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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 characteristics underlying OUD vulnerability. Current rodent models focus on how one or few traits interact in a linear manner to predict substance use disorder (SUD), 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 (SBM) network-based clustering approach was used to separate rats into subpopulations. Three distinct subpopulations (vulnerable, intermediate and resilient) emerged that predicted OUD vulnerability in both sexes, although females showed a more vulnerable phenotype, akin to what is observed in humans. Vulnerable subpopulations exhibited behavioral heterogeneity with respect to the most salient traits, another feature observed in humans. Hierarchical analyses revealed distinct sub-clusters within the vulnerable sub-population only. For both sexes, there was a high consumer/low seeker, low consumer/high seeker, and high consumer/high seeker sub-cluster. The presence of different clusters highlights the need for different therapeutic interventions for those afflicted with OUD. Furthermore, rats in the vulnerable group exhibited greater compulsive heroin taking and resistance to punishment, a cardinal feature of SUD. Subpopulations also differ in nucleus accumbens core dendritic spine morphology, a drug specific form of transient synaptic potentiation.