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ESTIMATION OF ALLELIC FREQUENCIES AT SOME LOCI, PREVIOUSLY ASSOCIATED WITH SUBSTANCE USE DISORDERS, IN UKRAINIANS AND IN THE 1000 GENOMES DATASET

Background/Aim. Substance use disorders (SUDs) are complex polygenic conditions in which genetics accounts for about 50% of the variability [Gerring et al. 2024]. Eastern European populations are understudied, so we aimed to compare the distribution of alleles in a sample of healthy volunteers from Ukraine with the 1000 Genomes (1000G) groups at the COMT-rs4680, ADH1B-ADH1C-rs1789891, and HTR2A-rs6313 loci, that are associated with SUDs in other populations. **Methods.** DNA was extracted using Zymo Quick-DNA Miniprep. Genotyping was done using custom-made primers, TaqMan probes produced by Metabion. We compared genotype frequencies among 264 individuals with the 1000G data using χ^2 test. **Results.** The allele frequencies in the Ukrainian population for the examined loci are: COMT-rs4680 A/G:48.81%/51.19%, HTR2A-rs6313 C/T:63.64%/36.36%, ADH1B-ADH1C-rs178989 A/C:12.17%/87.83%. Genotype frequencies at COMT-rs4680 have statistically significant differences from the African (AFR; $p = 5.98 \times 10^{-24}$), American (AMR; $p = 3.47 \times 10^{-8}$), and East Asian (EAS; $p = 3.22 \times 10^{-25}$) population groups, while being similar to South Asian (SAS) and European (EUR) ($p > 0.05$). For HTR2A-rs6313, statistically significant differences were found from the EUR ($p = 0.0017$), EAS ($p = 9.83 \times 10^{-24}$), and SAS ($p = 0.013$) groups, while AMR and AFR do not differ statistically ($p > 0.05$) from the Ukrainian population. Genotype frequencies at ADH1B-ADH1C-rs1789891 significantly differed from all superpopulations in the 1000G: EUR ($p = 0.03$), AFR ($p = 6.33 \times 10^{-149}$), AMR ($p = 0.02$), EAS ($p = 2.006 \times 10^{-15}$), and SAS ($p = 0.0075$). **Conclusions.** We found differences in allele distribution of the studied loci for the Ukrainian population compared to the groups from the 1000G project. Ukrainian genotype distributions at ADH1B-ADH1C-rs1789891 differ from all the 1000G superpopulations. For COMT-rs4680, there is similarity with SAS and EUR groups, for the HTR2A-rs6313, with AMR and AFR. For more detailed conclusions, more diverse reference databases should be used.

Keywords: substance use disorders, COMT, rs4680, ADH1B-ADH1C, rs1789891, HTR2A, rs6313.

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