

Effects of bupropion and naltrexone on the discriminative stimulus effects produced by 22 hours food deprivation



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Introduction

Bupropion inhibits dopamine and norepinephrine transporters and is clinically used to treat depression and as a smoking cessation aid. Naltrexone is an opioid antagonist and is clinically used to treat opioid and alcohol dependence. Studies show that bupropion decreases food intake in rats (Zarrindast, Hosseini-Nia, 1988). Naltrexone has also been shown to decrease food intake in rats (Kirkham, Blundell, 1987). Bupropion in combination with naltrexone decreases food intake in rats (Clapper, Athanacio, Wittmer, Griffin, D'Souza, Parkes, & Roth, 2013). Contrave®, a drug that combines naltrexone and bupropion, is currently in clinical trials for the treatment of obesity in humans. Contrave® has been found to reduce body weight in humans (Orexigen Therapeutics, 2013). In the present investigation, we examined the effects of bupropion, naltrexone, and combinations of bupropion and naltrexone in non-restricted rats trained to discriminate between 22- and 2-hr food deprivation to gain better understanding of neurochemicals mediating the discriminative stimulus effects of 22-hr food deprivation.

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

- Bupropion (3.2-32 mg/kg) was dissolved in 0.9% saline
- Naltrexone (1-10 mg/kg) was dissolved in 0.9% saline

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 session.

Generalization tests

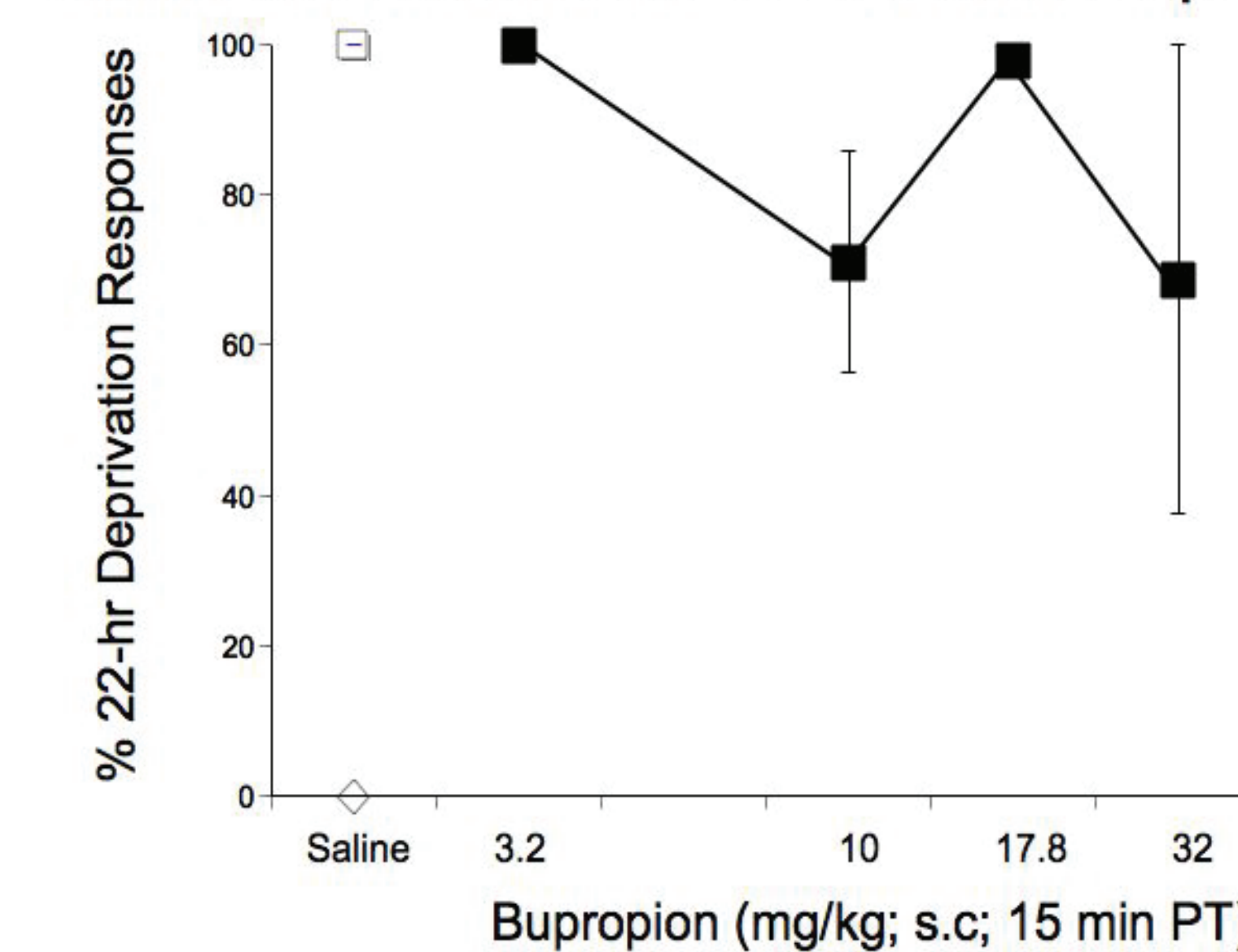
- Injections were made subcutaneously 15 minutes before the experimental session
- A cumulative dosing procedure was implemented during test sessions.
- Responses toward either lever were reinforced under a FR-15 reinforcement schedule.
- Saline was administered prior to the first response period.
- Bupropion (3.2-32 mg/kg), naltrexone (1-10 mg/kg), or the combination of bupropion (10 mg/kg) and naltrexone (1-10 mg/kg) was administered after the saline response period.
- Following the last response period for a session, subjects were placed in suspended cages with free access to food and water for one hour.
- A minimum of two training days occurred between test sessions, with subjects passing both a 2- and 22-hr session.
- Data were analyzed by ANOVA. If the results of the ANOVA were significant, Tukey post-hoc tests were implemented.

Results

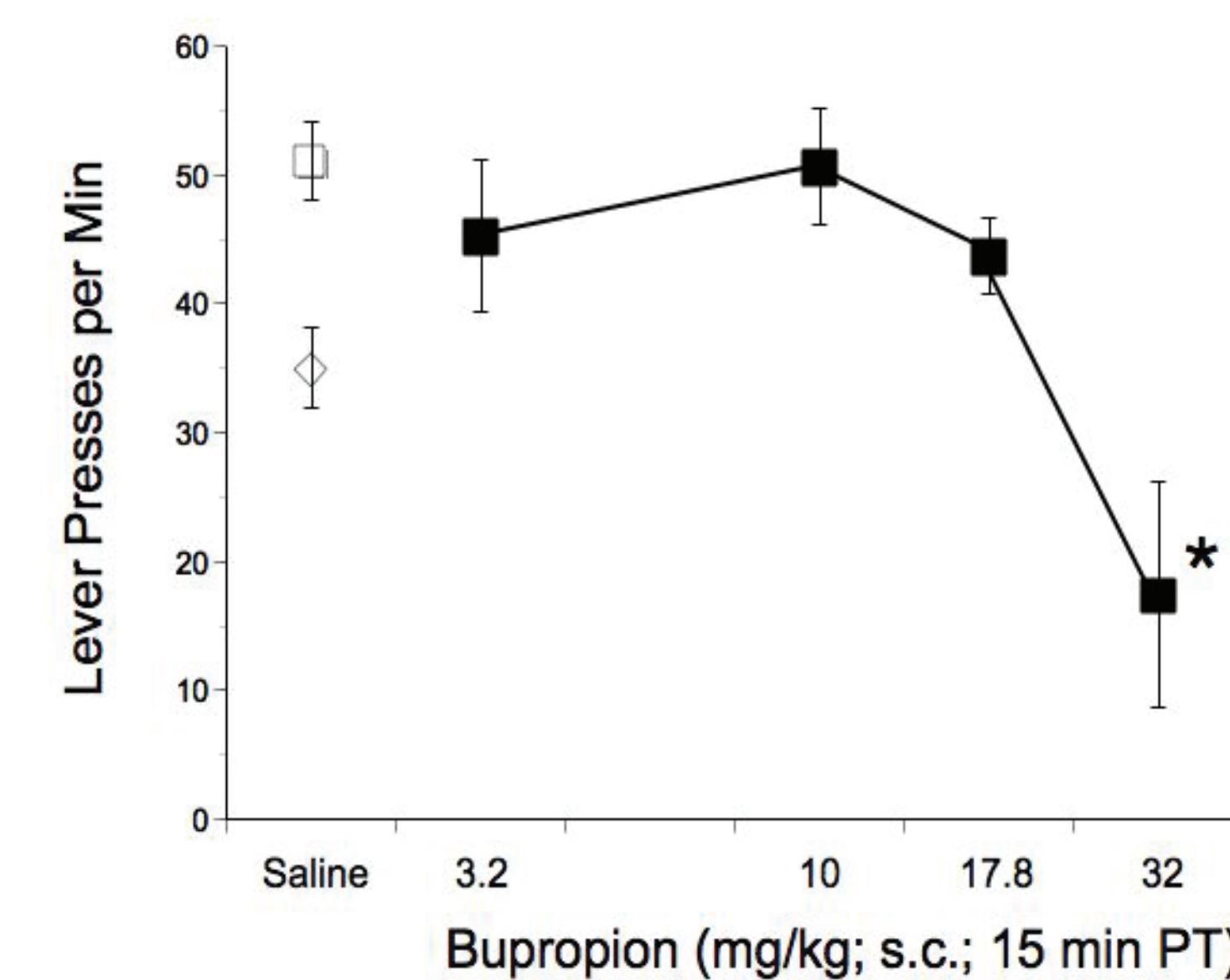
- Bupropion (3.2-32 mg/kg) did not affect the discriminative stimulus effects of 22-hr food deprivation. Bupropion (32 mg/kg) significantly decreased response rates and food intake. Smaller doses had no effect on lever pressing or food intake.
- Naltrexone (1-10 mg/kg) did not affect the discriminative stimulus effects of 22-hr food deprivation or rates of lever pressing. Naltrexone (10 mg/kg) significantly decreased food intake.
- Combinations of Bupropion (10 mg/kg) with naltrexone (1-10 mg/kg) did not affect the discriminative stimulus effects of 22-hr food deprivation or response rates. The combination of bupropion (10 mg/kg) and naltrexone (10 mg/kg) significantly decreased food intake.

Bupropion

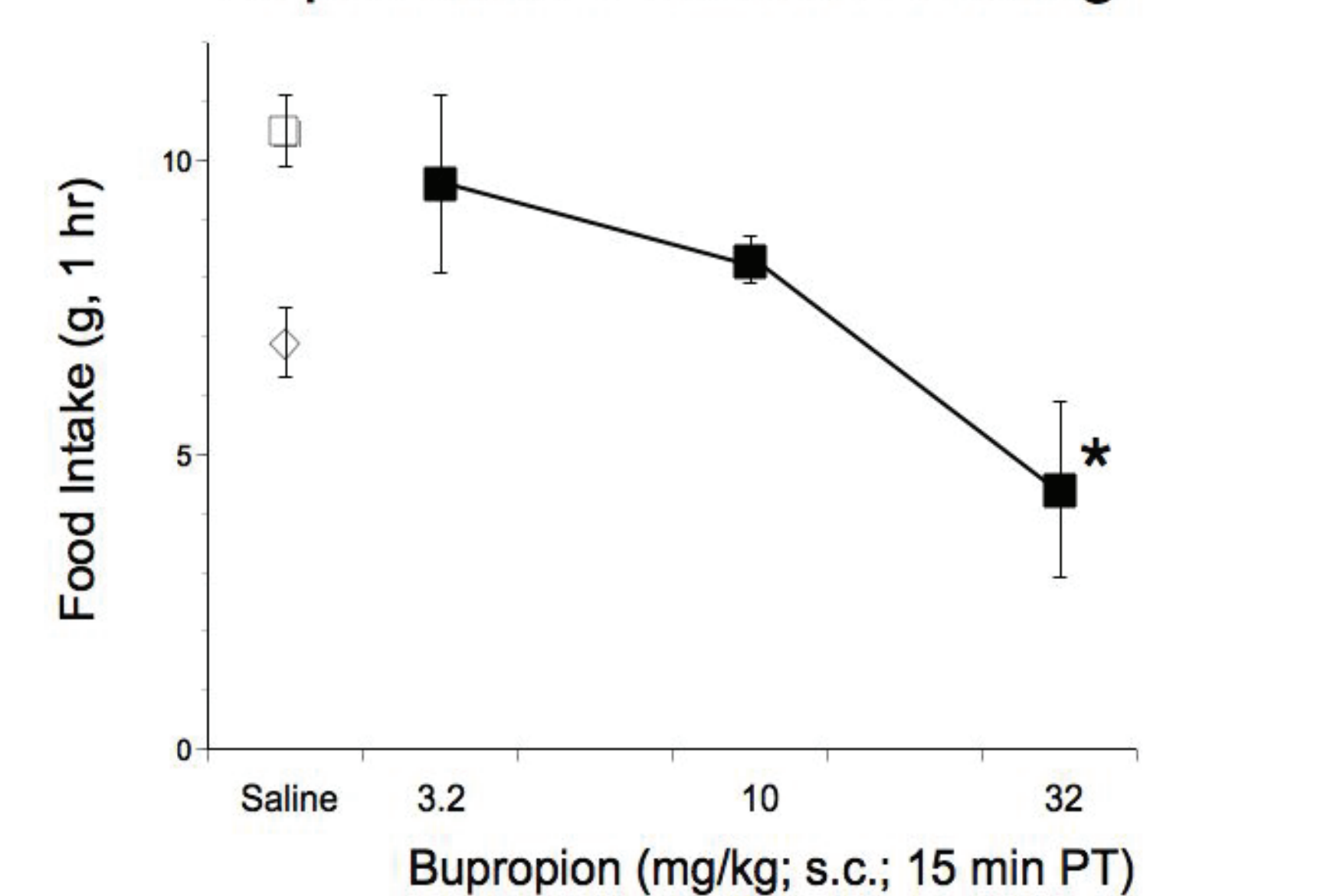
Effects of Bupropion on the Discriminative Stimulus Effects of 22-hr Food Deprivation



Bupropion Decreases Response Rate

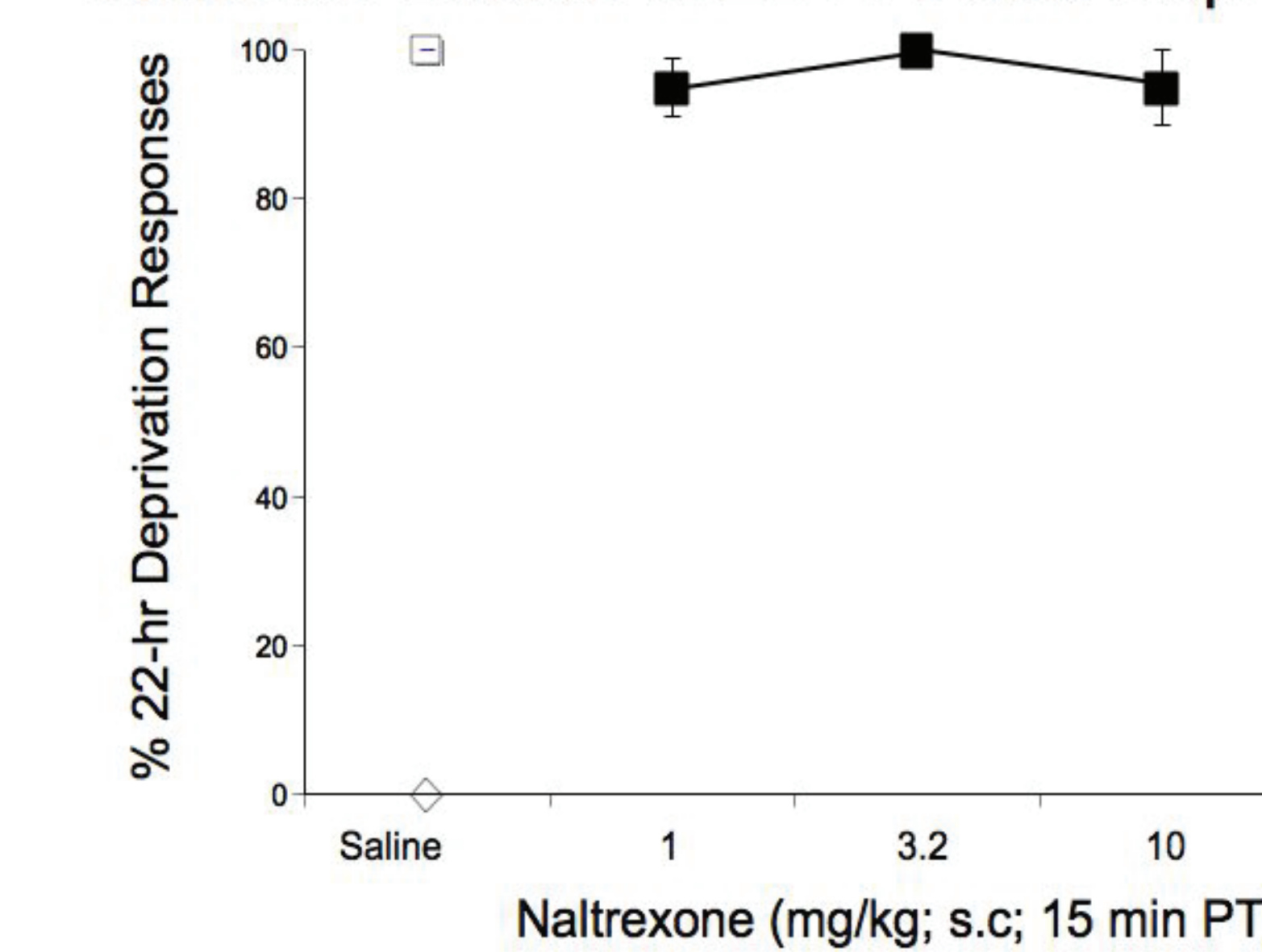


Bupropion Decreases 22 hr-Food Deprivation-Induced Feeding

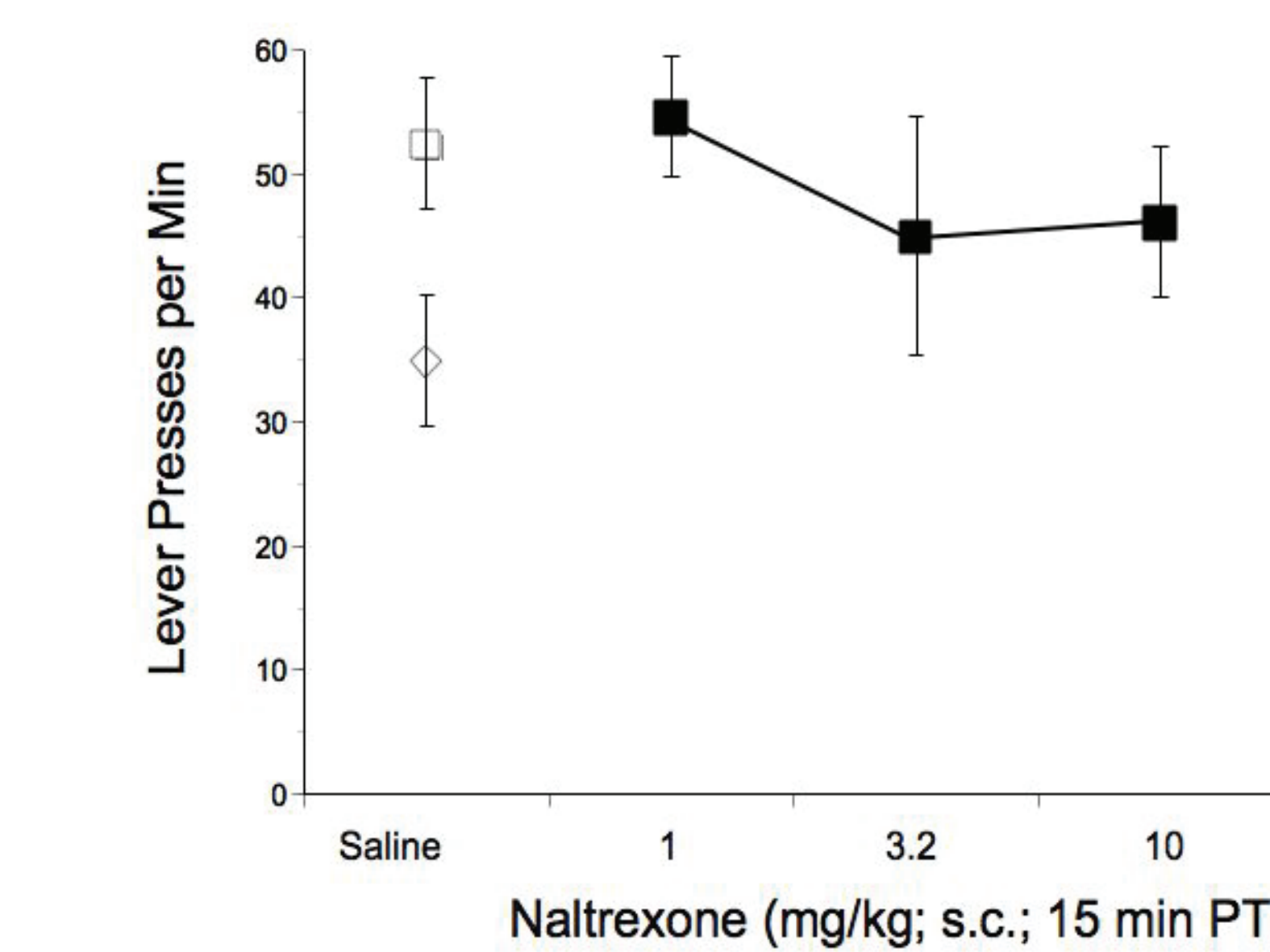


Naltrexone

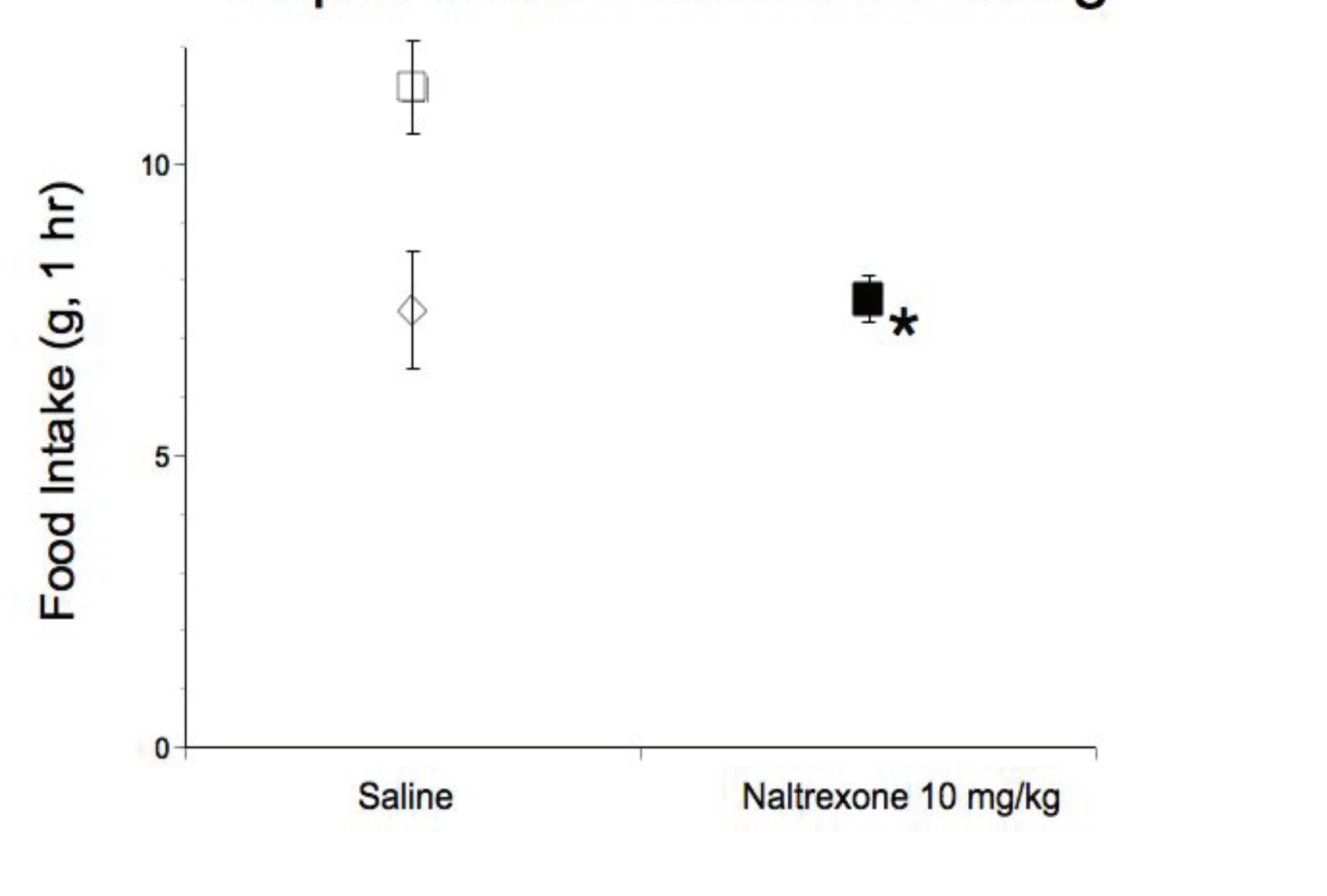
Naltrexone Does Not Alter the Discriminative Stimulus Effects of 22-hr Food Deprivation



Naltrexone Does Not Affect Response Rate

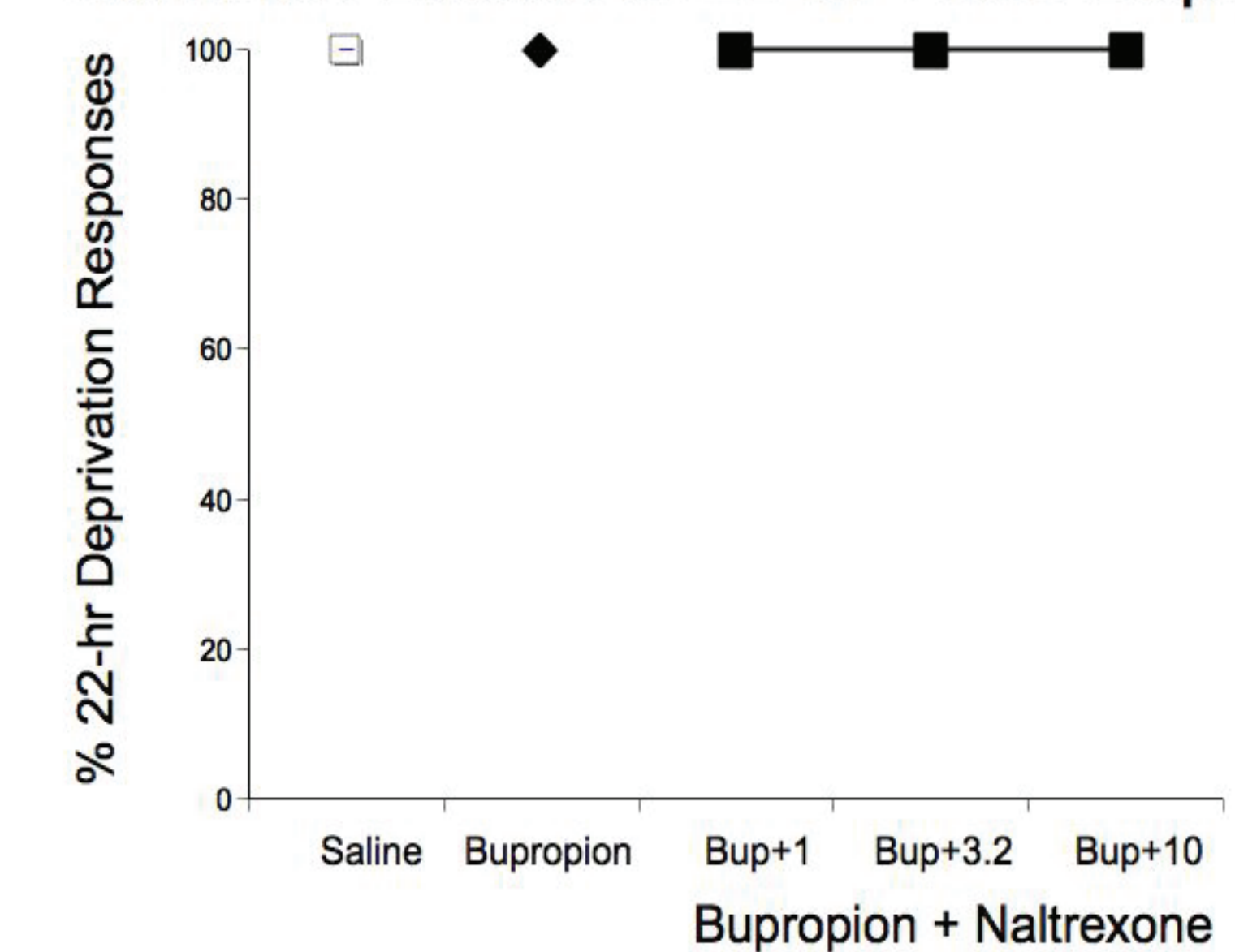


Naltrexone Decreases 22-hr Food Deprivation-Induced Feeding

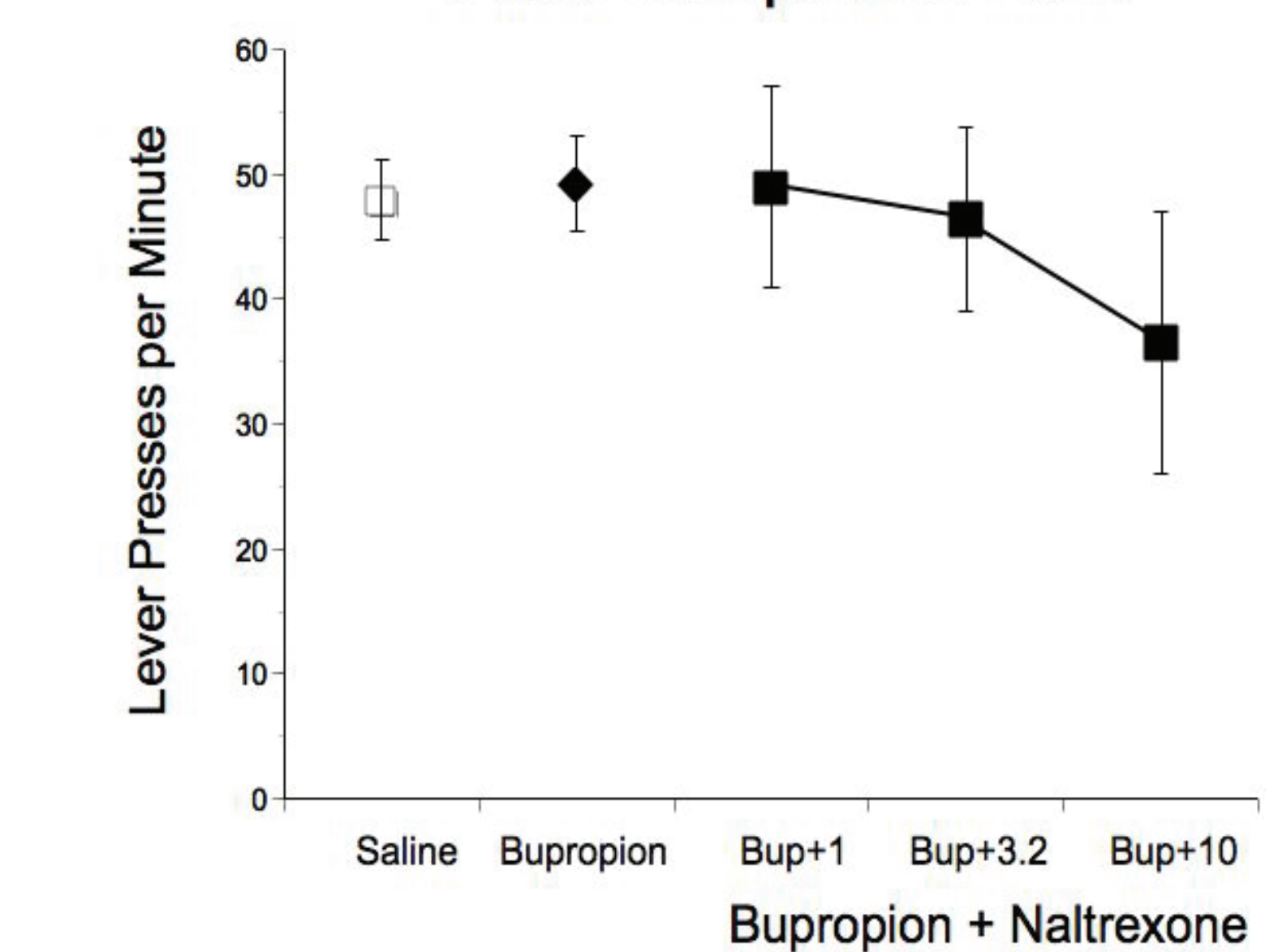


Bupropion + naltrexone

Bupropion + Naltrexone Does Not Alter the Stimulus Effects of 22-hr Food Deprivation



Bupropion + Naltrexone Does Not Alter Response Rate



Bupropion + Naltrexone Decreases 22-hr Food Deprivation-Induced Feeding



Conclusion

The discriminative stimulus was not affected by naltrexone, bupropion, or the combination bupropion (10mg/kg) with naltrexone (1-10 mg/kg). We found that naltrexone, bupropion, and the combination reduced food intake in rats. Our results demonstrate that bupropion decreased response rate while naltrexone and the combination did not have an effect on response rate. Our results suggest that the decrease in food intake is due to neurochemicals unrelated to the discriminative stimulus of 22-hr food deprivation.

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