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Study investigates genetic variants' role in increasing Parkinson's disease risk

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Boston University School of Medicine (BUSM) investigators have led the first genome-wide evaluation of genetic variants associated with Parkinson's disease (PD). The study, which is published online in *PLOS ONE*, points to the involvement of specific genes and alterations in their expression as influencing the risk for developing PD.

Jeanne Latourelle, DSc, assistant professor of neurology at BUSM, served as the study's lead author and Richard H. Myers, PhD, professor of neurology at BUSM, served as the study's principal investigator and senior author.

A recent paper by the PD Genome Wide Association Study Consortium (PDGC) confirmed that an increased risk for PD was seen in individuals with genetic variants in or near the genes SNCA, MAPT, GAK/DGKQ, HLA and RIT2, but the mechanism behind the increased risk was not determined.

"One possible effect of the variants would be to change the manner in which a gene is expressed in the brains, leading to increased risk of PD," said Latourelle.

To investigate the theory, the researchers examined the relationship between PD-associated genetic variants and levels of gene expression in brain samples from the frontal cortex of 26 samples with known PD and 24 neurologically healthy control samples. Gene expression was determined using a microarray that screened effects of genetic variants

on the expression of genes located very close to the variant, called cis-effects, and genes that are far from the variant, such as those on a completely different chromosome, called trans-effects.

An analysis of the cis-effects showed that several genetic variants in the MAPT region showed a significant association to the expression of multiple nearby genes, including gene LOC644246, the duplicated genes LRRC37A and LRRC37A2 and the gene DCAKD. Significant cis-effects were also observed between variants in the HLA region on chromosome 6 and two nearby genes HLA-DQA1 and HLA-DQA1. An examination of trans-effects revealed 23 DNA sequence variations that reached statistical significance involving variants from the SNCA, MAPT and RIT2 genes.

"The identification of the specific altered genes in PD opens opportunities to further study them in model organisms or cell lines with the goal of identifying drugs which may rectify the defects as treatment for PD," said Myers.

More information: dx.plos.org/10.1371/journal.%20pone.0046199

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