**Systemic Baclofen Decreases Gustatory Discrimination and Induces Conditioned Taste Aversion in Adult Rats**

G.N. Wilson, O.R. Biesan, J.L. Remus, L. Ramos, K. Ketchesin, & G.A. Mickley

Baldwin-Wallace College, Neuroscience Program and Department of Psychology, Berea, OH 44017

**Abstract**

Studies that aimed to evaluate drug-induced changes in learning and memory are challenged to parse out the effects of drug on sensory and appetitive systems as well as on neural systems in the brain. In the context of conditioned taste aversion (CTA), drugs that alter the sequence of events and affect their ability to learn or eat can manifest as malaise and drive the context-sensitive effects observed from these manipulations. Therefore, the current experiment examined the effects of baclofen (BAC), sodium chloride (LiCl), and their combinations on the acquisition of CTA. Our null hypothesis was that BAC would not alter the CTA paradigm in either SAC or SAC+LiCl at either 2 or 3mg/kg. Our data indicate that, depending on the dose, BAC can alter SAC taste that received the 3mg/kg dose of BAC compared to more conventionally SAC + lithium chloride (LiCl) paradigms. The results of the second experiment indicated that 2 and 3mg/kg (i.p.) BAC were effective in the suppression of SAC and water drinking (revealed in Experiment 1).

**Introduction**

- **Baclofen** ([BAC; 4-aminomethyl-5-chloro-1-phenylpyridine (bacitracin), a GABA,B receptor agonist, disrupts performance in a variety of memory tasks [1, 2, 9, 15]].
- **However, tests of GABAergic system manipulations on a conditioned taste aversion (CTA) have produced variable results.**
  - Chester and Cunningham (2012) showed that BAC does not alter ethanol-induced conditioned taste aversion in mice, nor does BAC, itself, have malaise-inducing properties at a dose of 2mg/kg. However, other labs have demonstrated that GABA,B knockout mice fail to acquire a CTA while GABA,B knockout mice fail to acquire a CTA (9).
  - The challenges of using drugs like BAC in the test memory in the context of an appetitive paradigm include the fact that GABAergic system manipulations especially cause hypolucosis, sedation, vomiting and hypothermia (4, 5, 15).
  - In order to separate out drug effects on learning/memory vs. drug effects on sensory or appetitive factors this investigation asked the following questions:
    - Does BAC alter basal food or liquid consumption?
    - Does BAC change basal intake, thus acting as a US or interfering with actions of a US?
    - Given the previous literature (see above), in our first experiment, we hypothesized that BAC would have no effects on taste discrimination or overall SAC consumption.
    - Results of the first experiment led to a second experiment in which we hypothesized that BAC at 3mg/kg would have the visceral effects of an unconditioned stimulus if used in a CTA paradigm.

**Experiment 1: Taste Discrimination and Hypodipsia Test**

- **Sensory manipulations reportedly cause hypodipsia, sedation, vertigo and nausea**; therefore, we evaluated the effect of BAC injections on SAC in the CTA paradigm. The rats that received BAC at 3mg/kg also showed a decrease in their water consumption at the time point tested in the experiment. The first day of fluid deprivation the animals were given 1.0% SAC.
- **Following the first fluid deprivation day, animals were subjected to saccharin (SAC 0.3%) and LiCl (0.15 M)**. We evaluated this treatment pattern described in Table 1.
- **On the fifth day of testing, animals were given an injection of either SAC (1.5 mg/kg) or LiCl (1.0 mg/kg).** There were three groups were injected with LiCl (1mg/kg) or was randomly presented with the solution of SAC taste for 10min.

**Hypodipsia Test**

- There was no indication on Day 5, that LiCl-induced hypodipsia was affected by BAC injection. A repeated measures ANOVA did not show a significant difference in water consumption from the Day 1 test (mean water consumption on Days 2 and 4) to water consumption on the LiCl-induced hypodipsia Test Day (Fig. 5). *p<0.05*
- In our study, BAC at 1mg/kg showed no decrease in water consumption in comparison to SAC + LiCl group and SAC group. However, at 2mg/kg BAC group at 3mg/kg BAC showed a decrease in water consumption in comparison to SAC + LiCl group and SAC group.

**Experiment 2: Effects of BAC on a SAC taste discrimination task**

- **High dose of Baclofen (2-3mg/kg)** may induce hypodipsia and affect SAC consumption, which in turn may affect the development of CTA.
- **Low dose of Baclofen (1mg/kg)** may alter SAC taste discrimination, which could affect the development of CTA.

**Summary & Conclusions**

- **Experiment 1 revealed that basilicous (1 and 2mg/kg) injection of BAC at 1mg/kg did not induce a CTA, as SAC consumption decreased significantly over the day.**
- **BAC at 1.5 mg/kg did not disrupt LiCl-induced hypodipsia, so the US effects of LiCl remain intact when co-administered with BAC.**
- **Both doses of BAC tested in experiment 2 (2 and 3mg/kg) did induce a CTA, as SAC consumption decreased significantly over the day.**
- **BAC at 1mg/kg did not disrupt LiCl-induced hypodipsia, so the US effects of LiCl remain intact when co-administered with BAC.**
- **Despite some variance in the literature (see above, 2, 3, 5, 11, 12), it is not surprising that BAC produces US properties, due to the cascade of neurophysiological effects it produces in the CNS (5, 15).**
  - Through direct action as a GABA receptor agonist, BAC indirectly reduces levels of a variety of neurotransmitters (e.g., neuropeptides, dopamine, acetylcholine, serotonin, glutamate, and GABA) (15).
  - Overall, our data indicated that BAC at 2 mg/kg (p) impairs sensorial abilities and decreases gustatory discrimination in rats.
  - Because these effects may be augmented by dose-dependent US properties of BAC that, when paired with the gustatory stimulus, SAC, induced a CTA in Experiment 2.
  - **BAC may still be used successfully in future CTA manipulations at a dose of 3mg/kg (p), since these data no longer change in any of the CTA manipulations.**
  - **Nevertheless, it is clear that BAC is a potent inducer of CTA and its effects on SAC consumption should be taken into consideration when designing future experiments with this drug.**

**References**

- [1] Baldwin-Wallace College, Neuroscience Program and Department of Psychology, Berea, OH 44017