Correlation of a hypocretin-2 receptor polymorphism with cluster headache susceptibility and a serotonergic 5-hydroxytryptamine receptor polymorphism with triptan treatment response

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Cluster headache (CH) is a primary neurovascular headache with an increased hereditary risk. The less common A allele of the CH associated *HCRTR2* gene polymorphism rs2653349, seems to reduce disease susceptibility. The *GNB3* gene polymorphism rs5443 was associated with positive triptan treatment response. Carriers of the mutated T allele are more likely to respond positively to triptans compared to C:C homozygotes. DNA from buccal swabs of 1464 non related individuals was collected and analysed. Gene distribution for the polymorphism rs2653349 was G:G=77.8%,G:A=20.3% and A:A=1.9%. The frequency of wild-type G allele was 92.3%. The frequencies for rs5443 polymorphism were C:C=44,8%,C:T=41.9% and T:T=13.3%.The frequency of wild-type C allele was 70.0%. The odds ratio of male vs. female volunteers for rs2653349 exhibited no statistically significant difference, but for rs5443 polymorphism a statistically significant difference (p=0,0292) between the genders could be demonstrated. Comparison of study population polymorphism frequencies vs. other populations showed that rs2653349 A allele appeared only 7.7% while in global and in European population the frequency was 12,1% and 18,4% respectively. Further, we observed that male homozygotes for the protective mutant allele are 2-fold more than female. Results indicate that investigated Greek population has great similarity to the European population regarding rs5443 allele and genotype distribution. Based on our results we could assume that the pathophysiology of CH is affected by multiple factors, however, the genotyping analysis of polymorphisms may play a significant role in susceptibility and treatment of CH suffering patients.