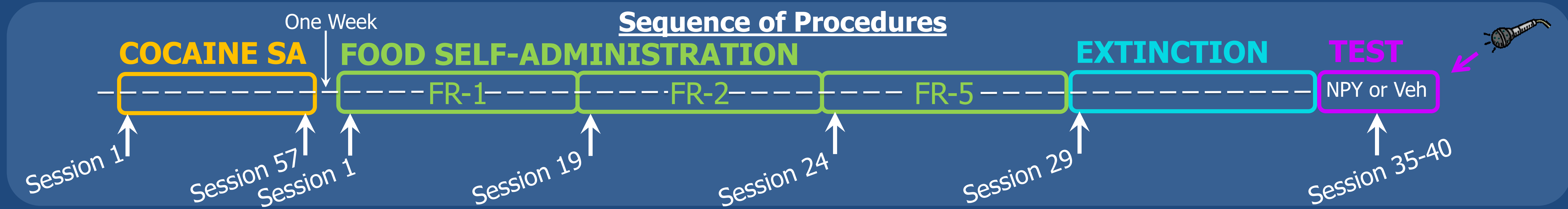




The Effect of Neuropeptide Y on Food-Induced Reinstatement and Vocalization in Rats

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Introduction

- Neuropeptide Y (NPY) is a polypeptide neurotransmitter, released into the central nervous system, which has several functions including the regulation of food intake.
 - NPY is an orexigenic. It increases food intake.
- Our laboratory recently found that increasing brain NPY also *reduces* cocaine-induced reinstatement and cocaine-induced 50 kHz ultrasonic vocalizations (USVs).
 - This was demonstrated in a rat self-administration (SA) model.
- The current study tests the idea that NPY-induced suppression of cocaine-induced behavior could be due to an increase in food-seeking by evaluating food-induced reinstatement and food-induced USVs in rats with a history of cocaine SA.
- Hypothesis:** Due to its natural orexigenic effects, ICV administration of NPY should induce food seeking, enhance the magnitude of food-induced reinstatement, and increase the number of 50 kHz USVs made during the reinstatement procedure.

Methods

- Subjects:** 16 male Long-Evans (hooded) rats implanted with injection catheters (right jugular vein) and microinjection cannula (lateral ventricle of the brain) were trained in cocaine self-administration (SA) and then in food SA.
 - Training included (a) acquisition of SA, (b) extinction by non-reinforced experience, and (c) reinstatement by reinforcer-primed exposure (see Sequence & Figs. 1 and 2).
- Design:** 2 x 2 factorial design [Reinstatement-Prime (Prime or No-Prime) x NPY (0 or 0.3 nmol, ICV)] with repeated measures on Reinstatement-Prime.
 - Cocaine SA:** The reinstatement model of relapse was used to evaluate the effect of NPY on (a) reinstatement of cocaine seeking, (b) cocaine-induced reinstatement of cocaine seeking, (c) cocaine-induced 50 kHz vocalizations.
 - Food SA:** The cocaine SA procedure was adapted for food SA to evaluate the effect of NPY on (a) reinstatement of food-seeking, (b) food-induced reinstatement of food-seeking, (c) food-induced 50 kHz vocalizations.
- Procedures:** Standard operant conditioning procedures were used in which snout pokes into an active (reinforcer-paired) or inactive (no programmed consequence) hole were measure for 3h (cocaine) or 30 min (food).
 - The fixed ratio (FR) schedule of reinforcement was FR1 for cocaine, FR1 to FR5 for food. A cue light and 25sec time-out period after each reinforcement was also applied.
- Vocalizations:** USVs were recorded during reinstatement (testing) using Avisoft Bioacoustics ultrasonic microphone and software (Berlin Germany).

Fig. 1: Rats learned to self-administer (SA) cocaine and that response extinguished when cocaine was withheld

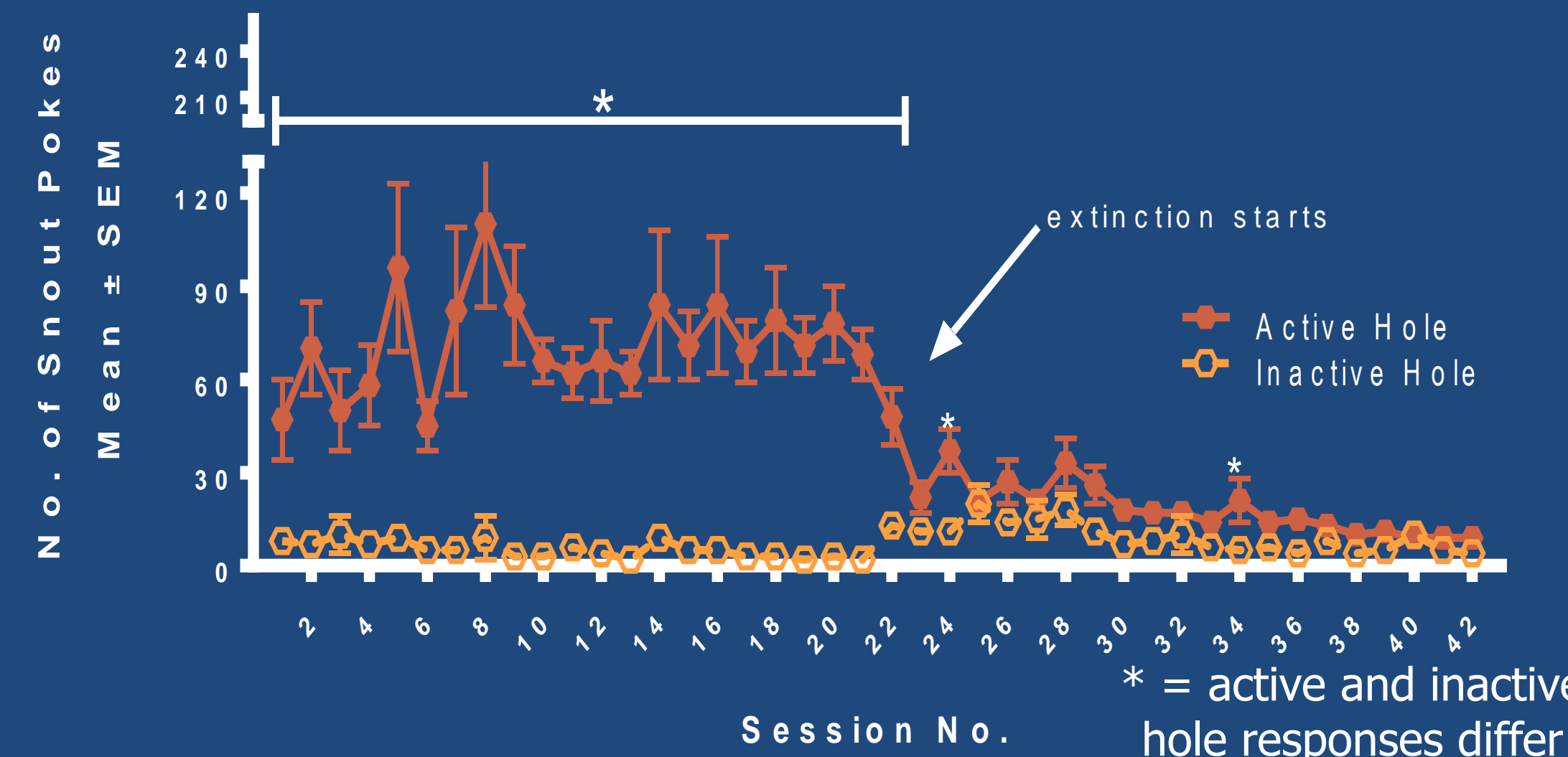


Fig. 2: Rats learned to SA food and that response extinguished when food was withheld

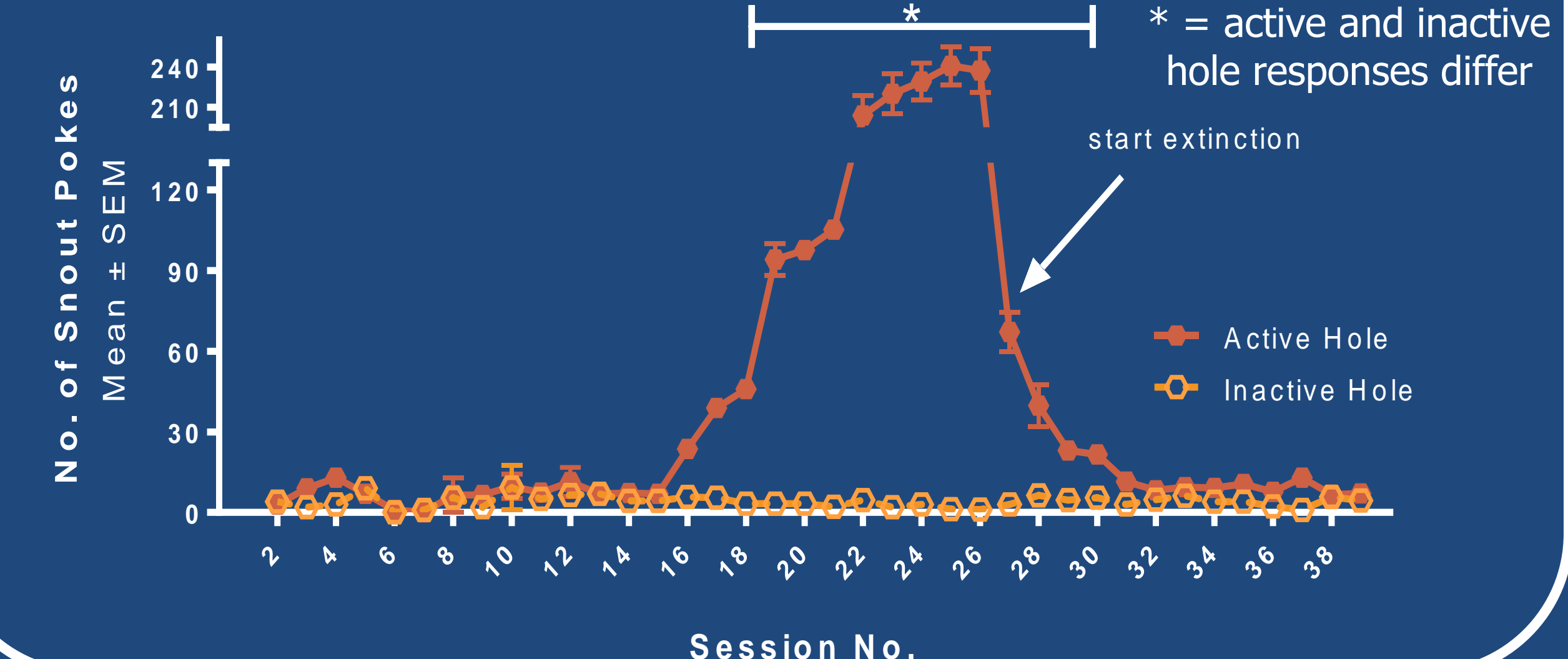


Fig. 3: A cocaine-prime at the end of extinction increased 50 kHz vocalizations: NPY decreased cocaine-induced vocalizations

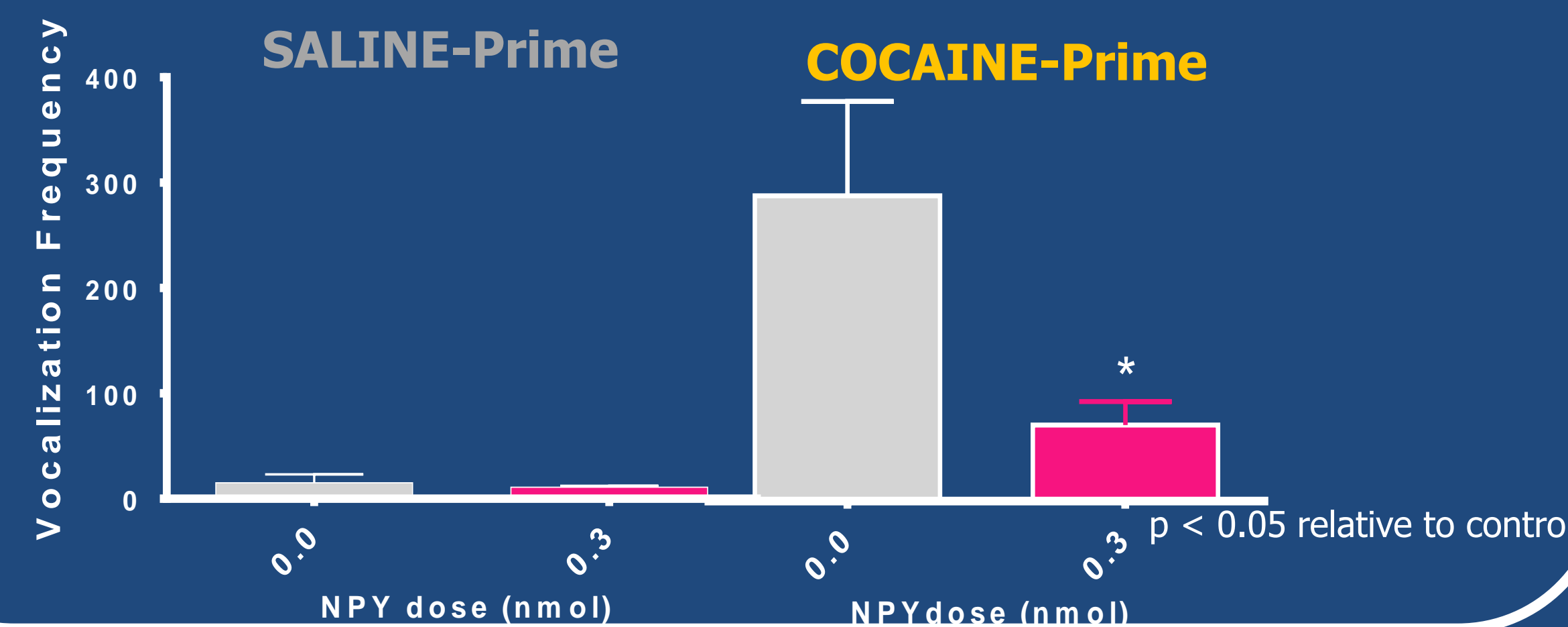


Fig. 4: A food-prime at the end of extinction had no effect on 50 kHz vocalizations limiting the test of the hypothesis on this measure

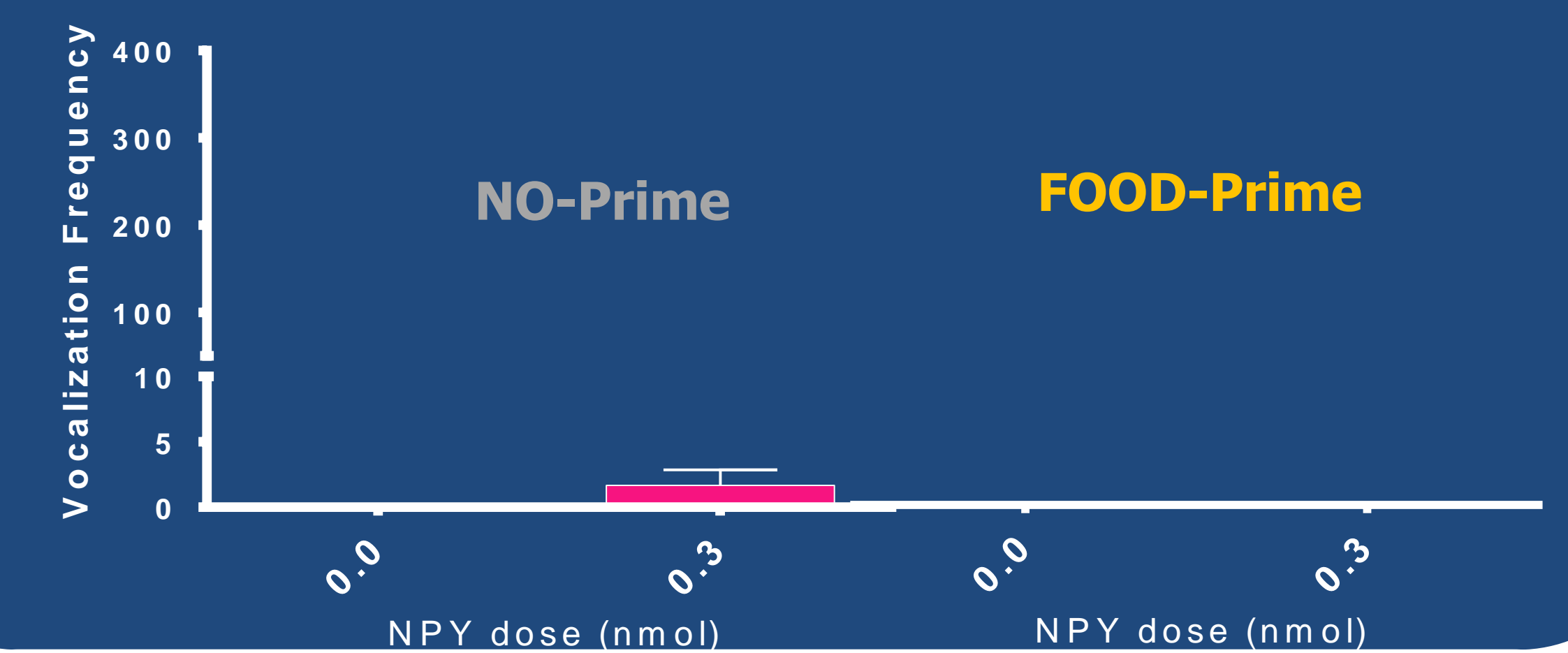


Fig. 5: A cocaine-prime at the end of extinction reinstated the SA response: NPY decreased cocaine-induced reinstatement

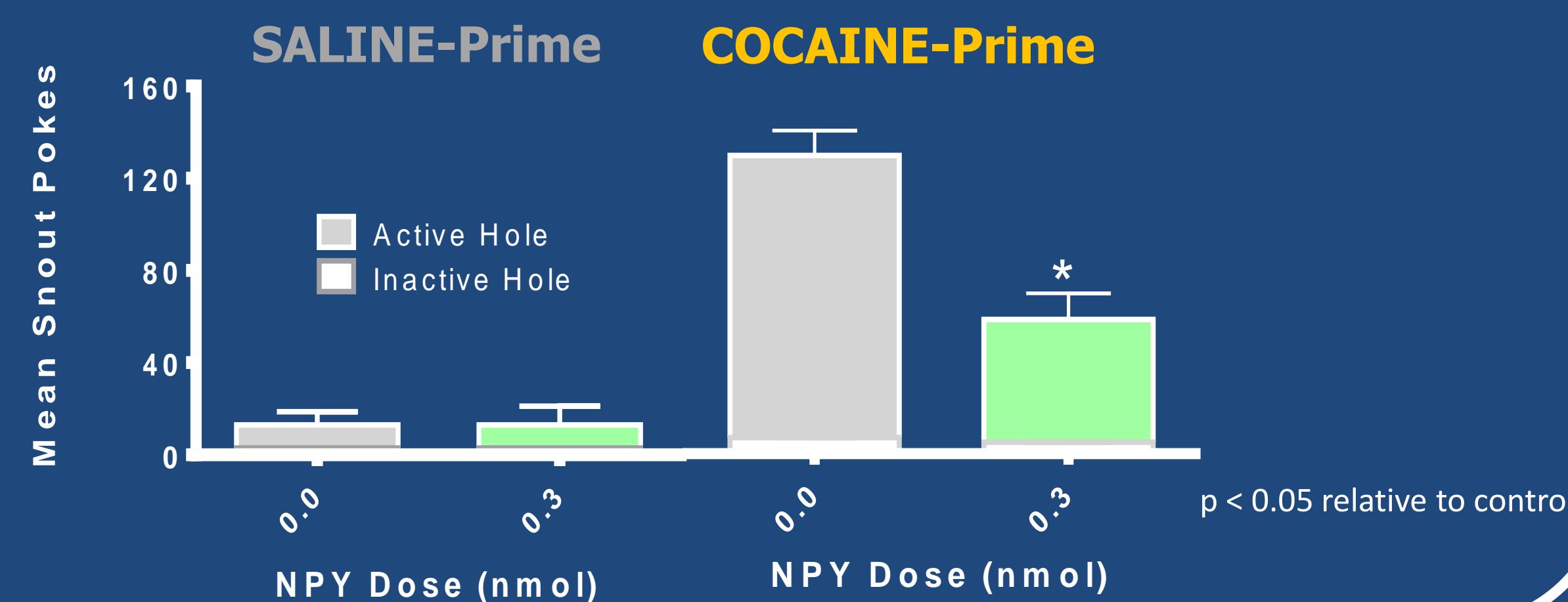
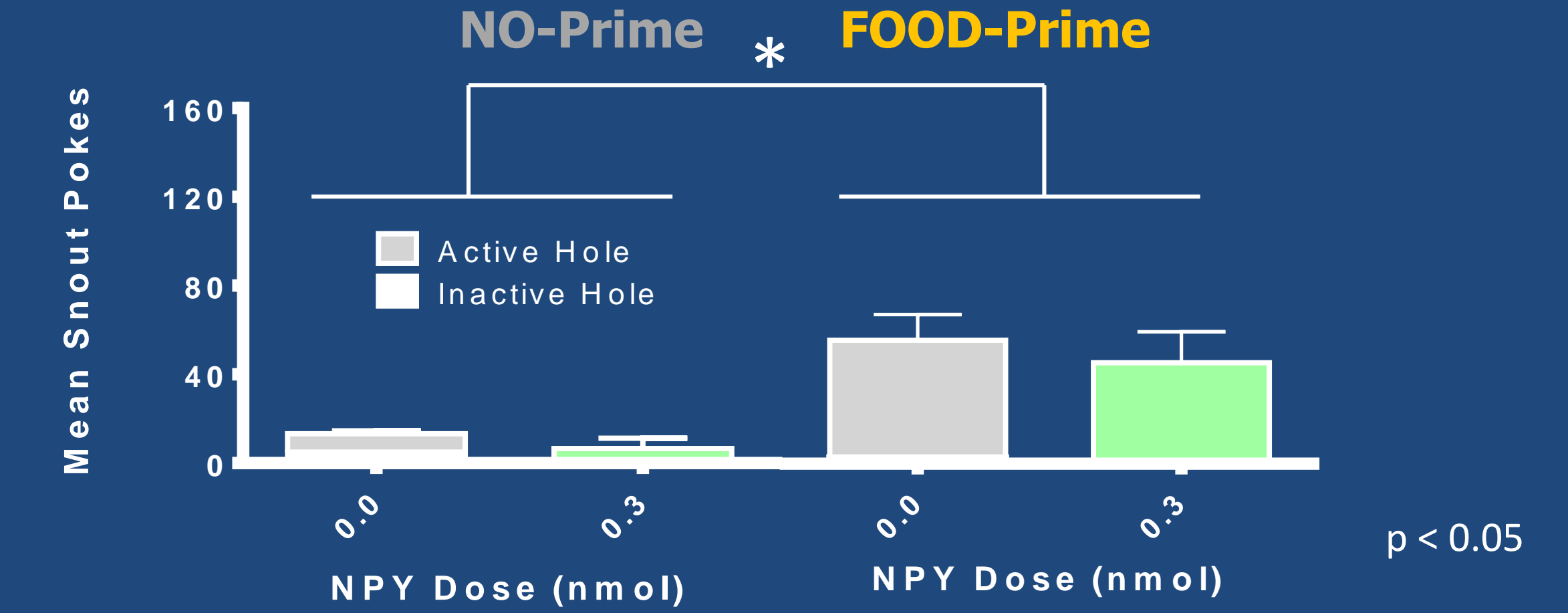


Fig. 6: A food-prime at the end of extinction reinstated the SA response: NPY had no effect on food-induced reinstatement



Conclusion

- Microinjection of NPY 30 min before reinstatement did not by itself induce, modify, or inhibit food reinstatement.
- USVs in the 50 kHz range were predominantly unaffected during a food-induced SA reinstatement test.
- The data does not support food seeking behavior as a reason for the decrease in cocaine-induced SA.

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