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ABSTRACT: Genes coding for the neuronal nicotinic acetylcholine receptor genes emerged as the top replicable associations with smoking behaviors from GWAS a little over a decade ago. In particular, a non-synonymous single nucleotide polymorphism

(SNP) in *CHRNA5*, rs16969968, leads to an amino acid change (D398N) which affects the pharmacological effects of the receptor. The goal of this analysis is to determine whether we can identify other variants/genes that may interact with SNP rs16969968. Using the UK Biobank, we used PLINK to perform a genome-wide gene-by-gene interaction analysis for cigarettes per day. We used raw (M=18.22, SD= 10.16) and log-transformed (M= 1.20, SD= 0.25) cigarette per day scores from 116,257 unrelated current and former smokers. Our preliminary results found no significant interaction effects between rs16969968 and genome-wide SNPs with this phenotype. It is possible that even with a large sample size such as UK Biobank, the power to detect GxG interactions at the genome-wide level is limited. Future exploratory analyses to examine specific subsets of genes (e.g. those that are known to be involved in nicotinic receptor biology) are in progress.

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