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Individual variation in addiction-related behaviors contributes to opioid dependence vulnerability

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A significant worldwide rise in opioid use disorder (OUD) has arisen, making the understanding of the behavioral, neurobiological and genetic components that contribute to OUD necessary to explore. In the current study, genetically heterogeneous outbred rats underwent various testing procedures to assess the behavioral determinants associated with vulnerability versus resilience to opioid dependence. Stress and anxiety-related behaviors, as well as analgesic thresholds, were first assessed. Rats then underwent 3 weeks of long-access heroin self-administration training, followed by a progressive ratio test and a within-session extinction training and heroin-induced reinstatement (0.25 mg/kg, s.c.). Extinction training (6 days) then commenced, after which a test for cue-induced reinstatement was performed. The paradigms assessing stress, anxiety and analgesic threshold were then repeated. We have shown that locomotor activity during the open field test acts as a predictor for drug-seeking behavior during the reinstatement tests. Furthermore, we created a composite index that encompasses these various behaviors to classify rats based on vulnerability to OUD. Tissue samples for analysis of genetic and epigenetic factors contributing to OUD vulnerability are currently being collated. However, we have shown that the gut microbiome and brain grey matter volume (GMV) changes as a function of heroin experience. Specifically, heroin experience results in a decrease in GMV in several cortical and sub-cortical areas associated with addiction, a finding consistent with human heroin addicts. These data highlight the translational validity of our model, and the benefit of focusing on a variety of behavioral and biological markers when assessing vulnerability to OUD.