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## The role of serotonergic and inflammatory system genes in individual differences in depression level

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KEYWORDS: depression, serotonin, inflammation, GxE-interaction

### ABSTRACT:

Depression is an important public health issue due to its high prevalence and socio-economic costs to society. A multifactorial nature of depression suggests the involvement of multiple genes of small effect and environmental factors in its development, thus requiring simultaneous examination of genetic and environmental predictors. Considering the role of serotonergic and inflammatory functioning in emotional regulation, the present study aimed to estimate both the main effect of polymorphic variants of serotonergic (*SLC6A4* 5-HTTLPR, *HTR1B* rs13212041, *HTR2A* rs7322347) and inflammatory (*TNF* rs1041981, *CRP* rs3093077, *IL1B* rs16944) system genes, and GxE-interactions in individual differences in depression in healthy individuals. The study included 999 mentally healthy individuals (80.5% women; 19.98±1.80 years) of Caucasian origin (327 Russians, 242 Tatars, 233 Udmurts, 112 Bashkirs and 85 of mixed ethnicity) from Russia. Depression was assessed using BDI. SNPs genotyping was performed using Real-Time PCR. Statistical analysis was conducted with PLINK v.1.9 followed by FDR correction for multiple testing. Statistical analysis revealed association of the *TNF* rs1041981 A-allele and decreased depression level in Russians ( $\beta = -1.44$ ;  $P = 0.04$ ), while the *SLC6A4* 5-HTTLPR LL-genotype was statistically significantly more frequent in men with enhanced depression score ( $\beta = 3.79$ ;  $P = 0.009$ ;  $P_{FDR} = 0.13$ ). As a result of stratification analysis we observed that birth season significantly affected association of *TNF* rs1041981 ( $\beta = -2.21$ ;  $P = 0.006$ ;  $P_{FDR} = 0.04$ ), *IL1B* rs16944 ( $\beta = -2.21$ ;  $P = 0.04$ ) and depression level in the total sample. The present study provides evidence that *TNF*, *IL1B* and *SLC6A4* genetic variants may contribute to depression susceptibility together with environmental factors in mentally healthy young adults.