A Genome-wide Scanning and Fine Mapping Study of COGA Data

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Abstract

A thorough genetic mapping study was performed to identify predisposing genes for alcoholism dependence using COGA data. The procedure was comprised of whole genome linkage and confirmation analyses, single locus and haplotype fine mapping analyses, and gene-environment haplotype regression. Stratified analysis was considered to reduce the ethnic heterogeneity and simultaneously family-based and case control study designs were applied to detect potential genetic signals. By using different methods and markers, we found high linkage signals at D1S225 (253.7 cM), D1S547 (279.2 cM), D2S1356 (64.6 cM) and D7S2846 (56.8 cM) with NPL scores of 3.92, 4.10, 4.44 and 3.55 respectively. We also conducted haplotype and odds ratio analyses, where the response was the dichotomous status of alcohol dependence, explanatory variables were the inferred individual haplotypes and the three statistically significant covariates were age, gender and max drink. The final model identified important AD-related haplotypes within a candidate region of *NRXN1* at 2p21 and a few others in the inter-gene regions. The relative magnitude of risks to the identified risky/protective haplotypes was elucidated.

Key words: Linkage; linkage disequilibrium; haplotype; ethnic heterogeneity.