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TITLE: The role of oxytocin receptor gene polymorphisms in depression-related traits: Gene-environment interactions.

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ABSTRACT:
Depression is an important public health issue due to its high prevalence and socio-economic costs to society. According to published findings, a multifactorial nature of depression development requires simultaneous examination of genetic and environmental factors. Considering the role of oxytocinergic functioning in emotional regulation, the present study aimed to estimate both the main effect of polymorphic variants and haplotypes of oxytocin receptor gene (*OXTR: rs53576, rs237911, rs7632287, rs2254298, rs2228485, rs13316193*), and G×E-interactions in individual differences in depression in healthy individuals considering modulating effect of environmental factors.
The study included 623 mentally healthy individuals (81.11% women; 19.53±1.75 years) of Caucasian origin (225 Russians, 218 Udmurts, 141 Tatars and 39 of mixed ethnicity) from Russia. Depression was assessed using BDI. SNPs genotyping was performed using

PCR-based KASP genotyping technology on “CFX96” DNA Analyzer (BioRad, USA). Statistical analysis included multiple linear/logistic regression followed by FDR-correction for multiple testing (PLINK v.1.09). Genotypes and 21 environmental parameters served as independent factors and depression level as dependent variable. The present study revealed a modulating effect of birth order on association between *rs237911* (β=-2.742; P=0.031) in the *OXTR* gene and depression level. GxE model including rs53576 (β=-2.52; P=0.017) in the *OXTR* gene and the level of paternal care significantly modulated interindividual differences in depression. Haplotype analysis revealed an association of the *OXTR GAG*-haplotype (rs53576-rs2228485-rs237911) and enhanced depression in total sample (β=4.967; P_{FDR}=0.034) and among women (β=5.256; P_{FDR}=0.028).
The present study indicated a modulating effect of environmental factors on *OXTR*-associated liability to depression in healthy individuals.

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