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Intragastric infusion and intraperitoneal injection of 0.15 M lithium chloride (LiCl) produce equivalent suppression in the conditioning of a taste aversion

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In a standard conditioned taste-aversion methodology, rats (*Rattus norvegicus*) ingested a novel saccharin solution and then received intragastric infusions or intraperitoneal injections of lithium chloride (LiCl) after a delay of either 0, 30, or 60 min. The two methods of administration of LiCl were found to produce equivalent aversions as assessed over three extinction trials. Both methods of administration showed a delay of reinforcement effect, that is, both of the zero-delay conditions resulted in enhanced suppression of drinking on the first extinction trial relative to the 30- and 60-min-delay conditions, which did not differ according to delay or method of administration.

Taste-aversion methodologies are being used in diverse fields of inquiry. In addition to the questions of associative flexibility around which these procedures developed, they have been adopted as robust and reliable experimental paradigms with which to investigate an increasing variety of issues.

Procedures used to induce conditioned taste aversions vary widely. In an influential study, Nachman and Ashe (1973) provided a comparison of dosage, concentration, and route of administration of lithium chloride (LiCl). They demonstrated that optimal taste aversions could be conditioned using an isotonic 0.15-molar (M) solution and that this effect was not dependent on volume or concentration of the LiCl treatment (their Experiment 1). In addition, they found no significant differences among intraperitoneal (i.p.) injection, intragastric (i.g.) infusion via a stomach tube, and subcutaneous routes of administration (their Experiment 2). In the latter comparison, however, a hypertonic 0.65-M dosage was used. Although dosages of LiCl vary somewhat (Grill, 1985), the current literature suggests that i.p. injection of 0.15 M is the most frequent treatment, followed closely by direct stomach infusion of 0.15 M.

There has been some question as to the accuracy of i.p. injection in rats. Lewis, Kunz, and Bell (1966) performed 137 such injections using an oily contrast media, after which they radiographed each subject. In 19.6% of the animals, at least part of the material was not injected into the peritoneal cavity. Fifteen animals were partially injected in the gastrointestinal tract, 5 subcutaneously, 3 retroperitoneally, and 2 in the urinary bladder.

The time course for different routes of LiCl treatment has not been evaluated (Cappell & LeBlanc, 1977; Domjan, Foster, & Gillan, 1979), and it is possible that route of administration could produce differences in the speed of action, delay of reinforcement, and, possibly, some physiological effect of the drug itself (Coussens, 1974). For example, Domjan et al. (1979) gave rats equal doses of LiCl either in one large injection or in two smaller injections separated by 35 min. They found that in most cases, the animals given two small injections showed stronger taste and odor aversions. They hypothesized that variations in drug administration might result in changes of such drug parameters as latency, duration, and intensity of the drug effects, variables about which little is known.

Finally, when examining sensitive associative phenomena, it is sometimes desirable to habituate subjects to the drug-administration procedure before experimental sessions are conducted (Braveman, 1977; Coussens, 1974; Domjan & Best, 1980; Domjan et al., 1979; Gamzu, 1977). The i.g. infusion procedure is a relatively safe and simple alternative to repeated sham i.p. injections, provided that i.g. infusion produces an equivalent behavioral response.

METHOD

Subjects and Apparatus

The subjects were 8 male and 22 female Sprague-Dawley rats weighing 197-257 g and housed individually in home cages, in which all conditioning and testing sessions took place. Food was removed, and a 500-ml glass water bottle with a rubber stopper and ball-point drinking tube 7.5 cm long and 31 mm in diameter (Popper & Sons, Inc., New Hyde Park, NY) was attached to the outside of each cage. This was wired

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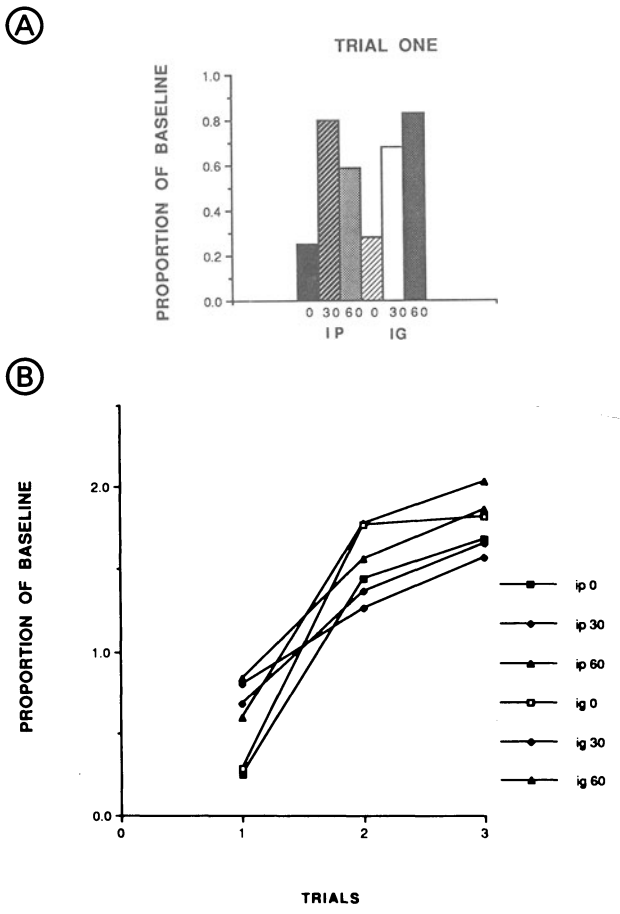

Figure 1. (A) Proportion of baseline consumption on first extinction trial. (B) Proportion of baseline consumption across three extinction trials.

to a Drinkometer (Model 5805, Lafayette Instrument Co., Lafayette, ID), which was in turn wired to a Lafayette Clock/Counter (Model 54035) such that the duration of the time that a rat's tongue touched the drinking tube was recorded in milliseconds. In the i.p. injection conditions, 3-cc, 22-ga plastic disposable syringes (Model 5572, Becton-Dickinson, Rutherford, NJ) were used. In the i.g. infusion conditions, 7.6-cm-long, 16-ga. animal feeding needles with a 3-mm diameter ball on the end (Model 160-8916, George Tiemann & Co.) were used.

Procedure

The subjects were randomly divided into six groups of equal size ($n=5$); three groups received i.p. injections, and the other three were administered i.g. infusions of LiCl orally. Of the three i.p. groups, one was injected immediately after drinking a flavored solution, one after a 30-min delay, and one after a 60-min delay, respectively. Identical delay conditions were used in the three i.g. infusion groups.

The subjects were first water deprived for 24 h and then given 4 days of habituation to drinking unadulterated distilled water from the water bottles. On the first two habituation days, they were given access to water for 10 min at 12-h intervals. On the second two days, they had access to water for 10 min at 24-h intervals. On Day 5, following 24 h of water deprivation, the subjects received a 0.2% (weight/volume) solution of sodium saccharin in distilled water in their bottles for 10 min, and the amount of time spent licking the novel solution was recorded. The subjects were then injected or infused with a 1.2% of body weight solution of 0.15 M LiCl (Nachman & Ashe, 1973), according to condition, and returned to their home cages. On Day 6, the subjects were allowed to recuperate from illness. Twenty-four hours after toxicosis treatment, they were given unadulterated distilled water in their bottles for 10 min. Starting on Day 7, the subjects received at 12-h intervals three consecutive 10-min taste-aversion test trials in which the 0.2% sodium saccharin water was presented in their bottles and time spent licking was recorded.

The time that each subject spent licking the sodium saccharin water on each of the test trials was divided by the time that the subjects spent licking the same water on the LiCl treatment day, thus providing the proportion of baseline lick time (Figure 1).

RESULTS AND DISCUSSION

A 2×3×3 mixed analysis of variance (ANOVA) (administration procedure × delay × trials) was computed. The administration procedure and delay condition were between-group variables, and consumption across trials was the within-subject measure. The ANOVA revealed a significant main effect for trials [$F(2,48) = 48.83, p < .01$], indicating a strong taste aversion that extinguished over trials. Tukey's post hoc comparisons showed significant differences between Trial 1 and Trials 2 and 3 ($p < .01$). There were no reliable differences between methods of administration or between delay conditions, and none of the interactions was significant.

The results of the present experiment demonstrated that when a 0.15-M LiCl solution was administered by i.g. infusion or by i.p. injection, the strengths of the resultant conditioned taste aversions were equivalent, and the avoidance subsequently extinguished over test trials. Consistent with the finding of previous experiments (Garcia, Ervin, & Koelling, 1966; Nachman, 1970; Revusky, 1968; Smith & Roll, 1967), aversions occurred in all delay conditions; the zero-delay condition for both the i.p. and i.g. groups generated a more robust effect than did the 30- and 60-min-delay groups.

These findings are consistent with previous research that used only i.p. injection (Garcia & Koelling, 1966) and indicate that robust aversions can be obtained using relatively painless isotonic i.g. LiCl and that these effects are equivalent to those obtained by i.p. injection. However, it is probably incorrect to assume that i.g. and i.p. administration elicit an identical physiologic response (see Dupre, Ross, Watson, & Brown, 1973).

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