

Polymorphisms of the interleukin-1 gene complex may influence alcohol dependence

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Cytokines are small proteins secreted by cells that serve as molecular messengers between cells. Pro-inflammatory cytokines - which function in the immune system - may be involved in alcohol dependence (AD). A study of three polymorphisms of the interleukin-1 gene complex (IL-1) and one of the tumor necrosis factor-alpha (TNF α) has found that IL-1 may directly contribute to AD among Spanish Caucasian males.

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

"Cytokines are proteins which mediate and regulate the inflammatory reaction in infectious and autoimmune diseases," explained Pilar A. Sáiz, associate professor of psychiatry at the University of Oviedo, Spain and corresponding author for the study. "Clinical observation of increased circulating levels of pro-inflammatory cytokines such as IL-1 and TNF α in patients with alcohol liver disease suggests that they might play a role on the pathogenesis of the disease. Additionally, these cytokines act in the central nervous system affecting the functionality of the serotonergic and dopaminergic systems, which have been also related to the pathophysiology of AD, and with the brain reward systems involved in alcohol reinforcement."

Sáiz and her colleagues recruited 200 (169 males, 31 females) AD patients from an outpatient detoxification unit, as well as 420 (216 males, 204 females) healthy individuals without a history of drug/alcohol/psychiatric problems (known as "controls"), from the north

of Spain. All of the Spanish Caucasian participants were genotyped for four polymorphisms -IL-1 α -889 C/T, IL-1 β +3953 C/T, IL-1RA (86bp)n, and TNF α -308A/G - and assessed at baseline and again at six months for alcohol intake, addiction severity, and biomarkers of alcohol intake.

"We found that AD male patients and healthy control male patients differed in the genotype frequencies of the IL-1RA [polymorphism](#) owing to an excess of the A1/A1 genotype in the AD males," said Sáiz. "On the other hand, analysis of the IL-1 gene complex revealed a higher frequency of the IL-1a -889C / IL-1b +3953C / IL-1RA A2 haplotype in the control group than among the AD patients, as well as in the abstainers after six months of follow-up compared to the nonabstinent patients."

A haplotype is a combination of alleles at multiple loci that are transmitted together on the same chromosome, Sáiz explained. Prior research has suggested that the study of single polymorphisms may miss more complex haplotype effects, she added.

"In short, this haplotype seemed to exert a protective effect and was related to better outcomes," said Sáiz. "These findings provide further tentative evidence of the role of the IL-1 gene complex in AD as well as evidence that the nature of the associations may be direct, gender-specific, or involve haplotype effects."

She cautioned readers to remember, however, that AD is influenced by both genetic and environmental factors. "We are talking about a multifactorial polygenic disorder caused by a combination of small variations in different genes, often in concert with environmental factors," she said. "In spite of great efforts, the exact genes related to the pathophysiology of alcoholism are yet unknown. Our work represents a small piece of the puzzle."

Source: Alcoholism: Clinical & Experimental Research

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