PARKINSON DISEASE

Five novel genetic loci identified to be associated with PD

A meta-analysis of data from five genome-wide association studies (GWAS), conducted by the International Parkinson Disease Genomics Consortium, has found 11 loci associated with Parkinson disease (PD), five of which are newly identified. According to the study's researchers, their findings may provide clues as to the underlying molecular causes of this movement disorder.

PD was long considered to be a non-genetic disease; however, the discovery of monogenic forms of this disorder (which account for 5–10% of all cases of PD) dispelled the earlier status quo. Several genetic variants that increase susceptibility to PD have also been discovered. Of note, the *MAPT* and *SCNA* genetic loci have consistently shown associations with PD in GWAS. A further four genetic loci—*BST1*, *LRKK2*, *GAK* and *HLA-DRB5*—have also demonstrated associations with this disorder in some studies.

The International Parkinson Disease Genomics Consortium set out to confirm the associations between the six previously identified loci and PD and to discover further genetic loci associated with this condition. To achieve these objectives, the consortium's researchers conducted a prospective meta-analysis of data from four previously reported PD GWAS and one additional dataset, which was

identified from The National Center for Biotechnology Information database of Genotypes and Phenotypes. Imputed sequence variants from samples in the 1000 Genomes Project were included in this discovery-phase analysis to increase its power. In total, the researchers analyzed 7,689,524 single-nucleotide polymorphisms (SNPs) in 5,333 case and 12,019 control samples from several European countries and the USA.

SNPs that passed genome-wide significance in the discovery phase were examined in the replication stage, which included 7,053 case and 9,007 control samples. From the replication analyses, 11 loci were identified that surpassed the threshold for genome-wide significance ($P < 5 \times 10^{-8}$), including the six previously identified loci and five novel loci—*ACMSD*, *STK39*, *MCCC1-LAMP3*, *SYT11* and *CCDC62-HIP1R*. The consortium's

researchers calculated that the population-attributable risk for all 11 loci combined was 60.3%.

As acknowledged by the consortium's researchers, GWAS have a number of limitations, including the fact that the detection of an association does not prove causality. In spite of these caveats, the researchers conclude that their meta-analysis—the first of its kind for data from PD GWAS—provides evidence that common genetic variation has an important etiological role in this movement disorder.

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