2015

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The Metabolism of Alcohol: Risk and Protective Factors

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Background

In 2013, it was reported by the National Institutes of Health that 59.4% of college aged students (18-22) drank alcohol in the past month of being asked, as compared to 50.6% of those not in college. They also found that 20% of college students met the criteria for at least one alcohol use disorder (AUDs).

Many genes have been linked to an increased risk for AUDs and how individuals with various ethnic backgrounds respond to alcohol. Genes that metabolize alcohol are obvious candidate genes for alcohol-related phenotypes. The purpose of this presentation is to synthesize information about the key genes involved in alcohol metabolism, as documented in the literature.

Gene Pathways

ADH1B: *1: risk allele, prevalent in Caucasians and American Indians⁴
*2: protective allele, prevalent in Asians (especially Eastern) and somewhat in Russians⁴
*3: protective allele, almost exclusive to African Americans⁴

ADH1C: *1: protective allele, predominant in Eastern Asia and black populations⁴
*2: risk allele, *1 and *2 equally distributed among Caucasians and American Indians⁴

CYP2E1: metabolizes ethanol to acetaldehyde and generates ROS⁸
CAT pathway= metabolizes ethanol to acetaldehyde in non-liver tissues⁸

Other important genes: CYP2E1* metabolizes ethanol to acetaldehyde and generates ROS⁸
CAT pathway= metabolizes ethanol to acetaldehyde in non-liver tissues⁸

ADH2: *1: risk allele; common allele⁴
*2: protective allele; found almost exclusively in Asians, but not those of Northern European ancestry⁴

Results

• Alcohol metabolism genes affect how individuals process and respond to alcohol.
• Main genes: alcohol and aldehyde dehydrogenase
  • ADH1B and ADH1C: first metabolize ethanol (alcohol) into the by-product acetaldehyde
  • ALDH2: acetaldehyde is then metabolized into the waste product acetate
• Many of the adverse effects associated with alcohol consumption are due to the build up of acetaldehyde:
  • Some of these effects include facial blushing, nausea, headaches, and other similar alcohol sensitivity symptoms⁸
  • Acetaldehyde builds up after alcohol consumption at different rates depending on the type of enzymes they produce
• Super-active alcohol dehydrogenase isoenzyme and slow aldehyde dehydrogenase enzyme= less likely to develop AUDs due to the negative effects from excess acetaldehyde in the body⁴,⁵,¹⁰
• Others are more likely to endorse increased drinking behaviors and AUDs since they don’t experience the same ill effects

In general, the more public knowledge about these genetics and their association with alcohol consumption and alcohol use disorder symptoms. Due to the diverse nature of the sample, the researchers are able to explore ethnic differences in these alcohol metabolism genes and their effects.

Implications

In, the more public knowledge about these genetics and research findings, the more at-risk individuals can get help and diagnosis. On college campuses, health centers can use this information to promote better preventative measures. A better understanding of aggregate effects of alcohol metabolism genes, as well more information regarding ethnic differences in the distribution of genetic variants which impact alcohol processing, will assist researchers and health professionals working with those at risk for AUDs.

Methods

The information about each gene was found through a literature search using databases including PubMed, Google Scholar, and cited references from relevant papers. For database searches, the names of the genes were used as well as terms such as AUDs, alcohol metabolism, and alcohol and aldehyde dehydrogenase. The focus of the presentation is relevant to college-aged students, but relies on research done in college and adult populations due to a lack of sufficient college-aged gene-based studies in this area.

Statistics

National and VCU student alcohol use

• About 20% of college students meet the criteria for an AUD⁴
• Roughly 25% of college students report academic consequences from drinking⁴
• About 50% of VCU students who have ever drank have blacked out⁴

Alcohol is metabolized to acetaldehyde, a toxic byproduct, by several enzymes in the liver as well as other tissues. Some enzymes produce reactive oxygen species (ROS) in the process. ROS and acetaldehyde cause negative reactions in the body which can deter people from drinking. Acetaldehyde is then metabolized to acetate, a waste product, by a different set of enzymes.

Acknowledgements

I would like to thank Amy Adkins and Greg Chartier for their mentorship and time and advice while overseeing this project. Thank you to Drs. Danielle Dick and Ken Kendler together with the VCU Library for Psychosocial and Behavioral Genetics and the VCU Library for their support for this project. This project could not have been done without the VCU students who assisted in participant recruitment with Spit for Science: they interviewed with Spittle for Science: their VCU student survey. Finally, thank you to IRROP for providing a forum for presentation.

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