Investigating cis-SNP/mRNA level associations of candidate Alzheimer's disease genes in different brain regions of patients

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The levels of many gene transcripts have been shown to be influenced by genetic variants. We hypothesize that some Alzheimer’s disease (AD) risk variants may act via modifying gene expression levels in the brain. To test the presence of AD risk variants that modify transcript levels, we measured mRNA levels of 13 AD candidate genes in the cerebellum and temporal cortex of pathologically-confirmed AD subjects and performed association studies with their cis-SNP genotypes residing within ±1cM flanking regions of these genes. Transcript levels were measured in the cerebella of 197 AD patients and in the temporal cortex of 88 ADs, using quantitative PCR. Genotypes of the cis-SNPs were obtained from the genome-wide associate study (GWAS) of these subjects was performed on the Illumina Hap 300 platform. Multivariate linear regression analyses was performed within PLINK using age, gender and ApoE genotypes as covariates. We identified 195 cis-SNP/mRNA associations in the cerebellum of ADs and 153 from their temporal cortex with nominally significant p-values<0.05. Our results suggest that the selected AD candidate genes may contain variants that influence their expression in the brain.

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