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Network-based clustering approach models multi-symptomatic opioid use disorder vulnerability

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There has been a significant rise in opioid use disorder (OUD) in the United States over the past decade, making it imperative to gain a better understanding of the behavioral and neurobiological characteristics underlying OUD vulnerability and resiliency. Current rodent models focus on how one or a few traits interact in a linear manner to predict substance use disorder, however, OUD consists of several symptoms that interact with one another and can vary across individuals. In the current study, male and female heterogeneous stock rats were assessed across several measures of heroin taking, refraining and seeking behaviors. To assess how behaviors interact conferring OUD vulnerability, a Bayesian stochastic block model network-based clustering approach was used to separate rats into an OUD vulnerable, resilient, and intermediate subpopulation. Relative to resilient rats, OUD vulnerable rats exhibit potentiated compulsive heroin-taking behavioral following a period of abstinence, withdrawal-induced ultrasonic vocalizations and heroin-taking in the presence of an adverse stimuli. Furthermore, using a hierarchical analysis, vulnerable OUD rats are comprised on distinct sub-clusters, exhibiting heterogeneity in salient traits conferring overall vulnerability, with differences between male and female rats observed. Using this model, we also show that OUD vulnerable and resilient rats exhibit distinct thalamo-striatal and top-down cortical processes following cued-reinstatement. Subpopulations also differ in nucleus accumbens neuroplasticity measures. Together, these findings highlight distinct adaptations associated with OUD vulnerability and resiliency using a model akin to human OUD. Current analyses are focused on assessing genetic differences between these distinct subpopulations.