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Dysregulated Oxycodone use in Select Inbred Rat Strains From the Hybrid Rat Diversity Panel

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Prescription opioids are considered the gold standard in analgesic pain medication but can lead to problematic drug use and the development of opioid use disorder (OUD). Little work has systematically assessed the factors that contribute to the development of OUD. A rodent genetic model was used to precisely measure specific phenotypes associated with the initiation of oxycodone use and the development of compulsive-like escalation of oxycodone use. Based on initial profiling of oxycodone intake parameters across all 15 inbred strains (M=107; F=104), we selected three “low-taking non-escalating”, and three “high-taking escalating” for additional phenotypic assessment of compulsive-like oxycodone use by quantifying intake during episodes of burst infusions. Our results suggest that the low- and high-taking strains are significantly different in the number of burst episodes ($F_{5,89} = 16.93$, $p < 0.001$), burst durations ($F_{5,88} = 8.99$, $p < 0.001$), the number of infusions per burst ($F_{5,88} = 7.49$, $p < 0.001$), and inter-infusion intervals ($F_{5,88} = 12.19$, $p < 0.001$). Among the high-taking strains, the M520/N displayed a significant increase in burst episodes from the first to the last long-access session ($t_{89} = 6.68$, $p < 0.001$), and had significantly more episodes of burst infusions compared with all other strains. The low-taking HXB23/lpcv strain maintained controlled oxycodone intake with no escalation in oxycodone intake, few burst episodes, and long inter-infusion intervals. These findings suggest that genetic contributions to oxycodone use may uniquely determine multiple specific features of opioid use.

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