Discriminative stimulus effects of naltrexone in rats with limited access to sucrose

Department of Psychology, University of Wisconsin- Eau Claire, 54702

Introduction

- Naltrexone (NTX) is an opioid antagonist that is not discriminable at typical doses in operant paradigms.
- Hoebel, Avena, and colleagues have demonstrated increases in opioid function in rats given daily, 12 hour access to 10%–25% sucrose solutions. We and others have shown chronic consumption of 32% sucrose increases opioid function.
- We wondered if we could establish naltrexone as a discriminative stimulus in rats given daily, 12 hour dark cycle access to sucrose solutions.

Naltrexone Discrimination: Acquisition

- Originally subjects had access to sucrose one hour prior to testing (Figure C).
- Access to sucrose solutions was postponed until after each daily testing session was complete (Figure D).
- Subjects continued to discriminate NTX from saline.

Acute Water Substitution

- Discrimination training was suspended and subjects were given 24 hour access to water for two weeks.
- Subjects were trained to discriminate between saline and NTX (3.2 mg/kg) for 11 sessions, with access only to water.
- After 14 days without access to sucrose, NTX was no longer able to serve as a discriminative stimulus.

Chronic Water Substitution

- Subjects were maintained on 12 hour access to either 10%, 25%, or 32% sucrose solutions.
- Subjects were trained with 0.1 mg/kg NTX.
- Subjects are currently being trained to reacquire the discrimination of 0.1 mg/kg NTX.

Results

- Naltrexone (3.2 mg/kg) was established as a discriminative stimulus in rats with chronic 12 hour access to sucrose (Figure A; representative subject- Figure B).
- Removal of daily sucrose access for 25 days altered the ability of NTX to serve as a discriminative stimulus (Figure E), again with no effect on rate (Figure F).
- Restoring daily sucrose access resulted in all subjects rapidly reacquiring the NTX and saline discrimination; representative subject (Figure G).
- Naloxone 0.1 mg/kg was discriminable by several subjects.
- We are currently attempting to train the subjects to reacquire the discrimination of 0.1 mg/kg NTX.
- Our results suggest that chronic sucrose consumption results in a long term change in endogenous opioid activity.

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