30) | 26.8 (2.6; 22-30) | 27.2 (2.3; 23-30) | 26.8 (2.5; 18-30) | 27.1 (2.5; 16-30) | 26.9 (2.5; 20-30) | 0.9816              |
| GDS-15 total score       | 2.2 (3.9)                                | 1.9 (3.7)                                  | 2.5 (4.6)       | 1.7 (2.2)          | 1.5 (1.8)        | 1.6 (2.0)        | 0.9198              |
| SCOPA-AUT total score    | 10.8 (6.2)                               | 11.2 (8.5)                                 | 11.3 (7.0)      | 8.2 (6.0)          | 8.5 (6.3)        | 8.3 (6.1)        | 0.4918              |
| Orthostatic systolic blood pressure drop | -3.1 (12.8) | -0.2 (11.2) | -1.3 (7.8) | 0.5 (10.7) | -1.0 (11.2) | -0.4 (10.9) | 0.7726              |
| Orthostatic diastolic blood pressure drop | -5.2 (6.4) | -3.9 (7.8) | -2.3 (7.0) | -3.5 (7.8) | -4.7 (7.6) | -3.3 (7.6) | 0.4713              |
| State trait anxiety score | 64.9 (18.6) | 63.0 (22.6) | 70.9 (24.2) | 60.9 (16.5) | 59.8 (15.8) | 59.5 (15.8) | 0.5323              |
| QUIP (≥ 1 disorder)      | 5 (28%)                                   | 5 (29%)                                    | 3 (27%)         | 41 (26%)           | 40 (27%)         | 41 (33%)         | 0.8616              |
| Epworth sleepiness scale (≥ 10) | 2 (11%) | 4 (22%) | 3 (27%) | 16 (10%) | 13 (9%) | 11 (9%) | 0.0686              |
| RBDSQ (≥ 5)              | 2 (12%)                                   | 4 (25%)                                    | 1 (9%)          | 36 (23%)           | 31 (21%)         | 26 (21%)         | 0.6986              |

Data are mean (SD) or n (%) unless otherwise stated. Hyposmia defined by UPSIT ≤ 15th percentile for age and sex. Five or fewer participants per group missed any one assessment except for the non-hyposmia group at year 2 (seven missed the SCOPA-AUT). p values were found using generalized estimating equations modeling the change from baseline at follow-up (continuous outcomes) or the binary response at follow-up (categorical outcomes) while adjusting for the baseline value. Significance level for comparisons is p < 0.0038 (after Bonferroni correction). UPSIT=University of Pennsylvania Smell Identification Test. MDS-UPDRS=Movement Disorder Society Unified Parkinson’s Disease Rating Scale. MOCA=Montreal Cognitive Assessment. GDS-15=Geriatric Depression Scale (15-item). SCOPA-AUT=Scales for Outcomes in Parkinson’s Disease-Autonomic. QUIP=Questionnaire for Impulsive-Compulsive Disorders in Parkinson’s Disease. RBDSQ=REM Sleep Behavior Disorder Screening Questionnaire.
Supplementary Table 2. Change in DAT specific binding ratios among LRRK2 G2019S carriers and comparison to healthy controls at baseline

|                | LRRK2 G2019S carriers | Healthy controls | p values |
|----------------|------------------------|------------------|----------|
|                | Baseline (N = 176)     | Year 2 (N = 140) | Baseline (N = 185) | Time effect | Group effect |
| Caudate SBR    | 2.97 (0.57; 1.38-4.30) | 2.89 (0.61; 1.27-4.59) | 2.99 (0.61; 1.56-5.20) | 0.1929      | 0.0520       |
| Putamen SBR    | 2.09 (0.51; 0.67-3.70) | 2.03 (0.54; 0.89-3.23) | 2.15 (0.54; 0.88-3.89) | 0.0865      | 0.0237       |
| Striatum SBR   | 2.53 (0.52; 1.17-4.00) | 2.46 (0.56; 1.12-3.85) | 2.57 (0.55; 1.22-4.24) | 0.0910      | 0.0292       |

Data are mean (SD; range). DAT imaging results were missing for 8 LRRK2 G2019S carriers at baseline, 18 LRRK2 G2019S carriers at year 2, and 1 healthy control at baseline. p values were found using one-sample t-tests assessing the percent change from baseline to year 2 among LRRK2 G2019S carriers (time effect) and inverse probability weighting methods comparing LRRK2 G2019S at year 2 vs healthy controls at baseline while adjusting for age and sex (group effect). Significance level for comparisons is p < 0.0167 (after Bonferroni correction). DAT=dopamine transporter. SBR=specific binding ratio.
Supplementary Table 3. Change in urine bis(monoacylglycerol)phosphate among *LRRK2* G2019S carriers

|                  | LRRK2 G2019S carriers | p value |          |          |          |
|------------------|------------------------|---------|----------|----------|----------|
|                  | Baseline (N = 176)     | Year 1  (N = 172) | Year 2  (N = 140) | Time effect |
| **Total di-18:1-BMP** | 17.5 (13.4)           | 18.6 (17.0)           | 20.3 (17.7) | 0.1523    |
| Median (min, max) | 14.2 (0.9, 72.0)      | 13.0 (2.3, 99.0)      | 14.8 (1.7, 76.5) |          |
| **Total di-22:6-BMP** | 77.3 (46.5)         | 81.0 (52.8)            | 85.5 (55.2) | 0.3304    |
| Median (min, max) | 63.8 (10.6, 245.6)    | 67.2 (7.5, 289.6)     | 72.6 (15.8, 320.8) |          |
| **2,2'-di-22:6 BMP**  | 61.3 (40.3)          | 61.9 (42.5)            | 65.9 (42.9) | 0.8168    |
| Median (min, max)  | 49.6 (8.1, 248.2)     | 47.0 (2.2, 244.2)     | 57.1 (12.8, 252.8) |          |
| **Missing BMP**      | 33                    | 32                   | 54       |           |

Data are mean (SD). p values were found using generalized estimating equations modeling the change from baseline at follow-up. Significance levels for comparisons are p < 0.0167 (after Bonferroni correction). BMP= bis(monoacylglycerol)phosphate.
|                          | LRRK2 G2019S carriers: phenoconverters | LRRK2 G2019S carriers: non-converters |
|--------------------------|----------------------------------------|----------------------------------------|
|                          | Baseline (N = 5)                       | Year 1 (N = 5)                         | Year 2 (N = 3)                          | Baseline (N = 171) | Year 1 (N = 167) | Year 2 (N = 137) |
| MDS-UPDRS total score    | 22.0 (12.7)                            | 24.2 (11.7)                            | 35.0 (19.3)                            | 8.5 (6.9)         | 9.1 (7.9)        | 8.8 (8.1)        |
| MDS-UPDRS Part I         | 6.4 (5.5)                              | 6.0 (2.9)                              | 7.7 (2.5)                              | 4.7 (3.8)         | 5.0 (4.2)        | 4.7 (4.1)        |
| MDS-UPDRS Part II        | 5.4 (3.4)                              | 5.2 (3.2)                              | 6.0 (2.6)                              | 1.0 (2.1)         | 1.3 (2.6)        | 1.3 (2.5)        |
| MDS-UPDRS Part III       | 10.2 (6.3)                             | 13.0 (7.2)                             | 21.3 (15.8)                            | 2.9 (3.8)         | 2.9 (3.6)        | 2.8 (3.7)        |
| MOCA total score, mean (SD; range) | 25.5 (2.6; 23-29) | 25.5 (1.0; 25-27) | 25.7 (0.6; 25-26) | 26.8 (2.4; 18-30) | 27.1 (2.5; 16-30) | 26.9 (2.4; 20-30) |
| GDS-15 total score       | 1.4 (1.7)                              | 1.2 (1.3)                              | 0.7 (1.2)                              | 1.7 (2.4)         | 1.5 (2.1)        | 1.7 (2.3)        |
| SCOPA-AUT total score    | 10.6 (7.7)                             | 10.4 (4.7)                             | 12.3 (2.5)                             | 8.4 (6.0)         | 8.7 (6.6)        | 8.5 (6.3)        |
| Orthostatic systolic blood pressure drop | -2.0 (9.9)                            | 1.0 (12.7)                             | -2.0 (7.8)                             | 0.2 (11.0)        | -0.9 (11.1)      | -0.4 (10.7)      |
| Orthostatic diastolic blood pressure drop | -0.6 (5.0)                            | -5.2 (4.3)                             | -4.7 (5.5)                             | -3.8 (7.7)        | -4.6 (7.7)       | -3.2 (7.6)       |
| State trait anxiety score| 64.6 (21.0)                            | 58.8 (12.8)                            | 58.7 (9.0)                             | 61.3 (16.6)       | 60.2 (16.7)      | 60.5 (16.9)      |
| QUIP (≥ 1 disorder)      | 0 (0%)                                 | 0 (0%)                                 | 1 (33%)                                | 46 (27%)          | 45 (28%)         | 43 (32%)         |
| Epworth sleepiness scale (≥ 10) | 0 (0%)                                 | 0 (0%)                                 | 0 (0%)                                 | 18 (11%)          | 17 (10%)         | 14 (11%)         |
| RBDSQ (≥ 5)              | 0 (0%)                                 | 1 (20%)                                | 0 (0%)                                 | 38 (23%)          | 34 (21%)         | 27 (20%)         |

Data are mean (SD) or n (%) unless otherwise stated. Among phenoconverters, there were no missing values except for the MOCA (one missing value at baseline and year 1); among non-converters, five or fewer participants missed any one assessment except for at year 1 (six missed the MDS-UPDRS total score and RBDSQ) and year 2 (10 missed the SCOPA-AUT; six missed the STAI). MDS-UPDRS=Movement Disorder Society Unified Parkinson’s Disease Rating Scale. MOCA=Montreal Cognitive Assessment. GDS-15=Geriatric Depression Scale (15-item). SCOPA-AUT=Scales for Outcomes in Parkinson’s Disease-Autonomic. QUIP=Questionnaire for Impulsive-Compulsive Disorders in Parkinson’s Disease. RBDSQ=REM Sleep Behavior Disorder Screening Questionnaire.
| Group | p values |
|-------|----------|
| LRRK2 G2019S carriers (N = 176) | LRRK2 R1441G carriers (N = 16) |
| Sex (female) | 0.7935 |
| Age, mean (SD; range) | 0.0035 |
| Education (≤ 12 years) | 0.0312 |
| Ethnicity (Hispanic/Latino) | <.0001 |
| Race (White) | <.0001 |
| Family history of PD (first-degree) | 0.2286 |
| UPSIT raw score, mean (SD; range) | <.0001 |
| UPSIT percentile | <.0001 |
| ≤ 15th | 8 (50%) |
| 16th-50th | 8 (50%) |
| > 50th | 0 (0%) |
| DAT deficit | 0.4437 |
| Missing DAT results | 0 |
| Caudate SBR | 0.7824 |
| Putamen SBR | 0.2469 |
| Striatum SBR | 0.5036 |
| MDS prodromal criteria (> 80%) | 0.6036 |

Data are mean (SD) or n (%) unless otherwise stated. DAT deficit defined as < 65% age/sex-expected lowest putamen SBR. Ethnicity and race were missing for one LRRK2 G2019S subject. p values for SBR measures were adjusted for age and sex using inverse probability weighting; all other p values were found using Fisher’s exact and Wilcoxon rank-sum tests. UPSIT=University of Pennsylvania Smell Identification Test. DAT=dopamine transporter. SBR=specific binding ratio. MDS=International Parkinson and Movement Disorder Society.