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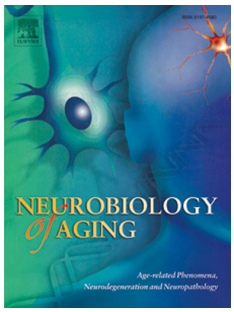

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Variants in *GBA*, *SNCA,* and *MAPT* Influence Parkinson Disease Risk, Age at Onset, and Progression

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Abstract

Multiple genetic variants have been linked to risk of Parkinson disease (PD), but known mutations do not explain a large proportion of the total PD cases. Similarly, multiple loci have been associated with PD risk by Genome-Wide Association Studies (GWAS). The influence that genetic factors confer upon phenotypic diversity remains unclear. Few studies have been performed to determine whether the GWAS loci are also associated with age at onset (AAO) or motor progression. We used two PD case-control datasets (Washington University and the Parkinson's Progression Markers Initiative) to determine whether polymorphisms located at the GWAS top hits (*GBA*, *ACMSD/TMEM163*, *STK39*, *MCCC1/LAMP3*, *GAK/TMEM175*, *SNCA*, and *MAPT*) show association with AAO or motor progression. We found associations between SNPs at the *GBA* and *MAPT* loci and PD AAO and progression. These findings reinforce the complex genetic basis of PD and suggest that distinct genes and variants explain the genetic architecture of PD risk, onset, and progression.