Pleiotropic effects of Chr15q25 nicotinic gene cluster and the relationship between smoking, cognition and ADHD


Journal of Psychiatric Research
DOI: http://dx.doi.org/10.1016/j.jpsychires.2016.06.002

Abstract

Polymorphisms in the CHRNA5-CHRNA3-CHRNB4 gene cluster (Chr15q25) have been robustly associated with nicotine dependence, including genome-wide studies, as well as with cognitive and neuropsychological measures. In addition, cognitive processes can be influenced by nicotine use through nicotinic acetylcholine receptors (nAChRs). Here, we evaluated the effect of polymorphisms in CHRNA5-CHRNA3-CHRNB4 gene cluster and their interaction with tobacco smoking status on cognition in patients with Attention Deficit/Hyperactivity Disorder (ADHD). Eight SNPs from the CHRNA5-CHRNA3-CHRNB4 gene cluster were evaluated on a clinical sample of 403 adults with ADHD. Cognitive performance was assessed using the Wechsler Adult Intelligence Scale-Revised (WAIS-R). Analyses of covariance were used to assess the influence of single markers and their interaction with smoking status in the Vocabulary and Block Design subtests of WAIS-R. Correction for multiple comparisons was applied. Lifetime smoking was associated to Vocabulary subtest. The TT genotypes of CHRNA5 SNPs rs588765 and rs514743 showed a trend towards association with, respectively, higher and lower scores on the Vocabulary subtest. There was a significant interaction between intergenic SNP rs8023462 and smoking on Vocabulary scores. Our results are consistent with an influence of variants in the CHRNA5–CHRNA3–CHRNB4 gene cluster on cognitive measures. The overall scenario suggests a pleiotropic role of Chr15q25 nicotinic gene cluster with complex influences in ADHD, tobacco smoking and cognitive performance, characteristics that can be partially interdependent and may share underlying genetic factors.