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Aversive, appetitive and flavour avoidance responses in the presence of contextual cues

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Abstract Appetitive, aversive and avoidance responses to a flavoured solution in distinct contexts were examined. Rats placed in either a white or black box were given access to saccharin. Consumption was followed by an injection of a toxin in one but not the other box. Rats showed more aversive responses in anticipation of and during the presentation of saccharin in the box paired with the toxin than in the box paired with vehicle. The reverse was true for appetitive responses. The acquisition of conditioned avoidance paralleled the acquisition of aversive and appetitive responses. These findings demonstrate that the toxin does not have to overlap exposure to contextual cues to produce conditioned aversive responses, that the aversive and appetitive responses to a flavour can be modulated by visually distinct environments that predict the toxin, and that conditioned avoidance and conditioned aversions develop simultaneously during acquisition. Thus, environmental cues can modulate anticipatory nausea and may prove helpful in the control of nausea in clinical settings.

Keywords Taste aversion · Taste avoidance · Taste reactivity · Anticipatory nausea · Gape · Contextual cues

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Introduction

Researchers make a distinction between conditioned flavour avoidance and conditioned flavour aversion (Cross-Mellor, Kavaliers & Ossenkopp, 2004, 2005; Grill & Norgren, 1978; Parker, 1995, 2003). Conditioned flavour avoidance is the learned response to avoid a flavoured solution and is almost always measured using a consumption test. Conditioned flavour avoidance can be achieved by pairing a flavoured solution with emetic agents, such as lithium chloride (LiCl) and chemotherapy drugs (Best, Brown & Sowell, 1984; Best, Batson, Meachum, Brown & Ringer, 1985; Martin & Storlien, 1976; Revusky & Garcia, 1970; Revusky & Martin, 1988; Symonds, Hall, Lopez, Loy, Ramos & Rodriguez, 1998), wheel running (Lett & Grant, 1996), rewarding drugs (Berger, 1972) and foot-shock (Pelchat, Grill, Rozin, & Jacobs, 1983). Conditioned flavour aversions are typically measured using the taste reactivity test (Grill & Norgren, 1978). With this method, an animal's orofacial and somatic responses to a flavoured solution, which has been previously paired with an emetic agent, are recorded. The flavoured solution is usually infused via an implanted intra-oral cannula, and indicators of either palatability, such as tongue protrusions (both lateral and rhythmic) and paw licking, or disgust, including gaping, chin rubbing, headshaking, paw wiping and flailing of the forelimbs (Berridge, 2000; Grill & Norgren, 1978), are measured.

Parker (2003) stated that not all instances of conditioned flavour avoidance are accompanied by an aversion to the flavoured solution and, consequently, the consumption test may not be adequate for assessing conditioned nausea. Parker (1995) found that while rewarding drugs could be used to produce conditioned flavour avoidance, this conditioned avoidance is not accompanied by orofacial or

somatic rejection reactions, suggesting that these drugs do not produce a conditioned flavour aversion. Furthermore, the conditioned flavour avoidance produced by rewarding drugs is not attenuated by anti-nausea treatments (Limebeer & Parker, 2000; Parker & Macleod, 1991), which are effective in reducing the aversive taste reactions to flavours paired with LiCl.

The study of avoidance and aversive reactions to flavoured solutions has been expanded to include reactions to contextual cues present at the time fluid is presented. Animals that drink in a context that is paired with the injection of a poison subsequently avoid other solutions in this conditioned context (Best et al., 1984; Best et al., 1985; Symonds et al., 1998; Symonds & Hall, 2002; Rodriguez, Lopez, Symonds, & Hall, 2000) and avoid the context when given a choice (Best, Best & Henggeler, 1977). The animals' aversive taste reactivity responses to these contexts, where the poison followed exposure, have not been examined. Results from tests, such as the blocking procedure, suggest that animals can associate the context with the toxin and therefore might show aversive reactions (see Symonds & Hall, 1997).

Aversive taste reactivity responses to a context have been demonstrated when a rat has been poisoned while in the context (Limebeer, Hall, & Parker, 2006; Limebeer, Krohn, Cross-Mellor, Litt, Ossenkopp, & Parker, 2008). In these experiments, rats were injected with LiCl before being placed in a target context and then infused with a saccharin solution via an implanted intraoral cannula on a test trial while in that context. The rats that were tested in the lithium-paired context gaped more than the rats in the unpaired context (i.e., in the absence of LiCl) when infused with saccharin. The gaping also occurred at inter-infusion intervals, suggesting that the rats were showing anticipatory gaping in the context when no fluid was present (Limebeer et al., 2006). To further investigate this conditioned gaping to a lithium-paired context, Limebeer et al. (2008) injected rats with LiCl prior to placement in either an odour-permeated context or a context alone with no added odour cues present, both in the absence of any flavoured solution. The rats trained in either the odour-permeated context or in the context devoid of added odour cues showed a gaping reaction when placed back in the lithium-paired context in the absence of illness.

The results of previous studies suggest, but have not shown, that there should be a strong relationship between fluid consumption and the aversive taste reactivity responses seen in a context. The study reported here documents this relationship and extends our understanding to the relationship of appetitive responses to consumption. In particular, we determined whether aversive taste reactivity responses can be obtained when an injection of LiCl follows exposure to a context, whether the responses could be shown when a discrimination between contexts was required, whether appetitive responses to a context occurred and whether acquisition of appetitive and aversive responses tracked fluid consumption. Rats were trained on a context discrimination task that was divided into Safe and Danger days. On Safe days, access to a saccharin solution was followed by an injection of saline; on Danger days, access to saccharin was followed by an injection of LiCl. In addition to measuring saccharin consumption, we scored both appetitive and aversive taste reactivity responses (Berridge, 2000; Grill & Norgren, 1978; Limebeer et al., 2006; Limebeer et al., 2008) both before and during access to the saccharin solution. As such, we were able to assess whether the context alone would come to elicit the appetitive or aversive responses. The usual taste reactivity test involves forced tasting of a solution through an implanted intra-oral cannula and subsequently assessing the animal's orofacial and somatic responses; however, the same orofacial and somatic reactions are also present when a solution is freely available to the animal (Pelchat et al., 1983). The latter method was used in our study so that the behavioural changes could be correlated with consumption.

Method

Subjects

Eight male Long-Evans rats, obtained from Charles River Company (St. Constant, Quebec, Canada) and weighing between 330 and 430 g at the start of the experiment, were used. The rats had been used previously in a water maze experiment. The rats were singly housed in clear plastic cages (45 × 25 × 21 cm) with metal lids, in a temperature controlled (20 ± 2°C) colony room that was maintained on a 12/12-h (light/dark) cycle with the lights on at 0800 hour. All rats had continuous access to food in their home cages. One week prior to the start of the experiment, the rats were put on a water deprivation schedule in which access to tap water was limited to 15 min each day. On experimental days, this drinking session occurred in the colony room immediately after all rats had finished the conditioning trial for the day. Animal care and all procedures used in the experiment were approved by Memorial University's Institutional Committee on Animal Care and followed the Canadian Council on Animal Care guidelines.

Apparatus

The training contexts were two rectangular wooden drinking chambers (one painted black and the other painted white), each with a recessed wooden lid and containing no floor. The inner dimensions of the boxes measured 25.40 ×

15.24 × 38.10 cm. Two holes were drilled in each chamber (one in the short side and one in the long side) to allow the insertion of a drinking tube. The boxes were placed on top of a square glass table (85.10 × 85.10 cm), which stood 73.70 cm from the floor, to allow the animals to be videotaped from underneath. Only one box was on the glass table at any given time, and the position on the table was identical for the black and white boxes.

During training, rats were given an intraperitoneal (ip) injection of either saline (0.9% NaCl; 3.0 ml/kg) or LiCl (0.47 M; 3.0 ml/kg), depending on the trial type. A 0.1% saccharine solution (1 g/1000 ml of water) stored at room temperature was the novel flavour that the rats could consume during the conditioning phase.

Procedure

Rats were tested in two squads of four rats. Each squad was trained on separate occasions; that is, once squad one had finished all trials, squad two was then started. The animals were transported daily from the colony room to the experimental room on the same rack that they were housed. This rack was then situated just outside of the experimental room. Rats remained on the rack in their home cage until their conditioning trial was about to begin. A single rat was carried in its home cage into the experimental room. The rat was weighed before being placed into the test box, which marked the start of a conditioning trial.

The conditioning phase consisted of Safe and Danger days. On Safe days, a rat was placed in a black or white box for 10 min and then given access to saccharin in the box for an additional 10 min. The rat was then removed from the training context and given an ip injection of saline before being returned to the home cage. On Danger days, a rat was placed in the box with the opposite colour for 10 min, given the same saccharin solution for an additional 10 min and then injected with LiCl before being returned to the home cage. The safe context was the white box for half of the rats (n = 4) and the black box for the other half (n = 4). The hole from which the spout of the drinking bottle entered the drinking chamber also differed on Safe and Danger days, as half of the rats received the saccharin solution through the hole on the long wall on Safe days, while the other half received the saccharin solution through the hole on the short wall on Safe days. The opposite box and hole were used on Danger days. There were two rats in each combination of box colour and drinking hole. The amount of fluid consumed was recorded in grams.

There were a total of 49 training days during the conditioning phase: 39 Safe days interspersed with 10 Danger days. The extra Safe days were given to all subjects to increase fluid consumption after a Danger day. Days 4, 9, 14, 20, 26, 31, 36, 40, 45 and 48 were Danger days; all other days were Safe days. This pattern of Safe and Danger days was irregular and ensured that rats did not learn a pattern which can sometimes underlie discrimination learning (Capaldi, 1967) For the purpose of statistical analyses, the conditioning phase was divided into ten 3-day cycles (safe–danger–safe). The extra Safe days were not analysed.

Scoring of videotaped behaviour

The rats' behaviour was recorded on all trials with a Canon high definition (HD) video camcorder (model HV-10.) This video was later scored for both aversive and appetitive taste reactivity responses. The responses of interest for this experiment were derived from the taste reactivity test developed by Grill and Norgren (1978) as well as from categorizations by Berridge (2000). Appetitive taste reactivity responses that were coded included paw licking and tongue protrusions. Paw licking was defined as the rat licking at its paws in bouts of licking. A bout started at the onset of the first paw lick and ended either when the rat stopped the behaviour or paused for longer than 1 s. A tongue protrusion was said to have occurred when the rat either licked out its tongue in a single protrusion, or rhythmically licked out its tongue. A rhythmic tongue protrusion is considered to have occurred when the animal starts and stops this behaviour, with a clear pause in between the bouts. Aversive taste reactivity responses that were coded included gaping and chin rubbing. A single gape was defined as large openings (and partial closings) of the rat mandible, with the corners of the mouth furled back, that occurred in a rhythmic fashion in quick succession. Chin rubbing was defined as the rat rubbing its chin either across the glass floor or on the sides of the test box. A single chin rub would occur once the rat's chin touched the surface, was rubbed across it, and lifted off again. Other aversive responses, including headshaking and flailing of the forelimbs, were also scored, but these were not included in the analyses because they were not observed to occur very often. This observation is consistent with Parker (1995). Hole-poking behaviour was also scored in this experiment. During the first 10 min of the trial, rats often poked their nose into the holes associated with fluid delivery. A single hole-poke was defined as the rat inserting its nose into a drinking hole, ending when the nose was completely removed from the hole. Oftentimes rats would leave their nose in the hole and move it about, but a new hole-poke was not scored until the nose had been completely removed and re-inserted. In addition to these behaviours, grooming (both in number of bouts and duration) and face-washing were also scored but not reported. Although face washing is part of the normal grooming regimen, it was coded separately in this study.

Berridge (2000) stated that a face-wash could be considered an aversive behaviour; however, in our study, it was observed more frequently to occur in conjunction with the normal grooming regimen. This finding is also consistent with that from Parker (1995). Any instances of a behaviour that was said to have occurred, but the observer was unsure at the time, were marked during scoring and later reviewed to determine if the behaviour had actually happened.

An independent observer scored some of the responses from the videotapes in order to test inter-rater reliability. A single day was chosen from the collection of videos in which a particular behaviour was known to have occurred. The independent observer then scored all eight rats for that given day for the particular measure in question. This process (pairing a particular day with a measure) was repeated until all of the responses were scored. The independent observer was blind to whether he was scoring responses occurring on a Safe or Danger day. All of the measures from the independent observer correlated significantly with the measures obtained by the experimenter (gapes = 0.922, chin rubs = 0.989, paw licks = 0.974, tongue protrusions = 0.800).

Results

All rats acquired the discrimination, consuming more saccharin in the safe context than in the danger context over the 10 cycles of training (see Fig. 1). A two-way [Cycle (1 – 10) × Days (safe–danger–safe)] analysis of variance (ANOVA) revealed a significant main effect of Cycle [$F(9,63) = 5.305$, $p < 0.01$] and Day [$F(2,14) = 5.525$, $p < 0.05$) and a significant Cycle × Day interaction [$F(18,126) = 9.537$, $p < 0.05$], reflecting acquisition of the discrimination. Follow-up *t*-tests showed that rats drank significantly less on the Danger day than on the subsequent Safe day on Cycles 7 [$t(7) = 1.970$, $p < 0.05$], 8 [$t(7) = 2.102$, $p < 0.05$], 9 [$t(7) = 2.843$, $p < 0.05$] and 10 [$t(7) = 3.218$, $p < 0.05$]. Based on the fluid consumption measure, the context discrimination emerged at cycle 7. In all subsequent analyses, planned comparisons of the rats' behaviour on the Danger day and the subsequent Safe day were conducted during the last four cycles. The comparisons were carried out on these two days because any differences would not be confounded by the additional Safe days that preceded a Danger day. All statistical decisions were the same when the preceding day was used.

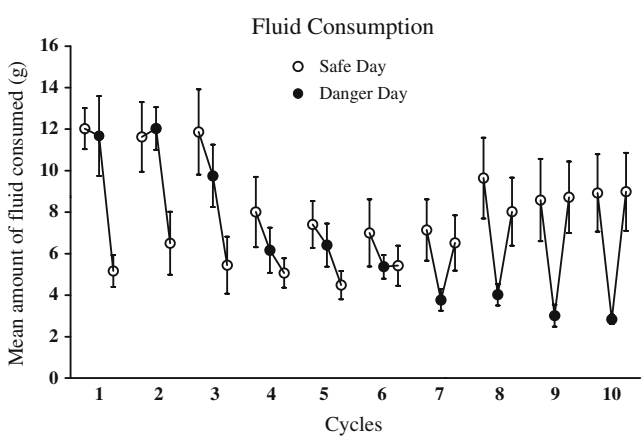

Fig. 1 Mean (±SEM) amount of fluid consumed (g) on each safe–danger–safe cycle (1 through 10)

Gaping

As can be seen in Fig. 2, rats gaped more on danger days than on safe days, both prior to and during saccharin presentation. A three-way (Cycle × Day × Interval; first 10 min vs. second 10 min) ANOVA revealed a significant main effect of Cycle [$F(9,63) = 6.312$, $p < 0.05$], Day [$F(2,14) = 14.704$, $p < 0.05$] and Interval [$F(1,7) = 5.833$, $p < 0.05$], as well as significant Cycle × Day [$F(18,126) = 6.602$, $p < 0.05$], Day × Interval [$F(2,14) = 7.651$, $p < 0.05$] and Cycle × Day × Interval [$F(18,126) = 3.358$, $p < 0.05$]

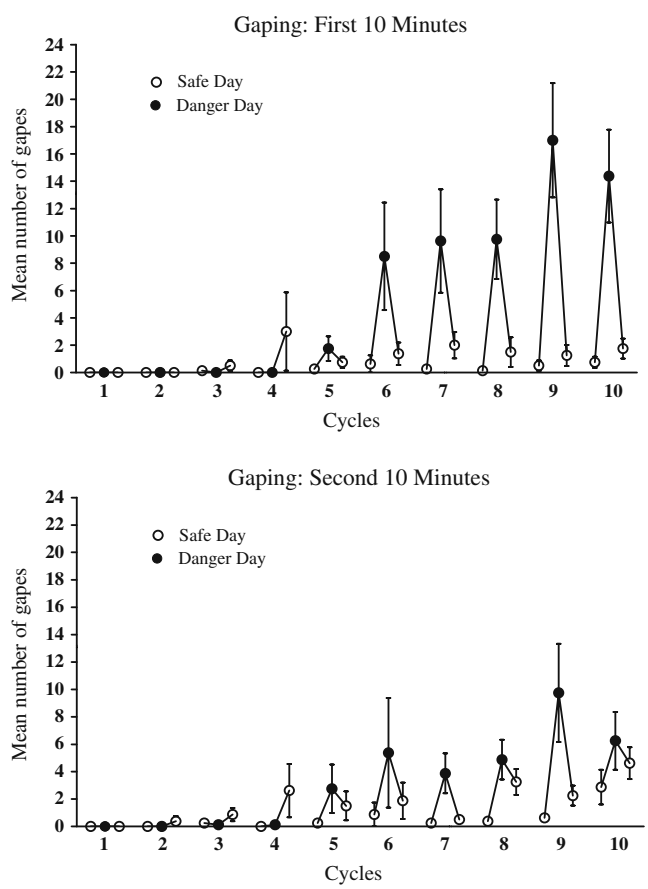

Fig. 2 Mean (±SEM) number of gapes on each safe–danger–safe (1 through 10) for the first (top panel) and second (bottom panel) 10-min interval, respectively

interactions. Follow-up t tests were conducted on the last four cycles for both the first and second 10 min, respectively, of the trial. During the first 10 min, rats gaped significantly more on the danger day relative to the subsequent safe day on Cycles 7 [$t(7) = 2.547$, $p < 0.05$], 8 [$t(7) = 3.066$, $p < 0.05$], 9 [$t(7) = 4.034$, $p < 0.05$] and 10 [$t(7) = 4.000$, $p < 0.05$]. During the second 10 min, rats gaped significantly more on the danger day than on the subsequent safe day on Cycles 7 [$t(7) = 2.527$, $p < 0.05$] and 9 [$t(7) = 2.149$, $p < 0.05$].

Chin rubbing

As can be seen in Fig. 3, rats chin rubbed more on Danger days than on Safe days both prior to and during saccharin presentation. A 10 × 3 × 2 repeated measures ANOVA revealed a significant main effect of Cycle [$F(9,63) = 8.913$, $p < 0.05$] and Day [$F(2,14) = 8.096$, $p < 0.05$], as well as significant Cycle × Day [$F(18,126) = 5.538$, $p < 0.05$], Cycle × Interval [$F(9,63) = 2.271$, $p < 0.05$], Day × Interval [$F(2,14) = 4.270$, $p < 0.05$] and Cycle × Day × Interval [$F(18,126) = 2.240$, $p < 0.05$] interactions. Follow-up t tests were conducted on the last four cycles for both the first and second 10 min, respectively, of the trial. During the first 10 min, rats made significantly more chin-rubbing responses on the Danger day than on the subsequent safe day on Cycles 8 [$t(7) = 2.374$, $p < 0.05$], 9 [$t(7) = 3.220$, $p < 0.05$], and 10 [$t(7) = 2.308$, $p < 0.05$]. During the second 10 min, rats made significantly more chin-rubbing responses on the danger day than on the subsequent safe day on Cycles 7 [$t(7) = 1.994$, $p < 0.05$], 8 [$t(7) = 2.560$, $p < 0.05$], 9 [$t(7) = 2.952$, $p < 0.05$] and 10 [$t(7) = 2.526$, $p < 0.05$].

Tongue protrusions

As can be seen in Fig. 4, rats tended to exhibit more tongue protrusions on safe days than on danger days, with this response occurring more during saccharin presentation. A 10 × 3 × 2 repeated measures ANOVA revealed significant main effects of Cycle [$F(9,63) = 6.370$, $p < 0.05$], Day [$F(2,14) = 4.646$, $p < 0.05$) and Interval [$F(1,7) = 14.460$, $p < 0.05$] and significant Cycle × Interval [$F(9,63) = 3.752$, $p < 0.05$] and Cycle × Day [$F(18,126) = 3.462$, $p < 0.05$] interactions. Follow-up t tests were conducted on the last

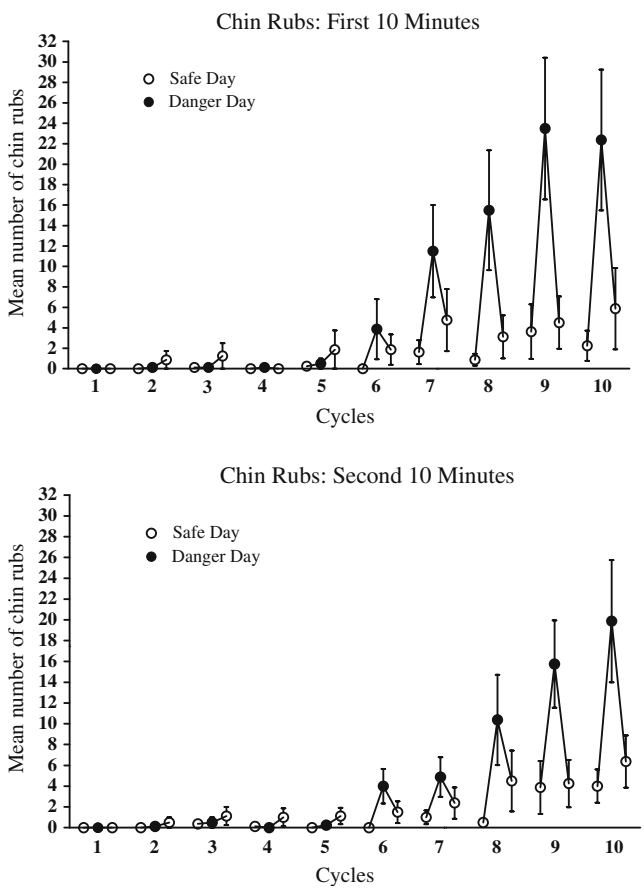

Fig. 3 Mean (±SEM) number of chin rubs on each safe–danger–safe cycle (1 through 10) for the first (top panel) and second (bottom panel) 10-min interval, respectively

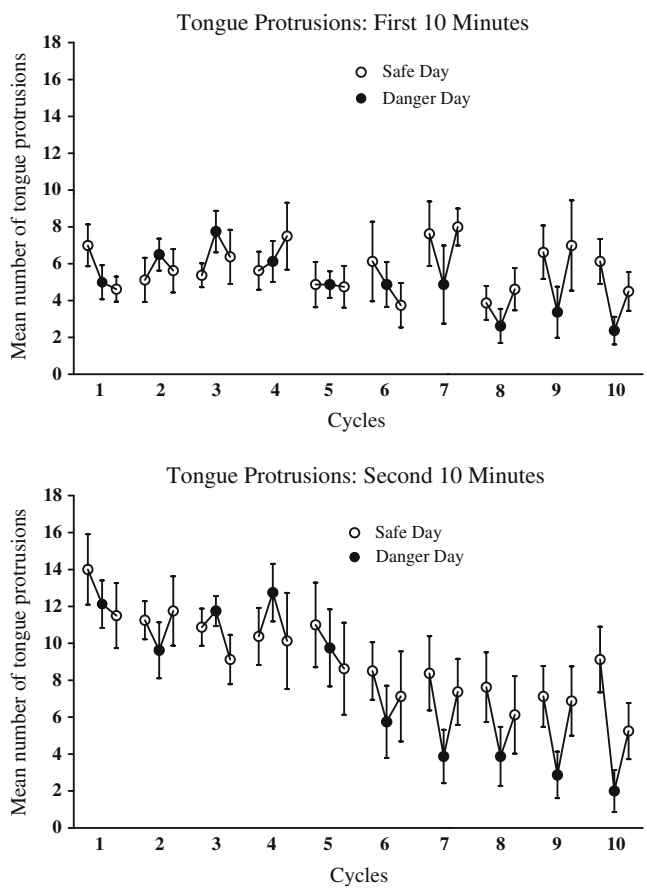

Fig. 4 Mean (±SEM) number of tongue protrusions on each safe–danger–safe (1 through 10) for the first (top panel) and second (bottom panel) 10-min interval, respectively

four cycles for both the first and second 10 min of the trial, respectively. During the first 10 min, rats demonstrated significantly more tongue protrusions on the safe day than on the preceding danger day on Cycle 8 [$t(7) = 2.428$, $p < 0.05$). During the second 10 min, rats demonstrated significantly more tongue protrusions on the safe day than on the preceding danger day on Cycles 7 [$t(7) = 1.997$, $p < 0.05$], 9 [$t(7) = 2.244$, $p < 0.05$] and 10 [$t(7) = 2.630$, $p < 0.05$].

Paw licking

As can be seen in Fig. 5, rats had a tendency to lick their paws more on Safe days than on Danger days, with this trend occurring more during saccharin presentation. A 10 × 3 × 2 repeated measures ANOVA revealed significant main effects of Cycle [$F(9,63) = 2.247$, $p < 0.05$], Day [$F(2,14) = 11.687$, $p < 0.05$], and Interval [$F(1,7) = 9.074$, $p < 0.05$] and significant Day × Interval [$F(2,14) = 5.203$, $p < 0.05$], and Cycle × Day [$F(18,126) = 1.891$, $p < 0.05$] interactions. Follow-up t tests were conducted on the last four cycles for both the first and second 10 min, respectively, of the trial. During the first 10 min, rats demonstrated significantly more paw licking on the safe day than on the preceding danger day on Cycle 10 [$t(7) = 2.049$, $p < 0.05$]. During the second 10 min, rats demonstrated significantly more paw licking on the safe day than on the preceding danger day on Cycles 7 [$t(7) = 2.252$, $p < 0.05$] and 8 [$t(7) = 2.671$, $p < 0.05$].

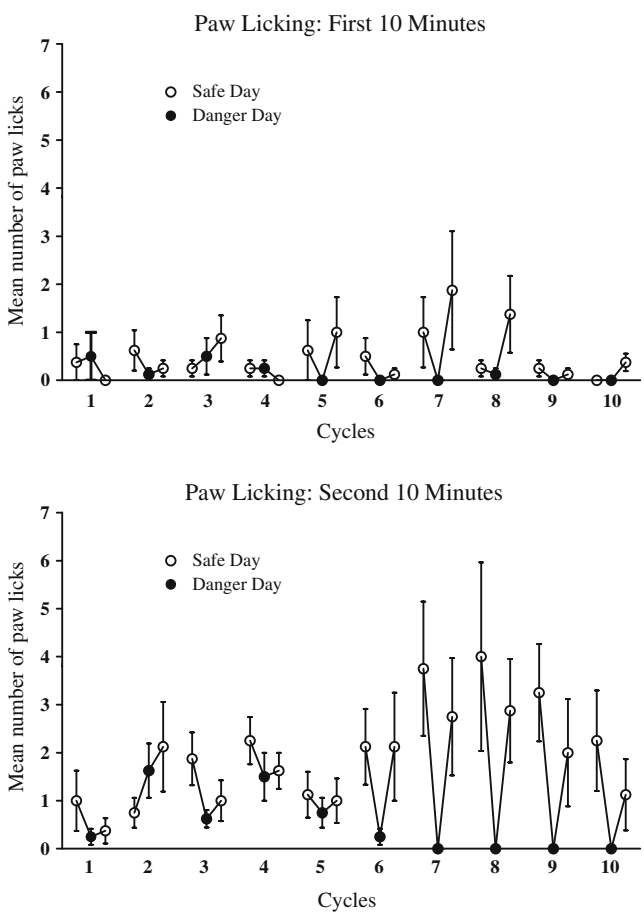

Fig. 5 Mean (±SEM) number of paw licks on each safe–danger–safe cycle (1 through 10) for the first (top panel) and second (bottom panel) 10-min interval, respectively

Hole-pokes

As can be seen in Fig. 6, on safe days, rats tended to poke their head into the hole associated with "safe" fluid delivery more than the hole associated with "dangerous" fluid delivery. There was no evidence of preferential hole-poking on Danger days. A 10 × 3 × 2 [Cycle × Day × Hole position (safe hole vs. danger hole)] repeated measures ANOVA revealed significant main effects of Cycle [$F(9,63) = 2.265$, $p < 0.05$], Day [$F(2,14) = 6.873$, $p < 0.05$] and Hole position [$F(1,7) = 21.374$, $p < 0.05$] and significant Cycle × Day [$F(18,126) = 3.936$, $p < 0.05$], Day × Hole position [$F(2,14) = 11.794$, $p < 0.05$] and Cycle × Day × Hole position [$F(18,126) = 2.710$, $p < 0.05$] interactions.

Follow-up t tests were conducted on the last four cycles. These analyses revealed that rats poked their heads into the safe hole more on the Safe day after a Danger day on cycle 8 [$t(7) = 2.953$, $p < 0.05$], cycle 9 [$t(7) = 2.650$, $p < 0.05$] and cycle 10 [$t(7) = 2.101$, $p < 0.05$]. Hole-pokes to the danger hole differed between the Safe day and the preceding Danger day on cycle 7 [$t(7) = 4.490$, $p < 0.05$]. However, hole-pokes to the danger hole did not differ between the Danger day and following Safe day on cycles 8, 9 and 10 ($p > 0.05$).

Correlations of taste reactivity responses with fluid consumption

Both the aversive and appetitive taste reactivity responses were correlated with fluid consumption. All measures were

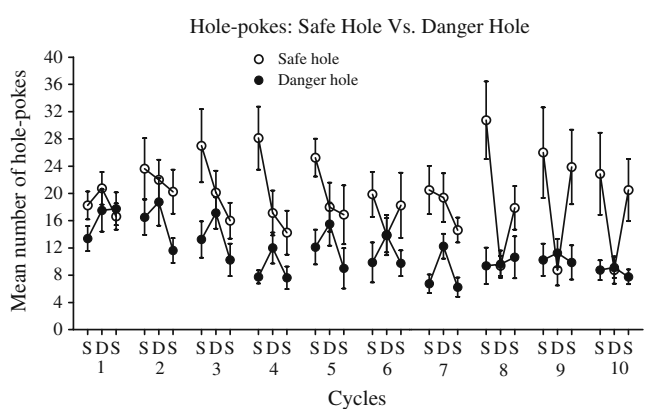

Fig. 6 Mean (±SEM) of hole-pokes on each safe–danger–safe cycle (1 through 10) for the first 10-min interval, respectively. *S* Safe, *D* danger

averaged across the last three cycles, giving us an averaged safe–danger–safe cycle. Even though fluid was not present during the first 10-min interval, the behaviours occurring during that interval were correlated with fluid consumption on that day.

Aversive responses

Gaping during the first 10 min of the Danger day was negatively correlated with fluid consumption ($r = -0.813$, $p < 0.05$). Both gaping ($r = -0.686$) and chin rubs ($r = -0.642$) during the second 10 min of the Danger day were negatively correlated with fluid intake (all $p < 0.05$). Chin rubs during both the first ($r = -0.744$) and the second ($r = -0.727$) 10-min interval of the first Safe day were negatively correlated with fluid consumption (all $p < 0.05$). Gaping and chin rubs on the second Safe day (regardless of interval) were not significantly correlated with fluid consumption (all $p > 0.05$).

Appetitive responses

Neither tongue protrusions nor paw licks during the first 10 min of the first Safe day were significantly correlated with fluid consumption (all $p > 0.05$). Both tongue protrusions ($r = 0.845$) and paw licks ($r = 0.903$) during the second 10 min of the first Safe day were positively correlated with fluid consumption (all $p < 0.05$). Tongue protrusions during both the first ($r = 0.693$) and second ($r = 0.827$) 10-min interval of the Danger day were significantly correlated with fluid consumption (all $p < 0.05$). Neither tongue protrusions nor paw licks during the first 10 min of the second Safe day were significantly correlated with fluid consumption (all $p > 0.05$). Both tongue protrusions ($r = 0.695$) and paw licks ($r = 0.721$) during the second 10 min of the second Safe day were positively correlated with fluid consumption (all $p < 0.05$).

General discussion

Rats in the present experiment responded differently to the white and black boxes after discrimination training. The contextual cues gained control over the expression of orofacial and somatic responses typically measured in taste reactivity paradigms (Berridge, 2000; Grill & Norgren, 1978). Rats showed an increase in aversive responses (i.e., gaping and chin rubbing) and a decrease in appetitive responses (i.e., paw licking and tongue protrusions) on Danger days. On Safe days, aversive responses became less frequent, and appetitive responses became more frequent. These trends became apparent once the rats had learned the discrimination, as evidenced in the consumption measures, which began at approximately Cycle 7 of the experiment. The timing of this learned discrimination is consistent with results from earlier studies in which only consumption measures were taken (e.g., Murphy & Skinner, 2005).

Our findings revealed that the observed changes in fluid consumption were related to both aversive and appetitive responses that were measured in parallel. Both tongue protrusions and paw licking were positively correlated with fluid consumption after the fluid was delivered on Safe days, while there was either a negative relationship or no relationship at all on Danger days. Gaping and chin rubbing were both negatively correlated with fluid consumption on Danger days. These findings with a single-flavoured solution presented in both a safe and danger context extend the findings of Parker (1995) who showed the same correlations when testing aversive and palatable solutions.

Data from our study show that the context and the unconditional effects of the LiCl do not have to overlap to produce aversive responding since rats injected with LiCl after removal from the context showed anticipatory aversive responses in the context. In previous studies, the animals were injected with LiCl prior to being placed in the context (Limebeer et al., 2006; Limebeer et al., 2008; Rodriguez et al., 2000). Future work will have to determine whether the acquisition of the aversive responses is limited to circumstances in which the animal has drunk in the context since the capacity of a context to suppress consumption is limited to situations where the animal drinks in a context prior to the injection of LiCl (Skinner, Martin, Pridgar, & van der Kooy, 1994; Symonds & Hall, 1997). Our study did not evaluate the effect of consumption on aversive responses to the context since the purpose was to monitor the development of conditioned avoidance, aversive and appetitive responses to a flavoured solution. The expression of aversive reactions was not limited to the time when the animal drank since the aversive reactions were apparent prior to the presentation of the fluid once the context discrimination had been acquired.

Our results demonstrate that it is possible for aversive, appetitive and avoidance responses to come under the control of environments that differ primarily on the basis of colour. This extends previous findings of avoidance learning to fluids in distinct environments (Lopez & Cantora, 2003; Loy, Alvarez, Rey, & Lopez, 1993; Murphy & Skinner, 2005; Rodriguez et al., 2000; Skinner et al., 1994; Symonds & Hall, 2002) and the demonstration of aversive responses to environments (Limebeer et al., 2006; Limebeer et al., 2008) in that strong olfactory and texture cues do not have to mediate those effects. Apparently, rats can associate boxes that differ primarily on the basis of visual cues with LiCl-induced sickness and that the reaction to a flavour that is repeatedly paired with LiCl (on ten occasions in this experiment) can be affected by a primarily visual discrimination that is learned.

The anticipatory aversive responses observed in our study are consistent with the suggestion of Limebeer et al. (2008) that the gaping response should occur in anticipation of an aversive solution as a reaction to the contextual signals for nausea. The appetitive measures (tongue protrusions and paw licking) did not occur in anticipation of the fluid but seemed to be limited to the presentation of the solution itself, suggesting that the context preceding an injection of LiCl can elicit anticipatory aversive responses. In contrast, appetitive responses are tied to palatability and are limited to the flavoured solution itself.

The appetitive measure of hole-poking occurred in anticipation of fluid presentation on Safe days. Rats hole-poked more on Safe days than on Danger days, and they poked the 'safe' hole significantly more than the 'danger' hole on Safe days. Finally, rats did not seem to have a preference for poking either hole on Danger days. It would appear that anticipation reflected in a motor response, such as hole-poking, can occur in anticipation of the flavoured solution.

Results from previous studies suggest that contextual cues can control fluid consumption (Skinner et al., 1994; Murphy & Skinner, 2005). The findings of our study indicate that this conditional control may not be limited to the avoidance response. Both the aversive and appetitive responses tracked the fluid consumption measures. Future work will be required to determine whether the differential responses observed in the two contexts reflect conditional control or an interaction between the association between context and LiCl and fluid consumption.

The observation that aversive and appetitive reactions to the flavoured solution vary in the two environments suggests that one might attenuate the aversive reactions and increase the appetitive reactions to flavours when the environments differentially predict the occurrence of a toxin. Implementation of discrimination training could potentially attenuate the deleterious effects on consumption produced by chemotherapy agents since the flavoured foods that were inadvertently paired with the toxin would be less aversive in the safe environment.

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