Supplemental Online Content

Ortega RA, Wang C, Raymond D, et al. Association of dual *LRRK2* G2019S and *GBA* variation with Parkinson disease progression. *JAMA Netw Open*. 2021;4(4):e215845. doi:10.1001/jamanetworkopen.2021.5845

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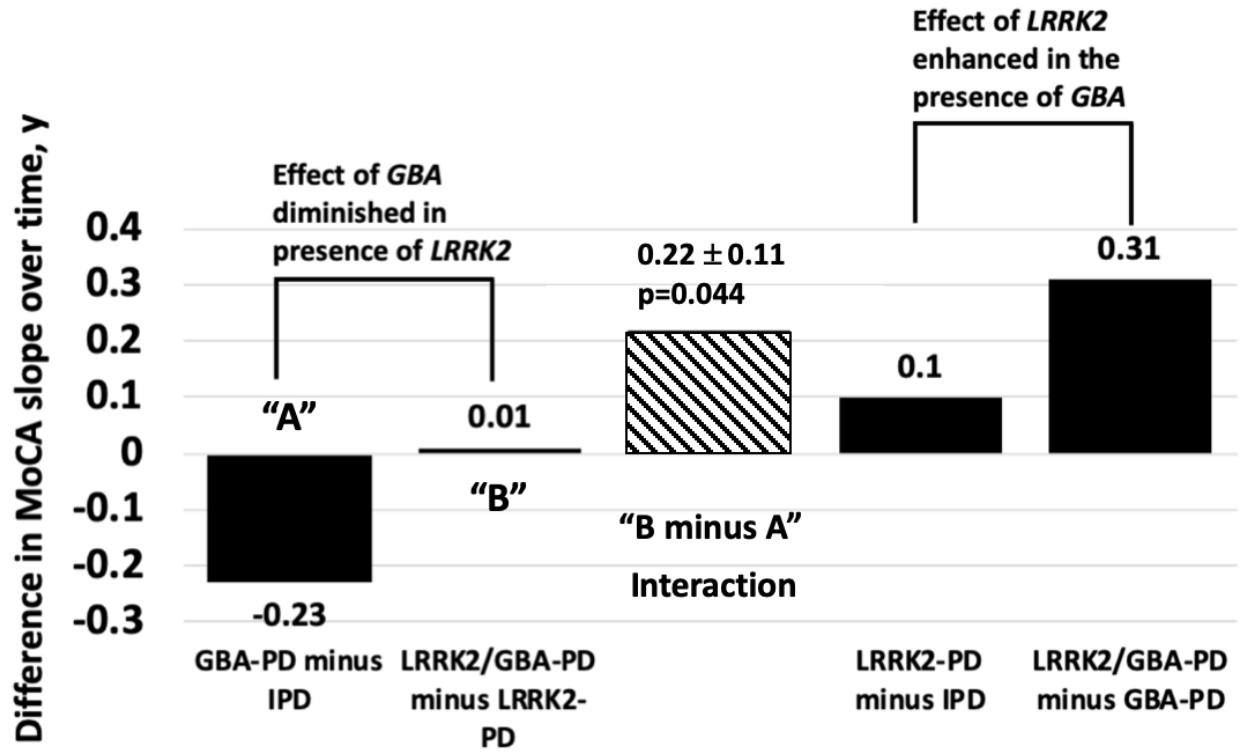
eTable. Interaction Between *LRRK2* and *GBA* for Rate of MoCA Decline

	Estimate: B ± SE[1]
Interaction effect between *LRRK2* and *GBA* mutations on the rate of cognitive progression*: B minus A**: Difference in presence of *LRRK2* - difference in absence of *LRRK2* ** As well as D minus C: Difference in presence of *GBA* – difference in absence of *GBA*	 0.22 ± 0.11 points/year p=0.044
Effect of *GBA* mutations on non-*LRRK2*-G2019S carriers: Decline among *GBA*-PD Decline among idiopathic PD A: Difference in absence of *LRRK2*-G2019S: *GBA*-PD minus idiopathic PD	 -0.52 ± 0.09 points/year -0.29 ± 0.05 points/year -0.23 ± 0.08 points/year p=0.005
Effect of *GBA* mutations on *LRRK2*-G2019S carriers: Decline among *LRRK2/GBA*-PD Decline among *LRRK2*-PD B: Difference in presence of *LRRK2*-G2019S: *LRRK2/GBA*-PD minus *LRRK2*-PD	 -0.21 ± 0.06 points/year -0.19 ± 0.06 points/year 0.01 ± 0.07 points/year p=0.845
Effect of *LRRK2* mutations on non-*GBA* carriers Decline among *LRRK2*-PD Decline among idiopathic PD C: Difference in absence of *GBA*:	 -0.21 ± 0.06 points/year -0.29 ± 0.05 points/year 0.10 ± 0.06 points/year

LRRK2-PD minus idiopathic PD	p=0.080
Effect of *LRRK2* mutations on *GBA* carriers: Decline among *LRRK2*/*GBA*-PD Decline among *GBA*-PD D: Difference in presence of *GBA-PD*: *LRRK2*/*GBA*-PD minus *GBA*-PD	 -0.21 ± 0.06 points/year -0.52 ± 0.09 points/year 0.31 ± 0.092 points/year p<0.001

[1] This table demonstrates the requisite estimates involved in deriving the interaction effect between *LRRK2* and *GBA* mutations on the rate of cognitive progression. The interaction effect can be estimated by subtracting the effect of harboring a *GBA* mutation on rate of cognitive decline among non-*LRRK2*-G2019S mutation carriers (e.g. slopes in *GBA*-PD minus idiopathic PD) from the effect of harboring a *GBA* mutation on the rate of cognitive decline among *LRRK2*-G2019S mutation carriers (e.g. slopes in *LRRK2*/*GBA*-PD minus *LRRK2*-PD). Similarly, it could be estimated by subtracting the effect of harboring a *LRRK2* mutation on rate of cognitive decline among non-*GBA* mutation carriers (e.g. slopes in *LRRK2*-PD minus idiopathic PD) from the effect of harboring a *LRRK2* mutation on the rate of cognitive decline among *GBA* mutation carriers (e.g. slopes in *LRRK2*/*GBA*-PD minus *GBA*-PD).

eFigure. Interaction Between *LRRK2* and *GBA* for Rate of MoCA Decline



eFigure 1. The interaction effect can be estimated by subtracting the effect of harboring a *GBA* mutation on rate of cognitive decline among non-*LRRK2* mutation carriers (e.g. slopes in *GBA*-PD minus idiopathic PD) from the effect of harboring a *GBA* mutation on the rate of cognitive decline among *LRRK2* mutation carriers (e.g. slopes in *LRRK2*/*GBA*-PD minus *LRRK2*-PD). Similarly, it could be estimated by subtracting the effect of harboring a *LRRK2* mutation on rate of cognitive decline among non-*GBA* mutation carriers (e.g. slopes in *LRRK2*-PD minus idiopathic PD) from the effect of harboring a *LRRK2* mutation on the rate of cognitive decline among *GBA* mutation carriers (e.g. slopes in *LRRK2*/*GBA*-PD minus *GBA*-PD). See also Supplemental table 1.