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**THE EFFECTS OF
BENZODIAZEPINES ON
FEEDING BEHAVIOR**

Benzodiazepines

- GABA agonists—increase effect of GABA, a general inhibitory NT
- Anti-anxiety drugs (7.3% U.S. population)
- Prescription versions: *Valium*, *Xanax*
- Chlordiazepoxide (CDP) *Librium*
- Side effect is weight gain



How do benzodiazepines lead to weight gain?

- Benzodiazepines stimulate feeding behavior
 - Caused by removal of anxiety (*motivation*)?
 - Caused by a change in palatability?
- Sucrose and other palatable stimuli
 - Increases consumption selectively
- Few studies of aversive stimuli

Our Experiment

Question: Does CDP increase palatability of appetitive and/or aversive stimuli?

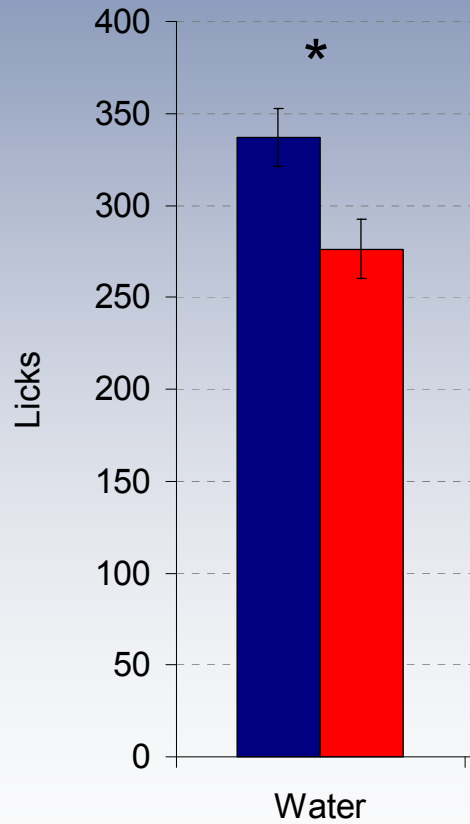
- Effects on palatability measured by changes in licking responses
- Tastants from 4 taste categories:
 - appetitive (sucrose)
 - aversive (sodium chloride, citric acid, quinine)
- Male and female Sprague-Dawley rats

Long Term Protocol

- Licking measured over 90 min in AC 108 lickometer
- 75 mM Sucrose, 500 mM NaCl, 30 mM Citric Acid, 0.5 mM Quinine
- Influenced by palatability and post-ingestive feedback mechanisms
 - Microstructural analysis of licking behavior
 - First minute licks (*palatability*)
 - Total number of licks (*satiety/palatability*)
 - Meal duration (*satiety*) & Meal Licks (*palatability*)
 - Pause Duration & Licking Rate (*palatability*)
- Hypothesis: If benzodiazepines selectively increase palatability, then microstructural analysis measures related to taste cues should increase under the influence of CDP as compared to saline with little or no change to measures related to satiety

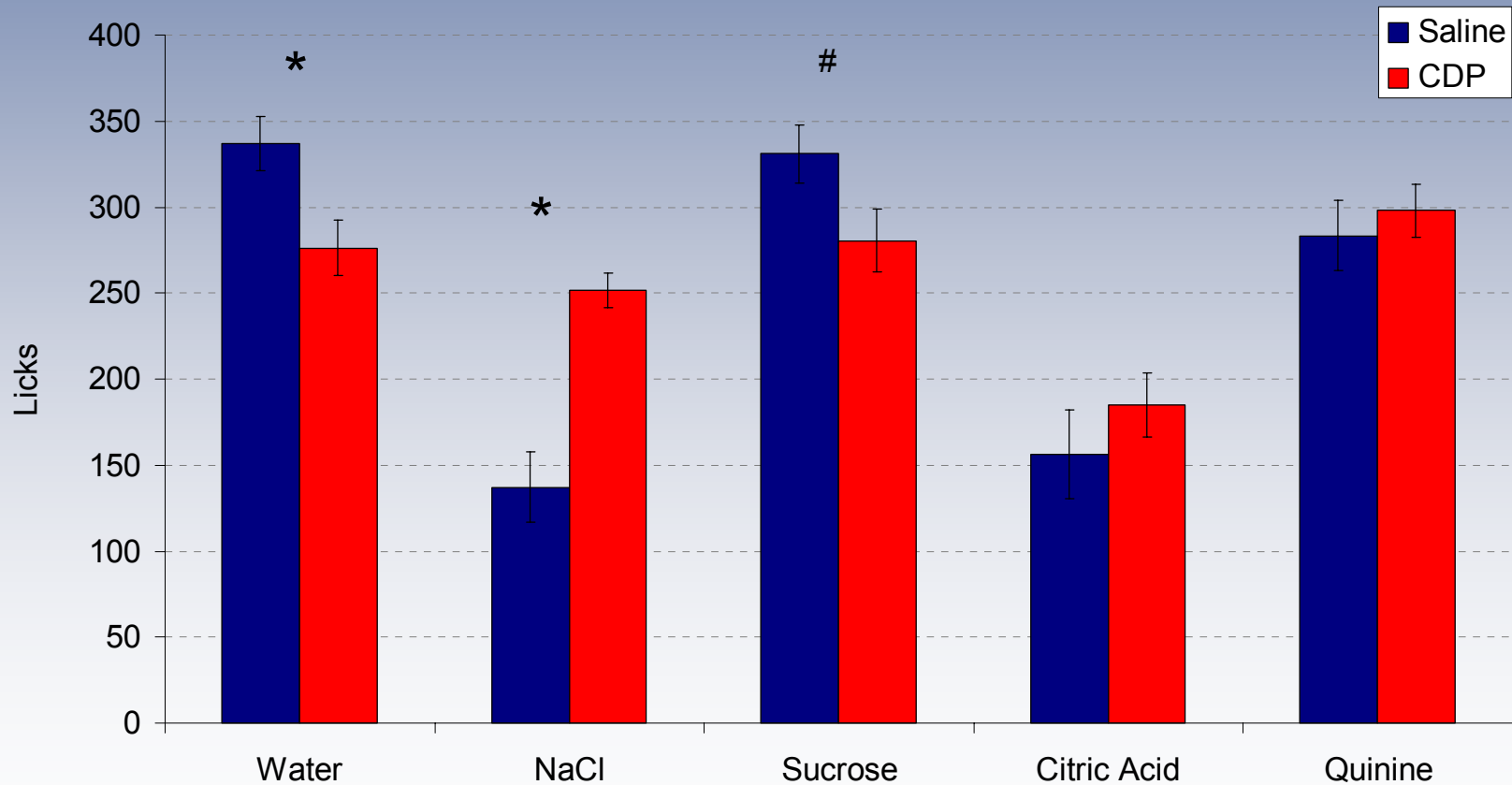
Long Term Results

First Minute Licks



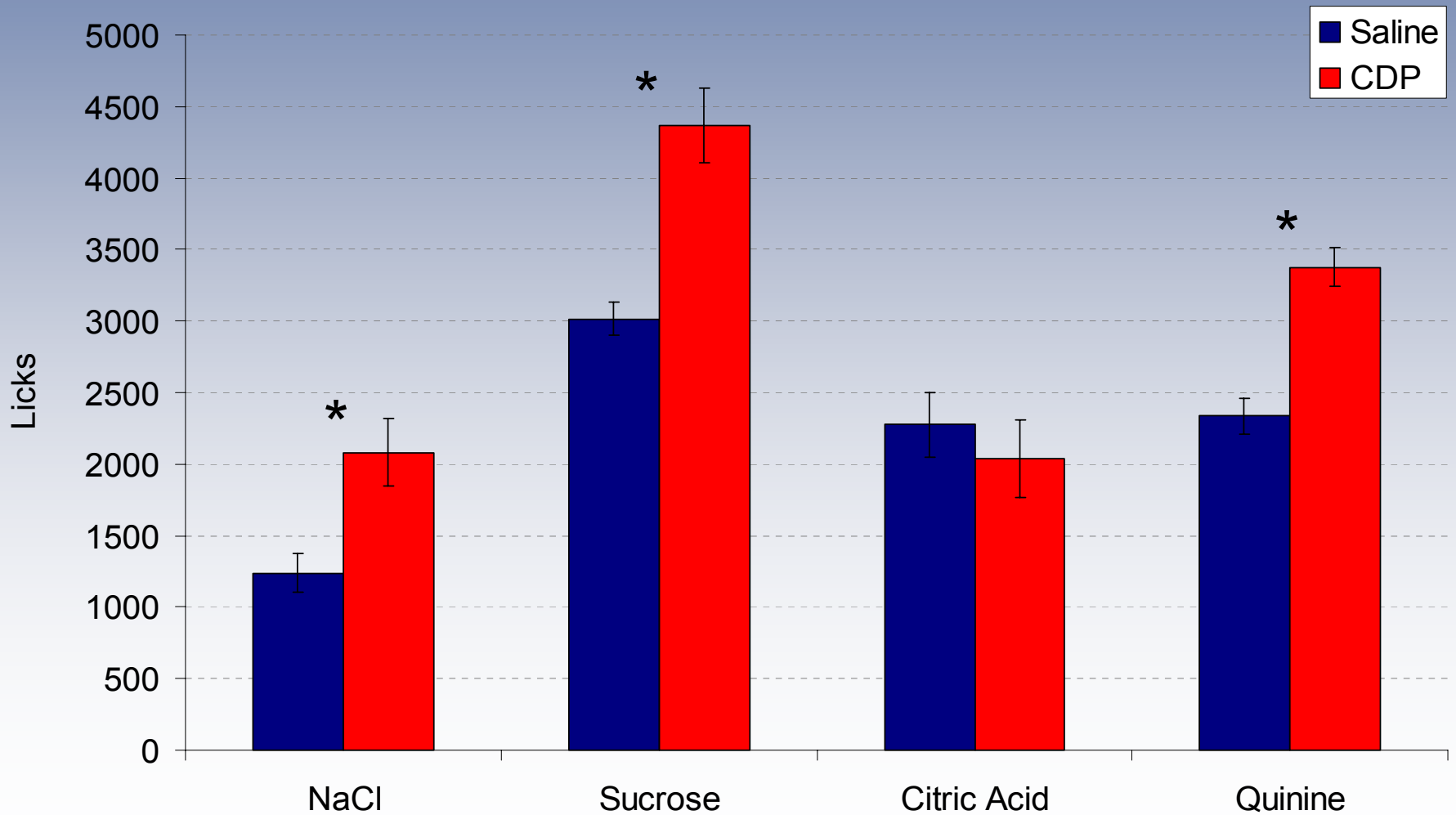
Long Term Results

First Minute Licks



Long Term Results

Session Licks

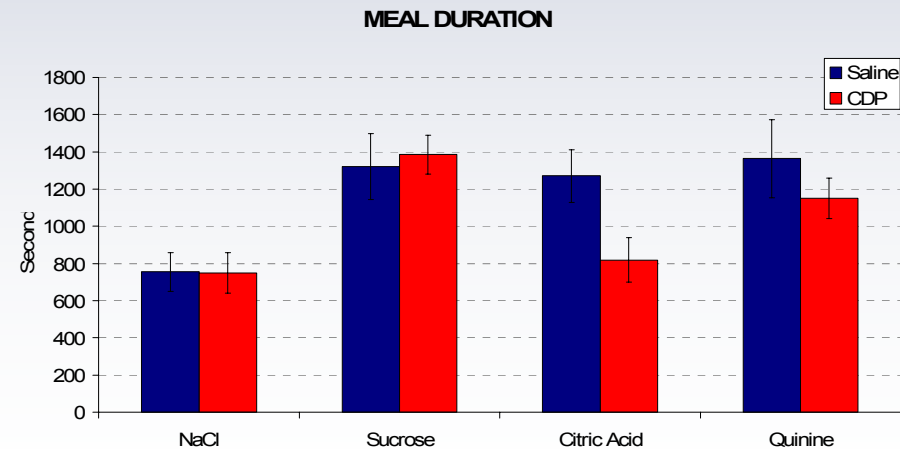


Long Term Results

Meals

(Groups of Licks; Pause >10min ends meal)

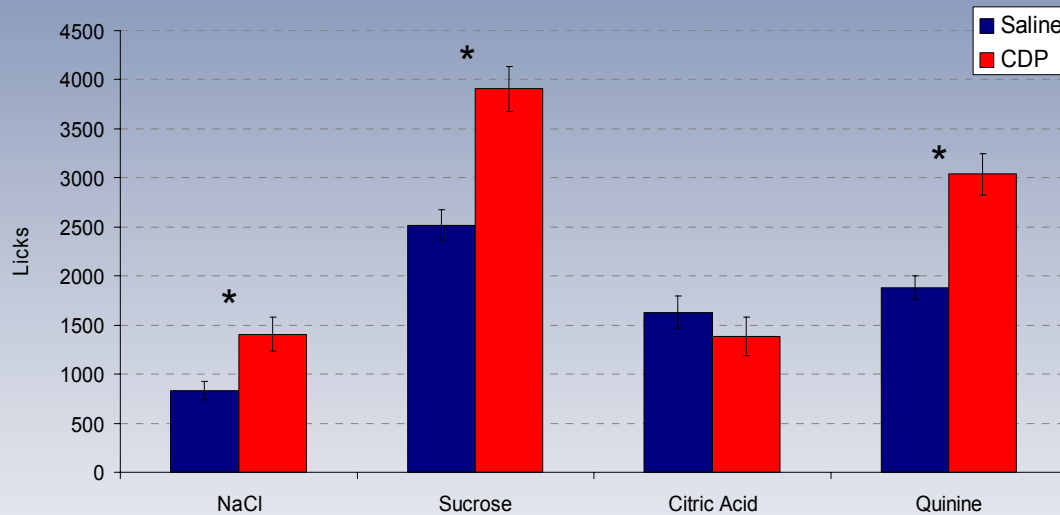
Changes in Meal Duration
associated with hunger / satiety



Long Term Results Meals

(Groups of Licks; Pause >10min ends meal)

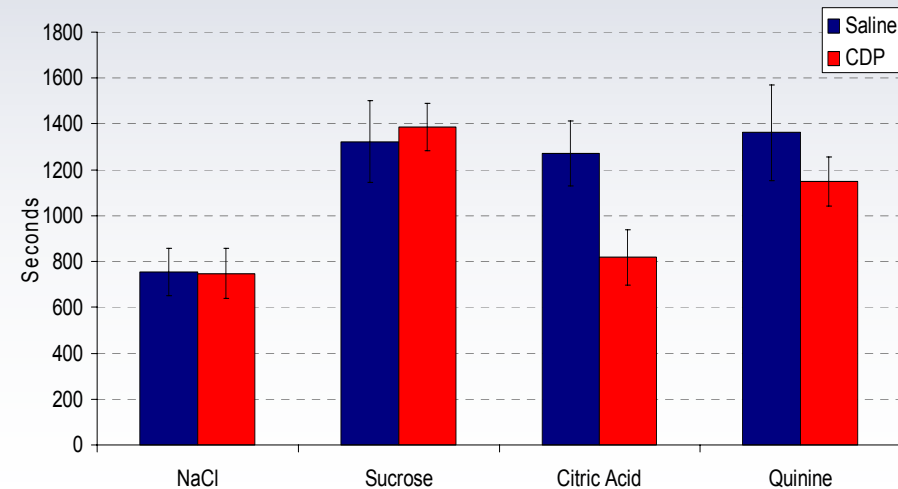
MEAL LICKS



Changes in Meal Licks associated with palatability

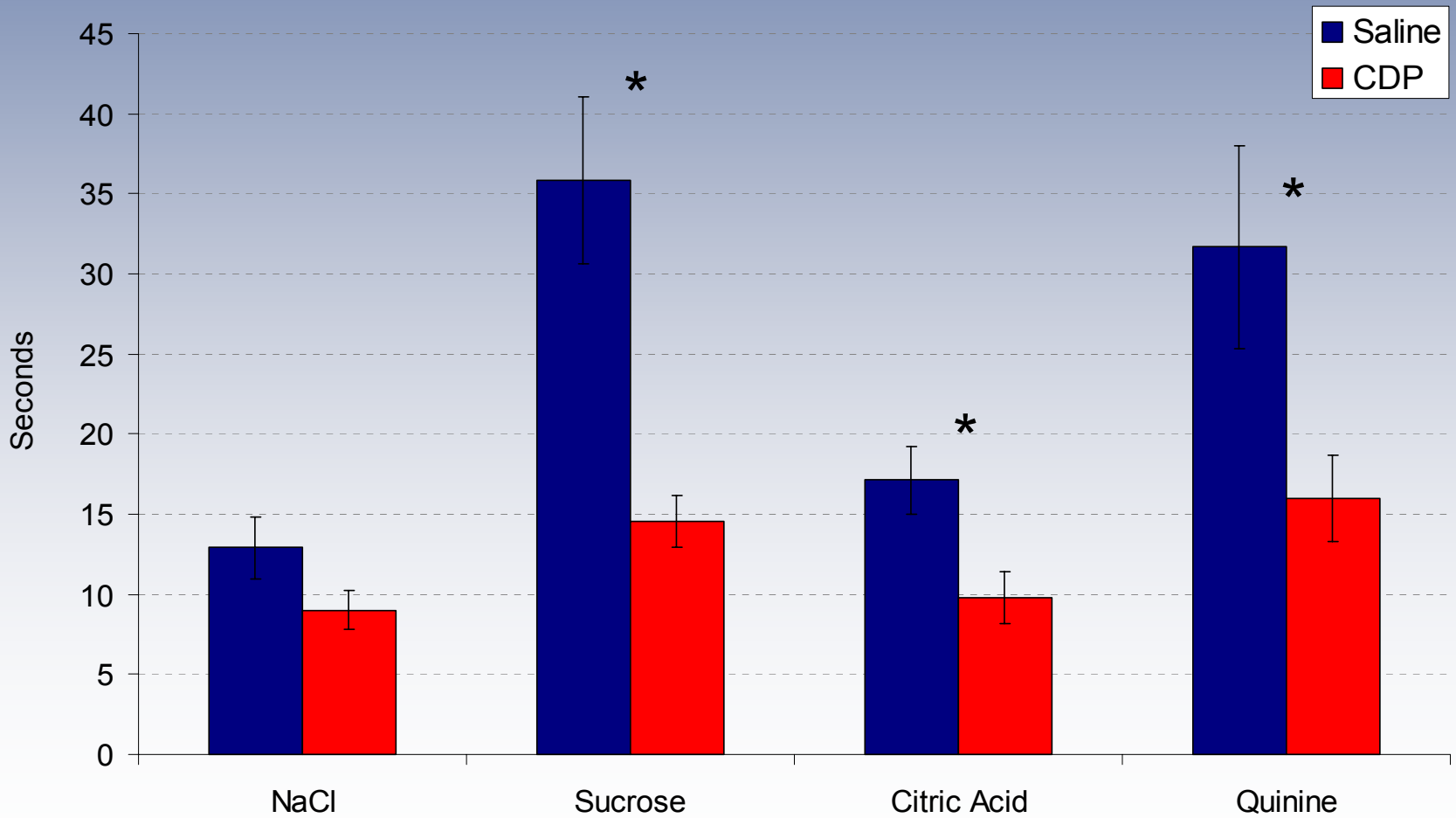
Changes in Meal Duration associated with hunger / satiety

MEAL DURATION



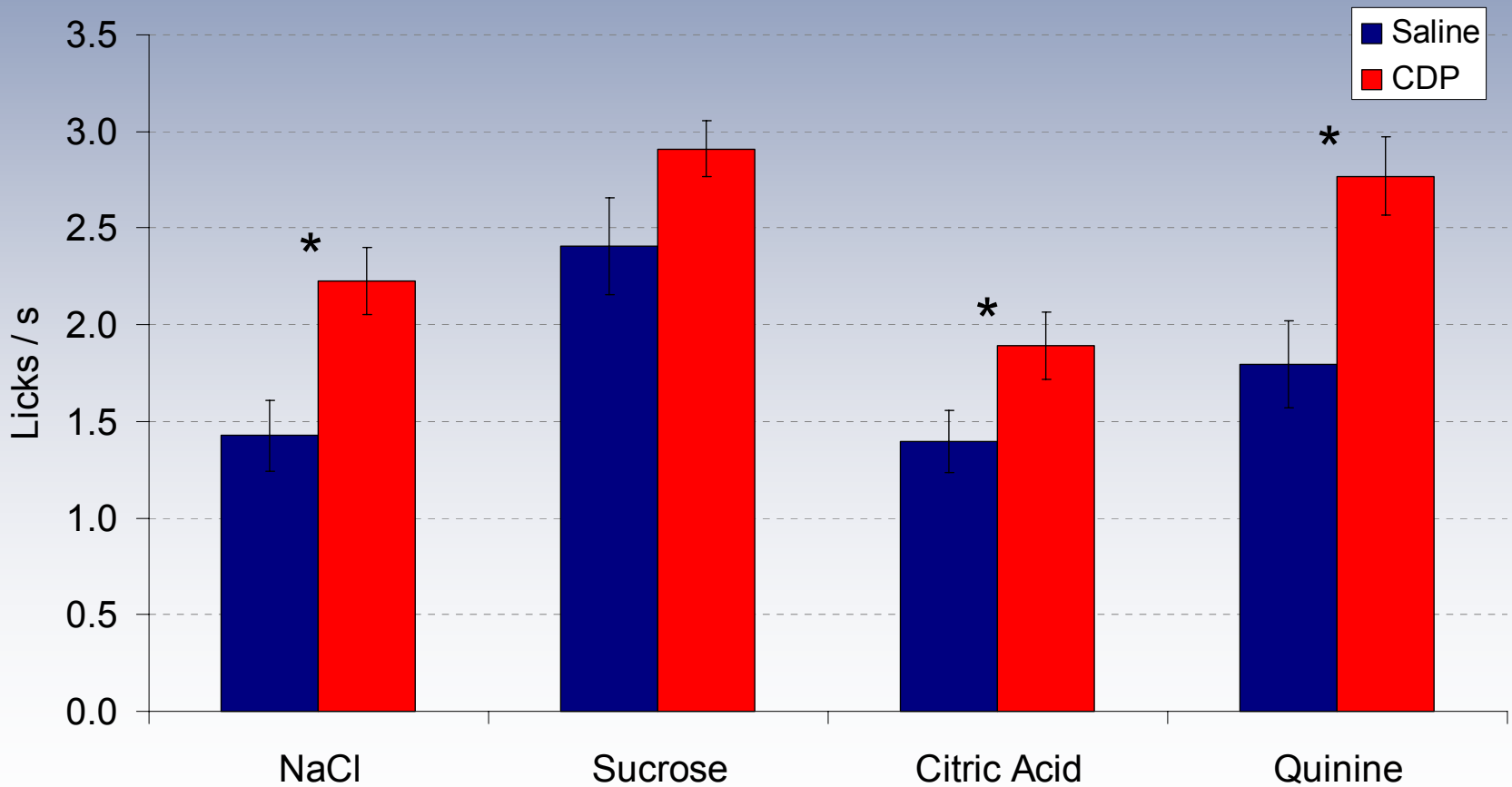
Long Term Results

Pauses within Meals



Long Term Results

Lick Rate

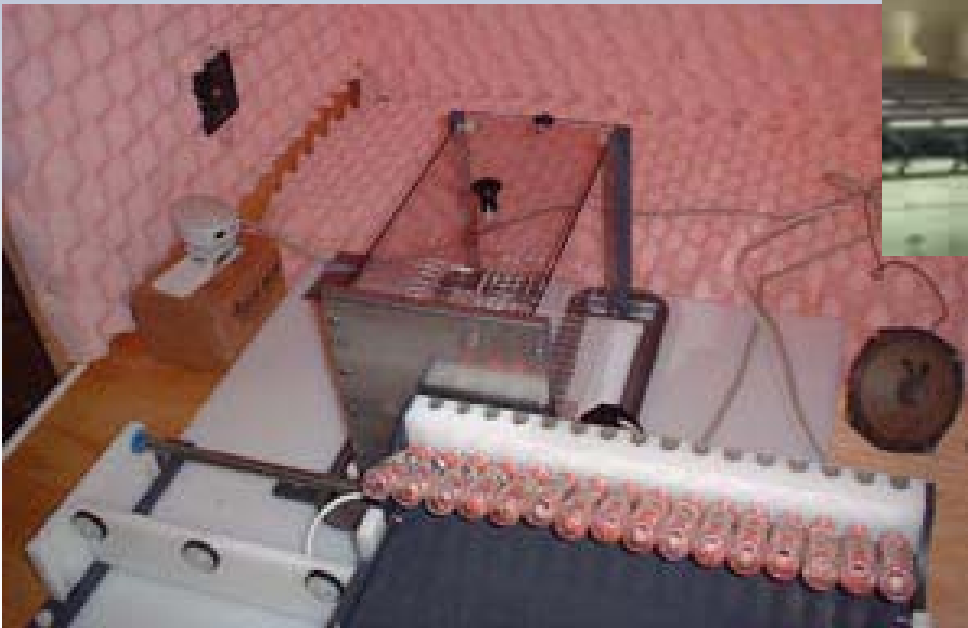


Short-Term Testing

- CDP or Saline, i.p. injections
- 15s stimulus trials
- 4 Tastants:
 - Sweet: Sucrose (25, 50, 100, 500 mM)
 - Salty: NaCl (125, 250, 500, 1000 mM)
 - Sour: Citric Acid (7, 15, 30, 60 mM)
 - Bitter: QHCl (0.003, 0.013, 0.05, 0.2 mM)
- Hypothesis: If benzodiazepines increase palatability, then licking should increase under the influence of CDP as compared to saline

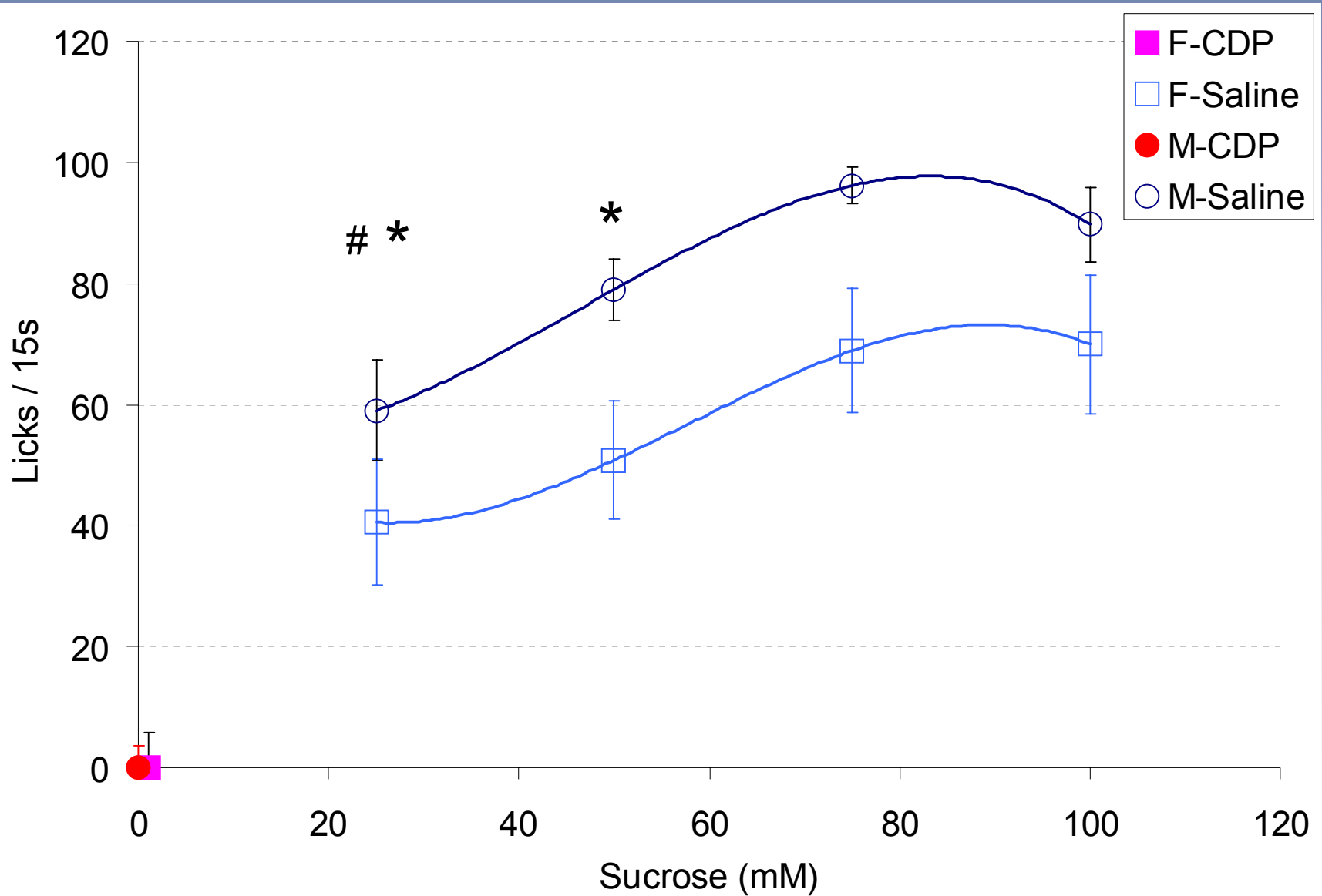
The Davis Rig

Phase 1: Short-term Testing



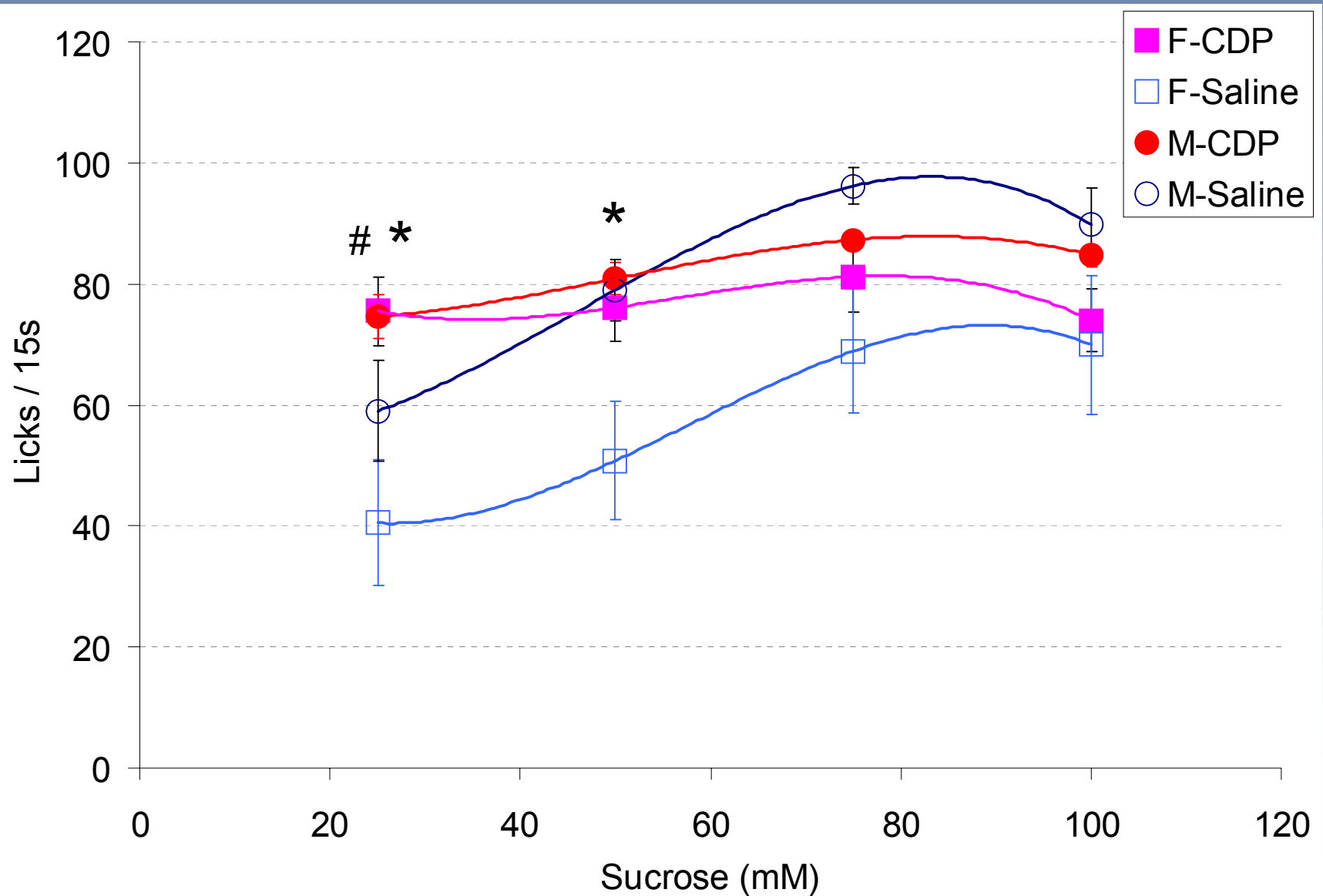
Short Term Results

Sucrose



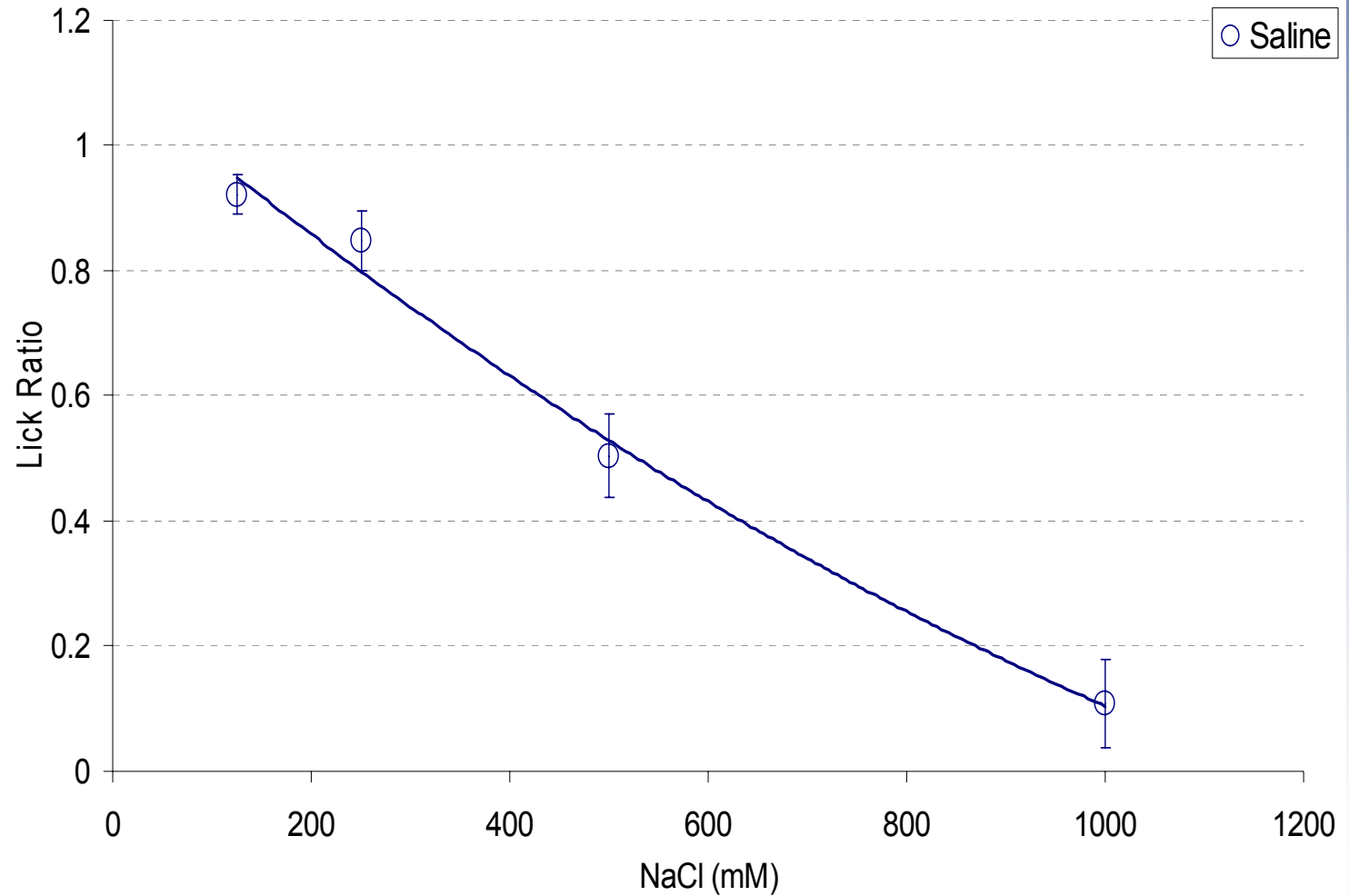
Short Term Results

Sucrose



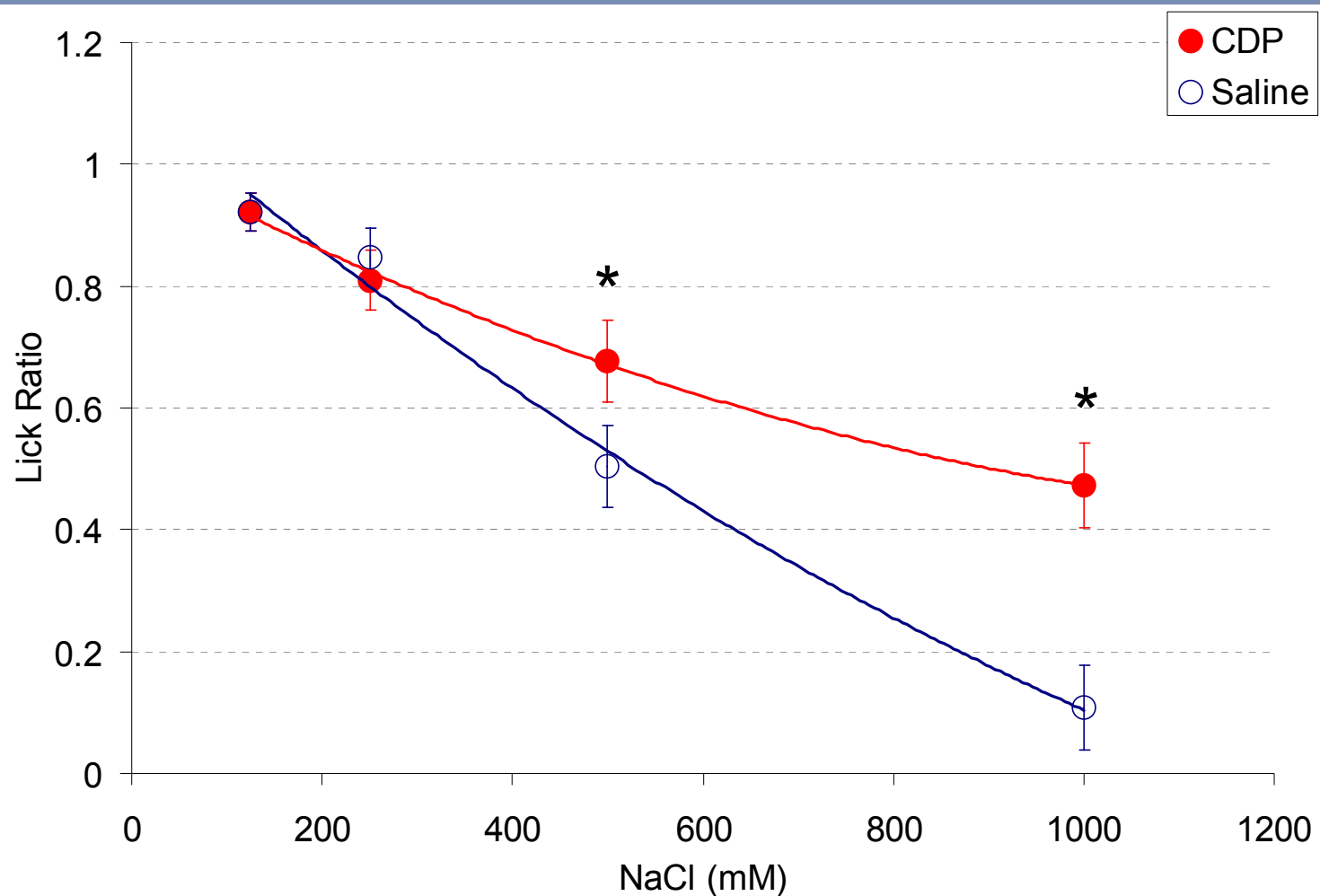
Short Term Results

Salty, Males Only



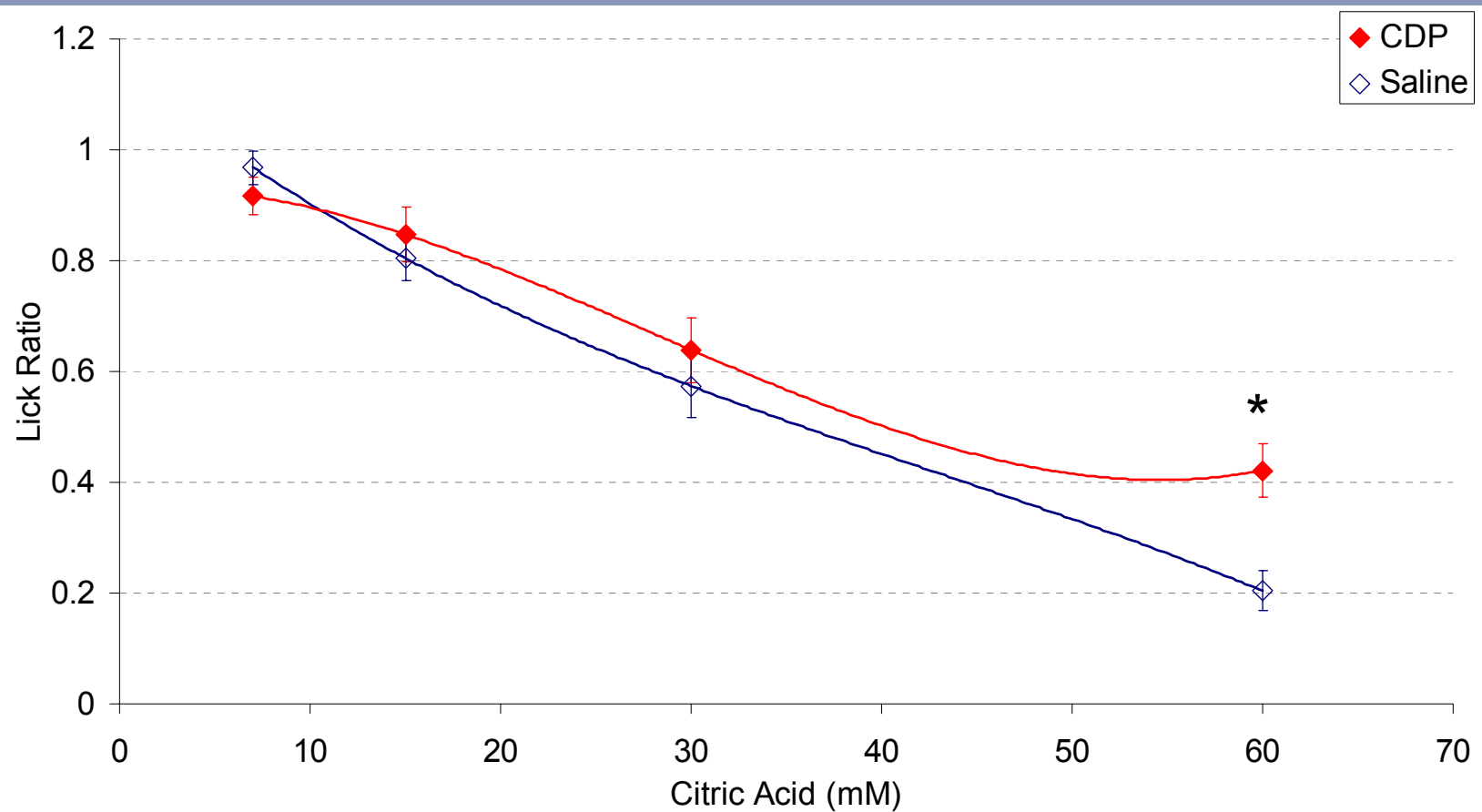
Short Term Results

Salty, Males Only

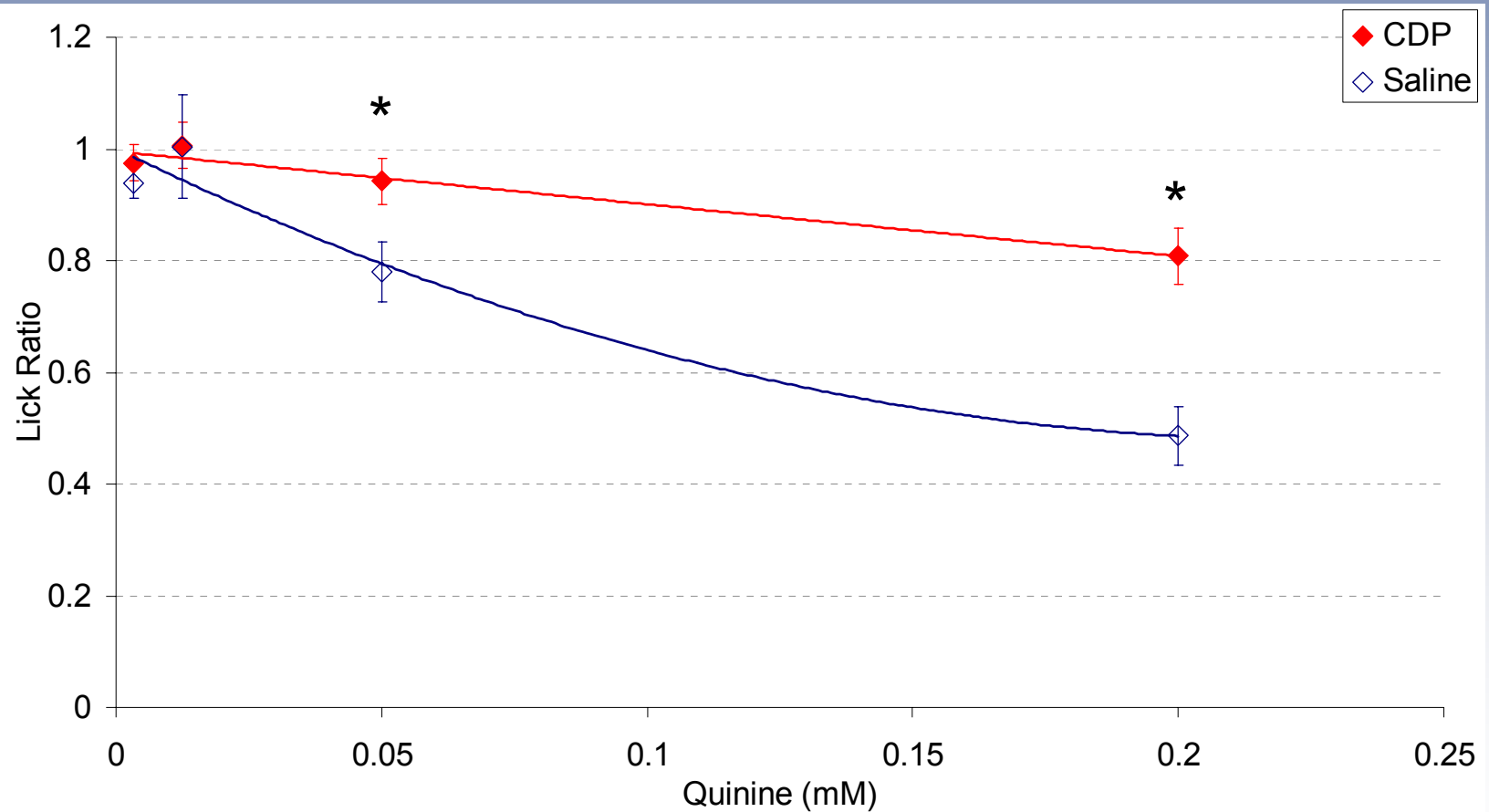


Short Term Results

Sour



Short Term Results Bitter



Results Summary

- Microanalysis of long-term testing showed effects for measures associated with palatability
 - First-minute licks, meal licks, pause duration, licking rate
- Short-term testing confirmed increases in palatability for both appetitive and aversive stimuli
 - Sucrose: ceiling effect, but CDP increased licking at lower concentrations
 - NaCl: more palatable after CDP for males
 - CA and Quinine: more palatable after CDP

Conclusions

- **Increase in palatability with benzodiazepines**
- **This research expands on previous reports:**
 - Both short term and long term testing
 - Analysis of licking behavior not just stimulus consumption
 - Both appetitive and aversive stimuli
- **Important Implications**
 - Taste system neurophysiology: GABA regulation of taste
 - Clinical relevance: Benzo side effects
 - Potential Applications: *Treatment for eating disorders related to changes in palatability*

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