

Genome-Wide Polygenic Risk Score Identifies Individuals at Elevated Parkinson's Disease Risk (4286)

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Objective: Here, for the first time, we apply a genome-wide polygenic risk score approach using 6.2 million variants to compute a Parkinson's Disease (PD) genome-wide polygenic risk score (PD-GPRS).

Background: PD is the second most common and fastest-growing neurological disorder. Polygenic Risk Scores (PRS) using hundreds to thousands of PD-associated variants support polygenic heritability.

Design/Methods: PD-GPRS was computed via the LDpred algorithm using a European Genome Reference Panel and PD-GWAS summary statistics published by Nalls et al. 2019. PD-GPRS validation and testing used Accelerating Medicines Partnership – Parkinson's Disease (AMP-PD) and FinnGen Consortia genomic data from 1,654 PD Cases and 79,123 Controls.

Results: PD odds for the top 8%, 2.5%, and 1% of PD-GPRS were three-, four-, and seven times greater compared with lower percentiles, respectively ($p < 1e-10$). PD age of onset and MDS-UPDRS motor scores also differed by PD-GPRS decile. Enrichment for phagosome related, dopamine signaling, immune related, and neuronal signaling pathways was found for genes nearest high PD-GPRS variants identified by MAF analysis.

Conclusions: PD-GPRS offers a promising screening tool to identify high-risk individuals for preventive lifestyle or new drug therapy trials.

Reference

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