Behavioral Evidence of Benzodiazepine-Induced Alterations of the Gustatory Evaluation of Accepted and Aversive Taste Stimuli.

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Introduction

Benzodiazepines are a class of anxiolytic drugs that facilitate the effectiveness of the GABA neurotransmitter to hyperpolarize cells. Benzodiazepine receptors are broadly distributed throughout the CNS including the gustatory nuclei of the hindbrain, the nucleus of the solitary tract (NST) and the parabrachial nucleus (PBN). Previous research has provided evidence that corticofugal projections utilize GABA in hindbrain gustatory nuclei in order to shape the afferent gustatory signal. GABA agonists appear to narrow the responsiveness of NST gustatory cells to taste stimuli.

Benzodiazepines have a well-documented hyperphagic effect on palatable taste stimuli and foodstuffs. The research suggests that the benzodiazepine-induced consumption is related to an enhancement of the gustatory evaluation of the ingesta. The majority of research has focused on sweet and fat tastants or foodstuffs with little research exploring the ability of benzodiazepines to influence the gustatory evaluation of aversive stimuli such as moderate concentrations of salt, sour, or bitter tastants.

This study examines the effect of chlordiazepoxide (CDP), the first synthesized benzodiazepine, on the ingestive behavioral responses to sweet, sour, salt, and bitter taste stimuli in both long-term and brief-access tests. We predicted that in addition to increasing the gustatory evaluation of sweet stimuli, CDP would also increase consumption of normally aversive salt, sour, and bitter taste stimuli.

Methods

Subjects: 24 adult Sprague-Dawley rats (male n=12, female n=12).

Long-Term Test Stimuli: Water, 75mM sucrose, 500mM NaCl, 0.05mM QHCl, 30mM citric acid

Brief-Access Test Stimuli: Water; 25, 50, 75, 100mM sucrose; 0.125, 0.25, 0.5, 1M NaCl; 0.003, 0.013, 0.05, 0.2mM QHCl; 7, 15, 30, 60mM citric acid

Behavioral Testing Procedures

Three days prior to the experiment, rats were placed and maintained on a 23-hr water restriction schedule *except the nights prior to brief-access testing of sucrose when rats were given free access to water*. All injections were administered i.p. 20 minutes prior to behavioral testing. Using a counterbalanced design, rats were tested for each taste stimulus on 2 consecutive days with half of the rats receiving a saline injection (150mM NaCl, 1ml/kg) and half of the rats receiving an injection of CDP (chlordiazepoxide, 10mg/ml/kg) on each test day. All taste stimuli were mixed daily.

Long-term behavioral tests were daily 90-min sessions in the AC-108 lickometer (DiLog Instruments) in which each lick was recorded. Microanalysis of the data categorized the licking patterns into meals (terminated by 10min pause) and bursts (terminated by 1s pause) of licking.

Brief-access tests were daily sessions in the MS-160 Davis Rig (DiLog Instruments) in which each lick was recorded during 15s stimulus presentations with 10s interstimulus intervals. Each test session consisted of 20 trials in which four tastant concentrations and water were presented in random order within 4 stimulus blocks. A lick ratio (licks tastant/licks water) was calculated for salt, sour, and bitter testing.

Data Analysis: All data were statistically analyzed using mixed factorial repeated measures ANOVA and post-hoc paired t-tests (SPSS).

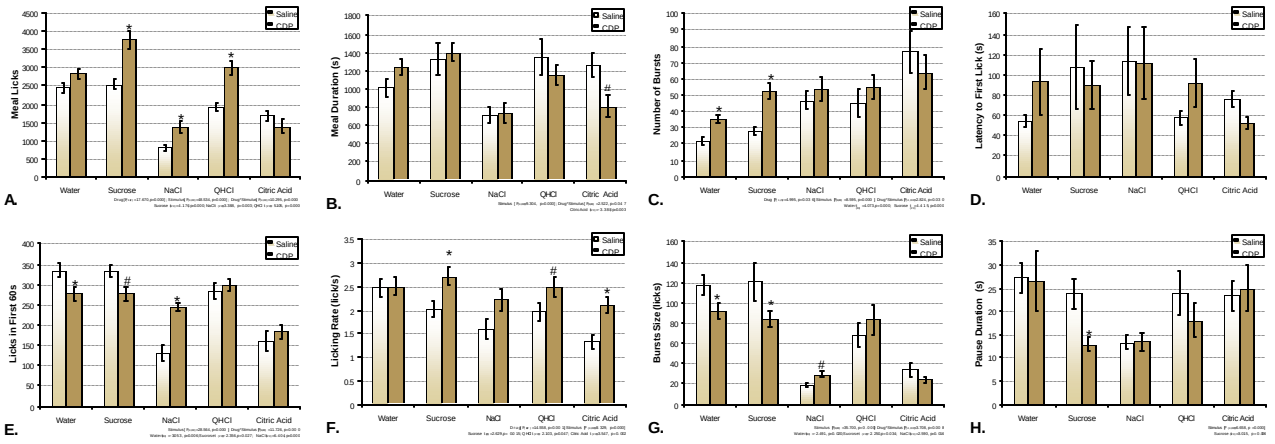

FIGURE 1. Microanalysis of licking during 90-min test sessions 20 min following saline or CDP injections. There were no sex differences therefore male and female data have been combined. CDP significantly increased **meal licks (A)** for salt, sweet, and bitter stimuli with no effect on water or sour stimuli. The **meal duration (B)** is associated with postingestive feedback and there was a reduction for only citric acid. The **number of bursts (C)** is also associated with postingestive cues and CDP increased consumption of both water and sucrose. There was no effect on the **latency to the first lick (D)** indicating a high motivation to consume the stimuli and no interference from olfactory cues. CDP-induced changes in the measurements associated with gustatory evaluation of the stimuli indicate that CDP increased acceptance of most tastants with increased **licks in the first minute (E)** for salt, increased **licking rates (F)** for sweet, bitter, and sour stimuli, increased **burst size (G)** for salt, and decreased **pause duration (H)** for sweet.

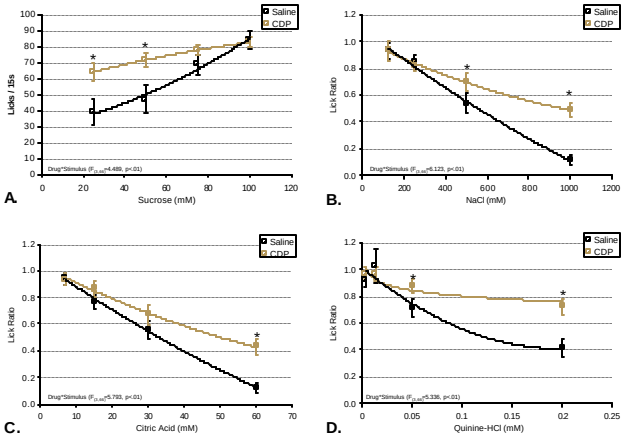

FIGURE 2. Brief-access testing in the MS-160 Davis Rig reveals CDP-induced increases in licking to low concentrations of **sucrose (A)** and moderate to high concentrations of **NaCl (B)**, **citric acid (C)**, and **quinine-HCl (D)**. There were no significant effects of sex *(data shown combined)* or differences in the latency to the first lick.

Discussion

Our results confirm previous research findings that CDP increases consumption of appetitive stimuli (sucrose) acting primarily through taste-mediated cues. Our results extend previous findings by showing that CDP also acts to increase the acceptance of aversive stimuli. Our behavioral findings support concurrent electrophysiological recordings of taste-responsive cells in the PBN which suggest that CDP suppresses responses to aversive stimuli and increases the proportion of cells responsive to sweet and salt stimuli. ***SEE POSTER #467, Saturday, JP Baird.***

FUTURE DIRECTIONS:

- Include additional taste stimuli such as ***non-nutritive sweet and umami*** in both the long-term and short-term tests
- Include ***additional concentrations*** of sucrose, NaCl, citric acid, & QHCl in both the long-term and short-term tests
- Examine the ***effect of additional benzodiazepine agonists*** besides CDP
- Examine the effect of benzodiazepine agonists on consumption of taste stimuli using ***water-replete*** rats in long-term tests.
- ***CNS site-specific benzodiazepine application*** during short-term testing.

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