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Genetic Correlates of Impulsivity in Bulgarian Substance Users

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This study examined the genetic basis of impulsivity in the context of substance use disorders. The multidimensional construct of impulsivity was analyzed using a battery of 23 self-report and neurocognitive indices of impulsivity and related traits. An exploratory GWAS was conducted in a sample of 380 Bulgarian participants, including 88 heroin users, 69 amphetamine users, 110 polysubstance users, and 118 controls. Genotyping was performed with the SmokeScreen array. After QC filtering, GWAS was conducted in PLINK v1.9 using linear regression model, with gender and age as covariates. FUMA was used for functional annotation of results, gene prioritization and interactive visualization. Several of the impulsivity and anxiety phenotypes reached genome-wide significance ($p < 5 \cdot 10^{-8}$). The most significant association was found with the total score of the Levenson's Self-Report Psychopathy Scale (LSRP) and rs116990828 in *UBAP2* gene ($p = 1.544 \cdot 10^{-17}$), previously implicated in alcohol dependence. The total Trait score of the State-Trait Anxiety Inventory (STAI-T) was associated with rs75676207 in *HOMER2* gene ($p = 2.868 \cdot 10^{-12}$), which has been associated with cocaine dependence and plasticity in alcohol use disorder. Several other promising results were found for impulsivity- and anxiety-related measures (risk taking on Balloon Analogue Risk Task, Anxiety Sensitivity on Substance Use Risk Profile Scale, ADHD on Wender Utah Rating Scale, Fagerstrom Test of Nicotine Dependence). Genes implicated in cognitive functioning, brain development and synaptic plasticity, as well as substance use and other psychiatric disorders were among the most promising results. These preliminary findings highlight the importance of deep phenotyping to unravel genetic effects in addiction.