Cannabinoid receptor 1 is linked to dependence on alcohol and other substances

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While researchers know that genetic factors play an important role in the development of alcohol dependence (AD), it is challenging to discover which particular genes may be involved. Prior evidence had established that the endogenous cannabinoid system is implicated in AD, with cannabinoid receptor 1 (CNR1) appearing to be the main candidate. New findings confirm the association between CNR1 and dependence on alcohol and other substances.

Results will be published in the February 2012 issue of *Alcoholism: Clinical & Experimental Research* and are currently available at Early View.

"Susceptibility to AD is determined by a complex interplay of environmental and genetic factors," said Rogelio González-Sarmiento, professor of medicine at University of Salamanca, Spain and corresponding author for the study. "Allelic variants within specific genes – such as single nucleotide polymorphisms – may be potential candidates for involvement in the development of AD. Animal models have shown that the CNR1 gene is involved in the reward system. In addition, more than 10 allelic variants have been described within this gene, and several previous studies in humans have shown a relationship of some of these allelic variants with dependence to several substances, including alcohol."

"Many neuronal circuits are potentially involved in AD and the cannabinoid system is very likely one of those circuits," agreed Antonio

J. Chamorro, a senior researcher at the University Hospital of Ourense, Spain. "There are other neurotransmitters that may be more important or have been more studied, but the goal of studying the genetics of AD is precisely to understand why some patients develop AD and some do not. That is, in some patients the endogenous cannabinoid system may play a more critical role than in other patients, and this can be due to genetic variants."

González-Sarmiento and his colleagues examined the relationship between three allelic variants of the CNR1 gene (rs6454674, rs1049353, and rs806368) that had previously been associated with addictive disorders. They genotyped these three polymorphisms from the blood cells of 298 male alcoholics: 187 were diagnosed with AD according to the "Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition" (DSM-IV) criteria, and 111 with alcohol abuse. All had been referred to the Alcoholism Unit of the University Hospital of Salamanca, Spain. An additional 155 healthy volunteers served as controls.

"We found that two specific haplotypes – a haplotype is a combination of alterations in the normal sequence of a gene that are likely to be inherited together – are more frequent in patients with AD than in patients who abuse alcohol," said González-Sarmiento.

"In other words," added Chamorro, "certain patients consuming a large amount of alcohol will be more likely to develop AD according to the possession of specific CNR1 polymorphisms. These results confirm the findings of other researchers that have shown a role for certain haplotypes of the CNR1 gene in [developing] dependence to several substances, including cocaine and alcohol. Therefore, it seems that the possession of certain genetic variants within the CNR1 gene may be a marker of a susceptibility to addictive disorders."

"We still have a road to be traveled in the field of the genetics of AD,"

noted González-Sarmiento. "It is well known that this disorder has a genetic basis but we have yet to refine this knowledge in order to be able to use it in the clinical care of alcoholic patients."

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