Supplementary Table 1. Sex differences in homocysteine and urate levels in PD and controls over 54 months

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Control** | | | | | | **PD** | | | | | |
|  |  | **Male** | | **Female** | | **t/z** | **p** | **Male** | | **Female** | | **t/z** | **p** |
|  |  | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** |
| *Urate (µmol/L)* | |  |  |  |  |  |  |  |  |  |  |  |  |
|  | *Baseline* | 372.5 | 71.9 | 280.7 | 68.8 | 6.3 | **<0.001** | 330.5 | 68.2 | 252.5 | 69.2 | 6.5 | **<0.001** |
|  | *18 month* | 391.3 | 78.7 | 286.1 | 69.2 | 6.5 | **<0.001** | 326.3 | 72.1 | 257.7 | 65.5 | 5.5 | **<0.001** |
|  | *36 months* | 374.5 | 65.6 | 284.9 | 66.6 | 5.7 | **<0.001** | 325.3 | 71.5 | 264.9 | 70.3 | 4.2 | **<0.001** |
|  | *54 months* | - | - | - | - | - | - | 340.0 | 104.4 | 221.1 | 55.7 | 4.4 | **<0.001** |
| *Homocysteine (µmol/L)* | |  |  |  |  |  |  |  |  |  |  |  |  |
|  | *Baseline* | 10.2 | 3.5 | 8.8 | 2.9 | -2.4 | **0.018** | 11.3 | 3.8 | 10.6 | 3.8 | -1.1 | 0.274 |
|  | *18 month* | 11.7 | 3.4 | 10.6 | 3.9 | -2.0 | 0.046 | 12.8 | 3.9 | 11.5 | 3.8 | -1.9 | 0.054 |
|  | *36 months* | 13.1 | 4.7 | 11.3 | 3.4 | -1.8 | 0.069 | 13.9 | 3.6 | 13.8 | 6.9 | -1.7 | 0.094 |
|  | *54 months* | - | - | - | - | - | - | 14.6 | 5.0 | 11.4 | 2.3 | -2.2 | **0.027** |

PD, Parkinson’s disease; SD, standard deviation. Significant results are highlighted in bold.

**Supplementary Table 2. Baseline predictors of motor severity and global cognition over 54 months using linear mixed effects modelling, adjusting for vascular risk factors and comorbidities**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | **β** | **SE** | **t** | **p-value** |  |
| **Predictors of MDS-UPDRS III** | |  |  |  |  |  |
| *Basic modela + urate* | |  |  |  |  |  |
|  | *Urate* | -0.02 | 0.02 | -1.01 | 0.316 |  |
|  | *Urate x Time* | 0.02 | 0.00 | 4.32 | **<0.001** | \*\*\* |
| *Basic modelb + homocysteine* | |  |  |  |  |  |
|  | *tHyc* | 0.36 | 0.29 | 1.26 | 0.211 | . |
|  | *tHyc x Time* | 0.46 | 0.12 | 3.94 | **<0.001** | \*\*\* |
| *Basic modelb + urate + homocysteine* | |  |  |  |  |  |
|  | *Urate* | -0.01 | 0.02 | -0.80 | 0.423 |  |
|  | *tHyc* | 0.45 | 0.30 | 1.50 | 0.136 | . |
|  | *Urate x Time* | 0.02 | 0.00 | 3.30 | **0.001** | \*\* |
|  | *tHyc x Time* | 0.32 | 0.12 | 2.59 | **0.010** | \* |
| **Predictors of MoCA** | |  |  |  |  |  |
| *Basic modelc + urate* | |  |  |  |  |  |
|  | *Urate* | 0.00 | 0.00 | -0.35 | 0.723 |  |
|  | *Urate x Time* | 0.00 | 0.00 | 1.44 | 0.150 |  |
| *Basic modeld + homocysteine* | |  |  |  |  |  |
|  | *tHyc* | 0.02 | 0.09 | 0.19 | 0.849 |  |
|  | *tHyc x Time* | 0.11 | 0.04 | 2.73 | 0.007 | \*\* |
| *Basic modeld+ urate + homocysteine* | |  |  |  |  |  |
|  | *Urate* | 0.00 | 0.00 | -0.67 | 0.502 |  |
|  | *tHyc* | 0.01 | 0.09 | 0.13 | 0.900 |  |
|  | *Urate x Time* | 0.00 | 0.00 | 1.02 | 0.311 |  |
|  | *tHyc x Time* | 0.11 | 0.04 | 2.51 | **0.013** | \* |

Motor severity determined by MDS-UPDRS III. Significant predictors highlighted in bold.

a Covariates included in model: age, sex, folate, B12, time, smoking status, type II diabetes, hypertension, ischemic heart disease, previous stoke or TIA, hypercholesterolemia, gout, folate x time and B12 x time

b Covariates included in model: age, sex, LEDD, folate, B12, time, smoking status, type II diabetes, hypertension, ischemic heart disease, previous stoke or TIA, hypercholesterolemia, gout, LEDD x time, folate x time and B12 x time Covariates included in model: age, years of education, motor severity, time and motor severity x time

c Covariates included in model: sex, age, MDS-UPDRS III, folate, B12, time, smoking status, type II diabetes, hypertension, ischemic heart disease, previous stoke or TIA, hypercholesterolemia, gout, MDS-UPDRS III, folate x time and B12 x time

d sex, age, LEDD, folate, B12, smoking status, type II diabetes, hypertension, ischemic heart disease, previous stoke or TIA, hypercholesterolemia, gout, time, LEDD x time, folate x time and B12 x time

MDS-UPDRS III, Movement Disorder Society Unified Parkinson’s Disease Rating Scale Part III; MoCA, Montreal Cognitive Assessment; LEDD, Levodopa equivalent daily dose; tHyc, serum homocysteine; TIA, transient ischemic attack.