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Comparison of Intravenous Self-Administration of Psychostimulants vs. Opioids in an Animal Model of Internalizing vs. Externalizing Temperament

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In humans, only a small portion who experiment with recreational drug use transition to substance use disorder (SUD). Multiple factors underlie this difference, including genetically mediated differences in temperament; with externalizing individuals often approaching drugs of abuse from a sensation-seeking pathway, while internalizing individuals approach drugs of abuse less for recreational reasons, but will following triggers like psychosocial stress. Our lab has used a selective breeding strategy based on locomotion in a novel environment to derive two lines of rats with distinct genotypes, behavioral and neurobiological phenotypes, selectively-bred high-responders (bHRs) and low-responders (bLRs). We have previously shown that temperamental differences between these rats influences their propensity to seek and take psychostimulants, in ways that reflect what's seen in humans. However, we hypothesized these differences in baseline drug seeking are partially drug-specific, where bLRs have higher preference for opioids than stimulants. Here, we used a free access self-administration paradigm of heroin or cocaine to determine whether these individual differences result in differential use patterns. For both drugs, we observed the expected phenotype differences, with bHRs seeking and taking more drug than bLRs. However, the differences were less pronounced for opioids than stimulants, implying increased opioid preference in bLRs relative to stimulants, and include a complex drug/sex/phenotype interaction. Work is ongoing to evaluate differential impact of cocaine on gene expression in the nucleus accumbens and hippocampus at the bulk and single nuclei levels. These findings advance our understanding of individual differences in genetics/gene expression as antecedents of addiction development.