

# The Hippocampus and Space Revisited

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The hippocampal formation has long been the focus of intense interest among neuroscientists. The discovery by Scoville and Milner (1957) that the mesial temporal lobe, including the hippocampal formation, played a central role in memory function in humans can be said to have started the modern era of research on this brain system. There followed two decades of animal research aimed at creating experimental models of the memory defects observed in humans, including my dissertation research, which met with scant success (Nadel, 1968). Indeed, when John O'Keefe and I started considering the hippocampus and its possible role in *spatial mapping* several years later, one of our greatest challenges was to analyze the extant lesion literature in terms of this theory with the minimum amount of special pleading. There were already several hundred such studies, varying extensively in terms of exact size and regional location of the lesion, the means by which the lesion had been created, the kind of animal used, the nature of the task, the kind of motivation employed, and so on. Yet, it was our feeling in 1976, when we terminated the review of the lesion literature, which was ultimately published in *The Hippocampus as a Cognitive Map* (O'Keefe and Nadel, 1978), that the spatial hypothesis successfully handled the vast preponderance of these lesion studies as well as what was then known about the physiology of the hippocampal formation.

In the years following publication of the book, most published lesion studies were concerned in some way with the spatial map hypothesis; most often, comparisons with rival hypotheses were involved. This was a frustrating period because, although many thought they were testing our ideas, too frequently the major themes we hoped to stress were misconstrued. In this article I dig back into the book we published in 1978 and reiterate some of the themes that were important to us then, and remain so now. By so doing, I hope to bring out some of the reasons why we thought, and continue to think, that space is so special as to warrant a structure as compelling as the hippocampal formation.

I will concentrate on three major issues. First, I will discuss at some length the fact that our theory was about a *spatial memory* system, not simply a "spatial" system. Second, I will discuss our assumption that the spatial memory system we allocated to the hippocampus was but one of many spatial systems, and that the role of these various systems can best be understood if one takes into consideration an animal's behavior in its natural habitat. Third, I will briefly discuss our view that in the human hippocampus, at least in the left hemisphere, the mapping system represents something more abstract than physical space.

Before turning to these substantive points, however, a brief digression into methods and first principles is in order. Some

years before the book was published, O'Keefe and I published a paper (Nadel and O'Keefe, 1974) in which we presented some of the reasons for hypothesizing that the hippocampal system is engaged in cognitive mapping. We also discussed an underlying principle guiding our approach to brain function in general and the hippocampal system in particular—the principle of multilevel analysis and proof. We asserted that one of the major problems with then-extant models of hippocampal function was that they depended upon data generated within a single domain of inquiry (lesions, physiology, anatomy, etc.). In so doing, they became subject to what we called "hypothesis drift"—as soon as contradictory data were reported, the hypothesis could be easily recast to accommodate the new facts. Because such hypotheses were tied to only one level of analysis, they could, and in fact did, drift all over the map. The notion that the hippocampus was involved in response inhibition was an excellent example (Nadel et al., 1975). We suggested that a meaningful hypothesis of the function of some brain area should be constrained by data generated from several levels simultaneously, using the method that has come to be called convergent operations. Thus, we argued that there was little point in deriving a theory of the hippocampus that made great sense in terms of the lesion data, but had nothing to say about physiology and anatomy.

In our theory we made an attempt to link our model to as many levels of data as possible; the success or failure of the spatial hypothesis must be viewed in this light. We felt, and still feel, that other models of hippocampal function must aspire to the same multilevel analysis, lest they fall prey to hypothesis drift or mere operationalism. Perhaps we were ambitious at the time, but 15 years later this should not be the case. We now know a great deal more about the details of hippocampal anatomy, physiology, pharmacology, behavioral involvement, and even its computational structure. All these facts, and more, should find their place in any respectable theory of hippocampal function. At the very least, one should not postulate theories that ignore, or flatly contradict, entire bodies of facts generated at another level. Since the writing of the book, another domain of evidence has emerged that must be woven into the tapestry—data from ecological/evolutionary studies. I will discuss these data at some length below, as I believe they provide some of the strongest evidence to date in favor of the view that the hippocampal system is quite specifically a spatial mapping system.

## THE HIPPOCAMPUS AS A SPATIAL MEMORY SYSTEM

The cognitive map theory of hippocampal function is, first and foremost, a theory about *memory* for spatial layouts and the ways in which animals use such a memory system for

adaptive behavior in the world. We could hardly have been thinking of anything else, given our exposure to Brenda Milner and her colleagues at the Montreal Neurological Institute. Notwithstanding what we thought was a clearly stated position on this point, a curious thing happened—it was somehow assumed that we were not discussing memory at all. It is true that we were not discussing the kind of *global* memory function thought to be disrupted in the amnesic syndrome.

The study of memory function in the hippocampus (and many other brain structures) has often proceeded under the implicit assumption that memory is a unitary phenomenon. While few investigators would state this assumption explicitly, it is none the less present, often specifying certain cortical areas as the site of permanent memory. Rather fewer researchers hold the other traditional view, associated with Lashley, that memory cannot be localized in this way. The trend of much recent research indicates that neither the non-localization nor the limited localization theories are completely acceptable. Instead, it appears that there are different types of memory, relating perhaps to different kinds of information, and that these are localized in many, possibly most, neural systems. We have hinted at this view by emphasizing the notion that behaviour, viewed at the molar level, consists of the use of particular hypotheses, each type resting on a different form of information. The memory for these would be stored in different neural areas, corresponding perhaps to those areas responsible for specific forms of information processing. Under this assumption there is no such thing as *the* memory area. Rather, there are memory areas, each responsible for a different form of information storage. The hippocampus, for instance, both constructs and stores cognitive maps (O'Keefe and Nadel, 1978, pp. 373–374).

Adherence to such a multiple-memory system view has now become the accepted norm (cf., Nadel and Wexler, 1985; Polster et al., unpublished observations), but when we espoused such a view in 1978 we had only Tulving (1972) to look to for support. Our limited-memory notion of hippocampal function was sufficiently different from the standard view that cognitive map theory was considered merely a theory about space, not memory. The reasons for this are historical, as noted in the passage quoted above: in the 1950s and 1960s the predominant view of memory was that there was an integrated memory function, presumably subserved by a centralized neural system. The *global amnesia* purportedly observed in H.M. encouraged many to adopt the view that some aspect of that centralized memory system had been disrupted in his case. This single memory "box" would be concerned with all kinds of information, following along lines laid out in the information-processing tradition within a resurgent cognitive psychology at that time. However, such an approach ignored the fact that H.M. and other patients were known early on to be not quite "global" in their defects (Milner, 1962). Some forms of learning remained, and Milner was certainly aware of the important implications of this fact.

Cognitive map theory presupposed a different understanding of the organization of learning systems than this traditional view. It followed along lines established by Tolman (1949), who emphasized that there were multiple forms of learning. We assumed that there were two classes of learning systems, corresponding roughly to the notions of "knowing that" and "knowing how." We created new names for these

two classes of learning systems: *locale* and *taxon*. These names were chosen to represent certain critical features of each of the learning systems. In the case of the *locale* system this was the fact that the memories it contained incorporated information about place and time; in the case of the *taxon* systems it was the fact that they were governed by the rule of category inclusion. Memories in *taxon* systems were organized in terms of features and their similarity/dissimilarity, while those in the *locale* system were not. There was also an important distinction between these learning systems in terms of the role of time/place context—it played a central role in *locale*-based memories, but was absent from *taxon*-based memories.

These distinctions were not entirely novel to us. Ryle (1949) and many others made roughly the same points, and I think it is reasonable to say that similar distinctions lie at the root of many subsequent modular memory proposals. Yet, there are important differences here, most prominently our insistence that the foundation for one of the systems—the *locale* system—lies in its inclusion of spatial information. In the years since our formulation of this theory, there has been much support for the view that the hippocampus is crucially important in the processing of spatial information (cf. Barnes, 1988). What has been rejected is our insistence that this spatial signature is the best way of describing hippocampal function. The past decade has witnessed the formulation of a number of alternative hypotheses; the core of most of these hypotheses is that there must be some more abstract characterization of the kind of information the hippocampus is responsible for processing than the (deceptively) simple notion of space we suggested. Notions such as working memory (Olton et al., 1979), temporary memory (Rawlins, 1985), declarative memory (Squire, 1987), and configural association (Sutherland and Rudy, 1989) have been proposed, among others. These views tend to accept our claim that spatial information is an important example of the kind of information processing engaging the hippocampus, but all go further to argue that spatial information is not the only kind of information the hippocampus is concerned with. Hence, we encounter the frequently asked question: do we remain insistent on the central role of spatial information in accounting for hippocampal function and, if so, why? In the next section I discuss some of the reasons why we think spatial memory is so special. This is preceded by a brief comment and one extended exception that, together, permit me to discuss some of the important data that have been generated in lesion and other studies of hippocampal function over the past 15 years. The brief comment: my reading of the general run of the rodent lesion literature in this time period is that it supports, with a small number of exceptions, our position that it is the spatial nature of a given task that determines whether or not hippocampal disruption will influence learning. Thus, when the spatial hypothesis has been directly contrasted with, for example, the working memory hypothesis or the temporary memory hypothesis, and when an appropriate spatial task has been used (see below), the spatial hypothesis has generally been supported (cf. Rasmussen et al., 1989; Jarrard and Davidson, 1990; for some recent examples). This work did not address the configural association hypothesis, which remained a plausible hypothesis, given their results.

The extended exception concerns evidence from single-unit recording studies that clearly demonstrates that the hippocampal cognitive mapping system is part of a memory system, as postulated in our early writings. The first finding of this sort was published by O'Keefe and Conway (1980), but more convincing evidence was reported by O'Keefe and Speakman (1987). They trained rats on both a reference-memory and working-memory version of a place learning task on a four-arm maze in a controlled-cue situation. After rats were trained to perform at a high level in this situation, microdrives were implanted and single cells were recorded that had stable fields in the environment. On a critical "probe" trial the animal was exposed to the situation but not permitted to enter the body of the maze. Then, the cues were all removed, and the animal was allowed to move through the maze. The critical question here was whether or not the place cells would retain their place specificity—the answer was a resounding yes for 27 of 30 cells recorded in the study. As the animals moved through the maze and environment, now devoid of any distinguishing cues, place cells continued to fire in the right locations; the animals continued to behave properly, seeking reward in the correct locations. Interestingly, on those trials on which the animal made a behavioral mistake, the place units fired incorrectly also. O'Keefe and Speakman concluded that the hippocampal spatial map system is a memory system, and that this internally represented memory of the environment, in combination with information about the animal's movements, permitted updating of the place-field representations and the correct unfolding of both neural activity and navigational behavior. A similar finding has been reported by Jones-Leonard et al. (1985). In this case, rats were exposed to a familiar environment in which place cells had been identified; the behavioral task involved forced choices on an eight-arm radial maze. Place field locations remained consistent under all but one circumstance. In this case, the room lights were turned off either before or after the animal had been exposed to the environment on that day. When the lights were off during first exposure to the environment, the place cells no longer fired in the locations where their activity had been consistently maximal in the past. When the lights were on as the animal was initially placed in the environment, and were then turned out, a different picture emerged. Place cells fired in the correct locations while the lights were on and maintained this correct firing even after the lights were turned off, even though the rat might not have been in the place field at the moment the lights went out. In discussing these studies, Leonard and McNaughton (1990) suggest that "the spatial selectivity of the discharge of place cells can be determined by the animals' memory of the spatial relationships of the visual features of the experimental environment" (p. 411). A recent study by Mizumori et al. (1989) provides even stronger evidence that the hippocampal system is capable of maintaining appropriate activity patterns in the absence of all the inputs normally associated with place cell activity. Injections of tetracaine into the medial septal region eliminated movement-induced theta modulation of hippocampal EEG, as well as causing a significant reduction in location-specific firing in hilar/CA3 place cells; however, there was no comparable change in the location-specific firing patterns of CA1 place cells. Mizumori et al. argue that this pattern of

results indicates that hippocampal circuits perform a "pattern-completion" operation essential to retrieving memories under reduced input conditions (cf. McNaughton and Nadel, 1989; McNaughton and Barnes, in press).

Though there remain subtle disagreements about just how the hippocampal system manages these memory effects, these studies show very clearly that the hippocampal cognitive map system is part of a memory system. They do not, however, show that memories are permanently stored in the hippocampus itself. This is a rather tangled issue, which I will not discuss at any length here, as it is not germane to the question of the special role of the hippocampal system in spatial memory. However, it is worth making a few comments. In 1978 O'Keefe and I claimed that long-term memories for spatial layouts were stored in the hippocampal formation. This claim has attracted a good deal of attention, much of it negative. The general point here is that the hippocampus is responsible for storing the results of a learning experience only for a limited time, during which information is somehow established in nonhippocampal (presumably neocortical) circuits. After a sufficient *consolidation* period, the hippocampus is no longer necessary for appropriate performance based on this prior learning (e.g., Squire et al., 1984). The evidence that is usually adduced in favor of this view comes from lesion studies, in which it is demonstrated that a certain time after learning, the hippocampus can be ablated without disruption of performance (Zola-Morgan and Squire, 1990; Winocur, 1990; Kubie et al., 1990). What is always overlooked in these discussions is the simple logical fact that such demonstrations say nothing about the status of memory storage in the hippocampus—they address only the question of whether there is adequate information outside the hippocampus to support performance. It is very interesting that the establishment of such adequate extrahippocampal storage takes time, but it does not logically follow that during the same time period information is disappearing from the hippocampal system. Such a claim demands a different kind of evidence, which has not yet been provided. There is indirect evidence from studies of synaptic plasticity (see below), and there is the conceptual argument based on storage capacity limitations, but there is no direct evidence indicating that the hippocampal memory trace slowly disappears in parallel with establishment of the neocortical engram. In any event, what is now being suggested is that the "temporary" period of hippocampal storage lasts on the order of several years. Surely, a duration this indefinite makes distinctions between "long-term" and "temporary" storage a matter of semantics.

To summarize, the major point of this section is that the hippocampal cognitive mapping system is a memory system whose information content is selective, and whose adaptive purpose is to provide the basis for behavior based on knowledge about environments gained in the past. I also will not discuss at any length the phenomenon of *long-term potentiation*, or *enhancement* (Lømo, 1966; Bliss and Lømo, 1973; McNaughton et al., 1978; and many hundreds of others in the years since), the best current example of a neurophysiologically plausible candidate for memory that has proven to be most easily elicited in the hippocampal formation. I consider the existence of LTP/E to be a relatively strong indicator that the hippocampus is involved in memory, but,

alone, it is not sufficient to prove the case. In any event, many questions remain about how long LTP/E lasts and what its duration signifies for the persistence of memories in the hippocampus itself, as noted already.

Finally, it is important to note another aspect of our 1978 theory that has attracted very little attention: the central role given to *exploration* in the creation of cognitive map representations.

The hippocampal locale system is assumed to form the substrate for maps of environments an animal has experienced; *these maps are established in the hippocampus during exploration, a species-specific behaviour pattern concerned with the gathering of information. . . . Exploration is a direct response of the animal to the detection of a mismatch by the locale system; in the absence of the hippocampus all forms of exploratory behaviour should disappear from the animal's repertoire* (O'Keefe and Nadel, 1978, p. 242, italics in the original).

Two forms of evidence were adduced in support of this notion: (1) the existence of a subclass of place cells in the hippocampal formation that responded maximally in a given location when something novel happened in that location (O'Keefe, 1979; O'Keefe and Nadel, 1978); and (2) evidence that hippocampal lesions interfered with normal exploratory behavior. Given the centrality of these assertions concerning exploration and the cognitive mapping system, it remains a considerable surprise to me that so few studies of exploration have been conducted in the past decade or so. With a few notable exceptions (e.g., Harley, 1979; Morris, 1983; Renner, 1990), the whole area of exploratory behavior and its relation to the cognitive map theory of hippocampal function has been ignored. One reason, perhaps, is that while exploration can be seen as an integral part of a spatial mapping theory, it does not relate in any obvious way to working memory, declarative memory, configural associations, and the like. Nonetheless, the facts connecting the hippocampus to exploration, which play a central role in cognitive map theory, remain to be explained by any successful theory that seeks a more abstract characterization of hippocampal function. The recent demonstration of "exploration-dependent modulation" of evoked activity in the dentate gyrus (Sharp et al., 1989; Green et al., 1990) only confirms the importance of this connection between exploratory behavior and the hippocampal information-storage system.

### THE SPECIAL NATURE OF SPATIAL INFORMATION

"Space plays a role in all our behaviour. We live in it, move through it, explore it, defend it. We find it easy enough to point to bits of it: the room, the mantle of the heavens, the gap between two fingers, the place left behind when the piano finally gets moved" (O'Keefe and Nadel, 1978, p. 5). These opening words of the book stated our central claim: space is ubiquitous and crucially important to almost everything we do. We argued that space is unlike color, motion, or other contingent properties of objects and the physical universe. Such things can be taken away, but space can not. The first reason, then, for viewing space as unusually important is its special status as an ineliminable property of our experience in the world.

Indeed, we argued that spatial information is so important that there are many brain systems devoted to representing various aspects of it. We drew crucial distinctions between these diverse forms of spatial information, but to a large extent these distinctions were not grasped by early interpreters. The most important distinction was related to that between *egocentric* and *nonegocentric* spatial systems, not least because we assumed that the hippocampal formation was critical for the latter, but unnecessary for the former.

According to this multiple spatial systems view, there should be many so-called spatial abilities that would be unaffected by lesions in the hippocampal formation, and a rather select class of such abilities that are affected. For example, many behavioral tasks demand that animals respond to an alley on the left (or right), or an object to one side or other of the experimental apparatus. Such tasks can be performed readily by animals with damage in the hippocampal system, but such performance says nothing about the cognitive map theory. It is only nonegocentric tasks, such as the *place learning* tasks designed by O'Keefe et al. (1975), Olton and Samuelson (1976), and Morris (1981; Morris et al., 1982), that truly and necessarily test the functions of the hippocampal cognitive mapping system as we described it, and they all demonstrate devastating deficits after damage to the hippocampal system.

Our emphasis upon these varied forms of spatial representation, and their underlying neural substrates, was embedded in a particular view of behavioral neuroscience that was not very popular in the 1970s and is only slightly more so now. It relates in a very central fashion to the main theme I wish to emphasize in this section of the paper: the fundamental importance of adopting a perspective on brain and behavioral organization that takes into account ecological, evolutionary, and ethological aspects of the animal under study. I will argue below that recent evidence from this approach, unknown at the time we wrote our book, provides one of the strongest reasons for insisting on the importance of space in describing hippocampal function.

We described our views on the methods used in behavioral neuroscience in the section of the book dealing with the results of single neuron recording studies, which had produced the initial, and strongest, evidence for the cognitive map theory. It is worth quoting this section at some length here, as the points it made bear repeating.

There are two fundamentally different approaches to the study of single-unit activity in the freely-moving animal. These roughly parallel the two different approaches to the study of behaviour we outline below . . . and have close affinities with the different types of experiment on hippocampal EEG . . . The first can be called *neuropsychological* and the second *neuroethological*. The neuropsychological approach draws its inspiration from the methodology of behavioural psychology which has dominated animal experimental psychology in most countries for the past 30 years. The experimenter addresses himself to a limited number of pre-ordained questions (usually one) about unit activity, and seeks to design a well-controlled study which will answer them. For example, he might want to know whether the unit responds to a particular stimulus or not, whether that response decrements when repetitively elicited, or whether changes in the animal's behaviour or attitude towards a stimulus are paralleled by a

change in the unit's responses. Often the stimulus and situation are chosen so as to be devoid of biological significance to the animal at the start of the experiment. The underlying assumption appears to be that the animal's biological constitution and its ecological niche are incidental, or irrelevant, to the behaviour of its neurones. Instead, interest centres on such abstract psychological concepts as learning, habituation, memory, and so on. The units in a particular neural area are treated as a group. Thus, we learn that in nucleus X 31 percent of the units responded only to the 2 Khz tone, 19 percent to the flashing light, 12 percent to both, and 38 percent to neither. This may be like concluding that there is a remarkable uniformity amongst computers, caryatids, chrysanthemums, and coprophagists, since they are all polysyllabic, begin with a hard C sound, and denote entities which fall at the same rate in a vacuum. . . . The advantages of the neuropsychological approach are clear: it affords a degree of control over the experimental situation which will eventually be necessary if the laws governing the operations of the nervous system are to be discovered. Its drawbacks result from its premature application. . . . At the rate of one or two questions per experiment, it will be many years before we hit upon the correct question, even with a good bit of luck and insight. . . .

The neuroethological approach differs from the neuropsychological one in several respects. First, it seeks to study the activity of single units in as naturalistic a setting as possible, in the belief that an animal's behaviour in its natural environment maximizes the possibility of producing changes in unit activity that are meaningfully related to that unit's function. It thus embodies the reasonable assumption that the brain of a particular animal is built to operate in a specific environment. (O'Keefe and Nadel, 1978, pp. 190-194)

The central point made here, with respect to single unit recording methodology, applies with equal force to the lesion literature. In particular, I would point out its relevance to any discussion of the apparent discrepancies in results obtained with rodents and primates. While the rodent literature has strongly supported the spatial/cognitive map theory, the primate lesion literature has generally moved off in a different direction (cf. Zola-Morgan and Squire, 1985; 1986). Here, the emphasis has been on the neuropsychological approach described above, and the conclusion has been that the hippocampal system in the monkey is involved in certain forms of both spatial and nonspatial memory, at least for some lengthy consolidation period. It has frequently been asserted that there is nothing particularly spatial about the defect seen after hippocampal damage in monkeys. An alternative perspective has recently surfaced in the work of Parkinson et al. (1988), who developed a task that selectively assesses location memory in monkeys. Their results indicated that "the hippocampus is critical for the rapid formation of object-place associations" (p. 4159). Indeed, recent single-neuron recording studies in primates have indicated that "place cells" can be found in the hippocampus of this species as well (Ono et al., 1989; Rolls et al., 1988; Feigenbaum and Rolls, unpublished observations).

The point to be made here is that many of the tasks used in the work with primates are highly artificial. It is hard to see exactly what real-world functions are being tapped in what is deemed the signature task for the primate hippocampus—the delayed nonmatching to sample (DNMS) task. In this situation, animals are first shown a novel object and then,

after a delay, are shown that object plus another new one. In the nonmatching task the animal must choose the new object, while in the matching task it must choose the one it had seen on the "sample" presentation. The fact that nonmatching is easier for monkeys than is matching indicates that the novelty of the objects plays an important role in solving this task. Is performance on this task then a function of an animal's ability to recognize novelty? If so, then since recognition memory depends upon the "ability to recognize a stimulus object as one that was seen recently, or as one seen in a particular time and place" (Squire and Zola-Morgan, 1983, p. 225), perhaps it is not surprising that the DNMS task is disrupted by hippocampal lesions. The real problem here lies in determining the relation between the true functions of the underlying brain system, and the capacities required by the kinds of artificial tasks used in the laboratory setting. There are two ways in which one might approach this question. First, one might argue that there is a specific capacity related to "matching-to-sample" (or nonmatching) that is at the root of hippocampal function, and that could be shown to provide the selective pressure driving hippocampal development in phylogeny (see below). Second, one might argue that hippocampal evolution was driven by some other capacity, perhaps even spatial mapping, but that by the process of exaptation, this brain system became specialized for a broader range of functions (Sherry and Schacter, 1987), such as working, temporary, declarative, or configural memory. What seems incontestable is that anyone seeking to propose a theory of hippocampal function should ask, and should provide an answer to, the following question: "What ecologically important function is being served by this brain system?"

It is my view that simply demonstrating the impact of a lesion in brain structure X on some abstract behavior or capacity Y does not tell us very much about what structure X is doing. Without some theory of what sort of information is involved in solving the task that supposedly requires capacity Y, we cannot begin to imagine what it is that structure X is doing, even though lesioning it has a clear-cut effect on an easily measured, but poorly understood, behavior. Nor can one take the view that structure X is simply a "memory" structure, independent of specifying what kind of information is being stored and/or retrieved by this structure. The clear thrust of the multiple memory systems view is that there are separate systems involved with different kinds of information, while no system is involved with memory *per se*, a position accepted by virtually all who are currently working on the hippocampus. This is also not a new idea; the core of it dates back at least to Johannes Muller and his law of specific nerve energies, which stated that the content of information carried by particular neurons is determined by which neurons are active. That is, activity in neurons in the visual system conveys visual experience, whether triggered by visual inputs to the retina, or tactual pressure applied directly to the eye. What matters is which neurons are active, not how they were made active. This notion has become quite prominent in recent connectionist models of memory that depend upon "content-addressable memory" rather than the "location-addressable" memories typical of digital computers and early information-processing models of cognition. The disadvantage of notions like "working memory", "declarative mem-

ory", "temporary memory", and "explicit memory" is that they say little about the *kind* of information the system is handling, hence they must fail to make unambiguous predictions about the results of various experiments, especially in animals, where the conscious awareness typically associated with explicit or declarative memory cannot be directly assessed. As a result, these notions are subject to hypothesis drift, or to being merely operational definitions rather than theories.

Thus, a major reason to persist in couching hippocampal function in spatial terms is the fact that the ability to move about in space in an effective fashion is indisputably an ecologically important form of behavior. The ability to make delayed matches from sample, for example, does not on its face have this sort of naturalistic validity. It seems incumbent on those who would replace a spatial theory with a more abstract notion of what the hippocampus is doing to relate their abstractions to the real world in which the hippocampal system, like all brain systems, evolved. To my knowledge such has not yet been done.

These ecological musings were just that in 1978, but in the years since publication of the book an entire domain has emerged that provides very strong support for the assertion that the hippocampal system is shaped by its spatial function. Two sorts of evidence are important here. First, two separate research groups have demonstrated a relation between the size of certain hippocampal structural parameters and performance on tasks usually influenced by hippocampal lesions. For example, Wimer et al. (1971) showed that performance on certain forms of avoidance behavior depended on the size of the mossy fiber pathway conveying fibers from the dentate gyrus to the CA3 field. Wimer et al. (1983) showed that there is a negative correlation between dentate granule cell density and two-way active avoidance performance. Note that hippocampal lesions have been shown to *facilitate* two-way-avoidance performance, hence the negative correlation fits the lesion result. Lipp, Schwegler, and their colleagues (see Lipp and Schwegler, 1989, for a review of these studies) have replicated and extended these findings to spatial maze learning, in which size of the infrapyramidal mossy fiber terminal field was seen to correlate positively with performance (Schwegler et al., 1988). They have also shown that the negative relation between mossy fiber extent and two-way active avoidance learning can be manipulated in individual animals epigenetically (Lipp et al., 1988). Variability in the extent of the mossy fiber system was created through early postnatal injections of thyroxine or saline. Performance on the two-way avoidance task was related to the extent of the infrapyramidal mossy fiber system in individual animals, regardless of the genetic strain from which they were drawn. Taken together, such results suggest that variations in the size of certain hippocampal structural parameters can influence performance on tasks also known to be influenced by hippocampal lesions. These studies do not, however, provide conclusive evidence that there is a relation between the size of the hippocampal formation and performance on spatial tasks in particular. More convincing evidence for this notion has emerged in recent years from a considerable number of studies done in a variety of species, which show that there is a relation between the extent to which a species utilizes space

(in the cognitive mapping sense) and the size of the hippocampal system.

This was first shown in birds, and has more recently been demonstrated in mammals as well. The critical first study was reported by Krebs et al. (1989), who measured the volume of the hippocampal complex relative to brain and body size in 35 species or subspecies of passerine birds. They showed that hippocampal size

is significantly larger in species that store food than in species that do not. Retrieval of stored food relies on an accurate and long-lasting spatial memory, and hippocampal damage disrupts memory for storage sites. The results suggest, therefore, that food-storing species of passerines have an enlarged hippocampal complex as a specialization associated with the use of a specialized memory capacity. Other life-history variables were examined and found not to be correlated with hippocampal volume (p. 1388).

For example, the hippocampus of the marsh tit is 31% larger than the hippocampus of the great tit, even though the remainder of the forebrain of the latter is larger. The authors concluded that the relation between hippocampal size and food storing behaviors "is likely to be related to the facts that food storing places special demands on spatial memory and that the hippocampus plays a role in spatial memory" (p. 1390). In this study the authors looked for, but did not find, any relation between hippocampal complex size and whether a particular species of birds engaged in migratory behavior. Others, however, have shown quite clearly that there is an important role for the avian hippocampal complex in homing and navigational behavior, whether or not the particular species is migratory.

In a series of studies, Bingman and his colleagues (Bingman et al., 1984; 1987; 1988a; 1988b; 1990; Bingman and Mench, in press) have assessed the effects of lesions in the hippocampus and parahippocampus of the pigeon on homing and navigational behavior. In the earlier studies these investigators showed that hippocampal ablations had little effect on navigational behavior in experienced adult homing pigeons. In the latest work, however, they have shown that hippocampal ablations in naive, young homing pigeons cause severe deficits in long-distance navigational behavior (Bingman et al., 1990) as well as in short-distance homing behavior (Bingman and Mench, in press). They conclude that

the hippocampus appears to be involved in the neural regulation of two independent spatial navigation systems in homing pigeons (Bingman, 1990): (a) one based on their navigational map, which supports navigation from distant unfamiliar locations, and (b) one based on the use of familiar landmarks in the vicinity of the home loft, which supports local navigation near home. In so far as these spatial navigation mechanisms can be assumed to be based on something like a cognitive map, the data from homing pigeons offer strong support for a cognitive mapping function (O'Keefe and Nadel, 1978) for the avian hippocampus (Bingman et al., 1990, p. 910).

Most important in the present context, these results for the avian hippocampal complex are exactly like those reported in the rodent. Bingman and Mench (in press) put it this way, in comparing their results to those obtained in the water-maze task in rats with hippocampal damage:

The paths taken by hippocampal lesioned rodents to arrive at their hidden goal is strikingly reminiscent of the flight paths taken by hippocampal lesioned homing pigeons. Together, rat and homing pigeon studies suggest the presence of a phylogenetically conservative cognitive mapping system whose neural control is in part regulated by the hippocampus and related structures.

The relation between the spatial demands of an animal's lifestyle (food-storing or not, homing and navigational needs, etc), and the size of the avian hippocampal complex, so convincingly demonstrated in the studies briefly reviewed above, has now been extended to the mammal, in an important set of experiments conducted in several species of voles. This work began with the demonstration of gender differences in spatial learning in species in which there are gender differences in natural range size, that is, if males and females of a given species of voles use space differently, this is mirrored by differences in their spatial maze performance when they are brought into the laboratory (Gaulin and Fitzgerald, 1986; 1989). The critical next step was taken by Jacobs et al. (1990), who demonstrated that there are gender differences in hippocampal size in a species of voles showing habitat range and spatial learning dimorphism, but not in a congeneric species of voles with an absence of such dimorphisms. They conclude that the evolution of hippocampal size is responsive to sexual selection for range size and spatial ability. Differences in range size between genders usually relates to whether a particular species is polygynous or monogamous; in the former case large differences in range size exist, while in the latter case such differences are usually absent. Since most mammals are polygynous, Jacobs et al. (1990) predict that "sex differences in hippocampal volume should be the dominant mammalian pattern" (p. 6351). Consistent with this speculation, we recently have shown significant differences in place learning between male and female rats (Warren et al., 1990). Similar differences in spatial ability between male and female rats have been reported by Williams et al. (1990). Thus, there is mounting evidence consistent with the view that it is the need for spatial information processing that drives hippocampal development in phylogeny (see also Cheng, 1986; Gallistel, 1990). This is an area of research that demands further investigation: Do these differences in hippocampal size go beyond what would be expected from allometric considerations? Are there gender differences in hippocampal size in humans? Are size differences genetically or epigenetically determined? Can these variations in hippocampal size be related to other proposed aspects of hippocampal function? One would hope that proponents of the "more-than-space" theories of hippocampal function will address at least the last of these questions in the near future.

### THE ROLE OF THE HIPPOCAMPUS IN HUMANS

Finally, and very briefly, I will toss in the towel and admit, as we did in 1978, that at least in the case of the human hippocampal system, there is more than merely spatial mapping going on.

The cognitive map in infra-humans should be viewed as a spatial map in which representations of objects experienced

in the environment are ordered within a framework generating a unitary space. However, the central property of the locale system is its ability to order representations in a structured context. The development of objective spatial representations is not the only possible use for such a system. . . . mapping structures can represent verbal, as well as non-verbal, information. For both of these forms the locale system will be shown to be central to a particular form of memory: that concerned with the representation of experiences within a specific context (O'Keefe and Nadel, 1978, p. 381).

The proposed role of the human hippocampus in locale memory, concerned with the representation of both physical space and what we (mis)labelled "semantic deep structure," was highly speculative when we wrote our book in 1978. In the intervening years, there has been considerable evidence in support of the first supposition—that the human hippocampus (at least in the right hemisphere) plays a role in spatial mapping—but little investigation of the second, more radical, claim. I will briefly review the data on spatial functions in the right hippocampus, then turn to the left hippocampus.

In a series of studies, Smith and Milner (1981; 1989) have demonstrated that in humans the "right hippocampal region also appears to have a special role in spatial learning and memory" (1989, p. 78). Most recently, Piggott and Milner (1990) have extended these findings in a complex scene recognition task, confirming a special role for the right hippocampal formation in spatial location memory. As with the work on primates, these authors express concerns over whether the defect observed in patients with right temporal lobectomy (which include damage to a variety of extrahippocampal structures, such as the amygdala) can be viewed as strictly a spatial defect, or whether it must be seen in a broader light. The critical test requires access to patients with damage restricted to the hippocampus in the right hemisphere; no such patients have yet been reported. It is clear from these data, however, that as in birds, rats, and monkeys, damage to portions of the hippocampal formation in humans has a devastating effect on the learning of any task involving memory for spatial location. That the defect in humans is specific to nonegocentric forms of spatial learning, as predicted, has recently been shown by Goldstein et al. (1989).

There is little more to be said now about the role of the hippocampus in the left hemisphere in "verbal mapping" than there was in 1978. To our dismay, there has been no systematic attempt to date to explore the possibility that the hippocampal formation has a central role to play in certain aspects of language. That there are verbal learning defects after damage to the hippocampus in the left hemisphere has been well-known for some time; the precise nature of these defects remains unclear, however. As we suggested in 1978, various forms of verbal learning, now referred to as *implicit* or *procedural* forms, are relatively intact in patients with amnesia incumbent upon hippocampal dysfunction. Other, more episode-bound, forms of verbal learning are seriously impaired by hippocampal dysfunction. What is lacking is a theory relating the specific functions of the hippocampal system to the types of memory problems encountered in verbal tasks. We provided a speculative model for such a theory in 1978, based on the early work of Jackendoff (1976) and others. More recently, Jackendoff and Landau (in press) have gone further



in showing how spatial cognition and spatial language might be related. We claimed in 1978 that a careful analysis of the verbal defects seen in human amnesic patients would add to their conclusion that there is some deep relation between the cognition of physical space, and the ways in which we talk about events in the world. This claim remains to be tested.

The major point to be made here, however, is that we did not insist on the purely spatial nature of the cognitive mapping system throughout phylogeny. One could then ask: if we were willing to admit a more abstract cognitive map into the human left hippocampus, why not admit a more abstract representational system into the monkey, rat, or even bird hippocampus? The answer then, as now, is simply that we did not, and still do not, see the need for such hypothesis drift. The beauty, if I may use that word, of the cognitive map hypothesis lay precisely in its specificity, detail, and lack of mere operationalism. We were referring to space, and we meant space, not abstractly, but concretely. The evidence from lesion studies comparing rival hypotheses does not suggest that we should abandon our spatial theory. The evidence from comparative studies suggests, in contrast, that we were on the right track when we insisted that it was the spatial nature of the information that characterized the hippocampal memory system. The evidence from work with human and nonhuman primates remains contradictory, but until those working with primate models propose a theory of what the hippocampus is doing that goes beyond operational definitions and how the structural facts fit this theory, we will not be displaced. One hopes that such a theory will address not only the results generated within the primate domain, but also the results of single-unit research and comparative analyses.

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