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Aversive Taste Reactivity: Reactivity to Quinine Predicts Aversive Reactivity to Lithium-Paired Sucrose Solution

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PARKER, L. A. *Aversive taste reactivity: Reactivity to quinine predicts aversive reactivity to lithium-paired sucrose solution.* PHARMACOL BIOCHEM BEHAV **47**(1) 73–75, 1994.—The ability of a rat's reactivity to the aversive taste properties of quinine to predict its' reactivity to the aversive taste properties of a lithium-paired sucrose solution were assessed. In phase 1, all rats were intraorally infused with 0.05% quinine solution over a 2-min taste reactivity (TR) test. On the basis of their composite aversive reactions, rats were divided into high reactors (HiQ) and low reactors (LoQ). In phase 2, rats were given three TR conditioning/testing trials in which they received a 2-min intraoral infusion of 0.5 M sucrose solution immediately followed by an IP injection of either 127.2 mg/kg lithium chloride or physiological saline. Among rats conditioned with lithium during phase 2, the phase-1 quinine HiQs displayed more aversive reactions than did the phase-1 quinine LoQs. This suggests that reactivity to the aversive properties of quinine may predict the strength of conditioned palatability shifts to a lithium-paired sucrose solution.

Individual differences Taste reactivity Sucrose Quinine Lithium Taste aversion Taste Palatability

GARCIA and colleagues (4) proposed that the avoidance of a lithium-paired flavor is motivated by an hedonic shift in the palatability of the flavored solution. This suggestion was based on the observation that the pattern of reactions elicited by a lithium-paired sucrose solution was similar to the pattern of reactions elicited by an unconditionally aversive-tasting quinine solution.

More recently, Grill and Norgren (5) developed a test that would systematically assess a rat's hedonic reaction to a tastant. The taste reactivity (TR) test directly measures a rat's orofacial and somatic reactions to a flavored solution that is infused across a rat's tongue. Palatable tastes such as sucrose elicit the ingestive responses of tongue protrusions, mouth movements, and paw licking. Unpalatable tastes such as quinine elicit the aversive reactions of chin rubbing, gaping, and paw treading. Grill and Norgren (5) reported that after having been paired with lithium, a sucrose solution elicits aversive reactions that are similar to those elicited by quinine solution.

Although it is clear by grouped data that rats react to the taste of a lithium-paired sucrose solution as if it is unpalatable (8), the within-group variability is high. Some rats demonstrate a greater palatability shift than others. It is conceivable that individual differences in reactivity to the aversive properties of quinine solution are related to the likelihood that a lithium-paired sucrose solution will become unpalatable to rats. The following experiment assessed whether the strength of a rat's aversive reactions to quinine would predict the strength of its' aversive reactions to a lithium-paired sucrose solution.

METHOD

Subjects

Subjects were 52 male Sprague–Dawley rats weighing between 328–460 g in Conditioning Trial 1. They were housed in individual stainless steel cages and maintained on ad lib rat chow and water throughout the experiment.

Procedure

One week after their arrival in the laboratory, rats were surgically implanted with intraoral cannulae as described by Parker (7). After a 1-week recovery period, they received two adaptation trials to the TR test procedure.

Adaptation trials. In each adaptation trial, rats were brought into the test room and placed in the glass test chamber (22.5 × 26 × 20 cm). The test chamber was illuminated by two 25-W lights hung on either side of a mirror that was hung at an angle beneath the test chamber. Their cannulae were attached to a syringe placed in the holder for the infusion pump (Model 22, Harvard Apparatus, South Natick, MA) by means of a 30-cm length of PE 90 tubing. After a 1-min

period, the infusion pump delivered water through the cannulae at the rate of 1 ml/min for a period of 2 min. Each rat received two adaptation trials, with each occurring on consecutive days.

Phase 1: Quinine test trial. One day after the final adaptation trial, all rats received an intraoral infusion of 0.05% quinine solution over a 2-min period in a manner identical to that of the adaptation training. In this quinine test trial, the orofacial and somatic responses of rats were videorecorded from a mirror hung at an angle beneath the test apparatus. The videotapes were then scored by means of an event recorder program called Observer (Noldus, Inc., Wageningen, The Netherlands) by a rater blind to experimental conditions. The behaviors measured included the aversive reactions of chin rubbing (mouth in direct contact with the floor or a wall and projecting the body forward), gaping (large-amplitude, rapid opening of the mandible with concomitant retraction of the corners of the mouth), and paw treading (sequential extension of one forelimb forward against the floor while the other forelimb is being retracted). The frequencies of each of these behaviors that occurred within the 2-min test were combined to produce a total aversive TR reaction score. The frequency of aversive reactions elicited by the quinine solution determined the subsequent grouping of rats into high quinine responders (HiQ; $n = 26$) and low quinine responders (LoQ; $n = 26$).

Phase 2: Conditioning/testing trials. Four days after the quinine test, rats received the first of three conditioning/testing TR trials. On each trial, both the high and low quinine responders were intraorally infused with 0.5 M sucrose solution (17%) over a 2-min period during which they were videorecorded. Immediately after the intraoral infusion, rats were injected IP with either 127.2 mg/kg lithium chloride or physiological saline solution in a volume of 20 ml/kg. The groups were thus as follows: HiQ/lithium ($n = 13$); LoQ/lithium ($n = 13$); HiQ/saline ($n = 13$); and LoQ/saline ($n = 13$). All rats received three such trials. The tapes were later scored for the behaviors described above as well as tongue protrusions (protrusions of the tongue on the midline or on either side of the mouth), mouth movements (low-amplitude, rhythmic openings of the mandible), and paw licking (licking the forelimb paws while they are held close to the mouth). These three ingestive reactions were combined to produce a composite ingestive reactions score for each rat.

RESULTS

Figure 1 presents the mean frequency of aversive reactions elicited by sucrose solution on each conditioning/testing trial for each group. A 2 × 2 × 3 mixed-factor analysis of variance (ANOVA) revealed a significant main effect of drug condition, $F(1, 48) = 42.3, p < 0.001$, quinine responsivity, $F(1, 48) = 4.7, p < 0.05$, and drug condition × quinine reactions interaction, $F(1, 48) = 4.6, p < 0.05$. The lithium-conditioned HiQs demonstrated more aversive reactions when infused with the lithium-paired sucrose solution than did the lithium-conditioned LoQs ($p < 0.05$), although both lithium-conditioned groups displayed more aversive reactions than did both saline groups ($p < 0.01$). Additionally, the drug condition × conditioning trial interaction was significant, $F(2, 96) = 32.1, p < 0.01$. The frequency of aversive reactions increased across conditioning/testing trials for the lithium-conditioned groups.

Figure 2 presents the mean amount of time during the TR conditioning/testing trials that rats in the various conditions

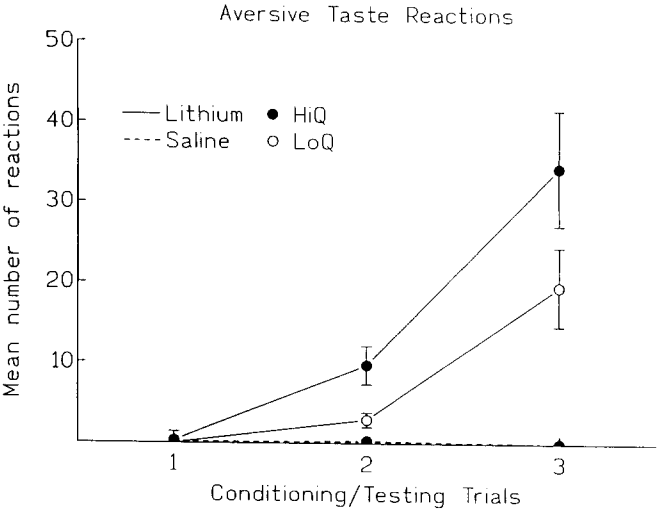

FIG. 1. Mean frequency of aversive reactions elicited by lithium- or saline-paired sucrose solution across conditioning/testing trials by the high (HiQ) and low (LoQ) quinine-reactive groups.

displayed ingestive reactions. The 2 × 2 × 3 mixed-factor ANOVA revealed a significant drug condition effect, $F(1, 48) = 39.7, p < 0.001$, and a drug condition × conditioning trials interaction, $F(2, 96) = 3.6, p < 0.05$. The lithium-conditioned rats displayed less ingestive responding than the saline-conditioned rats with each trial. However, the variable of reactivity to quinine solution did not modify the pattern of ingestive responding elicited by sucrose solution across trials.

DISCUSSION

Rats that were more sensitive to the aversive taste properties of quinine solution were also more sensitive to the aversive taste properties of a lithium-paired sucrose solution. This pre-

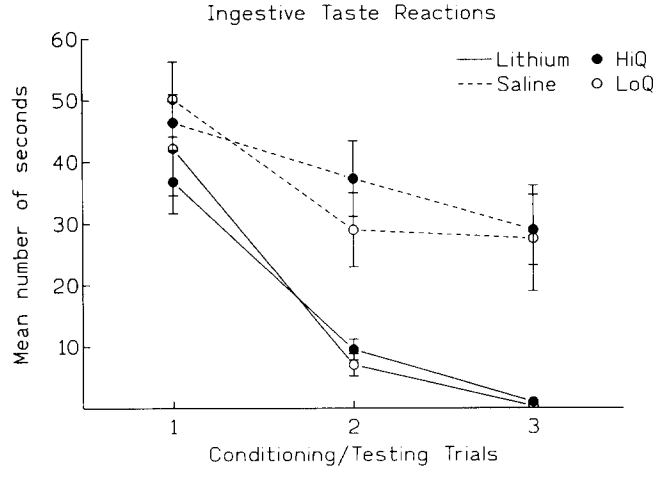

FIG. 2. Mean duration (s) of ingestive reactions elicited by lithium- or saline-paired sucrose solution across conditioning/testing trials by the high (HiQ) and low (LoQ) quinine-reactive groups.

dictive relationship suggests that the aversive reactions elicited by a sucrose solution that has previously been paired with lithium chloride may be mediated by the same mechanism that is responsible for the aversive reactions elicited by an unconditionally unpalatable quinine solution.

A rat's sensitivity to the aversive properties of quinine solution, however, did not predict a change in the degree of suppression of positive hedonic properties of sucrose solution across conditioning trials. Thus, the increased sensitivity of HiQ rats to the aversive properties of a lithium-paired tastant is not a function of their decreased sensitivity to the positive properties of sucrose. These results support a two-dimensional model of palatability proposed by Berridge and Grill (3) that suggests that positive hedonic and aversive properties of tastants vary independently of one another, that is, individual differences in reactivity to bitter tastants appear to vary independently of differences in reactivity to positive hedonic properties of tastants.

In humans, genetic differences in reactivity to phenylthiocarbamide (PTC) and 6-*n*-propylthiouracil (PROP) have been linked to differences in sensitivity to bitter tastes such as caffeine, KCl, benzoate, and saccharin (1,2). However, is not clear whether the ability of quinine reactivity to predict the strength of a palatability shift for a lithium-paired sucrose solution in rats is genetically mediated.

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