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Association of GBA Genotype With Motor and Functional Decline in Patients With Newly Diagnosed Parkinson Disease

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Study Question

Are variants in the *GBA* gene associated with the evolution of motor and functional impairment in patients with newly diagnosed Parkinson disease (PD)?

What Is Known and What This Paper Adds

GBA mutations are the most important known genetic risk factors for PD. This investigation's results provide evidence for an association between *GBA* variants and faster progression of motor and functional impairment in patients with PD.

Methods

For these longitudinal analyses, the investigators analyzed data from 440 patients with PD (60.7% male; mean baseline age, 69.9 ± 9.6 years) who participated in any of 3 cohort studies: the Norwegian ParkWest study, the Swedish NYPUM study, and the Scottish PINE study. Recruitment for these studies occurred between 2002 and 2009. Laboratory personnel used a combination of whole exome sequencing and various PCR assays to detect *GBA* variants in genomic DNA extracted from peripheral blood samples, and the participants underwent assessments at baseline and follow-up timepoints with Unified PD Rating Scale (UPDRS) sections designed to assess motor impairments and activities of daily living (ADL). The investigators used mixed linear regression models to analyze relationships between *GBA* genotypes and longitudinal changes in UPDRS scores.

Results and Study Limitations

Overall, 53 patients carried *GBA* mutations. Relative to the patients with idiopathic PD, those with *GBA* mutations experienced faster annual increases in UPDRS scores for motor impairments and ADL deficits. The present study's limitations include having few patients with specific *GBA* variants, which precluded analyses of the effects of specific variants, and relying on linear models, which might not have captured changes in score progression due to medication usage.

Table Between-Group Differences in Predicted Annual UPDRS Score Changes

Group	Mean annual change (95% confidence interval) in UPDRS scores for	
	Motor impairment	ADL deficits
Patients with *GBA* mutations	2.2 points/y (1.3–3.1 points/y)	1.5 points/y (1.1–2.0 points/y)
Patients with idiopathic PD	1.3 points/y (1.1–1.6 points/y)	1.0 points/y (0.9–1.1 points/y)

Study Funding and Competing Interests

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A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.

