Alcoholism Susceptibility Loci: Confirmation Studies in a Replicate Sample and Further Mapping

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Background: There is substantial evidence for a significant genetic component to the risk for alcoholism. A previous study reported linkage to chromosomes 1, 2, and 7 in a large data set that consisted of 105 families, each with at least three alcoholic members.

Methods: Additional genotyping in the 105 families has been completed in the chromosomal regions identified in the initial analyses, and a replication sample of 157 alcoholic families ascertained under identical criteria has been genotyped. Two hierarchical definitions of alcoholism were employed in the linkage analyses: (1) Individuals who met both Feighner and DSM-III-R criteria for alcohol dependence represented a broad definition of disease; and (2) individuals who met ICD-10 criteria for alcoholism were considered affected under a more severe definition of disease.

Results: Genetic analyses of affected sibling pairs supported linkage to chromosome 1 (LOD = 1.6) in the replication data set as well as in a combined analysis of the two samples (LOD = 2.6). Evidence of linkage to chromosome 7 increased in the combined data (LOD = 2.9). The LOD score on chromosome 2 in the initial data set increased after genotyping of additional markers; however, combined analyses of the two data sets resulted in overall lower LOD scores (LOD = 1.8) on chromosome 2. A new finding of linkage to chromosome 3 was identified in the replication data set (LOD = 3.4).

Conclusions: Analyses of a second large sample of alcoholic families provided further evidence of genetic susceptibility loci on chromosomes 1 and 7. Genetic analyses also have identified susceptibility loci on chromosomes 2 and 3 that may act only in one of the two data sets.

Key Words: Alcoholism, Nonparametric Linkage Analysis, Sibling Pair, Susceptibility Genes.