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TITLE: The role of arginine-vasopressin receptor gene polymorphisms in the development of anger-related traits

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ABSTRACT:

Introduction: Anger is an emotional reaction to threat, frustration or social provocation, which modulates an individual's risk for aggression. Molecular-genetic studies demonstrated the involvement of arginine-vasopressin system in affective psychopathology. However, many of them lack the analysis of GxE-interactions thus providing controversial findings. The present study aimed to estimate the main effect of *AVPR1A* (*rs1042615*, *rs3803107*) and *AVPR1B* (*rs28632197*, *rs33911258*) gene polymorphisms, as well as GxE effects on anger-related traits in healthy individuals.

Materials and Methods: The study involved 623 mentally healthy individuals from the Russian Federation (81.11% women; mean age 19.53±1.75 years). All participants were of Caucasian origin of several ethnic groups: Russians (N=225), Udmurts (N=218) and Tatars (N=180). Anger-related traits were assessed using Anger Scale of the Buss Perry Aggression Questionnaire (BPAQ-29). SNPs genotyping was performed used Real-Time PCR. Statistical analysis was conducted with PLINK v.1.9 followed by FDR correction for multiple testing.

Results: Statistical analysis revealed an association of *AVPR1A***rs3803107* T-allele ($P_{FDR}=0.03$; $r^2=0.01$) and *AVPR1B***rs33911258* G-allele ($P_{FDR}=0.03$; $r^2=0.01$) and de-

creased anger. Multiple regression analysis demonstrated that smoking ($P_{\text{FDR}}=0.01$; $r^2=0.16$), birth season ($P_{\text{FDR}}=0.04$; $r^2=0.04$) and place of residence ($P_{\text{FDR}}=0.04$; $r^2=0.02$) significantly modulated association of *AVPR1B***rs33911258* and anger, while birth season ($P_{\text{FDR}}=0.03$; $r^2=0.05$) significantly modulated association on the *AVPR1A***rs3803107* and anger in total sample.

Conclusion: Our findings provide evidence for specific effect of several environmental factors (smoking, birth season and place of residence) on the associations *AVPR1A* and *AVPR1B* gene polymorphisms and anger-related traits.

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