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journal homepage: www.elsevier.com/locate/l&mEnhanced latent inhibition in context aversion conditioning[☆]Geoffrey Hall^{a,*}, Michelle Symonds^a, Marcial Rodriguez^b^aDepartment of Psychology, University of York, YO10 5DD York, UK^bFaculty of Education and Humanities of Ceuta, University of Granada, Spain

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ABSTRACT

In four experiments, we investigated the effect of giving rats exposure to a distinctive environmental context before a phase of training in which an injection of LiCl was paired with that context. The results of Experiments 1 and 2 were consistent with the possibility that such preexposure served to retard subsequent conditioning to the context (i.e., produced a latent inhibition effect). Experiments 3 and 4 demonstrated that allowing the rats to consume a novel-flavored solution during preexposure enhanced the latent inhibition effect. The relevance of these findings both for theories of latent inhibition and for the use of preexposure as a clinical intervention for the reduction of conditioned nausea in humans is considered.

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Preexposure to the event that is to be used as the conditioned stimulus (CS) in a classical conditioning procedure usually retards subsequent conditioning—the well-known latent inhibition effect. The effect is exceptionally robust and has been demonstrated for a wide range of CSs and conditioning procedures (see Lubow, 1989). The experiments to be reported here were intended, first, to establish that the latent inhibition effect can be obtained in rats when the CS is a set of contextual cues and the unconditioned stimulus (US) is a state of nausea (induced by an injection of lithium chloride, LiCl). We then went on to investigate the proposal that the degree of latent inhibition might be enhanced by a procedure in which the CS is preexposed in conjunction with another, salient, cue. The basis for this proposal, which can be derived from an extension of the account of latent inhibition first put forward by Pearce and Hall (1980), is described in the introduction to Experiment 3.

That preexposure to a context might produce latent inhibition has practical as well as theoretical implications. One of the unwanted side-effects of cancer chemotherapy is that, after the initiation of a course of treatment, some patients come to experience nausea and vomiting when they return to the

[☆] We thank Jenny Wills for help in conducting Experiment 4.

* Corresponding author. Fax: +44 1904 433181.

E-mail address: g.hall@psych.york.ac.uk (G. Hall).

clinic (e.g., Andrykowski & Redd, 1987). The development of anticipatory nausea and vomiting (ANV) has been interpreted as being an instance of classical conditioning in which a context (the complex of stimuli that constitute the clinic) is a CS signaling the occurrence of a US, the state of nausea induced by infusion of a cytotoxic drug. The formation of this association allows the context to evoke nausea as a conditioned response (CR). (For reviews of evidence relevant to this analysis see Carey & Burish, 1988; Morrow & Rosenthal, 1996; Stockhorst, Klosterhalfen, & Steingrüber, 1998.) An implication of this interpretation of anticipatory nausea is that it should be possible to alleviate the problem by an intervention that acts to prevent or attenuate the formation of the association between the context and the US. In particular, it has been suggested that patients should be allowed to become fully familiar with the clinic before the start of treatment. Assuming that this preexposure to the clinic results in latent inhibition, the context–nausea association will be formed less readily and they will be less likely to suffer from anticipatory nausea (see Hall, 1997; Klosterhalfen et al., 2005).

The aim of the first two experiments reported here was to establish, using an animal model of context-evoked anticipatory nausea, that prior exposure to a context can indeed result in latent inhibition. Although it has been known for some time that contextual cues can become associated with drug-induced malaise (e.g., Best & Mickley, 1973), we have more recently developed a procedure that is intended to provide a closer parallel with the case in which patients develop ANV. In our procedure (Rodriguez, Lopez, Symonds, & Hall, 2000) rats are given an injection of LiCl immediately before being transferred to a novel and distinctive cage. They thus (as in the situation thought to give rise to ANV in the clinic) experience the nausea induced by the injection in the presence of the contextual cues provided by this cage. We have assessed the properties acquired by the contextual cues in two main ways. First, we have shown (Symonds & Hall, 2002) that the presence of these cues reduces the willingness of rats to consume a novel-flavored substance, an effect that matches the unconditioned response (UR) evoked by presentation of the US itself (i.e., by an injection of LiCl). This rejection of an otherwise palatable flavor is accompanied by the orofacial responses that have been taken to indicate a state of nausea in the rat (Limebeer, Hall, & Parker, 2006). Second, we have shown (e.g., Symonds & Hall, 1997) that the acquisition of a conditioned aversion to a novel flavor is blocked when conditioning is given in the presence of pretrained contextual cues. These observations are consistent with the view that the contextual cues have acquired the power to evoke a (conditioned) state of nausea. The experiments to be reported next make use of both these test procedures (the consumption test in Experiment 1; the blocking test in Experiment 2) to investigate the effects of preexposure to the context.

Experiment 1

Although, as we have already noted, latent inhibition has been readily demonstrated for a wide range of conditioning procedures, it is possible that context conditioning might constitute an exception. For this reason we adopted, in the present experiment, the most basic and straightforward experimental design, comparing just two groups, one given extensive exposure to the context prior to conditioning, and one given no preexposure. Only if it is possible to demonstrate a difference between these two groups will it be sensible to go on to further work to analyze the nature of the latent inhibition effect in this paradigm.

Our reasons for doubting the possible effectiveness of latent inhibition in context aversion conditioning were twofold. First, in unpublished studies from our laboratory (using, admittedly, rather short periods of preexposure) we have had difficulty in obtaining a reliable effect. Second, there are published studies on context conditioning, from experiments using shock as the US and freezing as the CR, that have shown that preexposure to the context can actually enhance rather than reduce the magnitude of the CR (e.g., Fanselow, 1990; Kiernan & Westbrook, 1993; Rudy & O'Reilly, 1999; Westbrook, Good, & Kiernan, 1994). This reversed latent inhibition effect has been explained in terms of the special properties of the context as a CS. As Rudy and O'Reilly (1999) point out, "a context" consists, in fact, of a complex and varied set of cues or elements; exposure to a context allows the possibility that these elements might be bound together in a representation of their conjunction. Conditioning will occur more readily, it is assumed, when the conjunctive context representation is available to the animal on the first conditioning trial. Kiernan and Westbrook (1993) offer much the same explanation

(although they express it in terms of standard associative learning theory; see McLaren, Kaye, & Mackintosh, 1998). They assume that the rats will be able to sample only a subset of the cues that make up the context at any one time. When animals are tested in the context after a conditioning trial, there is no guarantee that they will sample all the cues that were sampled and learned about on the conditioning trial, and the CR will be weak. Prior exposure to the context, however, will permit the formation of a network of associations among the contextual cues. Thus, even if a cue sampled on test is not one that was directly conditioned, it may, none the less, be able to make contact with the US representation by way of an associative link with one that was. The CR will be correspondingly more vigorous in animals given context preexposure.

Although this account is derived from studies of shock-based conditioning the processes described can be expected to operate in the context conditioning procedures of interest here. Whether any facilitatory effect of preexposure will outweigh that produced by the latent inhibition that the individual cues may be assumed to suffer, is an empirical matter. Kiernan and Westbrook (1993) found that facilitation occurred after relatively little preexposure (four 2-min trials) but were able to obtain latent inhibition with more extensive preexposure (four 20-min trials). Since the aim of the present experiment was simply to demonstrate the possibility that latent inhibition might occur with our own context conditioning procedure we chose to give extensive preexposure. Rats in the experimental condition were given eight 30-min sessions of exposure to the context before the conditioning trials in which the context was paired with an injection of LiCl. The question of interest was whether these subjects would show less evidence of context conditioning (i.e., less suppression of drinking on the consumption test) than control subjects that received the conditioning trials, but no preexposure to the context.

Method

Subjects and apparatus

The subjects were 16 male hooded Lister rats, with a mean ad lib weight of 415 g (range: 375–450 g at the start of the experiment). Throughout the experiment they were housed in pairs in their home cages where they were allowed continuous access to food. Access to water was restricted, as detailed below. The cages had walls and floor made of opaque plastic, and measured 35 × 22 × 20 cm. A layer of wood shavings covered the floor. The roof was made of wire mesh and held food and a water bottle (when available). The cages were situated in a colony room that was lit from 8.00 a.m. to 8.00 p.m. daily. Experimental treatments were given in a different set of cages (the context) located in a separate small room, dimly lit by a single 60-W red lamp, and containing a speaker which supplied a constant background white noise at 75 dBA, measured close to the cages. The walls and floor of these cages were made of transparent polycarbonate, and the roof of wire mesh with a hole through which a drinking spout could be inserted. The floors were covered with commercially obtained cat litter. The cages measured 30 × 18 × 18 cm. Fluids were presented by means of an inverted 50-ml centrifuge tube, equipped with a stainless steel, ball-bearing-tipped spout. Consumption was measured (to the nearest 0.5 g) by weighing.

Procedure

In order to establish a schedule of water deprivation, the standard water bottles were first removed overnight; for the rest of the experiment the rats were given access to water for two 30-min periods at 10.00 a.m. and at 5.00 p.m. After 2 days on this schedule the rats were randomly assigned to two groups of eight, and the preexposure treatment was initiated for the preexposed group. The rats were simply transferred to the experimental context cages for a 30-min session starting at 11.00 am on each of the next 8 days. Animals in the control groups remained in their home cages during this phase. It should be noted that water was not made available during the context exposure sessions, but was given in the home cage (at 10.00 a.m. for 30 min) prior to the experimental session. On the next day, all rats received an intraperitoneal injection of 0.15 M LiCl at 10 ml/kg of body weight, following which they were transferred for 30 min to the experimental context. After a recovery day in which no experimental treatments were given, all subjects received a further conditioning trial, identical to the first. After a further recovery day the rats were given a single test session. They were transferred at 11 a.m.

to the experimental cages where they were given access, for 30 min, to a drinking tube containing a solution of 3.4% sucrose (weight/volume).

Results and discussion

No data were recorded during the preexposure and conditioning phases. On the test session the control, nonpreexposed, group drank a mean of 7.3 ml (*SEM*: 0.66) of the sucrose solution. We take this low level of consumption (our previous experiments have shown that animals given this test without prior context conditioning drink at least 10 ml; e.g., [Rodriguez et al., 2000](#)) to indicate that the context had acquired aversive properties for this group. Rats in the preexposed group drank rather more (9.8 ml; *SEM*: 0.76), and the difference between the groups was statistically reliable, $F(1, 14) = 5.97$. (Here and elsewhere a significance level of $p < .05$ was adopted.) This outcome is what would be expected if the context was less aversive for the preexposed than for the nonpreexposed group. In the absence of a control group not given the conditioning procedure, we cannot know if the effect of preexposure is to abolish or merely to attenuate the effects of conditioning; but this result is consistent with the notion that some degree of latent inhibition can be obtained with this conditioning procedure, and is enough to encourage us to conduct further, more analytic, studies.

Experiment 2

The results of Experiment 1 are no more than consistent with the proposal that prior exposure to a context will produce latent inhibition; other interpretations are possible. For example, the training procedure used here means that preexposed subjects had experience of daily handling and received the final test in a context with which they were very familiar (control subjects remained in their home cages prior to conditioning and experienced the test context only twice, on the conditioning trials, prior to the test). If rats are less willing to drink in a novel than in a familiar context, this in itself could be enough to generate the difference between the groups obtained in Experiment 1. The observation that the neophobic response to a novel flavor is greater in a novel than in a familiar context ([Honey, Pye, Lightbown, Rey, & Hall, 1992](#)) adds weight to this suggestion.

To confirm that context aversion conditioning is susceptible to latent inhibition requires the use of a different test and in this experiment we turned to the blocking procedure (e.g., [Rodriguez et al., 2000](#); [Symonds & Hall, 1997](#)). In this procedure, the associative strength acquired by the context is assessed in terms of its ability to block the acquisition of an aversion to a novel flavor when the context and flavor are presented together and followed by an injection of LiCl. The aversion controlled by the flavor is then tested in a different context (the home cage) and thus test performance cannot be directly influenced by the familiarity of the test context. What is more, we might expect preexposure to the context to result in reduced consumption on the test (a context that has undergone latent inhibition will acquire little strength during conditioning and thus be poor at blocking the acquisition of an aversion by the flavor)—that is, the pattern of consumption on the test should be the opposite of that observed in the consumption test used in Experiment 1.

The design of the experiment is outlined in [Table 1](#). There were three experimental groups. As before we had an experimental group (group Eight in the table) given eight sessions of preexposure to the context and a control group (labeled None in the table) given no preexposure. We included a third group (Four), given four preexposure sessions, in order to see if a latent inhibition effect could be obtained with this reduced amount of preexposure. All received Li-context pairings of the context and an injection of LiCl, followed by a compound conditioning phase in which consumption of a sucrose solution (in the home cage) was followed by an LiCl injection and experience of the context. In the final test, sucrose was presented in the home cage. We expected, on the basis of our previous results, that the context would block acquisition of the flavor aversion in the group given no preexposure, and that therefore the rats in this group would drink sucrose readily on the test. Latent inhibition of context conditioning would be indicated if the groups given preexposure showed more of an aversion to sucrose (i.e., if the context was less effective at blocking the flavor aversion).

Table 1
Experimental designs

Group	Preexposure	Context conditioning	Compound conditioning	Test
<i>Experiment 2</i>				
None	—	Li–C	Suc–Li–C	Suc
Four	4 C->0	Li–C	Suc–Li–C	Suc
Eight	8 C->0	Li–C	Suc–Li–C	Suc
<i>Experiment 3</i>				
None	—	Li–C		Sal
Pre	6 C->0	Li–C		Sal
Pre (Sac)	6 C (Sac)->0	Li–C		Sal
Pre (H)	6 C (HCl)->0	Li–C		Sal
<i>Experiment 4</i>				
Pre (W)	4 C (W)->0	Li–C	Suc–Li–C	Suc
Pre (H)	4 C (HCl)->0	Li–C	Suc–Li–C	Suc

Note. C represents exposure to a distinctive context; Li, an intraperitoneal injection of lithium chloride given just before transfer to the context. In Experiments 3 and 4 some subjects were permitted to drink water (W), a saccharin solution (Sac), or a weak acid solution (HCl) during preexposure (Pre) to the context. Numbers refer to the number of preexposure trials. In Experiments 2 and 4, sucrose (Suc) was made available in the home cage; in Experiment 3, saline (Sal) was presented in the context.

Method

The subjects were 24 male hooded Lister rats with a mean ad lib weight of 376 g (range: 340–480 g) at the start of the experiment. After the deprivation schedule had been established, as in Experiment 1, the rats were divided into three groups of eight. One group received exposure to the context for 30 min each morning on each of the next 8 days; the second remained in the home cage for 4 days before four sessions of context preexposure were given; the third group received no preexposure to the context, but was maintained on the water deprivation schedule in the home cage. At the end of the preexposure phase, all the animals received two context conditioning trials in which exposure to the context followed an injection of LiCl. After a recovery day all subjects received a compound conditioning trial. On this they were given access to 15 ml of a 3.4% sucrose solution in the home cage for 30 min, starting at 11.00 a.m. They were then given an injection of LiCl prior to being moved to the context cages for the next 30 min. A further recovery day followed. During the final test phase, all subjects received access to the sucrose solution in their home cages on each of the next 3 days. Details not specified here were the same as those described for Experiment 1.

Results and discussion

No data were recorded during the preexposure and context conditioning phases. On the compound conditioning trial the subjects drank the sucrose readily and there was no difference among the groups. The group mean scores were 11.4 ml for the Eight group, 12.6 ml for the Four group, and 13.0 ml for the group given no preexposure ($F < 1$). This treatment successfully established an aversion in all groups. Group mean scores for consumption of sucrose presented in the home cage are shown in Fig. 1; it shows an initial suppression of consumption in all groups that waned over the course of the nonreinforced test trials. There was a clear difference among the groups, with the group given eight preexposure trials showing the strongest aversion, the four preexposure group somewhat less, and the no-preexposure group least of all. An ANOVA was conducted on the data summarized in the figure with group and trial as the variables. There was a main effect of group, $F(2,21) = 12.56$, and a main effect of trials, $F(2,21) = 59.51$. The interaction was not significant ($F < 2$). Pairwise comparisons using Tukey's test showed that each of the preexposed groups differed significantly from the nonpreexposed group, but that there was no difference between the two preexposed groups.

These results are what would be expected if preexposure to the context generated latent inhibition. In the group given no preexposure, the context conditioning trial would be capable of establishing a strong aversion to the context, with the result that the presence of contextual cues on the compound

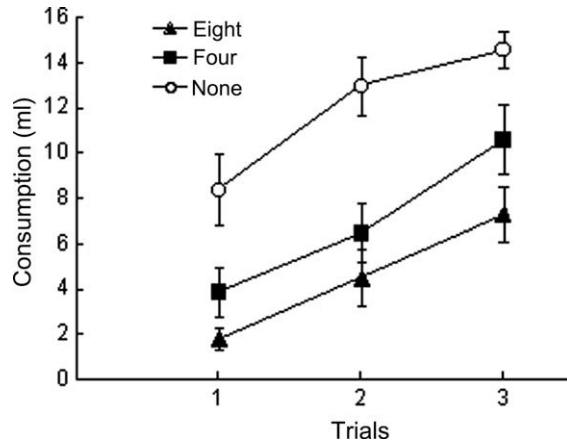


Fig. 1. Experiment 2: Mean scores (plus and minus SEMs) for consumption of a sucrose solution presented in the home cage. All subjects had received aversion conditioning with a compound of sucrose and a distinctive context. Prior to this, the groups had received different amounts of context exposure (none, four trials, or eight trials) and context aversion conditioning.

conditioning trials would be able to block acquisition of the aversion sucrose. Preexposure, by attenuating context conditioning, appeared to reduce the blocking effect and allow an aversion to sucrose to be established. The size of the aversion (and thus, the size of the latent inhibition effect) was greatest in the group given eight preexposures, but that seen in the group given only four preexposure was still substantial (and indeed these two groups did not differ significantly in their test performance). Taken together with those of Experiment 1, these results provide converging evidence to suggest that contextual cues may be susceptible to latent inhibition in this training paradigm.

Experiment 3

Experiments 1 and 2 provide evidence of the occurrence of latent inhibition of a context in context aversion conditioning. It may be noted, however, that a substantial amount of preexposure was required (and indeed, as we have already noted, in other experiments modeled on the procedure use in Experiment 1, we have found little sign of the effect in subjects given fewer than four preexposure sessions). This is a matter of practical concern if we want to use the latent inhibition procedure as a means for reducing context conditioning (and ANV) in the clinic—a busy hospital could not easily arrange for each patient to have eight sessions of preexposure to the clinic prior to the start of chemotherapy. What is needed is a procedure that will enhance the rate at which latent inhibition occurs.

One possibility emerges from the account of latent inhibition outlined by Hall (1991) on the basis of the model of conditioning proposed by Pearce and Hall (1980). According to the latter, the associability of a stimulus can be changed by experience; specifically, it will decline when the stimulus is consistently followed by a given consequence, and will fall to zero when it fully predicts that consequence. Hall (1997) conceptualized the latent inhibition procedure in the same general way, suggesting that nonreinforced preexposure involved a learning process in which the subject learns, over a series of trials, about the consequences of the stimulus (in this case that no event follows). In developing this interpretation, Rodriguez and Hall (in press) pointed out that it makes the prediction that latent inhibition should develop more quickly when the event to be used as the CS is presented in compound with another salient cue during preexposure. According to the Pearce–Hall model, the outcome of the trial (the occurrence of no event) will come to be predicted more readily in these circumstances, than when the target stimulus is presented alone. As a consequence the associability of the target stimulus will fall to zero during compound training in fewer trials than would be required if the stimulus was presented alone. Rodriguez and Hall acknowledged that such potentiation of latent inhibition might be found only with appropriately chosen stimuli, as the effect could well be

disrupted as a consequence of generalization decrement if the added stimulus interfered with the sensory or perceptual processing of the target stimulus; but they successfully demonstrated a potentiation effect with an odor as the target stimulus and a taste as the element added during preexposure.

In the present experiment, we applied the same strategy to preexposure in which the target stimulus was a context. There were four groups of rats (see Table 1), all of which received context conditioning followed by a consumption test, as in Experiment 1. As in that experiment, for one group the context was novel at the time of conditioning, whereas another group received prior exposure to the context. Because we were seeking to demonstrate a potentiation of latent inhibition we were concerned to use a level of preexposure that would produce some degree of latent inhibition, but not so much that an enhancement could not be observed. To this end, we chose six preexposure trials. The rats in the other two groups also received six context preexposure trials, but these subjects also experienced the concurrent presentation of what we assumed would be a salient stimulus, a novel flavor. The question of interest was whether the presence of a flavor during preexposure would increase the amount of latent inhibition obtained. For one group of rats the flavor used was the sweet taste of saccharin; for the other group it was the sour taste of acid. We chose acid for one of the groups on the basis of previous studies showing that this flavor is able to overshadow contextual cues when both are presented on a conditioning trial (Symonds & Hall, 1999)—according to the theory under investigation, the process that produces overshadowing during compound conditioning (a rapid decline in associability) should produce enhancement of latent inhibition with nonreinforced exposure to the compound. We used saccharin for the other group in the hope of demonstrating that any effect obtained was independent of the hedonic value of the flavor.

Method

The subjects were 32 male hooded Lister rats with a mean ad lib weight of 395 g (range: 350–450 g) at the start of the experiment. After the deprivation schedule had been established as in Experiment 1, the rats were divided into four groups of eight. Three groups received exposure to the context for 30 min each morning on each of the next 6 days; the other group remained undisturbed in the home cage over this period. Two of the preexposed groups received access to 15 ml of a flavored solution on each preexposure session. For one group the solution was of 0.1% (weight/volume) sodium saccharin; for the other group it was 0.01 M HCl. At the end of the preexposure phase, all the animals received two context conditioning trials in which exposure to the context followed an injection of LiCl. After a recovery day, all received a test session during which a saline solution (0.15 M) was made available in the context. Saline was used for the consumption test, rather than the sucrose used in Experiment 1, as in this experiment some of the subjects had already experienced a sweet solution

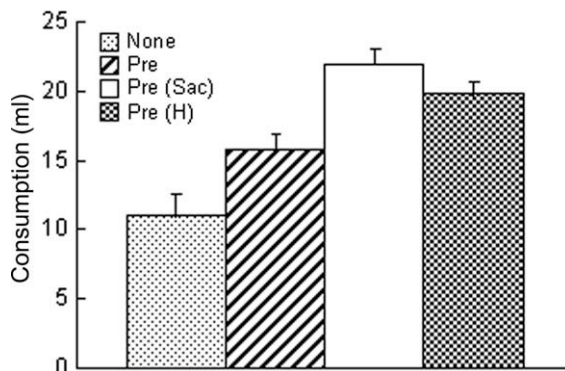


Fig. 2. Experiment 3: Mean scores (plus SEMs) for consumption of a sucrose solution presented in an aversively conditioned context. Prior to context conditioning the Pre groups had received six trials of preexposure to the context. For Pre(Sac) a saccharin solution was available in the context during preexposure; for Pre(H) an acid solution was available.

(saccharin) in preexposure. In other respects procedural details were the same as those described for Experiment 1.

Results and discussion

On the first day of context preexposure, the subjects drank less than the full amount of fluid made available; a mean of 9.6 ml for subjects for group Pre (Sac), and a mean of 8.9 ml for group Pre (H). There was a moderate increase in consumption over the course of preexposure, so that on the final day, consumption of the fluids offered to both groups had reached similar levels, group Pre (Sac) drinking 10.4 ml, and group Pre (H) drinking 10.5 ml.

The results of principal interest, group means for consumption of saline on the test, are shown in Fig. 2. It is evident that the group given no preexposure to the context consumed least and the difference between this group and that labeled Pre in the figure replicates the result obtained in Experiment 1. This difference, we have suggested, represents latent inhibition of context aversion conditioning in the preexposed group. The two groups allowed to drink a distinctive flavor during preexposure drank more than either of the other groups; that is, the context aversion appeared to be weak in these subjects, as would be expected if the presence of the flavor during preexposure enhanced latent inhibition. A one-way ANOVA showed there to be a difference among the groups, $F(3,28) = 14.73$. Pairwise comparisons using Tukey's test failed to reveal a significant difference between the Pre group and that given no preexposure (i.e., the basic latent inhibition effect was not statistically reliable in this case). There was, however, a significant difference between the None group and each of the other two preexposed groups, suggesting that latent inhibition had been potentiated in each of these groups. In addition there was a significant difference between the Pre(Sac) group and the Pre group.

Although the results just described are consistent with the proposal that consumption of the novel flavor during preexposure produced a potentiation of latent inhibition, we must consider alternative interpretations. One possibility is in terms of the effects that could be produced by the formation of associations between the context and the flavors presented in them. Most obviously, the formation of an association between the context and the sweet taste of saccharin might be capable of endowing the context with positive properties that would oppose the effect of later aversive conditioning, making the context a less aversive place on test, and promoting consumption. The fact that rats trained with the (somewhat aversive) acid solution also showed a high level of consumption on the test (relative to the group preexposed to the context alone) argues against this particular interpretation. It may be noted, however, that the rats were water-deprived during preexposure and so access to fluid, whether this was flavored with saccharin or with acid, would be likely to be a positive experience. This in itself might be enough to increase the amount consumed on the test in the rats given this preexposure treatment. Another possibility is that flavor neophobia contributed to the amount consumed by the various groups in the test. Although the test flavor (saline) was novel for all groups, those given flavors during preexposure had the opportunity to habituate any neophobic responses to acid or to saccharin. To the extent that this habituation generalizes to a novel flavor, we might expect such preexposure to result in a higher level of consumption of saline than would follow from exposure to the context alone. The next experiment was designed to address these possibilities.

Experiment 4

In this experiment, we attempted to replicate the central finding of Experiment 3, but with procedural modifications designed to help rule out alternative interpretations. As before one group received access to a novel-flavored solution (acid in this case) during preexposure to the context. The control group was given access to unflavored water in the context during this phase. Both groups, therefore, had the opportunity to form an association between the contextual cues and the alleviation of thirst. Additionally, in this experiment we used, not a consumption test, but the blocking procedure as described for Experiment 2. With this procedure, conditioning (and hence the degree of latent inhibition) is assessed by measuring the consumption of a fluid presented in the home cage, making direct associations between the context and other cues less likely to contribute to the outcome. Furthermore,

with this test procedure, latent inhibition would be demonstrated by a low level of consumption in the final test. If preexposure in the presence of a novel flavor enhances latent inhibition, we would expect consumption on test to be even lower in this case; generalization of the habituation of neophobia predicts the opposite result.

Method

The subjects were 16 male hooded Lister rats with a mean ad lib weight of 419 g (range: 360–460 g) at the start of the experiment. After the deprivation schedule had been established, the rats were divided in two groups of eight. One group, the Pre(W) group of Table 1, received exposure to the context for 30 min each morning on each of four consecutive days. A drinking tube containing 15 ml of water was available on each trial. The second group, the Pre(H) group of the table, was treated identically, apart from the fact that the drinking tube contained acid. We chose four preexposure trials for this study as the results of Experiment 2 (Fig. 1) showed that, with this test procedure, four trials will produce a substantial latent inhibition effect, but not one so strong that it is incapable of being enhanced (see the results for subjects given eight preexposures in Fig. 1).

All subjects next received two context conditioning trials in which exposure to the context followed an injection of LiCl, followed, after a recovery day, by a single compound conditioning trial. On this they were given access to 15 ml of a 3.4% sucrose solution in the home cage, followed by an injection of LiCl prior to being moved to the context cages for the next 30 min. During the test phase, given after a recovery day, the subjects received access to the sucrose solution in their home cages on three consecutive days. Details not specified here were the same as those described for Experiment 2.

Results and discussion

On the first day of context preexposure, the rats drank less than the total amount made available; a mean of 11.0 ml for the Pre(W) group, and 9.5 ml for the Pre(H) group. Consumption of water increased over the course of preexposure (reaching 14.3 ml on the final session); that of HCl did not (10.6 ml on the final session). The difference between the groups on the final session was statistically reliable, $F(1, 14) = 14.14$. On the compound conditioning trials all subjects consumed the sucrose solution readily, the group mean scores being 14.1 ml for the Pre(W) group and 13.6 ml for the Pre(H) group ($F < 1$).

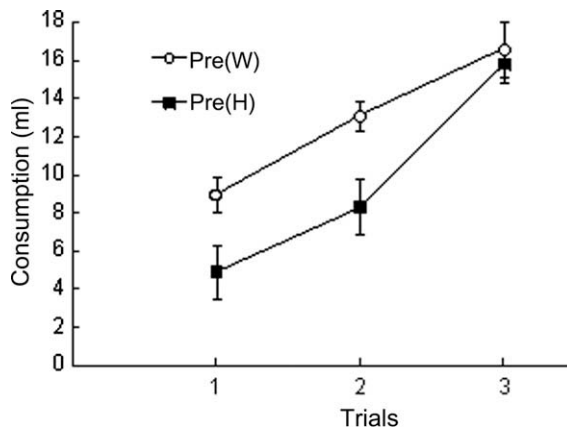


Fig. 3. Experiment 4: Mean scores (plus and minus SEMs) for consumption of a sucrose solution presented in the home cage. All subjects had received aversion conditioning with a compound of sucrose and a distinctive context. Prior to this, the subjects had received context aversion conditioning preceded by exposure to the context, with water available in the context for the Pre(W) group, and an acid solution available for the Pre(H) group.

Fig. 3 shows the amount of the sucrose solution consumed over the three test trials. Both groups showed evidence of an aversion, with consumption being suppressed on Trial 1, but recovering over the course of the test. The group given access to the flavored solution during context preexposure consumed less than the group given unflavored water. An ANOVA with group and trial as the variables showed there to be a significant effect of group, $F(1, 14) = 4.43$, of trials, $F(2, 14) = 106.32$, and a significant interaction between the variables, $F(2, 28) = 5.49$. An analysis of simple effects showed that the groups differed on Trial 1, $F(1, 42) = 5.67$, and on Trial 2, $F(1, 42) = 8.00$, but not on Trial 3 ($F < 1$).

The difference between the groups in their test performance is what would be expected if the presence of a flavored solution during preexposure enhanced latent inhibition to the context in the Pre(H) group. Enhancement of latent inhibition would result in poor context conditioning in the next phase of training. The context would then be less effective for that group than for the Pre(W) group in blocking the acquisition of an aversion to sucrose on the compound conditioning trial. The outcome would be the result obtained, a greater aversion to (less consumption of) sucrose in the final test. Taken together with those of Experiment 3, the results of this study provide support for the proposal of [Rodriguez and Hall \(in press\)](#), that the presence of a salient cue during preexposure will potentiate the acquisition of latent inhibition by another cue with which it is compounded.

General discussion

The first aim of these experiments was to demonstrate that preexposure to a set of contextual cues could retard context aversion conditioning (i.e., produce a latent inhibition effect). Evidence to support this view was provided by Experiment 1, in which the aversion controlled by the context was tested by assessing its ability to suppress consumption of an otherwise palatable solution. It was confirmed in Experiment 2, in which the strength of the context was measured by assessing its ability to block standard flavor-aversion conditioning. Neither of these experiments, on its own, provides indisputable proof of the existence of the effect, free from alternative interpretations. It may be noted, however, that in the first procedure the occurrence of latent inhibition was evidenced by a higher level of test consumption in the preexposed than in the nonpreexposed group, whereas the reverse was true with the second procedure. It cannot be argued, therefore, that the results are a consequence of some general change in levels of consumption produced by experience of handling during preexposure or by familiarity with the distinctive context.

The second aim was to investigate a possible procedure for enhancing the amount of latent inhibition produced by a given amount of preexposure to the context. According to the extension of the [Pearce and Hall \(1980\)](#) put forward by [Rodriguez and Hall \(in press\)](#), preexposure in which the target cue is compound with another salient cue might be capable of potentiating the extent to which latent inhibition occurs to the target cue. We tested this proposal, using a novel flavor as the added cue, with both the consumption test (Experiment 3) and the blocking test (Experiment 4). In both cases results consistent with a potentiation of latent inhibition were obtained. And again, the fact that the effect showed as an increase in consumption with one test procedure, but as a decrease in consumption with the other, helps rule out alternative explanations.

According to the analysis offered by [Rodriguez and Hall \(in press\)](#) the mechanism responsible for potentiation of latent inhibition is essentially that used by the [Pearce and Hall \(1980\)](#) model to explain overshadowing of conditioning. In both cases it is assumed that asymptote is reached more quickly when training is given with a compound cue than with just an element of the compound. At asymptote the associability of each element of the compound falls to zero. In the case of overshadowing this means that no more associative strength can be acquired, with the result that the CR acquired under these conditions will be weaker than that produced when the target element is conditioned alone. In the case of nonreinforced exposure, it means that negative transfer to subsequent conditioning (i.e., latent inhibition) will be evident after fewer trials when the target is exposed in compound with another. An implication of this analysis is that the combination of cues that is capable of producing an enhancement of latent inhibition should also result in an overshadowing effect when reinforced training is given; that is, the acquisition of a conditioned context aversion should proceed less readily when a salient flavor is made available on conditioning trials than when the context is presented alone.

At first sight, this prediction appears to be challenged by the results of several experiments claiming to show that the presence of the novel flavor during conditioning will actually potentiate rather than overshadow context conditioning (e.g., Best, Brown, & Sowell, 1984; Boakes, Westbrook, & Barnes, 1992; Mitchell & Heyes, 1996). But a review of the details of these and other related experiments led Symonds and Hall (1999) to the conclusion that the potentiation effect they demonstrated might be artifactual (specifically that direct generalization of the aversion established to the flavor present during training to the flavor subsequently in the test of context conditioning might be responsible for many of the results). Symonds and Hall conducted a series of experiments looking for the potentiation effect in a test procedure free from this potential artifact (they used the blocking procedure described for the present Experiments 2 and 4). They consistently found an overshadowing effect, using contextual and flavor stimuli that were the same as those used in the experiments reported here. The entire pattern of results therefore, is consistent with the predictions we have derived from the Pearce and Hall (1980) model.

Whether this interpretation of the potentiation effect can be shown to be correct will depend on the outcome of further research; but whatever its source, the results reported here encourage the conclusion that it may be possible to devise a form of the latent inhibition procedure that could be of clinical usefulness. The idea of applying latent inhibition in a clinical context is not novel (see, e.g., Lubow, 1998, for suggestions for applying the procedure in the treatment of fear and phobia); the results reported here encourage further exploration of the possibility that the latent inhibition procedure might also be developed as an intervention for the alleviation of anticipatory nausea. They suggest that, for rats, context aversion conditioning is indeed susceptible to latent inhibition, and that, under appropriate conditions, the effect can be obtained after rather few exposures. Preliminary work with human subjects (Klosterhalfen et al., 2005) indicates that parallel effects may be obtained with this species. But in the experiment just cited, nausea was induced by rotation, and the context was that supplied by the distinctive laboratory housing the rotation chair. It will need direct study to confirm that latent inhibition effects can be obtained when the context is a clinic and the nausea is induced by infusion of a cytotoxic drug.

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