

Genetically Influenced Responses to Alcohol Affect Brain Activation

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A study by researchers at the University of California, San Diego School of Medicine suggests that differences in brain activation in individuals with a low level of response to alcohol may contribute to their inability to recognize modest levels of alcohol intoxication. Their findings could provide the potential to identify individuals who are at risk for developing an alcohol-use disorder before it develops – in essence, providing a marker for this vulnerability.

In a study to be published in the January 2012 issue of *Alcoholism: Clinical & Experimental Research* and currently available at the journal's *Early View*, researchers used functional magnetic resonance imaging (fMRI) to examine brain activation in young men and women in San Diego, ages 18 to 25, with both low and high level of response (LR) to alcohol.

“We found significant differences in brain activation between individuals with high and low levels of response to alcohol while performing a cognitive task, possibly reflecting difference in the amount of brain activity used to deal with a cognitive challenge,” said Marc A. Schuckit, MD, Distinguished Professor of Psychiatry at UC San Diego, who headed the study.

A low level of response to alcohol is a genetically influenced characteristic, or phenotype, that reflects at least in part a low brain response to alcohol, and carries significant risk for the later development of alcoholism. This study addressed the physiological underpinnings of a low and high LR, finding significant differences in brain activation during a cognitive task, possibly reflecting differences in the amount of brain activity used to deal with a cognitive challenge.

“While some genes that contribute to LR have been provisionally identified, the mechanism through which the low LR operates in the brain has not been extensively studied,” said Schuckit. “This report confirms prior reports from our group that used a different cognitive task to show that people with a low LR process information differently from those with a high LR even when tested with placebo. The differences between LR groups after placebo and alcohol across different cognitive tasks may help explain why low LR subjects might have more problems recognizing the effects of moderate doses of alcohol. If you aren't able to recognize the effects of


lower doses of alcohol, you are more likely to drink heavy amounts per occasion, which both directly and indirectly increases your risk for alcohol problems.”

Schuckit and his colleagues examined 98 (52 females, 46 males) young, healthy drinkers who were not alcohol dependent and who had been identified in prior testing as clearly having low or high LRs to alcohol. The subjects in the two LR groups were matched to be similar on recent drinking histories, age, gender, race, and histories of smoking and using illicit drugs. All participants were evaluated during two, event-related fMRI sessions while performing a cognitive task. The two groups were given either a placebo or an amount of alcohol roughly the equivalent of three standard drinks, in random order. Treated subjects developed identical blood alcohol levels during the sessions.

After placebo, those with a low LR seemed to exert more cognitive effort in performing a cognitive task than those with high LRs. But after alcohol, the low LR subjects seemed to do the task with less effort than they had after placebo. In contrast, the high LR subjects had to work harder to do the task after alcohol than after placebo.

“When the low LR people drink modest amounts of alcohol, they may not perceive much change in how their brain is working,” said Schuckit. “If a modest dose of alcohol produces a situation where you don’t have to exert as much effort to think about how a challenging task that needs to be done – as might be true for low LR subjects – perhaps drinking is a bit more rewarding for you, compared to people who find that modest alcohol doses actually impairs their thinking, as is seen for high LR subjects.”

“The real issue for clinicians is that the low LR is an important, genetically influenced risk factor for later alcohol problems,” Schuckit added. “These results can also inform researchers interested in how the low LR might actually work to affect how intoxicated a person might feel.”

Additional contributors include Susan Tapert, Scott C. Matthews, Martin P. Paulus, Neil J. Tolentino, Tom L. Smith, Ryan S. Trim, Shana Hall and Alan Simmons of the University of California, San Diego. The study was funded by the National Institute on Alcohol Abuse and Alcoholism. This release is supported by the Addiction Technology Transfer Center Network at www.ATTCnetwork.org 

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Media Contact: Debra Kain, 619-543-6163, ddkain@ucsd.edu

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