Non-reinforced flavor exposure attenuates the effects of conditioned taste aversion on both flavor consumption and cue palatability.

Dominic Michael Dwyer[1], Patricia Gasalla[2] & Matías López[2]

1 = Cardiff University, Cardiff, UK: 2 = University of Oviedo, Oviedo, Spain

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Address for correspondence:
Dominic Dwyer
School of Psychology
Cardiff University
Tower Building, Park Place
Cardiff
CF10 3AT, UK
Tel: +44 (0)29 2087 6285
Email: DwyerDM@cardiff.ac.uk

Abstract

Non-reinforced exposure to a cue tends to attenuate subsequent conditioning with that cue – an effect referred to as latent inhibition (LI). The two experiments reported here examined LI effects in the context of conditioned taste aversion by examining both the amount of consumption and the microstructure of the consummatory behavior (in terms of the mean size of lick clusters). This latter measure can be taken to reflect affective responses to, or the palatability of, the solution being consumed. In both experiments, exposure to a to-be-conditioned flavor prior to pairing the flavor with nausea produced by lithium chloride attenuated both the reduction in consumption, and the reduction in lick cluster sizes, typically produced by taste aversion learning. In addition, there was a tendency (especially in the lick cluster measure) for non-reinforced exposure to reduce neophobic responses to the test flavors. Taken together, these results reinforce the suggestion from previous experiments using taste reactivity methods that LI attenuates the effects of taste aversion on both consumption and cue palatability. The current results also support the suggestion that the failure in previous studies to see concurrent LI effects on consumption and palatability was due to a context specificity produced by the oral taste infusion methods required for taste reactivity analyses. Finally, the fact that the pattern of extinction of conditioned changes in consumption and lick cluster sizes was not affected by pre-exposure to the cue flavors suggests that LI influenced the quantity but not quality of conditioned taste aversion.

It is well established in rats that pairing a novel taste with illness induced by the injection of an emetic drug (e.g., lithium chloride, LiCl) results in decreased consumption of the taste when it is subsequent contacted, a learning paradigm termed conditioned taste aversion (see Reilly & Schachtman, 2009, for a recent review on this phenomenon). Although taste aversions produced by different methods are often considered together, it has been argued by Parker and colleagues (see Parker, 2003; Parker, Limebeer, & Rana, 2009) that a reduction in the consumption of a taste previously paired with aversive consequences may be motivated by two different processes; the association of the taste with the nausea, or by its association with a potential danger (e.g., that produced by a novel change in rat´s physiological state). This distinction is largely based on the presence or absence of aversive (rejection) reactions in the taste reactivity test introduced by Grill and Norgren (1978). In this test, rats are infused with a flavored solution via a cannula implanted in their oral cavity and the orofacial reactions elicited by the flavor are recorded. Rats usually display rejection reactions, such as gaping, chin rubbing, and paw treading, when infused with unpalatable solutions such as bitter tasting quinine. Critically, rats also display the same rejection reactions to otherwise palatable tastes (such as sweet sucrose) that have been previously paired with nausea produced by LiCl administration, reflecting a shift in hedonic value, or palatability, of the taste (e.g., Parker, 1982; Pelchat, Grill, Rozin, & Jacobs, 1983). In contrast when sucrose is paired with peripheral pain (electric shock), the consumption of that solution is reduced to a degree comparable to that induced by pairing the solution with LiCl, but does not produce a change in palatability of the taste stimulus as measured by the taste reactivity test (e.g. Pelchat et al., 1983). This was interpreted in terms of the solution becoming a danger signal without a change in its affective properties. Further evidence that taste aversion learning is mediated both by internal nausea linked to disgust

reactions as well as by other mechanisms includes the fact that that rats can suppress intake of flavors paired with rewarding drugs, such as cocaine or amphetamine, that do not result in the production of rejection reactions to the conditioned stimulus flavors (e.g., Parker, 1982; 1995), and that antiemetic drugs that can interfere with the establishment of disgust reactions to a LiCl-paired flavor without affecting the amount consumed of the flavored solution (e.g., Limebeer & Parker, 2000).

It is also well established that exposure to a stimulus prior to it being paired with some reinforcing event will attenuate (or even prevent) learning about the cue-event relationship. This phenomenon is referred to as latent inhibition (LI) and has been demonstrated with a wide variety of preparations including when the cue stimulus is a flavor, and the subsequent event is the administration of LiCl (for reviews, see Lubow, 1989; 2009). But while it has long been known that flavor pre-exposure reduces conditioned taste aversion as measured by voluntary fluid ingestion in simple consumption tests, its effects on taste palatability are not well understood. In particular, the possibility that latent inhibition might affect the quality of learning produced by taste aversion learning (i.e. whether taste aversion learning produces changes in the palatability of the cue flavor or not) has yet to be conclusively addressed. In a recent study conducted to evaluate whether flavor pre-exposure concurrently attenuates the effects of taste aversion on both fluid consumption and conditioned disgust reactions as an index of palatability, we found that pre-conditioning flavor exposure not only disrupts suppressed consumption, but also attenuates the establishment of conditioned disgust reactions to flavor paired with LiCl (López, Gasalla,Vega, Limebeer, Tuerke, Bedard, & Parker, 2010). However, the effects of pre-conditioning exposure to saccharin on acquired consumption and disgust reactions differed as a function of how the saccharin exposure was performed. That is, when rats were given intraoral

infusions of saccharin prior to conditioning with LiCl, saccharin pre-exposure resulted in attenuated conditioned disgust reactions in the taste reactivity test, but did not attenuate the reduction in flavor ingestion during a voluntary consumption test; in contrast, when pre-exposed to the solution by bottle, the taste aversion induced reduction in consumption of saccharin was attenuated, but there was no effect of exposure on the acquisition of conditioned disgust reactions to saccharin. In short, latent inhibition effects on either consumption or disgust reactions required a common method of fluid delivery during pre-exposure and testing.

This apparent dissociation in latent inhibition effects on consumption and taste reactivity measures might relate to the context specificity of latent inhibition whereby a change of context between exposure and test will attenuate or abolish the latent inhibition effect (e.g. Boakes, Westbrook, Elliot, & Swinbourne, 1997; Hall & Channell, 1986; Lovibond, Preston, & Mackintosh, 1984). In the experiments by López et al. (2010) taste reactivity analyses were performed during intraoral fluid delivery, while consumption was assessed by giving free access to the test solution in a bottle. On the grounds that the method by which fluid access was given would presumably be highly salient to the rats, López et al. suggested that it would act as a contextual cue, and so exposure to the flavor before training should only influence conditioned taste aversion when the exposure and test methods of fluid delivery matched (which is exactly the pattern of results that was observed). However, while context-based latent inhibition effects certainly offer an account of the apparent dissociation in the taste reactivity and consumption measures, this account cannot be tested by traditional taste reactivity methods because the reliance on intraoral infusion means that the fluid delivery context will be perfectly correlated

with the type of response being assessed[1]. Moreover, it is at least possible that consumption and taste reactivity reflect two different aspects of the conditioned response and that flavor exposure might influence them independently. In terms of Konorski's (1967) distinction between preparatory and consummatory conditioning, bottle-based consumption tests afford preparatory responses (e.g. approach or withdrawal from the bottle) while intraoral infusion does not, but intraoral infusion does afford consummatory responses (including hedonic reactions). This division between consummatory and preparatory responses has previously been considered in light of the fact that the hedonic effects of conditioned taste aversion appear to extinguish faster than the effects on consumption (Cantora, López, Aguado, Rana, & Parker, 2006; Dwyer, 2009).

With these issues in mind, the goal of the present studies was to determine whether latent inhibition in taste aversion has concurrent effects on consumption of, and hedonic reactions to, the target taste when the possibility of context effects produce by fluid delivery methods is removed. This was achieved by the microstructural analysis of licking behaviour during voluntary consumption (for reviews of this methodology see, Davis, 1973; 1989; Dwyer, 2012). The ingestive behavior of rats consuming fluids consists of sustained runs of rapidly occurring rhythmic licks (referred to here as clusters) separated by pauses of varying lengths. It is consistently observed that palatable sugar solutions increase the quantity of fluid consumed, the number of licks, and the number of licks per cluster (e.g., Davis & Perez, 1993; Davis & Smith,

[1] While taste-reactivity analyses can be performed under free-consumption conditions this produces confounds based on the amount of consummatory contact with the cue flavor - if the solution is aversive then rats do not consume enough reliably elicit aversive behaviors, and if the solution is not aversive then appetitive responses can be swamped by actual consumption. While the connection between the fluid delivery context and the type of response being assessed could be broken in theory, this would come at the cost of reducing the sensitivity of the taste-reactivity assessment.

1992); in contrast, the aversive taste of quinine reduces the rate of licking and the size of licking clusters (e.g., Spector & St. John, 1998). Also, pairing an otherwise palatable taste with LiCl results in a reduction of the lick cluster size similar to that produced by quinine (Baird, John, & Nguyen, 2005; Dwyer, 2009). Moreover, amphetamine based aversions do not produce the same degree of a change in lick cluster size as do aversions produced by LiCl (Dwyer, Boakes, & Hayward, 2008; but see also Arthurs, Lin, Amodeo, & Reilly, 2012; Lin, Arthurs, Amodeo, & Reilly, 2012). In addition, it has been demonstrated that the administration of benzodiazepine drugs, which modulate ingestion responses in the taste reactivity test and enhance hedonic reactions to food in humans, enhance lick cluster size (e.g., Cooper, 2005; Higgs & Cooper, 1998). All these findings indicate that the analysis of the microstructure of licking behavior can be taken as an effective indicator of rodents´ hedonic reactions. Moreover, the measurement of licking behavior does not affect the means of fluid delivery (it relies on simple electrical means to record the time of each lick to a freely available bottle) and so does not produce a context change similar to that created by the use of intraoral fluid delivery. Thus the current experiments, using the latent inhibition paradigm, examined both the amount of consumption and the microstructure of licking behavior in order make an unambiguous assessment of concurrent changes in consumption and taste palatability following flavor pre-exposure in taste aversion learning.

Experiment 1

The design of Experiment 1 is shown in Table 1. Half of the animals (Group LI) were exposed to 0.1% (w/w) saccharin without any experimentally defined consequences across four drinking sessions, while the remainder (Group Control) received water. Following this exposure

phase all animals received two sessions in which saccharin was paired with intraperitoneal injections of lithium chloride (LiCl). The responses to saccharin were then examined across ten drinking sessions in extinction. Throughout the initial exposure, conditioning, and test phases, the timing of all licks was recorded to allow for the analysis of lick cluster sizes. On the basis of previous analyses of latent inhibition in conditioned taste aversion, rats in Group LI should consume more saccharin than those in Group Control during the test phase (i.e., after saccharin was paired with LiCl). Furthermore, to the extent that latent inhibition also attenuates the degree to which conditioned taste aversion influences hedonic reactions then lick cluster sizes elicited by saccharin should be larger in Group LI than in Group Control.

Method

Subjects.

Twenty-four male Lister hooded rats (*Rattus Norvegicus*) were obtained from Harlan, Bicester, UK for the purposes of the study. Their weights before the beginning of the study ranged from 289g to 361g, with a mean weight of 333g. The rats were housed in pairs in a room illuminated between the hours of 0800-2000, where they had ad-lib access to food and received 60 min access to water per day approximately, 1 hr after the experimental sessions.

Apparatus and Stimuli.

Rats were trained and tested in twelve custom-made drinking chambers (Med Associated Inc., St Albans, USA). These measured 32 × 15 × 12 cm (L × W × H), with steel mesh flooring and with white acrylic walls. The drinking chambers were located in a room separate from that containing the home cages. Fluids were made accessible through drinking spouts made of stainless steel, attached to 50ml cylinders. These could be inserted on the left or right hand side

of the lid (made of wire mesh). The distance between the holes for the bottles was 8cm. Only the left hand side was used for the current studies. A contact sensitive lickometer registered the time of each lick to the nearest 0.01s. This was recorded by a computer using MED-PC software (Med Associates Inc.). The amount of fluid consumed by each rat was measured by weighing the drinking bottle before and after each session. The stimuli were tap water or solutions of 0.1% (w/w) saccharin.

Procedure.

All experimental drinking sessions were 15 min in duration and there was one session on each day. To acclimatize the rats to the experimental apparatus they were given two 15-min sessions with access to water. The following four sessions comprised the exposure phase: rats in Group LI received saccharin in each session, while those in Group Control received water (see Table 1). Following the exposure phase, all rats received a 2-day conditioning phase in which exposure to saccharin was followed by an intraperitoneal injection of LiCl (0.15M at 5ml/kg bodyweight) on both days. The test phase consisted of ten drinking sessions in which saccharin was presented without any experimental consequences.

Data Analysis.

In addition to the consumption data, the mean cluster size for each rat was extracted from the record of licks for analysis. A cluster was defined as a set of licks each separated by an inter-lick-interval of no more than 0.5 s. This criterion is used by Davis and his co-workers (e.g., Davis & Perez, 1993; Davis & Smith, 1992) and in the majority of our previous studies using lick analysis techniques (for a review see, Dwyer, 2012). Although other criteria have been used (e.g., Dwyer, Pincham, Thein, & Harris, 2009; Spector, Klumpp, & Kaplan, 1998), parametric analyses suggest that there is little practical difference between them as most pauses greater than

0.5 s are also greater than 1 s (e.g., Davis & Smith, 1992; Spector, et al., 1998). Mixed analyses of variance (ANOVA) were used to analyze the test data with factors of exposure condition (LI vs. Control) and session (Conditioning 1 and 2, Tests 1-10). All tests reported here used a criterion for significance of $p = 0.05$.

On several occasions no licks were recorded for individual rats (test session 1 – three rats from group control, test session 2 – two rats from group control, test sessions 6, 8, and 9 – one rat from group control). Consumption was correspondingly very low at these times suggesting that these were genuine absences of licking, rather than a failure of the recording equipment. As lick cluster size measures are undefined in the absence of any recorded licks, these empty cells were replaced with the relevant group means for that session in the analyses reported below. A preliminary analysis using only the animals for which data was available for every test session revealed the same general pattern of effects suggesting that this treatment of the data did not generate spurious effects.

Results

Table 2 shows the data averaged across the exposure phase. Consumption of saccharin in Group LI was higher than consumption of water in Group Control, $t(22) = 5.63$, $p < .001$, SED = 0.55, but the mean lick cluster sizes did not differ between groups, $t < 1$.

Figure 1 shows the data from the conditioning and tests sessions (consumption in Panel A and lick cluster size in Panel B). Inspection of Panel A suggests that consumption of saccharin was generally lower for the Control than the LI group, and that consumption in both groups dropped from the level seen on conditioning session 1, before partially recovering across testing in extinction. ANOVA conducted on the amount consumed revealed significant effects of

exposure condition (LI vs. Control), $F(1, 22) = 9.90$, $p = .005$, MSE = 3.67), session, $F(11, 242) = 73.43$, $p < .001$, MSE = 2.93, but no interaction between these two factors, $F(11, 242) = 1.41$, $p = .167$, MSE = 2.93. Simple effects analyses revealed that the difference between the Groups LI and Control was significant on every session (lowest $F(1, 22) = 4.35$, $p = .049$, MSE = 8.79, for test session 10) except for test session 1 ($F(1, 22) = 2.08$, $p = .164$, MSE = 3.31). In addition, consumption was significantly lower than on conditioning session 1 in all subsequent sessions for both Group LI (lowest $F(1, 22) = 24.85$, $p < .001$, MSE = 0.82, for the comparison to test session 10) and Group Control (lowest $F(1, 22) = 31.08$, $p < .001$, MSE = 0.82, for the comparison to test session 10).

Inspection of Panel B suggests similar results for the analysis of mean lick cluster sizes. These were generally lower for the Control than the LI group, and mean lick cluster sizes in both groups dropped from the level seen on conditioning session 1. Unlike with consumption, this recovery did approach initial levels of lick cluster size by the end of extinction testing. ANOVA conducted on the lick cluster size data revealed significant effects of exposure condition (LI vs. Control), $F(1, 22) = 13.58$, $p = .001$, MSE = 62.13), session, $F(11, 242) = 20.76$, $p < .001$, MSE = 96.27, but no interaction between these two factors, $F < 1$. Simple effects analyses revealed that the difference between the Groups LI and Control was significant on conditioning session 2, and test sessions 3 – 9 (lowest $F(1, 22) = 5.33$, $p = .031$, MSE = 161.04, for test session 5), but not on conditioning session 1, and test sessions 1, 2, and 10 (highest $F(1, 22) = 3.94$, $p = .060$, MSE = 90.55, for conditioning session 1). In addition, in Group LI lick cluster size was significantly lower than on conditioning session 1 in conditioning session 2, test sessions 1 – 5 and 7 (lowest $F(1, 22) = 5.29$, $p = .031$, MSE = 26.80, for the comparison to conditioning session 2), but was not significantly different from the initial level on test sessions 6 or 8 – 10 (highest

$F(1, 22) = 3.44$, $p = .077$, MSE = 32.9, for the comparison to test session 6). In Group Control lick cluster size was significantly lower than on conditioning session 1 in conditioning session 2, test sessions 1 – 9 (lowest $F(1, 22) = 5.33$, $p = .031$, MSE = 17.46, for the comparison to test session 9), but was not significantly different from the initial level on test session 10 ($F < 1$).

In summary, exposure to saccharin prior to taste aversion conditioning with LiCl resulted in both higher levels of consumption, and higher lick cluster sizes compared to a non-exposed control. This is consistent with exposure producing a latent inhibition effect that was apparent in both consumption and lick microstructure measures. In addition, the effects of the taste aversion treatment on consumption were more resistant to extinction treatment than were the effects of taste aversion on lick cluster size in both the LI and control conditions. It should also be noted that the effects produced by stimulus pre-exposure were not affected by the stage of conditioning or extinction test. The fact that the difference between the LI and control groups remained consistent across sessions suggests that exposure may have attenuated a neophobic reaction to the saccharin solution[2]. In this light, it is interesting that studies of neophobia reduction using taste reactivity (Neath, Limebeer, Reilly, & Parker, 2010) and lick microstructure methods (Lin, Amodeo, Arthurs, & Reilly, 2012) have produced inconsistent effects. The evidence that there was an attenuation of neophobia raises the question of whether pre-conditioning exposure to the flavor stimulus affected learning of the CS-US relationship or simply changed the pre-conditioning baseline against which learning took place. Before considering the theoretical

[2] In the present case the difference in lick cluster sizes between the exposed and non-exposed groups during the initial conditioning session (i.e. when the control group first had access to saccharin) did not reach standard levels of statistical significance (albeit that at $p = .06$, it would have been significant on a 1-tailed test).

implications of the results of Experiment 1 in more detail, we sought to replicate and extend them to a within-subject design.

Experiment 2

In Experiment 1, the fact that exposure influenced consumption (and to an extent lick cluster size) at the start of the conditioning phase meant that it is hard to completely disentangle any effects of neophobia attenuation from latent inhibition more generally. The design of Experiment 2 is shown in Table 1. Half of the animals (Group LI) were exposed to two separate CS flavors (NaCl and maltodextrin - although presented without consequences in the exposure phase these were to be counterbalanced between the CS+ and CS-), while the remainder (Group Control) received water. Following this exposure phase all animals received a two-day conditioning phase where the CS+ flavor was paired with the IP injection of LiCl on one day and the CS- flavor was paired with the IP injection of NaCl on the other. The responses to the CS+ and CS- were then examined across 16 drinking sessions in extinction (these alternated between the CS+ and CS-). As in Experiment 1, both consumption and mean lick cluster size measures were taken throughout. Using a within-subject manipulation of the taste aversion manipulation means that we were able to compare both conditioned and unconditioned differences in the responses to the flavored solutions. The comparison between the LI and control conditions of the responses averaged across the CS+ and CS- during the conditioning phase allows for the assessment of unconditioned differences in the response to the stimuli. More importantly, the CS+ and CS- will be equally familiar in the LI group and equally unfamiliar in the control group. Therefore, if CS exposure merely affects the pre-conditioning baseline, then there should be no difference in the size of the difference between the CS+ and CS- across exposure conditions.

However, if pre-exposure to the CSs affects learning then the size of the CS+ vs CS- difference should be lower in the LI condition than in the control condition.

Method

Subjects, Apparatus and Stimuli.

Twenty-four male Lister hooded rats, obtained from the same source and maintained in the same fashion as in Experiment 1, were used. These animals had previously been used in an unrelated flavor preference experiment where they were exposed to fructose and Kool Aid flavors (Kraft Foods USA, Rye Brook, NY, USA) in different experimental chambers than used here. Their weights before the beginning of the study ranged from 354g to 441g, with a mean weight of 400g. The drinking chambers used were the same as described for Experiment 1. To ensure that the rats previous experience with sweet tastes did not interfere with the current study the stimuli were tap water or solutions of 1% (w/w) NaCl, or 4% (w/w) maltodextrin (C*Dry MD 01904, Cerestar-UK, Manchester, UK).

Procedure.

All experimental drinking sessions were 15 min in duration and there was one session on each day. To acclimatize the rats to the experimental apparatus they were given one 15-min session with access to water. The following eight sessions comprised the exposure phase: rats in Group LI received alternating sessions with NaCl and maltodextrin, while those in Group Control received water (see Table 1). Following the exposure phase, all animals received a two-day conditioning phase. On the first conditioning day all rats received NaCl in the drinking session: for half of the rats in both groups LI and Control this was followed by an intraperitoneal

injection of LiCl (0.15M at 5ml/kg bodyweight); the remainder of the rats received an intraperitoneal injection of NaCl (0.9% at 5ml/kg bodyweight). On the second conditioning day all rats received maltodextrin in the drinking session: rats that had received LiCl on the first conditioning session now received an injection of NaCl while the remainder received an injection of LiCl. Thus, for both the LI and Control groups the CS+ and CS- were counterbalanced between NaCl and maltodextrin. A single pairing of the CS+ with LiCl was used because Experiment 1 indicated that one pairing was sufficient to produce changes in consumption and lick cluster size in this general protocol. The test phase consisted of 16 drinking sessions alternating between the CS+ and the CS-.

Data Analysis.

The data was prepared for analysis in the same general manner as in Experiment 1. In addition, as will be seen below, there were large unconditioned differences in the lick cluster sizes elicited by NaCl and maltodextrin during the exposure phase (these continued into the conditioning and test phases). Thus a factor of solution counterbalance (CS+ = NaCl vs CS+ = maltodextrin) was added to the analysis of the consumption and lick cluster size data from the conditioning and test phases.

Results

Table 2 shows the data averaged across the exposure phase. Taking first the LI group, while consumption of the solutions to become the CS+ and CS- was equivalent, there was a tendency for consumption of maltodextrin to be lower than that of salt. These trends were stronger in the lick cluster size data. An ANOVA was performed on the consumption data from the LI group with factors of whether that solution was to be paired with LiCl or not (CS+/CS-)

and the nature of the solution (Salt/Maltodextrin). This revealed that there was no main effect of CS, $F < 1$, that the main effect of solution type approached standard levels of significance, $F(1,10) = 3.66$, $p = .085$, MSE = 2.32, and that there was no interaction between these factors, $F < 1$. A similar analysis of the lick cluster size data revealed no main effect of CS, $F < 1$, a significant effect of solution type, $F(1,10) = 24.88$, $p = .001$, MSE = 49.77, and no interaction between these factors, $F < 1$. In addition, consumption of the flavored solutions as a whole in Group LI was higher than consumption of water in Group Control, $t(22) = 6.90$, $p < .001$, SED = 0.61, but the mean lick cluster sizes did not differ between groups, $t(22) = 1.64$, $p = .115$, SED = 2.99.

Figure 2 shows the data from the conditioning and tests sessions (consumption in Panel A and lick cluster size in Panel B). Inspection of Panel A suggests that, in both the LI and Control groups, consumption of the CS+ dropped following the conditioning session before recovering across extinction testing – with the initial reduction being smaller in the LI than Control groups. That is, pre-exposure to the CS+ and CS- attenuated, but did not prevent, the formation of a conditioned taste aversion. The consumption data was subjected to a mixed ANOVA with within-subject factors of CS (CS+/CS-) and test session, plus between subject factors of exposure group (LI/Control) and stimulus assignment (CS+ = NaCl/CS+ = maltodextrin). The most theoretically relevant results from the analysis were as follows: There was a main effect of CS, $F(1,20) = 93.14$, $p < .001$, MSE = 25.60, a session by CS interaction, $F(8,160) = 34.18$, $p < .001$, MSE = 4.25, and an exposure by CS interaction, $F(1,20) = 5.77$, $p = .026$, MSE = 25.60. Respectively, these confirmed that pairing the CS+ with LiCl produced an aversion, this aversion reduced over extinction testing, and that the size of the conditioned difference between the CS+ and CS- was attenuated by exposure to the CS solutions. The remainder of the full 4-way

ANOVA was as follows: There was a main effect of test session, $F(8,160) = 42.39$, $p < 0.001$, MSE = 4.53, as well as interactions between session and exposure condition, $F(8,160) = 2.77$, $p = 0.007$, MSE = 4.53, and session and stimulus assignment, $F(8,160) = 2.39$, $p = 0.019$, MSE = 4.53. There was also an interaction between CS and stimulus assignment, $F(1,20) = 21.75$, $p < .001$, MSE = 25.60, such that the CS+ vs. CS- difference was attenuated, but still significant, when the salt was the CS+ solution (means not shown). There was no interaction between CS, exposure condition, and stimulus assignment, $F(1,20) = 1.63$, $p = .217$, MSE = 25.60, indicating that the theoretically important CS by exposure interaction was not influenced by stimulus assignment. Finally, there were no significant interactions between session, CS, and exposure condition, $F(8,160) = 1.83$, $p = .076$, MSE = 4.25, between session, CS, and stimulus assignment, $F(8,160) = 1.71$, $p = .099$, MSE = 4.25, nor a 4-way interaction between session, CS, exposure condition, and stimulus assignment, $F < 1$.

In order to further explore the effects of exposure on conditioning, simple effect tests were performed to compare the LI and Control groups for consumption of both the CS+ and CS-. These revealed that consumption of the CS+ was greater in the LI than the Control group on test sessions 1-4 (lowest $F(1, 20) = 4.94$, $p = .038$, MSE = 9.63, for test session 2), but consumption of the CS+ did not differ between groups at any other time (highest $F(1, 20) = 1.45$, $p = .242$, MSE = 16.17, for test session 5). Consumption of the CS- did not differ between the LI and Control groups on any session (highest $F(1, 20) = 2.24$, $p = .150$, MSE = 6.20, for test session 6). In addition, in group LI consumption of the CS+ was significantly reduced relative to the conditioning session baseline on test sessions 1-4 (lowest $F(1, 20) = 5.22$, $p = .033$, MSE = 1.01, for the comparison to test session 4), but was not significant different to the baseline on test sessions 5-8 (highest $F(1, 20) = 2.45$, $p = .133$, MSE = 1.22, for the comparison to test session

4). In group LI consumption of the CS- did not differ from the conditioning session baseline during any subsequent test (highest $F(1, 20) = 2.94$, $p = .102$, MSE = 0.80, for the comparison to test session 5). In group Control consumption of the CS+ was significantly reduced relative to the conditioning session baseline on test sessions 1-5 (lowest $F(1, 20) = 5.33$, $p = .032$, MSE = 1.35, for the comparison to test session 5), but was not significant different to the baseline on test sessions 6-8 (highest $F(1, 20) = 2.19$, $p = .155$, MSE = 1.22, for the comparison to test session 6). In contrast to group LI, in group Control the consumption of the CS- did exceed that of the conditioning session baseline on test sessions 2-8 (lowest $F(1, 20) = 8.40$, $p = .009$, MSE = 0.80, for the comparison to test session 5), but was equivalent to baseline consumption on test session 1 ($F < 1$). Finally, with respect to the possibility of neophobia reduction, an analysis of consumption during the conditioning phase averaged across the CS+ and CS- revealed that there was no difference between the LI and Control groups, $F(1, 20) = 1.56$, $p = .222$, MSE = 5.91.

Turning to the lick cluster size data in Panel B of Figure 2, for both the LI and Control groups, the mean lick cluster size elicited by the CS+ reduced following the conditioning session before recovering across extinction testing – with the initial reduction being smaller in the LI than Control groups. Thus, pre-exposure to the CS+ and CS- attenuated, but did not prevent, taste-aversion produced changes in affective responses to flavored solutions. In addition, the mean lick cluster sizes (across both the CS+ and CS-) appeared somewhat lower for the Control group than the LI group during the conditioning session – an effect consistent with a neophobic response. The lick cluster data was subjected to the same mixed ANOVA as the consumption data: Within-subject factors of CS (CS+/CS-) and test session, plus between subject factors of exposure group (LI/Control) and stimulus assignment (CS+ = NaCl/CS+ = maltodextrin). The most theoretically relevant results from the analysis were as follows: There was a main effect of

CS, $F(1,20) = 2625$, $p < .001$, MSE = 395.80, a session by CS interaction, $F(8,160) = 8.36$, $p < .001$, MSE = 140.69, and an exposure by CS interaction, $F(1,20) = 16.59$, $p = .001$, MSE = 395.80. Respectively, these confirmed that pairing the CS+ with LiCl reduced the lick cluster size for the CS+, this reduction decreased over extinction testing, and that the size of the CS+ vs CS- difference was attenuated by exposure to the CS solutions. In addition to these theoretically critical effects, there was also a main effect of test session, $F(8,160) = 5.11$, $p < 0.001$, MSE = 212.07, but no interactions between session and exposure condition, $F(8,160) = 1.16$, $p = 0.325$, MSE = 212.07, or session and stimulus assignment, $F(8,160) = 1.15$, $p = 0.333$, MSE = 212.07. There was also an interaction between CS and stimulus assignment, $F(1,20) = 43.71$, $p < .001$, MSE = 395.80, such that the CS+ vs. CS- difference was only present when the maltodextrin was the CS+ solution (means not shown). There was an interaction between CS, exposure condition, and stimulus assignment, $F(1,20) = 6.74$, $p = .017$, MSE = 395.80, reflecting the fact that the CS by exposure condition interaction was carried by the conditions in which Maltodextrin was the CS+. Finally, there was no significant interaction between session, CS, and exposure condition, $F < 1$, a significant interaction between session, CS, and stimulus assignment, $F(8,160) = 4.59$, $p < .001$, MSE = 140.69, but no 4-way interaction between session, CS, exposure condition, and stimulus assignment, $F < 1$.

In order to further explore the effects of exposure on conditioning, simple effect tests were performed to compare the LI and Control groups for mean lick cluster sizes elicited by the CS+ and CS-. These revealed that lick cluster size for the CS+ was greater in the LI than the Control group during the conditioning session, as well as test sessions 1-5 (lowest $F(1, 20) = 4.56$, $p = .045$, MSE = 301.40, for test session 4), but lick cluster sizes for the CS+ did not differ between groups at any other time (highest $F(1, 20) = 4.08$, $p = .057$, MSE = 549.27, for test

session 7). Lick cluster sizes for the CS- did not differ between the LI and Control groups on any session (highest $F(1, 20) = 2.98$, $p = .099$, MSE = 274.77, for the conditioning session). In addition, in group LI lick cluster sizes for the CS+ were significantly reduced relative to the conditioning session baseline on test sessions 1-3 (lowest $F(1, 20) = 7.75$, $p = .011$, MSE = 20.58, for the comparison to test session 3), but was not significant different to the baseline on test sessions 4-8 (highest $F(1, 20) = 2.98$, $p = .100$, MSE = 23.75, for the comparison to test session 4). In group LI lick cluster size for the CS- did not differ from the conditioning session baseline during any subsequent test (highest $F(1, 20) = 3.06$, $p = .096$, MSE = 32.94, for the comparison to test session 8). In group Control lick cluster size for the CS+ was significantly reduced relative to the conditioning session baseline on test sessions 1-3 (lowest $F(1, 20) = 5.03$, $p = .036$, MSE = 20.58, for the comparison to test session 3), but was not significant lower than the baseline on test sessions 4-8 (highest $F(1, 20) = 1.62$, $p = .218$, MSE = 23.75, for the comparison to test session 4). In group Control the lick cluster size for the CS- did not differ from that of the conditioning session baseline on any test session (highest $F(1, 20) = 1.61$, $p = .219$, MSE = 33.51, for the comparison to test session 2. Finally, with respect to the possibility of neophobia reduction, an analysis of lick cluster sizes during the conditioning phase averaged across the CS+ and CS- revealed that these were lower in group Control and in group LI, $F(1, 20) = 5.35$, $p = .031$, MSE = 240.03.

In summary, exposure to the cue flavors prior to taste aversion conditioning with LiCl resulted in a reduction in the subsequent differences between the CS+ and CS- flavors for both consumption and lick cluster size measures relative to non-exposed controls. While there was also some evidence for exposure reducing neophobic responses (especially in terms of the differences between groups LI and Control for the lick cluster measure during the conditioning

phase) the use of a within-subject manipulation of aversion conditioning meant that any neophobia reduction could be parceled out of the exposure effect on learning itself. In addition, the effects of taste aversion persisted for longer on consumption than they did on lick cluster size, but in neither case did the effects of extinction interact with the effects of exposure condition.

General Discussion

The main purpose of these experiments was to provide a demonstration of the attenuating effects of flavor pre-exposure (i.e., latent inhibition) on taste aversion learning as assessed by microstructural analysis of licking behavior as a means to ascertain whether latent inhibition has concurrent effects on consumption and hedonic responses. Although latent inhibition effects in taste aversion have been examined extensively using consumption tests (i.e., prior exposure attenuates subsequent suppressed consumption of an illness-paired flavor), the effect of flavor pre-exposure on taste palatability is not well known. In Experiment 1, non-reinforced exposure to saccharin prior to aversive conditioning with LiCl resulted in attenuated conditioned taste aversion, as assessed by the amount consumed from a bottle containing the solution (i.e., the typical latent inhibition effect in taste aversion learning). More interestingly, the pre-exposure treatment also reduced the effects of taste aversion on the size of licking clusters as compared to a non-exposed control, indicating that the effects of taste aversion on hedonic reactions had also been attenuated. That is, latent inhibition attenuates the effects of taste aversion on both consumption and taste palatability. In addition, it was found in this experiment that conditioned changes in taste palatability extinguished more rapidly than did consumption. Experiment 2 used a within-subject design to preclude any interpretation of the above-described pattern of results in

terms of attenuating neophobia to the cue flavor. As in Experiment 1, flavor pre-exposure attenuated the formation of a conditioned taste aversion as measured by consumption and lick cluster size. More specifically, the exposure to the cue flavors (CS+ and CS-) prior to aversive conditioning with LiCl resulted in a reduction in the subsequent differences between the CS+ and CS- flavors for both consumption and lick cluster size measures. Again, conditioned changes in taste palatability extinguished more rapidly than did consumption. Therefore, the concurrent effects of latent inhibition on lick cluster size and consumption indicate that pre-conditioning exposure to the CS flavors attenuates the changes in both consumption and taste palatability produced by conditioned taste aversion in a way that was independent of exposure effects on neophobia.

The current results are largely consistent with previous experiments (López et al., 2010) using the taste reactivity methodology to examine changes in cue palatability following flavor pre-exposure in the taste aversion learning paradigm. López et al. (2010) demonstrated for the first time that flavor pre-exposure not only disrupts suppressed consumption, but also attenuates the establishment of conditioned disgust reactions to a LiCl-paired taste. However, the attenuating effects of flavor pre-exposure on both consumption and taste reactivity appeared to depend on a common method of fluid delivery during pre-exposure and testing. As noted in the introduction, the methods of flavor presentation differentially affected the consumption of the flavor and the display of disgust reactions. When the rats were intraorally infused with the flavor during pre-exposure, they did not display rejection reactions but showed a reduction in flavor consumption; in contrast, when the solution was provided by bottle during the pre-exposure phase, the rats displayed disgust reactions, but they drank the solution in the consumption test. López et al. (2010) interpreted this pattern of results as consistent with the idea that the

contextual cues provided by the fluid delivery method (especially the intraoral infusion) can modulate the expression of latent inhibition in taste aversion learning. There is already some evidence that changing the fluid delivery method between pre-exposure and conditioning attenuates the latent inhibition effect on consumption measures in taste aversion learning (e.g., Fouquet, Oberling, & Sandner, 2001; Yamamoto, Fresquet, & Sandner, 2002), as the strength of the taste aversion is weakened by changing the method of fluid exposure between conditioning and testing (e.g., Limebeer & Parker, 2006). The current experiments, which demonstrate concurrent effects of latent inhibition on consumption and palatability without the contextual confound of different fluid delivery methods, are thus consistent with the suggestion that the absence of concurrent latent inhibition effects on consumption and palatability observed in the previous study by López et al. (2010) was due to a context effect produced by the oral taste infusion method required for taste reactivity analyses.

Considered in this way, latent inhibition appears to produce the same general pattern of effects on lick cluster and taste reactivity measure in the context of conditioned taste aversion. Thus, latent inhibition joins a number of other manipulations which have parallel effects on these two measures (for a review see Dwyer, 2012). Such results suggest that microstructural analysis of lick patterns and taste reactivity may be complementary measures which both assess taste palatability or hedonic responses. However, it should be noted that there are at least some places where taste reactivity and lick microstructure measures diverge. This is apparent in the current context when the effects of flavor exposure on neophobia are considered. As previously noted, a study by Neath et al. (2010) using the taste reactivity method found that repeated intraoral exposure to saccharin caused an increase in consumption in an intake test but not an increase in hedonic reactions to the fluid in the taste reactivity test. In contrast, a recent study by Lin,

Amodeo, et al. (2012) found that repeated exposure to saccharin results in an attenuation of the neophobic response to this solution as revealed by an increase in consumption and, importantly, an increase in the size of lick clusters. Although not designed as an explicit test of the effects of flavor exposure on neophobia our own studies reflect this pattern of results: Both of Experiments 1 and 2 here provided at least some suggestion that lick cluster sizes were indeed larger following flavor exposure, while our previous study of latent inhibition in taste aversion (López et al., 2010) did not see any evidence of flavor novelty on unconditioned taste reactivity responses. Taken at face value, these results appear to represent a dissociation between taste reactivity and lick microstructure measures, with the former suggesting that the reduction in neophobia with exposure does not affect the palatability of a taste, while the latter suggests that it does. While it is premature to offer a definitive interpretation here, it is worth noting that (broadly speaking) taste reactivity analyses are aimed at making a qualitative distinction as to whether a pattern of facial responses are appetitive or aversive while lick microstructure analyses provide a more quantitative measure. It is thus possible that release from neophobia might not change a taste from being aversive to being appetitive (hence the lack of a taste reactivity change) but merely change the degree to which it is appetitive (or aversive).

Finally, the results of the present experiments may also provide some information about hedonic processes underlying extinction of conditioned taste aversions. Previous studies examining the microstructure of licking during extinction of a taste aversion have shown that reduction in lick cluster size associated with a learned change in palatability extinguishes more quickly than does the avoidance of the flavor previously paired with the lithium (Dwyer, 2009). That is, the suppressed consumption appears to be more resistant to extinction than learned changes in taste palatability as indicated by the lick cluster size. Similarly, taste reactivity

experiments show that a conditioned palatability shift precedes extinction of suppressed consumption (Cantora, et al., 2006). The pattern of results obtained in the current study is consistent with these results: In Experiment 1 consumption in the last extinction trial was significantly lower than on the first conditioning session for both Group LI and Group Control but lick cluster size did return to baseline levels for both groups; while in Experiment 2 the differences in consumption between the CS+ and CS- reduced more slowly than did the differences in lick cluster size (for both the LI and Control groups). We (Cantora, et al., 2006; Dwyer, 2009) have previously suggested that the difference in extinction rates for hedonic and consumption measures might result from preparatory responses associated with approaching the drinking bottle being more resistant to extinction than are the consummatory responses (including hedonic ones) directed to the taste itself (e.g., Konorski, 1967; Wagner & Brandon, 1989). The current data is entirely consistent with this general idea, and the fact that prior exposure to the conditioned flavors has little or no effect on the relative speed of extinction suggests that there is little reason to think that latent inhibition differentially influences preparatory and consummatory responses in taste aversion. That is, latent inhibition appears to have affected the amount of learning about the CS-US relationship in conditioned taste aversion without affecting the nature of what was learnt.

To summarize, we found that latent inhibition attenuates the effects of taste aversion on both consumption and taste palatability as assayed by the size of licking clusters. That is, non-reinforced exposure to a flavor to-be associated with illness resulted in faster recovery of the size of licking clusters and consumption after taste aversion treatment. The fact that the lick cluster and consumption changes were seen concurrently, and that exposure did not materially affect the relative speed of extinction in consumption and lick cluster measures, suggests that latent

inhibition influences taste aversion through a single mechanism rather than having separate effects on preparatory and consummatory process – in short, latent inhibition appears to have had quantitative but not qualitative effects on conditioned taste aversion. That said, differences do remain between studies using taste reactivity and lick microstructure methods. While some of these differences might well be attributable to context effects based upon fluid delivery methods, further studies will be needed to determine conclusively how the type of measure (e.g. amount consumed, lick microstructure, taste reactivity) are related to the processes involved in taste aversion learning.

Author note

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Table 1

Design of Experiments 1 and 2

	Exposure	Conditioning	Test
Experiment 1			
LI	4 × saccharin	2 × saccharin → LiCl	10 × saccharin
Control	4 × Water		
Experiment 2			
LI	4 × CS+, 4 × CS-	CS+ → LiCl & CS- → NaCl	8 × CS+ & 8 × CS-
Control	8 × Water		

Note: There was one 15 min drinking session per day in both experiments (followed 1 hr later by 1 hr access to water in the home cage). In both experiments the conditioning and tests phases were the same in the LI and control conditions. In Experiment 1 saccharin was presented at 0.1% (w/w). In Experiment 2, CS+ and CS- were counterbalanced between 1% (w/w) NaCl, and 4% (w/w) maltodextrin. All injections (5 ml/kg 0.15 *M* LiCl or 5ml/kg 0.9% NaCl) were given by the intraperitoneal route and occurred immediately after the end of the relevant drinking session.

Table 2

Exposure Phase data from Experiments 1 and 2

	Solution	Consumption (g)	Lick Cluster Size
Experiment 1			
LI	Saccharin	11.9 (0.5)	32.6 (2.4)
Control	Water	8.8 (0.2)	35.4 (2.4)
Experiment 2			
LI	CS+ Salt	13.7 (0.9)	48.3 (3.6)
	CS+ Maltodextrin	12.4 (0.8)	36.8 (3.8)
	CS- Salt	13.4 (0.7)	51.1 (5.3)
	CS- Maltodextrin	12.3 (0.7)	33.9 (3.3)
Control	Water	8.8 (0.4)	36.3 (5.6)

Note: Data is shown as mean (with SEM). In Experiment 2, data from the LI group is shown as a function of whether that solution was to be paired with LiCl or not (CS+/CS-) and as a function of the nature of the solution (Salt/Maltodextrin)

Figure Legends

Figure 1. Experiment 1: Shows mean consumption (panel A) and lick cluster size (panel B) per session for both the LI and Control groups (error bars indicate SEM). C1 and C2 refer to conditioning sessions 1 and 2, while T1-T10 refer to extinction test sessions 1-10.

Figure 2. Experiment 2: Shows mean consumption (panel A) and lick cluster size (panel B) per session for both the CS+ and CS- flavors for the LI and Control groups (error bars indicate SEM). C refers to the conditioning session while T1-T8 refer to extinction test sessions 1-8.

Figure 1

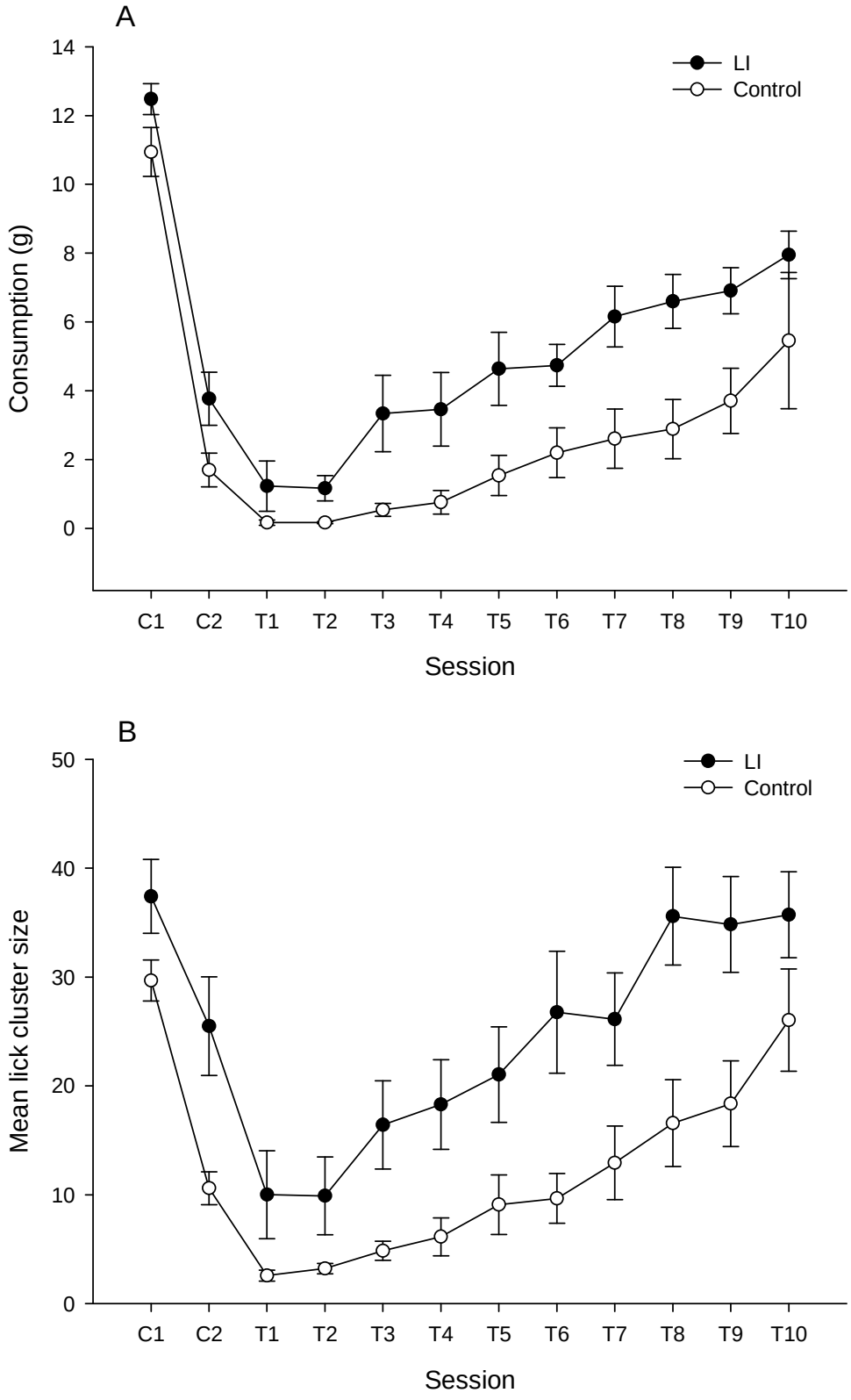
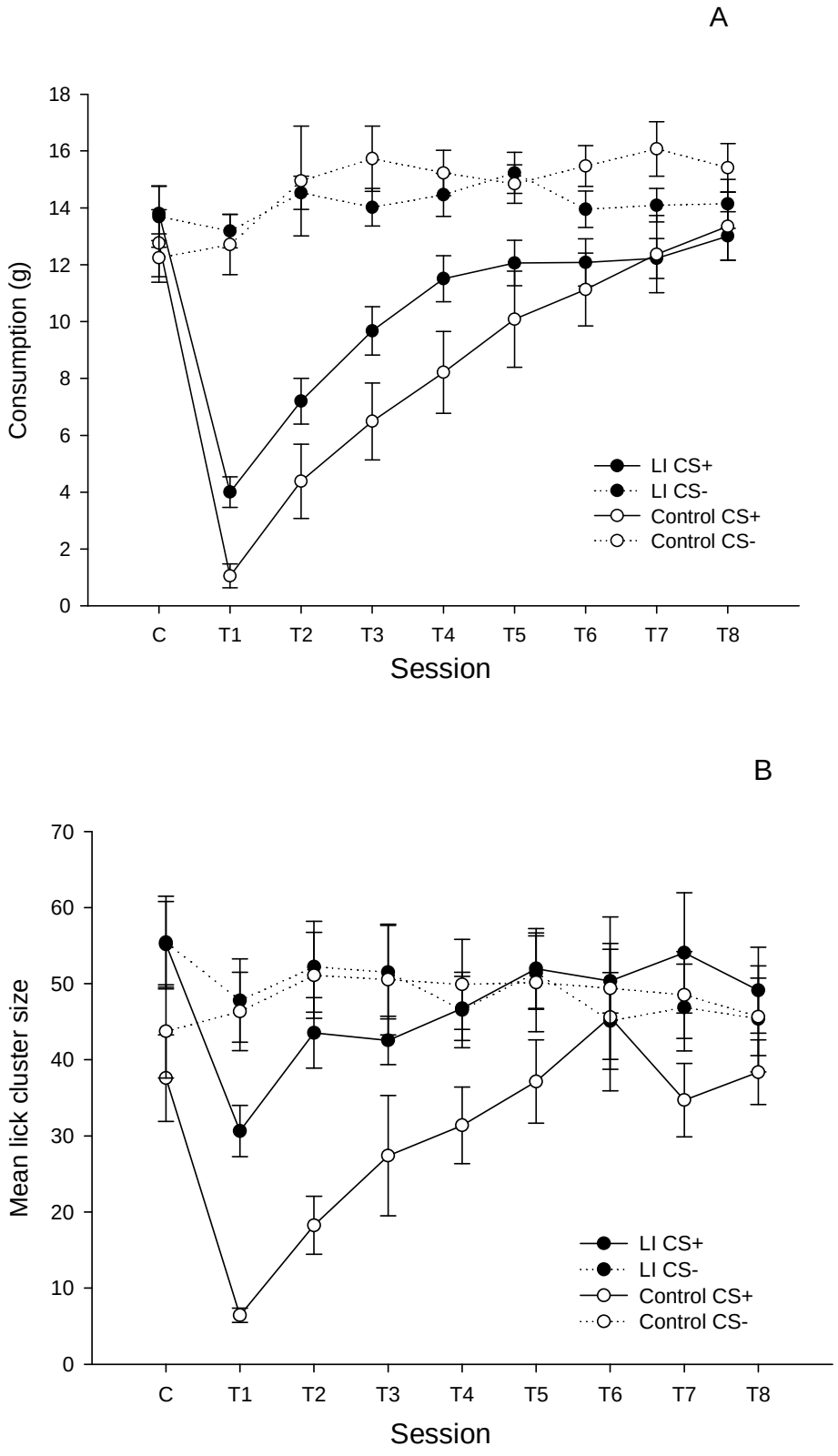

A
LI
Control
Consumption (g)
0
2
4
6
8
10
12
14
C1
C2
T1
T2
T3
T4
T5
T6
T7
T8
T9
T10
Session
B
LI
Control
Mean lick cluster size
0
10
20
30
40
50
C1
C2
T1
T2
T3
T4
T5
T6
T7
T8
T9
T10
Session

Figure 2


A
Consumption (g)
0
2
4
6
8
10
12
14
16
18
C
T1
T2
T3
T4
T5
T6
T7
T8
Session
LI CS+
LI CS-
Control CS+
Control CS-
B
Mean lick cluster size
0
10
20
30
40
50
60
70
C
T1
T2
T3
T4
T5
T6
T7
T8
Session
LI CS+
LI CS-
Control CS+
Control CS-

References

Arthurs, J., Lin, J.-Y., Amodeo, L. R., & Reilly, S. (2012). Reduced palatability in drug-induced taste aversion: II. Aversive and rewarding unconditioned stimuli. *Behavioral Neuroscience, 126,* 433-444. doi: 10.1037/a0027676

Baird, J. P., John, S. J. S., & Nguyen, E. A. N. (2005). Temporal and qualitative dynamics of conditioned taste aversion processing: Combined generalization testing and licking microstructure analysis. *Behavioral Neuroscience, 119,* 983-1003. doi: 10.1037/0735-7044.119.4.983

Boakes, R. A., Westbrook, R. F., Elliott, M., & Swinbourne, A. L. (1997). Context dependency of conditioned aversions to water and sweet tastes. *Journal of Experimental Psychology: Animal Behavior Processes, 23,* 56-67. doi: 10.1037/0097-7403.23.1.56

Cantora, R., López, M., Aguado, L., Rana, S. A., & Parker, L. A. (2006). Extinction of a saccharin-lithium association: Assessment by consumption and taste reactivity. *Learning & Behavior, 34,* 37-43.

Cooper, S. J. (2005). Palatability-dependent appetite and benzodiazepines: new directions from the pharmacology of $GABA_A$ receptor subtypes. *Appetite, 44,* 133-150. doi: 10.1016/j.appet.2005.01.003.

Davis, J. D. (1973). The effectiveness of some sugars in stimulating licking behavior in the rats. *Physiology & Behavior, 11,* 39-45. doi: 10.1016/0031-9384(73)90120-0.

Davis, J. D. (1989). The microstructure of ingestive behavior. *Annals of the New York Academy of Sciences 575,* 39-45. doi: 10.1016/0031-9384(73)90120-0.

Davis, J. D., & Perez, M. C. (1993). The acquired control of ingestive behavior in the rat by flavor-associated postingestional stimulation. *Physiology & Behavior, 54*, 1221-1226. doi: 10.1016/0031-9384(93)90352-G.

Davis, J. D., & Smith, G. P. (1992). Analysis of the microstructure of the rhythmic tongue movements of rats ingesting maltose and sucrose solutions. *Behavioral Neuroscience, 106*, 217-228. doi: 10.1037/0735-7044.106.1.217.

Dwyer, D. M. (2009). Microstructural analysis of ingestive behaviour reveals no contribution of palatability to the incomplete extinction of a conditioned taste aversion. *Quarterly Journal of Experimental Psychology, 62*, 9-17. doi: 10.1080/17470210802215152

Dwyer, D. M. (2012). Licking and liking: The assessment of hedonic responses in rodents. *Quarterly Journal of Experimental Psychology, 65*, 371-394. doi: 10.1080/17470218.2011.652969

Dwyer, D. M., Boakes, R. A., & Hayward, A. J. (2008). Reduced palatability in lithium- and activity-based, but not in amphetamine-based, taste aversion learning. *Behavioral Neuroscience, 122*, 1051-1060.

Dwyer, D. M., Pincham, H. L., Thein, T., & Harris, J. A. (2009). A learned flavor preference persists despite the extinction of conditioned hedonic reactions to the cue flavors. *Learning & Behavior, 37*, 305-310. doi: 10.3758/LB.37.4.305.

Fouquet, N., Oberling, P., & Sandner, G. (2001). Differential effect of free intake versus oral perfusion of sucrose in conditioned taste aversion in rats. *Physiology & Behavior, 74*, 465-474. doi:10.1016/S0031-9384(01)00585-6.

Grill, H. C., & Norgren, R. (1978). The taste reactivity test. I: Mimetic responses to gustatory stimuli in neurobiologically normal rats. *Brain Research, 143,* 263-279.doi: 10.1016/0006-8993(78)90568-1.

Hall, G., & Channell, S. (1986). Context specificty of latent inhibition in taste-aversion learning. *Quarterly Journal of Experimental Psychology, 38B,* 121-139.

Higgs, S., & Cooper, S. J. (1998). Effects of benzodiazepine receptor ligands on the ingestion of sucrose, intralipid and maltodextrin: an investigation using a microstructural analysis of licking behavior in a brief contact test. *Behavioral Neuroscience, 112,* 447-457. doi: 10.1037/0735-7044.112.2.447.

Konorski, J. (1967). *Integrative activity of the brain*. Chicago: University of Chicago Press.

Limebeer, C. L., & Parker L. A. (2000). The antiemetic drug ondansetron interferes with lithium-induced conditioned rejection reactions, but not lithium-induced taste avoidance in rats. *Journal of Experimental Psychology: Animal Behavior Processes, 26,* 371-384. doi: 10.1037//0097-7403.26.4.371.

Limebeer, C. L., & Parker L. A. (2006). Effect of conditioning method and testing method on strength of lithium-induced taste aversion learning. *Behavioral Neuroscience, 120,* 963-969. doi: 10.1037/0735-7044.120.4.963.

Lin J.-Y., Amodeo, L. R., Arthurs, J., & Reilly, S. (2012). Taste neophobia and palatability: The pleasure of drinking. *Physiology & Behavior, 106,* 515-519. doi: 10.1016/j.physbeh.2012.03.029.

Lin, J.-Y., Arthurs, J., Amodeo, L. R., & Reilly, S. (2012). Reduced palatability in drug-induced taste aversion: I. Variations in the initial value of the conditioned stimulus. *Behavioral Neuroscience, 126,* 423-432. doi: 10.1037/a0027674

López, M., Gasalla, P., Vega, M., Limebeer, C.L., Rock, E.M., Tuerke, K. J., Bedard, H., & Parker, L.A. (2010). Latent inhibition of conditioned disgust reactions in rats. *Learning & Behavior, 38*, 177-186 .doi: 10.3758/L.B.38.2.177.

Lovibond, P. F., Preston, G. C., & Mackintosh, N. J. (1984). Context specificity of conditioning, extinction, and latent inhibition. *Journal of Experimental Psychology: Animal Behavior Processes, 10*, 360-375.

Lubow, R. E. (1989). *Latent inhibition and conditioned attention theory*. New York: Cambridge University Press.

Lubow, R. E. (2009). Conditioned taste aversion and latent inhibition: A review. In S. Reilly & T. R. Schatchman (Eds.), *Conditioned taste aversion. Behavioral and neural processes* (pp. 37-57). New York: Oxford University Press.

Neath, K. N., Limebeer, C. L., Reilly, S., & Parker, L. A. (2010). Increased liking for a solution is not necessary for the attenuation of neophobia in rats. *Behavioral Neuroscience, 124*, 398-404. doi: 10.1037/a0019505.

Parker, L. A. (1982). Non-consummatory and consummatory behavioral CRs elicited by lithium-paired and amphetamine-paired flavors. *Learning and Motivation, 13*, 281-303.

Parker, L. A. (1995). Rewarding drugs produce taste avoidance, but not taste aversion. *Neuroscience & Biobehavioral Reviews 19*, 143-151. doi: 10.1016/0149-7634(94)00028-Y.

Parker, L. A. (2003). Taste avoidance and taste aversion: Evidence for two different processes. *Learning & Behavior, 31*, 165-172. doi: 10.3758/BF03195979.

Parker, L. A., Limebeer, C. L., & Rana, S. A. (2009). Conditioned disgust, but not conditioned taste avoidance, may reflect conditioned nausea in rats. In S. Reilly & T. R. Schachtman

(Eds.), *Conditioned taste aversion. Behavioral and neural processes* (pp. 92-113). New York, NY: Oxford University Press.

Pelchat, M. L., Grill, H. J., Rozin, P., & Jacobs, J. (1983). Quality of acquired responses to tastes by Rattus norvegicus depends on type of associated discomfort. *Journal of Comparative Psychology*, *97*, 140-153. doi: 10.1037/0735-7036.97.2.140.

Reilly, S., & Schatchman, T.R. (2009). *Conditioned taste aversion. Behavioral and neural processes*. New York: Oxford University Press.

Spector, A. C., Klumpp, P. A., & Kaplan, J. M. (1998). Analytical issues in the evaluation of food deprivation and sucrose concentration effects on the microstructure of licking behavior in the rat. *Behavioral Neuroscience*, *112*, 678-694.doi: doi: 10.1037/0735-7044.112.3.678.

Spector, A. C., & St. John, J. (1998). Role of taste in the microstructure of quinine ingestion by rats. *American Journal of Physiology: Regulatory, Integrative and Comparative Physiology*, *274*, 1687-1703.

Wagner, A. R. & Brandon, S. E. (1989) Evolution of a structured connectionist model of Pavlovian conditioning (AESOP). In S.B. Klein & R.R. Mowrer (Eds.), *Contemporary learning theories: Pavlovian conditioning and the status of traditional learning theory* (pp. 149-189). Hillsdale, NJ: Erlbaum.

Yamamoto, J., Fresquet, N., & Sandner, G. (2002). Conditioned taste aversion using four different means to deliver sucrose to rats. *Physiology & Behavior*, *75*, 387-396. doi: 10.1016/S0031-9384(01)00671-0.