Research report

Dorsal hippocampus inactivation impairs spontaneous recovery of Pavlovian magazine approach responding in rats

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HIGHLIGHTS

- Spontaneous recovery was observed for a distally but not recently extinguished cue.
- Dorsal hippocampal inactivation with muscimol eliminated spontaneous recovery.
- Dorsal hippocampus appears involved in controlling extinction by temporal context.

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ABSTRACT

Destruction or inactivation of the dorsal hippocampus (DH) has been shown to eliminate the renewal of extinguished fear [1–4]. However, it has recently been reported that the contextual control of responding to extinguished appetitive stimuli is not disrupted when the DH is destroyed or inactivated prior to tests for renewal of Pavlovian conditioned magazine approach [5]. In the present study we extend the analysis of DH control of appetitive extinction learning to the spontaneous recovery of Pavlovian conditioned magazine approach responding. Subjects were trained to associate two separate stimuli with the delivery of food and had muscimol or vehicle infused into the DH prior to a single test-session for spontaneous recovery occurring immediately following extinction of one of these stimuli, but one week following extinction of the other. While vehicle treated subjects showed more recovery to the distally extinguished stimulus than the proximal one, muscimol treated subjects failed to show spontaneous recovery to either stimulus. This result suggests that, while the DH is not involved in the control of extinction by physical contexts [5], it may be involved when time is the gating factor controlling recovery of extinguished responding.

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1. Introduction

When the rat is given repeated temporal pairings of a conditioned stimulus (CS) and an unconditioned stimulus (US), for example a tone and food, presentations of the CS elicit conditioned responding (CR), such as magazine approach. The learning that CS–US pairings produces is commonly understood in terms of new associative connections developing between neural representations of the CS and US. During an extinction phase, repeated nonreinforced presentations of the CS attenuate the propensity of CSs to elicit CRs. However, subjects tested

following a delay between extinction and the test session (e.g., 1 week) show a reemergence of CRs in response to the CS – an effect referred to as spontaneous recovery [6,7]. Some theoretical approaches to Pavlovian learning (e.g., [8]) assume that extinction only partially weakens the CS–US association, and the presence of spontaneous recovery confirms that the original learning was not completely abolished [9]. However, other findings suggest that under some circumstances associations can survive extinction treatments fully intact [10,11] and this result challenges the assumption that extinction results in at least partial weakening of the underlying CS–US association. Given such findings together with other key results reported in the literature (e.g., [12]), other mechanisms (e.g., contextual occasion setting, acquired context inhibition, attention decrements to the CS, inhibitory stimulus-response associations) are also currently thought to play a critical role in explaining extinction [9,13–15].

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While the study of extinction has exploded in recent years, much of this work has focused on the molecular mechanisms involved in response loss. Consequently, not as much attention has been devoted to the study of the neural mechanisms of related phenomena, like spontaneous recovery. To account for spontaneous recovery at the psychological level, many mechanisms have been proposed (reviewed by Robbins [16]). For example, Pavlov [6] suggested that a CS-focused “internal inhibition” process develops during extinction and may be more labile than an excitatory learning process that develops during initial training. If so, this more labile process would dissipate more completely over time, and this would lead to spontaneous recovery.

Another explanation of spontaneous recovery is that it is a special form of “renewal” [17–20]. The renewal effect refers to the finding that extinguished conditioned responding recovers when the CS is tested outside of the extinction context (e.g., [21]). That renewal and spontaneous recovery may be related is suggested by the fact that spontaneous recovery and renewal combine additively to test performance when the two are manipulated in the same experiment [22]. In order to account for the renewal effect, Bouton [18,19] suggested that during extinction training new inhibitory learning develops, and, further, that the extinction context gates the expression of this inhibitory learning through a “negative occasion setting” process (e.g., [48–50]).

Bouton [17–20] extended this analysis to explain spontaneous recovery by assuming that the time at which extinction takes place is processed by the animal as a type of context cue. Accordingly, spontaneous recovery occurs because the delay between extinction and test removes the organism from the temporal context of extinction, and, therefore, it removes the negative occasion setting that the temporal extinction context engages. Thus, while changes in physical contexts are responsible for renewal after extinction, the passage of time involves a change in temporal contexts and this promotes spontaneous recovery.

Neurobiologically focused studies of fear conditioning have begun to identify structures in the brain that are important for extinction and renewal phenomena and resemble the kind of modulatory mechanisms suggested by Bouton [23–25]. In particular, investigations of the renewal effect have suggested that the dorsal hippocampus (DH) is crucial for the expression of context-dependent extinction [1–3, 51]. When the DH is inactivated (and in some cases destroyed) prior to testing, differences in fear recovery to the CS across different contexts are no longer observed. These findings are commonly understood as implying that the DH is involved in the contextual modulation of extinction. However, while most of the supporting evidence comes from fear conditioning studies, Campese and Delamater [5] have shown recently that inactivation or destruction of the DH does not impair ABA or ABC renewal in an appetitive magazine approach task with rats. While these results conflict with the findings from the fear conditioning literature on DH function, it is worth noting that there have been no investigations of the role of the DH in spontaneous recovery either in aversive or appetitive tasks. Given our earlier findings of no effect on appetitive renewal, we may anticipate no effect of DH inactivation on appetitive spontaneous recovery as well. However, this presupposes that the neural networks mediating spontaneous recovery and renewal are one and the same, and this is unlikely, especially if temporal and physical contexts are differentially involved in these two phenomena.

In the present study the role of the DH was determined by inactivating the structure prior to a test for spontaneous recovery involving two stimuli, one extinguished proximally to the test, the other distally, as a within-subject manipulation. The design used here (see Table 1) was suggested by Rescorla [7] and ensures that both stimuli are tested in the same session, eliminating potential differences in various subject factors at the time of test

Table 1
Presents the design used. S1 and S2 were the 15 s stimuli (tone or light). Plus signs indicate reinforcement with food, while minus signs indicate nonreinforcement. Groups specified with MUS and VEH, received either muscimol or its saline vehicle into the dorsal hippocampus 15 min prior to tests. All phases of this study were conducted in the same physical context. ‘A’ refers to the acquisition and ‘Ext’ to the extinction phases. There were two of each of these phases, first for S1 and then for S2.

						Infusions
A1	Ext 1	Rest	A2	Ext 2	Test	
S1+	S1-	3 Days	S2+	S2-	(VEH) S1-, S2- ?	
					(MUS) S1-, S2- ?	

(e.g., general activity differences, maturational changes). One of the stimuli (S1) was conditioned for 3 days and then extinguished in a single session. Following a three-day break period a second stimulus (S2) similarly was conditioned for 3 days and then extinguished in a single session. Immediately following the S2 extinction session, subjects were removed from the chambers and either muscimol or vehicle was infused into the DH 15 min prior to being returned for a test session with both S1 and S2. Control subjects are expected to show more recovery to S1 than S2 because the test occurs outside of the temporal extinction context of S1 (one-week following S1 extinction), but within the temporal extinction context of S2 (immediately after the S2 extinction session). If the DH is important for temporal modulation of extinction, subjects with compromised DH function would be anticipated to show impaired spontaneous recovery, i.e., low levels of responding to both S1 and S2 during the test.

2. Methods

2.1. Experimental subjects

Subjects were 32 experimentally naïve Long–Evans male rats weighing between 295 g and 346 g at the start of the study. The subjects were bred and housed in standard clear-plastic tubs 10.5 in. × 19 in. × 8 in. with woodchip bedding within a colony room on a 14:10 light:dark schedule. Subjects had free access to water while in their home tubs and were maintained within a ±5 g range of their target weights with supplemental feedings of home cage chow given after experimental sessions on a given day. The study was run in two replications at different times with 16 animals in each. All methods employed here were approved by the institutional animal care and use committee at Brooklyn College which follows the recommendations set out in the *Guide for the Care and Use of Laboratory Animals*.

2.2. Surgeries

Subjects were anaesthetized using a 0.001% body weight injection of sodium pentobarbital at a 50 mg/mL concentration resulting in a dose of 50 mg/kg. Subjects were treated with a 1.35% body weight injection of atropine sulfate concentrated at 0.4 mg/mL 10 min following injection of the sodium pentobarbital in order to aid respiratory function. The scalp was then shaved and the rat placed in a Stoelting stereotaxic apparatus for implantation of bilateral guide cannulas (Plastics One: 22 gauge, 10 mm long beyond pedestal with a 5 mm separation). Lubricant was placed on the cornea to maintain moisture and the head swabbed with a 10% ethanol solution. An incision was made over the midline of the skull and the fascia pushed aside to reveal bregma and lambda. Once bregma and lambda were confirmed to lie on the same horizontal plane, the unit was calibrated for placement over the dorsal hippocampus by touching both tips of the cannula unit

onto bregma and recording the coordinates for each tip. Two holes were drilled over the dorsal hippocampus and an additional 4 holes were drilled around the unit for placement of jeweler's screws. The cannulas were placed at the following coordinates: 3.8 AP, 2.5 ML, 2.5 DV and then fixed into place using dental cement. Once the cement was dry the edges of the incision to the scalp were sutured and antibacterial ointment was applied to the wound. The guide cannulas were plugged with obturators (Plastics One: 24 gauge, projected 0.5 mm beyond tips of guide) and covered with a dust cap. Subjects were placed in a recovery area until locomotor activity was observed and then returned to their home tub for 1-week recovery with food freely available. Following surgery, obturators were changed every other day until the completion of the study.

2.3. Infusions

Infusions into the dorsal hippocampus were done one hemisphere at a time. A Hamilton syringe attached to PE 50 tubing was connected to a 28 gauge injector (Plastics One), which extended 1 mm beyond the tip of the guide cannula. For subjects in the first replication, the syringe was automated by a KD scientific pump; however, the syringe was operated manually in the 2nd replication. In both cases, 1 μ L of solution was infused into each hippocampus at a rate of 0.32 μ L/min when using the pump, or over a 40 s period when infused by hand. Subjects were restrained during this process and remained connected to the infusion line for an additional 2 min following each infusion to allow for diffusion of the drug. Muscimol was concentrated at 1 mg/mL in physiological saline. The order of infusion was counterbalanced across animals with regard to cerebral hemisphere.

2.4. Histology

Subjects were anaesthetized using the sodium pentobarbital and transcardially exsanguinated with 0.9% saline and perfused using a 10% formalin solution. When extracted, brains were cryoprotected in a 20% sucrose + 10% formalin solution and stored in 10% formalin until sectioning between 3 and 4 days later. Sections were cut 40 μ m thick and placed in distilled water for mounting onto 2% bovine gelatin coated standard microscope slides. The samples were stained with cresyl echt violet for nissl bodies using the standard protocol. Slides were held in xylene and then covered slipped using Permunt and let to dry. The locations of the infusions were assessed under an Optimus light microscope using Paxinos and Watson's [26] atlas of the rat brain as a reference.

2.5. Apparatus

Rats were trained in a set of eight identical standard BRS Foringer conditioning chambers (30.5 cm $\times$ 24.0 cm $\times$ 25.0 cm) that were housed in individual light and sound attenuating shells. The two end walls of each chamber were made out of aluminum, while the side walls and ceiling were made from transparent Plexiglas. The floors consisted of 0.60 cm stainless steel rods spaced 2.0 cm apart. A recessed food magazine measuring 30 mm $\times$ 36 mm $\times$ 20 mm (length $\times$ width $\times$ depth) was located on one end wall of the chamber 12.0 mm above the grid floor. Positioned approximately 3 mm deep on the side walls of the food trough and 3 mm above the base of the magazine were an infrared emitter and detector which enabled the automatic recording of head entries inside the magazine. Head entries into the magazine were registered by the breaking of the infrared beam in the food trough.

All of the conditioning boxes were equipped with a 7.6 cm diameter 8 ohm speaker (Radio Shack) mounted outside the magazine side of the chamber. This speaker delivered a computer generated

1500 Hz tone (T) amplified by a Radio Shack amplifier. The volume of the tone CS was 4 dB above the 78 dB background noise produced by fans mounted on the light and sound attenuated outer shells of the chambers for ventilation. The boxes also contained a 6 W light bulb (L) positioned at the base of the shell just behind the chamber. When activated these stimuli (T and L) remained on for fifteen seconds. Both stimuli terminated with the delivery of two 45 mg food pellets (Noyes, Formula A/I) delivered to the food magazine.

2.6. Magazine training

Subjects underwent 2 sessions of magazine training, with one session each day for two days. During each session, subjects had food pellets delivered to the food trough on a variable time 60 s schedule for 20 min.

2.7. Acquisition and extinction

S1 was trained on days 1–3. For half of the subjects S1 was the Tone CS, while for the other half S1 was the Light CS. In each session the 15 s CS was presented 20 times and reinforced with two food pellets presented at the offset of the stimulus. All sessions had an intertrial interval that averaged 3 min, with a range of 1–5 min. On day 4 the S1 stimulus was extinguished. Session parameters were identical to the training phase, except that the stimulus was presented without reinforcement. There was then a 3-day break period during which time the rats remained in their home cages. On days 8–10 the excitatory training of S2 occurred, followed on day 11, by the extinction of S2, which was accomplished exactly as described for S1. Immediately after this session subjects were infused and then tested.

2.8. Testing

There was a single test session that occurred on day 11. Immediately following the end of the extinction session for S2, animals were removed from the training chambers and given either vehicle or muscimol infusions into the DH (see above for details). Fifteen minutes following the infusions subjects were returned to the chambers and tested for spontaneous recovery to both S1 and S2. During this session, each stimulus was tested under extinction 8 times using the same average intertrial interval and range as the previous phases of the study. The order of stimulus presentations during the test session was T, L, T, L, T, L, T, L, T, L, T, L, T, L, T, L. Group assignments were made on the basis of average responding to S1 and S2 on the last day of training for each stimulus. Data from extinction were not used for matching due to the need to quickly remove, infuse and return animals to the conditioning chambers after the extinction of S2.

3. Results

Out of the 32 subjects that started this study, 7 were not included in the data. Five of the subjects reacted in a highly abnormal way to the infusions just prior to the test session. Specifically, rats either rolled over onto their backs repeatedly or they became very slow in their movements and were generally inactive. Two subjects from the control group and 3 subjects from the muscimol group were excluded due to these problems. The other two animals were excluded due to inaccurate cannula placement. Ultimately, 13 vehicle and 12 muscimol treated subjects were included in the analysis.

For all of the subjects, magazine training was successful as seen by subjects retrieving food from the magazine shortly after delivery.

Fig. 1. Depicts mean magazine responses during acquisition (left panel) and extinction (right panel) for S1 and S2 in difference score form (CS-Pre).

3.1. Acquisition and extinction

Magazine entry data from the acquisition and extinction phases are presented in Fig. 1 below in the form of difference scores (CS-Pre CS, both 15 s) for S1 and S2. The data are collapsed across replication because preliminary analyses showed that this factor did not significantly interact with CS or Block factors. While CRs increased over blocks during training for both CSs, responding to S2 was higher. This was very likely due to some form of stimulus generalization from prior training of S1 since S2 was trained second. This was confirmed by a CS (S1, S2) $\times$ Block (1–6) repeated measures ANOVA that revealed significant main effects for both Block, $F(5, 120) = 34.51$, $p < 0.01$, and CS, $F(1, 24) = 5.21$, $p = 0.032$. No significant CS $\times$ Block interaction was observed. During extinction, responding to both stimuli declined over blocks. The extinction data were analyzed in the same way as acquisition data. The analysis revealed a significant main effect for Block, $F(1, 24) = 18.849$, $p < 0.05$. Once again, no significant CS $\times$ Block interaction was observed, and additionally there was no significant CS main effect during extinction.

3.2. Test data

Magazine entry data from the test session are presented below in Fig. 2 in the form of difference scores (CS-Pre CS, both 15 s) during the two stimuli as well as during the 10-s post CS periods for the two stimuli. Post CS responding is sometimes used to reflect conditioning (e.g., [5]) since this period coincides with when the animals would normally be consuming the food US. Preliminary analyses showed no effect of replication, therefore the data were collapsed

Fig. 2. Depicts mean magazine responses during S1 and S2 for control subjects on the left and muscimol treated subjects on the right during the test session.

across this factor. The subjects infused with vehicle prior to testing showed more spontaneous recovery of magazine approach CRs to S1 than to S2 during the stimuli. Animals infused with muscimol did not show spontaneous recovery to S1 as responding was equally low in all recording intervals.

The data were analyzed using a CS (S1, S2) $\times$ Recording Interval (CS, Post CS) $\times$ Infusion (Mus, Veh) split plot ANOVA. This analysis yielded a significant main effect of Recording Interval, $F(1, 23) = 19.47$, $p < 0.01$, and a Recording Interval $\times$ Infusion interaction, $F(1, 23) = 7.76$, $p = 0.01$. Additional results of this analysis include a marginally significant main effect of Stimulus, $F(1, 23) = 4.169$, $p = 0.053$, a significant main effect of Infusion, $F(1, 23) = 7.812$, $p = 0.01$ and, most critically, a significant Stimulus $\times$ Infusion interaction, $F(1, 23) = 5.754$, $p < 0.05$. The Recording Interval $\times$ Stimulus $\times$ Infusion interaction was not significant. To assess the basis of the significant Stimulus $\times$ Infusion interaction separate one-way ANOVAs were conducted for each group with a pooled error term. Analysis of vehicle subject data revealed a significant overall main effect, $F(3, 36) = 12.012$, $p < 0.05$, and post hoc tests [27] showed that these subjects displayed more spontaneous recovery to S1 than S2, $F(3, 36) = 4.78$, $p < 0.05$. These post hoc tests also found that more responding was seen in CS compared to Post CS recording intervals $F(3, 36) = 6.47$, $p < 0.05$. No difference was found between S1 and S2 in the Post CS interval. A one-way analysis on the data from subjects infused with muscimol did not show a significant overall effect. Therefore, no further tests were conducted on these data. This analysis confirms the impressions of the data stated above.

The results of the analysis above confirm that more responding was seen to S1 than S2 for vehicle but not muscimol treated subjects, and this confirms that spontaneous recovery was only seen in vehicle animals. Another measure of spontaneous recovery involves a comparison between responding to each CS at the end of extinction and the start of testing. We observed that responding to S1 during the first test trial was significantly greater than during the last extinction trial, but only for subjects infused with vehicle, $t(12) = 2.37$, $p = 0.035$ (the means for S1 on the last extinction and first test trials, respectively, were: Vehicle = 3.1, 10.2, Muscimol = 6.0, 3.3). Responding to S2 did not show spontaneous recovery in either group. However, muscimol animals responded less to this cue on the first test trial than on the last extinction trial, $t(22) = 2.12$, $p = 0.045$ (the means for S2 on the last extinction trial and first test trial, respectively, were: Vehicle = 3.1, 3.7, Muscimol = 4.3, 0.0).

In order to determine if the disruptive effects of muscimol on spontaneous recovery may be related to a general reduction in responding, an additional analysis was performed on baseline (Pre CS) responding during the test session. This analysis found that subjects treated with muscimol showed somewhat higher baseline rates than vehicle subjects, $t(23) = 2.17$, $p = 0.04$ (Means: Vehicle = 0.6, Muscimol = 1.7), a result that is opposite to what would be expected if muscimol generally lowered responding. This confirms that muscimol's disruptive effects on spontaneous recovery were on the ability of S1, specifically, to elevate responding above baseline levels, and not to generally impair performance.

Results of the histological analysis are presented in Fig. 3 below, which shows the locations of the infusion sites for the subjects included in this study. The injection sites were mostly located around -3.36 posterior to bregma at the dorsal most portion of the hippocampus, with few sites found ventral to that boundary.

4. Discussion

Subjects infused with the saline vehicle prior to the test session displayed more recovery of magazine approach CRs to S1 than to

Fig. 3. Depicts the intracerebral infusion sites for subjects included in the study. Sites for subjects in the vehicle group during the renewal tests are represented by white squares and muscimol by black. The coordinates from which the atlas figures derive are found to the right of each atlas figure and are relative to Bregma.

S2. This result is consistent with previous findings of spontaneous recovery in this within-subjects experimental design [7]. Subjects infused with muscimol, however, failed to display such differences. These results suggest that the DH plays a role in spontaneous recovery in an appetitive task. However, the exact role is unclear.

One rather trivial explanation for our findings is that muscimol infusions may have exerted non-specific motor effects that reduced overall levels of magazine approach responding. While this possibility cannot be completely ruled out here, it is worth noting that elsewhere we found that with the same infusion parameters muscimol had no impact on magazine CRs in various renewal designs [5]. Further, in the present study muscimol did not reduce baseline (Pre CS) levels of responding during the test session, relative to vehicle animals. Thus, we think it is unlikely that this mechanism explains the present results.

As noted above, one popular approach to understanding spontaneous recovery is to regard it as a form of renewal. The design of the present experiment can be construed as an ABC versus ABB renewal design where S1 was conditioned in one temporal context (A), extinguished in another (B), and tested in a third (C), while S2 was conditioned in A but extinguished and tested in B. An alternative possibility would be an AAB versus AAA renewal design because training and extinction sessions were separated only by 24 h. In either case, the critical feature is that S1, but not S2, was tested outside of its extinction context. Therefore, the DH may be important in determining how temporal contexts modulate extinction learning in appetitive conditioning. For instance, the DH may be critical for control by a temporal negative occasion setting function analogous to that normally assumed to explain renewal effects

when physical contexts are manipulated [13,18,19]. It is interesting that in the present circumstance when S1 was tested in a different temporal context from extinction, the muscimol animals behaved as though the extinction memory was retrieved. Corcoran and Maren [1,2] and Maren and Hobin [4] also observed that the fear extinction memory seemed to be retrieved in DH-inactivated animals when tested either in the same or different physical context from extinction. In the absence of a fully functioning modulatory process, the animals may resort to their most recently experienced contingency.

A simpler explanation, perhaps, is that the DH may be important for recognizing that the temporal context at the time of test is different from that of S1 extinction. From that perspective, the test would functionally be occurring in the extinction context for DH-inactivated subjects and this would be expected to result in no recovery to S1. Other data suggest that discrimination of time, per se, is not influenced by hippocampal manipulations [28]. More specifically, Kyd et al. [28] showed that pretraining hippocampal lesions did not diminish the ability of animals to respond differentially after a trace interval to a stimulus presented at different durations (e.g., 10 versus 30 s). Thus, the hippocampus is unnecessary for rats to discriminate when a single stimulus is presented at two different short durations. In the present setting the animals were asked to discriminate between two different time periods in their life, separated by one week, and so it is possible that this type of temporal discrimination may engage the hippocampus whereas those over smaller time scales might not. We think this is unlikely, however, because Iordanova et al. [29] reported no harmful effects of hippocampal lesions on a relatively simple time of day discrimination. Nevertheless, it may be noted that a time of day discrimination is still shorter than that required in our spontaneous recovery experiment that was more on the order of a week, and so we cannot completely rule out this possibility.

Regardless of which of these two explanations – temporal context occasion setting or temporal context discrimination – may be correct, our findings reported here and elsewhere [5] suggest that spontaneous recovery and renewal phenomena may depend on different neural substrates in an appetitive learning preparation with rats. Whether or not these two phenomena have similar or different substrates in aversive learning situations is an open question. At the same time, however, while the present findings together with our renewal data [5] point to dissociable neural substrates for these two phenomena, these findings do not rule out the possibility that a similar psychological mechanism may be at the root of both of these recovery phenomena. Spontaneous recovery and renewal may both be dependent on the removal of the subject from an extinction context in order to promote response recovery. However, the DH may be involved in modulating appetitive extinction learning when the context is temporal over fairly large time scales and not physical (as in renewal). This idea is supported by findings from Honey and his colleagues ([29–31]) who showed that hippocampal lesions or inactivations impaired performance in a task in which time cues were jointly encoded with item and context information. Thus, the DH seems especially engaged by tasks that require hierarchical encoding of events with time cues (see also [32,52]), and this seems required of an occasion setting mechanism [13,18,19].

The present results suggest that the DH is involved in response recovery following extinction; however, they do not address how spontaneous recovery might arise at a neural network level. The neural mechanisms involved in extinction of conditioned freezing have been extensively reviewed elsewhere (e.g., [9,25,33,34]), and the conclusion in that system is that extinction works through interactions among the hippocampus [1,2,33,35], the infralimbic prefrontal cortex (IL), and the amygdala (e.g., [33,36–41]). The

hippocampus appears to be important for the contextual modulation of fear extinction memories [2]. When in the extinction context, the hippocampus might stimulate the IL, which, in turn, would suppress activity within the amygdala (e.g., [33]). The presence of direct projections from the hippocampus to the IL [42] supports this possibility [43]. In renewal or spontaneous recovery experiments, when testing occurs outside of the extinction context the hippocampus may not stimulate the IL, and this could result in renewal because amygdala neurons are not being suppressed. Spontaneous recovery may work in a similar way but where the hippocampus plays a key modulatory role for temporal contexts.

The circuitry involved in appetitive learning and extinction is far less well understood than is the aversive system [24,44]. However, Rhodes and Killcross [45,46] have demonstrated that the IL plays an important role in modulating appetitive extinction in rats, similar to what has been reported in fear conditioning (e.g., [35,47,53]). Thus, it remains plausible to think that hippocampal–IL–amygdala interactions may be responsible for spontaneous recovery in an appetitive task, even though the hippocampus appears to be less critical in appetitive renewal tasks [5].

In summary, the present study examined the role of the dorsal hippocampus in spontaneous recovery of an extinguished appetitively conditioned magazine approach response in rats. We observed that rats responded more to a stimulus that had undergone extinction one week prior to a test session compared to another stimulus that was extinguished immediately before the test. DH inactivation with muscimol prior to the test session eliminated this spontaneous recovery effect, suggesting that the DH may be especially involved in modulation of extinction learning by temporal context cues in an appetitive Pavlovian learning task. Further work will be required to more fully specify the neural circuits involved in spontaneous recovery in both appetitive and aversive Pavlovian conditioning paradigms.

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