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The Internal Exposome, Opium Use, and Opioid Use Disorder

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Opioid use disorder (OUD) is a clinical diagnosis based on the qualitative criteria defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). Our study focused on finding objective biological markers associated with OUD, to assist future studies of genetic susceptibility to OUD development among those exposed to opiates. These findings could also reveal metabolic perturbations that could inform new drug targets or nutritional intervention strategies.

We used urine specimens from 510 participants of the Golestan Cohort Study, which has enrolled more than 50,000 adults, living in Golestan Province in northeast Iran, 8,500 of them reporting chronic opiate use. The selected individuals either reported no opiate use (80 controls) or reported opiate use (n=430 further classified as having or not having OUD using a validated questionnaire).

Untargeted analysis of urine was conducted using a UPLC-Q-Exactive HFX Mass Spectrometer, and using a Bruker 700 Nuclear Magnetic Resonance (NMR) spectrometer. Data were modelled using logistic regression, multivariate analysis, and hypothesis testing with the comparison of these phenotypes: opium users vs non-users, and opium users diagnosed as OUD positive vs OUD negative. Comparisons were stratified by tobacco use, route of exposure (ingestion or inhalation), and level of opium intake.

Opium exposure resulted in perturbations in endogenous metabolites involved in one carbon metabolism, Krebs cycle, tryptophan metabolism, mediation of cell signal transduction, and neuroexcitatory activity. A subset of metabolites were associated with OUD. Metabolites of illicit drugs, tobacco products, carcinogens, phthalates, and plants also contributed to the phenotypes investigated.