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### **Intermittent oral oxycodone self-administration in inbred strains of rats is heritable**

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The steady rise in prescription opioids such as oxycodone has led to widespread abuse in the US. Given the importance of drug pharmacokinetics, we have designed an oral operant self-administration procedure to model the pattern of drug intake of most human users/abusers of oxycodone who initiate using oral tablets. We trained male and female Lewis rats to lick on a spout to obtain oxycodone (60  $\mu$ l drops) under a fixed ratio 5 schedule. Rats were not deprived of food or water before operant training. Rats were first trained in five 1-h daily sessions to obtain 0.025 mg/ml oxycodone. Thereafter, session length was increased to 4-h and training was conducted on alternate days. The oxycodone dose was gradually increased to 0.2 mg/ml. Females licked  $3,360 \pm 809$  per session to obtain  $2.6 \pm 0.52$  mg/kg oxycodone during the last three fixed-ratio sessions. Males consumed significantly less oxycodone than females. We then tested this procedure on six inbred strains of rats, including Brown Norway, Fisher 344, Lewis, Spontaneous Hypertensive Rat, WMI, WLI (Wistar-Kyoto More Immobile and Less Immobile). The estimated heritability ( $h^2$ ) for number of licks on the active spout and oxycodone intake was 0.46 and 0.37, respectively. In contrast, the  $h^2$  for inactive licks was 0.07. These results supported the hypothesis that oral oxycodone intake is a heritable trait in rats. We plan to use the hybrid rat diversity panel to map aspects of oxycodone addiction.