Research report

Attenuation of context-specific inhibition on reversal learning of a stimulus–response task in rats with neurotoxic hippocampal damage

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Abstract

Rats with hippocampal or sham lesions were trained on a stimulus–response task developed for the 8-arm radial maze. After reaching a stringent learning criterion, different context manipulations were performed. In Experiment I, the different groups were transferred to an identical radial maze in a different room to determine the context specificity of the discrimination learning. Experiment I revealed that although rats with hippocampal lesions did not show a normal context detection effect, the expression of the discrimination was not context dependent for either the lesion or sham groups. In Experiment II, animals were trained to criterion on the discrimination task and then both groups were divided into sub-groups based on whether they would experience reversal training in the same or different context from original training. Experiment II indicated that animals with hippocampal lesions and shams reversed in a different context were significantly enhanced in reaching the learning criterion compared to either counterparts that were reversed in the same context. Reversal learning in rats with hippocampal lesions was faster than sham animals in the same context suggesting that the context-specific inhibition effect was hippocampal-based. After learning the reversal task, the groups of animals trained and reversed in different contexts were brought back into the original training context to test for competitive effects. Animals with hippocampal lesions that were reversed in the different context, did not show a competition between the most recently acquired discrimination and a context-specific association acquired during original training whereas sham animals in the same condition did. Taken together these results suggest that rats with hippocampal lesions do not acquire normal context-specific inhibition during discrimination learning.

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1. Introduction

There is evidence suggesting that the rat hippocampus is involved in place [45,47,41]; context [20,57]; and relational learning and memory [53,7]. Although debate persists on the precise conditions under which the rat hippocampus is critical for these paradigms, one theory suggests that rats with hippocampal damage have difficulty in acquiring these tasks when simple associative solutions are not available to them during training [44,58,35]. This view suggests that rats with hippocampal damage are impaired on these different categories of learning and memory paradigms (place, context, relational learning) because the computational requirements are similar. This critical computation may be the formation of a representation that encompasses various elements that define a specific event and the context in which it occurred [58]. In the intact animal, the hippocampus always appears to be encoding relationships among all elements of an experience into a representation of the event [33,16,43].

Early theorists have posited a general role for the hippocampus in a neural process similar to that of inhibition [10,29,17] in which associative processes lead to inhibition of behaviour because a conditioned stimulus (CS) becomes associated with non-reinforcement. This rather limited view of hippocampal function was initially abandoned and replaced by spatial, contextual, and relational theories of the hippocampus.
However, recent work suggests that the idea of the hippocampus being involved to some extent in inhibition of certain behaviors is worth reconsidering, and may not be entirely incompatible with more recent functions ascribed to the hippocampus. Of particular interest to the present study is the function of the hippocampus and the relationship between discrimination learning and reversal, as well as latent inhibition and context conditioning. Modern views of reversal learning suggest that it should be considered an interference paradigm because the original contextual cues of the testing situation are the same but the stimulus–response (S–R) requirements are different. That is, the context acts as a retrieval cue for the S–R memory and when the discrimination is reversed the context re-activates the old S–R representation thereby interfering with new learning in that situation [20,6].

One discrimination task that was developed for the eight-arm radial maze is an example of a task that lends itself to contextual manipulations because the task solution does not involve the use of spatial cues. Briefly, for this task lights were affixed along the inner side of each arm on the radial maze. On each day four of the eight arms were pseudo-randomly chosen to be lit and contained food. A rat was then placed on the central platform and allowed to forage throughout the maze. If a rat obtained a pellet from a lit arm the light for that arm would be turned off. Entries into the unlit arms were scored as errors. Following each training day, a new selection of baited arms was made. This task requires extensive amounts of training, the acquisition curve is slow, and is not dependent on stimulus-outcome associations [48,39,40,54] which taken together is consistent with the idea that this task is acquired in an incremental S–R manner [25].

Using the S–R task described above, McDonald et al. [36] have shown that reversal learning in this paradigm was enhanced when animals were reversed in a context that was different from the one used during original training. One possible explanation for the interference effect shown in the group of rats reversed in the same context is that an inhibitory association was accrued to the non-reinforced dark arm. A similar explanation is used for the well-known latent inhibition paradigm that is characterized by a behavioral profile of reduced conditioned responding to a CS that has a history of non-reinforcement.

Since evidence suggests that inhibitory associations acquired during latent inhibition training show strong context specificity [59,9,31,18] and the hippocampus has been implicated in context memory processes, the effects of hippocampal lesions on the context-specific inhibitory association found in the S–R task paradigm should be of considerable importance in understanding these processes and brain areas mediating such effects. Therefore, the purpose of the present experiment was to further evaluate the role of hippocampus in context detection, reversal learning and context-specific inhibition.

2. Materials and method

2.1. Animals and handling

Fifty-eight Long Evans male rats from Charles River colonies were used for the study. Upon arrival, animals were housed individually on a 12:12 light/dark cycle, and had food and water available to them ad libitum. A week following surgery animals were placed on a food deprivation schedule to reduce them to 90% of their free-feeding body weights. All rats weighed approximately 300–340 g at the beginning of the experiment. Animals were handled for 5 min each by the experimenter for 4–5 days prior to experimental training. During this handling phase each rat received 10 Fruit-Loops per day.

2.2. Surgery

Rats were divided into two groups; hippocampal lesions [32] and sham controls [26]. All animals were administered atropine (5 mg/kg body weight) in order to avoid respiratory problems, and then anaesthetized using sodium pentobarbital (65 mg/kg body weight) administered i.p. Valium (10 mg/kg body weight) was also injected i.p. to both groups prior to surgery to prevent the possible development of seizures in the lesion animals. During surgery drops of mineral oil were applied to the animal’s eyes for protection. Hair was removed from the top of the animal’s head with an electric shaver, and the scalp was cleaned with alcohol and betadine. Sham animals had their scalps cut along the midline, but no penetration of the brain tissue was performed. Bilateral neurotoxic lesions of the hippocampus were produced by using a 5 mg/ml solution of NMDA in pH balanced phosphate buffer injected over 3 min through 30-ga cannulae attached to a Harvard minipump. The injection coordinates were calculated from a level head with respect to bregma: 3.1 mm posterior (p), 1 mm lateral (l), and 3.6 mm ventral (v); 3.1 (p), 2 (l), 3.6 (v); 4.1 (p), 2 (l), 4 (v); 4.1 (p), 3.5 (l), 4 (v); 5 (p), 3, (l), 4.1 (v); 5 (p), 5.2 (l), 5 (v); 5 (p), 5.2 (l), 7.3 (v); 5.8 (p), 4.4 (l), 4.4 (v); 5.8 (p), 5.1 (l); 6.2 (v); 5.8 (p), 5.1 (l), 7.5 (v). Rats assigned to the hippocampal group received twenty injections (ten per side), the first eight injections were 0.25 ul, while the remaining two were 0.4 ul of NMDA solution. Each intra-cranial injection was infused at a rate of 0.20 ul/min. Animals were monitored until they were completely awake and...
active in their home cages. Following surgery animals were allowed 1 week to recover before training began.

2.3. Histology

On completion of behavioural procedures, each hippocampal lesioned animal was perfused intracardially with a 0.9% saline solution, followed by a 10% formalin solution. The brains were sectioned (40 micron section), and the tissue was stained with cresyl violet.

2.4. Apparatus

2.4.1. Training context A

An eight-arm radial maze constructed from wood and painted white was used as the experimental apparatus. The maze was elevated 60 cm from the floor. The centre platform was 40 cm in diameter, and each arm was 60 cm in length and 9 cm wide. Small light bulbs were affixed on the inner side of each arm, which could be turned on/off by a control panel, and a beige coloured food cup was located at the end of each arm. The maze was placed in a testing room that was 305 cm long and 216 cm wide. The north and east walls were covered with black plastic sheets, and a large blue circle (34 cm in diameter) constructed from cardboard was mounted on the west wall. A wooden partition was placed diagonally against the southwest corner in order to change the perceived shape of the room. Other cues in the room included an overhead lamp, a chair, a grey plastic pail and the experimenter (seated).

2.4.2. Training context B

A white eight-arm radial maze with identical dimensions as the one in context A was used as the apparatus. The training room was 360 cm long and 302 cm wide, all walls were beige and had wire mesh surrounding them. Extra-maze cues included a wooden stand against the west wall, a poster mounted asymmetrically on the north wall, and a poster mounted diagonally on the east wall. Other cues in the room included a black lamp (200 cm in height) located in the southeast corner, a chair, a grey plastic pail, a convex door, and the experimenter (seated).

3. Experiment I: context detection in S–R learning

McDonald et al. [36] have previously shown that the expression of a S–R task on the radial maze was not dependent on the context in which it was learned. Results suggested that transient disruptions in performance were likely due to a novelty effect associated with the new context, and this was confirmed by an additional experiment that showed no decline in choice accuracy scores or alterations in latencies when novelty was controlled for. In the present study, Experiment I was performed to determine whether rats with hippocampal lesions would detect a change in their training context, and to see if there would be any effect of a context-shift on the expression of the S–R task.

3.1. Procedure

3.1.1. Pre-exposure

For 2 days consecutively each animal was allowed to freely explore the radial maze located in room A for 10 min. No food cups or food were present on the maze, and all arm lights were turned off during this habituation session. After each rat was pre-exposed the maze was wiped down with a soap and warm water solution.

3.1.2. Acquisition

Thirty animals (16 hippocampals, and 14 sham controls) were trained to go to lit arms, which were baited with food, and to avoid darkened arms which were not baited. Throughout training, the lighting in the room remained dim to increase the salience of the lights on the maze. On each trial, four pseudo-randomly selected arms were lit, with a rule that no more than two adjacent arms could be lit, and food was placed into their food cups. Trials were run twice a day with each trial beginning when the rat was placed onto the centre platform facing the north wall. Immediately after the rat left a lit arm (indicated by front two paws outside the threshold of the arm), having eaten the food located there, the lights in that arm were turned off. The trial ended when all food reward was eaten or 10 min had elapsed. At the end of the first trial the animal was placed onto the experimenter’s arm and covered with a towel while the same four arm lights were turned on and food cups were re-baited. If 10 min had elapsed during the first trial the second trial was not run. After each animal, the maze was wiped down with a solution of soap and warm water to eliminate the possibility that rats were following scent trails from the previously trained rat. Latency to complete the task and all arm entries were recorded for each trial. An animal was considered to have been in an arm when all four paws were inside the threshold of the arm. Entries into unlit arms, and lit arms (when the food was not retrieved) were scored as errors. Choice accuracy scores were calculated by dividing the number of correct choices by the total number of entries and then multiplying by 100. Daily mean percent scores were calculated for each group. Trials were run until each group of animals reached a criterion of 85% or higher on their choice accuracy for 2 consecutive days.

3.1.3. Context shift

Each group of animals was divided into two subgroups by matching their choice accuracy percentages
over the last 2 days of training. One of the sixteen rats with a hippocampal lesion had to be eliminated from the study because of seizure activity that was observed during training. The remaining hippocampal group was subdivided into Group 1 = 87.27%, \( n = 7 \); Group 2 = 87.04%, \( n = 8 \), and the sham control group was subdivided into Group 1 = 85.19%, \( n = 7 \); Group 2 = 85.6%, \( n = 7 \). Groups 1 remained in the same context and were trained, using the same procedures as in acquisition, until the original training criterion was reached. Groups 2 were transferred to context B and were given identical training as Groups 1 until the original training criterion was met.

3.2. Results

3.2.1. Histology

Of the sixteen subjects that underwent hippocampal surgery four of them were dropped from the study. Two animals were eliminated from the analysis because of incomplete damage, and the other two because of seizure activity. Acceptable lesions were extensive and consistently large. Fig. 1 is a photomicrograph representing the extent of hippocampal damage in rats with neurotoxic lesions. One animal had very slight unilateral thinning of the cortex at the injection sites. The damage included extensive bilateral damage to both dorsal and ventral aspects of the structure. Five animals had some unilateral sparing of the most ventral aspects of the hippocampus. The neurons spared unilaterally in the ventral hippocampus of these five subjects resided exclusively in the CA3 or CA1 region. The subiculum was essentially unaffected in this group of animals except that some of the lesions encroached in the transition zone between hippocampus and subiculum \( (n = 4) \). The parahippocampal cortex (entorhinal and perirhinal cortex) was unaffected in this group of animals.

3.2.2. Statistics

All analyses were considered to be significant at the \( P < 0.05 \) level.

3.2.3. Acquisition

Fig. 2 represents the S–R task acquisition curves for sham and hippocampal lesion groups. As can be seen, the subjects with hippocampal lesions had higher
accuracy scores at the beginning of training. An ANOVA with repeated measures was computed on the 40 days of training required by the lesion group to reach criterion and indicated significant effects of Group $F(1, 24) = 5.16$, Day $F(39, 936) = 29.91$, and a Group × Day interaction $F(39, 936) = 1.93$. To assess whether the groups of animals were different throughout the acquisition phase, planned comparisons were performed on the beginning (day 1), middle (day 20) and end (day 40). This revealed that there were differences between the groups of animals at the beginning, but not by the middle, or end of training. Although the sham animals required more training to reach criterion, their accuracy scores remained high and consistent for the remaining trials.

3.2.4. Context shift

The effects of the context shift on expression of the S−R task in sham and subjects with hippocampal lesions can be seen in the top panel of Fig. 3. Clearly, the context shift had dramatic effects on performance of the sham animals as the group that were transferred to the different context exhibited a significant initial decline in accuracy scores. Interestingly, this pattern of data was not obtained with the lesioned animals. The context shift did not significantly alter choice accuracy performance in rats with hippocampal lesions. A three-way ANOVA with repeated measures on choice accuracy scores was conducted that confirmed these overall impressions and revealed significant effects of Group $F(1, 22) = 7.64$, Context $F(1, 22) = 6.36$, and a Group × Context interaction $F(1, 22) = 9.47$. Planned comparisons performed within the sham group (between context) indicated significant differences on the first and second day of the context shift. Although sham animals transferred to the different context required 10 days of training before reaching the criterion, their choice accuracy scores accelerated greatly and were above 80% on the third day following the context shift. This transient affect of the context shift was likely a result of novelty induced exploratory behaviour [36]. A similar analysis executed within the hippocampal group (between context) showed no significant differences in choice accuracy scores, as their performance levels remained high. The bottom panel of Fig. 3 represents the total amount of training required by all groups to reach the 85% criterion over two consecutive days. While this data clearly showed that the sham animals’ accuracy scores were transiently affected by the context shift, this context manipulation did not disrupt accurate responding in the lesion group.

In addition to choice accuracy scores, trial latencies were also analysed to evaluate performance following the context shift (Fig. 4). An ANOVA with repeated measures revealed significant effects of Day $F(2, 24) = 5.68$, and a Group × Day interaction $F(2, 24) = 8.63$, however, there was no effect of Group $F(1, 12) = 3.86$, $P > 0.05$). Planned comparisons revealed that sham and

![ACQUISITION (L+, D-)](image)

Fig. 2. Acquisition curves of the S−R task for rats with hippocampal lesions and sham controls on an eight-arm radial maze. During this discrimination turning into the light arm was reinforced (L+) and turning into the dark arm was not reinforced (D−). Choice accuracy scores were reflected as daily mean correct percentages (±SE). Rats with hippocampal lesions (dark circles) showed an initial acquisition enhancement when compared to sham animals (open squares) but by day 40 this effect was no longer present.
animals with hippocampal lesions were only different on day 1 of the context shift. A within group analysis performed on trial latency for the sham animals indicated significant differences when comparing latencies between the pre-shift and the shift (day 1) trial blocks, as well as differences between the shift block (day 1) and the post-shift block (day 2). However, no differences were obtained when comparing latency scores for the pre-shift and post-shift (day 2) trial blocks. The hippocampal group revealed a different pattern of results. Specifically, differences in trial latencies were only obtained when comparing the pre-shift with the post-shift (day 2) data blocks. This data suggests that although both groups were able to detect a
change in their training environment, the sham animals were more greatly affected by the context shift than the rats with hippocampal lesions.

One caveat concerning this data set is the fact that the lesion and sham groups required different amounts of training to reach the strict learning criterion on this task. This is clearly indicated in Fig. 1 in which the sham group took significantly longer than the hippocampal lesion group to reach criterion. This pattern of data might pose an interpretative problem because it is possible that fewer training trials might weaken the ability of a subject to detect a change in context. One piece of evidence against this interpretation of the difference found between the sham and lesion group is data found in the original study [36] reporting context effects on the S/C1/R habit task. This experiment showed that a group of animals, that reached criterion in 28 training days, which is 12 less days than required by the hippocampal group in the current experiment, showed a strong context detection effect. This data suggests that the number of training trials required to reach criterion is not a critical factor in determining whether a particular group of animals will show the context detection effect on this task.

4. Experiment II: effects of context on reversal learning of the S–R task

Previous work has shown that rats given reversal training in the same context, as original training, were impaired compared to rats reversed in a different context [36]. One interpretation of this pattern of data is that during initial acquisition in the original training context, an inhibitory association was acquired to the dark arm which interfered with reversal learning in rats remaining in that context [59,36]. We were interested in using this task on rats with hippocampal lesions to determine the effects of damage to this brain system on reversal learning in the same or different context from initial training.

4.1. Procedure

4.1.1. Pre-exposure and acquisition
Twenty-eight different animals (16 hippocampals, 12 sham controls) of approximately the same age and weights were used, and followed the same procedures used in Experiment I.

4.1.2. Reversal learning
Each group of animals were divided into two subgroups that were matched by their choice accuracy percentages over the last 2 days of training. One of the sixteen lesioned animals had to be dropped from the study because of seizure activity during the initial acquisition. The hippocampal group was subdivided into Group 1 = 89.92%, n = 7; Group 2 = 89.88%, n = 8, and the sham control group was subdivided into Group 1 = 90.78%, n = 6; Group 2 = 90%, n = 6. Groups 1 remained in context A and underwent reversal training until the same criterion was met. The same procedures were followed as in acquisition, except that food was placed into food cups of the unlit arms instead of lit arms. Immediately after an animal left an unlit arm, having eaten the food, the arm light was turned on. Groups 2 were transferred to context B and also underwent reversal training. The procedures were identical to that of Groups 1.

4.1.3. Competition
Previous results [36] have shown that rats reversed in a different context will show chance performance to the initial discrimination when brought back into the original context. The chance performance reflected a competition between what the animal had most recently learned and an existing representation that was associated with the original context. We were interested in determining whether rats with hippocampal lesions would also show a similar pattern of performance to the initial discrimination. Accordingly, animals (hippocampals and sham controls) that completed reversal training in a different context were transferred back to the original context. On the initial day four arms were lit, however, none of the arms on the maze were baited with food. For each trial a rat was placed onto the centre platform facing the north wall, and the first 8 arm

Fig. 4. Mean amount of time (s) required to complete a training trial (±SE) by rats with hippocampal lesions (dark circles) and shams (open squares) on the pre-shift, shift (day1), or post-shift (day2) data blocks.
entries were recorded. The rat was then placed onto the experimenter’s arm and covered with a towel before the second trial began. For the following days four arms were randomly lit and food was placed into their food cups to prevent extinguishing, or an inhibitory association from being attached to the light stimulus. The same training procedures as in the original learning phase were implemented for the proceeding 4 days.

4.2. Results

4.2.1. Histology

Of the sixteen animals that underwent hippocampal surgery two of them were eliminated from the study. One animal was removed because of extensive damage to temporal and perirhinal cortex, the other animal was dropped because of continued seizure activity. Acceptable lesions were extensive and consistently large. Fig. 5 is a photomicrograph representing the extent of hippocampal damage of rats with neurotoxic lesions. Three animals had slight thinning of the cortex at the injection sites. The damage included extensive bilateral damage to both dorsal and ventral aspects of the structure. Four animals had slight unilateral sparing of the most ventral aspects of the hippocampus that was found in the ventral CA3, CA1 region, and in one case the dentate gyrus. The subiculum was largely unaffected by this lesion procedure except for slight encroachment of the lesion border in the transition zone between the hippocampus and subiculum in some of the animals (n = 3). The parahippocampal cortex was unaffected by this lesion procedure.

4.2.2. Statistics

All analyses were considered to be significant at the $P < 0.05$ level.

4.2.3. Acquisition

Fig. 6 represents the learning curve for animals with hippocampal lesions and sham controls. As illustrated in this figure, animals with hippocampal lesions initially learned the S–R task at a faster rate, however, the sham animals progressed quickly and eventually reached the criterion first. An ANOVA with repeated measures on choice accuracy was performed on the 33 days necessary for the shams to acquire the visual discrimination task and revealed no significant effect of Group $F(1, 24) = 0.57, P > 0.05$, but a significant effect of Day $F(32$,
Fig. 6. Acquisition curves (L+, D–) for the S–R task for rats with hippocampal lesions and sham controls on an eight-arm radial maze. Choice accuracy scores were reflected as daily mean correct percentages (±SE). Rats with hippocampal lesions (dark circles) showed an initial acquisition enhancement when compared to sham animals (open squares) but by the middle of training this effect was no longer present. 768) = 54.30, and a marginally significant Group × Day interaction $F(32, 768) = 1.44, P > 0.05$ were obtained. To further evaluate the groups’ learning curves, planned comparisons were performed indicating significant differences at the beginning (day 1), but not at the middle (day 16) or end (day 33) of training. Despite the fact that animals with hippocampal lesions required more training, their remaining accuracy percentages were consistently high until they reached criterion.

4.2.4. Reversal acquisition

Once criterion was reached, both groups of animals either underwent reversal training in the same or different context. Fig. 7 represents the reversal learning curve for animals trained in the same or different context. As illustrated, animals reversed in a different context had higher choice accuracy scores and more readily reached criterion than their counterparts that remained in the same context. A Three-way ANOVA was computed on the 12 days required by the lesioned and sham animals to readily reach criterion and reversed in the same context. As can be seen in Fig. 7 the same and different context rats with hippocampal lesions showed a stronger perseveration for the original discrimination at the beginning of reversal training and this likely resulted in the statistical differences observed. As illustrated in Fig. 7, the groups of animals reversed in the different context were faster at reaching criterion than sham animals remaining in the same context.

Although the lesion rats reversed in the same context required more training then those that were transferred to another context, they were significantly faster at reaching criterion than sham animals remaining in the same context. As illustrated in Fig. 7, the groups of animals reversed in the same and different context had higher choice accuracy scores and more readily reached criterion than their counterparts that remained in the same context. A Three-way ANOVA was computed on the 12 days required by the lesioned and sham animals to readily reach criterion and reversed in the same context. As can be seen in Fig. 7 the same and different context rats with hippocampal lesions showed a stronger perseveration for the original discrimination at the beginning of reversal training and this likely resulted in the statistical differences observed. As illustrated in Fig. 7, the groups of animals reversed in the different context were faster at reaching criterion than the groups of animals remaining in the same context. It is important to note that this result can not be explained by suggesting that novelty to the...
different context could have facilitated reversal learning because McDonald et al. [36] have also shown enhanced reversal acquisition in a different context when exposure to both contexts were equated. Therefore, the observed enhancement likely resulted from the fact that the groups of animals transferred to a different context were able to learn the reverse contingencies away from contextual inhibition that would have been associated with the original training room.

In the same context, sham animals required substantially more reversal training than the lesion group to reach criterion. To further assess this data an ANOVA with repeated measures on choice accuracy scores was executed on the same context groups encompassing the 18 days required by animals with hippocampal lesions to reach criterion and revealed significant effects of Day $F(17, 187) = 23.37$, and a Group x Day interaction $F(17, 187) = 4.22$. Significant group differences were obtained at the beginning (Day 1) and end of training (Day 18). The difference obtained at the end of training can be clearly seen in Fig. 7, as the animals with hippocampal lesions were performing at higher levels than the sham animals by the 16th day of reversal, and quickly reached criterion thereafter.

4.2.5. Competition

Fig. 8 shows the choice accuracy scores to the initial S–R for groups of animals reversed in the different context when brought back to the original training context. As can be seen in this figure, sham animals displayed chance performance to the original S–R ($L+$, $D-$), whereas rats with hippocampal lesions perseverated on the most recently learned response. A One-way ANOVA was performed on the first 4 arm selections made on trial block one (no reinforcement), and indicated a significant effect of Group $F(1, 11) = 5.18$. An interesting pattern of results were obtained when a further analysis was performed on all eight arm selections, specifically, rats with hippocampal lesions showed a greater tendency to respond to the most recently learned association, whereas sham animals were more likely to enter arms not previously sampled, and this probably gave rise to the larger Group effect $F(1, 11) = 46.36$. The remaining days of competition testing were conducted with reinforcement associated with the original discrimination, and a repeated measures ANOVA on choice accuracy percentages revealed significant effects of Group $F(1, 11) = 44.33$, Day $F(3, 33) = 3.66$, and a Group x Day interaction $F(3, 33) = 3.93$. This pattern of data suggests that the sham, but not lesioned animals, showed a competition effect when brought back to the original training context. Presumably, rats with hippocampal lesions perseverated on the newly learned response because they did not have an existing representation associated with the original context competing for behavioural control.

![Fig. 8. Results of the competition test for rats with hippocampal lesions and shams that were given reversal training in a different context. Choice accuracy scores were reflected as daily mean correct percentages ($\pm 5E$). Animals with hippocampal lesions were represented with dark circles and shams with open squares. No food was present on the maze during the first trial block, but was associated with lit arms for the subsequent days of training ($L+$, $D-$).](image-url)
A caveat associated with the interpretation of Experiment I could be applied to the pattern of acquisition data found in Experiment II. As can be seen in Fig. 6, the hippocampal lesion group took longer to reach criterion than the sham group. Varying degrees of initial training between the two groups could provide an alternative explanation for the competition data. We have completed various lesion experiments using this paradigm since the data collected in the current paper and have not found a relationship between the number of training trials to criterion and the strength of the context-specific inhibition effect. For example, recent data obtained in our laboratory suggests that this is not the reason why the hippocampal lesion group did not show the normal competition effect. In that experiment, a group of normal animals required 40 training trials, which was 14 more training days than the lesion group, to reach criterion. These animals were still able to show a normal context-specific inhibition effect and competition, suggesting that the number of training trials needed to reach criterion is not a crucial factor in producing the inhibition or competition effects reported.

5. Discussion

The results reported in the present study support the idea that the hippocampus is involved in context-specific learning and memory processes. Experiment I showed that during a context shift, although choice accuracy scores remained high in animals with hippocampal damage their trial latencies was altered. Sham animals were more affected by the context shift as their choice accuracy and latency scores were transiently disrupted. These data are interpreted as evidence that shows that both groups of animals have a capacity to detect a change in their environment, however, S–R learning is not dependent upon the context in which it is learned. The results of Experiment II revealed that groups of animals reversed in a different context were faster in reaching criterion than groups of animals reversed in the same context. Presumably, this effect would have occurred because reversal learning was acquired in a context that was different from the one in which original learning took place. Interestingly, we also found that, in the same context, animals with hippocampal lesions showed enhanced reversal acquisition rates compared to sham animals. This suggests that sham animals are more affected by some context-specific inhibitory association than the lesion animals. Finally, groups of animals reversed in the different context were brought back to the original context to determine whether the context-specific inhibitory association, presumably attached to the dark arm in the original training context, would compete with the most recently acquired discrimination for behavioural control. Results indicated that sham animals showed a competition effect but the animals with hippocampal damage did not. A previous study has shown that this pattern of effects was not due to unequal exposure to the same and different context [36]. Taken together, results of these experiments suggest that although animals with hippocampal lesions have some form of a context representation (context detection), it is different than sham animals and appears to be incapable of supporting context-specific inhibition processes expressed during discrimination reversal learning and the competition test.

5.1. Context detection

Consistent with other reports [2,18,36] rats trained on discrimination tasks detected a change in the training context, but the learning was not context-dependent. This pattern of data is consistent with the idea that there are no context-US associations that modulate CS-US or S–R associations to produce discriminative behaviour in the discriminative task on the radial maze. The present findings indicate that rats with hippocampal damage showed an increase in trial latencies when the discrimination was performed in a new context. The increases in trial latency likely resulted from the fact that the animals with hippocampal lesions spent more time rearing and sniffing in the new environment. This pattern of behaviour in the lesion group is interesting when considered alongside a recent report demonstrating that rats with hippocampal damage showed dishabituated exploratory behaviour when a familiar chamber was moved into a new context [42]. One interpretation of the ability of rats with hippocampal damage to detect context manipulations is that the relational information is available to them but that this information does not have access to voluntary behaviour [42]. Alternatively, rats with hippocampal lesions might have another context representation available to them. The latter view is supported by recent reports that, under certain conditions (low cue ambiguity), the amygdala might support a primitive context representation [37,16,1]. It is also possible that there is another simple context representation based on circuits centered on the entorhinal cortex that is independent of this brain structures’ projections to the hippocampus [50]. Interestingly, this alteration in behaviour did not greatly affect performance of the visual discrimination task. A possible explanation for this apparent ability of lesioned animals to continue performing the discrimination, following the context shift, is that removal of the hippocampal-based learning and memory system enhances dorsal striatum-based control of voluntary movement [40], and would therefore compel the animals to enter the correct arms indicated by the appropriate stimulus feature.
5.2. Reversal learning

It is generally agreed that one functional effect of hippocampal damage in rats is impairments in discrimination reversal learning [20,44]. This effect has been used as empirical support for both behavioural inhibition, and spatial/contextual theories of hippocampus. Interestingly, rats with neurotoxic lesions of the hippocampus in the present study showed no impairments in discrimination reversal learning. A possible explanation for our inability to replicate this effect is that most of the studies reporting impairments have used electrolytic or aspiration lesions of the hippocampus or the fornix [30,55,46,61,5,12]. There is strong evidence to suggest that these lesion techniques can produce different effects on behaviour when compared to selective neurotoxic lesions of the structure [52,26,33,38,8,14,15]. The results of the present experiment are also inconsistent with demonstrations of enhanced contextual control over behaviour in rats with damage to the hippocampal system [61,62,60].

5.3. Context-specific inhibition effect

Why do control rats given reversal training in the original training context display a context-specific inhibition effect compared to the rats given reversal training in a different context when it was shown that the original discrimination was not context dependent? We have previously argued that this effect was due to the extra training required to extinguish the context-specific inhibitory association between the dark arm and non-reinforcement during original training [36]. In the present experiment, rats with hippocampal lesions given reversal training in the original context did not show this effect caused by the inferred inhibitory association. This is similar to various reports showing that rats with hippocampal damage are impaired on latent inhibition tasks in which the inhibition of learning might be based on a CS non-reinforcement association [24,34].

The present results also showed that rats with hippocampal lesions reversed in a different context did not show a competition effect when brought back to the original context. We have characterized the chance performance exhibited by normal rats on the competition test as being the result of a competition between the most recently learned response (L−, D+) and another representation linked to the original context. According to this view, animals that do not acquire this association would not show a competition effect and continue to use the most recently acquired S–R habit in the inappropriate training context. Indeed, rats with hippocampal lesions performed at very poor levels on the competition test suggesting that these animals did not have a neural representation affiliated with the original context competing with the dorsal striatal-based S–R habit system for behavioural control.

The assumptions in the current paper concerning what is learned about the non-reinforced dark arm during acquisition of the S–R task are tempered by a current lack of research using this paradigm, and discrimination reversal paradigms in general. For example, it is possible that the subjects in the current experiment are showing non-associative decrements in CS processing [56,19] and/or an avoidance habit to the dark arm [32]. However, even if this information was acquired, there is little evidence in the literature to suggest that either of these learning processes show context-specificity [23]. Our assumption that the dark arm has inhibition properties, similar to that found in latent inhibition paradigms, in the present experiments is not without empirical support in the current data set (context specificity) and other work in the literature, but further research will be required to confirm this hypothesis.

Another interesting issue concerning the context-specific inhibition effect reported here, is that it is difficult to ascertain whether the pre-training lesions affected the acquisition of the context associations, the nature of the S–R association, or the expression of these associations in behaviour. Future research using post-training manipulations and reversible lesions will help to clarify these issues [34,49].

5.4. Multiple functions of the hippocampus

New evidence points towards a multi-faceted role for the hippocampus that can be functionally differentiated in relation to its intrinsic anatomical structure [22,41,3,51,13–15]. The specific subsystems theorized by these research groups are different, in many cases incompatible and a serious analysis of these differences is beyond the scope of the present paper. Our working hypothesis is that each component of the three dimensional organization of the hippocampus is necessary for different classes of learned behaviours: (1) the dorsal hippocampus in highly efficient place navigation; (2) the longitudinal circuitry (association fibers) in the hippocampus being necessary for discriminative context-US conditioning; (3) and the ventral hippocampus in active inhibition of the amygdala-based learning and memory system. Further analysis of these possible subsystems within the hippocampus may broaden current understanding of the role for the hippocampus in CS-no event associations [27,24,34], negative occasion setting [23], decrements in CS processing [28,19] and conditioned inhibition effects [4]. The simple discrimination task developed for the radial maze exploited in the current set of experiments should prove to be an important addition to current paradigms used to address these important and complex research problems.
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