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TITLE: The role of inflammatory system genes in non-verbal intelligence in mentally healthy individuals

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ABSTRACT:
A multifactorial nature of cognitive abilities (including non-verbal intelligence) suggests the involvement of multiple genes of small effect and environmental factors in its development, thus requiring simultaneous examination of genetic and environmental factors. Recently, pathways involved in immune function and inflammatory response, especially interleukin and cytokine signaling (i.e. *TNF*, *IL1B*, *CRP*) were related to cognitive impairments. However, the data on their involvement in cognitive abilities is scarce.
In order to assess the possible involvement of inflammatory genes in cognitive processing, the present study aimed to estimate both the main effect of *IL1B*, *CRP* and

TNF gene polymorphisms and G×E-interactions in individual differences in non-verbal intelligence in healthy individuals.

The study included 897 mentally healthy individuals (79% women; 19.74±1.51 years) of Caucasian origin (428 Russians, 200 Tatars, 117 Udmurts, and 152 of mixed ethnicity) from Russia. The assessment of non-verbal intelligence was conducted via Raven's progressive matrices. SNPs genotyping was performed using PCR-based KASP genotyping technology on "CFX96" DNA Analyzer (BioRad, USA). Statistical analysis included multiple linear/logistic regression (FDR-correction, PLINK v.1.09). Genotypes and 21 environmental parameters served as independent factors and non-verbal intelligence as dependent variable.

Statistical analysis revealed association of increased non-verbal intelligence and *TNF* rs1041981 A-allele in men (β=1.75; P_{FDR}=0.035) and *IL1B* rs16944 A-allele in Tatars (β=1.645; P_{FDR}=0.005). Moreover, GxE model demonstrated that sibship size modulated the association of *TNF* rs1041981 A-allele and non-verbal intelligence (β=1.90; P=0.005).

The present study indicated the involvement of inflammatory system genes (*TNF*, *IL1B*) in individual variation in cognitive abilities in healthy individuals.

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