Supplemental Methods

Multivariate regression analysis of subgroups

Due to the variety of recruitment practices, available data, and laboratory capabilities of the multiple study centers involved, we opted to follow up our results from the Mantel-Haenszel procedure with a series of multivariate logistic regression models. We partitioned our analysis into pre-specified subgroups stratified by study center, Ashkenazi status and sequencing-depth. Independent variables of mutations N370S and L444P were then assessed in subsequent iterations of these models to evaluate associations with Parkinson disease. Logistic regressions included all samples with complete outcome, predictor and covariate data; missing data was the only exclusion criterion. Regression models in Ashkenazi samples were adjusted for site, and in non-Ashkenazi samples were adjusted for self-reported ethnicity. In these models, ethnicity and site were considered collinear. Cases from Haifa were only included in the logistic regression models as the lack of controls excluded their inclusion in the Mantel-Haenszel analysis.

While results from this multivariate regression modeling across subgroups are described in the paper, a detailed summary of these models are shown in the table below. These ORs were generally larger for comparisons among Ashkenazi and than non-Ashkenazi subjects for L444P and N370S risk across all sequencing levels (p-values < 0.01), although interaction analyses in combined multivariate models (including both Ashkenazi and non-Ashkenazi) utilizing an identical covariate set showed the interactions between Ashkenazi-status and either mutation to be non-significant.

Supplemental table 1: Detailed results from regression analyses

Non-Ashkenazi cases and controls

Mutation	Sequencing depth of coverage in the GBA region	N in Model (% cases)	OR	95% CI		P-value
Any mutation	full	2632 (59.64)	6.51	3.62	11.74	<0.001
Any mutation	6-9 mutations	5039 (50.06)	5.75	3.31	9.99	<0.001
N370S	full	2632 (59.64)	4.48	1.28	15.6	0.019
N370S	2 mutations	5039 (50.06)	3.27	1.55	6.87	0.002
L444P	full	2632 (59.64)	8.31	2.92	23.6	<0.001
L444P	6-9 mutations	5039 (50.06)	8.99	3.79	21.35	<0.001
Any mutation	any	8174 (51.71)	6.16	4.15	9.15	<0.001
N370S	any	8174 (51.71)	3.3	1.79	6.1	<0.001
L444P	any	8174 (51.71)	9.68	4.98	18.83	<0.001
E326K	any	1567 (66.82)	0.66	0.27	1.58	0.349
T369M	any	1562 (66.25)	0.59	0.25	1.38	0.022

Ashkenazi cases and controls

Mutation	N in Model (%	OR	95% CI		P-value

		cases)				
Any mutation	full	242 (72.72)	3.37	0.974	11.64	0.055
Any mutation	6-9 mutations	901 (64.37)	7.42	4.08	13.52	<0.001
N370S	Full	242 (72.72)	3.66	0.82	16.32	0.089
N370S	6-9 mutations	901 (64.37)	6.03	3.06	11.89	<0.001
L444P	6-8 mutations	901 (64.37)	5.11	0.641	40.76	0.124
Any mutation	Any	1143 (66.72)	6.48	3.78	11.09	<0.001
N370S	Any	1143 (66.72)	5.62	3.04	10.39	<0.001
L444P	Any	1143 (66.72)	4.95	0.621	39.38	0.131
E326K	Any	242 (72.72)	0.4	0.024	6.62	0.52
T369M	Any	242 (72.72)	0.17	0.015	1.98	0.16

*The following values were underpowered and therefore are not reported in this table; in non Ashkenazi subjects, semi coverage for any mutation, N370S or L444P; in Ashkenazi subjects, partial coverage for any mutation, N370S or L444P, and full coverage for L444P.

+ Coverage: full=sequencing of all *GBA* exons; 2 mutations=screening for N370S and L444P only; 6-9 mutations= screening for N370S, L444P, and IVS2+1g>a, c.84insG, V394L, D409H, R463C, Rec, and R496H