

Mnemonic Theories of Hippocampal Function

David S. Olton, Cynthia G. Wible, and Matthew L. Shapiro
Johns Hopkins University

Although mnemonic interpretations of hippocampal function in people have been readily accepted for many years, similar interpretations of hippocampal function in animals have received a number of challenges. This article reviews two of these challenges, shows how they were resolved in favor of some kind of mnemonic interpretation, and then suggests ways in which these types of interpretations must change in order to encompass new data.

The appearance of a severe amnesic syndrome in patient H.M. following bilateral removal of the temporal lobes led quickly to the development of mnemonic descriptions of hippocampal function. Subsequent experiments and conceptual analyses of the behavioral impairments following temporal lobe damage in humans have continued to support a mnemonic interpretation of hippocampal function (Corkin, 1984).

In animals, however, mnemonic descriptions of hippocampal function have had much less consistent acceptance. Two challenges have been particularly important. These suggested that (a) the behavioral changes following lesions of the hippocampus in animals could not be explained as a failure of memory, and (b) single-unit activity in the hippocampus reflected processes involved in cognitive mapping rather than memory.

This article reviews briefly these two challenges and the way they have altered mnemonic interpretations of hippocampal function. It then concludes with a suggestion that although the hippocampus clearly participates in memory, a more global theoretical framework is necessary to encompass all the phenomena associated with hippocampal function.

Do Hippocampal Lesions in Animals Cause Amnesia?

The initial experiments examining the behavioral changes produced by lesions of the hippocampus in animals generated two particularly confusing sets of results. First, impairments did not always appear in behavioral tests that involved learning and memory. Second, the impairments that did occur could not always be encompassed by mnemonic explanations.

Many different resolutions of these apparently discrepant results in animals and humans were offered (Isaacson, 1972; Iversen, 1976; Weiskrantz, 1971), one of which had devastating implications for mnemonic interpretations of hippocampal

function in animals. In this view, brains of people had a different functional organization than the brains of animals, mnemonic explanations of hippocampal function in animals were wrong, and animal models of human memory were not possible.

Fortunately for comparative neuropsychology, all these conclusions were proven wrong. Four lines of evidence were particularly instrumental in producing this change of opinion.

First, experimental evidence indicated that amnesic patients had normal performance in some types of mnemonic tasks, as did animals following hippocampal lesions (Cohen, 1984; Milner, Corkin, & Teuber, 1968; Squire & Cohen, 1984). Second, new experimental procedures were developed for animals; in these tests, which were designed to be similar to those in which human amnesics had impairments, animals with hippocampal lesions also had a severe impairment (Kesner, 1985; Mishkin, 1982; Olton, 1983; Squire & Zola-Morgan, 1983). Third, the more cognitive approach to the analysis of psychological processes encouraged, in turn, the development of comparative cognition, an approach that was able to apply the same conceptual framework to the analysis of performance in both animals and humans (Hulse, Fowler, & Honig, 1978; Roitblat, 1982; Terrace, 1984). Fourth, theoretical explanations of memory and amnesia came to emphasize the heterogeneity of memory processes; the presence of normal memory processes in amnesic syndromes was no longer surprising, but a pivotal component of both experimental design and theoretical explanations (Mishkin, Malamut, & Bachevalier, 1984; Squire & Cohen, 1984). These four developments all converged to the conclusion that following temporal lobe lesions in both animals and humans, similar types of memory processes were both spared and impaired; hippocampal function in animals was similar to that in humans after all, and mnemonic interpretations were appropriate in both cases.

In retrospect, the apparent discrepancies between the effect of temporal lobe lesions in humans and animals were due mainly to an inappropriate comparison of results from two different types of tasks. This problem can be illustrated best by visualizing a 2×2 table with the type of individual being tested on one dimension (animals, humans), and the type of behavioral test on the other (ones in which performance is impaired in amnesic syndromes, and ones in which performance is spared in amnesic syndromes). Most of the early comparisons were made along the diagonal of this table:

The production of this article was supported in part by Research Grant MH24213 from the National Institute of Mental Health to David S. Olton.

The authors thank Debbie Harris for typing the manuscript and Richard F. Thompson for the opportunity to contribute to this special issue.

Correspondence concerning this article should be addressed to David S. Olton, Department of Psychology, The Johns Hopkins University, Baltimore, Maryland 21218.

Animals were tested in tasks in which performance was spared in amnesic syndromes, and humans were tested in tasks in which performance was impaired. Given this type of analysis, which confounded the effects of two different variables simultaneously, apparent contradictions had to result.

Do Single Units in Animals Have Mnemonic Correlates?

A second challenge to the mnemonic interpretations of hippocampal function in animals came from the observation that many complex spike units in the hippocampus had a striking *place field*, an area of the environment in which the rate of activity was markedly elevated as compared with the baseline rate. Experiments manipulating the stimuli in the environment showed that the activity of these units was influenced by the topological organization of extramaze distal cues. These findings led to an explanation of hippocampal function that emphasized spatial cognitive mapping rather than memory (O'Keefe, 1979; O'Keefe & Nadel, 1978, 1979).

Subsequent experiments confirmed the ubiquity of place correlates of complex spike units. These correlates were more complicated than those initially described for the simple place field. In a given environment, unit activity was influenced by the direction of movement (McNaughton, Barnes, & O'Keefe, 1983), and it often had many separate areas of increased and decreased firing rate, which resulted in a complicated mosaic of rate changes (Kubie, Muller, & Fox, 1986). Between different environments, the baseline rate of activity changed markedly (Kubie & Ranck, 1983), as did the discriminative stimuli influencing the position of the place field (Kubie, Muller, & Fox, 1986). Nonetheless, the data consistently demonstrated that single-unit activity was influenced by spatial variables, and this fact was taken as evidence that mnemonic interpretations of hippocampal function must be wrong.

More recent experiments examining the activity of single units in other types of tasks demonstrate that this conclusion is invalid; complex spike units clearly have nonspatial mnemonic correlates. Thus the presence of spatial correlates can not be used to imply the absence of mnemonic correlates.

One experiment tested rats in a cued match-to-sample procedure (Wible et al., in press). The apparatus was a straight runway with two compartments at the choice point. One compartment was black, and the other one was white. Chocolate milk was used as reinforcement for a standard match-to-sample procedure. Each trial had two phases. For the *sample phase*, the entrance to one compartment was blocked so the rat was forced to enter the other compartment. For the *choice phase*, the block was removed so the rat had access to both compartments. However, reinforcement was available only in the same compartment that was entered during the sample phase. The left-right position of the compartments was changed in a pseudorandom fashion so that the compartment cues were relevant and the spatial cues were irrelevant.

A bundle of microwires was implanted and lowered to find unit activity. Data were recorded with standard electrophysiological techniques. When the activity from a complex spike unit was adequately discriminated from background activity, the rat was given at least 80 trials.

The rate of activity was analyzed while the rat was in the goal compartment. Unit activity was correlated with three dimensions: the phase of the task (sample or choice), the color of the compartment (black or white), and the location of the compartment (left or right). The resulting data were analyzed with a three-way analysis of variance to identify significant behavioral correlates of unit activity.

Of the 27 units recorded, 19 had clear correlates with one or more of these three dimensions, and only a few units responded to just the spatial location of the rat. The most common finding was an interaction of two dimensions. For example, some units responded most when the rat was in a particular compartment during a particular phase of the task (e.g., the black compartment during the sample phase).

Single units in the primate hippocampus showed a similar pattern during three different tasks. A delayed-response task used lights as stimuli. Two lights were located on a panel. For each trial, one *cue light* was turned on and then turned off for a delay period. Two *choice lights* were then turned on. The monkey was rewarded for responding to the choice light that had also been the cue light at the start of that trial. The majority of units showing behavioral correlates were responsive only during the delay. Many of these *delay units* responded differentially either to the cue light, the cue and choice lights, or only the choice light. All of these units had a maximal response rate that reflected the interaction of the delay with the discriminative stimuli (Watanabe & Niki, 1985).

During an object-place task, monkeys were presented with a screen divided into 9 locations by a 3 × 3 grid. During each trial, an object appeared in 1 of the 9 locations. Each object was presented in a location twice. If the object had been presented in that location before, the monkey was rewarded for responding. If the object had not been presented in that location before, the monkey was required to remember a stimulus in conjunction with a location. During a stimulus-response association task, the monkey was required to touch one stimulus three times, but to withhold response to a second stimulus. In both tasks, the majority of units did not respond to either the response or the stimulus alone, but they did respond to some combination of the two (Rolls, Miyashita, Cahusac, & Kesner, 1985).

In summary, when spatial environments emphasize temporally constant features, single units in the hippocampus do have spatial correlates. However, when spatial environments emphasize temporally changing features, single units in the hippocampus have mnemonic correlates. Thus, the presence of spatial correlates cannot be used to refute mnemonic interpretation of hippocampal function (Deadwyler, West, Christian, Hampson, & Foster, 1985; Fuster & Jervey, 1983).

New Mnemonic Theories of Hippocampal Function

This review demonstrates that some kind of mnemonic interpretation of hippocampal function in animals is still appropriate. However, it also demonstrates that new theories are necessary, ones that incorporate the challenges described here.

One significant development is an emphasis on temporal factors as they relate to hippocampal function. Time must play a critical role in memory because the ability to take information obtained at one time and apply it at another time is, by definition, memory. Furthermore, H.M., the classic patient with temporal lobe amnesia, has a distorted sense of time (Richards, 1973).

The Scalar Timing Theory has provided both the conceptual frameworks and the experimental procedures to examine temporal discriminations in animals (Church, 1978; Gibbon & Church, 1984; Gibbon, Church & Meck, 1984). In one experiment, rats were trained on a signaled fixed-interval procedure until the usual scalloped response function was obtained (Meck, Church & Olton, 1984). Two types of probe trials followed. During *peak trials*, the signal remained on for approximately twice as long as the usual fixed interval, and no reinforcement was given to mark the end of the fixed interval. All rats produced a response rate function that showed a clear peak sometime during the signal; the time at which this peak rate occurred was called the *peak time*. Control rats had a peak time at the time when reinforcement was usually delivered in the fixed-interval schedule. Rats with fimbria-fornix lesions had a significantly shorter peak time; they remembered the time of reinforcement as earlier than the actual time of reinforcement.

In *gap trials*, the same procedure was used except that the stimulus was turned off for a short interval (the gap) soon after it began. Normal rats had a rightward shift of the peak time by an amount equal to the duration of the gap, which showed that they followed a *stop rule*. During the gap, they stopped timing, remembered the duration of the signal prior to the gap, and added that value to the duration of the signal following the gap. Rats with fimbria-fornix lesions had a rightward shift of the peak time by an amount equal to the duration of the gap plus the duration of the signal prior to the gap, which showed that they followed a *reset rule*. During the gap, they stopped timing, forgot the duration of the stimulus prior to the gap, and began timing again from the beginning when the stimulus was presented after the gap. In the context of the Scalar Timing Theory, these results indicate that fimbria-fornix lesions disrupted both reference memory (the remembered time of reinforcement gained from performance during many trials, assessed by peak trials) and working memory (the remembered duration of the stimulus prior to a gap in an individual trial, assessed by gap trials). They also indicate that the hippocampus must be critically involved in the processing of temporal information, a conclusion that has been reached on the basis of other data as well (Rawlins, 1985; Solomon, 1979, 1980). Temporal discriminations must be an integral component of memory, or they must fortuitously involve the same neural mechanisms that are required for memory.

New descriptions of hippocampal function must encompass the spatial, temporal, and mnemonic phenomena described here. The cognitive processes involved in the perception of space, time, and memory may all be interrelated, psychologically and neurophysiologically. If the hippocampus is involved in all three of these processes, any description of hippocampal function must be able to incorporate all of them.

In the same way that a cognitive map establishes the topological interrelations among different places, a temporal map may establish the chronological interrelation among different events. Both types of maps require the interrelation of components within the map, a process that must involve memory in order to establish the correct contextual framework. The hippocampus may be the brain structure that allows each of the various components of a place and an event to be linked together and compared with other places and events (Marr, 1971; Teyler & DiScenna, 1986).

From this view, chronological and topological interrelations require many of the same comparison processes and representations (Olton, in press; Neisser, in press), and they both involve the hippocampus. An ideal theory is one that is able to describe these processes in sufficiently abstract terms that the theory can be applied to all of the phenomena in which this comparison process is instantiated.

References

- Church, R. M. (1978). The internal clock. In S. H. Hulse, F. Fowler, & W. K. Honig (Eds.), *Cognitive processes in animal behavior* (pp. 277-310). Hillsdale, NJ: Erlbaum.
- Cohen, N. J. (1984). Preserved learning capacity in amnesia: Evidence for multiple memory systems. In N. Butters & L. R. Squire (Eds.), *The neuropsychology of memory*. New York: Guilford Press.
- Corkin, S. (1984). Lasting consequences of bilateral medial temporal lobectomy: Clinical course in experimental findings in H.M. *Seminars in Neurology*, 4, 249-259.
- Deadwyler, S. A., West, M. O., Christian, E., Hampson, R. E., & Foster, D. C. (1985). Sequence related changes in sensory evoked potentials in the dentate gyrus: A mechanism for item-specific short-term information storage in the hippocampus. *Behavioral and Neural Biology*, 44, 201-212.
- Fuster, J. M., & Jervey, J. P. (1983). Inferotemporal neurons distinguish and retain behaviorally relevant features of visual stimuli. *Science*, 212, 1175-1178.
- Gibbon, J., & Church, R. M. (1984). Sources of variance in information processing theories of timing. In H. L. Roitblat, T. G. Bever, & H. S. Terrace (Eds.), *Animal cognition* (pp. 465-488). Hillsdale, NJ: Erlbaum.
- Gibbon, J., Church, R. M., & Meck, W. H. (1984). Scalar timing in memory. In J. Gibbon & L. Allan (Eds.), *Annals of the New York Academy of Sciences: Timing and time perception* (pp. 52-77). New York: New York Academy of Science.
- Hulse, S. H., Fowler, H., & Honig, W. K. (Eds.). (1978). *Cognitive processes in animal behavior*. Hillsdale, NJ: Erlbaum.
- Isaacson, R. L. (1972). Hippocampal destruction in man and other animals. *Neuropsychologia*, 10, 47-64.
- Iverson, S. D. (1976). Do hippocampal lesions produce amnesia in animals? *International Review of Neurobiology*, 19, 1-49.
- Kesner, R. P. (1985). Correspondence between humans and animals in coding of temporal attributes: Role of hippocampus and prefrontal cortex. *Annals of the New York Academy of Sciences*, 444, 122-136.
- Kubie, J. L., & Ranck, J. B., Jr. (1983). Sensory-behavioral correlates in individual hippocampus neurons in three situations: Space and context. In W. Seifert (Ed.), *Neurobiology of the hippocampus* (pp. 433-447). London: Academic Press.
- Kubie, J. L., Muller, R. U., & Fox, S. E. (1986). Firing fields of hippocampal place fields: Interim report. In G. Buzsaki & C. H. Vanderwolf (Eds.), *Electrical activity of the archicortex*. Budapest, Hungary: Akademiai Kiado.

- Marr, D. (1971). Simple memory: A theory for archicortex. *Philosophical Transactions of the Royal Society of London*, 262(B), 23-81.
- McNaughton, B. L., Barnes, C. A., & O'Keefe, J. (1983). The contributions of position, direction and velocity to single unit activity in the hippocampus of freely moving rats. *Experimental Brain Research*, 52, 41-49.
- Meck, W. H., Church, R. M., & Olton, D. S. (1984). Hippocampus, time, and memory. *Behavioral Neuroscience*, 98, 3-22.
- Milner, B., Corkin, S., & Teuber, H-L. (1968). Further analysis of the hippocampal amnesic syndrome: 14-year follow-up study of H.M. *Journal of Neuropsychologia*, 6, 215-234.
- Mishkin, M. (1982). A memory system in the monkey. *Philosophical Transactions of the Royal Society of London*, 298(B) 85-95.
- Mishkin, M., Malamut, B., & Bachevalier, J. (1984). Memories and habits: Two neural systems. In G. Lynch, J. L. McGaugh, & N. M. Weinberger (Eds.), *Neurobiology of learning and memory* (pp. 65-77). New York: Guilford Press.
- Neisser, U. (in press). A sense of where you are: Functions of the spatial model. In P. Ellen & C. Thinus-Blanc (Eds.), *Cognitive Processes and Spatial Orientation in Animal and Man*. Dordrecht, The Netherlands: Martinus Nijhoff.
- O'Keefe, J. (1979). A review of the hippocampal place cells. *Progress in Neurobiology*, 13, 419-439.
- O'Keefe, J., & Nadel, L. (1978). *The hippocampus as a cognitive map*. Oxford: Clarendon Press.
- O'Keefe, J., & Nadel, L. (1979). Precis of O'Keefe and Nadel's: The hippocampus as a cognitive map. *The Behavioral and Brain Sciences*, 2, 487-533.
- Olton, D. S. (1983). Memory functions and the hippocampus. In W. Seifert (Ed.), *Neurobiology of the hippocampus* (pp. 335-373). New York: Academic Press.
- Olton, D. S. (in press). Temporally constant and temporally changing spatial memory: Single unit correlates in the Hippocampus. In P. Ellen & C. Thinus-Blanc (Eds.), *Cognitive processes and spatial orientation in animal and man*. Dordrecht, The Netherlands: Martinus Nijhoff.
- Rawlins, J. N. P. (1985). The hippocampus as a temporary memory store. *The Behavioral and Brain Sciences*, 8, 479-497, 514-528.
- Richards, W. (1973). Time reproductions by H.M. *Acta Psychologica*, 37, 279-282.
- Roitblat, H. L. (1982). The meaning of representation in animal memory. *The Behavioral and Brain Sciences*, 5, 353-372.
- Rolls, E. T., Miyashita, Y., Cahusac, P., & Kesner, R. O. (1985). The responses of single neurons in the primate hippocampus related to the performance memory tasks. *Society for Neuroscience Abstracts*, 11, 525.
- Solomon, R. (1979). Temporal versus spatial information processing theories of hippocampal function. *Psychological Bulletin*, 86, 1272-1279.
- Solomon, R. (1980). A time and a place for everything? Temporal processing views of hippocampal function with special reference to attention. *Physiological Psychology*, 8(2), 254-261.
- Squire, L. R., & Cohen, N. J. (1984). Human memory and amnesia. In J. McGaugh, G. Lynch, & N. Weinberger (Eds.), *Neurobiology of Learning and Memory*. New York: Guilford Press.
- Squire, L. R., & Zola-Morgan, S. (1983). The neurology of memory: The case for correspondence between the findings for man and non-human primate. In J. A. Deutsch (Ed.), *The physiological basis of memory* (pp. 199-267). New York: Academic Press.
- Terrace, H. S. (1984). Animal cognition. In H. L. Roitblat, T. G. Bever, & H. S. Terrace (Eds.), *Animal cognition* (pp. 7-28). Hillsdale, NJ: Erlbaum.
- Teyler, T. J., & DiScenna, P. (1986). The hippocampal memory indexing theory. *Behavioral Neuroscience*, 2, 147-154.
- Watanabe, T., & Niki, H. (1985). Hippocampal unit activity and delayed response in the monkey. *Experimental Brain Research*, 325, 241-254.
- Weiskrantz, L. (1971). Comparison of amnesic states in monkey and man. In L. E. Jarrard (Ed.), *Cognitive processes of non-human primates* (pp. 25-46). New York: Academic Press.
- Wible, C. G., Shapiro, M., Findling, R. L., Lang, E. J., Crane, S., & Olton, D. S. (in press). Mnemonic correlates of unit activity in the hippocampus. *Experimental Brain Research*.

Received May 14, 1986 ■