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Impact of *P2RX7* and *TNF/LTA* gene polymorphisms in non-verbal intelligence in mentally healthy individuals

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Motivation and Aim: The study of cognitive functions as an important part of mental health has become challenging because of the enhanced requirements for effective intellectual activities in all fields of social functioning [1]. Nonverbal intelligence as one of cognitive abilities implies an individual's ability to use problem-solving strategies and manipulate visual information without using verbal skills [2]. The heritability (percent of individual differences accounted for genes) of intelligence in infancy is estimated at about 20 %, increases to about 40 % in middle childhood and may be as high as 80 % in adulthood [3]. Nowadays, the study of nonverbal intelligence from a biological point of view is considered the most justified. Inflammatory mediators belong to one of the promising and poorly studied biological systems in relation to non-verbal intelligence [4]. In this regard, the purpose of this work was to study the SNPs of genes involved in regulation of inflammatory mediators (*TNF/LTA rs1041981, rs1800629,* and *P2RX7 rs2230912*) and their role in the formation of individual differences in the level of nonverbal intelligence in mentally healthy individuals.

Methods and Algorithms: The study involved 1011 mentally healthy individuals (Russians, Tatars and Udmurts) from Republic of Bashkortostan (80 % women) (mean age 19,79 ± 1,69 years). A written inform consent was obtained from all the participants after they were acquainted with all the procedures. SNPs genotyping was performed via real-time PCR with a fluorescent detection using the KASP method. Detection was carried out on the CFX96 DNA Analyzer (Bio-Rad, USA) with the endpoint fluorescence analysis. The level of nonverbal intelligence was measured using a black-and-white version of the Raven Progressive Matrices [5]. Statistical analysis was conducted with Plink v.1.09.

Results: As a result of haplotypic analysis we detected the association of the *TNF/LTA*AA* haplotype (*rs1041981*, *rs1800629*) ($\beta_{ST} = 1.19$; $p = 0.033$; $p_{perm} = 0.047$) with an enhanced level of nonverbal intelligence in individuals without cognitive decline. In the present study we also conducted the analysis of gene-by-environment (G×E) interactions estimating the effect of 14 socio-demographic parameters. As a result of G×E interactions we observed that sibship size significantly affected the association

of the *rs1041981* in the *TNF/LTA* gene ($\beta = 2.08$; $\beta_{ST} = 0.16$; $p = 0.001$) and a dose-dependent effect of *P2RX7 rs2230912* minor *G*-allele on a decreased level of nonverbal intelligence among smoking individuals ($\beta = –1.70$; $\beta_{ST} = –0.10$; $p = 0.022$).

Conclusion: The results obtained within the framework of this study confirm the role of the inflammatory mediator's system in the formation of differences in the level of nonverbal intelligence in mentally healthy individuals.

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