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APOE-controlled effect of inflammatory system gene variants on non-verbal intelligence in young adults

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ABSTRACT:

Although multiple studies indicated the role of APOE gene in cognitive decline, the evidence of APOE effect on genetic associations of inflammatory system genes and cognitive abilities (including non-verbal intelligence, NVI) is scarce. The aim of the study was to estimate the main effect of inflammatory gene variants on individual differences in non-verbal intelligence in mentally healthy students and to clarify the necessity to control for unfavorable *APOE* E4-alleles while performing genetic testing even at young age. The study included 1011 mentally healthy individuals (80% women; 19.79±1.69 years) of Caucasian origin (535 Russians, 231 Tatars, 160 Udmurts, and 85 of mixed ethnicity) from Russia. NVI score was assessed via Raven's progressive matrices. The *IL1b* rs16944, *IL1A* rs1800587, *CRP* rs3093077, *TNF* rs1041981 and rs1800629, *P2X7R* rs2230912 gene variants were genotyped using PCR. Statistical analysis included multiple linear regression models (additive, dominant, recessive) conducted controlling for sex, ethnicity and *APOE* E4-allele in total sample and in men and women separately (PLINK v.1.09). While stratifying by *APOE* E4-allele and controlling for sex and ethnicity in the total sample, there was a significant effect of *TNF* rs1800629 A-allele (β=1.79; P=0.019), *TNF* rs1041981 A-allele (β=1.49; P=0.019) and *TNF AA*-haplotype (rs1041981, rs1800629) (β=1.53; P=0.033) on higher NVI in dominant model. The same effect was observed in men while controlling for *APOE* E4-allele: *TNF* rs1800629 A-allele was associated with higher NVI (β=1.75; P=0.021). The findings obtained evidence in a modulating effect of *APOE* E4-allele on the association between *TNF* gene variants and non-verbal intelligence in young adults.

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