Evaluation of the abuse liability of oxycodone in male and female rats using two approaches: intravenous self-administration and conditioned place preference

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In collaboration with the NIH HEAL Initiative Preclinical Screening Platform for Pain (PSPP), we evaluated the abuse liability properties of oxycodone in the intravenous self-administration and conditioned place preference (CPP) tests in male and female Sprague Dawley rats. Intravenous drug self-administration took place in sound attenuated operant chambers (Med Associates, VT) where rats pressed an active lever that delivered the test compound intravenously through a jugular vein catheter. Rats were allowed to self-administer saline (negative control), morphine (0.6 mg/kg/infusion) or oxycodone (0.01, 0.03, 0.06 and 0.1 mg/kg) by pressing the active lever on an FR3 schedule. Acquisition training lasted 20 days. In male and female rats, oxycodone (0.03, 0.06 and 0.1 mg/kg/infusion) showed higher infusion rate compared to saline. In the CPP study, an independent group design (N=16) was used for both male and female rats with five treatment groups (saline, cocaine 15 mg/kg, and oxycodone 1, 3 and 5 mg/kg) injected intraperitoneally (IP). Perceptive cues were applied to create a distinctive texture and visual features for the two compartments. A 10-day protocol was used in this study. The study was videotaped on Day 1 (baseline) and on Day 10 (bias test). The time spent in the different chambers was scored by an experimenter blinded to the treatment. Days 2-9 of the test were conditioning days in which differentiation between "drug compartment" and "saline compartment" was achieved. Rats were treated with saline on days 2, 4, 6 and 8, and with either cocaine or oxycodone on days 3, 5, 7, 9. Animals were confined in the "drug compartment" or "saline compartment" immediately after drug administration for 20 minutes. Compared to saline, cocaine, used as the positive control, induced significant CPP. Oxycodone (1, 3 and 5 mg/kg; IP) induced even larger bias between the two compartments ($P<0.001$) in both male and female rats. These data confirm the high abuse potential of oxycodone in male and female rats and both assays can be used to screen the potential abuse liability of novel therapies as part of the NIH HEAL Initiative's PSPP program towards discovering novel non-addictive analgesics.