



## Short report

## Enhanced consumption of an aversively conditioned taste following the presentation of a “medicine” taste

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## ABSTRACT

Rats given presentations of a citric acid solution while recovering from LiCl-induced illness (i.e., a “medicine effect” treatment) subsequently drank more of an aversively conditioned NaCl solution at test, when the NaCl presentation was immediately preceded by citric acid. That is, citric acid passed a summation test of conditioned inhibition. Such an effect was not observed in a group given explicitly unpaired presentations of LiCl and citric acid. It is proposed that enhanced consumption of an aversive taste due to the previous presentation of a “medicine” taste can provide an animal model of human maladaptive behavior in regards to food consumption.

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## 1. Introduction

Systematic research using standard tests of conditioned inhibition (i.e., summation and retardation tests; Rescorla, 1969b) in conditioned taste aversion (CTA) has been scarce, providing both success (e.g., Lambert et al., 1989) and failure (e.g., Delamater et al., 1986). Furthermore, such research focused on answering questions of theoretical, but not applied, relevance. Interestingly, the summation test of conditioned inhibition in a CTA preparation could provide insight into a case of human maladaptive behavior known as *risk compensation*, or the adjustment of behavior to perceived changes in risk—an effect that comprises a tendency to behave cautiously as perceived risk increases and, conversely, to behave recklessly as perceived risk decreases (see Adams, 1995). For example, research has shown that seatbelt use increases the number of car accidents (Peltzman, 1975), and that sunscreen use increases risk of skin cancer (Autier et al., 1999). These paradoxical effects make sense in light of risk compensation theory: both seatbelts and sunscreen make us feel protected (i.e., from injury/death in case of car accident and from sunburn/skin cancer, respectively); in turn, this feeling of safety encourages reckless driving and prolonged sun exposure. A similar process might be postulated to underlie the summation test of conditioned inhibition in the CTA preparation. This test consists of the compound presentation of two tastes, an aversively conditioned taste and a putative inhibitor. The putative inhibitor is said to pass the test if it effectively enhances consumption of the aversive taste relative to a condition lacking exposure

to the putative inhibitor at test. In other words, this test could be viewed as involving risk compensation: a substance that is known to be harmful is consumed in larger amounts (i.e., reckless behavior) due to the feeling of safety elicited by the putative inhibitor (i.e., reduction in perceived risk).

In a first attempt to develop such an animal model of human maladaptive behavior, the present experiment evaluated whether the presentation of a putative inhibitor for illness can enhance the consumption of an aversively conditioned taste in a CTA preparation with rats. Two groups received treatments aiming to endow a citric acid solution with inhibitory value: Group Med received a “medicine effect” treatment (e.g., Garcia et al., 1967; Green and Garcia, 1971), in which citric acid was presented while the animals were recovering from the illness induced by a previous lithium chloride (LiCl) administration (e.g., Barker and Weaver, 1991; Hasegawa, 1981; Zahorik and Bean, 1975); and Group UP received explicitly unpaired presentations of LiCl and citric acid (e.g., Rescorla, 1969a). Following treatment with citric acid and LiCl, both groups received one pairing of a NaCl (salt) solution with LiCl. Testing then consisted of the presentation of the citric acid solution, immediately followed by the NaCl solution (i.e., a serial compound). The consumption of NaCl at test in these two groups was compared to that of Group Water, which received a treatment identical to that of Group Med, but was given water instead of citric acid at test. Citric acid would pass the summation test of conditioned inhibition for Groups Med and UP if these groups subsequently drank NaCl in higher amounts than Group Water. Additionally, the following control groups were included: Group PE was preexposed to citric acid prior to the first LiCl injection, and Group Novel was presented with the citric acid solution for the first time during testing. In these two groups, the citric acid solution lacked inhibitory value

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and, hence, was expected to have no detectable impact on NaCl consumption. Finally, Group NoAv never received a pairing of NaCl with LiCl and, accordingly, was expected to consume this taste in large amounts.

## 2. Method

### 2.1. Subjects

The subjects were 72 Wistar, naïve, young adult rats (36 males and 36 females), obtained from Charles River, Inc. (Raleigh, NC). Rats were 96 days old at the beginning of the experiment, and their body weights ranged from 348 to 437 g for males and from 202 to 315 g for females. The animals were housed individually in 48.26 cm × 26.67 cm × 20.32 cm Plexiglas cages on a 12:12-h light:dark cycle, with all the experimental sessions occurring during the light period. Subjects had free access to food in the home cage. Prior to initiation of the experiment, water availability was progressively reduced to 30 min per day, provided approximately 1 h after any scheduled treatment.

### 2.2. Apparatus

All the experimental manipulations were conducted in the home cages. The animals were maintained in the laboratory since their arrival until termination of the experiment with no interruption. Daily access to water was provided in 500-ml plastic bottles fitted with stainless steel spouts, attached to the front of each cage. In the experimental sessions, liquid rations were provided in 8 oz (i.e., approximately 236.5 ml) glass bottles fitted with stainless steel spouts containing ball bearings, also attached to the front of each cage. The amount of liquid intake was assessed by the difference between bottle weight before and after the liquid presentations.

Two distinct tastes were employed in this study, a .9% (w/v, .15 M) NaCl solution, and a 1% (w/v, .05 M) citric acid solution. Solutions were made using tap water and provided at room temperature (20 °C/68 °F). Gastrointestinal illness was induced by a 15 ml/kg of body weight intraperitoneal (i.p.) injection of .12 M LiCl. All solutes were obtained from Sigma–Aldrich Chemie GmbH (Steinheim, Germany).

### 2.3. Procedure

The design of the experiment is summarized in Table 1. Prior to the start of the experiment, subjects were assigned to one of five experimental groups, matched for body weight. The critical groups in this study (i.e., Groups Water, Med, and UP) had a larger sample ( $n = 16$ , 8 males and 8 females per group) than control Groups PE, Novel, and NoAv ( $n = 8$ , 4 males and 4 females per group). (A male rat from Group Novel died prior to the start of the experiment, thereby resulting in  $n = 7$ .) Unless explicitly stated otherwise, all subjects were given a single 10-min experimental session per day,

which started at approximately 13:00. Also, all subjects received additional 20-min access to tap water soon after the session. Consumption during each session was recorded.

#### 2.3.1. Pretraining

On Days 1–4, tap water was presented with the glass bottle. This treatment acclimated subjects to drinking from the lick tubes at the daily treatment time.

#### 2.3.2. Phase 1

Phase 1 treatment took place on Days 5–10. On these days, Group PE received a presentation of the citric acid solution, whereas the other groups received a presentation of tap water.

#### 2.3.3. Phase 2

Phase 2 treatment took place on Days 11–25. On Days 11, 14, 17, 20, and 23 all subjects received an i.p. injection of LiCl, after which they were immediately returned to the home cage. Seventy-five minutes after being injected with LiCl, Groups Water, Med, and NoAv were given a presentation of the citric acid solution, whereas Groups UP, PE, and Novel received a presentation of tap water. Days 12, 15, 18, 21, and 24 consisted of recovery days, on which tap water was presented with the glass bottle, while allowing the subjects to recover from the impact of the LiCl injection. On Days 13, 16, 19, 22, and 25, Group UP received a presentation of the citric acid solution, whereas the other groups were given a presentation of tap water.

#### 2.3.4. Phase 3

Phase 3 treatment was conducted on Days 26–28. On Day 26, Groups Water, Med, UP, PE, and Novel received a presentation of the NaCl solution, whereas Group NoAv received a presentation of tap water. These fluid presentations were followed immediately by an i.p. injection of LiCl, after which the animals were immediately returned to the home cage. Seventy-five minutes after being injected with LiCl, Groups Water, Med, and NoAv were given a presentation of the citric acid solution, whereas subjects in Groups UP, PE, and Novel received a presentation of tap water. Day 27 consisted of a recovery day. On Day 28, Groups UP and NoAv received a presentation of the citric acid and NaCl solutions, respectively, whereas the other groups were given a presentation of tap water.

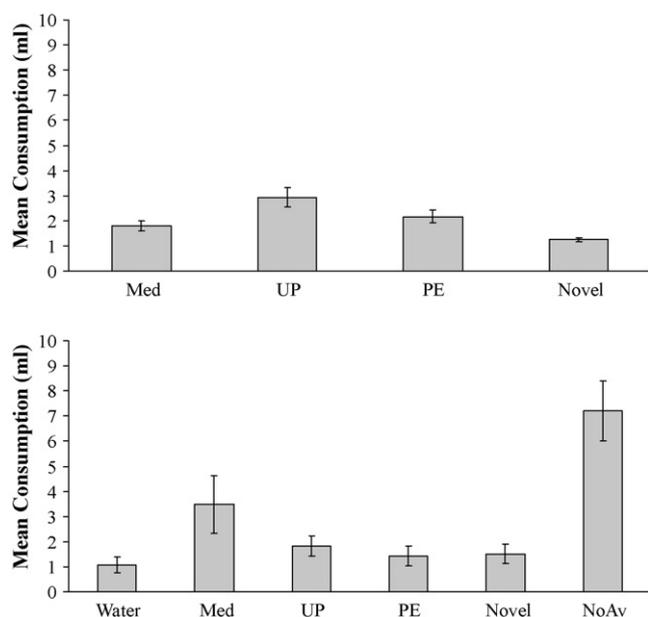
#### 2.3.5. Test

Testing took place on Day 29. On this day, all subjects received a 5-min presentation of the NaCl solution. For Groups Med, UP, PE, and Novel this presentation of NaCl was immediately preceded by a 5-min presentation of the citric acid solution, whereas for Groups Water and NoAv it was preceded by tap water. The volume of water presented to the animals in these groups was yoked to the volume of the citric acid solution consumed by the animals in Group Med. Analyses were conducted excluding the data from those subjects in Groups Med, UP, PE, and Novel that failed to consume at least 1 ml of citric acid during testing. The application of this criterion

**Table 1**  
Design of the experiment.

Group	Phase 1 (Days 5–10)	Phase 2 (Days 11–25)	Phase 3 (Days 26–28)	Test (Day 29)
Water	6 W	5 LiCl → 75' → C	1 N → LiCl → 75' → C	1 W → N
Med	6 W	5 LiCl → 75' → C	1 N → LiCl → 75' → C	1 C → N
UP	6 W	5 LiCl / 5 C	1 N → LiCl / 1 C	1 C → N
PE	6 C	5 LiCl	1 N → LiCl	1 C → N
Novel	6 W	5 LiCl	1 N → LiCl	1 C → N
NoAv	6 W	5 LiCl → 75' → C	1 LiCl → 75' → C / 1 N	1 W → N

Note. N = NaCl solution; C = citric acid solution; W = tap water; LiCl = lithium chloride i.p. injection. '→' means 'immediately followed by', '→ 75' →' means 'followed, after a 75-min delay, by', and '/' means that the trial types were interspersed within a single phase. The numbers denote the number of presentations of each trial type in each phase. See text for further details.



**Fig. 1.** Top panel: mean consumption at test of the citric acid solution. Bottom panel: mean consumption at test of the NaCl solution. Error bars depict standard error of the means.

removed the data from 5, 2, and 1 subjects from Groups Med, UP, and Novel, respectively. An alpha level of  $p < .05$  was adopted for all statistical analyses.

### 3. Results

The top panel of Fig. 1 depicts the consumption of citric acid at test. A one-way ANOVA among groups on the mean citric acid consumption yielded significant differences,  $F(3, 35) = 5.00, p < .01$ . Pairwise comparisons showed that Group UP consumed more citric acid than Groups Med and Novel,  $F_s(1, 35) > 8.07, p_s < .01$ . Also, Group PE differed from both Groups UP and Novel, although these differences were marginally significant,  $p_s > .08$ . Finally, citric acid consumption in Group Med was comparable to that of Groups PE and Novel,  $p_s > .28$ .

The bottom panel of Fig. 1 depicts the consumption of NaCl at test. A one-way ANOVA among groups on the NaCl consumption yielded significant differences,  $F(5, 57) = 9.41, p < .01$ . Pairwise comparisons were conducted on the NaCl consumption scores and showed that Group Med consumed more NaCl than Group Water,  $F(1, 57) = 7.36, p < .01$ . Groups UP, PE, and Novel consumed similar amounts of NaCl,  $p_s > .69$ , and in amounts that were comparable to that of Group Water,  $p_s > .36$ , and lower than that of Group Med, although these latter differences fell short of significance,  $p_s > .05$ . However, NaCl consumption in Group Med was larger than the combined consumption of Groups PE and Novel,  $F(1, 57) = 4.83, p < .05$ . Finally, Group NoAv consumed more NaCl than the rest of the groups,  $F_s(1, 57) > 12.50, p_s < .01$ .

Additional analyses were conducted to ascertain if consumption of citric acid and NaCl differed between males and females. A Group  $\times$  Sex ANOVA on the citric acid consumption scores showed no main effect of sex,  $p > .57$ , or an interaction,  $p > .91$ . An analogous ANOVA on the NaCl consumption found no main effect of sex,  $p > .39$ , but yielded a significant interaction,  $F(5, 51) = 2.68, p < .05$ . Pairwise comparisons showed that, in Group NoAv, the NaCl solution was consumed in larger amounts by males ( $M = 9.46$  ml,  $SEM = 1.01$ ) than by females ( $M = 4.92$  ml,  $SEM = 1.48$ ),  $F(1, 51) = 9.14, p < .01$ . No sex-

related difference was found in the consumption of NaCl for the rest of the groups,  $p_s > .16$ .

### 4. Discussion

The results of test found that the presentation of citric acid enhanced the subsequent consumption of NaCl for Group Med relative to Group Water, an effect that was not detected in Groups UP, PE, and Novel. Also, Group Med's NaCl consumption was higher than the combined consumption of NaCl in Groups PE and Novel (i.e., the control groups for which citric acid had no inhibitory value), a result that indicates that the enhanced NaCl consumption of Group Med was not due to a generalization decrement caused by the mere presentation of citric acid at test. In sum, citric acid passed the summation test of conditioned inhibition for Group Med, but not for Group UP. It seems like, at least in the CTA preparation and with the present experimental parameters (e.g., nature and concentration of the tastes), the "medicine effect" treatment received by Group Med was more effective in endowing citric acid with inhibitory value than was the explicitly unpaired treatment received by Group UP.<sup>1</sup>

As mentioned in Section 1, the summation test of conditioned inhibition could be used as an animal model of risk compensation in humans. In the specific case of CTA, the summation test of conditioned inhibition could be used to model reckless consumption of potentially harmful foods caused by medicine-induced safety. For example, the summation test parallels the use of over-the-counter medicines (e.g., antacid tablets or anti-hangover caplets) in order to indulge in foods or drinks (e.g., fatty or spicy foods, alcoholic beverages) that, when consumed in large amounts, could be potentially harmful. (Antacids are usually taken *after* the ingestion of harmful foods to *relieve* pain associated with heartburn, but they can also be taken *before* the ingestion of harmful, but tasty, foods in order to *prevent* heartburn.) Such maladaptive human behavior is no more puzzling than the behavior of the rats in Group Med which, upon the first presentation of NaCl following its pairing with illness, consumed this taste in larger amounts due to the presence of citric acid, a taste previously associated with recovery from illness. Related to this finding, Pineño et al. (2008) observed that the neophobic response typically elicited by a novel taste was attenuated by the presentation of a conditioned inhibitor of illness. Specifically, rats consumed more of a novel taste when presented along with a conditioned inhibitor than when presented alone or together with another novel taste. Given the important role of the neophobic response in avoiding the ingestion of potentially toxic substances, the large consumption of a novel taste constitutes another example of reckless behavior arising from the presence of the conditioned inhibitor. The enhanced consumption of a novel taste (Pineño et al.) or an aversively conditioned taste (present study) due to the compound presentation of a conditioned inhibitor provides a simple paradigm to study in the animal laboratory how a highly adaptive psychological mechanism (i.e., inhibitory learning) might inadvertently lead to a maladaptive behavior in humans (i.e., risk compensation).

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<sup>1</sup> It is worth noting that, in spite of the explicitly unpaired procedure being widely recognized as a robust conditioned inhibition treatment, some studies reported a failure to detect conditioned inhibition using this procedure (e.g., Frey and Butler, 1977; Rauhut et al., 2001).

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