http://dx.doi.org/10.7124/bc.000AE3

Genetic effects of variation at *ADH1B-ADH1C* locus on substance use disorders and physical health traits

V.V. Bashynska[1], O. Zahorodnia[2], Y. Borysovych[2], Y. Zaplatnikov[2], V. Vasilyeva[2], I. Arefiev[2], D. Krasnienkov[3], O. Zabuga[3], N. Darvishov[2], D. Osichanskaya[4], A. Karapetyan[4], O. Melnychuk[5], O. Boiko[5], G.M. Zil'berblat[5], O.I. Turos[1], I.O. Prokopenko[6], M.A. Kaakinen[6,7]

[1] O.M. Marzeiev Institute of Public Health, NAMS of Ukraine
50, Hetman Pavlo Polubotka Str., Kyiv, Ukraine, 02094
[2] Taras Shevchenko National University of Kyiv
64/13, Volodymyrska Str., Kyiv, Ukraine, 01601
[3] D.F. Chebotaryov Institute of Gerontology, NAMS of Ukraine
67, Vyshhorodska Str., Kyiv, Ukraine, 04114
[4] MedLux Medical Centre
6/8, Nikolsko-Botanicheskaya Str., Kyiv, Ukraine, 01033
[5] Kyiv City Psychoneurological Hospital №3
7, Pavlova Str., Glevakha, Kyiv region, Ukraine, 08631
[6] University of Surrey
Stag Hill, University Campus, Guildford, United Kingdom, GU2 7XH
[7] Imperial College London
South Kensington Campus, London, United Kingdom, SW7 2AZ
vitalina.bashynska@health.gov.ua

Introduction. Substance use disorders (SUDs), including drug (DD), alcohol (AD) and nicotine (ND) dependence, are global threats for physical and mental public health. In Ukraine, ~350,000 people inject drugs, and ~6% of adult population have alcohol abuse. We may expect an increase of this problem as a consequence of war and acute social problems. SUDs are highly co-morbid with each other and there is evidence for co-morbidity with other health-related traits. This suggests underlying shared genetic effects. **Aim.** We investigated association of a validated in other populations GWAS-identified AD risk locus *ADH1B-ADH1C* rs1789891 with a range of SUDs in Ukrainians and evaluated its potential effects on other traits in GWAS summary statistics from Biobanks. **Methods.** We genotyped rs1789891 at *ADH1B-ADH1C* in a multivariate dataset including 507 individuals with and without SUDs from Ukraine (mean age 32.6±9.6 years, among them 133 individuals without any SUDs) using PCR. We performed logistic regression for DD, AD, and ND, adjusting for sex and other SUDs phenotypes. We further conducted a phenome-wide association study of rs1789891 in summary statistics from UK Biobank (UKBB) and FinnGen. **Results.** rs1789891 in Ukrainians was associated with AD (p = 0.0087) and DD (p = 0.0321), with the direction of effect corresponding to GWAS data, but not with ND, or alcohol consumption. rs1789891 showed an association in the UKBB with alcohol intake frequency ($p = 2.45\times10^{-24}$) and suggestive evidence for associations with F10 AD ($p = 3.27\times10^{-8}$), Waist/Hip circumference ratio ($p = 3.02\times10^{-6}$), and Non-insulin-dependent diabetes mellitus ($p = 3.03\times10^{-6}$). In FinnGen, rs1789891 was significantly associated with different definitions of Alcohol use disorder ($p = 1.8\times10^{-11}$–1.5×10^{-6}) and Substance abuse ($p = 5.7\times10^{-8}$), and there was a suggestive evidence for associations with Acute renal failure ($p = 1.2\times10^{-4}$), and death from Alcohol related diseases ($p = 1.7\times10^{-4}$). **Conclusion.** Variations at ADH1B-ADH1C may have pleiotropic effects on SUDs as well as some physical health traits. **Grants.** University of Surrey Faculty Research Support Fund, US-Ukraine Biotech Initiative Small Research Grant, Crowd.Science.

Keywords: genetic association study, substance use disorders, Ukrainians, multi-phenotype study, *ADH1B-ADH1C,* pleiotropy.