A polymorphism of the μ-opioid receptor is linked to alcohol misuse among adolescents

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A genetic study has examined the association between a polymorphism of the μ-opioid receptor (OPRM1) gene and alcohol misuse among adolescents. Results suggest that teens who carry the G allele (A118G) of the OPRM1 gene are at increased risk for alcohol problems because they experience alcohol as more pleasurable or rewarding than teens without A118G.

While many genetic studies have examined alcoholism among adults, identifying genes that are associated with alcohol misuse during youth is equally important, given that genetic and environmental influences on alcoholism vary across development. New findings show an association between a polymorphism of the μ-opioid receptor (OPRM1) gene and alcohol misuse among adolescents.

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

"Our current knowledge about the genetics of alcohol misuse during adolescence comes almost exclusively from family and twin studies," explained Robert Miranda, Jr., assistant professor in the department of psychiatry and human behavior at Brown University and corresponding author for the study. This research, he said, generally shows that environmental factors, such as peer influence, are predominantly responsible for the initiation of alcohol use.

"But the relative importance of environmental and genetic factors appears to shift considerably over the course of adolescence," Miranda Jr. added, "with genetics playing an important role once teenagers begin to drink. Although family and twin studies can disentangle genetic and environmental influences, they cannot identify the specific genes that confer risk for alcoholism in youth. Our goal was to test if and how the OPRM1 gene, which was previously shown to be associated with alcoholism in adults, is associated with alcohol misuse among adolescents."

Researchers genotyped 187 adolescents (98 boys, 89 girls), with a mean age of 15.4 years, for a single-nucleotide polymorphism (SNP) of the OPRM1 gene called A118G (rs1799971). Miranda Jr. and his co-authors also assessed participants for alcohol-use disorders (AUDs) and other psychiatric diagnoses, gathered continuous measures of alcohol misuse, and examined drinking motives.

"Our findings provide the first evidence to suggest that teenagers who carry a certain variant of the OPRM1 gene experience more alcohol-related problems and are more likely to meet diagnostic criteria for an AUD," said Miranda, Jr. More specifically, 51.9 percent of youth with an AUD carried at least one copy of the G allele compared to 16.3 percent of youth without an AUD.

"In addition," he said, "we found that adolescent drinkers with this variant reported drinking to enhance how they feel more often than those without this variant, and this difference explained, at least in part, why youth with this OPRM1 variant were more likely to experience alcohol-related problems."

"What is very notable about this study is that it provides good evidence of the particular mechanism by which variations in the OPRMI receptor gene may contribute to alcohol problems in adolescence," added Peter R.

Finn, professor of psychological and brain sciences at Indiana University, Bloomington. "The G allele, or variant, of the OPRMI gene is associated with the function of the body's own natural opiate system. Research suggests that the G allele is associated with experiencing more pleasure and greater intoxication after drinking."

This means that individuals with the G allele of the OPRMI receptor gene may be more likely to drink because they experience alcohol as more pleasurable than individuals without the G allele.

"Interestingly, Miranda's study showed that adolescents who had the G allele were more likely to report drinking alcohol for its pleasurable effects than drinking for other reasons, which is consistent with the idea that they might experience alcohol as being more pleasurable in the first place," said Finn. "Finally, the results suggested that the presence of the G allele is associated with greater sensitivity to the pleasurable effects of alcohol which, in turn, was associated with more alcohol problems. In other words, the reason the G allele is associated with more alcohol problems in adolescence is because it increases teenagers' sensitivity to the rewarding effects of alcohol."

"This study may have important implications for developing more effective treatment strategies for adolescents, particularly in terms of pharmacological interventions," noted Miranda, Jr. "Identifying genetic influences on adolescent alcohol misuse may help advance medication development research with youth, in part, by shedding light on the types of youth most likely to benefit from particular pharmacological treatments. Opioid receptor antagonists, such as naltrexone hydrochloride, blunt the reinforcing effects of drinking alcohol and this effect is more pronounced in carriers of the genetic variant investigated in this study."

"This is simply one step in the very broad and extensive research into the

genetic and environmental influences on alcohol problems," said Finn. "The research suggests a role for a particular gene in a particular mechanism that contributes to the development of alcohol problems in adolescence; however, there are many genes and many different mechanisms that contribute to the complex set of problems that we refer to as 'alcohol problems' or AUDs. In addition, there may be other genes that contribute to the same mechanism. Nonetheless, this study provides very interesting results that make a lot of intuitive sense."

Source: Alcoholism: Clinical & Experimental Research