

P-706 - MAJOR DEPRESSIVE DISORDER IS INFLUENCED BY A GENETIC INTERACTION OF VEGF AND TNF ALPHA

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Altered serum levels of vascular endothelial growth factor (VEGF) and tumor necrosis factor alpha (TNFalpha) have been implicated in therapy response of depression. We analyzed effects of 4 functional SNPs of VEGF and TNF alpha genes on MDD to test their possible role in pathomechanism of MDD. We recruited 293 inpatients diagnosed for major depressive disorder (MDD) and 443 healthy volunteers. MDD was diagnosed by DSM-IV criteria and measured by Montgomery-Asberg Depression Scale (MADRS). DNA was extracted from buccal mucosa samples given by all participants. Likelihood ratio tests for case-control and multivariate linear analysis for quantitative phenotype models were performed in SPSS 17.0 software. We identified a protective allele against MDD as the frequency of G allele of rs1800629 (previously associated with lower TNFa serum level) was 2.7 fold higher in the control group compared to MDD group (LRT=4.197; p=0.040). Higher frequency of the same allele was found among SSRI responders compared to non-responders (LRT=6.281; p=0.012). Significant GxG interactions were shown within MDD group: epistatic effect of allele variants and also genotypes of the four investigated SNPs were significant on MADRS score (for risk alleles: $p_{\text{modell}}=0.024$; $p_{\text{interaction}}=0.005$; Adj.R²=0.259; for genotypes: $p_{\text{modell}}=0.035$; $p_{\text{interaction}}=0.007$; Adj.R²=0.371). These findings suggest that TNFalpha and VEGF genes are associated with MDD and SSRI response. Our results support the molecular crosstalk between VEGF and TNFalpha pathway by a genetic interaction. This study was supported by the Hungarian Scientific Research Fund Grant (OTKA CK 80289/2009).