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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

![Bar graph showing licks over water with an asterisk (*) indicating significance.](image)
Long Term Results
First Minute Licks

- Water
- NaCl
- Sucrose
- Citric Acid
- Quinine

Saline vs. CDP*
Long Term Results
Session Licks

Licks

<table>
<thead>
<tr>
<th></th>
<th>NaCl</th>
<th>Sucrose</th>
<th>Citric Acid</th>
<th>Quinine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Saline</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CDP</strong></td>
<td></td>
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</tbody>
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* Denotes significant difference.
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

**MEAL DURATION**

- Changes in Meal Duration associated with hunger / satiety
Long Term Results
Pauses within Meals

Saline
CDP

NaCl  Sucrose  Citric Acid  Quinine

Seconds
Long Term Results
Lick Rate

<table>
<thead>
<tr>
<th>Substance</th>
<th>Licks / s</th>
<th>Saline</th>
<th>CDP</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl</td>
<td>1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sucrose</td>
<td>3.0</td>
<td>3.5</td>
<td></td>
</tr>
<tr>
<td>Citric Acid</td>
<td>2.0</td>
<td></td>
<td>2.5</td>
</tr>
<tr>
<td>Quinine</td>
<td>2.5</td>
<td></td>
<td>3.0</td>
</tr>
</tbody>
</table>

* Significant difference
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

![Graph showing the relationship between Sucrose concentration and licks per 15s for different groups: F-CDP, F-Saline, M-CDP, and M-Saline. The graph includes error bars and significant markers (#, *).]
Short Term Results
Sucrose

Licks / 15s vs Sucrose (mM)
Short Term Results
Salty, Males Only

![Graph showing the relationship between NaCl (mM) and Lick Ratio for Saline. The graph indicates a decrease in Lick Ratio as NaCl concentration increases.]
Short Term Results
Salty, Males Only

![Graph showing lick ratio against NaCl concentration for CDP and Saline groups.](image-url)
Short Term Results
Sour

![Graph showing lick ratios versus citric acid concentrations for CDP and Saline groups.](image)
Short Term Results

Bitter

![Graph showing lick ratio against quinine concentration for CDP and saline with asterisks indicating significant difference.](image)
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*
Special thanks to:

Dr. Baird (Amherst College) for his help in analyzing the long term data

Tyler Toomes for his help with data collection

Dr. Pittman for his continuing guidance and support throughout this study