Supplementary Notes

1. The pattern of hippocampal lesions was very similar to that reported in other recent studies from our lab in which the same surgical procedures were followed (1, 2). On average, hippocampal lesions destroyed about 67% of the hippocampus proper (range: 35% - 95%). In all of the rats with hippocampal lesions, there was some sparing in the dorsal and ventral planes. Twenty-nine of the lesioned rats sustained damage that affected 50% or more of the hippocampus proper (Mean: 71%; Range: 50% - 95%). These lesions affected all the hippocampal subfields (CA1-CA3, dentate gyrus) and, to varying degrees the anterior portion of the subiculum. The latter point is potentially important in view of Bunsey and Eichenbaum’s (3) finding that the effects of hippocampal lesions on the food preference task were most pronounced when the lesions were extended to dentate gyrus and subiculum. Whether this effect was due to lesion size or particular involvement of dentate gyrus and/or subiculum could not be determined. In the present study, there was no effect of lesion size in either task and there appeared to be no difference related to extent of damage to other hippocampal regions. It is difficult to make direct comparisons with Bunsey and Eichenbaum (3) in that our coordinates were more anterior than theirs and, as a result, our rats sustained less damage to subiculum. In the rest of the rats with hippocampal lesions, the average lesion destroyed 41% of the hippocampus proper (range: 35% - 48%). In all lesioned rats, extra-hippocampal damage was minor or non-existent.
2. Our finding of a difference favoring the CXT-D condition at long delays in the food preference test may relate to (a) the natural tendency of the original preference to decline over time in the environment in which it was acquired, as normal rats are drawn adaptively to novel foods (4), and (b) the possibility that at long delays, context-independent memory and context-dependent memory related to the same event co-exist to varying degrees, consistent with our framework (see paper). Though at long delays, normal rats tend to rely more on context-independent memory, the lingering presence of context-dependent memory may influence rats’ behavior. In this case, in the CXT-S condition the two types of memory evoked competing responses. Context-dependent memory would discourage selection of the target food in the same environment where it may not be biologically adaptive to persist with that response, and context-independent memory, which evokes a less precise representation of the environment, would favour selection of a previously experienced and safe food. The prediction that follows is that, at long delays, normal rats would show greater preference for the target food in CXT-D (where the cues evoked the memory for the learned preference without competing influences from context-dependent memory) than in CXT-S (where the memories were in conflict), which, in fact, is what we found. The result, in effect, supports our hypothesis that memories are transformed over time, though the two types may continue to interact with each other. We did not observe this interaction in contextual fear conditioning for a number of possible reasons, but the most likely is that the two types of memory evoked the same freezing response, rather than acting in opposition to one
another. Consequently, one would expect virtually the same performance in the
two conditions, which is what we found.

3. A series of 2 x 2 ANOVAs were conducted to compare performance of
hippocampal and control groups in the same or different contexts at short and
long delays. The ANOVA for the CXT-S condition of the food preference task
confirmed significant main effects of group (F\(_{1,36} = 4.59, p = .04\)) and delay (F\(_{1,36}
= 17.45, p < .001\)). The group x delay interaction was in the expected direction
and at the margin of the conventional standard of statistical significance (F\(_{1,36} =
3.17, p = .08\)). In the CXT-D condition of this task, only the group x delay
interaction was significant (F\(_{1,30} = 7.64, p = .01\)). This interaction was due to the
development of the context-independent memory in the controls and the lack of
such an effect in the hippocampal animals.

In the CXT-S condition of the fear conditioning task, the ANOVA yielded a
highly significant main effect of group (F\(_{1,23} = 23.61, p < .001\)). The effect of
delay and the group x delay interaction were not significant (both F_s < 1). This
outcome shows that, even though rats with hippocampal lesions were able to
acquire a food preference without the benefit of contextual cues, their rate of
forgetting was faster than that of controls. This could be due to an inefficient
learning strategy, an impoverished representation of the memory trace, retrieval
failure, or some combination of these deficits. In the CXT-D condition of the fear
conditioning task, the main effects of group (F\(_{1,24} = 6.11, p = .02\)) and delay (F\(_{1,24}
= 15.79, p < .001\)) were highly significant, as was the group x delay interaction
(F\(_{1,24} = 23.70, p < .001\)). The results of these analyses clearly reflect the
impairment of hippocampal groups in contextual fear conditioning and their lack of responsiveness to contextual manipulations.

4. In demonstrating the effects in two different tasks we are able rule out several other possible explanations related to the role of the hippocampus. For example, it is conceivable that, when the animals were shifted to the new context, the hippocampus contributed to a distraction from the task at hand by eliciting exploration of the new context, leading to less freezing or less food consumption. Conversely, the change may have increased the animal's anxiety due to the novelty of the situation and induced freezing. However, during testing in the fear-conditioning task, control animals were more active in the new environment and, in the food preference task, ate less of the target food in the new environment, thereby ruling out a simple fear-based explanation. As a further indication that fear was not a factor in the food-preference task, when rats were tested in the new environment, the following table shows that the total amount of food eaten by all groups did not differ across any of the test conditions.
Table 1

Mean total amount of food eaten and mean percent target food eaten during the food preference test (numbers in brackets represent standard deviations)

<table>
<thead>
<tr>
<th>Delay</th>
<th>Context Same</th>
<th>Context Different</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amount of food eaten (g)</td>
<td>Percent target food eaten (%)</td>
</tr>
<tr>
<td>24 hours</td>
<td>HPC 9.73 (2.29) 73.08 (9.29) 10.40 (2.37) 68.57 (21.04)</td>
<td>Control 10.17 (2.50) 74.38 (11.90) 10.31 (2.57) 60.33 (8.29)</td>
</tr>
<tr>
<td>8 days</td>
<td>HPC 11.43 (3.41) 51.75 (13.99) 11.60 (2.47) 59.33 (9.41)</td>
<td>Control 10.75 (3.31) 65.79 (8.80) 12.06 (1.92) 75.07 (2.66)</td>
</tr>
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</table>

5. The finding that normal rats’ preference for the target food was context-sensitive contrasts with an earlier report by Alvarez, Wendelken, and Eichenbaum (5) that normal rats performed equally well on this task when tested in an environment that was the same or different than that used in training. However, there are several important procedural differences between that study and the present one. For example, Alvarez et al (5) tested their animals in the same home cage in both environments and allowed the rats two to three days of habituation and feeding in the different test environment before testing. In our study, rats in the CXT-D condition were tested in a different box and were not exposed to that environment before the test. As well, in the Alvarez et al (5) study, rats were tested only 2.5 hours after training, as compared to 24 hours in the present study. Prior
experience with the test environment would have rendered that environment quite familiar which, at a very short delay, would have been conducive to generalization of the strong food preference, thereby minimizing the context effect. In fact, there was only minimal (anecdotal) evidence that animals in the Alvarez et al (5) study noticed the difference between the same and different environments.

6. Our framework bears some resemblance to McClelland et al’s (6), and O’Reilly and Rudy’s (7) computational models but departs from them in two important ways. In those models, detailed, specific (episodic) representations which depend on the hippocampus, modify or strengthen neocortical representations that capture the general features of episodes, and lay the basis for semantic memory. The idea that semantic memories are derived from episodic ones is appealing, and consistent with the data we report in this study. It must be acknowledged, however, that an alternative view cannot be ruled out, namely that the episodic and semantic memories are formed independently of one another. There is evidence that without the hippocampus, humans and animals can form semantic or schematic memories, albeit slowly and with difficulty in adulthood (8-10, but see 11) but perhaps more easily in early childhood (12). A second, important proviso relates to evidence that episodic memories are not always lost or degraded once semantic memories are formed. In humans, we have shown that even semantic memories, such as knowledge of famous people, continue to be influenced by episodic memories that individuals have of these famous people.
This influence is absent in people with medial temporal-lobe damage (14). Similarly, deficits on semantic fluency tests are associated with hippocampal damage (15). Finally, performance on tests of gist memories of repeated events (such as family dinners) is associated with the hippocampal activation on fMRI which is sensitive to the vividness and personal significance of those repeated events (16). Thus, there is a growing body of literature from humans and animals that retention and retrieval of detailed, specific representations of past episodes continue to depend on the hippocampus regardless of their age (17-19).

7. Our study has shown that by the time the hippocampus is no longer needed for contextual fear conditioning and acquired food preferences, behavior is governed by gist or schematic memories. We do not know, however, what type of memory controls behavior in normal animals during the middle periods when the hippocampus is still needed. One possibility is that, during that time, context-dependent memories still dominate, as they did shortly after acquisition; alternatively, there may be a transition to schematic or gist dominance, with the hippocampus still contributing to varying degrees. To examine these possibilities, we tested the effects of altered context in normal rats at a 2-day delay for acquired food preference, and at a 7-day delay for contextual fear conditioning. If context-dependent memories dominate, the results should resemble those we obtained shortly after acquisition. On the other hand, if gist memories are gaining in influence, then the results would resemble those we obtained at the longest delays. In both tasks, no distinction was observed between performance in the same and
altered context (p’s > .37). It may be noted that the temporal parameters associated with consolidation or the transformation process can vary with lesion size and training procedures in both the food preference (3, 20, 21) and contextual fear conditioning tasks (22-24), although the essential relationships with respect to hippocampal involvement in the process are unchanged. For the size of our lesions and the procedures followed, the temporal effects of hippocampal lesions that we describe are consistent with previous reports (20, 22). Overall, our results indicate that gist memories continue to require hippocampal support as they emerge, perhaps by drawing on information mediated by the hippocampus. Such a result is consistent with the possibility that there is a dynamic interplay between the diminishing context-dependent memories and the emerging gist memories, an idea that warrants further investigation (25).
References


