

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



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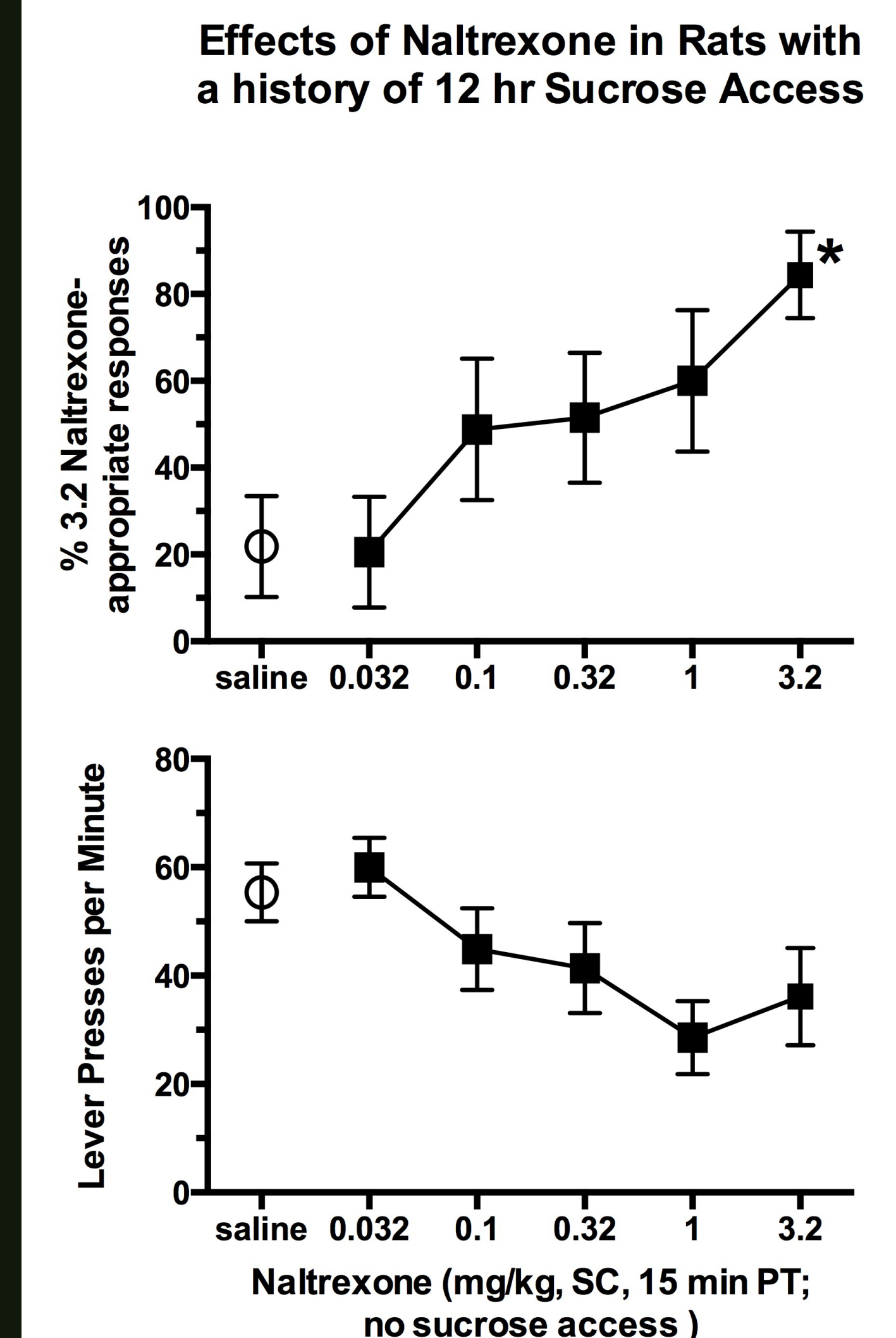
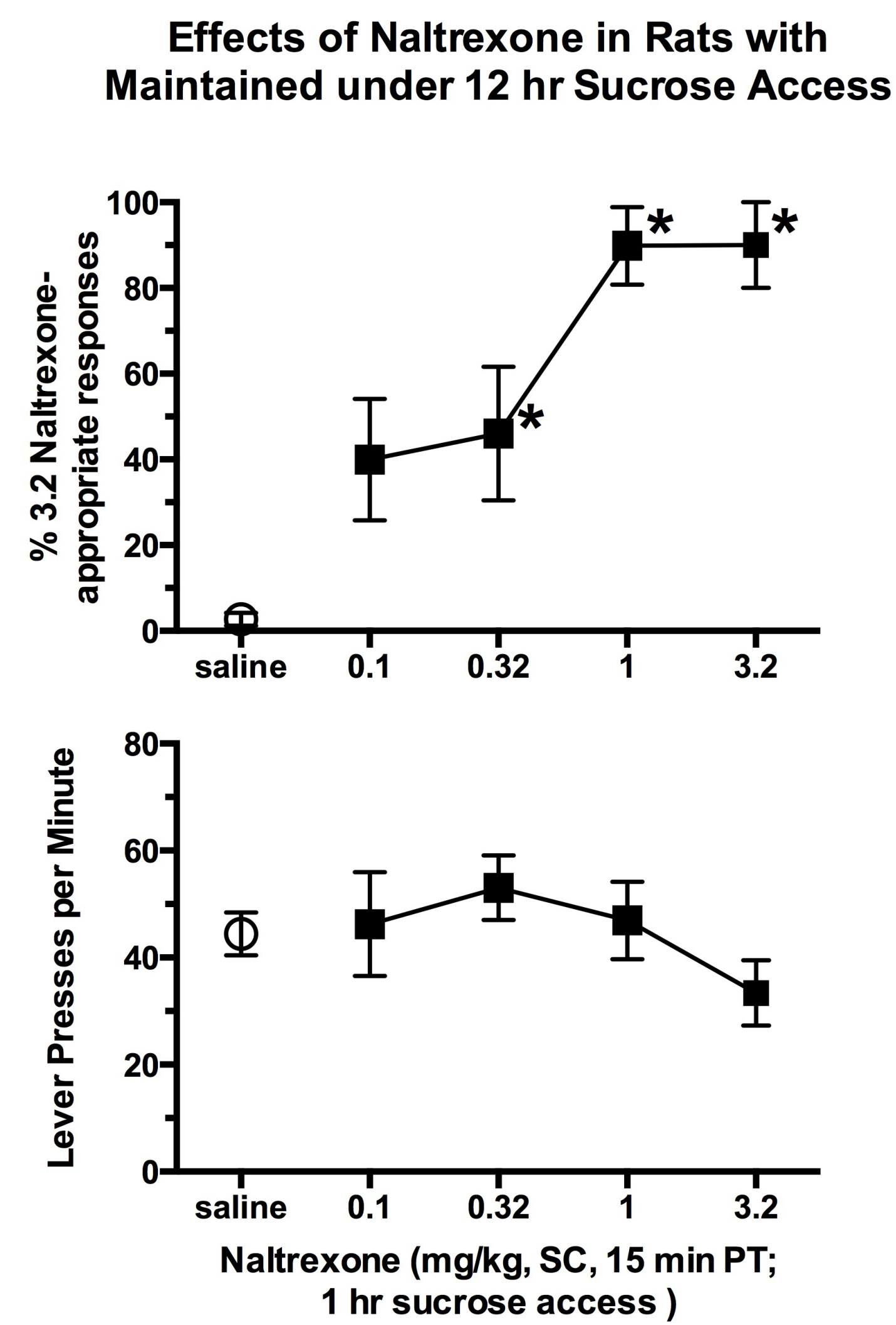
Introduction

-Naltrexone (NTX) is an opioid antagonist that is not discriminable at typical doses in operant paradigms.

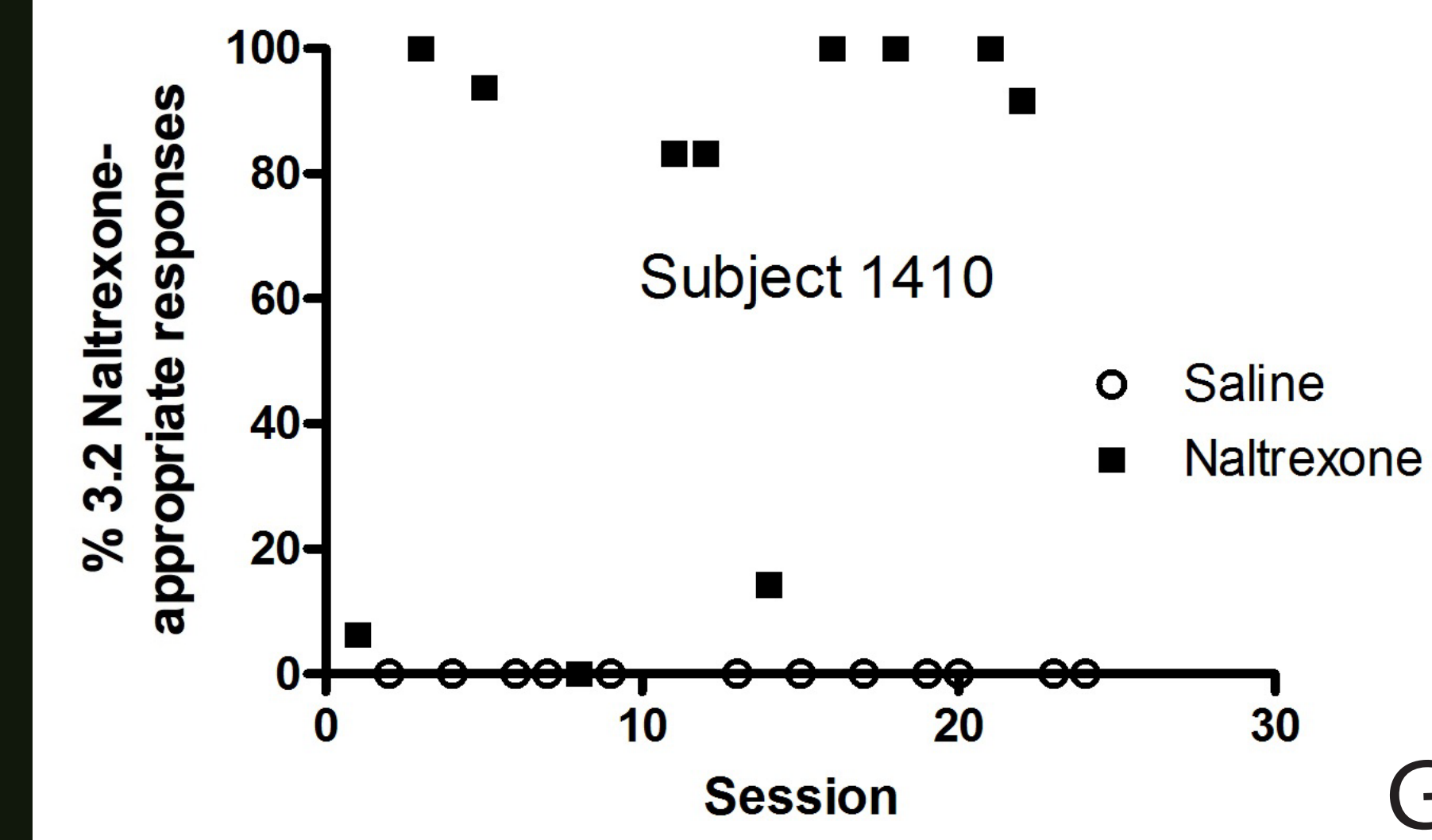
-Hoebel, Avena, and colleagues have demonstrated increases in opioid function in rats given daily, 12 hour access to 10% - 25% sucrose solutions. We and others have shown chronic consumption of 32% sucrose increases opioid function.

-We wondered if we could establish naltrexone as a discriminative stimulus in rats given daily, 12 hour dark cycle access to sucrose solutions.

Naltrexone Dose Effect Curves



Reacquisition with Sucrose



-Following chronic water substitution, subjects were again given daily 12 hour dark cycle access to sucrose and 12 hour light cycle access to water for two weeks.

-Subjects then resumed training, which resulted in rapid reacquisition of the 3.2 mg/kg naltrexone discrimination (Figure G).

Results

-Naltrexone (3.2 mg/kg) was established as a discriminative stimulus in rats with chronic 12hr 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).

-Naltrexone 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.

Acute Water Substitution

-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).

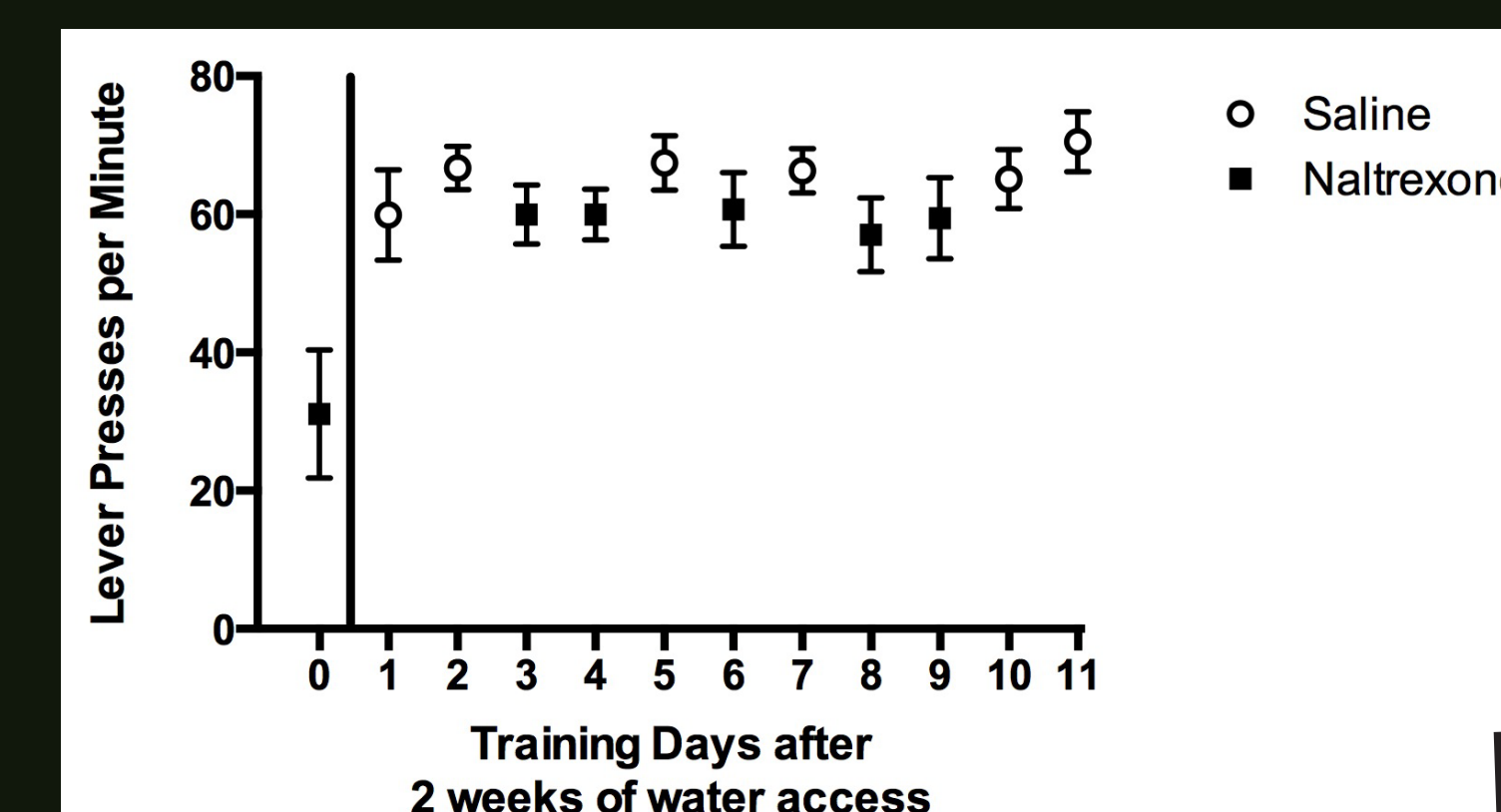
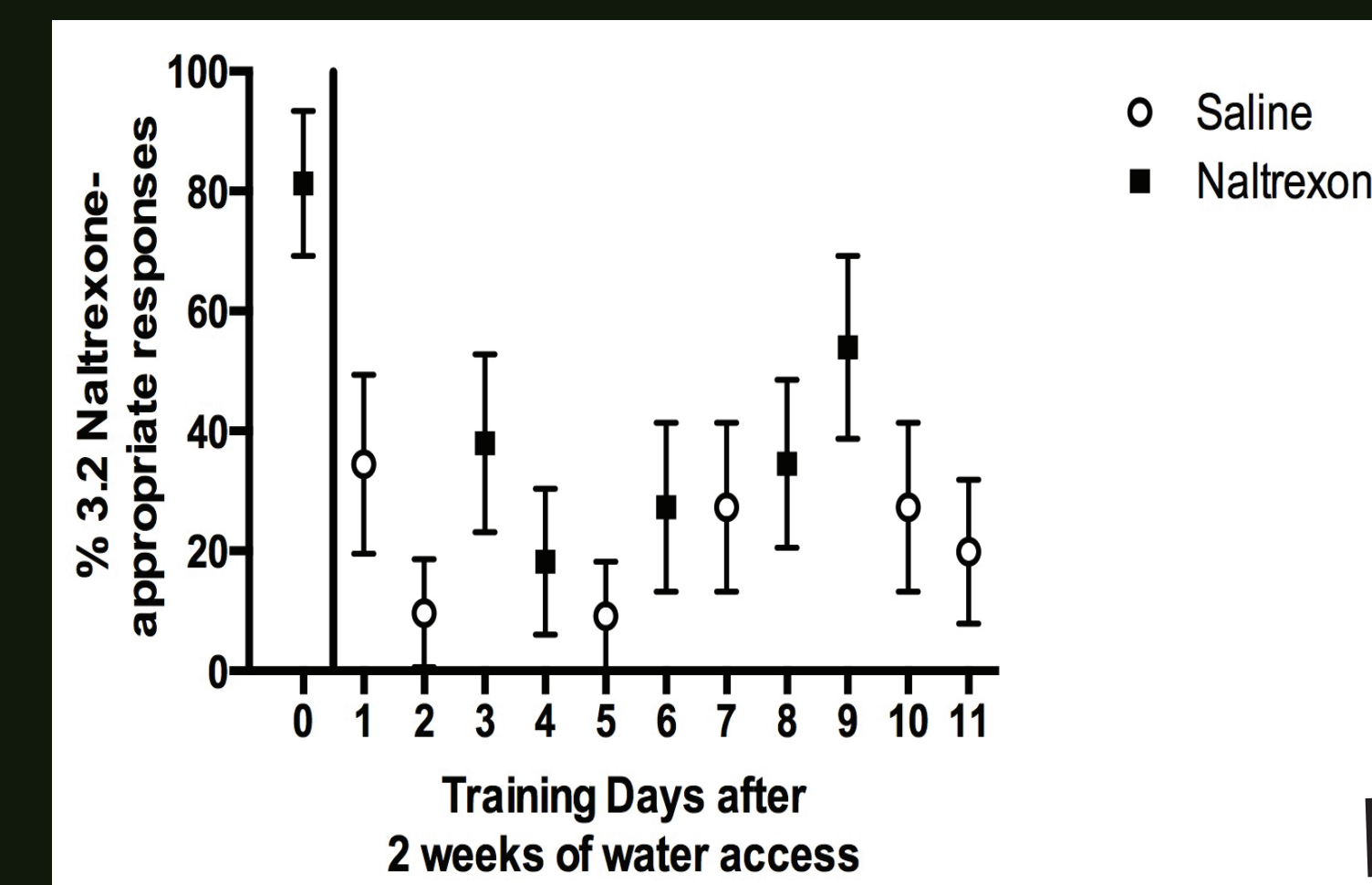
-Subjects continued to discriminate NTX from saline.

Chronic 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.

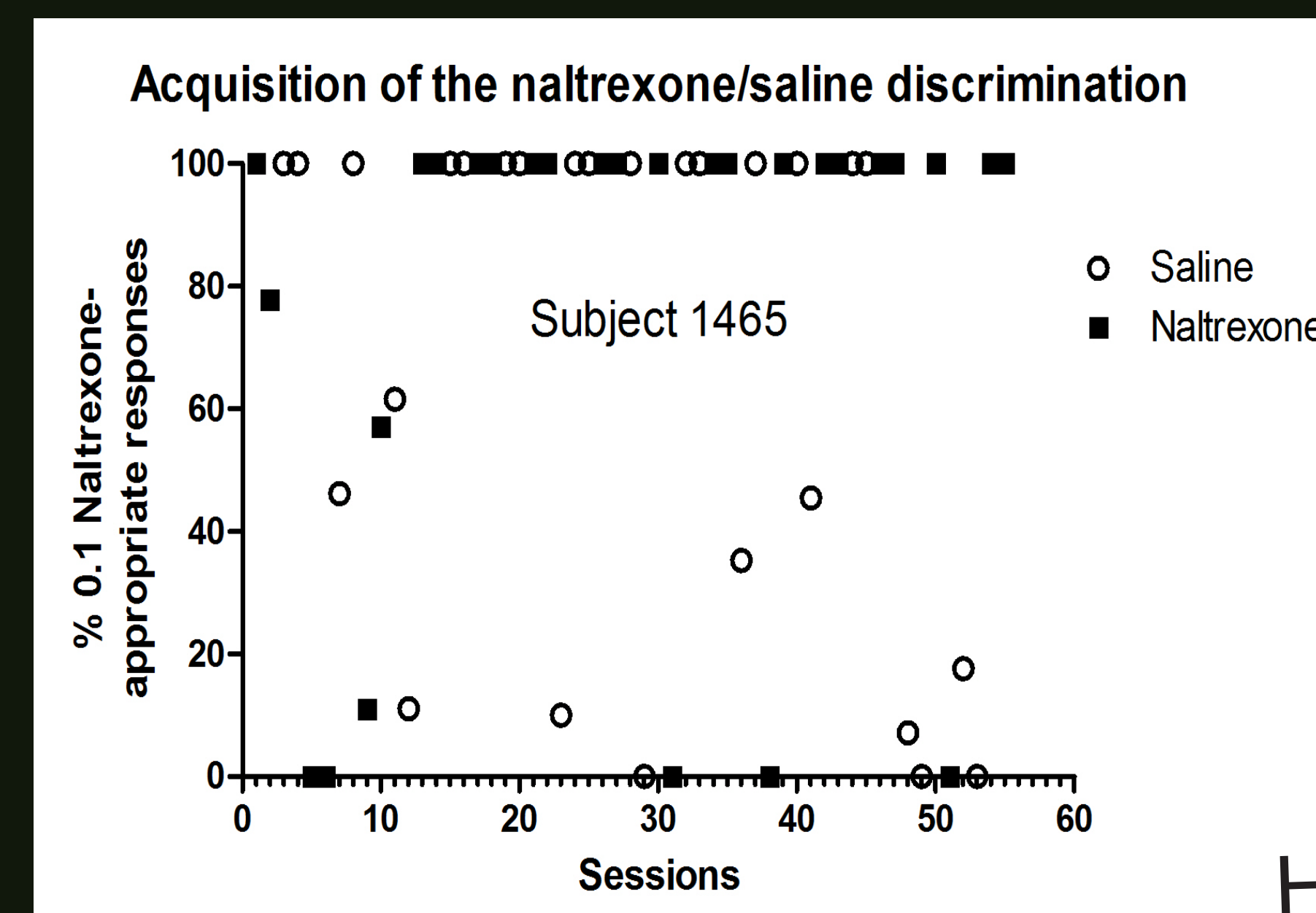


Can Smaller Doses of Naltrexone be Discriminated?

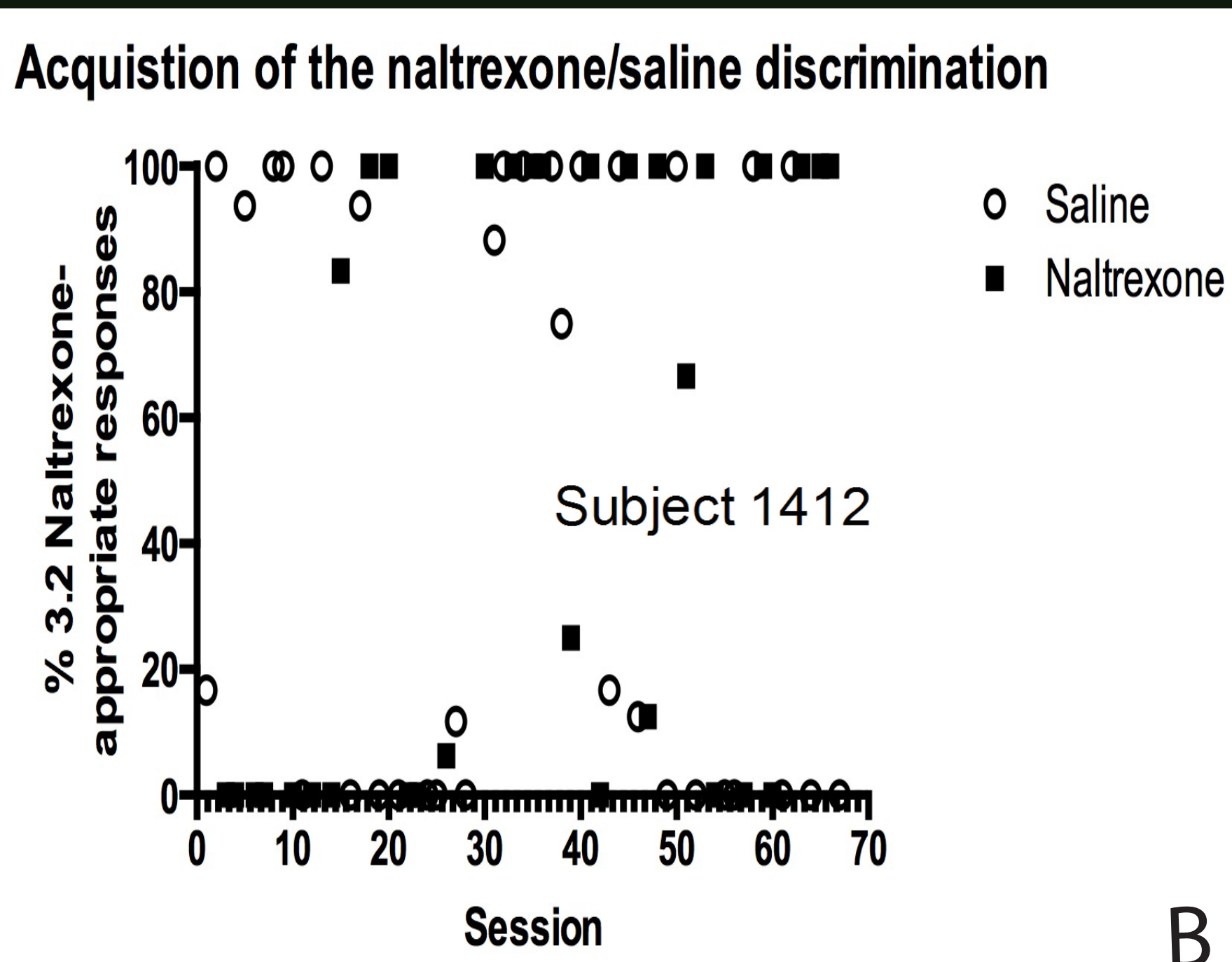
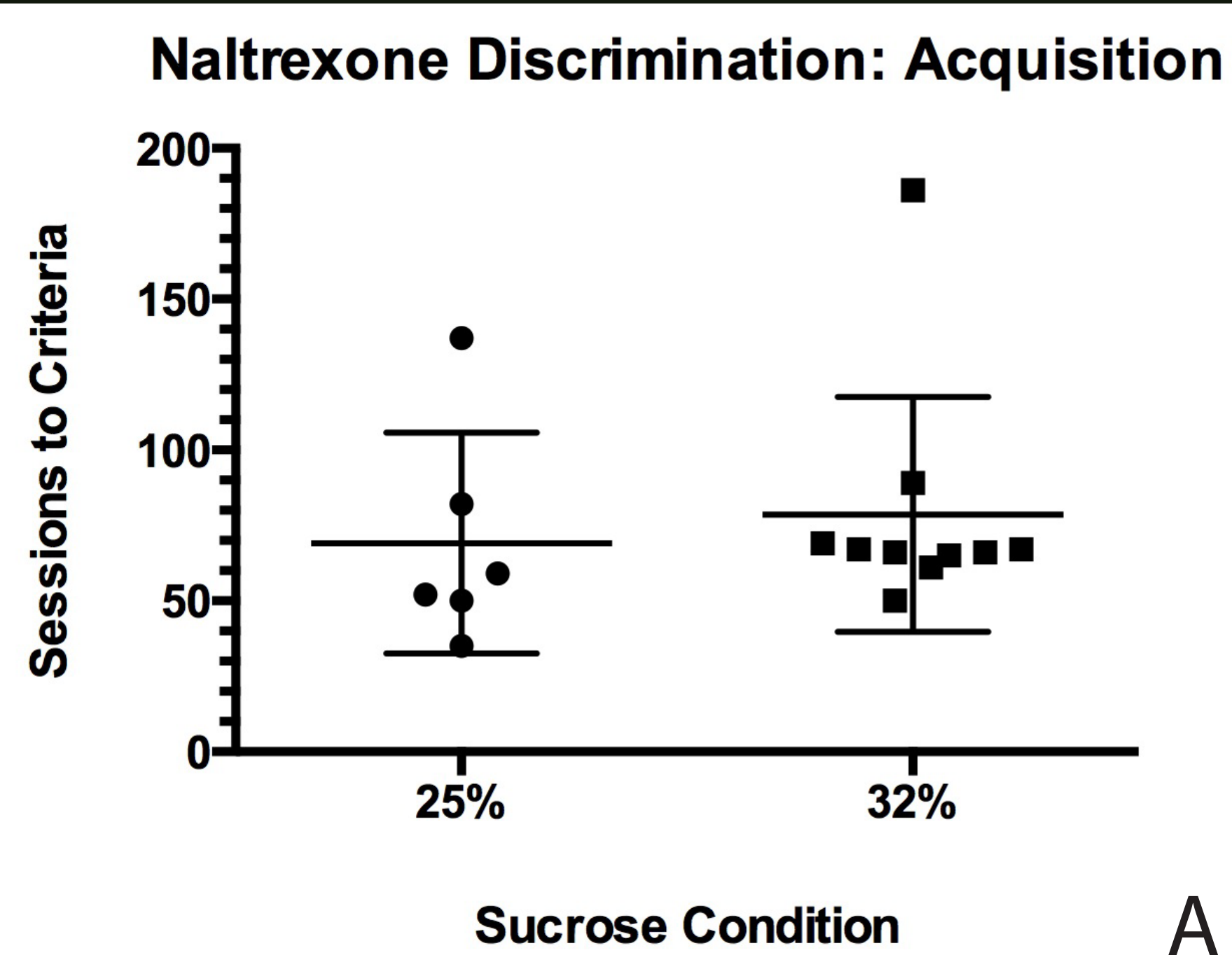
-Subjects were maintained on 12 hour access to either 10%, 25%, or 32% sucrose solutions.

-Subjects were trained with 0.1 mg/kg NTX.

-Subjects are currently being trained to reacquire the discrimination of 0.1 mg/kg NTX.



Naltrexone Discrimination: Acquisition



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