# Supporting Online Material for

## Paradoxical False Memory for Objects After Brain Damage

Stephanie M. McTighe, Rosemary A. Cowell, Boyer D. Winters, Timothy J. Bussey, Lisa M. Saksida*

*To whom correspondence should be addressed. E-mail: lms42@cam.ac.uk

Published 3 December 2010, *Science* **330**, 1408 (2010)
DOI: 10.1126/science.1194780

**This PDF file includes:**

**Supporting Online Material**

## 1. Materials and Methods

### Behavioral Experiments

### General Methods

### Subjects

In Experiment One the subjects were 23, and in Experiment Two 24 male Lister Hooded rats, weighing approximately 250-300 g at the start of testing. The rats were housed on a reversed 12 hour light/12 hour dark cycle (lights on 19:00-07:00), in groups of two. All behavioral testing was conducted during the dark phase of the cycle. Rats were food deprived to 85-90% of their free feeding weight, except during recovery from surgery where food was available *ad libitum*. Water remained available *ad libitum* throughout. All experimentation was conducted in accordance with the UK Animals (Scientific Procedures) Act 1986.

### Surgery

Rats were randomly assigned to receive either a sham or a peri-postrhinal (PPRh) lesion, which includes damage to the PRh, postrhinal, and entorhinal cortices, but not the hippocampus. We chose PPRh lesions because lesions centred on perirhinal cortex, combined with the object recognition task, has served as one of the predominant models of memory impairment (*S1*). It is unclear exactly what relative contribution perirhinal, postrhinal and entorhinal cortex lesions have on object recognition, what is clear is that hippocampal damage does not impair performance on this task when conducted using the same apparatus and object stimuli used in the present study (*S2, S3*). Therefore, the current model may best be considered a model not of dense global amnesia, but of the aspect of amnesia associated with impairments in recognition of objects and people. This is a critical function, the impairment of which causes untold distress in patients suffering from diseases such as Alzheimer's Disease.

Before surgery, all animals were deeply anaesthetized with 100 ml/kg Avertin [10 g of 2,2,2-tribromoethanol in 5 g of tertiary amyl alcohol, diluted in a solution of 40 ml of ethanol and 450 ml of PBS] and placed in a stereotaxic frame with the incisor bar set at +5.0. The scalp was incised and retracted to expose the skull. Craniotomies were performed bilaterally directly above the target region. Prior to each injection the dura was pierced to expose the cortex.

For the PPRh lesions, injections of 0.2 μl of 0.9 M NMDA (N-methyl D-aspartic acid) dissolved in sterile phosphate buffer (pH 7.4) were made using a 1 μl Hamilton syringe. Each animal received 5 injections to each hemisphere (see Table S1). Injections were made over 2 minutes at a rate of 0.1 μl/min, and the needle was left in situ for 4 minutes following each injection to allow for diffusion of the neurotoxin. Sham control animals received the same initial surgical procedure, including craniotomy, but no injections were performed.

At the completion of surgery, the scalp was sutured, and an antibiotic powder was applied. Animals were then administered sub-cutaneously with 5 ml of glucose saline.

### Apparatus

Decoupled delayed spontaneous object recognition was conducted in a Y-shaped apparatus, specifically designed to minimize the contribution of spatial and contextual cues (*S2, S3*). The apparatus had high, homogeneous white walls which prevented the rat from seeing out of the apparatus and viewing other stimuli in the room. This also directed the animals' attention to the objects. The walls were constructed from white Foamalux and were 40 cm high. Each arm was 27 cm long and 10 cm wide. The starting arm had a guillotine door, which was 18 cm from the end of the arm, forming a start box area where the rat was held before beginning the sample and choice phases. The apparatus was wiped clean with a dry paper towel between rats, but no other cleaning took place. A lamp illuminated the apparatus. Trials were recorded by a video camera mounted above the apparatus. There were four identical copies of each "junk object" used in the experiment, object heights ranged from 4 to 23.5 cm. All objects were firmly attached to the floor of the apparatus with Blu-tack to ensure the same view of the objects was always presented, and to prevent them from being displaced or knocked over. As far as could be determined, the objects had no natural significance for the rats, and they had never been associated with a reinforcer.

A specially designed visually restricted holding area was also used in this experiment. This comprised a cylindrical dark container made of black plastic, height = 69 cm, diameter = 39 cm, with a black material covering designed to keep out light. This holding area was cleaned between rats.

## Behavioral Testing

When the standard spontaneous object recognition procedure is used, the requirement that two items be simultaneously compared precludes determination of whether the novel item is viewed as familiar, or vice versa, as the amount of exploration to one objects affects the amount of exploration to the other (as both objects cannot be explored simultaneously), and the presence of one item affects how the other is evaluated. Thus, the effect of judging all stimuli as familiar rather than all as novel cannot be tested in the standard version of object recognition. We designed a novel variant of the task specifically for this reason.

### Decoupled Delayed Spontaneous Object Recognition Habituation

Rats received two days of habituation of five minutes before the start of object recognition. Animals were held in individual holding cages while habituation took place. Each rat was taken from the holding cage and placed into the start box, with the guillotine door lowered. The guillotine door was then raised by the experimenter, allowing the rat to enter the Y maze arena. Once the rat had fully exited the start box, the guillotine door was lowered and the rat was allowed to explore the arena for five minutes. After five minutes had elapsed, the rat was removed from the arena and returned to the holding cage.

After the first stage of object recognition, animals received ten days of habituation to the visually restricted holding area, prior to reduced interference object recognition testing. Each rat was taken from the holding cage and placed into the individual visually restricted holding area for a period of one hour. When one hour

had elapsed, the animal was taken from this holding area back to its individual holding cage.

**Decoupled Delayed Spontaneous Object Recognition Testing**

Trials consisted of two phases: the study and the test phase. In the study phase, two identical objects were placed in the apparatus, one at the end of each arm. Objects were wiped with 50% ethanol/water solution on a cloth before being put into the apparatus. The rat was placed in the start box with the guillotine door lowered. The door was then raised and the rat was allowed to enter the arena and explore for 3 minutes, timed from when the rat fully exited the start box. Exploration of a particular object was defined as the rat having its nose directed at the object at a distance of 2 cm or less, or touching the object with its nose. After 3 minutes, the rat was then removed from the apparatus and placed into a holding cage for one hour.

The test phase could take one of two forms – the "novel" condition or the "repeated" condition. In the "novel" condition, two identical novel objects would be placed in the apparatus. In the "repeated" condition, two new identical copies of the study object would be placed in the apparatus. New identical copies were used to prevent the use of olfactory cues. When the one-hour delay had elapsed, the rat was again placed in the start box with the guillotine door shut, then allowed to enter the arena and explore for another 3 minutes.

Animals were first tested on this standard version of the task for four daily trials; they were then tested for four days on the reduced interference version, and then placed back onto the standard version for another four days, for a total of 12 trials per rat. 12 object pairs were used, so each rat viewed a different pair each day. The order in which the rats received the 12 object pairs was counterbalanced across rats. The order in which rats received novel and repeated trials was counterbalanced within each four day subset, to ensure that each rat received two novel and two repeated trials in the standard condition, then two of each trial type in the reduced interference condition, etc. Which object of the pair was viewed in the study phase was also counterbalanced so that both objects were viewed an equal number of times in the study phase in novel and repeated trials.

We used a delay of one hour between study and test, a delay at least as long as those at which impairments in OR following this lesion have been observed previously (*S3*). It is well established in the literature that rats with PPRh lesions are not impaired on object recognition tasks at short delays (*S4, S5*), indicating intact basic perceptual function and short term memory ability.

**Reduced Interference Condition**

The current study was designed to parallel studies in human amnesics in which the "minimal interference" condition consisted of spending the delay in a dark, quiet room (see e.g., *S6*). Therefore, trials in the reduced interference condition were conducted identically to the standard version of the task, except that during the delay animals were taken from the Y apparatus and placed directly into the visually restricted holding area for one hour. After one hour, animals were taken directly from the visually restricted holding area, and placed into the test phase. Rats received four trials in this form; two "novel" trials and two "repeated" trials. Because we house our rats on a reversed 12 hour light/12 hour dark cycle, and all behavioral testing for this study was conducted during the dark phase of the cycle, it is highly unlikely that the rats were sleeping more in the visually restricted condition.

**Data Collection**

Exploration was recorded by the experimenter using a computer program written in Visual Basic 6.0. Two keys corresponded to the left and right objects. Object exploration in both the study and test phases was recorded by pressing the appropriate key at the onset of a bout of exploration and then pressing it again at the offset.

**Data Analysis and Statistics**

Total study and test exploration was calculated by the scoring program. Trials on which a rat had explored for less than 15 seconds in the study phase were excluded, as the rat was deemed not to have adequately explored the object for encoding. For each rat, the test exploration was expressed as a proportion of the study exploration by simply dividing test exploration by study exploration. Therefore a score of 1 corresponded to equal exploration in the study and test phases, whereas a score of 0.5 corresponded to the rat exploring half as much in the test phase as it had in the study phase. Each rat's average score for the novel and repeated conditions was calculated in each experimental stage (standard conditions stage 1; reduced interference; standard conditions stage 2), and these were used to compute a group average.

Repeated measures ANOVA with a within subjects factor of condition (novel, repeated) and a between subjects factor of lesion (peri-postrhinal, sham) was used to analyze the exploration score data for each of the three phases in experiment one, and experiment two. The same test was also done on the study exploration times as a control condition. Post hoc independent samples t tests using Bonferroni correction were performed on the novel and repeated conditions where a significant interaction was seen in the ANOVA.

**Histology**

At the completion of behavioral testing, rats were anaesthetized by IP injection with 2 ml of Euthatal and perfused transcardially with phosphate buffered saline (PBS), followed by 10% neutral buffered formalin. The brains were removed and postfixed in formalin for at least 24 hours before being immersed in 20% sucrose solution until they sank. Sixty μm sections were cut on a freezing microtome through the full extent of perirhinal and postrhinal cortex. Every fifth section was mounted on a gelatin-coated glass slide and stained with cresyl violet. Slides were examined under a light microscope to verify the extent of peri-postrhinal lesions.

**Results**

**Experiment One: Object Recognition under Standard Interference and Reduced Interference Conditions**

**Histology**

Lesion reconstructions are depicted in Figure S1. Two animals were excluded from the lesion group for having significant damage outside of the peri- and postrhinal cortices, leaving a group size of nine. Of the remaining animals, the lesion was much as intended; cell loss was observed throughout the rostral-caudal extent of PRh and continued caudally throughout PPRh. All had some bilateral damage to

lateral entorhinal cortex, with sparing of medial entorhinal cortex.. Eight showed some degree of incidental TE damage, one showed a small degree of unilateral mechanical damage to the overlying cortex, one showed unilateral caudate damage anteriorly, one showed a small amount of subiculum damage, and one showed partial amygdala damage bilaterally.

**Sample exploration**

For phase one (standard conditions), repeated measures ANOVA showed no effect of condition ($F_{(1,19)} = 2.83$, $p > 0.05$), no effect of lesion ($F < 1$) and no interaction ($F < 1$). For phase two (reduced interference), repeated measures ANOVA showed no effect of condition ($F < 1$), no effect of lesion ($F < 1$) and no interaction ($F_{(1.19)} = 3.62$, $p > 0.05$). For phase three (standard conditions – repeat), repeated measures ANOVA showed no effect of condition ($F < 1$), no effect of lesion ($F < 1$) and no interaction ($F < 1$).

**Exploration ratio data**

For phase one (standard conditions), repeated measures ANOVA showed a significant effect of condition ($F_{(1,19)} = 15.38$, $p < 0.001$), an effect of lesion ($F_{(1,19)} = 5.39$, $p < 0.05$) and a significant interaction ($F_{(1,19)} = 13.58$, $p < 0.005$). Post hoc t tests using Bonferroni correction showed a significant difference in the novel condition ($t_{19} = 3.88$, $p < 0.001$), and no difference in the repeated condition ($t_{19} = 0.76$, $p > 0.05$). For phase two (reduced interference), repeated measures ANOVA showed a significant effect of condition ($F_{(1,19)} = 18.33$, $p < 0.001$), no effect of lesion ($F < 1$) and no interaction ($F < 1$). For phase three (standard conditions – repeat), repeated measures ANOVA showed a significant effect of condition ($F_{(1,18)} = 33.97$, $p < 0.001$), a significant effect of lesion ($F_{(1,18)} = 14.59$, $p < 0.005$) and a significant interaction ($F_{(1,18)} = 16.17$, $p < 0.005$). Posthoc t tests using Bonferroni correction showed a significant difference in the novel condition ($t_{18} = 4.62$, $p < 0.001$), and no difference in the repeated condition ($t_{18} = 0.33$, $p > 0.05$).

## Experiment Two: Replication of Object Recognition under Standard Interference Conditions

**Histology**

One animal was excluded for having large bilateral damage outside of the peri and postrhinal cortices, leaving a lesion group size of eleven. Of the remaining animals, the lesion was much as intended; cell loss was observed throughout the rostral-caudal extent of PRh and continued caudally throughout PPRh. All had some bilateral damage to lateral entorhinal cortex, with sparing of medial entorhinal cortex. All showed some degree of incidental TE damage, and one animal showed a small amount of unilateral damage to CA1 in the hippocampus and subiculum.

**Sample exploration**

Repeated measures ANOVA showed no effect of condition ($F < 1$), no effect of lesion ($F_{(1,21)} = 1.89$, $p > 0.05$) and no interaction ($F < 1$).

**Exploration ratio data**

Repeated measures ANOVA showed a significant effect of condition ($F_{(1,21)}$ = 38.28, $p < 0.001$), no effect of lesion ($F_{(1,21)}$ = 1.09, $p > 0.05$) and a significant interaction ($F_{(1,21)}$ = 13.59, $p < 0.005$). Post hoc t tests using Bonferroni correction showed a significant difference in the novel condition ($t_{21}$ = 2.89, $p < 0.01$), and no difference in the repeated condition ($t_{21}$ = 1.54, $p > 0.05$). See Figure S2.

## Computational Simulations

### Stimuli

Four pairs of stimuli were used. In each pair, there was a four-featured sample object and a four-featured novel object; the two objects in a pair shared no features, reflecting a situation in which the objects are easily discriminable. Neither the sample nor the novel stimulus in any pair was replicated in any other pair, but individual features were allowed to appear in more than one object pair (*S7*). The stimuli were constructed according to the distribution of visual features likely to be found in a set of unique junk objects, such as were used in the rat experiments reported in this article.

### Object Recognition Task

There were two conditions: 'Standard Interference' and 'Reduced Interference'. In the Standard Interference condition, networks were presented with a number of interfering objects between encoding of stimuli and test of recognition memory. In the Reduced Interference condition, no interfering objects were presented. In both conditions, each network was tested on four object sets, to give four trials per network.

In the Standard Interference condition, on each trial, a network was exposed to the sample object and allowed to ‘encode’ the object for 20 cycles; as in (*S7*), each cycle sharpened incrementally the peak of activation representing the sample object. Following the sample encoding phase, each network was presented with 1200 interfering stimuli, each of which was encoded for a single cycle, before proceeding to the choice phase in which memory for the sample object was tested. As in (*S7*), the interfering stimuli were four-featured objects constructed from a limited pool of features (only sixteen values were available for each of the four features). Each interfering object was selected at random, with replacement, from the set of all possible four-featured combinations and presented for one encoding cycle each time it was selected. In practice, the set of possible four-featured combinations was so large that any one object was unlikely to be selected more than once during the delay. The final 'choice' phase of each trial occurred immediately after interference: each network was presented with both the sample and the novel object and the representations of the two objects were assessed to obtain an index of their relative familiarity, or 'recognition score'. At the beginning of each new trial, each network was reset to the state it had assumed at the end of pre-training.

In the Reduced Interference condition, networks proceeded directly from sample encoding to the choice phase, without interference. Trials were otherwise identical to those in the Standard Interference condition.

### Calculation of Exploration Time and Exploration Ratio

In previous publications with the same computational model, we have reported recognition scores analogous to the discrimination ratios reported in typical object

recognition tasks with rats. Because the present rat study employs a novel recognition memory paradigm in which, on any given trial, we measure the exploration of an individual stimulus rather than the relative exploration of two stimuli, we devised a new dependent variable from the model. 'Exploration time' was extracted from the model by taking the inverse of the familiarity index (*S7*) for a given stimulus. We report a ratio of choice exploration time to sample exploration time, where sample exploration time is the inverse of the familiarity index of a stimulus when it is presented following pre-training but prior to encoding, and choice exploration time is from the inverse of the familiarity index following encoding and, if applicable, interference.

**Networks and Lesions**

Two groups of six networks were tested: Group ‘Control’ consisted of networks that contained only the 'Perirhinal Cortex' layer; Group ‘Lesion’ consisted of networks that contained only the 'Caudal Layer', that is, networks were unable to use the stimulus representations in the 'Perirhinal Cortex' layer, in simulation of perirhinal cortex lesions. Each network was initialized and pre-trained before encoding of stimuli and testing of recognition memory began (*S7*).

In fact, there are two possible ways to simulate control networks: either reading out a familiarity signal from both caudal and perirhinal layers and taking the average of these; or reading out a familiarity signal from only the perirhinal cortex layer, since this component of the network provides the optimal information for discriminating the stimuli (as was done in generating the data in Figure S3). It is not clear which solution would be used by the brain, and therefore the choice between these two options for the calculation of control behavior is somewhat arbitrary. We simulated control networks in both ways, and found the general pattern of results to be the same in both the standard interference condition and the reduced interference condition. The principal difference between control networks constructed in the two ways is that exploration of the novel object in the 'Standard Interference' condition is lower in the case where control networks' behavior is dependent on both layers than in the case where control networks' behavior is generated by the perirhinal layer alone. This occurs because interference causes familiarity of the caudal representations to increase, and this increased familiarity comes to influence exploration behavior because the overall familiarity score is an average across the two layers; this contrasts with control networks containing only a perirhinal layer, in which the representations are not rendered more familiar by interference.

**Results**

The model simulation for standard interference (Figure S3A) predicts that control animals will explore the choice phase object more extensively on 'novel' trials than on 'repeated' trials. By contrast, it predicts that animals with perirhinal cortex lesions will explore the choice phase object to a similar degree regardless of trial type and that, importantly, their exploration of the choice object on novel trials will be lower than that of control animals. In other words, assuming exploration time is inversely related to familiarity, when the delay between sample and choice phases is filled with rich visual experience, the model predicts that lesioned animals will behave as though the novel object is familiar, rather than as though the familiar object is novel. The model simulation for reduced interference (Figure S3B) predicts a different pattern of results, namely that if animals are shielded from rich visual

experience to reduce interference, lesioned animals will show the same pattern of exploration as control animals, with greater exploration on 'novel' choice trials than on 'repeated' choice trials.

## 3. Supporting Figures

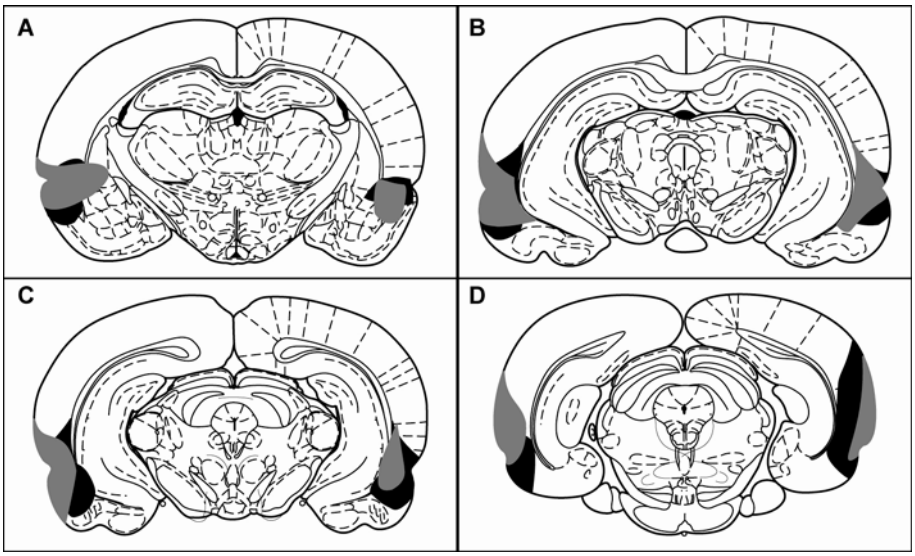


**Figure S1** Coronal sections illustrating the extent of the largest (black) and the smallest (gray) lesions of the perirhinal and postrhinal cortices. Damage was observed throughout, and is illustrated at: (A) bregma -3.14; (B) bregma -5.20; (C) bregma -5.80; and (D) bregma -6.80.

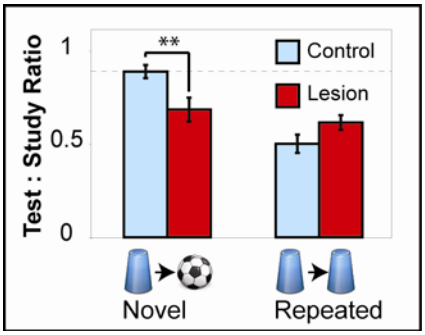


**Figure S2** Performance of rats with perirhinal cortex damage on the standard condition, with standard interference-filled delay, object recognition task (replication). (** = $p < 0.01$)

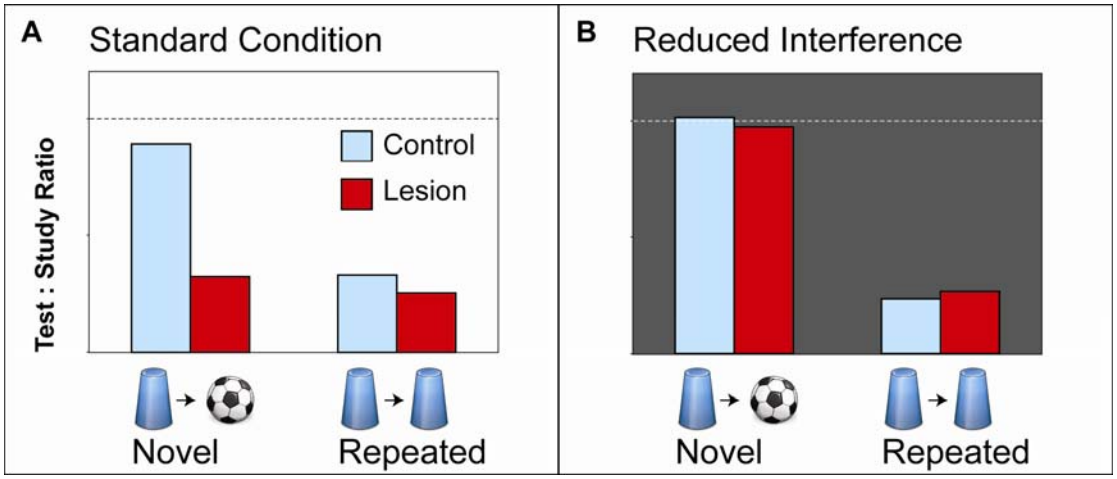


**Figure S3** (A) Computational simulations indicate that the prediction of the representational-hierarchical view is that an animal with damage to perirhinal cortex can be impaired at object recognition memory not because the familiar object looks novel, but because the novel objects looks familiar. (B) Blocking interference during the delay rescues the performance of the lesioned networks.

## 4. Supporting Tables

| Injection | Anteroposterior (mm) | Mediolateral (mm) | Dorsoventral (mm) |
|---|---|---|---|
| 1 | +3.9 | ±5.9 | +2.0 |
| 2 | +2.4 | ±6.1 | +1.6 |
| 3 | +0.6 | ±6.2 | +2.5 |
| 4 | -0.8 | ±6.2 | +2.7 |
| 5 | -0.8 | ±6.2 | +4.3 |

Table S1 – Injection coordinates for peri-postrhinal lesions (from (*S8*); distances in mm).

| Rat | Study Novel | Test Novel | Ratio Novel |
|---|---|---|---|
| 1 | 51.86 | 23.66 | 0.46 |
| 1 | 38.11 | 21.46 | 0.56 |
| 2 | 25.42 | 17.08 | 0.67 |
| 2 | 31.66 | 16.26 | 0.51 |
| 3 | 68.67 | 36.96 | 0.54 |
| 3 | 52.24 | 29.39 | 0.56 |
| 4 | 72.58 | 42.61 | 0.59 |
| 4 | 45.18 | 33.64 | 0.74 |
| 5 | 41.41 | 25.65 | 0.62 |
| 5 | 37.55 | 13.19 | 0.35 |
| 6 | 41.02 | 17.61 | 0.43 |
| 6 | 49.15 | 23.92 | 0.49 |
| 7 | 39.10 | 16.26 | 0.42 |
| 7 | 34.93 | 35.63 | 1.02 |
| 8 | 59.30 | 25.45 | 0.43 |
| 8 | 29.77 | 11.84 | 0.40 |
| 9 | 47.53 | 21.59 | 0.45 |
| 9 | 30.31 | 22.41 | 0.74 |

Table S2 – Standard Condition, Novel Trials, Peri/postrhinal lesion (PPRh) rats raw exploration data in seconds. In this and following raw data tables, any trial on which less than 15 seconds of exploration was recorded in the study phase has been excluded due to insufficient encoding of the study object.

| Rat | Study Familiar | Test Familiar | Ratio Familiar |
|---|---|---|---|
| 1 | 39.60 | 19.56 | 0.49 |
| 1 | 15.83 | 14.66 | 0.93 |
| 2 | 62.03 | 21.61 | 0.35 |
| 2 | 35.43 | 13.81 | 0.39 |
| 3 | 31.31 | 25.33 | 0.81 |
| 3 | 42.28 | 30.38 | 0.72 |
| 4 | 38.56 | 35.76 | 0.93 |
| 4 | 32.75 | 17.54 | 0.54 |
| 5 | 28.27 | 10.61 | 0.38 |
| 5 | 37.93 | 25.27 | 0.67 |
| 6 | 27.69 | 20.25 | 0.73 |
| 6 | 27.07 | 16.21 | 0.60 |
| 7 | 57.63 | 17.64 | 0.31 |
| 7 | 34.07 | 19.63 | 0.58 |
| 8 | 44.03 | 5.94 | 0.13 |
| 8 | 50.34 | 16.95 | 0.34 |
| 9 | 28.46 | 14.28 | 0.50 |
| 9 | 15.31 | 6.03 | 0.39 |

Table S3 – Standard Condition, Familiar Trials, PPRh rats raw exploration data

| Rat | Study Novel | Test Novel | Ratio Novel |
|---|---|---|---|
| 1 | 62.71 | 25.43 | 0.41 |
| 1 | 41.58 | 39.39 | 0.95 |
| 2 | 27.75 | 29.78 | 1.07 |
| 2 | 16.88 | 22.48 | 1.33 |
| 3 | 38.40 | 20.60 | 0.54 |
| 3 | 42.70 | 38.20 | 0.89 |
| 4 | 24.99 | 43.99 | 1.76 |
| 4 | 24.61 | 18.32 | 0.74 |
| 5 | 76.92 | 26.27 | 0.34 |
| 5 | 45.55 | 35.87 | 0.79 |
| 6 | 59.01 | 44.51 | 0.75 |
| 6 | 27.75 | 16.53 | 0.60 |
| 7 | 44.78 | 36.35 | 0.81 |
| 7 | 40.84 | 46.14 | 1.13 |
| 8 | 39.41 | 38.39 | 0.97 |
| 8 | 50.90 | 40.33 | 0.79 |
| 9 | 34.02 | 42.29 | 1.24 |
| 9 | 32.82 | 32.62 | 0.99 |
| 10 | 50.35 | 25.69 | 0.51 |
| 10 | 39.16 | 36.44 | 0.93 |
| 11 | 47.19 | 33.33 | 0.71 |
| 11 | 32.36 | 35.24 | 1.09 |
| 12 | 56.99 | 48.03 | 0.84 |
| 12 | 32.02 | 20.58 | 0.64 |

Table S4 – Standard Condition, Novel Trials, control rats raw exploration data

| Rat | Study Familiar | Test Familiar | Ratio Familiar |
|---|---|---|---|
| 1 | 42.47 | 15.38 | 0.36 |
| 1 | 32.89 | 15.18 | 0.46 |
| 2 | 56.57 | 30.62 | 0.54 |
| 2 | 48.09 | 27.65 | 0.57 |
| 3 | 51.10 | 20.60 | 0.40 |
| 3 | 44.09 | 27.75 | 0.63 |
| 4 | 40.65 | 12.95 | 0.32 |
| 4 | 35.87 | 12.80 | 0.36 |
| 5 | 40.26 | 12.70 | 0.32 |
| 5 | 16.59 | 7.02 | 0.42 |
| 6 | 30.16 | 14.82 | 0.49 |
| 6 | 58.06 | 13.33 | 0.23 |
| 7 | 41.93 | 20.19 | 0.48 |
| 7 | 42.03 | 15.47 | 0.37 |
| 8 | 46.39 | 25.41 | 0.55 |
| 8 | 18.00 | 19.36 | 1.08 |
| 9 | 48.09 | 21.82 | 0.45 |
| 9 | 23.50 | 14.62 | 0.62 |
| 10 | 34.87 | 20.01 | 0.57 |
| 10 | 34.82 | 9.82 | 0.28 |
| 11 | 32.03 | 15.13 | 0.47 |
| 11 | 29.55 | 20.40 | 0.69 |
| 12 | 32.76 | 15.76 | 0.48 |
| 12 | 20.32 | 12.60 | 0.62 |

Table S5 – Standard Conditions, Familiar Trials, control rats raw exploration data

| Rat | Study Novel | Test Novel | Ratio Novel |
|---|---|---|---|
| 1 | 23.51 | 21.78 | 0.93 |
| 1 | 17.96 | 25.05 | 1.39 |
| 2 | 29.44 | 31.81 | 1.08 |
| 2 | 52.99 | 18.81 | 0.35 |
| 3 | 64.07 | 51.44 | 0.80 |
| 3 | 34.14 | 30.59 | 0.90 |
| 4 | 51.85 | 40.94 | 0.79 |
| 4 | 34.53 | 32.17 | 0.93 |
| 5 | 23.12 | 11.54 | 0.50 |
| 5 | 57.63 | 41.62 | 0.72 |
| 6 | 38.15 | 24.19 | 0.63 |
| 6 | 32.30 | 37.14 | 1.15 |
| 7 | 33.88 | 35.16 | 1.04 |
| 7 | 36.44 | 24.35 | 0.67 |
| 8 | 24.59 | 28.24 | 1.15 |
| 8 | 39.88 | 26.19 | 0.66 |
| 9 | 19.65 | 26.13 | 1.33 |

Table S6 – Reduced Interference, Novel Trials, PPRh rats raw exploration data

| Rat | Study Familiar | Test Familiar | Ratio Familiar |
|---|---|---|---|
| 1 | 23.50 | 8.38 | 0.36 |
| 1 | 28.26 | 12.15 | 0.43 |
| 2 | 20.76 | 16.80 | 0.81 |
| 2 | 34.74 | 15.81 | 0.46 |
| 3 | 25.55 | 33.81 | 1.32 |
| 3 | 36.90 | 18.60 | 0.50 |
| 4 | 46.31 | 35.16 | 0.76 |
| 4 | 22.81 | 20.84 | 0.91 |
| 5 | 20.58 | 12.31 | 0.60 |
| 5 | 29.91 | 4.67 | 0.16 |
| 6 | 27.91 | 10.22 | 0.37 |
| 6 | 52.76 | 17.12 | 0.32 |
| 7 | 20.76 | 19.35 | 0.93 |
| 7 | 31.91 | 11.63 | 0.36 |
| 8 | 21.42 | 16.50 | 0.77 |
| 8 | 26.42 | 6.51 | 0.25 |
| 9 | 25.38 | 7.03 | 0.28 |

Table S7 – Reduced Interference, Familiar Trials, PPRh rats raw exploration data

| Rat | Study Novel | Test Novel | Ratio Novel |
|---|---|---|---|
| 1 | 52.23 | 13.18 | 0.25 |
| 1 | 42.83 | 16.22 | 0.38 |
| 2 | 19.45 | 22.30 | 1.15 |
| 3 | 28.07 | 29.50 | 1.05 |
| 3 | 36.82 | 16.20 | 0.44 |
| 4 | 17.09 | 25.02 | 1.46 |
| 4 | 30.25 | 18.58 | 0.61 |
| 5 | 21.39 | 19.23 | 0.90 |
| 5 | 42.24 | 34.70 | 0.82 |
| 6 | 26.39 | 21.30 | 0.81 |
| 6 | 45.77 | 37.29 | 0.81 |
| 7 | 15.22 | 15.33 | 1.01 |
| 8 | 30.01 | 34.10 | 1.14 |
| 8 | 16.36 | 19.69 | 1.20 |
| 9 | 22.98 | 26.44 | 1.15 |
| 9 | 37.61 | 23.36 | 0.62 |
| 10 | 31.60 | 12.63 | 0.40 |
| 10 | 25.72 | 16.36 | 0.64 |
| 11 | 36.99 | 40.16 | 1.09 |
| 12 | 20.28 | 15.59 | 0.77 |
| 12 | 48.88 | 45.22 | 0.93 |

Table S8 – Reduced Interference, Novel Trials, control rats raw exploration data

| Rat | Study Familiar | Test Familiar | Ratio Familiar |
|---|---|---|---|
| 1 | 24.47 | 12.36 | 0.51 |
| 1 | 58.78 | 18.66 | 0.32 |
| 2 | 49.23 | 17.08 | 0.35 |
| 2 | 62.99 | 17.46 | 0.28 |
| 3 | 42.42 | 15.58 | 0.37 |
| 3 | 23.62 | 11.45 | 0.48 |
| 4 | 15.87 | 7.32 | 0.46 |
| 5 | 38.79 | 9.05 | 0.23 |
| 5 | 46.63 | 42.01 | 0.90 |
| 6 | 48.68 | 11.84 | 0.24 |
| 6 | 39.49 | 13.83 | 0.35 |
| 7 | 26.26 | 18.08 | 0.69 |
| 7 | 21.42 | 5.63 | 0.26 |
| 8 | 20.45 | 14.78 | 0.72 |
| 8 | 32.20 | 7.24 | 0.22 |
| 9 | 23.49 | 19.76 | 0.84 |
| 9 | 43.51 | 12.72 | 0.29 |
| 10 | 34.90 | 28.55 | 0.82 |
| 11 | 20.13 | 1.04 | 0.05 |
| 11 | 20.92 | 1.72 | 0.08 |
| 12 | 15.44 | 25.23 | 1.63 |
| 12 | 44.27 | 18.60 | 0.42 |

Table S9 – Reduced Interference, Familiar Trials, control rats raw exploration data

| Rat | Study Novel | Test Novel | Ratio Novel |
|---|---|---|---|
| 1 | 26.98 | 25.92 | 0.96 |
| 1 | 20.36 | 17.11 | 0.84 |
| 2 | 18.07 | 7.55 | 0.42 |
| 3 | 30.87 | 23.30 | 0.75 |
| 3 | 34.87 | 24.84 | 0.71 |
| 4 | 16.67 | 5.84 | 0.35 |
| 4 | 36.80 | 14.87 | 0.40 |
| 5 | 29.46 | 13.41 | 0.46 |
| 6 | 42.55 | 16.14 | 0.38 |
| 6 | 24.65 | 19.16 | 0.78 |
| 7 | 20.39 | 17.03 | 0.84 |
| 8 | 16.31 | 11.10 | 0.68 |

Table S10 – Standard Condition (repeat), Novel Trials, PPRh rats raw exploration data

| Rat | Study Familiar | Test Familiar | Ratio Familiar |
|---|---|---|---|
| 1 | 15.78 | 5.89 | 0.37 |
| 1 | 22.03 | 16.92 | 0.77 |
| 2 | 21.97 | 6.75 | 0.31 |
| 2 | 27.75 | 8.73 | 0.31 |
| 3 | 30.14 | 16.83 | 0.56 |
| 3 | 22.80 | 16.42 | 0.72 |
| 4 | 27.27 | 16.72 | 0.61 |
| 4 | 39.23 | 16.95 | 0.43 |
| 5 | 27.53 | 14.67 | 0.53 |
| 5 | 15.25 | 7.70 | 0.50 |
| 6 | 45.75 | 13.50 | 0.30 |
| 6 | 34.68 | 17.65 | 0.51 |
| 7 | 18.25 | 11.97 | 0.66 |
| 7 | 24.10 | 12.29 | 0.51 |
| 8 | 23.05 | 10.56 | 0.46 |
| 8 | 28.65 | 17.37 | 0.61 |

Table S11 – Standard Condition (repeat), Familiar Trials, PPRh rats raw exploration data

| Rat | Study Novel | Test Novel | Ratio Novel |
|---|---|---|---|
| 1 | 37.00 | 31.35 | 0.85 |
| 1 | 29.72 | 22.46 | 0.76 |
| 2 | 25.38 | 16.11 | 0.63 |
| 2 | 38.97 | 36.15 | 0.93 |
| 3 | 21.48 | 17.13 | 0.80 |
| 3 | 28.40 | 38.42 | 1.35 |
| 4 | 15.17 | 22.25 | 1.47 |
| 5 | 29.56 | 45.29 | 1.53 |
| 5 | 17.78 | 26.53 | 1.49 |
| 6 | 29.17 | 23.72 | 0.81 |
| 6 | 27.46 | 37.55 | 1.37 |
| 7 | 18.28 | 19.23 | 1.05 |
| 8 | 25.31 | 44.85 | 1.77 |
| 8 | 20.23 | 30.20 | 1.49 |
| 9 | 36.03 | 31.42 | 0.87 |
| 9 | 23.07 | 33.22 | 1.44 |
| 10 | 27.08 | 27.27 | 1.01 |
| 10 | 31.49 | 34.33 | 1.09 |
| 11 | 21.17 | 23.44 | 1.11 |
| 11 | 46.00 | 29.27 | 0.64 |
| 12 | 25.73 | 32.57 | 1.27 |

Table S12 – Standard Condition (repeat), Novel Trials, control rats raw exploration data

| Rat | Study Familiar | Test Familiar | Ratio Familiar |
|---|---|---|---|
| 1 | 29.79 | 17.23 | 0.58 |
| 1 | 25.90 | 14.67 | 0.57 |
| 2 | 17.92 | 9.64 | 0.54 |
| 2 | 27.77 | 12.86 | 0.46 |
| 3 | 25.53 | 7.40 | 0.29 |
| 3 | 34.46 | 15.08 | 0.44 |
| 4 | 19.95 | 16.14 | 0.81 |
| 4 | 21.85 | 17.22 | 0.79 |
| 5 | 16.03 | 10.81 | 0.67 |
| 5 | 43.98 | 14.30 | 0.33 |
| 6 | 15.53 | 8.58 | 0.55 |
| 6 | 17.86 | 10.61 | 0.59 |
| 7 | 21.16 | 7.37 | 0.35 |
| 7 | 49.51 | 14.63 | 0.30 |
| 8 | 17.44 | 6.59 | 0.38 |
| 9 | 16.42 | 17.95 | 1.09 |
| 9 | 29.83 | 14.76 | 0.49 |
| 10 | 17.43 | 14.36 | 0.82 |
| 11 | 31.08 | 12.16 | 0.39 |
| 12 | 23.33 | 9.06 | 0.39 |

Table S13 – Standard Condition (repeat), Familiar Trials, control rats raw exploration data

## 5. Supporting References and Notes


S1. B. D. Winters, L. M. Saksida, T. J. Bussey, *Neuropsychologia*, (Feb 2, 2010).
S2. S. E. Forwood, B. D. Winters, T. J. Bussey, *Hippocampus* **15**, 347 (2005).
S3. B. D. Winters, S. E. Forwood, R. A. Cowell, L. M. Saksida, T. J. Bussey, *J Neurosci* **24**, 5901 (Jun 30, 2004).
S4. S. J. Bartko, B. D. Winters, R. A. Cowell, L. M. Saksida, T. J. Bussey, *J Neurosci* **27**, 2548 (Mar 7, 2007).
S5. A. Ennaceur, N. Neave, J. P. Aggleton, *Behavioral Brain Research* **80**, 9 (1996).
S6. N. Cowan, N. Beschin, S. Della Sala, *Brain* **127**, 825 (Apr, 2004).
S7. R. A. Cowell, T. J. Bussey, L. M. Saksida, *J Neurosci* **26**, 12186 (Nov 22, 2006).
S8. G. Paxinos, C. Watson, *The rat brain in stereotaxic coordinates*. (Academic Press, London, ed. third, 1998).