Genetic differences that make you sleepy when you drink can also protect against alcohol dependence

May 4 2010

Genetic differences in alcohol-metabolizing enzymes can significantly alter an individual's risk for developing alcohol dependence (AD). One variant of the alcohol dehydrogenase enzyme, ADH1B*3, is observed almost exclusively in populations with African ancestry and has also been associated with reduced rates of AD. A new study has found that greater levels of sedation in African Americans with ADH1B*3 may explain their lower rates of AD.

Results will be published in the July 2010 issue of *Alcoholism: Clinical & Experimental Research* and are currently available at Early View.

"In one study looking at genetic samples from a number of African groups, the ADH1B*3 variant was found in almost every group," explained Denis M. McCarthy, associate professor of psychology at the University of Missouri and corresponding author for the study. "Furthermore, prior studies had shown that those with ADH1B*3 had reduced drinking and risk for AD, and this was thought to be due to the different form of ADH enzyme that people with this allele have. The goal of our study was to see if those with ADH1B*3 had different subjective and physiological response to alcohol compared to those who do not. This would be one explanation for why they drank less than others - they have a different experience from drinking."

This focus on minority populations such as African Americans is sorely

needed, added Lara Ray, assistant professor in the department of psychology, and faculty member in the Brain Research Institute, at UCLA. "In the pharmacogenomics era, failure to account for genetic differences in various ethnic groups may perpetuate or even expand health disparities. In this study, the authors do a very nice job of addressing unique risk and protective genetic factors for alcoholism in African Americans.

Researchers provided a moderate alcohol dose - 0.72 g/kg for males, 0.65 g/kg for females - to 91 African American adults (52 females, 39 males) aged 21 to 26 years. All participants were genotyped for ADH1B*3 as well as additional polymorphisms that might contribute to alcohol response. Measures such as breath alcohol concentrations (BrACs), self-reports on sedation and stimulation, and pulse rates were collected both prior to alcohol consumption as well as for 2.5 hours following consumption.

Results showed that ADH1B*3 was associated with higher levels of sedation, as well as a sharper increase in pulse rate immediately following alcohol consumption.

"The unique part of this study is showing that people with this allele have a different experience when they drink -they get more sedated, particularly when their BrAC is high," said McCarthy. "This would be one explanation for their reduced drinking behavior - people are less likely to drink heavily when doing so makes them tired rather than stimulated or disinhibited. It is important for genetic research to go beyond demonstrating that a gene is related to a drinking disorder and instead demonstrating the steps by which the gene can exert its influence on that disorder."

Ray agrees. "This study provides a behavioral mechanism by which this gene may confer protection against the development of alcoholism, such

that carriers of the ADH1B*3 alleles may have a more negative response to alcohol when they drink, due to differences in alcohol metabolism, which in turn protects them against heavy drinking and the subsequent development of alcohol problems," she said.

"I think the sum of research on these genes - ADH and aldehyde dehydrogenase (ALDH) variants - has important implications for understanding why people drink and how we might help people reduce problematic drinking," said McCarthy. "The treatment of AD by Antabuse™ (disulfiram) actually mimics what happens in people with ALDH2*2 variants, blocking the breakdown of acetaldehyde. It may be that eventually we can do something similar to reduce heavy alcohol use or other consequences of use by increasing the speed at which alcohol is broken down. There is also extensive research on alcohol-related birth defects and cancers, the risk for which can be affected by these genetic variants. For example, people with ADH1B*3 who still drink might be at increased risk for cancers that result from acetaldehyde."

"It is important for readers to realize that alcoholism is a disorder of complex genetics and that multiple genes and environmental factors are needed to explain this multifaceted disorder," said Ray. "This study provides evidence of genetic influences on one pathway to alcoholism; other pathways may lead to the same outcome as evidenced by the heterogeneity of alcoholism."

Provided by Alcoholism: Clinical & Experimental Research