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Neural Mechanisms of Declarative Memory

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During the last two decades, considerable progress has been made toward understanding the brain mechanisms supporting memory representation. This success is due in great part to insights gained from studies of amnesia where memory breaks down into identifiable constituent elements that are differentially lost or spared after localized brain damage. In particular, studies of human amnesia associated with damage to the hippocampal region have shown that this part of the brain supports a capacity for declarative memory, the memory of everyday facts and events that can be brought to conscious recollection and are subject to verbal and other explicit means of expression (Cohen and Squire 1980; Cohen 1984; Corkin 1984; Squire et al. 1993). Our efforts have been directed at improving the resolution of this characterization through studies of hippocampal memory function in animals. This work is focused on key unresolved questions about the fundamental associative mechanisms, critical circuitry, and neural coding schemes that underlie declarative memory.

Characterization of human declarative memory as involving "conscious" and "explicit" recollection has been exceedingly useful for the understanding of hippocampal function in humans, but offers little direction for the development of animal models. Yet, there has been considerable progress in the study of hippocampal function in animals revealing that, as in humans, damage to the hippocampal region results in a selective impairment in some forms of memory while other memory performances are spared (for review, see Cohen and Eichenbaum 1993). Indeed, *two* kinds of dissociation have been prominent in this literature. In monkeys, several studies have shown that damage to the hippocampal region results in a selective impairment in object recognition memory, as well as in several related object memory tasks that involve rapid acquisition and extended retention (Mishkin 1982; Zola-Morgan and Squire 1985). In contrast, incremental learning of stimulus-reward associations and motor skills were completely preserved in animals with hippocampal region damage despite their deficits on object memory tasks. In rats, several dissociations have been demonstrated (see Eichenbaum 1994), the most prominent of which is that damage to the hippocampus results in impairments on spatial learning and memory versus sparing of various forms of stimulus-response and stimulus-reward association (O'Keefe and Nadel

1978; Nadel 1991). Furthermore, electrophysiological studies in rats have shown that hippocampal neurons encode spatial relations among environmental stimuli such that many hippocampal cells can be described as "place cells" that fire only when the animal is in a particular location of its environment, regardless of its orientation or ongoing behavior (O'Keefe 1976). Thus, there are strong parallels between dissociable forms of memory in animals and in humans, although the commonalities among object recognition memory and spatial memory in animals and declarative memory in humans are vague at best.

The connections between these types of memory may be further drawn by examining two general distinctions of hippocampal-dependent memory that are revealed in the studies across species and are differentially emphasized in experiments on monkeys and rats (Eichenbaum et al. 1992a, 1994). First, there is a *temporal distinction* by which the hippocampal region has been shown to be critical to very rapid acquisition of information and to persistent memory representations bridging the gap between short-term and long-term memory. Capacities for rapid acquisition and prolonged memory persistence are evident in a broad range of human memory tasks and are particularly prominent in the studies on object recognition in monkeys. Second, there is a *representational distinction* by which the hippocampal region is involved in aspects of memory organization and expression that mediate capacities for declarative memory in humans and are particularly evident in studies on spatial learning in rats. In this paper, we summarize some of our own explorations of the temporal and representational distinctions of hippocampal memory function using a rodent model system. Our data suggest that the neural mechanisms underlying these distinctions are dissociable and may be supported differentially by specific components of the hippocampal system.

MAJOR PATHWAYS OF HIPPOCAMPAL PROCESSING

Before we describe our results, we provide a brief review of the anatomy of the hippocampal system to introduce the components of the system that are the focus of the experiments described below (Fig. 1). The hippocampus is connected with other structures of the brain via two pathways, one that might be thought of

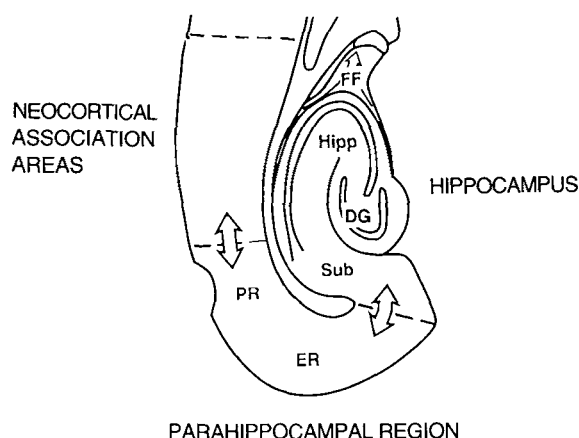


Figure 1. Simple schematic diagram of cortical-hippocampal connections illustrated on the outline of a horizontal rat brain section. (DG) Dentate gyrus; (ER) entorhinal cortex; (FF) fimbria-fornix; (Hipp) hippocampus proper; (PR) perirhinal cortex; (Sub) subiculum.

as the pathway bearing specific memory representations and the other that likely mediates modulatory and timing functions of the hippocampus. The information-bearing circuit involves the convergence of wide-ranging inputs directed from virtually every cortical association area into the parahippocampal region, a set of cortical structures including the perirhinal cortex, entorhinal cortex, and parahippocampal gyrus (Amaral and Witter 1989; Witter et al. 1989; Burwell et al. 1995). The parahippocampal region sends the major cortical inputs from intermediate layers II and III to the hippocampus proper within each of its major subfields, including the dentate gyrus, CA3, CA1, and the subiculum. Hippocampal outputs of this pathway return to deep layers of the parahippocampal region, and then this area projects heavily back to the same cortical association areas that were the origin of its inputs. Thus, the information-bearing pathway consists of two stages of bidirectional interaction: direct interactions between the cortex and parahippocampal region, and interactions between the cortex and hippocampus itself mediated via the parahippocampal region. In this paper, we present evidence that direct cortical-parahippocampal interactions are sufficient to support some memory functions independent of the hippocampus, and that the hippocampus itself mediates a distinct memory-processing function.

The pathway mediating modulatory and timing circuits of hippocampus involves bidirectional connections between subfields within the hippocampus itself and several subcortical nuclei (primarily the septal complex, mammillary bodies, and anterior thalamus) via the fornix (Fig. 1). The functions of this pathway are not the focus of the present paper. However, in some of the studies described below, we transected the fornix as one way to produce a selective dysfunction of the hippocampus, taking advantage of the fact that fornix transection disrupts subcortical connections of

hippocampus while sparing bidirectional cortical-parahippocampal connections as well as the subcortical connections of the parahippocampal region, which do not pass through the fornix.

CRITICAL ROLE OF THE PARAHIPPOCAMPAL REGION IN RECOGNITION MEMORY

As introduced above, one way the temporal properties of declarative memory have been studied extensively is with a simple recognition memory test known as delayed nonmatch to sample. In the task originally designed for monkeys, animals are presented with a novel sample object and rewarded for displacing it (Gaffan 1974; Mishkin and Delacour 1975). Then, after a variable memory delay, they are presented with two objects, one identical to the sample and the other a novel object. In this choice phase, monkeys are rewarded for selecting the novel, nonmatching object (this rule is easily learned because monkeys are naturally attracted to novel objects). The delayed nonmatch-to-sample task is ideal for measuring the persistence of memory representations for single, isolated stimuli. Indeed, to the extent that memory performance can be related specifically to variations in the length of the memory delay, it would seem this task selectively assesses the temporal distinction of hippocampal memory processing.

We have described the role of components of the hippocampal system in recognition memory using two strategies, neuropsychological studies that determine the effects of damage to different hippocampal structures on performance of the delayed nonmatch-to-sample task, and electrophysiological studies that characterize the firing properties of neurons in different components of the hippocampal region of animals performing this task. In both lines of study, we exploited rats' superb olfactory learning and memory in the development of a variant of the delayed nonmatch-to-sample task, called continuous delayed nonmatch-to-sample (cDNM), which employed odor cues and involved a stimulus presentation protocol suitable for characterizing neural firing patterns to single memory stimuli as well as behavioral responses in accordance with the nonmatch memory contingency (Otto and Eichenbaum 1992a,b). On each trial, one of a large set of odors was presented with the contingency that an appropriate response to the odor was rewarded only if that odor was different from (that is, a nonmatch with) the immediately preceding odor. Rats were trained initially with a very brief interval between odor presentations. Subsequently, the interstimulus interval was manipulated to vary the retention delay, allowing an assessment of the persistence of memory as in the earlier studies on monkeys.

In an initial experiment, we compared the effects of selective ablation of the parahippocampal region versus fornix transection that selectively disrupts hippocampal function (Otto and Eichenbaum 1992a).

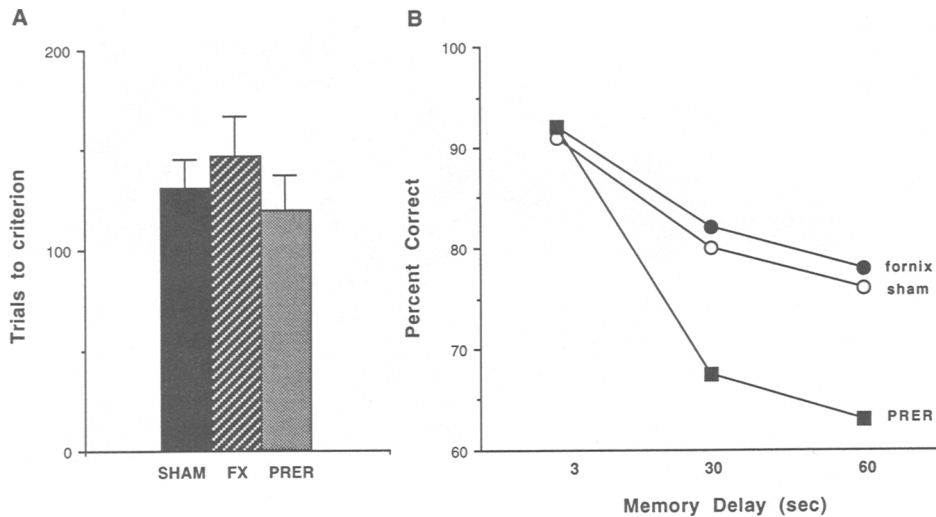


Figure 2. Performance of sham-operated rats (SHAM) and rats with transection of the fornix (FX) or lesions of the parahippocampal region (PRER) on initial acquisition of the cDNM task (A) and when the memory delay was increased (B).

Normal rats acquired the task within approximately 150 trials, and neither lesion affected the acquisition rate (Fig. 2A). In subsequent tests across memory delays, intact rats showed 90% or better retention at the shortest delay, and their memory performance gradually declined as the retention interval was increased (Fig. 2B). Rats with damage to the parahippocampal region also showed good retention at the shortest delay, but their performance declined abnormally rapidly, showing a severe deficit within 1 minute. In contrast, rats with fornix lesions performed identically with normal rats both during task acquisition and across delays, showing both intact performance at the short delay and the same gradual memory decay as normal rats. These findings indicated that neither the parahippocampal region nor the hippocampus is critical to the perception of the odor cues, nor is either component of the system necessary for acquisition of the nonmatch rule or short-term memory for odors. However, the parahippocampal region is critical to mediating a memory representation that persists beyond immediate memory in rats, as it is in monkeys. Furthermore, we may infer from these results that through its direct, reciprocal connections with the cortex, the parahippocampal region is sufficient to mediate the persistence of single-item memories independent of hippocampal processing.

In complementary electrophysiological studies, we have also examined the response properties of neurons in the parahippocampal region and in the hippocampus in rats performing the odor-guided cDNM task (Young et al. 1995). In our studies on the parahippocampal region, we examined the firing patterns of cells in these areas both during the period when rats were sampling the odor cues, in order to assess the extent to which odors were selectively encoded, and during the memory delay to determine the capacity of these areas to maintain an odor memory representation. For the

latter, we focused on the trial period at the end of the memory delay, that is, immediately preceding the initiation of trials succeeding a particular odor presentation. At this time, the overt behavior of the animal is consistent (it is approaching the stimulus port), allowing us to determine if neural activity varies with the identity of the preceding odor just before the recognition judgment must be made.

We found that a substantial proportion of cells in each of the subdivisions of the parahippocampal region and subiculum encode the identity of the odor cues during the odor sampling period (Fig. 3A). Some of these cells fired selectively or differentially to odors at odor onset and ceased firing when odor sampling was concluded, much as one would expect of a sensory neuron (Fig. 4A). In addition, other cells showed striking odor-specific activity during odor sampling and then throughout the delay period, such as the example shown in Figure 4B. Indeed, substantial numbers of cells in each of the subdivisions of the parahippocampal region demonstrated selective or differential firing patterns that were apparent in our systematic analysis of firing patterns at the end of the delay period (Fig. 3B).

To assess odor memory representations in the hippocampus itself, we recorded from CA1 pyramidal neurons of rats performing the cDNM task (Otto and Eichenbaum 1992b). A large proportion of hippocampal cells was actively associated with virtually every identifiable behavioral event in the task. A substantial subset of these cells was selectively active during the odor stimulus sampling period, and the activity of some of these hippocampal cells reflected the match or nonmatch relationship critical to performance in this task (Fig. 5). In contrast to cells in the parahippocampal region, no hippocampal cells fired associated with the sampling of a particular odor or with particular combinations of odors that composed specific

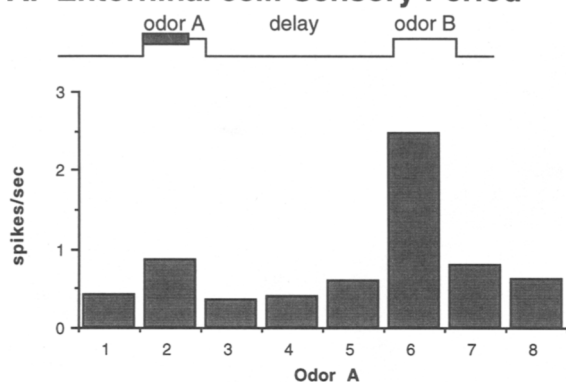
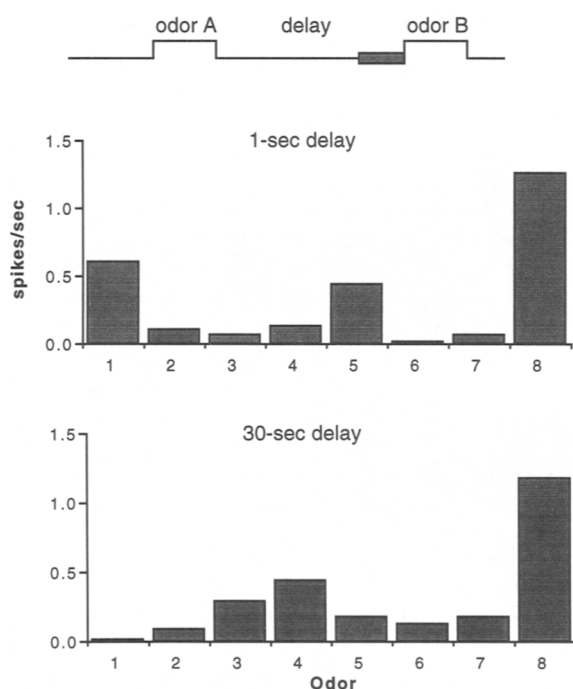
A. Entorhinal cell: Sensory Period**B. Entorhinal cell: Memory Period**

Figure 3. Neural activity in the parahippocampal region associated with delayed nonmatch-to-sample performance. Firing rates are shown for 0.5-sec periods of odor cue sampling or at the end of the memory delay associated with each of eight different odors. (A) Firing patterns of a cell that was selectively active during the odor sampling period. (B) Firing patterns of a cell that was differentially activated at the end of the memory delay regardless of the length of the delay.

matching comparisons. Rather, hippocampal cellular activity reflected all comparisons with the same outcome. We interpreted this finding as entirely consistent with the results of our lesion studies. It appears that the hippocampus itself is not involved in the encoding and storage of representations for specific items in this task. Instead, it appears that the hippocampus encodes abstract relations among cues, as it does in many other test situations. Thus, for example, the match/mismatch relationship reflected in the activity of hippocampal

cells in animals performing the cDNM task can be viewed as analogous to the spatial relations among cues reflected in the firing patterns of hippocampal place cells when rats explore open fields (O'Keefe 1979). Indeed, across a broad range of tasks, hippocampal cells encode all manner of relations among salient stimuli as well as behavioral actions (Eichenbaum and Cohen 1988; Eichenbaum 1993, 1996; Deadwyler et al. 1995). In the cDNM task, "relational" cells in the hippocampus may mediate memory for match and nonmatch trial outcomes, even though this information contributes little directly to performance on this simple recognition task. Consistent with our data from the lesion study, the parahippocampal region, but not the hippocampus, maintains specific and persistent representations sufficient to support recognition performance.

THE HIPPOCAMPUS, MEMORY FOR STIMULUS RELATIONS, AND FLEXIBLE MEMORY EXPRESSION

The above-described findings on hippocampal neuronal firing patterns, among a substantial body of other neuropsychological and electrophysiological evidence, led us to suggest that the hippocampus is critical for mediating the organization of memories according to the relevant relationships among remembered stimuli (Eichenbaum et al. 1992a, 1994; Cohen and Eichenbaum 1993). In addition, we have proposed that such a relational representation supports the ability to express knowledge about indirectly related items in the memory organization in a variety of ways outside repetition of learning events. We have assessed the role of the hippocampus in several different memory tasks, each of which requires the animal to learn an organization of relationships among odor cues, and each of which requires the animal to use its memory representations flexibly, that is, in situations that challenge the animal to employ the learned memory organization outside repetition of the learning trials.

Three such tasks that exploit rats' superb memory capacities with odors are described here. Each experiment focused on the role of the hippocampus itself and exploited some aspect of "natural" rodent behavior in using odor memory cues. However, the tasks differed in the nature of the learned association and how it was expressed in behavior. A brief summary of our results emphasizes both the generality of associations supported by the hippocampus and its common role in mediating relational organizations and flexible memory expression.

Paired Associate Learning

One memory test that requires learning specific relationships among cues is the paired associate task. The verbal paired associate task has been exceedingly useful in understanding cognitive aspects of associative

A. entorhinal cell e26t 10-2

B. entorhinal cell e26t 11-1

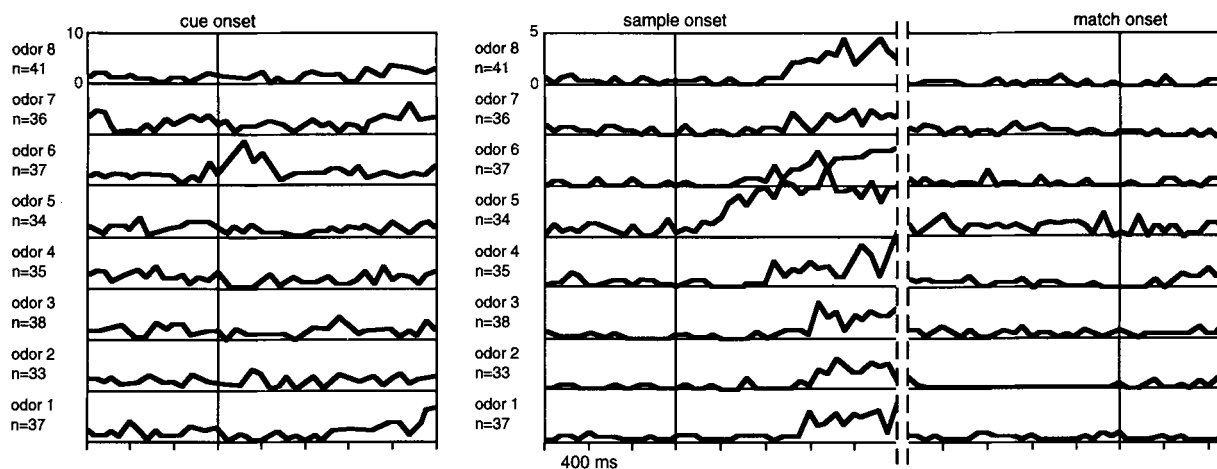


Figure 4. Neural activity in the parahippocampal region associated with delayed nonmatch-to-sample performance. (A) Responses of a cell during the 2 sec following the onset of different odors. (B) Activity of another cell during the cue sampling period and during the last 2 sec of that delay period; i.e., prior to the onset of the subsequent odor matching cue.

learning in humans and is often applied in the assessment of human amnesia. It seemed to us that a paired associate task adapted for animals was the simplest paradigm that we could exploit for neurobiological studies on the learning of new associations between distinct and neutral stimulus events. The paired associate task as typically used for humans involves presentation of a list of arbitrarily paired words followed by testing in which the subject is cued with the first item of each pair and must recall the second item. For rats, we designed an analogous task using odor stimuli and a recognition format that required subjects to distinguish in each of a series of trials the appropriate associate for a sample odor (Bunsey and Eichenbaum 1996). Exploiting rodents' natural foraging strategies that employ olfactory cues, animals were trained with stimuli that consisted of distinctive odors added to a mixture of ground rat chow and sand through which they dug to obtain buried cereal rewards. On each paired associate trial one of two sample odors initially presented was followed by two choice odors, each assigned as the "associate" of one of the samples and baited only when preceded by that sample (Fig. 6A,B). Following training on two sets of overlapping odor-odor associations, subsequent probe tests were used to characterize the extent to which learned representations supported two forms of flexible memory expression: *transitivity*, the ability to judge inferentially across stimulus pairs that share a common element; and *symmetry*, the ability to associate paired elements presented in the reverse of training order.

Intact rats learned paired associates rapidly, and hippocampal damage did not affect acquisition rate on either of the two training sets (Fig. 6C). Intact rats also showed strong transitivity across the sets with a preference of approximately 2:1 in favor of choice items in-

directly associated with the presented sample (Fig. 6D). In contrast, rats with selective hippocampal lesions were severely impaired in that they showed no evidence of transitivity. In the symmetry test, intact rats again showed the appropriate preference of approximately 3:1 in the direction of the symmetrical association (Fig. 6E). In contrast, rats with hippocampal lesions again were severely impaired, showing no significant capacity for symmetry. These findings indicate that some form of representation that supports stimulus-stimulus learning is intact in rats with selective hippocampal damage, as previously reported for rats and monkeys with hippocampal region damage (Saunders and Weiskrantz 1989; Murray et al. 1993; Cho and Kesner 1995; Eichenbaum and Bunsey 1995), as well as for human amnesiacs (Musen and Squire 1993; Moscovitch 1994). However, this form of representation does not support the inferential expression of indirect or symmetrical associations among stimuli—such "flexibility" in representation and memory expression relies on the hippocampus itself.

Serial Order Learning

The paired associate task described above involves learning that odor elements are associated with one another, perhaps the simplest kind of relationship that can exist between remembered items. However, we and other investigators (see, e.g., McClelland et al. 1995) believe that declarative memory organizations in humans, as well as spatial memories dependent on hippocampal function in rats (O'Keefe and Nadel 1978), involve learning a systematic organization of many interrelated items. A task that was developed to examine the capacity for expression of a systematic organization is the serial order learning test. In this task, subjects

continuous Delayed Non-match to Sample

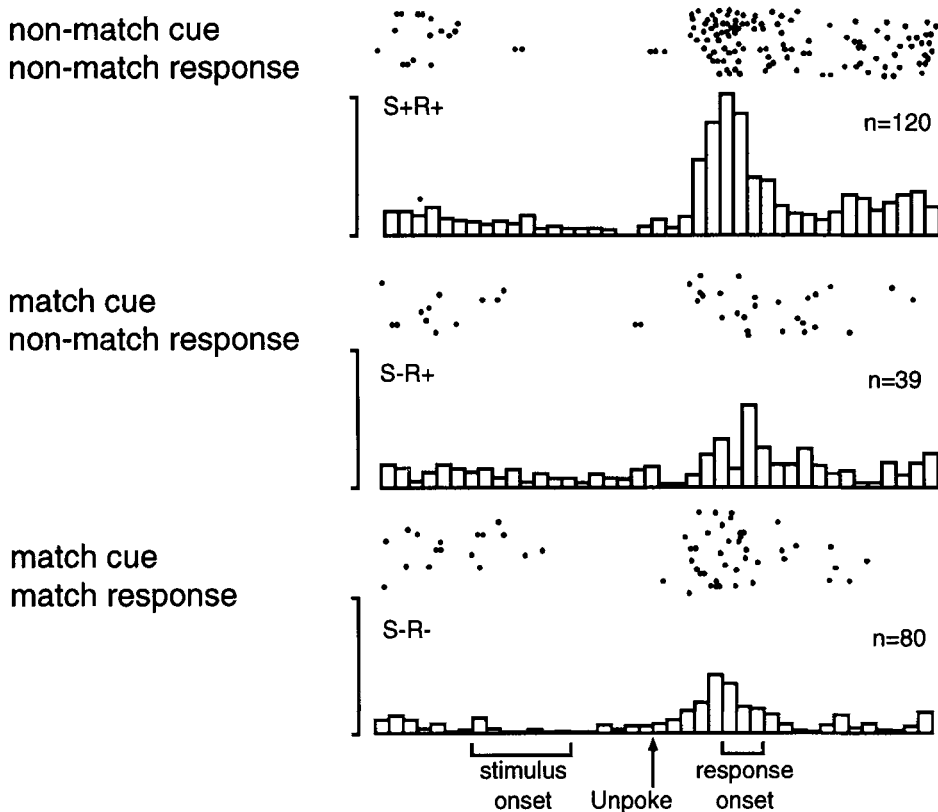


Figure 5. Neural activity in the hippocampus associated with delayed nonmatch-to-sample performance. The “unpoke” represents the instant when the rat ceases odor sampling and begins to make the discriminative response. See text for description.

learn pairwise comparisons that can be organized as a serial ordering of arbitrary stimuli. Thus, a typical training set involves comparisons $A > B$, then $B > C$, then $C > D$, then $D > E$, where rats are trained to select items to the left of the “ $>$ ” over those on the right. This set of comparisons can be efficiently represented by the serial organization $A > B > C > D > E$. A central asset of the serial representation is that it can be expected to support novel judgments about nonadjacent items in the ordered series, in particular, the judgment $B > D$. Note that each stimulus (with the exception of A and E) is associated with reward on only half of the choices, so the choice of B over D cannot be made solely on the basis of differential reward history. A direct control for the capacity for such a noninferential judgment is provided in presentation of the $A > E$ comparison, where the appropriate selection of A can be based on acquisition of a preference for this object whose selection was always followed by reward, and avoidance of object E, whose selection was never followed by reward. It has previously been determined that children acquire the capacity for serial organization, revealed by consistent transitive judgments of this type, at about age 6 (Bryant and Trabasso 1971). Several experiments have shown that chimpan-

zees (Gilliam 1981), new world monkeys (McGonigle and Chalmers 1977), and rats (Davis 1992) can also learn this type of one-dimensional serial organization.

Using the same foraging behavior described for our paired associate task above, subjects were initially rewarded for selecting the appropriate item in adjacent premise pairs ($A > B$, $B > C$, etc.) with blocks of 10 trials for each of the pairs presented in sequence (Dusek and Eichenbaum 1996). Then the number of trials in training blocks was gradually reduced until each pair was presented only once, and finally, all the premise pairs were intermixed in the same session. In the probe testing sessions we presented the critical probe pair $B > D$, as well as the nontransitive probe $A > E$, 10 times intermixed among 180 repetitions of the premise pairs. Because rats rapidly extinguish on nonrewarded probe trials, the expected choice on each of these tests (B and A, respectively) was rewarded on these probe trials. To test whether any observed differences in performance on these probes could have been due to learning the new pairings within the 10 presentations, we included additional testing sessions where new odor pairs were presented on 10 intermingled trials with one of each pair consistently rewarded.

We found that intact rats can acquire each of the

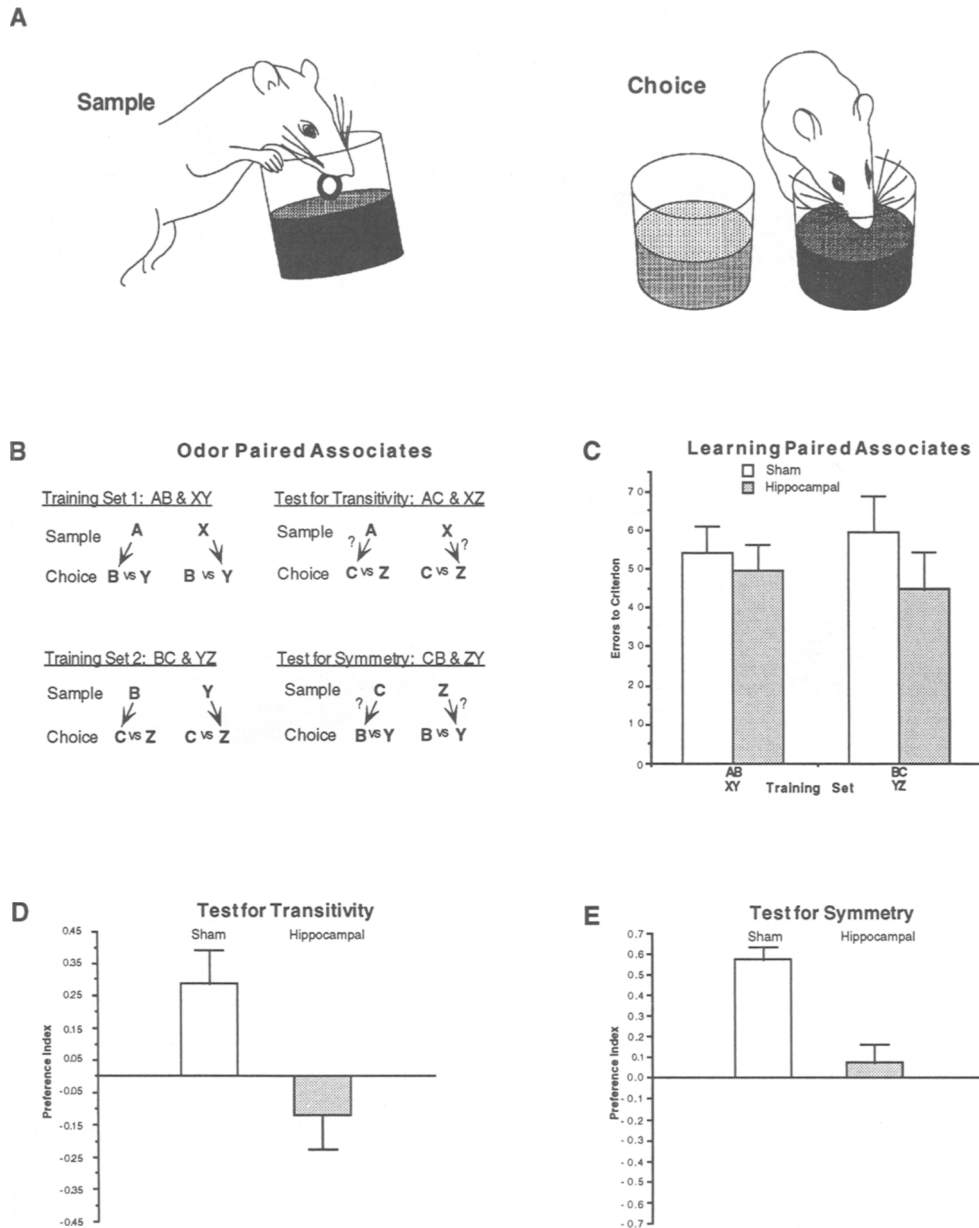


Figure 6. Inferential expression of odor-odor associations in sham-operated rats and rats with selective neurotoxic lesions of the hippocampus. (A) Rat and stimulus cups during sample and choice phases of the task. (B) Schematic diagram of paired associate training and probe testing. Letters represent odor stimulus items; arrows without question marks indicate trained pairings, whereas arrows with question marks indicate expected transitive and symmetrical choices. (C) Errors to criterion on acquisition of the two sets of paired associates for sham-operated and hippocampal subjects. (D) Preference indices on the test for transitive inference. For these probe trials, a preference score was calculated as $(X-Y)/(X+Y)$, where X and Y were the digging times in the transitive and alternate choices, respectively. (E) Preference indices on the test for symmetrical expression.

premise pairs of the serial order problem, and they perform well on concurrent presentations of all of these pairings during probe testing (Fig. 7). Furthermore, normal rats made the appropriate transitive judgment between stimuli B and D about as accurately as their overall performance on the premise pairs. Rats with fornix transection or perirhinal-entorhinal cortex lesions also acquired the premise pairs at the normal rate and performed them in concurrent presentations. However, rats with either fornix transection or removal

of the parahippocampal region showed no capacity for the transitive inference. They performed much worse than normal rats on the B > D transitive judgment, and their performance was not better than that expected by chance. In the control trials, intact rats and rats with fornix or perirhinal-entorhinal lesions accurately selected stimulus A over stimulus E, which could be guided by a bias for stimulus A and a bias against E. This finding indicates that the deficit in rats with fornix or parahippocampal lesions was not due merely to the

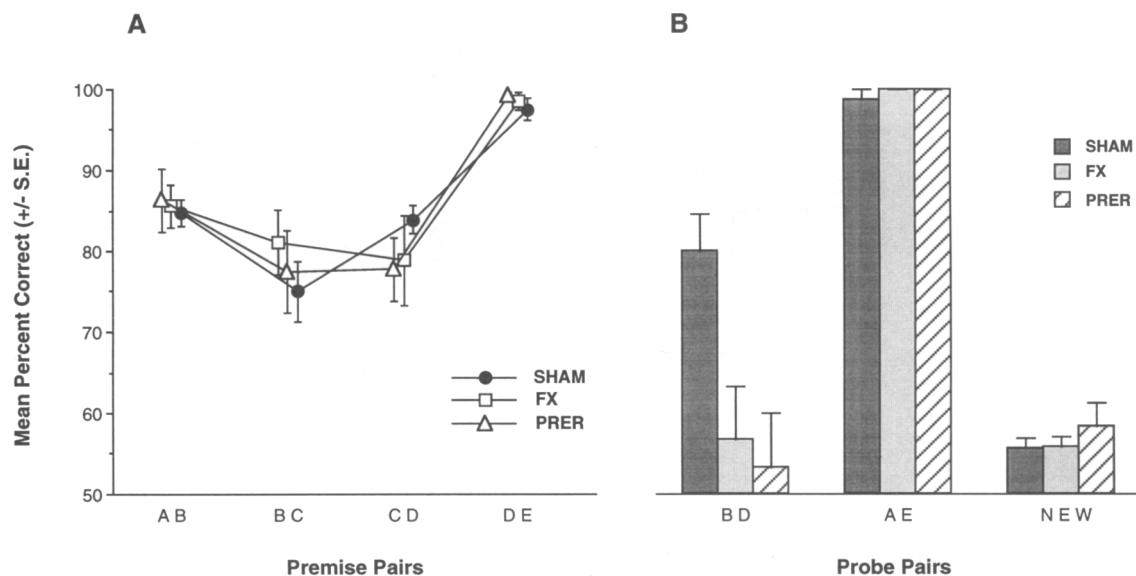


Figure 7. Transitive inference in serial ordering by sham-operated rats (SHAM) and rats with transection of the fornix (FX) or lesions of the parahippocampal region (PRER). (A) Performance levels after training on the premise pairs A > B, B > C, C > D, and D > E. (B) Performance on probe trials: BD involves the critical transitive judgment, AE can be solved by a nontransitive judgment, and columns labeled NEW reflect the extent of learning of two new odor pairings. See text for explanation.

novelty of the stimulus presentation when no transitive judgment was required. Finally, none of the groups learned the new pairs in the few intermixed trials on the novel discriminations. This pattern of results, combined with those from paired associate learning, indicates that some form of stimulus-stimulus representations can be acquired independent of the hippocampus itself, although these representations are "hyper-specific," that is, they can only be expressed within the confined context of reproduction of the learning event (Eichenbaum et al. 1992b). Only a hippocampally mediated representation can support the flexible expression of associations among items within a larger organization in various and even novel situations.

Social Learning of Odor-odor Associations

To further investigate the range of hippocampal involvement in natural forms of stimulus association, we also assessed the role of the hippocampal region in a type of social olfactory learning and memory that relies on flexible expression of an odor-odor association. The paradigm we used, called the social transmission of food preferences (Galef 1990), involves alterations in food selection patterns consequent to experience with a conspecific that has recently eaten a particular food. When an "observer" rat encounters another ("demonstrator") rat that has recently eaten a distinctively scented food, the probability that the observer will later select that same food over other foods increases. This form of social learning is interpreted within the adaptive heuristic that a food recently consumed by a conspecific is safe. In a series of studies, Galef (1990)

has shown that the mechanism underlying this learning involves an association between two odors present in the observer rat's breath, the odor of the recently eaten food and an odorous constituent of rat's breath, carbon disulfide. It is of particular importance that exposing the observer to the distinctive food odor alone, or to carbon disulfide alone, has no effect on later food preference. Thus, the shift in food choice cannot be attributed to mere familiarity with the food odor. In contrast, exposure to the scented food mixed with carbon disulfide, even without the social context in which this association is usually experienced, increased later consumption of food with the same odor. The clear conclusion from these studies is that the formation of a specific stimulus-stimulus association, in the absence of any primary reinforcement, is both necessary and sufficient to influence later food selection.

Following on a previous observation that this type of learning is dependent on the hippocampal region (Winocur 1990), we investigated the role of the hippocampus itself in this task, assessing both immediate memory and delayed (24 hour) memory for social exposure to the odor of a novel food (Bunsey and Eichenbaum 1995). Normal rats showed strong memory in both tests (Fig. 8B). In contrast, rats with damage selective to the hippocampus itself showed intact short-term memory but completely forgot the association within 24 hours. These findings, similar to the pattern of sparing of immediate memory and impairment in delayed recall in human amnesiacs, indicate that the hippocampus is not required for perceptual or motivational components of learning or for the ability to express a learned food selection. However, the hip-

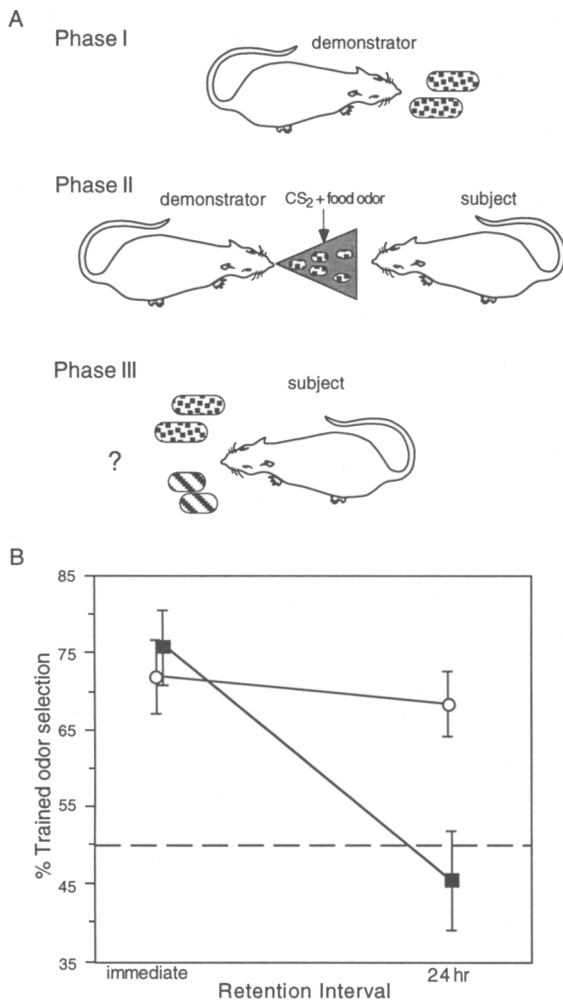


Figure 8. (A) Training and testing on a "naturalistic" odor-odor association. In Phase I, a "demonstrator" rat is given a distinctively scented food. Then, in Phase II, the demonstrator is presented to an experimental subject for a brief period of social interaction. In Phase III, subjects are presented with the same food or another distinctively scented food, either immediately or after a 24-hr delay. (B) Effects of hippocampal lesions on performance in an immediate or 24-hr delayed retention test.

poampus itself is required for long-term expression of this natural stimulus association in guiding behavior in a test well outside the original learning situation.

CONCLUSIONS

The findings described here support the view that the contributions of the hippocampal system to declarative memory can be fractionated into distinct components. One component is the ability to form representations following a single experience and to maintain the memory for an extended period through interfering events. Complementary neuropsychological and electrophysiological evidence presented here indicates that this function can be supported by the

parahippocampal region even in the absence of hippocampal processing.

With regard to the hippocampus itself, the findings presented here provide compelling evidence for a role of the hippocampus itself in relational memory representation and in flexible memory expression. This capacity should be thought of as an extension of classic views on human memory, such as William James's (1890) description of memory as involving an elaborate network of associations that can be applied across a broad range of situations, as distinct from habits that depend on rigid associative sequences. These findings are also entirely consistent with present-day characterizations of human declarative memory, such as Cohen's (Cohen and Eichenbaum 1993) description of declarative memory as "promiscuous" in its accessibility by novel routes of expression.

Taken together, the results of the studies presented here provide a preliminary picture of the processes that mediate declarative memory. It appears the parahippocampal region contributes to declarative memory by "buffering" specific representations that can be accessed and manipulated by the hippocampus. Then the hippocampus represents the critical relations among the items held by the parahippocampal region and, indeed, has access to the much larger organization of item representations in cortical association areas via the parahippocampal region. We presume the full relational memory organization comes about through multiple iterations of cortical input to the parahippocampal region and temporary storage there. This might be followed by hippocampal relational processing that adds to or restructures interconnections among parahippocampal and then cortical representations. Over extended time periods, new experiences that bear on the established organization reactivate established representations as well as add new ones, and these are processed together by this hippocampal circuit to weave the new information into the established relational network. Precisely because this network is so extensive and systematically interconnected, access to items via novel routes and in novel experiences not only is possible, but also occurs continuously as we express memories to guide almost every aspect of daily life.

ACKNOWLEDGMENTS

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