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ENIGMA-Addiction: Gene-brain associations with SUD

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Background and Rationale: ENIGMA-Addiction is an international, multi-site data pooling endeavor that seeks to identify the neurobiological and genetic correlates of SUD. While it continues to expand, it currently contains over 15,000 participants from 14 countries and includes current and former addicts, recreational users, and longitudinal cohort studies. The motivation for the large sample size is to be able to identify gene-brain associations that are reliable and reproducible.

Hypotheses: We sought to determine if there are brain markers (volumetric differences) between SUD cases and controls and if these are common or different across different drugs of abuse.

Results: Brain structure was examined in a mega-analysis of data pooled from 23 laboratories, including 3,240 individuals, 2,140 of whom had substance dependence on one of five substances: alcohol, nicotine, cocaine, methamphetamine, or cannabis. Lower volume or thickness was observed in many brain regions in individuals with substance dependence. The greatest effects were associated with alcohol use disorder. A set of affected regions related to dependence in general, regardless of the substance, included the insula and the medial orbitofrontal cortex. Furthermore, a support vector machine multivariate classification of regional brain volumes successfully classified individuals with SUD on alcohol or nicotine relative to nondependent control subjects.

Discussion: Results indicate that dependence on a range of different substances shares a common neural substrate and that differential patterns of regional volume could serve as useful biomarkers of dependence on alcohol and nicotine. Future aims will search for genetic correlates of these addiction-general and drug-specific putative biomarkers.