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LRRK2 G2019S mutations may be increased in Puerto Ricans

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We read with interest the article by Shino et al. that reported a higher familial aggregation of Parkinson's Disease (PD) among Hispanics1. In their evaluation of incident PD cases in Northern California, they propose that there is an increased rate of genetic and/or shared environmental factors in this group. We are interested in identifying genetic risk factors among Hispanics in the United States, and performed a pilot study of the *LRRK2* G2019S mutation in Hispanic, non-Hispanic, and non-Jewish Caucasian subjects participating in genetics research at Beth Israel Medical Center in New York, who were seen initially as patients or self-referred for genetic studies. Our pilot work suggests that there may be a higher rate of G2019S mutations in Puerto Ricans, and supports that further evaluation of this population is warranted.

We analyzed G2019S mutations in 104 individuals who met strict criteria for idiopathic PD2. 19 were of Hispanic descent, and 8 of these were of Puerto Rican background. 85 were non-Hispanic non-Jewish Caucasians. Three cases with the *LRRK2* G/A mutation (2.85%)

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Dr. Cabassa has nothing to disclose.

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were identified. Two were of Puerto-Rican descent, constituting 25% (2/8) of all Puerto Ricans sampled. Both Puerto Rican cases were women, with onset at ages 53 and 42 years respectively. The latter had an uncle with PD and the former did not have a family history of parkinsonism. They were not known to be related. The third case was a man of Irish/German background, with onset at age 58 and a brother with PD. The frequency of mutations was greater in Puerto Ricans than non-Puerto Ricans, (25.0% vs. 1.0% Fischer's exact, p=0.01). Mean age at onset and gender did not differ between groups (Table 1). In a logistic regression model adjusting for age at onset of PD, the odds of carrying a G2019S mutation was still greater in the Puerto Rican PD cases compared with non-Puerto Ricans, although the confidence intervals were broad (OR=28.24, 95% CI: 2.16–368.67, p=0.011). While there was a trend, the difference in PD between all Hispanics (11.1%) and non-Hispanic Caucasians (1.16%) was not significant.

Puerto Ricans may be of a Spanish, Taino and Black African descent, and genetic admixture is not uncommon.3 The relative admixture in our cases was not known. Spanish colonization and immigration to Puerto Rico as well as Ashkenazi Jewish influence may contribute to the increased rate of G2019S mutations, as this mutation is increased in Spaniards4 as well as in Ashkenazi Jews2. It is of interest that a prior North American screen identified two cases with *LRRK2* mutations among twenty Hispanic individuals screened, one with the G2019S mutation and one with the R1441G mutation5. Of note, the Consortium of Risk for Early Onset Parkinson Disease (CORE-PD), a multicenter study of subjects with PD onset younger than 51 years did not report an increased rate of *LRRK2* G2019S mutations in Hispanics overall. However, both of their mutation positive cases were Puerto Rican6, and the subtotal of Puerto Rican cases was not indicated. *LRRK2* mutations do not appear to be at increased frequency in Mexicans.7

We did not screen for other *LRRK2* mutations, including the R1441G mutation, which is increased in Spaniards of Basque origin4. As descendants from the latter group settled in California and the Southwest, it is possible that this other *LRRK2* mutation may also account for increased rates in US Hispanics. Further, some of the increased familial aggregation noted in Hispanics may be due to parkin mutations, as these are increased in Hispanics in the US6.

The main limitation to our pilot data is the small number of Puerto Ricans sampled. However, our rate of G2019S mutation carriers in non-Jewish Caucasians is similar to that in other such mixed populations that include both sporadic and familial PD and early and late-onset PD. Thus further evaluation for *LRRK2* mutations in Hispanic populations in the US should be considered, in both early and late onset cases, as these may constitute an important etiology of PD, particularly among Puerto Ricans.

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Table 1

Demographics and Mutation Frequency

	All subjects (n=104)	All Hispanics (n=19)	Puerto Ricans (n=8)	Non-Puerto Rican Hispanics (n=11)	Non-Hispanic Caucasians (n=85)
Gender, % Female (n)	50.96% (53)	52.63% (10)	60% (6)	47.06% (8)	50.59% (43)
Age at PD onset, mean ± SD**	53.37±12.31	54.58±12.90	54.0 ± 12.32	55.0 ± 13.89	53.09 ± 12.23
LRRK2mutation, % positive (n)*	2.88% (3)	10.53% (2)	25% (2)	0% (0)	1.18% (1)
Family History of PD	31.37% (32/102)	22.22% (4/18)	25% (2/8)	20% (2/10)	33.33% (28/84)

* Proband reported family history of Parkinson disease in first, second or third degree relatives, data not available for three subjects;

** Age onset unknown for three subjects