

Polymorphisms in the GluR5 glutamate receptor subunit gene (GRIK1) and alcohol dependence

HRVOJE GALIĆ¹, HRVOJE BEKINA¹, FILIP MARTINEZ¹, GORDANA NEDIĆ ERJAVEC², MATEA NIKOLAC PERKOVIĆ², KORONA NENADIĆ ŠVIGLIN³, FRAN BOROVEČKI⁴, NELA PIVAC², DUBRAVKA ŠVOB ŠTRAC²

¹UNIVERSITY OF ZAGREB, FACULTY OF SCIENCE, DEPARTMENT OF BIOLOGY, ZAGREB, CROATIA

²RUĐER BOŠKOVIĆ INSTITUTE, DIVISION OF MOLECULAR MEDICINE, ZAGREB, CROATIA

³PSYCHIATRIC HOSPITAL VRAPČE, CENTER FOR ALCOHOLISM AND OTHER ADDICTIONS, ZAGREB, CROATIA

⁴UNIVERSITY OF ZAGREB, FACULTY OF MEDICINE, CENTER FOR TRANSLATIONAL AND CLINICAL RESEARCH, DEPARTMENT FOR FUNCTIONAL GENOMICS, ZAGREB, CROATIA;

UNIVERSITY HOSPITAL CENTER ZAGREB, ZAGREB, CROATIA

hgalic2212@gmail.com

Glutamate, major excitatory neurotransmitter in the brain, has an important role in mediating the effects of alcohol and development of alcohol dependence. GRIK1 gene, encoding the GluR5 subunit of glutamate kainate receptors, has been associated with alcoholism, while certain GRIK1 polymorphisms have significant influence on the action of topiramate, drug used in alcoholism treatment.

The aim of this study was to investigate the association of GRIK1 gene polymorphisms (rs2832407 and rs2186305) with alcohol dependence in subjects of Croatian origin.

Genotyping was performed in 276 alcohol-dependent and 298 healthy subjects by using Real-Time PCR after extraction of DNA from the blood with salting out procedure. We compared the frequency of GRIK1 genotypes and alleles, between alcohol-dependent and healthy subjects using χ^2 test, considering the effects of gender and smoking. The distribution of genotypes and alleles of GRIK1 polymorphisms has been investigated in alcohol-dependent patients subdivided according to age of onset of alcohol abuse, suicidal and aggressive behavior, and type of alcoholism according to Cloninger classification. Haplotype analysis of polymorphisms has been conducted using Haploview version 4.2 software.

There were no significant differences in the distribution of genotypes and alleles of GRIK1 polymorphisms between alcohol-dependent and control individuals, as well as between different subsets of alcohol-dependent patients. A low degree of linkage disequilibrium (LD) was revealed for rs2832407 and rs2186305. In the analysis of polymorphism rs2186305 statistically significant difference was found in the frequency of carriers of genotype CC versus T allele carriers between healthy women and women addicted to alcohol ($p = 0.0188$; χ^2 - test), suggesting an association between this polymorphism with alcoholism, but only in women.

The results should contribute to a better understanding of the role of the GRIK1 gene and glutamate receptors in the development of alcoholism, as well as to the research of new potential therapeutic targets.

Keywords: alcohol dependence, GRIK1, genotype, haplotype, polymorphism

[HTTP://DX.DOI.ORG/10.17486/GYR.3.2218](http://dx.doi.org/10.17486/GYR.3.2218)