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Phenotypic differences in oxycodone responses in the inbred rat strains

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The opioid epidemic has become a national crisis in the United States over the last decade. To better understand the genetic contributions to opioid use disorder, oxycodone-induced behavioral responding was measured in the Spontaneously Hypertensive Rats (SHR/Ola), Brown Norway w/polydactyly-luxate (BN-Lx), and ACI inbred rat strains. Male and female rats were tested longitudinally across a battery of oxycodone-induced behaviors. Rats were trained to self-administer oxycodone (0.15 □g/kg/inf, iv) on a fixed-ratio 1 schedule in ten 2-hr sessions followed by 14 consecutive 12-hr self-administration sessions. A progressive ratio test was conducted before and after the long-access phase to evaluate the motivation to self-administer oxycodone. The tail immersion test was used to examine thermal sensitivity and oxycodone-induced analgesia before and after the oxycodone self-administration protocol. The SHR/Ola strain was resistant to oxycodone-induced analgesia and showed minimal tolerance after chronic self-administration. In contrast, BN-Lx and ACI strains displayed similar robust analgesic responses that diminished after chronic oxycodone self-administration. Acquisition and maintenance responding during the self-administration procedure were similar across strains, although a striking difference emerged in the progressive ratio test. The SHR/Ola strain showed minimal escalation in the motivation to self-administer oxycodone compared with BN-Lx and ACI. These initial studies suggest there are genetic contributions to these behavioral phenotypes associated with opioid use disorder and support our plans to use the Hybrid Rat Diversity Panel to map phenotypic and gene expression differences related to oxycodone behaviors across the genome.