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Sensation seeking behavior contributes to opioid dependence vulnerability in a sex-dependent manner

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There has been a significant rise in opioid use disorder (OUD) in the United States over the past decade, making the understanding of the behavioral components that contribute to OUD necessary to explore. In the current study, male and female heterogeneous stock rats underwent various testing procedures to assess the behavioral determinants associated with vulnerability versus resilience to OUD. Stress and anxiety-related behaviors, as well as analgesic thresholds, were assessed both prior to and following heroin experience. Rats then underwent 3 weeks of long-access heroin self-administration training, a progressive ratio test, extinction training and different tests of reinstatement of drug-seeking behavior. Rats were characterized based on a high level (high-responder, HR) versus a low level (low-responder, LR) of locomotor activity in an open field test. The HR/LR model is commonly used to examine individual variation in the acquisition of drug-taking behavior. We show that male HRs consume more heroin, are more motivated to work for heroin and have a higher relapse propensity relative to male LRs. Female HRs and LRs do not differ in any measures. Next, a Bayesian stochastic block model was applied to separate rats into clusters based on behavior over the course of training. Results show a higher representation of HRs in the cluster conferring OUD vulnerability, and more LRs in the resilient cluster. These data suggest that sensation-seeking behavior is one component of addiction liability, albeit in a sex-dependent manner, highlighting the benefit of focusing on a variety of behavioral factors when assessing vulnerability to OUD.