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Comparative Response to Alcohol in Individuals with ADH1B*1 and ADH1B*3 Polymorphisms

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The primary pathway of alcohol metabolism involves the oxidation to acetaldehyde, catalyzed by alcohol dehydrogenases (ADH), followed by further oxidation by aldehyde dehydrogenase. The ADH1B gene, which encodes for ADH1B enzyme is one of the most validated genetic risk factors for alcohol use disorder (AUD). Out of the three major alleles of ADH1B gene, the *ADH1B*3* allele is unique to people of African descent and certain Native Americans tribes. It is associated with a high alcohol elimination rate and intense, unpleasant response to alcohol intake that may be protective from AUD. This study combines oral intake and intravenous alcohol challenge clamping technique to evaluate the moderating effect of *ADH1B*3* polymorphism on the neurobehavioral and electrophysiological effects of alcohol.

Participants were healthy, non-dependent alcohol drinkers, who received 30mg% of oral alcohol and 60mg% of intravenous alcohol on separate occasions. During each session, continuous electroencephalography (EEG), event related potentials to cognitive tasks, battery of subjective scales (e.g., the bodily sensation scale, BSS), motor, and eye movement tasks were acquired from each participant.

The results show dose-dependent effect of *ADH1B1*3* and *ADH1B3*3* genotypes on the severity discomfort in the BSS and on the reduction of alpha power in several EEG electrodes, suggestive of reduction in the relaxing effect from alcohol compared to *ADH1B1/1* genotype. These effects were independent of the increased alcohol elimination rate from *ADH1B*3* allele. This study suggests that there may be an indirect effect of this ADH1B enzyme on alcohol risks in addition to its direct effect on alcohol metabolism.