Race and ADH / ALDH

Alcohol and aldehyde dehydrogenase isoenzymes in North American Indians.
Rex, Douglas K., et al.
Alcoholism: Clinical and Experimental Research, Vol 9(2), Mar-Apr, 1985. pp. 147-152.
Abstract:

Determined alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) isoenzyme phenotypes in autopsy liver samples from 50 Native Americans (age range at death 8 mo to 90 yrs) who lived in New Mexico. 46 of the livers had sufficient ADH activity to allow phenotyping at the ADH_2 and ADH_3 loci. Results show that ADH and ALDHphenotypes among Native Americans living in New Mexico were similar to those of Caucasian populations and quite different from those of Orientals.

Protective association of genetic variation in alcohol dehydrogenase with alcohol dependence in native American Mission Indians.
Wall, Tamara L., et al.
The **American** Journal of Psychiatry, Vol 160(1), Jan, 2003. pp. 41-46.
Abstract:

Two alcohol dehydrogenase genes (ADH2 and ADH3 on chromosome 4) and one aldehyde dehydrogenase gene (ALDH2 on chromosome 12) exhibit functional polymorphisms. The goals of this study were to determine whether any associations exist between the ADH2, ADH3, and ALDH2 polymorphisms and alcohol dependence in 30 NativeAmerican Mission Indians (aged 18-73 yrs) and to determine if any associations exist between these polymorphisms and the endophenotype, maximum number of drinks ever consumed in a 24-hour period. Each participant completed an interview with the Semi-Structured Assessment for the Genetics of Alcoholism. A blood sample was collected from each participant for genotyping at the ALDH2, ADH2, and ADH3 loci. 60% of all participants (72% of men and 53% of women) met lifetime DSM-III-R criteria for alcohol dependence. A significant difference in the ADH2 allele distributions was found between alcohol-dependent and non-alcohol-dependent participants. Those with alcohol dependence were significantly less likely to have the ADH23 allele and significantly more likely to have the ADH21 allele than those who were not alcohol dependent. Individuals with ADH23 reported a lower number of maximum drinks ever consumed in a 24-hour period, compared to those without this allele.

Ethnicity and the Subjective Effects of Alcohol.
Cook, Travis A. R. and Wall, Tamara L.
Mind-altering drugs: The science of subjective experience. Earleywine, Mitch, (Ed); pp. 154-182; New York, NY, US: Oxford University Press; 2005. x, 402 pp.
Abstract:

First, this chapter reviews the pathway of alcohol metabolism and the associations of aldehyde dehydrogenase (ALDH2) and alcohol dehydrogenase (ADH2 and ADH3) gene variations with alcohol-related behavior in different ethnic groups. Next, the authors discuss the subjective effects of alcohol in Native Americans (who have the highest rates of alcohol dependence and alcohol-related mortality of all ethnic groups in the US) and Jews (who have low rates of alcohol abuse and dependence compared with other ethnic or religious groups in the US). Finally, genetic associations with other drugs are addressed.

ALDH22 is Associated With a Decreased Likelihood of Alcohol-Induced Blackouts in Asian American College Students.

Luczak, Susan E., et al.
Journal of Studies on Alcohol, Vol 67(3), May, 2006. pp. 349-353.

Abstract:

Objective: A recent report found the heritability estimate for alcohol-induced blackouts was 53%. The present study was designed to determine whether possession of two specific genetic variations, an aldehyde dehydrogenase ALDH22 allele and an alcohol dehydrogenase ADH1B2 allele, were associated with lower rates of lifetime blackouts. Method: Asian American college students (N = 403) of Chinese and Korean descent were genotyped at the ALDH2 and ADH1B loci and assessed for lifetime alcohol-induced blackouts and the maximum number of drinks ever consumed in a 24-hour period. Results: Participants who had an ALDH22 allele had approximately one third the risk of having a lifetime blackout of participants without this allele. Rates of experiencing a lifetime blackout did not significantly differ by ADH1B2 status. Possessing an ALDH22 allele was associated with decreased risk of lifetime blackouts even after controlling for maximum number of drinks ever consumed in a 24-hour period and ethnicity. Conclusions: These findings suggest the protective effects of possessing an ALDH22 allele include a lowered risk of experiencing alcohol-induced blackouts.

Variations in ADH and ADLH in Southwest California Indians.

Ehlers, Cindy L.
Alcohol Research & Health, Vol 30(1), 2007. pp. 14-17.

Abstract:

Native Americans as a group have the highest rates of alcohol-related deaths of all ethnicities in the United States; however, it remains unclear how and why a greater proportion of individuals in some Native American communities develop alcohol-related problems and alcohol use disorders (AUDs). One potential factor that can influence responses to alcohol are variations in alcohol-metabolizing enzymes. Researchers have analyzed the frequencies of variants in the alcohol-metabolizing enzymes alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) in some NativeAmerican populations. So far the studies have yielded no evidence that an ALDH2 variant, which has shown protective effects in other populations, is found in either American Indians or Alaska Natives. A variant of the ALDH1 enzyme that is encoded by the ALDH1A12 allele, however, was found in a small proportion of a group of Southwest California Indians and had a protective effect against alcoholism in that population. Furthermore, a variant of the ADH1B enzyme that is encoded by the ADH1B3 allele was found in a similar proportion of Southwest California Indians and also was associated with a protective effect. However, these findings do not explain the high prevalence of alcoholism in the tribes investigated.

Health-related effects of genetic variations of alcohol-metabolizing enzymes in African Americans.

Scott, Denise M., and Taylor, Robert E.
Alcohol Research & Health, Vol 30(1), 2007. pp. 18-21.

Abstract:

Alcohol metabolism involves two key enzymes--alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH). There are several types of ADH and ALDH, each of which may exist in several variants (i.e., isoforms) that differ in their ability to break down alcohol and its toxic metabolite acetaldehyde. The isoforms are encoded by different gene variants (i.e., alleles) whose distribution among ethnic groups differs. One variant of ADH is ADH1B, which is encoded by several alleles. An allele called ADH1B3 is unique to people of African descent and certain Native American tribes. This allele is associated with

more rapid breakdown of alcohol, leading to a transient accumulation of acetaldehyde. African Americans carrying this allele are less likely to have a family history of alcoholism and experience a less rewarding subjective response to alcohol. Moreover, children of mothers with this allele are less vulnerable to alcohol-related birth defects. The enzyme ALDH1 also is encoded by several alleles. Two of these alleles that are found in African Americans--ALDH1A12 and ALDH1A13--may be associated with a reduced risk of alcoholism.

ADH and ALDH polymorphisms and alcohol dependence in Mexican and Native Americans.

Ehlers, Cindy L., et al.

The **American** Journal of Drug and Alcohol Abuse, Vol 38(5), Sep, 2012. pp. 389-394.

Abstract:

Background: Ethanol is primarily metabolized in the liver by two rate-limiting reactions: conversion of ethanol to acetaldehyde by alcohol dehydrogenase (ADH) and subsequent conversion of acetaldehyde to acetate by aldehyde dehydrogenase (ALDH). ADH and ALDH exist in multiple isozymes that differ in their kinetic properties. Notably, polymorphisms within the genes that encode for these isozymes vary in their allele frequencies between ethnic groups, and thus, they have been considered as candidate genes that may differentially influence risk for the development of alcohol dependence across ethnic groups. Objectives and methods: Associations between alcohol dependence and polymorphisms in *ADH1B, ADH1C*, and *ALDH2* were compared in a community sample of Native Americans (n = 791) living on reservations and Mexican Americans (n = 391) living within the same county. Results: Two Mexican Americans and no Native Americans possessed one *ALDH22* allele. Presence of at least one *ADH1B2* allele was found in 7% of the Native Americans and 13% of the Mexican Americans, but was only associated with protection against alcohol dependence in the Mexican Americans. Presence of at least one *ADH1B3* allele was found in 4% of the Native Americans and 2% of the Mexican Americans, but was associated with protection against alcohol dependence only in the Native Americans. No associations between alcohol dependence and polymorphisms in *ADH1C* were found. Conclusions and Scientific Significance: Polymorphisms in *ADH1B* are protective against alcoholism in these two populations; however, these findings do not explain the high prevalence of alcoholism in these populations.

Association and ancestry analysis of sequence variants in ADHand ALDH using alcohol-related phenotypes in a Native American community sample.

Peng, Qian, et al.

American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, Vol 165(8), Dec, 2014

Abstract:

Higher rates of alcohol use and other drug-dependence have been observed in some Native American (NA) populations relative to other ethnic groups in the US. Previous studies have shown that alcohol dehydrogenase (ADH) genes and aldehyde dehydrogenase (ALDH) genes may affect the risk of development of alcohol dependence, and that polymorphisms within these genes may differentially affect risk for the disorder depending on the ethnic group evaluated. We evaluated variations in the ADH and ALDH genes in a large study investigating risk factors for substance use in a NA population. We assessed ancestry admixture and tested for associations between alcohol-related phenotypes in the genomic regions around the ADH1–7 and ALDH2 and ALDH1A1 genes. Seventy-two ADH variants showed significant evidence of association with a severity level of alcohol drinking-related dependence symptoms phenotype. These significant variants spanned across the entire 7 ADH gene cluster regions. Two significant associations, one in ADH

and one in ALDH2, were observed with alcohol dependence diagnosis. Seventeen variants showed significant association with the largest number of alcohol drinks ingested during any 24-hour period. Variants in or near ADH7 were significantly negatively associated with alcohol-related phenotypes, suggesting a potential protective effect of this gene. In addition, our results suggested that a higher degree of NA ancestry is associated with higher frequencies of potential risk variants and lower frequencies of potential protective variants for alcohol dependence phenotypes.