D68 Association Between Alcohol Dependence and Glutamate Acid Decarboxilase (GAD 67) Gene Polymorphisms in a Male Italian Population

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After attending this presentation, attendees will understand the proposed methodological approach in analysis of biological factors associated with alcohol use disorders.

This presentation will impact the forensic science community by providing novel insights into the biological understanding of alcohol dependence.

Alcohol consumption has been associated with personal, familial, and social problems including school drop-out, productivity losses at work, as well as driving impairment with road accidents. Alcohol consumption has also been considered as one of the major contributing factor in violent crime.

Facing alcohol related problems is highly related to alcohol use disorder prevention and treatment. A contribution to a better understanding of the biological factors associated with alcohol use disorder (abuse and dependence) can be found in genetic studies.

The essential feature of Alcohol Dependence (AD) is a cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues to use the substance despite significant substance–related problems. In general, the development of AD of alcohol use disorder has been linked to environmental and biological factors. The role of biological factor has been widely published in studies relating gamma aminobutyric acid (GABA) to alcohol use disorder. Acute and chronic effects of ethanol have in fact been linked to a GABAergic system involvement.

Even though many studies have focused attention on GABA A receptor, this study concentrated on the glutamate decarboxylase (GAD), the rate limiting enzyme in GABA synthesis, believing it could be of potential interest in relation to AD development. In particular the isoform GAD 67, responsible for maintaining basal GABA levels as suggested by rodent studies (GAD67 knockout mice is usually lethal) was studied.

Based on these premise, a genetic association study was conducted in a rather homogeneous sample of individuals of Western European origin and of the Veneto Region in Italy, trying to provide novel insights into the biological understanding of the disorder.

Methods: The research has been structured as a case-control study. The patient group included 350 Caucasian males coming from Veneto region, North-east Italy, 140 of whom were alcohol dependent according to the DSM IV TR criteria, and 210 controls recruited from blood donors. Twenty-six SNPs localized in the coding and in the untranslated regions of the GAD 67 gene with a *Genotyping System* were analyzed. Fisher chi-square test for allelic and genotype distributions and Hardy-Weinberg equilibrium (HWE) analysis for cases and controls were performed. Ten SNPs at the GAD67 gene were valid for further statistics.

Preliminary results show a difference in genotype distribution (p=0.0030) between alcoholic subjects and controls of SNP rs 11542313 localized in exon 3 of the GAD 67 gene that is responsible for a silent mutation (HIS37HIS).

Discussion: This is the first genetic study regarding GAD 67 gene in relation to the condition of alcohol dependence in an Italian population coming from the same region (Veneto). These results put in evidence a statistical association between one SNP of GAD 67 and the condition of alcohol dependence (AD). In order to clarify the possible meaning of this association, further genetic analysis is being undertaken. In particular, investigation of other genetic polymorphisms both up and down stream from rs 11542313 that could interfere with splicing and/or GAD 67 mRNA stability will be researched.

Alcohol Dependence, Glutamate Decarboxylase, SNPStream

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