The role of dopamine receptor genes in drinking patterns, alcohol dependence, and related psychiatric phenotypes: Data from the longitudinal Finnish twin studies

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Abstract

Alcoholism is one of the most costly problems in the world, both in terms of societal cost ($184.6 billion in 1998) and personal cost to the affected individual and their family. As a disease, alcoholism has been demonstrated to be over 50% heritable, yet also influenced by environmental stimuli. The predisposition to alcohol dependence is thought to be influenced by genes affecting the pathways involved in reward, executive cognitive function, anxiety/dysphoria, and neuronal plasticity. Genetic variation across the dopamine receptor genes has been suggested to play a role in alcohol use through its involvement in reward pathways. This study integrates methods from quantitative genetics and statistical genetics to better understand genetic influences on drinking patterns and drinking problems across adolescence and into young adulthood. Using data from a population-based, longitudinal twin-family study, we examined the association between genetic markers genotyped across five dopamine receptor genes (DRD1 – DRD5) with drinking frequency assessed at ages 16, 17, 18, and mid-20s, drinking problems assessed at ages 18 and mid-20s (RAPI scores), and alcohol and nicotine dependence symptoms assessed via interview in the mid-20s (SSAGA interview). There was no evidence of population stratification with these SNPs. Family-based association analyses suggested some evidence of a dominant association with drinking frequency at age 16 (p=.02) with two SNPs on DRD4. The p-value was not significant at ages 17, 18, or 25, but there were trend level results with p< 0.1 for the two SNPs at these ages. There wasn’t a trend of association across the genes between these SNPs and the other phenotypes analyzed, but a few individual SNPs were found to be significant, most notably a SNP at DRD2 (rs4245149). In addition to the association analyses, we fit common pathway models to drinking frequency assessed across the four time points to create multivariate phenotypes. This model showed that there is a common factor influencing drinking patterns across these time points. Future analyses will utilize this multivariate phenotype in association analyses.