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# Supplementary Materials for

## Preserved visual memory and relational cognition performance in monkeys with selective hippocampal lesions

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**This PDF file includes:**

## Supplemental results and discussion

### Temporal Order

Although there were no robust post-operative group differences in how or how well monkeys with hippocampal damage solved temporal order problems, the statistically significant 3-way interaction between timepoint, group, and symbolic distance merited expanded exploratory analysis. Further analysis found a significant phase (pre vs. post lesion) x symbolic distance 2-way interaction ($F_{1,8}$ =29.013, p = .001), but no other 2-way interactions were significant (symbolic distance x group, and phase x symbolic distance, p > .05). Note that the significant two-way interaction does not involve lesion group specifically. Based on the significant 3-way interaction, we ran follow-up ANOVAs corrected for multiple comparisons (Bonferroni corrected $\alpha = .007$) to determine if particular symbolic distances drove this effect and found significant lesion x phase interactions only at symbolic distances 1 and 3 (SD 1: $F_{1,8} = 19.183$, p = .002; SD 2: $F_{1,8} = 7.478$, p = .026; SD 3: $F_{1,8} = 23.752$, p = .001; SD 0: $F_{1,8} = 0.113$, p = .745).

One possible explanation for the observed significant interactions is that monkeys with hippocampal damage performed poorly on the initial post-operative session but then improved. To investigate this hypothesis, we ran a repeated measures ANOVA on post-operative data which revealed no significant interaction of lesion x session: $F_{4, 32} = 1.323$, p = .283. When symbolic distance was included as a factor, the 3-way ANOVA was significant at conventional levels but just outside significance with the Bonferroni corrected $\alpha$ of .007: symbolic distance x post-operative session x lesion: $F_{5.148,41.182} = 2.438$, p = .008 (Figure S3), indicating that monkeys with lesions may have increased in accuracy over time but that this depends on the symbolic distance of the test items. Follow-up analyses revealed that this effect was driven by symbolic distance 3, which was the only symbolic distance that produced a significant session x lesion interaction: $F_{4,32} = 3.077$, p = .030 (SD 0, 1, and 2: p > .05). The relatively low accuracy in initial postoperative testing on the symbolic distance 3 tests may have been caused by differences in the extent to which working memory was sufficient to solve the task. Because the retention interval (RI) between images was 0.5 seconds, trials with shorter symbolic distance, and thus shorter delays, could have been solved with working memory, whereas the longer symbolic distance 3 trials potentially could not. In contrast, the RI used in the analogous rodent studies was 2.5 mins, which may indicate the involvement of the hippocampus only at longer RIs (7). However, fornix transections in monkeys produced a memory deficit with a RI of just 1 second (44), implicating the hippocampus even at short RIs. So, it is unlikely that the small differences in RI caused by differences in symbolic distance are relevant to interpreting these findings. Also note that SD 3 trials are the easiest trials, and therefore not necessarily where a lesion effect would be most expected. Regardless, a memory loss at one symbolic distance that abates within a few days is

inconsistent with the prediction of amnesia. A second explanation for the three-way interaction effect is that it represents a Type I error. If lesions had a robust effect on temporal order memory in this task, we would expect to see a significant group difference on post-lesion accuracy, but we found no such effect (see main text, Figure 3, and Figure S3).

Overall, we interpret these results as showing a lack of robust evidence that the hippocampus contributes to performance on this temporal order task, but the evidence for a transient effect on some trial types indicates a need for more research.

Simultaneous Chaining

For within-list performance, a repeated-measures mixed ANOVA revealed a 3-way interaction, suggesting that accuracy might differ between lesion groups as a function of the combination of test time (pre vs. post lesion) and symbolic distance: group (control vs. lesion) x phase (pre vs. post-operative) x symbolic distance: $F_{3,24} = 4.35$, $p = .014$; Figure 8A. However, this 3-way interaction was not significant when we used a corrected alpha level to protect against the multiplicity inherent in multiway ANOVA (69) (Bonferroni corrected $\alpha = .007$). There was a main effect of symbolic distance ($F_{3,24} = 25.30$, $p < .001$) but no other main effects or 2-way interactions were significant ($p > .05$). Thus, it is unlikely that the three-way interaction is the result of the hippocampal lesions.

For between-list performance, a repeated-measures ANOVA revealed no significant three or two-way interactions ($p > .05$), indicating no effect of lesion on accuracy: group (control vs. lesion) x phase (pre vs. post-operative) x symbolic distance: $F_{2.364,18.111} = 0.07$, $p = .948$; Figure 8B. There was a significant main effect of phase ($F_{1,8} = 5.94$, $p = .041$) and symbolic distance ($F_{1.549,12.390} = 19.63$, $p < .001$), revealing that all monkeys regardless of group decreased slightly in accuracy after surgery but still showed a robust SDE throughout testing.

As described in the main text, these results indicate that the hippocampus is not necessary for successfully executing well-learned lists from long-term memory and, critically, flexibly ordering images from within or between lists on probe test pairs.

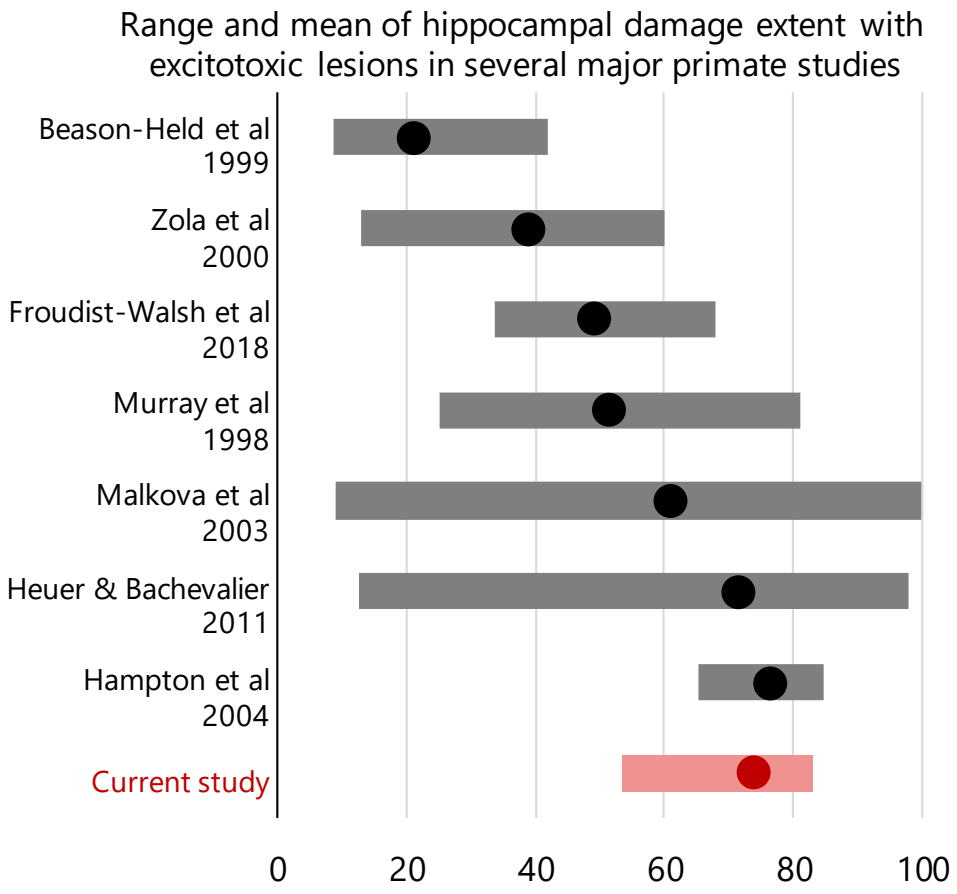


**Figure S1. Lesions in this study compared favorably to those in other published reports**. Mean (dots) and range (bars) of several major studies of neurotoxic hippocampal lesions in monkeys.

**Table S1. MRI estimated hippocampal damage**

| Monkey | Surgeries | % Volume reduction[a] | | | % Estimated damage[b] | | |
|---|---|---|---|---|---|---|---|
| | | Left | Right | Total[c] | Left | Right | Total[c] |
| Ap | 2 | 61.2 | 59.1 | 60.2 | 77.6 | 74.9 | 76.3 |
| Be | 1 | 42.8 | 59.0 | 50.7 | 53.4 | 74.8 | 63.7 |
| Ne | 1 | 60.8 | 56.2 | 58.6 | 77.1 | 71.1 | 74.2 |
| Es | 2 | 43.0 | 49.0 | 46.0 | 53.6 | 61.5 | 57.5 |
| Mi | 2 | 60.5 | 65.2 | 62.8 | 76.7 | 83.0 | 79.8 |
| **MEDIAN** | | **60.5** | **59.0** | **58.6** | **76.7** | **74.8** | **74.2** |
| **MEAN** | | **53.6** | **57.7** | **55.6** | **67.7** | **73.1** | **70.3** |

[a] (1 -( postoperative volume / preoperative volume))*100

[b] Calculated based on Malkova et al., (2001)

[c] Calculated from total hippocampal volume (i.e., left volume + right volume)

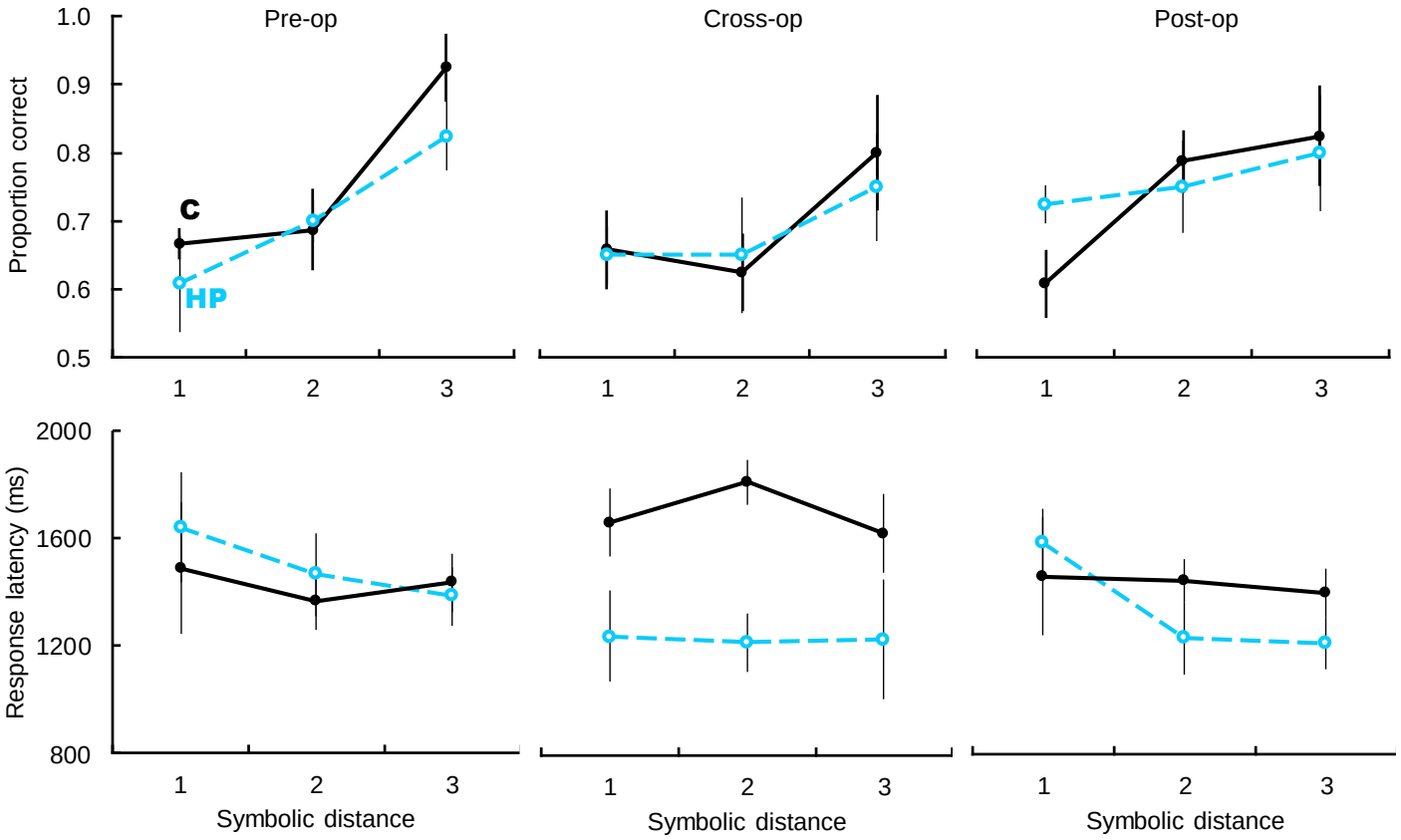


**Figure S2. Hippocampal damage did not affect transitive inference performance, even when considering only internal test pairs.** Accuracy (±SEM), top row, and response latency (±SEM), bottom row. Conventions as in Figure 2.

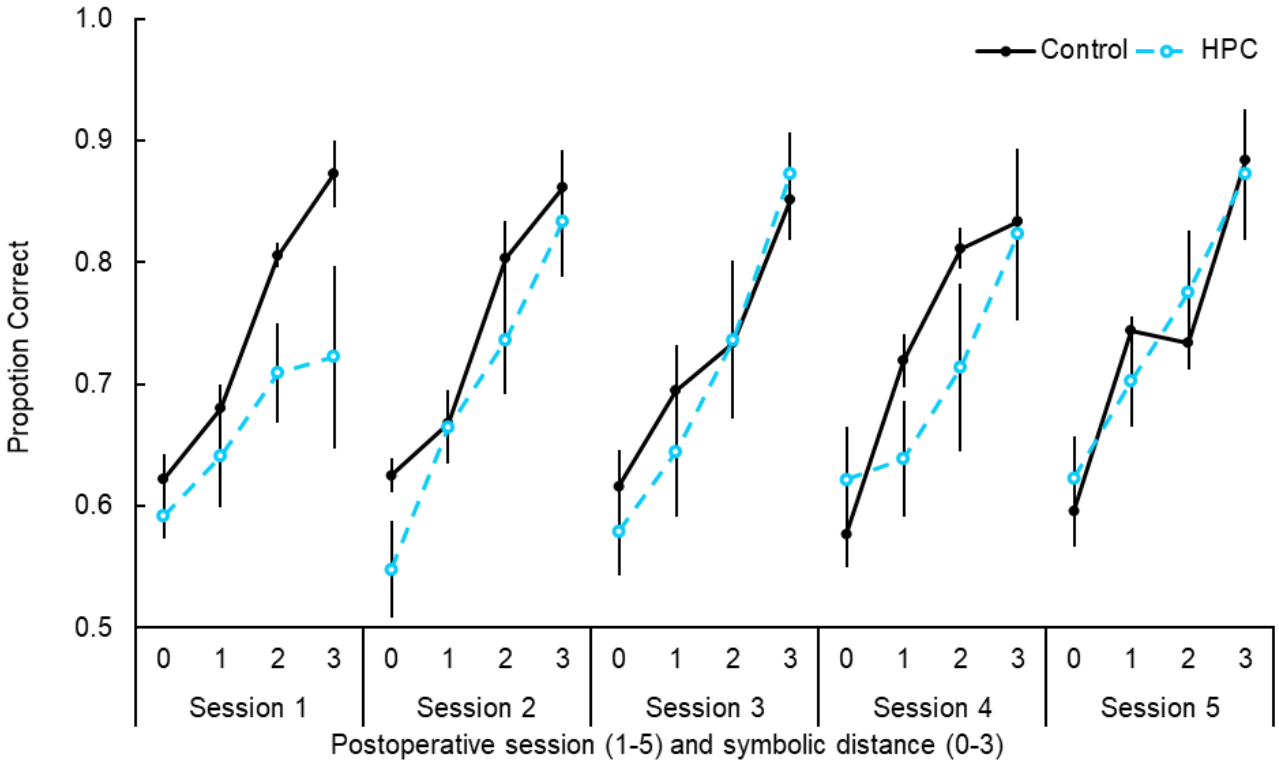


**Figure S3. Potential transient effect of selective hippocampal damage on memory for temporal order.** Proportion correct (±SEM) as a function of postoperative session, symbolic distance, and group (control = filled black dots, hippocampal = open blue dots). Compare to Figure 3 in this paper and Fortin et al., 2002, Figure 2.

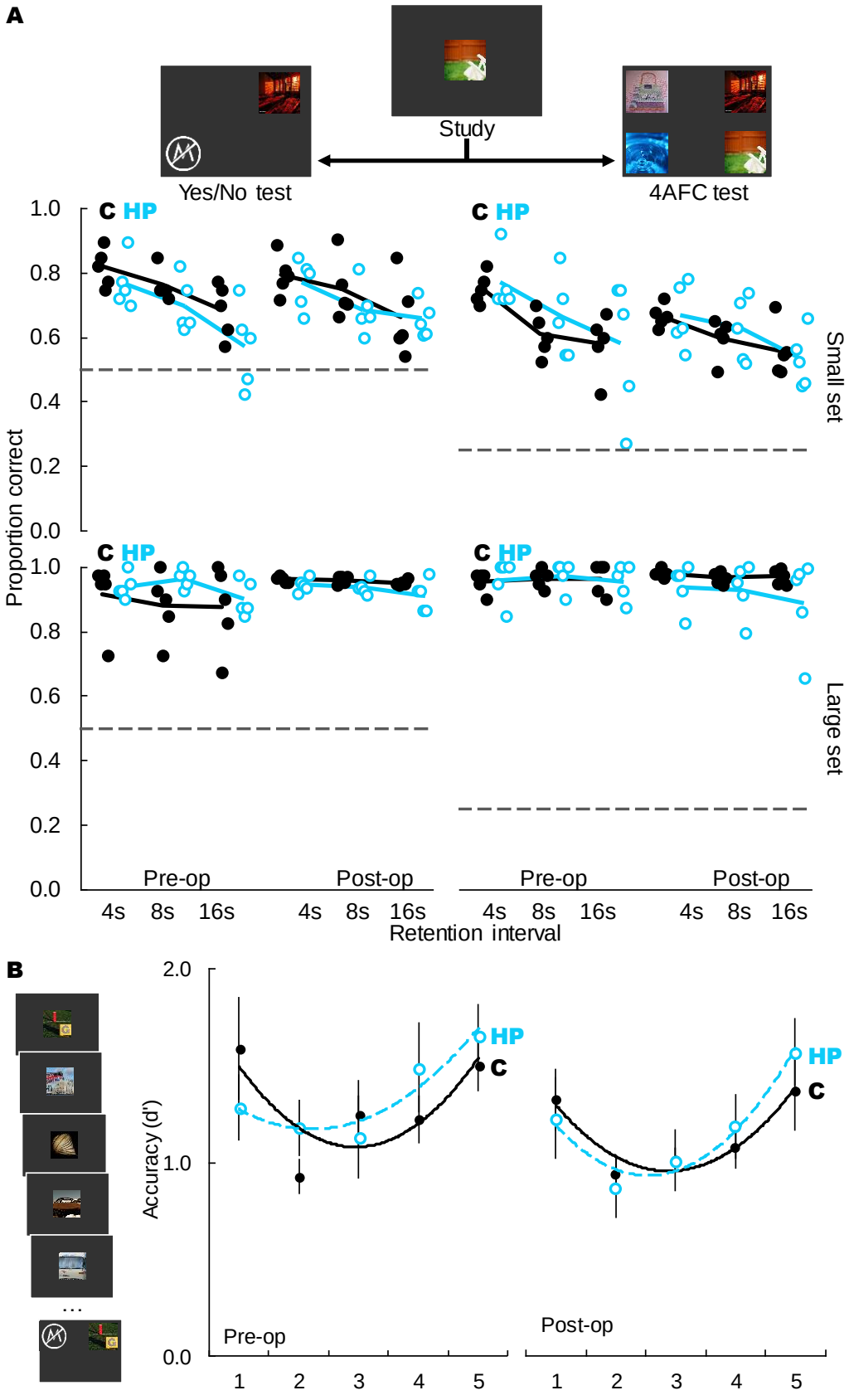
A
Study
Yes/No test
4AFC test
C HP
Small set
Large set
Proportion correct
1.0
0.8
0.6
0.4
0.2
0.0
Pre-op
Post-op
4s 8s 16s
Retention interval
B
Accuracy (d')
2.0
1.0
0.0
HP
C
1 2 3 4 5

**Figure S4. Selective hippocampal damage did not impair image recognition performance.** A) Example test screens for the yes/no and four alternative forced choice (4AFC) recognition tests and proportion correct for control monkeys (solid black circles) and monkeys with selective hippocampal damage (open blue circles) as a function of recognition paradigm (yes/no or 4AFC), image set size (small or large), retention interval (4, 8, or 16 seconds), and experimental timepoint (pre- or post-surgery). Accuracy was higher with the large set (4AFC: $F_{(1,8)} = 232.47$, $p < .001$ , partial $\eta^2 = .97$; YN: $F_{(1,8)} = 150.75$, $p < .001$ , partial $\eta^2 = .95$) and at shorter retention intervals (4AFC: $F_{(2,16)} = 14.76$, $p < .001$ , partial $\eta^2 = .65$; YN: $F_{(2,16)} = 9.82$, $p = .002$ , partial $\eta^2 = .55$), and these factors interacted (4AFC: $F_{(2,16)} = 10.71$, $p = .001$ , partial $\eta^2 = .57$; YN: $F_{(2,16)} = 9.82$, $p = .002$ , partial $\eta^2 = .55$). However, there were no main effects of lesion group or interactions with lesion group or any other factor (all $F < 3.11$, all $p > .085$). Lines represent group means, each dot represents one monkey, and dots are jittered along the x axis to allow better visualization of individual performance. B) Diagram of 5-item list recognition test and accuracy (±SEM), as expressed by d', for control monkeys (solid black circles) and monkeys with selective hippocampal damage (blue open circles) as a function of the position of the tested item from the list (1-5), and experimental timepoint (pre-operation or post-operation). We found a significant effect of list position ($F_{(4,32)} = 12.47$, $p < .001$ , partial $\eta^2 = .61$) and a significant U-shaped quadratic contrast ($F_{(1,8)} = 28.75$, $p = .001$ , partial $\eta^2 = .78$). The serial position effect was not affected by hippocampal damage (main effect of group: $F_{(1,8)} = 2.22$, $p = .175$; timepoint × group: $F_{(1,8)} = 1.94$, $p = .202$; list position × group: $F_{(4,32)} = 1.78$, $p = .158$; timepoint × list position × group: $F_{(4,32)} = 1.78$, $p = .157$). Stimuli images from Flickr under a Creative Commons CC BY 2.0 Generic License.

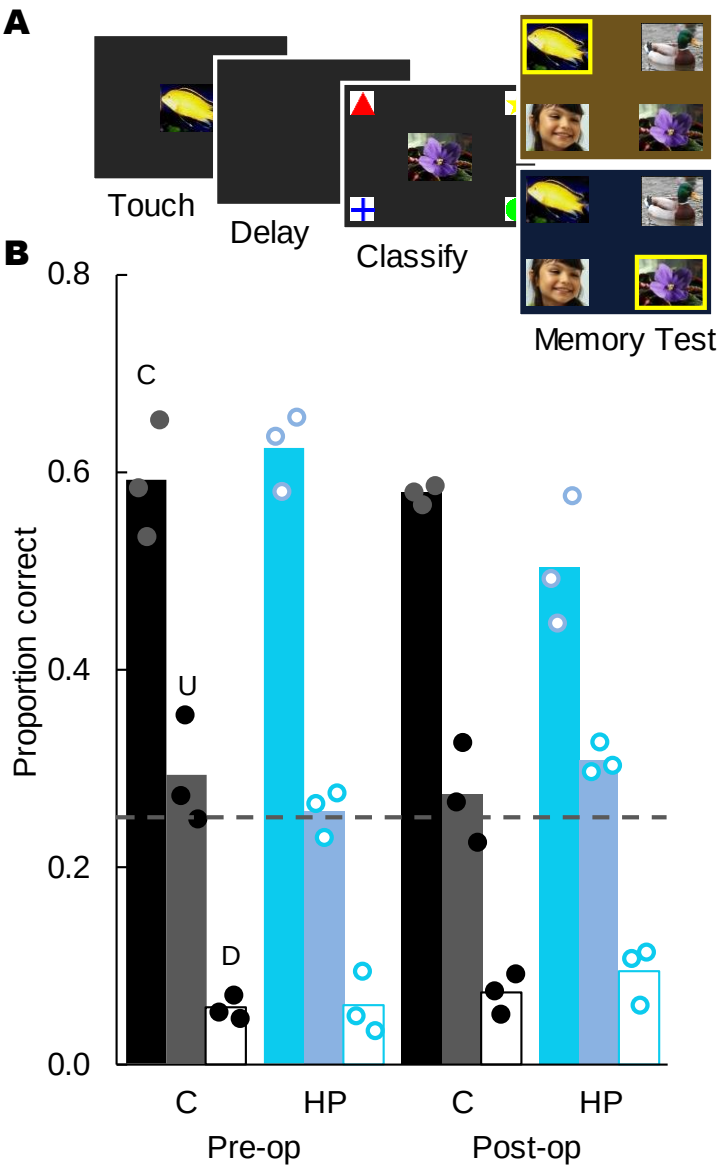


**Figure S5. Hippocampal damage did not impair source memory.** A) Trial progression in which the monkeys studied two samples in two different ways, by touching one and classifying the other, and then were unpredictably cued at test via the background color of the screen to report either the touched or classified sample. Item memory was operationalized as the ability to discriminate the two studied images from the two unstudied distractors and source memory was operationalized as the ability to discriminate between the two studied images. B) Proportion choice of the cued sample (C), the uncued sample (U), and the unstudied distractors (D) at test as a function of group and experimental timepoint. Proportion choice of the distractors is the average of the two unstudied distractors. Post-operatively, the two groups did not differ in item memory, as measured by false alarms to the unstudied distractor ($t_4 = 0.91$, $p = .41$), or source memory, as measured by false alarms to the uncued sample ($t_4 = 1.92$, $p = .13$). The dashed gray line indicates chance (0.25). Dots represent individual monkeys and are jittered on the x axis to visualize individual performance. Stimuli images from Flickr under a Creative Commons CC BY 2.0 Generic License.

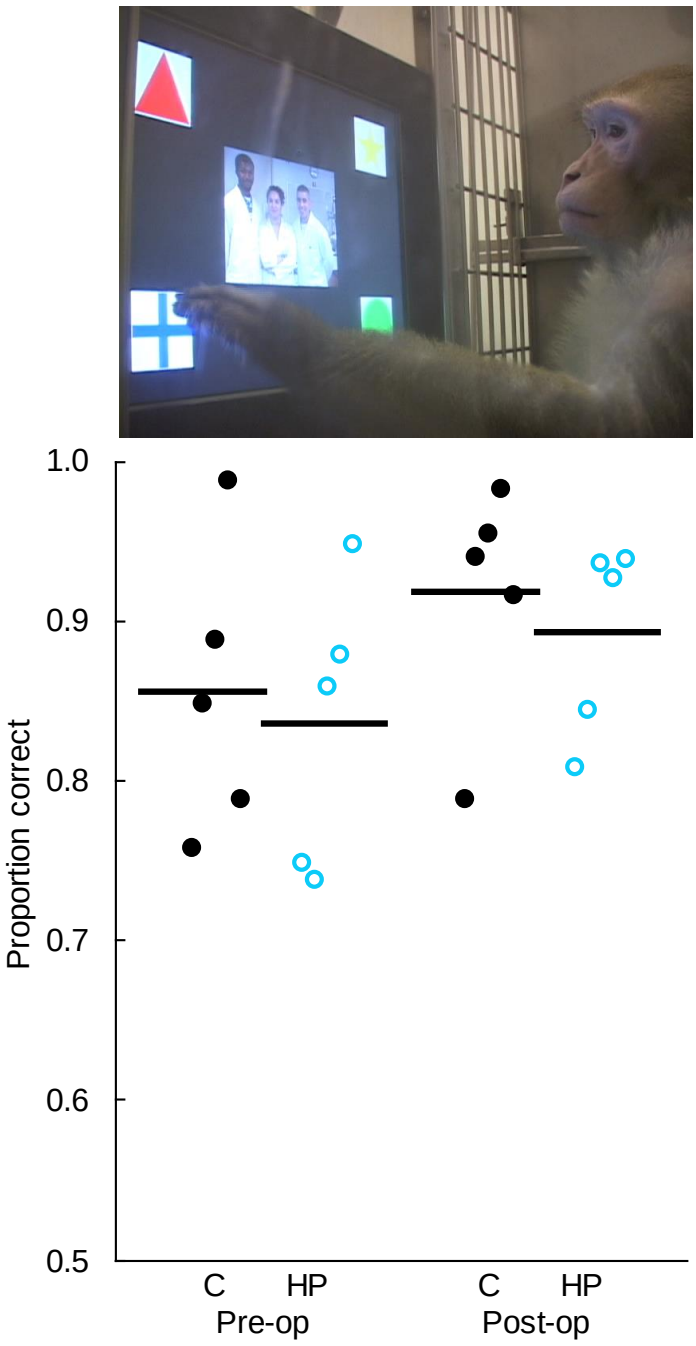


**Figure S6. Selective hippocampal damage did not impair perceptual classification.** Top: A monkey correctly classifies the central image as showing people by touching the associated symbol. Bottom: Hippocampal damage did not impair perceptual classification; pre: $t_8 = 0.43$, $p = .68$; post: $t_8 = 0.77$, $p = .46$. Proportion correct for control monkeys (C; solid black circles) and monkeys with selective hippocampal damage (HP; open blue circles) as a function of experimental timepoint (pre- or post-surgery). Lines represent group means, each dot represents one monkey, and dots are jittered along the x axis to allow better visualization of individual performance. Chance is 0.25. Photo Credit: Benjamin M. Basile, Emory University.