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## **Cocaine self-administration profiles in the Founder Strains of the Collaborative Cross**

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### Background/Rationale

Cocaine addiction places a significant health burden and substantial economic costs on society. Identifying biological mechanisms underlying addiction vulnerability will open up avenues for treatment and prevention. We aimed to identify biological mechanisms of addiction vulnerability by surveying intravenous cocaine self-administration (IVSA) in the genetically diverse founder strains of both the Collaborative cross and the Diversity Outbred population.

### Methods

Mice from these eight strains were tested on the cocaine IVSA paradigm. Following acquisition, individuals completed a full dose-response curve (0.032 – 1.8 mg/kg/infusion). Next, the extinction of drug-paired responses was recorded, following the removal of the drug. Relapse propensity was quantified using reinstatement in presence of drug-paired cues.

### Results

The eight inbred strains varied in their cocaine self-administration profiles based on acquisition of self-administration behavior, dose-response functions, extinction and reinstatement of drug-seeking responses. The PWK/PhJ strain displayed multiple addiction vulnerability phenotypes with a greater proportion of individuals acquiring cocaine IVSA and doing so at a higher rate. Additional PWK/PhJ addiction vulnerability traits included self-administering a higher number of infusions across the multiple drug doses during dose-response phase, prolonged extinction of drug-paired responses and rapid reinstatement in the presence of drug-paired cues. In contrast, 129S1/SvImJ strain displayed very low levels of drug-paired responses and did not progress through the subsequent phases of the study. Heritability estimates of addiction-relevant traits were also computed.

### Conclusions

These data provide the first comprehensive survey of cocaine self-administration phenotypes and demonstrate heritable strain differences in cocaine-seeking behaviors confer differential susceptibility to addiction.