Associations of Genetic SNPs With AD, Neuropathology, and Gene Expression Offers Novel Insight Into AD

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Alzheimer’s disease (AD), the most common form of dementia, affects approximately 5.8 million Americans aged 65 or older. AD causes brain atrophy and memory loss due to buildup of ß-amyloid plaques and hyperphosphorylated tau tangles. Exploring Single Nucleotide Polymorphisms (SNPs) associated with AD-related phenotypes for association with AD neuropathology/risk can reveal important AD markers and therapeutic targets. The experiment determined if candidate genetic SNPs are associated with specific neuropathological features of AD and expression of specific genes. In phase one, data was downloaded from 3 AMP-AD datasets (AD-knowledge portal), genotypes of 9 targeted SNPs were selected from these datasets and tested for association with amyloid and tau deposits (Braak/Thal). In phase two, APOC1 and NECTIN2 SNPs were genotyped from AD/non-AD DNA samples present in the research facility using TaqMan assays, and tested for associations with AD neuropathology/risk. In phase three, a gene-SNP pair was identified using the GTEx Database and previous eQTL data, 50 AD samples were selected with SNP carriers/non-carriers, cDNA was created, qPCR was performed, then the APOC1 SNP was tested for association with APOC1 gene expression. The results validated the NECTIN2 SNP significantly associated with higher Braak/Thal levels, and showed the NECTIN2 SNP associated with AD. The APOC1 SNP, however, doesn’t associate with AD, the expression of APOC1 in Carriers vs. Non-Carriers of AD patients, but may initiate CAA. The results suggest the NECTIN2 SNP may be responsible in AD pathology/risk and provide more insight into genetic roles of the formation of AD.

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