

Genetic signs of alcoholism in women studied for the first time

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(Medical Xpress)—Research done at the UPV/EHU-University of the Basque Country has determined the frequency of genetic variants linked to alcoholism for the Spanish population, and its incidence not only in individuals with a high level of alcohol intake, but also in individuals with alcohol dependence. Furthermore, the broad presence of women in the sample has made it possible, for the first time, to associate some of these genetic variants with a high level of alcohol intake in women. The results have been published in various top, international journals worldwide, like the journal *Addiction*, a leader in the field of misused substances.

[Alcohol](#) intake is a significant health and economic problem in Spain. Between 2% and 20% of the Spanish population are reckoned to be individuals who abuse alcohol intake, and even though it is not a unique problem since the aetiology of this imbalance has been established in genetics and in environmental variables, many studies have shown that there are genetic endowments that can confer greater susceptibility to alcoholism. For example, some variations in enzyme-encoding [genes](#) that break down the alcohol molecule are known to be closely associated with a higher intake, since they cause a variation in its metabolization rate which can be up to 30 times higher.

The pieces of research conducted by David Celorrio-Herrera of the BIOMICS research group at the UPV/EHU has focused on the study of different genetic variants in samples of the Spanish population for whom it has been possible to determine a statistically significant incidence in

[alcohol abuse](#). Specifically, the enzyme-encoding genes involved in the alcohol metabolization process and genes that encode receptors and enzymes linked to the dopaminergic system have been analysed. "The aetiology of addiction is due to a disorder in the system that regulates dopamine, since this [neurotransmitter](#) modulates the reward-response system in the brain," remarks Celorrio.

The incidence of single nucleotide polymorphisms (SNPs) —variations of a single "letter" on specific points of the gene— has been studied in all the cases. Within the family of metabolic genes the SNPs of the genes ADH1A-ADH1B-ADH1C, ADH4, ADH6, ALDH2 and CYP2E1 have been analysed; "70 % of the alcohol is broken down by enzymes encoded by these genes" points out Celorrio. Of the genes in the [dopaminergic system](#), the SNPs analysed correspond to the genes TH, SLC18A2, DRD1, DRD2, DRD3, MAOA and COMT, "being the ones linked to the entire useful life of the dopamine: its production, delivery, action in the presence of receptors and destruction," adds the author. The incidence of the two families of genes has been analysed in two groups of population samples: 1-excessive consumers and 2-patients with dependence.

Among the excessive consumers, polymorphisms that significantly increase the risk associated with the hazardous intake of this substance were found in the ADH1B and DRD2 genes for both sexes and in the MAOA gene in women only. The analysis of the environmental variables together with the hazardous intake of alcohol displayed a high-risk profile: men, smokers, heavy consumers of meat and low consumers of fruit and vegetables, with occupations not requiring a high level of qualifications and physically not very active.

On the other hand, a significant association of alcohol dependence with polymorphisms in genes of the metabolism and dopaminergic route was observed with an SNP of the ADH1B gene in both sexes and with SNPs of TH, COMT, DRD2 in men only, whereas the association with DRD3

occurred in women alone.

The study of excessive consumers was carried out on a sample of 1,533 individuals (653 cases and 880 controls) originating in the EPIC (European Prospective Investigation into Cancer and Nutrition) project, of whom half were men and the other half women. The critical value of inclusion in this group was the intake of alcohol in excess of 70 g/day in men and 42 g/day in women, values very similar to the WHO classification for the group of "individuals with hazardous intake".

The large size of the sample enabled stratification by sex and adjustment by environmental variables which affect [alcohol intake](#) to be done, "which makes the results obtained highly reliable," explains Celorrio. "Until now, the Spanish Caucasian population has been studied by means of small samples and with very few women," he adds. The results relating to the metabolic genes have been published in the journal **Addiction**.

Due to obtainment difficulties, in the study on patients with dependence it was not possible to have such a large sample, so the author prudently stresses that the results obtained are not so conclusive. The gathering of these samples was conducted in collaboration with various alcoholism treatment centres: the Psychiatric Hospital of Vitoria-Gasteiz, the mental health clinics Novia Salcedo and Uribe-Kosta in Bizkaia, the Hospital Donostia in Donostia-San Sebastian and the Zuria Outpatients' Hospital for Drug Dependence in Iruñea-Pamplona, and were compiled over more than three years.

More information: *Addiction*. 2012 Dec; 107(12):2117-27. [doi: 10.1111/j.1360-0443.2012.03970.x](https://doi.org/10.1111/j.1360-0443.2012.03970.x). Epub 2012 Aug 20

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