Clinical and imaging characteristics of non-manifest LRRK2 and GBA carriers: The PPMI cohort
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Objective:
To examine baseline prevalence of Parkinson's disease (PD) clinical features and DAT abnormalities in a cohort of non-manifest carriers (NMC) of GBA and LRRK2 compared to Healthy controls (HC).

Background: Monogenetic forms of Parkinson's disease represent a unique and potentially informative subset of all PD cases. More information is needed regarding these cases, particularly in the period before signs of parkinsonism become manifest.

Design/Methods:
Parkinson's Progression Markers Initiative (PPMI) is a longitudinal ongoing controlled study of at baseline de novo PD participants, HC and carriers of PD relevant genetic mutations. All participants are assessed annually with a spectrum of motor and non-motor scales, DAT imaging and biologic variables.

Results:
The study enrolled 194 LRRK2 (91% G2019S) and 132 GBA(96 %N370S) NMCs via worldwide recruitment initiative. NMCs average age was 61.9(7.1), 60% female, 87% had first degree PD relative. 25% of LRRK2 and 9% of GBA NMCs had abnormal DAT scan. Compared to HC, both LRRK2 and GBA NMCs had higher scores on MDS-UPDRS Total, Part I, II, III and lower MOCA scores that were independent of DAT results. There was no difference in sleepiness and RBD scores in NMCs compared to HC. Hyposmia was significant only in LRRK2 and predicted abnormal DAT scan but not in GBA NMCs. GBA NMCs compared to LRRK2s had higher MDS-UPDRS Part I score but better hyposmia scores and no difference in RBD scores.

Conclusions: Our data demonstrate evidence of subtle PD motor and non-motor signs in NMCs that can precede DAT abnormalities and provide comparison between LRRK2 and GBA NMCs. Longitudinal data will be essential to establish risk factors for phenoconversion.