Effects of duloxetine in rats trained to discriminate between 2 and 22 hr food deprivation

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

Introduction

Duloxetine is a serotonin and norepinephrine reuptake inhibitor used clinically to treat depression and generalized anxiety disorders. We tested the effects of duloxetine in rats trained to discriminate 22 hr food deprivation from 2 hr food deprivation in a two-lever, operant choice task. After rats learned the discrimination, subjects were food restricted for 22 hr and administered saline and duloxetine (3.2-17.8 mg/kg, s.c.) before generalization tests. Food intake was measured for 1 hr after generalization tests. Duloxetine (10-17.8 mg/kg) significantly decreased the discriminative stimulus effects of 22 hr deprivation, rate of lever pressing, and significantly reduced food intake induced by 22 hr deprivation. These findings are consistent with our laboratory’s previous findings with sibutramine and offer further evidence that serotonin and noradrenaline are important in regulating internal states associated with food intake and food consumption.

Method

Subjects and apparatus
- Male Sprague-Dawley rats were housed in individual cages in a room with 12:12 light/dark cycle.
- 45 mg food pellets (Bioserve F#0021) were delivered as reinforcers in standard two-lever operant chambers (Med-Associates).

Drug
- Duloxetine (3.2-17.8 mg/kg) was dissolved in 0.9% saline and administered s.c.

Behavioral training
- Condition appropriate lever presses (left lever presses following 22 hr food deprivation, and right lever presses following 2 hr deprivation) were reinforced under a FR-15 reinforcement schedule.
- Training continued until subjects emitted greater than 80% condition-appropriate responses both prior to the first reinforcer delivery for each training cycle and for the complete training sessions.

Generalization tests
- A cumulative testing procedure was implemented during test sessions.
- Responses toward either lever were reinforced under a FR-15 reinforcement schedule.
- Saline (s.c.) was administered prior to the response period.
- Duloxetine (3.2-17.8 mg/kg, 30 min PT) was administered prior to subsequent response periods.
- Following the last response period for a session, subjects were placed in suspended cages with free access to food and water for one hour.
- Data were analyzed by ANOVA. If the results of the ANOVA were significant, Tukey post-hoc tests were implemented.
- A minimum of two training days occurred between test sessions, with subjects passing both a 2- and 22 hr session.

Figures

Effects of Duloxetine on the Discriminative Stimulus Effects of 22- hr Food Deprivation

Effects of Duloxetine on Response Rate

Effects of Duloxetine on Food Intake

Results and Conclusion

- Administration of duloxetine (5.6-17.8 mg/kg, s.c.) significantly decreased the discriminative stimulus effects of 22 hr food deprivation.
- Duloxetine (10-17.8 mg/kg, s.c.) also resulted in significantly decreased rates of lever pressing.
- Duloxetine (5.6 - 17.8 mg/kg, s.c.) reduced food intake induced by 22 hr food deprivation.

These findings are consistent with our laboratory’s previous findings with sibutramine, and offer further evidence that serotonin and norepinephrine are important in regulating internal states associated with food consumption. Further investigation is necessary to determine the mechanisms through which these two neurotransmitters interact with neural systems in order to regulate physiological and behavioral aspects of food consumption. Understanding these processes may provide important insight into an array of abnormal regulation of food intake such as obesity.

Previous Results

- Chemicals that increase eating and reduce effects similar to 22-hr food deprivation: ghrelin, neuropeptide Y
- Chemicals that increase eating and do not induce effects similar to 22-hr food deprivation: butorphanol (DAMGO), orphanin FQ, pentobarbital
- Chemicals that decrease eating and reduce the effects of 22-hr food deprivation: cholecystokinin, sibutramine, amphetamine
- Chemicals that decrease eating and do not reduce the effects of 12hr food deprivation: exendin-4, naloxone, oxytocin, imipramine, chlorpromazine

Acknowledgements

- University of Wisconsin-Eau Claire Office of Research and Sponsored Programs
- University of Wisconsin-Eau Claire Faculty/Student Research Collaboration
- University of Wisconsin-Eau Claire Student Travel for the Presentation of Research Results
- University of Wisconsin-Eau Claire Differential Tuition Program