Supplementary Online Content

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eMethods. Cognitive Assessment and Motor Progression Analysis

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Cognitive Assessment and Motor Progression Analysis

Parkinson's Disease Cognitive Genetics Consortium – Cognitive Assessment

Seven sites from the Parkinson's Disease Cognitive Genetics Consortium (PDCGC) participated in this study: Rush University Medical Center, and the University of Pennsylvania, Feinstein Institute for Medical Research, Johns Hopkins University, Mayo Clinic Jacksonville, and Pacific Northwest Morris K. Udall Centers of Excellence for Parkinson's Disease Research. The Pacific Northwest Udall Center consists of two sites, one in Seattle, WA (Veterans Affairs Puget Sound Health Care System/University of Washington) and the other in Portland, OR (Portland Veterans Affairs Medical Center/Oregon Health and Science University).

All participants underwent detailed psychometric testing under the supervision of a neurologist, psychiatrist, or a neuropsychologist experienced in the assessment of patients with PD. The neuropsychological battery administered to participants has been described elsewhere and includes tests of global cognition, learning and memory, verbal fluency, working memory/executive function, and visuospatial abilities.[1, 2] Raw scores were converted to standard z-scores using published age-adjusted normative data from controls when available.[3-7] The cognitive data from participants enrolled at PANUC-Seattle, PANUC-Portland, Johns Hopkins University, the University of Pennsylvania, and Rush University were reviewed at diagnostic consensus conferences, and participants were classified as having no cognitive impairment, mild cognitive impairment, or dementia using previously described procedures.[8-10]

Statistical Analysis-Motor Progression

To assess the association between *GBA* genotype and rate of motor progression while accounting for the effects of dopamine replacement therapy (DRT), we performed a two-stage, adjusted-outcome regression. In the first stage, a linear mixed effect (LME) model was used to obtain adjusted MDS-UPDRS III scores; in the second stage, the effect of genotype on MDS-UPDRS III performance was estimated using multiple linear regression. First, we modeled the association between MDS-UPDRS III score and levodopa equivalent dose (LED), controlling for sex, age, and disease duration at each assessment. A random intercept for subject was included to account for the correlation between repeated (first, last) scores for an individual. The residuals from this LME model yielded adjusted MDS-UPDRS III scores that account for subject characteristics and LED. Next, a linear regression model was fit to estimate the association between *GBA* genotype and the adjusted MDS-UPDRS III score at the last assessment, using the adjusted MDS-UPDRS III score at the first assessment, the follow-up time between assessments, and study site as covariates. The resulting regression coefficient for genotype is the estimated difference in the adjusted MDS-UPDRS III score at the last assessment comparing *GBA* carriers to non-carriers with the same adjusted MDS-UPDRS III score at the first assessment and the same follow-up time between assessments. A significant coefficient indicates that genotype is associated with rate of motor symptom progression. A P-value < 0.05 was considered significant.

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