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Increased Drinking Stimulated by Exposure to Lithium-Conditioned Taste Cues: Effects of Conditioning Trials and Drug Dose[1]

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DOMJAN, M., G. A. GEMBERLING AND D. J. GILLAN. *Increased drinking stimulated by exposure to lithium-conditioned taste cues: Effects of conditioning trials and drug dose.* PHARMAC. BIOCHEM. BEHAV. 12(5) 789–795, 1980.—Rats first received differential conditioning in which the oral infusion of one flavored solution (the CS+) was followed by lithium injection and the oral infusion of a different solution (the CS−) was followed by no drug treatment. The intake of a novel palatable flavor was then measured after infusion exposure to either the lithium-conditioned CS+, the taste of tap water, or the CS−. Exposure to the CS+ stimulated more drinking than comparable exposure to tap water following 2–8 differential conditioning trials (Experiment 1), following conditioning with lithium doses of 0.75–3.0 mEq/kg (Experiment 2), and in comparison with both exposure to water and exposure to the CS− (Experiment 3). However, the phenomenon was not closely related to the degree of aversion subjects acquired to the lithium-paired taste solution. These results indicate that a complete characterization of the changes in drinking which are elicited by lithium-conditioned stimuli requires recognition of not only the suppression of intake commonly observed in the presence of the conditioned stimuli, but also the enhancement of intake evident as an after-effect of the lithium-conditioned stimuli.

Lithium Drug-conditioning Conditioned responses Taste-aversion conditioning Drinking

AN increasingly popular technique for the study of Pavlovian conditioning involves pairing exposures to a novel flavored solution with the administration of an aversive drug. Most experiments using this technique have measured how ingestion of the flavored solution is altered by the conditioning procedure, and typically a suppression in the intake of the drug-paired solution is observed [1,9]. Animals also suppress their intake of palatable solutions if these are presented during exposure to an exteroceptive stimulus, such as an olfactory cue, which was previously paired with an aversive drug [4,8].

In addition to the suppression of drinking that occurs in the presence of drug-paired stimuli, recent research has shown that subjects increase their intake of palatable solutions following exposure to drug-conditioned taste and exteroceptive stimuli [3, 6, 8]. This enhanced drinking aftereffect of drug-conditioned stimuli is opposite to the suppression of intake evident during the drug-conditioned cues and is also opposite to the unconditioned effects of the drug on ingestion [5]. The increased drinking effect clearly results from the conditioned properties of the drug-paired stimuli because the phenomenon is diminished by extinction of these stimuli and is not elicited by cues that were previously paired with the absence of drug treatment [6]. However, because most of the previous research has been focussed on identifying the test procedures that permit observation of the phenomenon [3, 6, 8], little is known about how the drug conditioned increased drinking is learned and how the response is governed by conditioning processes. The present experiments were designed to provide information relevant to these issues.

EXPERIMENT 1

In previous experiments, the increased drinking effect has been observed following 3–12 drug conditioning trials [3,6, 8]. However, because these experiments also differed in many other respects, they cannot be used to provide clear evidence of the relationship between the extent of conditioning and the magnitude of the enhanced drinking effect. Experiment 1 was conducted to provide this information. Independent groups of subjects received 1, 2, 4, or 8 differential conditioning trials, with the taste of one solution (CS+) paired with the injection of lithium chloride and the taste of a different solution (CS−) presented in the absence of drug treatment. The CS+ and CS− flavors were infused into the oral cavity through a fistula to provide precisely-controlled contact with the tastes. Following the initial differential conditioning phase, all subjects received two drinking tests with a novel vanilla solution. One of these tests occurred shortly after infusion exposure to the CS+ flavor, and the other occurred shortly after similar exposure to tap water.

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These test sessions allowed us to determine to what extent exposure to the CS+ elevated intakes above control levels. Exposure to tap water was considered to be satisfactory for the control tests because other research had shown that animals drink as much after the oral infusion of tap water as they drink after the oral infusion of a flavored solution (CS−) that was never paired with an aversive drug, and these two control procedures are interchangeable in measurements of the enhanced drinking effect ([6] see also Experiment 3). Following the two vanilla test sessions, each subject also received drinking tests with the CS+ and CS− flavors to evaluate the degree of aversion it learned to the drug-conditioned stimulus.

METHOD

Twenty-four male and twenty-four female 50–60 day-old Sprague-Dawley rats were individually housed in hanging wire-mesh cages and received continuous access to Purina Rat Chow. All animals had a fistula implanted in the cheek to permit the infusion of taste solutions into the oral cavity. During ether anesthesia, a section of Clay-Adams P. E. 205 Polyethylene tubing was passed under the skin of the neck, with one end exiting at the back of the neck and the other entering the oral cavity just anterior to the right molar teeth. The two ends were flared and held in place by polyethylene washers and by a wire suture attached to the oral end and affixed to subcutaneous tissue in the cheek. Approximately 1 week was allowed for recovery, after which access to water was restricted to 30 min daily in the home cage while food remained continuously available. On treatment days, this water access occurred after the experimental procedures. The water was always mixed with Terramycin to help control infections and respiratory disease.

Two sessions of adaptation to the infusion procedure were conducted on alternate days starting 7–8 days after the beginning of the water deprivation schedule. Within 2 min before each session, the cannulas were rinsed with 2–3 ml of tap water. The subjects were then placed individually in a wire-mesh cage whose walls had been extended to prevent the rats from jumping out. Each animal's cannula was connected with flexible Tygon formula B44-3 tubing to a 50 ml syringe in a Harvard Model 941 infusion pump, and tap water was infused into the oral cavity for 5 min at a rate (1.2 ml/min) slow enough to allow animals to swallow the fluid [7]. The animals were wiped dry with a paper towel after each infusion experience to remove any fluid which they did not swallow.

Following the adaptation sessions, subjects received differential flavor-aversion conditioning. The oral infusion of one solution (CS+) was followed 0.5–1.5 min later by an intraperitoneal injection of 0.15 M lithium chloride (2.25 mEq/kg), whereas the oral infusion of a different taste (CS−) was followed by an injection of 0.15 M sodium chloride (2.25 mEq/kg). Each infusion lasted 5 min and was administered at 1.2 ml/min after the cannula had been rinsed with 2–3 ml of water. CS+ and CS− trials occured in a strictly alternating order starting with the CS+, and 2–3 days separated successive trials. On both CS+ and CS− treatment days, the daily 30 min access to water was delayed for at least 90 min after the lithium or saline injection. A 2% (volume/volume) solution of cider vinegar (4.5% acidity) and a 1% (weight/volume) solution of sodium chloride served as the CS+ and CS− solutions. The assignment of flavors as the CS+ and CS− was counterbalanced in each group for both male and female subjects. Group 1 received one CS+ and one CS− conditioning trial, whereas Groups 2, 4, and 8 received 2, 4, and 8 CS+ and CS− trials, respectively. Six male and 6 female rats served in each group.

One day after the last differential conditioning session, 6 subjects in each group (3 for which the vinegar solution served as CS+ and 3 for which the sodium solution served as CS+) received a 5-min oral infusion of the CS+ solution at 1.2 ml/min, were injected with 2.25 mEq/kg .15 M sodium chloride, and were then returned to the home cage. Fifteen minutes after the end of the infusions, the subjects received access to a 3% (volume/volume) solution of vanilla extract (Piedmont) in the home cage for 120 min in graduated centrifuge tubes provided with stainless steel drinking spouts. The remaining 6 subjects in each group were treated the same way except that they received an oral infusion of tap water instead of the CS+ solution before the vanilla test. The 120-min vanilla test was repeated 2 days later. Animals that had been exposed to the CS+ 15 min before the first vanilla test received an oral infusion of tap water before the second test, and animals that were previously tested after an infusion of water were now tested after exposure to the CS+ flavor. Intakes during both test sessions were recorded at 10-min intervals to the nearest 1/4 ml. Exposure to tap water rather than the CS− flavor was used to establish control levels of vanilla intake. This procedure avoided possible complications in the event that different degrees of generalized aversion to the CS− occurred as a function of different numbers of conditioning trials.

To determine the strength of the aversion animals learned to the CS+ as compared to the CS− flavor, each subject received a 60-min one-bottle test with the vinegar solution one day after the last vanilla test. Two days later, each subject received a comparable drinking test with the sodium chloride solution. This test sequence insured that the order in which the animals were tested with CS+ and CS− was counterbalanced in each group.

RESULTS

Conditioned Aversions to CS+ and CS−

The amount each group drank of the CS+ and the CS− flavors during the postconditioning tests at the end of the experiment is presented in Fig. 1. Each group drank less of the CS+ than of the CS− solution. However, this discrimination increased as differential conditioning progressed. Only 6 of the 12 subjects that received one CS+ and one CS− conditioning trial drank less of the CS+ than of the CS− flavor. In contrast, every subject that received 2 or more differential conditioning trials drank less of the CS+ than of the CS− solution.

Evaluation of the CS+ and CS− intakes with a 2 (CS)×4 (Conditioning Trials) analysis of variance revealed a significant effect of type of CS solution (CS+ vs CS−), $F(1,40)=460.77$, $p<0.01$, number of conditioning trials, $F(3,40)=15.68$, $p<0.01$, and a significant CS×trials interaction, $F(3,40)=33.01$, $p<0.01$. This interaction occurred because there was a significant effect of conditioning trials on the intake of the CS+ flavor, $F(1,44)=30.39$, $p<0.01$, but not on the intake of the CS− flavor, $F<1.0$. Animals that received only one conditioning trial did not drink significantly less of the CS+ than of the CS− flavor, $t(11)=0.80$, $p>0.05$. However, each of Groups 2, 4, and 8 learned significant aversions to the CS+ as compared to the CS− solution, $ts(11)=4.43, 8.58, 9.84$, $ps<0.01$, respectively.

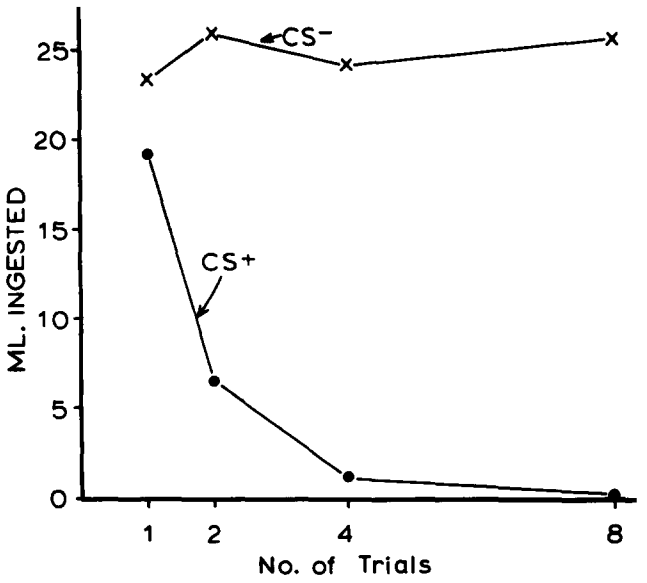

FIG. 1. Mean intakes of the CS+ and CS− flavored solutions during a test session conducted after 1, 2, 4, or 8 differential conditioning trials in Experiment 1.

Aftereffects of Exposure to CS+

The amount animals drank during successive 10-min periods of the two vanilla test sessions is presented in Fig. 2 for each group. Subjects drank more vanilla after an oral infusion of the drug-conditioned CS+ solution than after control infusions of tap water. This enhanced consumption stimulated by exposure to the CS+ was evident throughout the vanilla test sessions and occurred regardless of how many differential conditioning trials subjects previously received. However, subjects that received 4 or 8 conditioning trials drank more overall than subjects that received 1 or 2 conditioning trials.

The total amount of vanilla each of the 4 groups drank following CS+ and water exposure was evaluated with a 4×2 analysis of variance. This calculation revealed a significant effect of the number of conditioning trials, $F(3,44)=3.72$, $p<0.05$, and a significant effect of the type of stimulus (CS+ or water) that preceded the vanilla test, $F(1,44)=32.14$, $p<0.01$. However, the interaction between these two variables was not significant, $F<1.0$.

Because we were primarily interested in the effects that a lithium-conditioned stimulus (CS+) would have on drinking following different numbers of conditioning trials, we also compared with t tests the amount of vanilla each group drank following exposure to the CS+ and exposure to water infusion. Vanilla consumption was not significantly enhanced by exposure to CS+ after one conditioning trial, $t(11)=1.86$, $p>0.05$. However, significant increases in intake were observed following CS+ infusion in groups that received 2, 4, and 8 conditioning trials, ts (11)=4.33, 3.17, and 2.28, respectively, ps <0.05.

DISCUSSION

The present findings confirm that exposure to a lithium-conditioned stimulus increases the subsequent intake of a palatable flavor more so than does prior exposure to water

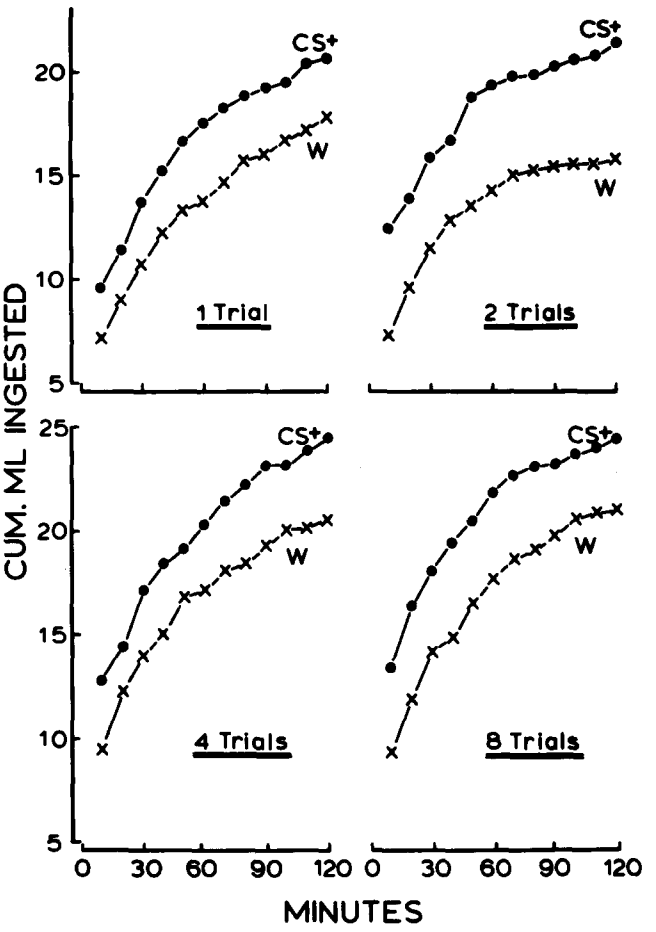

FIG. 2. Mean cumulative vanilla consumption during a test session started 15 min after infusion exposure to the CS+ flavor (CS+) or to tap water (W) in Experiment 1. (Subjects previously received 1, 2, 4, or 8 differential conditioning trials.)

[3, 6, 8]. This effect was no doubt a result of the conditioned properties of the CS+ because previous research showed that drinking following a stimulus paired with the absence of lithium (CS−) is not significantly different from drinking after exposure to water ([6] see also Experiment 3), and extinction of the excitatory properties of the CS+ reduces the increased drinking effect [6]. However, the phenomenon was not very sensitive to variations in the conditioned aversiveness of the CS+: significant increased drinking effects were observed in all groups that received 2 or more conditioning trials, and a significant interaction was not observed between amount of conditioning and the magnitude of the CS+ stimulated drinking. It may be that the enhanced drinking effect reflects a drug-conditioned response that is learned very rapidly and reaches asymptotic strength in only two conditioning trials.

EXPERIMENT 2

Experiment 2 was designed to determine whether the increased drinking that occurs after exposure to a lithium-conditioned stimulus is a function of the dose and distribution of lithium treatments given during conditioning. Independent groups received two conditioning trials with 0.75, 1.5, or 3.0 mEq/kg lithium injected as the unconditioned

stimulus. A fourth group received the same total amount of lithium as subjects that were injected twice with 3.0 mEq/kg except that for this group the lithium was given in 8 conditioning trials, with 0.75 mEq/kg lithium given on each trial.

METHOD

Forty-eight male 50–60 day-old Sprague-Dawley rats were used in procedures identical to those of Experiment 1 in all unspecified respects. After recovery from the cannula operation and adjustment to the water deprivation schedule, each animal received 4 infusion adaptation sessions conducted on successive days. During the next 4 days, subjects in Groups 2–0.75, 2–1.5, and 2–3.0, received 2 CS+ and 2 CS− conditioning trials in alternation starting with the CS+ trial. For Group 2–0.75 (n=12), each CS+ trial ended with a 0.75 mEq/kg IP injection of 0.15 M lithium chloride (5 ml/kg), whereas each CS− trial ended with a 0.75 mEq/kg injection of 0.15 M sodium chloride. For Groups 2–1.5 and 2–3.0 (ns=12), each conditioning trial ended with 1.5 mEq/kg and 3.0 mEq/kg injections, respectively. The higher drug doses were achieved by administering larger injections of the 0.15 M lithium and sodium solutions (10 ml/kg and 20 ml/kg for Groups 2–1.5 and 2–3.0 respectively). Group 8–0.75 (n=12) was treated the same way as Group 2–0.75 except that it received 8 CS+ and 8 CS− trials in alternation during the conditioning phase. As in Experiment 1, the assignment of vinegar and sodium chloride flavors as the CS+ and CS− was counterbalanced across groups.

One to two days after the last differential conditioning trial, 6 subjects from each group (3 for which the vinegar solution served as the CS+ and 3 for which the sodium chloride solution was the CS+) received a 5-min oral infusion of the CS+ flavor, followed by an injection of sodium chloride. (The injected dose in this phase was the same as that used during conditioning.) Fifteen minutes after this treatment, the animals received access to a 3% solution of vanilla for 120 min in the home cage. The remaining 6 subjects in each group were treated the same way except that they received an oral infusion of tap water instead of the CS+ before the vanilla test. Each subject received another vanilla test 2 days later preceded by infusion of the solution (tap water or the CS+) it was not given before the first vanilla test.

One day after the second vanilla test, each animal was allowed to drink the CS− solution for 30 min in its home cage before its daily 30-min access to water. Starting the next day, 4 similar one-bottle tests were conducted with the CS+ solution. These test sessions occurred at 1–2 day intervals.

RESULTS

Conditioned Aversions to CS+ and CS−

The amount each group drank of the CS+ and CS− flavors during the postconditioning tests is presented in Fig. 3. All animals drank substantial amounts of the CS− flavor, and there were no significant differences between groups in this consumption, $F(3,44)=2.42$, $p>0.05$. Intakes were very much suppressed during the first of the subsequent drinking tests with the CS+ flavor. However, CS+ consumption gradually increased with repeated testing. Group 8–0.75 evidenced the greatest aversion to the CS+ flavor, and the aversions of groups that received 2 conditioning trials were directly related to the conditioning lithium dose. Evaluation of these data with a 4 (Groups) × 4 (Test Trials) analysis of variance revealed a significant effect of both Groups, $F(3,44)=8.70$, $p<0.01$, and Test Trials, $F(3,132)=94.65$, $p<0.01$. The interaction between Groups and Test Trials was also significant, $F(9,132)=2.24$, $p<0.05$.

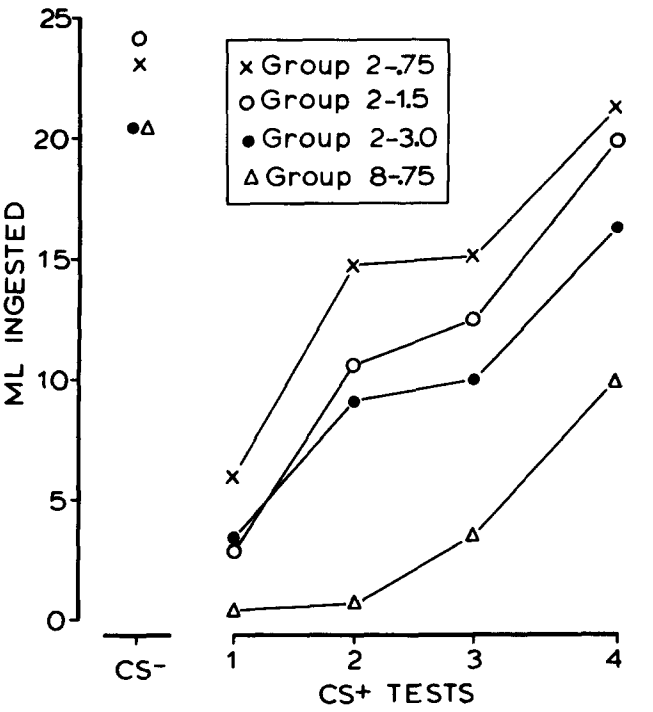

FIG. 3. Mean intakes during one postconditioning test with the CS− flavor and four test sessions with the CS+ flavor for various groups in Experiment 2.

Aftereffects of Exposure to CS+

The amount animals drank during successive 10-min periods of the two vanilla test sessions is presented in Fig. 4. Groups 2–3.0 and 8–0.75 drank more overall than the other two groups. However, irrespective of the lithium dose used during conditioning or the number of conditioning trials administered, animals drank more following infusion exposure to the CS+ flavor than they drank following similar exposure to tap water. Furthermore, this increased drinking stimulated by the CS+ was evident throughout the test sessions with each group.

The total vanilla consumption of each of the 4 groups following infusion exposure to the CS+ or water was evaluated with a 4×2 analysis of variance. This analysis revealed a significant effect of Groups, $F(3,44)=8.30$, $p<0.01$, and a significant effect of the type of stimulus (CS+ or water) that preceded the vanilla test, $F(1,44)=185.19$, $p<0.01$. However, the interaction between these two variables was not significant, $F(3,44)=2.69$, $p>0.05$.

Individual comparisons were also made with t tests of the total amount of vanilla each group drank after exposure to the CS+ and exposure to water. The increased consumption after exposure to the CS+ was significant in each group: ts (11)=6.20, 4.80, 8.05, and 8.39 for Groups 2–0.75, 2–1.5, 2–3.0, and 8–0.75 respectively, all ps < 0.01.

To determine whether increasing the conditioning lithium dose from 0.75 to 3.0 mEq/kg increased the enhanced drink-

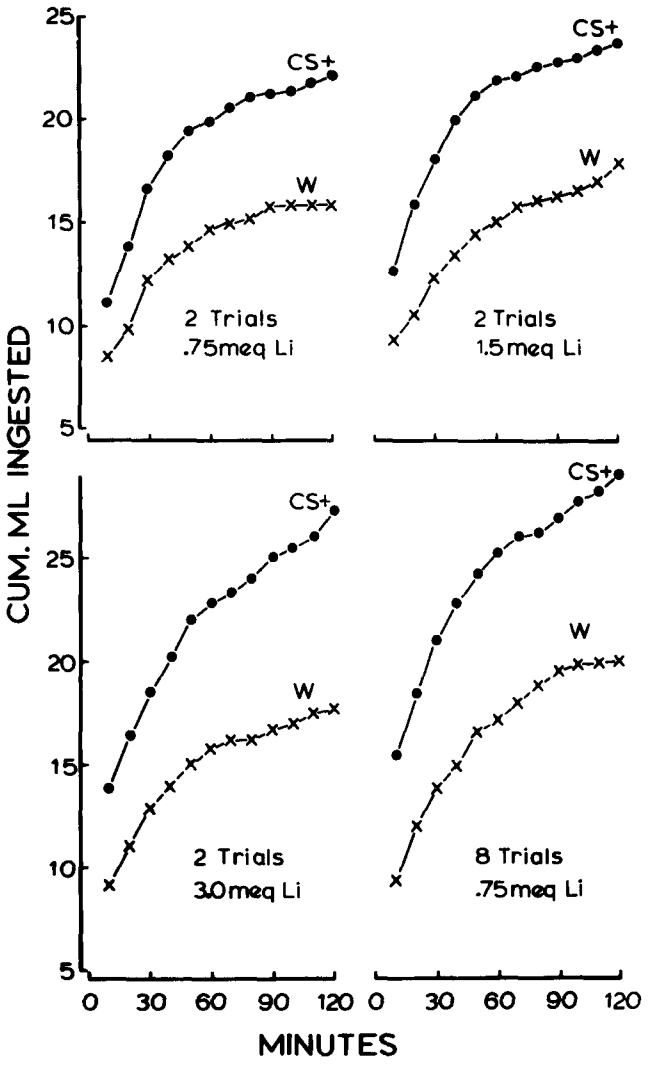

FIG. 4. Mean cumulative vanilla consumption during a test session started 15 min after infusion exposure to the CS+ flavor (CS+) or to tap water (W) in Experiment 2. (Some subjects previously received 2 conditioning trials in which the CS+ flavor was paired with injections of 0.75, 1.5, or 3.0 mEq/kg lithium chloride. Other rats received 8 conditioning trials with the 0.75 mEq/kg lithium.)

ing effect, the total vanilla intakes of Groups 2–0.75, 2–1.5, and 2–3.0 following CS+ and water infusion were included in a 3×2 analysis of variance. This revealed a significant main effect of conditioning dose $F(2,33)=4.18$, $p<0.05$, and confirmed that the CS+ stimulated more drinking than water infusion, $F(1,33)=120.02$, $p<0.01$. However, the interaction between these variables was not significant, $F(2,33)=3.18$, $p>0.05$.

The vanilla intakes of Groups 2–0.75 and 8–0.75 were likewise included in a separate analysis of variance to determine whether in this experiment the enhanced drinking effect was a function of the number of conditioning trials. This analysis also revealed a significant main effect of Groups, $F(1,22)=35.66$, $p<0.01$, and a significant effect of exposure to the CS+, $F(1,22)=107.02$, $p<0.01$. However, the interaction again was not significant, $F(1,22)=2.96$, $p>0.05$.

Finally, the vanilla intakes of Groups 2–0.30 and 8–0.75 after CS+ and water infusion were compared. These two groups received the same total amount of lithium during conditioning, but the drug was administered in 8 trials for Group 8–0.75 and 2 trials for Group 2–3.0. The only significant effect revealed by this analysis was that subjects drank more vanilla after infusion exposure to the CS+ than after exposure to water, $F(1,22)=134.36$, $p<0.01$. This increased drinking effect did not interact with distribution of the drug in 8 as compared to 2 conditioning trials, $F < 1.0$, and the main effect of drug distribution was also not significant, $F(1,22)=2.76$, $p>0.10$.

DISCUSSION

The present results confirm that exposure to a lithium-conditioned stimulus increases the subsequent intake of a palatable solution and extend this observation to situations in which high (3.0 mEq/kg) and low (0.75 mEq/kg) doses of lithium are used during conditioning. The extent to which exposure to a lithium-conditioned stimulus increased drinking in Experiment 2 was unrelated to variations in the dose and distribution of lithium used during conditioning. Furthermore, as in Experiment 1, the enhanced drinking effect was not closely related to the degree of aversion subjects acquired to the lithium-paired flavor. These results are somewhat puzzling because other evidence clearly indicates that the increased drinking effect is a result of the conditioning of the lithium-paired stimulus [6]. As was noted earlier, the enhanced drinking effect may be learned very rapidly and may reach asymptotic strength much sooner than the conditioned suppression of intake that is elicited by the CS+ flavor.

EXPERIMENT 3

In both Experiments 1 and 2, the enhanced drinking effect was measured against a baseline that involved ingestion of a palatable vanilla solution after the oral infusion of tap water. We previously showed that the amount animals consume following the infusion of tap water is not significantly different from how much they drink after infusion exposure to a taste solution (CS−) that was not previously paired with lithium malaise [6]. However, this earlier research involved a between-group experimental design, and the animals were tested only after extensive conditioning of a CS+ flavor (6 conditioning trials with 2.25 mEq/kg lithium). Therefore, conclusions based on this research may not be applicable to the present Experiments 1 and 2 which involved lower drug doses and fewer conditioning trials in some cases and were conducted with a within-subject experimental design. Experiment 3 was performed to provide more information on the comparison of infusion-exposure to tap water and exposure to a CS− flavor as control procedures with which to assess the enhanced drinking effect. In contrast to earlier similar comparisons [6], Experiment 3 employed a within-subject design, and the animals only received two CS+ conditioning trials with a low dose of lithium before the test session.

Each animal in Experiment 3 received two 120-min drinking tests with the vanilla solution following the initial phase of taste-aversion conditioning, as in Experiments 1 and 2. One group of animals was exposed to the CS+ flavor before one vanilla test session and a CS− flavor before the other test session (Group CS+/CS−). Another group was exposed to the CS+ flavor and tap water before the vanilla drinking

tests (Groups CS+/W), and the third group of animals was tested after infusion exposure to the CS− flavor and tap water (Groups CS−/W). Groups CS+/CS− and CS+/W provided measurements of the enhanced drinking effect against control procedures that involved exposure to CS− and tap water prior to the drinking tests, and Group CS−/W provided a direct comparison of two control procedures, CS− and W infusion.

METHOD

Twenty-five male 50–60 day-old Sprague-Dawley rats were used in procedures identical to Experiments 1 and 2 in all unspecified respects. After recovery from the cannula operation and adjustment to the water deprivation schedule, each animal received four infusion adaptation sessions conducted on successive days. During the next four days, two CS+ and two CS− conditioning trials were conducted in alternation starting with the CS+ trial. Each CS+ trial ended with a 1.5 mEq/kg IP injection of 0.15 M lithium chloride, whereas each CS− trial ended with a 1.5 mEq/kg IP injection of 0.15 M sodium chloride.

Starting 2–3 days after the last differential conditioning trial, each animal received two 120-min drinking tests with the vanilla solution. The animals were assigned to three groups for these test sessions, with the assignment of vinegar and sodium chloride flavors as the CS+ and CS− stimuli counterbalanced across groups. For Group CS+/CS− (n=8), one vanilla test session was preceded 20 min earlier by a 5-min oral infusion of the CS+ flavor and the other test session was preceded by a similar exposure to the CS− flavor. Group CS+/W (n=8) received exposure to the CS+ flavor before one of the test sessions and tap water before the other test, and Group CS−/W (n=9) was tested after exposure to the CS− flavor and tap water. The order of the two types of tests was perfectly counterbalanced for Groups CS+/CS− and CS+/W. For Group CS−/W, 5 animals were exposed to the CS− before the first test and tap water before the second test; the remaining 4 animals were tested in the reverse order. As in Experiments 1 and 2, immediately after the oral infusions that preceded the vanilla tests, the animals were injected with the physiological saline (1.5 mEq/kg).

On the third and fourth days after the second vanilla test, each animal received a 30 min drinking test with the CS+ and CS− flavors before its daily 30-min access to water. The order of the CS+ and CS− test sessions was counterbalanced across groups.

RESULTS

Conditioned Aversions to CS+ and CS−

Each animal drank much less of the CS+ than of the CS− solution during the test sessions at the end of the experiment. The mean intakes of the CS+ and CS− flavors were 3.5 ml and 20.2 ml (Group CS+/CS−), 3.1 ml and 19.8 ml (Group CS+/W), and 1.9 ml and 20.0 ml (Group CS−/W), respectively.

Aftereffects of Exposure to CS+, CS−, or Water

The amount animals drank during successive 10-min periods of the two vanilla test sessions is summarized in Fig. 5. The test intakes of Groups CS+/CS− and CS+/W show that animals drank more vanilla following exposure to the CS+ flavor than they drank after exposure to the CS− flavor or to tap water. However, exposure to the CS− flavor and to tap water did not produce appreciably different levels of consumption (see results for Group CS−/W).

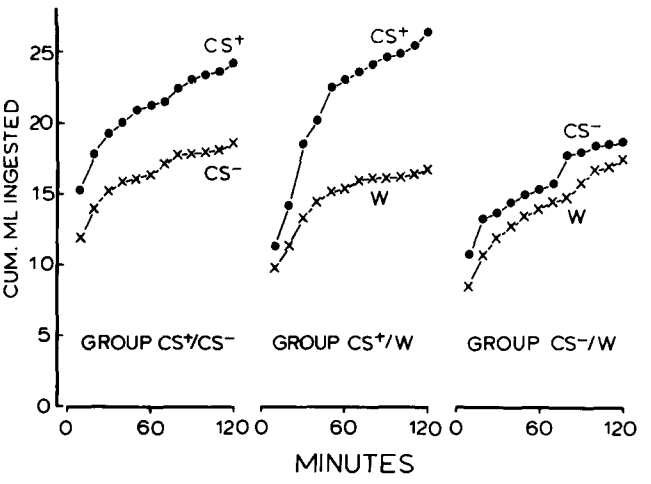

FIG. 5. Mean cumulative vanilla consumption following exposure to CS+ and CS− (Group CS+/CS−), CS+ and tap water (Group CS+/W), and CS− and tap water (Group CS−/W) in Experiment 3.

The total vanilla consumption of each group during the two test sessions was first evaluated with individual t-tests. Groups CS+/CS− drank significantly more following exposure to the CS+ flavor than following exposure to the CS−, $t(7)=3.88$, $p<0.01$. Groups CS+/W showed a similar significant difference in intake between the effects of exposure to CS+ and water, $t(7)=4.53$, $p<0.01$. However, the difference in drinking following the oral infusion of the CS− flavor and tap water was not significant in Group CS−/W, $t(8)=1.42$, $p>0.05$.

We also directly compared the magnitude of the enhanced drinking effect in Groups CS+/CS− and CS+/W by including the total intake scores of these animals in a 2 (Groups) × 2 (Test Conditions) analysis of variance. This analysis confirmed that animals drank more following exposure to the CS+ flavor than after esposure to control procedures, $F(1,14)=35.12$, $p<0.01$. However, there was no significant difference between the overall intakes of the two groups, $F<1.0$. The interaction between Groups and Test Conditions was also not significant, $F(1,14)=2.43$, $p>0.05$. This last finding indicates that the magnitude of the enhanced drinking effect was not significantly influenced by which control procedure was used, exposure to CS− or exposure to tap water.

DISCUSSION

Several aspects of the present experiment show that comparable results are obtained when the enhanced drinking effect is measured against control procedures that involve infusion-exposure to a CS− flavor or infusion-exposure to tap water. First, a significant enhanced drinking effect was produced by exposure to drug-paired CS+ flavor whether the control procedure involved exposure to a CS− flavor or exposure to tap water. Second, the magnitude of the enhanced drinking effect was not significantly different for Groups CS+/CS− and CS+/W. Finally, infusion-exposure to the CS- flavor and to water did not produce significantly different levels of consumption in Group CS−/W.

The present comparison of control procedures involving

exposure to a CS− flavor and tap water differed in several important respects from previous research [6]. Two CS+ conditioning trials were conducted before the test sessions instead of 6, the dose of lithium used during taste-aversion conditioning was reduced by 33%, and a within-subject experimental design was used instead of a between-subject design. In spite of these differences, the present study confirmed that measurement of the enhanced drinking effect is not significantly influenced by the type of control procedure (exposure to CS− or tap water) that is used. The present results, together with the earlier findings [6], show that exposure to a CS− flavor and to tap water are interchangeable control procedures for the enhanced drinking effect over a wide range of taste-aversion conditioning parameters.

GENERAL DISCUSSION

The present experiments confirm that exposure to a lithium-conditioned taste solution (CS+) stimulates more drinking of a palatable vanilla solution than does exposure to tap water or to a taste solution that was not paired with lithium (CS−). The present experiments also demonstrate that this enhanced drinking effect is observed with a large range of procedures. Exposure to a lithium-conditioned CS+ stimulates enhanced drinking following 2–8 taste-aversion conditioning trials, conditioning with a wide range of lithium doses (0.75–3.0 mEq/kg), and whether the control procedure involves exposure to tap water or exposure to a CS− flavor.

The enhanced-drinking effects produced by drug-conditioned stimuli in the present experiments (see also [3, 6, 8]) are contrary to the suppression of intake most other investigators have focussed on in studies of the conditioning of taste stimuli with drug treatments [1,9]. The fact that lithium-conditioned stimuli also increase drinking in a large range of situations provides another measure of the conditioned effects of drug-paired stimuli. Furthermore, given the present results, descriptions of conditioning that only detail the suppression of drinking produced by the presentation of a lithium-conditioned stimulus [1,9], do not fully characterize the changes produced by consistently pairing a stimulus with drug administration. In addition to the drug-conditioned suppression of ingestion that is commonly observed, one must consider that conditioning also results in increased drinking elicited as an aftereffect of the drug-conditioned stimulus [8].

There is a great deal of evidence from a variety of sources that the enhanced drinking effect is a reflection of the conditioned properties of the drug-paired CS+ stimulus ([6,8] see also Experiment 3). Therefore, it is rather remarkable that the phenomenon was not influenced by variations in the number of conditioning trials or the dose of the conditioning lithium injections in Experiments 1 and 2. This insensitivity of the enhanced drinking effect to conditioning parameters may be related to the various homeostatic control system that discourage excessive drinking under normal circumstances [2]. Homeostatic constraints that restrict the intake of large quantities of fluid may preclude observations of larger increased drinking effects following more extensive conditioning of the drug-paired stimulus. Another possibility is that the enhanced drinking effect is learned very rapidly and reaches asymptotic strength much sooner than the conditioned suppression of intake that occurs while the CS+ flavor is present.

Domjan, Gillan, and Gemberling [8] recently suggested that the enhanced drinking effect may be a manifestation of an opponent process conditioned to the lithium-paired CS+. This interpretation predicts that more extensive differential conditioning and conditioning with higher lithium doses should produce greater enhanced drinking effects, because opponent processes are assumed to grow with use and be directly related to drug dose [10]. The present experiments do not confirm these predictions. If the failure to observe a relationship between conditioning parameters and the increased drinking effect cannot be attributed to the measurement problems noted above, then the present findings would require a re-evaluation of the conditioned opponent process interpretation of the increased drinking phenomenon.

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