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Oxycodone oral self-administration in inbred rats identifies different patterns of vulnerability

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Although the misuse of most opioids requires injection or inhalation to produce rapid subjective effects, the exceptionally strong abuse liability of oxycodone is evident even when consumed orally. We designed an intermittent operant oral self-administration procedure in rats to model the pattern of oxycodone consumption in humans. This model starts with limited initial drug intake, followed by increasing drug concentrations during extended 4-h sessions on alternating days, progressive ratio test, extended access in 16-h sessions, extinction, and cue-induced reinstatement. We studied 25 inbred strains using this protocol (149 females and 108 males). Mean oxycodone intake (mg/kg) during 4-h sessions (0.1 mg/ml oxycodone, 60µl per reward using a fixed-ratio 5 schedule) ranged from 0.09±0.02 (HXB23) to 3.57±0.45 (LE/Stm) in females and 0.07±0.01 (M520) to 2.07±0.32 (WMI) in males. While across strains, females consumed more oxycodone than males, intake in 4-h ($r=0.54$, $p=0.02$) and 16-h ($r=0.70$, $p=0.003$) sessions was strongly correlated between sexes. Different patterns of escalation emerged when rats switched from 4-h to 16-h sessions: many strains maintained similar intake despite increased drug availability, while others drastically escalated (e.g. 7.7-fold in females and 4.9-fold in males of the FXLE15 strain). Together, these data demonstrated strong effects of genetic control on drug intake. While we are still increasing phenotyped strains, we anticipate genetic mapping using whole genome sequencing-based markers will identify genes contribute to these patterns of oxycodone-driven behavior.