

Do Hippocampal Pyramidal Cells Signal Non-Spatial as Well as Spatial Information?

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ABSTRACT: It is generally agreed that the rat hippocampus is involved in spatial memory. Whether this is its sole or primary function, or merely one component of a broader function, is still debated. It has been suggested, for example, that the hippocampus stores information about flexible relations between stimuli, both spatial and non-spatial. In this paper, I reiterate the basic tenet of the cognitive map theory that the processing and storage of spatial information is the primary and perhaps the exclusive role of the hippocampus in the rat, and that data that appear to contradict this have been misinterpreted. These data are found in reports of non-spatial correlates of unit activity recorded in the awake animals and reports of deficits on non-spatial tasks following hippocampal lesions. In this paper, I examine both claims and suggest alternative explanations of the data. The first part of the paper contains a review of some of the properties of hippocampal place cells, which might be misinterpreted as non-spatial in "non-spatial" tasks. For example, if an animal is trained to carry out a sequence of stereotyped actions in different parts of an environment, there will be a strong correlation between the performance of each behaviour and the animal's location, and it is necessary to rule out the locational correlate as the cause of the firing pattern. The second part of the paper looks at the results of experiments on conditioning and non-spatial discrimination tasks and concludes that the results are less supportive of a more general relational theory of hippocampal function than has been suggested. Furthermore, there is often a discrepancy between the correlates of unit firing in non-spatial tasks and the absence of an effect of hippocampal damage on these same or similar tasks. It is concluded that, contrary to the claims of its detractors, the cognitive map theory is still the theory of hippocampal function that is most clearly specified, makes the most testable predictions, and for which there is the strongest experimental support. *Hippocampus* 1999;9:352–364. © 1999 Wiley-Liss, Inc.

map theory states that this is the sole function of the hippocampus in the rat, that the structure was designed to carry out this specific function, and that its components are wired up to achieve that purpose. It is, of course, possible to modify such a system to accomplish different or additional functions by adding components or by changing the data that is fed into it. For example, Nadel and I have suggested that the addition of a temporal component to the basic spatial map in the human provides the basis for an episodic memory system. Similarly, in a second, separate development in the human we envisaged the dedication of the left hippocampus to linguistic functions by the alteration of its input from the neo-cortex (see also O'Keefe, 1996). Both of these enhancements were viewed as modifications incorporated into the basic spatial function and neither was seen as requiring significant alterations of the way in which the system worked. For example, the temporal component of the human episodic memory system would consist of the addition of a fourth dimension to the three-dimensional spatial mapping system.

An alternative view is that the hippocampus is a more general memory system concerned with a wide range of relational associations and not confined to just spatial ones (Cohen and Eichenbaum, 1993). In this view, the prominent role of the hippocampal system in spatial navigation and spatial memory reflects the prominence of spatial relations in the physical world and is not intrinsic to the biological functions of the system itself. Not all relations, however, require the hippocampus and here the trouble begins. The major problem with this neo-Guthrian view is the methodological one of delimiting the range of hippocampally-dependent relationships so that the theory is testable. On the face of it, any situation in which an animal finds itself can be described as an infinite set of relationships and it is difficult to see how the brain, much less the hippocampus, could be expected to identify and encode all of them. Eichenbaum and colleagues have attempted to specify more precisely those relationships that depend upon the hippocampus as opposed to those that do not. They have suggested, for example, that hippocampally-dependent relationships are those that are "flexible," i.e., usable

INTRODUCTION

There is general agreement that one of the functions of cells in the hippocampal formation of the rat is to signal the animal's location in an environment. Furthermore, it is widely accepted that damage to this structure leads to severe spatial impairments in this animal. These findings have been interpreted as support for the idea that the hippocampus in animals such as the rat operates as a dedicated spatial module, a cognitive map (O'Keefe and Nadel, 1978). The strong interpretation of cognitive

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under circumstances other than those in which they were learned; or, alternatively, those that cannot be coded by a single neocortical module; or, most recently, those that involve elements discontinuous in time and space (Wallenstein et al., 1998). There are problems with each. The flexibility criterion fails the empirical test: the clearest and simplest example of a flexible relationship is that required to solve the delayed non match-to-sample task. In this task, the animal earns a reward by choosing the stimulus that is different from a recently presented sample. The animal must respond differently on the choice phase of the task than on the acquisition phase, requiring flexibility. As we shall see, this relationship does not seem to be well represented in the firing of hippocampal cells nor do hippocampal lesions prevent the animal from solving the problem as well as normal controls. The second attempt to delimit the class of hippocampally-dependent relations uses a negative criterion. Relations that can be represented and stored in a single neocortical module do not require the hippocampus; only those based on information stored in two different modules do. This essentially defers the problem until the nature of stimulus processing in all of the neocortical modules that feed into the hippocampus is better understood. This leaves the final version, which identifies the set of relations dependent on the hippocampus as those noncontiguous in space and time. This has the merit of being clear and testable, and makes contact with a prior history of thinking about hippocampal function. A role for the hippocampus in the processing of temporal information was originally suggested by Solomon (1979) and Rawlins (1986). It is also closer in spirit to the extension of the cognitive map theory developed for the human (O'Keefe and Nadel, 1978), which is viewed as storing and relating spatio-temporal events as well as purely spatial information. It should be noted, however, that even here the results on delayed match-to-sample tasks are not supportive since there is often a delay between the training and testing phases, introducing a temporal discontinuity to the relationship.

A second major problem with the relational theory is that, although it purports to handle the place cell data, it only does so in a superficial manner and does not account for the fine details. For example, as I shall show later in this article, it fails to account for the fact that the (contiguous) adjacent walls of the testing box have an influence on the location and shape of place fields; nor does it account for the fact that the absolute firing rate of the place cell codes, at least in part, for the animal's speed of movement through the field. Furthermore there is no a priori reason to believe that the representations of different walls of a testing box are stored in different neocortical modules.

In the final analysis, the success of the relational theory will depend on the ability of its proponents to identify a set of non-spatial hippocampal unit responses that are consistent across experiments, and a set of non-spatial deficits in animals with lesions restricted to the hippocampus, which can be explained in terms of these unit responses. Notice here that it is not sufficient for Eichenbaum and colleagues to demonstrate non-spatial single unit responses in the hippocampus as evidence in favour of their theoretical position and against the cognitive map theory. The unit responses must also be of a nature that is predicted by the relational theory. There might be other correlates of hippocampal

unit firing patterns that are neutral as between spatial and relational theories and that will neither count for nor against either theory. For example, as we shall see, there are cells that fire as an animal moves from one part of an environment to another during olfactory discrimination tasks that, even if they turn out not to correlate with velocity, speed, or some other spatial variable, do not, on the face of it, provide support for (or against) the relational theory. Similarly, the demonstration of hippocampal cells responding to simple olfactory cues would not constitute evidence for or against either theory since these are neither relational nor spatial.

In the first part of this paper, I will discuss some of the spatial properties of the place cells that, in ostensibly non-spatial experiments, might be interpreted as non-spatial correlates: different hippocampal place cells fire in different locations so that, as an animal moves around the environment in a structured, repetitive task, different cells will appear to be correlated with different aspects of the task; under certain circumstances, complex-spike cells only fire when the animal moves in one direction through the place field and this might give the appearance of a behavioural correlation such as the approach to a goal; some place cells have additional secondary correlates in the place field such as a variation in the within-field firing rate as a function of speed of movement; some place cells (misplace cells) fire exclusively or maximally when the animal sniffs in a particular location. In the second part of the paper, I shall turn to the question of whether the firing of hippocampal pyramidal cells represents non-spatial information independent of place as has been suggested by some authors. Here I will conclude that there is, at present, little strong and consistent evidence that these cells have a major role in non-spatial perceptual or memory processes in the rat, rabbit, or monkey. Further, where there is evidence for non-spatial neuronal responses, there is frequently a discrepancy between the type of information that the cells are reported to encode and the absence of an effect of a hippocampal lesion on the animal's ability to use that information.

Representation of an Environment Within the Hippocampus

As a rat moves around an environment, each pyramidal cell becomes active in a particular location. The representation of the environment in the CA1 field of the hippocampus by a group of these place cells is a distributed one. The firing fields of a small number of pyramidal neurones are sufficient to represent an environment, and neighboring cells are as likely to code for distant regions of an environment as they are to code for nearby regions. Figure 1A shows the place fields of 15 CA1 pyramidal cells recorded simultaneously from a single tetrode while the animal moved around a 40 cm by 40 cm box, searching for small bits of rice. If we assume that cells that are anatomically closer to one electrode of the tetrode will have spikes of a larger amplitude on that tetrode, we can get some idea of the topographical relationship between the place fields of cells and their anatomical relationship to each other. In Figure 1, I have arranged the cells in a rough topographical ordering on the basis of the size of the

potential on the different electrodes. Two conclusions can be drawn from this picture. First, the fields of the 15 cells cover a considerable area of the environment and, second, there does not appear to be any obvious topographical relationship between the field locations and the anatomical locations of the cells relative to each other within the hippocampus. This lack of topography contrasts with the claim that there is a tendency for the place fields of neurones recorded on the same electrode to show similar place fields on a radial arm maze (Shapiro et al., 1997). I have no explanation for this discrepancy.

The conclusion that a small number of cells is adequate to represent the environment is strengthened by the inclusion of additional cells recorded on other electrodes at the same time as those shown in Figure 1A. In all, 35 cells with place fields on the box were recorded at the same time and their fields are represented in Figure 1B. Here the fields are represented by their relationship to the environment and not to their anatomical location within the hippocampus. Several aspects of the place field phenomenon can be seen from Figure 1B. Firstly, the 35 cells cover a large proportion of the environment. On the basis of similar recordings, Wilson and McNaughton (1993) calculated that approximately 130 place cells would be sufficient to allow the hippocampus to compute the animal's location in an environment to an accuracy of 1 cm/s and about 380 cells for an accuracy of 1 cm/0.1 s. As an animal moves around an environment in a behavioral task, one would expect a sequence of place cells to become active in succession. If the sequence of behavioral acts exhibited in the task is repetitive and stereotyped, one would expect a good correlation between each behavior and the firing of specific cells, since each behavior will tend to occur in the same location on each trial.

A second property of the place cells recorded in an open field environment is shown in Figure 2. This picture shows the firing fields of 4 of the cells from Figure 1B. For each cell, the central panel shows the firing field without regard to the direction in which the animal is moving. In the surrounding panels are shown the same firing fields when the animal's direction of movement is taken into account. It is clear that the fields in the different directions are more or less equivalent. It was this property of omnidirectionality (see O'Keefe, 1976, 1979; Muller et al., 1987) that originally suggested that these cells were not coding for simple sensory stimuli but were instead computing the more abstract concept of place or location. In contrast, a majority of place cells recorded from animals engaged in repetitive stereotyped tasks, which require them to run through the place fields in a limited number of directions, will have fields that are directional (McNaughton et al., 1983). That is, the cells fire as the animal goes in one direction through the field but not in the other. Furthermore, the same cells can be omnidirectional in open field environments and directional on the radial arm maze (Muller et al., 1994). An example of directionality is shown in Figure 3, which illustrates data from 3 cells recorded on a linear track while the animal shuttled from one end to the other in order to obtain food at each end. One might be tempted to describe the firing correlates of these cells as goal-approach except that in this situation there are two goals and the firing only occurs in the approach to one of these. It is, therefore, necessary to qualify the

description as one of approach to the West or East goal, i.e., to add a spatial component to the behavioral description.

Sensory Control Over the Location and Shape of the Hippocampal Place Cells

Why do the hippocampal place cells fire in particular locations in an environment? The way to answer this question is to study modifications of the environment that lead to changes in the location of the place fields or in the shapes of those fields. Burgess and I (O'Keefe and Burgess, 1996) recorded place cells in 4 rectangular boxes that varied in the length of one or both dimensions. There was a small and a large square and two rectangles each with one dimension equal to that of one of the squares. One of the rectangles was a 90° rotation of the other. The results suggest that each place field is composed of the summation of two or more Gaussians where the location of the centre, amplitude, and width of each Gaussian is determined by its distance to a particular wall in a particular direction. Gaussians that are centred close to the wall that controls them are higher and more sharply peaked than ones centred farther away. There are two notable features of these findings. The first is that the experiment was conducted in such a way that there was no distinctive sensory cue intrinsic to each wall that the animal could use to differentiate any one wall from another. The same four planks of wood were regularly interchanged to form the walls of the box. It follows that the animal must have been using some other source of information to identify each wall. We have suggested that this information consists of the allocentric direction of the wall from the animal and that this information is provided by the head direction cells found in the postsubiculum and the anterior thalamus (Taube et al., 1990a,b). The sources of directional input in the experiments under discussion were not identified but were probably distant visual cues from the room external to the recording box and internal proprioceptive and vestibular (idiothetic) cues. A second question is how the animal determines its distance from the relevant wall. In the original paper, this was not identified. McNaughton (1996) has suggested that distance in an enclosed box is calculated primarily on the basis of self-motion cues. He suggests that the animal registers each physical contact with a wall and monitors the amount of movement from that wall as an indication of distance. We believe that this is too narrow a view and prefer to stick with the suggestion incorporated in the original cognitive map theory (O'Keefe, 1976; O'Keefe and Nadel, 1978), that several ways of measuring distance are available to an animal. In experimental paradigms in which there are many visual cues to distance, we believe that these are the primary sources of distance information. For example, in our model of hippocampal control of navigation (O'Keefe and Burgess, 1996), we suggested that the animal could calculate its distance to a wall on the basis of the vertical height, on its retina, of the line where the wall meets the floor. Other alternatives are the vertical height of the wall or the distance between the two edges of the wall. Under circumstances in which strong and salient visual cues are not available, the rat may use self-motion information as it moves away from identified features

15 SIMULTANEOUSLY RECORDED PLACE CELLS -ORDERED WF'S

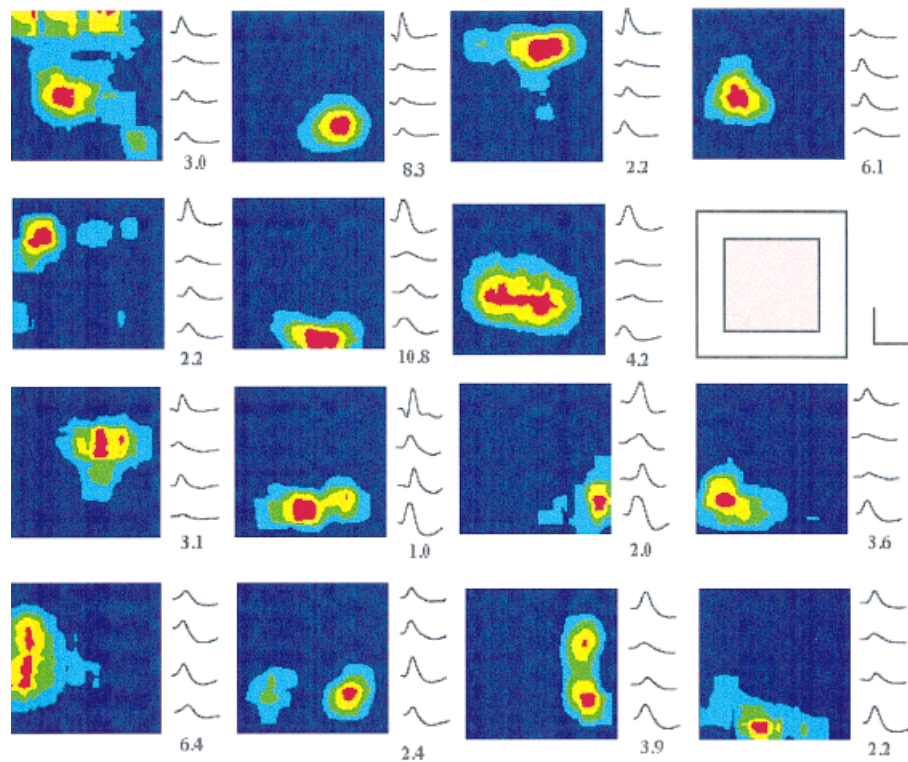


FIGURE 1. A: Place fields of 15 complex-spike cells recorded simultaneously in the CA 1 field of the hippocampus of a rat searching for grains of rice on a small 40 cm x 40 cm open platform. Inset: The surface area of the holding box relative to the overall camera view. The waveform for each cell as recorded on the tetrode is shown to the right of the place field. Cells with larger amplitudes are placed closer to the centre of the figure and those larger on electrode 1 are placed towards the upper left-hand corner; those larger on electrode 2 are placed towards the upper right-hand corner, and so on. Firing rates within the place fields are represented as a false color map, with each color representing a successive 20% of the peak firing

rate. Peak firing rate within each field is shown below the waveform. Calibrations for the spike waveform are 375, 300, 300, and 250 μ V, respectively, from top to bottom and 1 ms (after O'Keefe et al., 1998). B: Place fields of 35 simultaneously-recorded hippocampal complex-spike cells arranged according to field location. Fields towards the northwest of the box are shown in the upper left, those toward the northeast in the upper right, and so on. Cells with double fields are placed with respect to the stronger field. Notice that the fields collectively cover a large proportion of the environment (Reproduced with permission from O'Keefe et al. [1998] and The Royal Society; *Phil Trans R Soc B* 353:1333-1340.)

of the environment such as the walls of the box. Evidence for this comes from experiments showing that the speed at which an animal moves through the place field is coded by rarely encountered speed cells (O'Keefe et al., 1998) and more robustly by the firing rates of the place cells themselves (McNaughton et al., 1983; Wiener et al., 1989). Czurko and colleagues (1999) have recently confirmed these findings and identified one of the sources of speed information. They recorded from place cells with fields in a running wheel and showed that the firing rates of the cells increased linearly with the speed of running in the wheel. The spatial nature of these cells was confirmed by manipulations that showed that moving the wheel to other locations in the environment or rotating it relative to the environment abolished the cell firing. Therefore, the primary identification of location in this situation is based on environmental cues and the fields are directional. Since there is no movement of the animal's head relative to the environment, the speed signal cannot be coming from the vestibular system or from optic flow information but

must be derived from the motor system itself. This fits with long-standing evidence that at least one component of the hippocampal theta rhythm in the rat EEG is generated by inputs from the motor system (O'Keefe and Nadel, 1978).

One of the major weaknesses of the relational theory is that it does not account for the details of the place cell data. The O'Keefe and Burgess (1996) results cited above show that for many cells the primary factors determining their firing fields consisted of two of the four walls of the box and that these were always two adjacent walls and never two opposite walls. I suggest that this distribution is not that which would be predicted by the relational theory. Cells responding to two opposite walls would have fields consisting of strips running from one wall to the other and according to relational theory should account for at least one third of the data. Even more surprising, the most recent formulation of the relational theory (Wallenstein et al., 1998) suggests that all of the cells should fall into this latter class because the hippocampus is only required for spatial stimuli that are discontinuous and

35 SIMULTANEOUSLY RECORDED PLACE CELLS

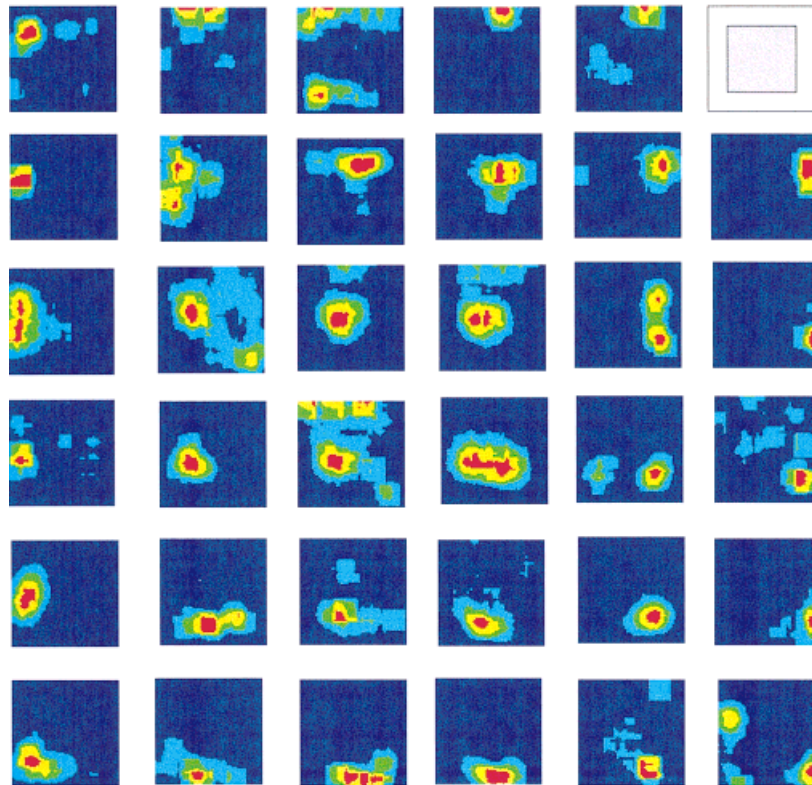


FIGURE 1 (Continued).

would not be interested in the relationship between the abutting walls that meet at the intersection. In its attempt to include the data from spatial experiments within its framework, the relational theory fails to account for the specific details of these experiments.

Misplace Cells Fire Maximally When the Animal Sniffs in the Cell's Spatial Firing Field and May Signal the Presence of Unexpected Objects or the Absence of Expected Objects There

Not all hippocampal place cells have simple locational correlates. Although many complex-spike cells can be classified as simple place cells, others have more complex properties. The firing rate of complex place cells is dependent on factors in addition to location (O'Keefe, 1976). For example, some cells increase their firing rates if the animal experiences a particular object in the place field or engages in a particular behavior there. Others do so when the animal either finds something new there or fails to find something expected there. These cells are called *misplace* cells. A good example of a misplaced cell is one that fired maximally when the animal went to a location and found its usual feeding bowl there but empty of food. Maximal firing was seen during the ensuing exploratory sniffing at the cup and immediate environs. The same experience and behavior elsewhere in the environment were not associated with increased firing. It is important, therefore, in experiments that report complex-spike firing correlated with sniffing during olfactory discriminations, to consider the

possibility that these cells are misplaced cells that are location specific. In order to rule this out, it is necessary to demonstrate that the cell fires when the animal engages in the same behavior in response to the same odor in a different location.

Do Hippocampal Pyramidal Cells Signal Things Other Than Place?

In several reviews (Cohen and Eichenbaum, 1993; Wallenstein et al., 1998) Eichenbaum and colleagues have suggested that hippocampal pyramidal cells respond to the non-spatial as well as the spatial aspects of the appropriate tasks. They report that they and others have found evidence for cellular responses during behaviors such as cue-sampling and approach to a goal. In other experiments, pyramidal cells have been reported to respond during classical conditioning, either to the conditioned stimulus itself or during the trace period between the conditioned stimulus and the unconditioned stimulus. In this section, I will review these results and suggest that many of the findings are due to secondary correlates of the cells such as arousal or movement or are simply different ways of looking at the spatial response to the cells as described above. I will concentrate on those aspects of the data that specifically support the relational theory and just briefly mention other correlates that do not necessarily lend specific support to either the spatial or the more general relational theories.

First, it is important to distinguish between complex-spike pyramidal cells and theta interneuron cells since, in many

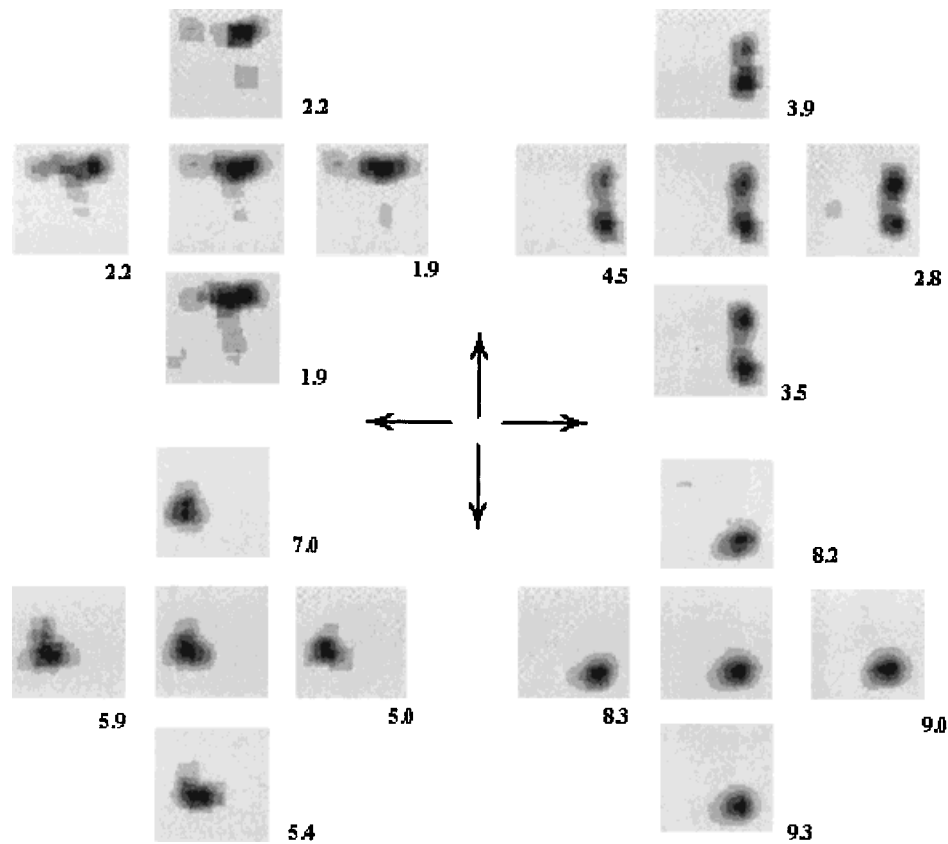


FIGURE 2. Omnidirectional firing pattern in 4 hippocampal complex-spike cells. For each cell, the central panel shows the overall firing pattern irrespective of the direction of movement of the animal through the place field. In the surrounding panels, the firing fields have been separated according to the direction of movement. Northward direction is at the top, eastward to the right, southward at

the bottom, and westward to the left. Peak firing rate is shown at the bottom right of each panel. Notice that each cell fires in the appropriate location irrespective of the animal's direction of movement (Reproduced with permission from O'Keefe et al. [1998] and The Royal Society; *Phil Trans R Soc B* 353:1333–1340.)

situations, these have different behavioral correlates. In the rat, the theta cells and in particular those in the dentate gyrus increase their firing rates during arousal irrespective of the animal's location. In contrast, the complex-spike cells decrease their low baseline firing rate during arousal if the animal is outside the place field. In contrast, they increase their firing within the place field as a function of the animal's speed of movement. Therefore, if one compares the firing rates of complex spike cells during two behaviors with different arousal levels or EEG states (for example LIA vs. theta) outside the field or different running speeds inside the field, there may be a small but significant difference in firing rate. The situation is slightly different in the rabbit where both theta and some complex-spike cells show an excitatory arousal response during immobility.

Second, in tasks that encourage the animal to move from one place in the environment to another in a stereotyped manner, the place cell firing becomes uni-directional, tempting one to describe it as goal-directed. As we shall see, however, experiments that explicitly tested this possibility have not supported it. Finally, there is often a mismatch between the results of single unit and lesion experiments on non-spatial tasks. In contrast to the reports of correlations between hippocampal unit activity and some

aspect of a task, there is often an absence of an effect of selective lesions of the hippocampus on that task. While this might be interpreted as evidence for redundancy across brain regions in the performance of the task, it might equally well mean that the hippocampus is only incidentally or peripherally involved in the

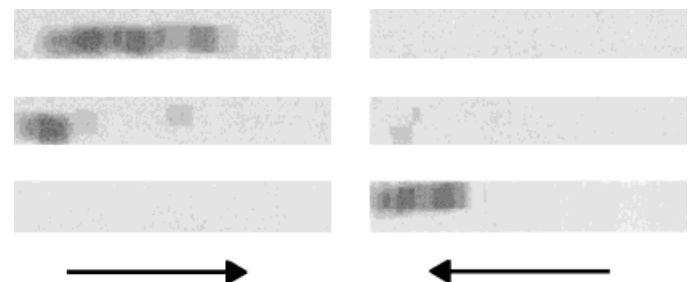


FIGURE 3. Directional firing of three place cells on a linear track. Firing in the eastward direction is shown on the left and in the westward direction on the right. The top two cells fire when the animal runs eastwards and the bottom (bottom) when it runs westward. Peak rates are 9Hz (top), 10 Hz (middle), and 7 Hz (bottom) (O'Keefe, unpublished data).

task, perhaps monitoring the location where the task is carried out or the level of arousal during the performance of the task.

Hippocampal Units During Non-Spatial Learning

I will only consider studies that attempted to isolate single units. Multi-unit recording in the hippocampus lumps complex-spike and theta cells together. Due to the lack of topography of the place representation in the hippocampus, recording from several complex-spike cells at the same time tends to cancel the spatial signal, allowing the arousal and movement correlates of the theta cells to dominate the recordings.

I will consider experiments in terms of the animal used, starting with the rat, moving on to the rabbit next, and considering the monkey last. Each section begins with the simplest paradigms, moving to progressively more complex ones. In general, the simplest paradigms typically involve conditioning to a single cue and do not require the animal to move around the environment. More complex tasks might require the animal to locomote around the environment or to remember a stimulus across a delay or to compare two stimuli.

Rats

Hippocampal unit activity has been recorded during both appetitive and aversive conditioning, using a single stimulus (CS) or two stimuli (CS⁺ and CS⁻). In the latter task, the animal is required to learn to discriminate between the stimuli, responding to one but ignoring the other. In the differential conditioning paradigm, the animal typically learns first to respond to both stimuli and only subsequently to inhibit its response to the CS⁻. Delacour (1984) trained rats on an aversive differential conditioning paradigm in which two different tones served as the conditioning stimuli and mild electric shock to the neck during slow-wave sleep as the unconditioned stimulus. Increased muscle tone as measured by the neck EMG was used as the conditioned response (CR). The cortical EEG served as an independent measure of arousal. Over the course of conditioning, two independent factors were in operation: during the early stages, both the CS⁺ and the CS⁻ elicited cortical arousal and muscle activation; during later stages, there was a reduction of the cortical arousal to both stimuli back to baseline and a differentiation of the EMG response. The neck muscle response to the CS⁺ remained high while that to the CS⁻ steadily declined to baseline. Delacour recorded both complex-spike cells and theta/granule cells in the hippocampus. The majority (8/9) of complex-spike cells had inhibitory responses to both stimuli, which increased and then decreased over the course of conditioning in parallel with the cortical arousal response. None of these units differentiated between the CS⁺ and the CS⁻ at any time during conditioning. In contrast, the responses of the theta/granule cells were primarily excitatory and followed the pattern of the EMG response. Their firing rate increased to both stimuli during the early stages of training but returned to baseline in response to the CS⁻ while continuing high to the CS⁺ as behavioral discrimination took place. Five of 6 cells in this category differentiated between the two stimuli by the end of training. It is interesting that thalamic cells recorded in this study also fell into two distinct classes with similar responses to the

hippocampal cells: cells recorded in the centre median acted similarly to the complex spike cells while those recorded in the dorsomedial nucleus resembled the theta cells. This strongly suggests that these responses are general ones to be found in several brain areas and are not restricted to the hippocampus. Delacour (1984) suggested that the response of the complex-spike cells was a reflection of general arousal whereas the pattern of activity of the theta/granule cells was a reflection of the learnt differential increase in neck muscle activations to the two conditioned stimuli. Following conditioning, the animals were moving to the CS⁺ and this was reflected in the theta cell movement correlate.

Christian and Deadwyler (1986) reported a similar pattern of responses in complex-spike and theta cells recorded during an appetitive conditioning task, ruling out an important role for the rewarding or punishing (i.e., motivational) aspects of the task. They trained thirsty rats to poke their noses into a small antechamber in the wall of a box in order to receive a water reward. In some animals, the availability of reward was signalled by a tone and no discrimination was required; in others a differential CS⁺/CS⁻ procedure was used. Complex-spike projection cells and theta interneurons were identified by the strictest criteria, including the use of electrical stimulation of hippocampal efferent fibres to antidromically activate complex-spike but not theta cells. Following successful conditioning to the single tone stimulus, theta cells showed a consistent increase in firing rate in the 200-ms period following tone onset. In contrast, no change from the background rate was seen in the complex spike cells. During two-tone differential conditioning, the theta cells showed an increase to both stimuli with a greater increase to the CS⁺. In contrast, the pyramidal cells registered no change to either. Head movement recordings showed that the onset of theta cell activity preceded the onset of the nose poke movement and that the changes in theta cell firing occurred in parallel to the acquisition of the conditioned EMG response and disappeared with subsequent extinction. Again no changes in firing pattern were seen in complex-spike cells during the course of acquisition. In contrast, as we shall see below, these same cells were found to have place correlates during a spatial task in the same experiment.

In a subsequent study from the same group, Foster et al. (1987) did find a small but significant increase in the overall activity of complex-spike cells to both conditioned stimuli but still no differential activity to the CS⁺. A differential response to the two stimuli did occur in their population of theta cells. The CS⁺ caused an initial increase in firing, which reached a peak about 80–100 ms after tone onset and continued at this increased level of activity throughout the entire 1-s period; the CS⁻ also caused a phasic response that peaked at about the same time as the CS⁺ but was followed by a decline in activity to baseline after the initial response. Recall that this is the same pattern that was reported by Delacour (1984) in an aversive task.

The simplest explanation for the pattern of results observed in these studies is that there are two independent central processes being conditioned: non-specific arousal and preparation for the motor response. Both act to control the firing of theta and granule cells but only one of these, arousal, influences the pyramidal cells. The initial short-latency response of the theta and granule cells to

either a CS⁺ or a CS⁻ is an activation reflecting an arousal input from the brainstem; at about the same time, a small percentage of pyramidal cells can, in some studies, also show an arousal response: depending upon the stage of training, this can either be an inhibitory or a weak excitatory response. The later phase (>200 ms after CS onset) of the unit activity is related to the behavioral response. For the theta and granule cells, there is a prolonged activation continuing throughout the CS⁺ period but no response to the CS⁻. The pyramidal cells do not participate in this second longer-latency phase, in line with the results of lesion studies that suggest that damage to the hippocampus has no effect on simple delay classical conditioning in the rat (Kim and Fanselow, 1992; Phillips and Le Doux, 1992).

Eichenbaum and his colleagues have studied the behavioral correlates of hippocampal cells in various olfactory discrimination tasks and recorded two major behavioral correlates: some cells fired when the animal sniffed at the odor cues while others changed their firing rates during various stages of the approach to the cues or to the goal. In a successive go/no-go discrimination (Eichenbaum et al., 1987), the rat was presented with one odor of a pair and had to poke its nose into the single odor port in response to the CS⁺ but not to the CS⁻. Water reward was available on the other side of the box, requiring the animal to shuttle continuously between the two opposite sides of the box. Two behavioral correlates of unit response were identified: cells that fired when the animal was sniffing at the odor (14.8%), and cells that fired when the animal approached the sniff port or ran from the sniff port to the water cup at the other end of the box (60%). A further 9.5 % were classified as theta cells. The goal approach cells may be identical to unidirectional place cells and at least some of the cue-sampling cells may be equivalent to the misplace cells. Many of these cue-sampling units had firing patterns that were maximally synchronized to the onset of cue sniffing. No evidence was found for cells that preferred one odor over another. Almost all fired more to the positive stimulus, which signalled the availability of water reward in another part of the environment. In addition, there was evidence that on the trials that followed a CS⁻ trial, the cells gave a larger response than on ones that followed a CS⁺. A follow-up study (Otto and Eichenbaum, 1992) looked at complex-spike cell firing during a continuous recognition olfactory memory task in which any one of 32 different odors could be presented and the availability of water nearby was signalled by a mismatch between the current and previous stimulus. Again, cells that had peak firing rates at different points in the task were found, including 12% (32/265) that peaked during the cue sampling period. The important unit responses for the relational theory in these experiments are ones signalling a match or mismatch between successive stimuli on which the animal could base its response. Somewhat disappointingly, however, only eight cells (3%) had firing patterns that could be classified as signaling a mismatch between successive stimuli. Since the behavioral correlates of unit firing were identified using a number of simple *t*-tests with alpha set at .05, uncorrected for multiple comparisons, at least this number of cells would be expected by chance.

In a forced-choice simultaneous odor discrimination, Wiener et al. (1989) presented the animal with a simultaneous odor

discrimination in which both the CS⁺ and CS⁻ were presented at the same time from two odor port and reported that 22% (62/281) of complex-spike cells had increased activity during cue sampling. However, closer examination of these data showed that only 13% of cue-sampling cells discriminated between odors irrespective of location while fully 44% took stimulus location into account. For example, one cell fired best to a particular odor presented at the left port. Somewhat more surprising, 44% of cup-approach cells also had responses that depended on the position of the prior nose poke or on the odor/position interaction, suggesting that the cup approach response in this ostensibly non-spatial task may depend on whether the animal turns towards the left or right on its exit from the sniff port, perhaps passing through a place field on one side of the sniff port as it turns in one direction.

In two experiments, Eichenbaum and his colleagues (Eichenbaum et al., 1987; Wiener et al., 1989) asked whether cells that were related to events in their olfactory discrimination task also had place fields in the same or different tasks. In the first study, they found that 43% of cells with correlates in the odor discrimination task had place fields in the same environment. In the second study, they recorded some complex-spike cells in a spatial task, some in their odor discrimination task, and a third group in both tasks. They found 75% of complex-spike cells tested in the spatial task had place fields as opposed to 58% with correlates in the odor discrimination task. Of cells collected in both tasks, 85% (82/97) had place fields as opposed to 54% (52/97) that had correlates in the odor task.

One can conclude several things from these studies on rats. In conditioning tasks in which the animals were not required to move around the environment to any great extent, most or all of the hippocampal cells taking part in the conditioning response were theta cells. Complex-spike cells, by contrast, did not take part or showed a slight inhibition of their resting firing rate. In discrimination tasks, in which the animals were required to move between different locations in the environment, increased activity in different cells was correlated with different behaviors that occurred in different locations. There is no evidence that these responses reflect relationships between stimuli and they are, therefore, not obviously evidence in favor of the relational over the spatial theory. It seems reasonable to ask whether the correlate is in fact with the animal's location rather than with its behavior. The cells that fire selectively during approach to the sniff port or the reward cup have much in common with place cells recorded on linear tracks. Recall that under conditions that constrain the animal to move along narrow pathways, the place cells are unidirectional. In order to distinguish a goal-oriented response from a motivationally neutral place response, it is necessary to have two identical goals in the environment or two different goals that can be interchanged. O'Keefe (1976) reported that interchanging the water and food at the end of a three-armed maze did not change the location of complex-spike firing fields on the maze. Speakman and O'Keefe (1990) reversed the location of the goal in a spatial memory task and found almost no cells that altered their place fields in the environment as a result. O'Keefe and Recce (1993) used a linear track with food reward at both ends and found that some cells fired as the rat ran in one direction while

other cells fired in the opposite direction. Further, they found that cell firing was better correlated with the animal's location than with temporal variables such as the time since it started its run. It would not seem warranted to describe the cells reported in the experiments of Eichenbaum and colleagues as goal-approach cells in the absence of similar manipulations (but see the following discussion of Wood et al., 1999).

A small number of complex-spike cells respond to the CS⁺ in a differential go/no-go discrimination but in general very few hippocampal cells code for the specific odor quality or other task relevant variables and many take the location of the odor into account. Very few cells signalled the match or mismatch between successive stimuli. As we have seen, many place cells fire at an increased rate when the animal sniffs at a location when the stimulus in that location has been altered in some way and these results from odor discrimination paradigms may provide additional information about the conditions under which this mismatch response occurs.

Recently, Wood et al. (1999) have carried out an important experiment in which they tried to address some of these concerns. They recorded from hippocampal cells during a variant of a successive olfactory discrimination task in which they tried to dissociate location, odor, and the match/mismatch aspects of the task. Rats were trained on an open platform to approach a small cup containing sand scented with one of nine odors. On each trial, the cup was placed in one of nine locations. If a cup had a different odor from that of the previous one, it contained food the animal could dig for (non-match); if the odor was the same, there was no food (match). An analysis of variance showed that 10 cells of 127 (7.8%) responded to odor in the absence of any other correlate, 14 (11%) solely to location, and 13 (10.2%) solely to the match/mismatch aspect of the task. The remainder of the responsive cells took interactions between these variables into account. In all, 25 cells had non-spatial correlates and 40 took location into account. A further 26 changed their firing rate as the animal approached any of the cups. These latter may simply be movement- or speed-related and, since this was not measured, will not be discussed further. These results are notable since they report a higher percentage of cells with a match/mismatch correlate irrespective of location than previous reports from this laboratory. Furthermore, there are many fewer purely spatially-coded cells. On the face of it, these results provide strong evidence for the more general relational theory. It is not clear from the report, however, how much of the differences between match and non-match can be attributed to the different behaviors of digging and turning away from the cup, which were used as the response measures as opposed to the relational judgment itself. It will also be interesting to see whether, unlike other successive mismatch discrimination tasks, this one can be shown to be disrupted by selective hippocampal damage.

Fornix Lesions Have Only a Mild Effect on Olfactory Discrimination Tasks

Eichenbaum and his colleagues (Eichenbaum et al., 1988) have examined the effects of fornix lesions on both simultaneous and

successive odor discrimination tasks similar to those in which units were recorded. They found that both simultaneous and successive discriminations were mildly impaired (on one of three problems in each case) if a spatial, left vs. right, response was required but that the lesioned animals were actually superior on two of the three successive discrimination problems in which a go/no-go non-spatial response was required. In a different study, there was no effect of a fornix lesion on a successive go/no-go discrimination but the lesioned animals were significantly better at reversal of the original reward contingency (Eichenbaum et al., 1986). Thus, the only consistent deficit in the lesioned animals was a spatial one perhaps because of the difficulty these animals have in breaking irrelevant response habits (see O'Keefe and Nadel, 1978, pp 277–283). One might have thought that the reversal of an olfactory discrimination was a good example of a task that would be easier for animals that had formed a flexible relationship between reward valence and response and should be particularly deficient in animals with hippocampal damage according to the relational theory.

Rabbits

Several laboratories have recorded the activity of single units and multiple units from the hippocampus during classical conditioning of the nictitating membrane response (NMR) in rabbits. Following Gormezano, Thompson (1976) suggested that this learning paradigm is ideal for the study of the formation of associations. In simple delay conditioning, the UCS overlaps the last portion of the CS so that both terminate together. In trace conditioning, the CS ends before the UCS begins and there is a temporal gap between the two. As we saw with classical conditioning in the rat, there is an important role for arousal in this form of learning. Experiments that manipulate the animal's arousal have shown that this has strong effects on learning rates and that this effect is reflected in the baseline rate of theta activity in the hippocampal EEG. Berry and Swain (1989) showed that the pre-training background amount of hippocampal theta was a good predictor of learning rates in delay conditioning and that this variable was strongly influenced by the level of arousal. Following mild water deprivation, there was more theta, higher arousal, and a faster rate of learning. A similar pattern was found in trace conditioning (Kim et al., 1995).

As noted above, the theta and complex-spike cells in the CA 1 field of the rabbit hippocampus are more easily activated by arousing stimuli than their counterparts in the rat. Furthermore, there is clear evidence that EEG theta activity gets conditioned to various aspects of the task during classical conditioning experiments. Powell and Joseph (1974) conditioned the corneo-retinal potential in the rabbit using mild electric shock to the eye as the UCS. This was preceded by one of two conditioned stimuli. During the early stages of learning, before differential responses to these two stimuli had been established, there was a high incidence of theta to both; after differential conditioning, when the CS⁺ but not the CS⁻ consistently elicited the UCS, a considerably higher amount of theta occurred to the CS⁺. During this second phase of conditioning, there was a differential response of the neck EMG

to the CS⁺. This pattern of responses is similar to that seen in the rat (see above) and, as suggested there, probably indicates that the early theta activity was related to general arousal while the later theta was related to the motor response.

Single Unit Recording in the Hippocampus During Nictitating Membrane Conditioning of Rabbits

Berger et al. (1983) recorded the activity of single units in the rabbit hippocampus during simple delay NMR conditioning. They sorted the units into three major classes on the basis of their responses to electrical stimulation of the fornix, their spontaneous firing rate, and the duration of their action potential: theta cells were orthodromically activated from fornix stimulation and fired with theta-like bursts of six to eight hertz synchronised to the ongoing EEG theta activity; pyramidal cells had lower spontaneous rates, sometimes fired a complex spike and could be activated antidromically by fornix stimulation; silent cells fired infrequently and could not be antidromically or orthodromically activated from fornix stimulation. Both theta cells and pyramidal cells increased their firing rates during the CS period while the silent cells never did. Theta cells were typically activated by the CS to fire a series of theta-like bursts, which often continued throughout the trial and in some cases continued into the post trial period beyond the termination of the trial. One type of theta cell increased its overall level of activity during the trial while another type showed an overall decrease in activity. Pyramidal cells formed the majority of cells recorded and typically emitted one or more bursts of spikes during the trial, some showing a pattern of activity that closely modeled the nictitating membrane response with others being more selective, firing during different time epochs of the trial. "Silent" cells, which constituted 11% (19/178) of the neurons recorded, had exceptionally low spontaneous firing rates (<0.2/s), were not activated by the stimulating electrodes, and did not participate in the conditioned response. As we shall see below, this estimate of the percentage of cells in this category may be low.

Weiss et al. (1996) recorded single units from rabbit hippocampus during trace conditioning of the NMR. They also reported the existence of the same three classes of cells reported by Berger and colleagues in their delay conditioning experiments but in other respects, the results differ markedly. Weiss et al. (1996) found a much larger percentage of silent cells that did not participate in the conditioning (37/93 or 40%) and they did not find anywhere near the number of units that were significantly excited during the CS or trace period in the conditioned animals in comparison with unpaired controls. In CA1, 14% of pyramidal cells were excited during the CS period as opposed to 9% in the controls; 11% were excited during the trace period as opposed to 9% in the controls. In contrast to the findings of Berger and colleagues (1983), but in agreement with the data from rats reviewed above, the increase in inhibitory responses relative to the controls was twice as large as the increase in excitatory responses. McEchron and Disterhoft (1997) obtained similar results in animals when recordings were taken after asymptotic performance had been reached. In addition, they recorded from some animals

during the earlier stages of learning. They found that the maximal hippocampal unit activation occurred on the trials just *prior* to the onset of the first signs of NMR learning. Furthermore, they found that as behavioral conditioning proceeded and the conditioned responses appeared more frequently, the hippocampal unit responses actually diminished. Finally, when looked at on a trial-by-trial basis, there was no correlation between the unit activity and the occurrence of the conditioned response. This pattern suggests that the hippocampus is not involved directly in the generation or timing of the motor response. Rather, it may be involved only indirectly, being required perhaps in the creation of a temporary behavioral state that precedes the motor learning but is a necessary condition for it to occur.

Lesions of the Hippocampus Do Not Affect Delay Classical Conditioning But Alter the Timing of the Conditioned Response in the Trace Version of the Task

It is generally accepted that damage to the hippocampus has no effect on the learning (or retention) of simple classical conditioning in which there is an overlap of the CS and UCS. In fact, some experiments report that the lesioned animals showed more rapid learning when the interval between the onset of the CS and UCS is shorter (150 ms) or longer (600 ms) than in the normal 300-ms interval (Port et al., 1986). On the other hand, there is an effect of hippocampal lesions on trace conditioning especially if the trace interval is longer than 500 ms. Although the lesioned animals usually learn to produce a CR in response to the CS, the timing of this response is different from that seen in the normal animals. In normal animals, the CR occurs just before the UCS while in lesioned animals it often occurs at a different time point. Whether this point is earlier or later than in normal animals appears to depend on the UCS that is employed. With the traditional UCS, an air puff, the CS in lesioned animals occurs just after the CS while with peri-orbital shock it occurs later than in normal animals (Port et al., 1986). It would appear that the main effect of the lesion is on the timing of the response and not on whether it is learnt or not. In only one of four experiments were the lesioned rabbits clearly deficient at learning trace conditioning when short latency responses were taken into account (Moyer et al., 1990). Although the animals in this experiment did generate some short latency responses, these never became numerous enough so that they reached the criterion for learning. The major difference between the Moyer et al. (1990) experiment, which produced a clear learning deficit, and the other three experiments, which produced changes in the timing of the conditioned response (Port et al., 1986; Solomon et al., 1986; James et al., 1987), was in the size of the lesion. The Moyer et al. (1990) lesions were large ablation removals of the entire hippocampus while the other three were restricted to the dorsal hippocampus. While this might suggest that complete lesions are necessary to produce a deficit in learning, it is also possible that the large removal of the Moyer et al. lesions affected structures in addition to the hippocampus. We know from work on the rat hippocampus that large lesions of this nature can affect afferents to the retrohippocampal structures and it will be interesting to see whether the deficit in NMR

conditioning occurs following selective neurotoxic lesions restricted to the hippocampus.

If we compare the effects of hippocampal lesions on the NMR with the results of single unit recording experiments, we are left with the paradox that delay conditioning, in which there are a sizeable number of pyramidal cells whose temporal activation profile precedes and models the CR, does not require the hippocampus whereas trace conditioning, during which very few such unit responses are found, does require an intact hippocampus.

The interpretation of the altered timing response following dorsal hippocampal lesions is unclear. Why, for that matter, does the conditioned response occur just prior to the unconditioned stimulus in normals? The whole rationale of the NMR learning paradigm was to rule out any instrumental contribution to the learning and, in particular, the possibility that the conditioned response would protect the eye from the UCS or otherwise attenuate its impact (Thompson, 1976). If, on the other hand, one accepts that the conditioned response in these conditioning paradigms is a reflection of the prediction of the unconditioned stimulus, then the timing of the CS is important and the lesion results would suggest that the hippocampus is involved in setting up the conditions under which the short-term prediction of stimuli can occur. What might this process be? One possibility is that a certain level of arousal is necessary to bridge the temporal gap between the CS and UCS in trace conditioning and that level of arousal is dependent on hippocampally-mediated conditioning to the background context.

Nadel and Willner (1980) originally suggested that the hippocampus is involved in the conditioning to the spatial context that occurs in these tasks in addition to the association to the target CS (see, e.g., Kim and Fanselow, 1992). Additional evidence for such a role comes from a context shift experiment. Although lesions of the hippocampus have no effect on simple delay conditioning, they do affect the role of the background cues, i.e., the room in which conditioning takes place. Penick and Solomon (1991) showed that simple delay conditioning was disrupted in normal rabbits when the animal was moved into a new room after conditioning was completed but hippocampal-lesioned animals were not affected. This result fits nicely with the idea that the hippocampus provides spatial contextual information that allows the conditioning of fear to the background situation to take place. Under these circumstances, the background stimuli can act as an occasion setter, which promotes the association between the CS and UCS. We can speculate that the silent complex-spike cells that do not appear to participate in the conditioning of task may be place cells that signal the animal's location in the environment and provide the information about the background cues or location in which conditioning takes place. This information might not be necessary for simple delay conditioning but it might be essential for trace conditioning.

We can conclude that the hippocampus has a minimal role in the acquisition of the NMR but that under certain circumstances it has a role to play in the timing of the conditioned response. This is particularly important in those paradigms such as trace conditioning where the CS-UCS interval is markedly different from 300 ms and normals generate a CR just prior to the UCS.

The mechanism of hippocampal involvement might be dependent on a more fundamental role in spatial context conditioning.

Monkeys

The monkey is closer to man than the rat and we would, therefore, expect that the monkey hippocampus might have incorporated some of the features that the cognitive map theory attributes to the human. For example, the incorporation of a linear sense of time might have converted the monkey hippocampus into an episodic memory system as well as a spatial navigation system. There are cells in the monkey hippocampus that respond to simple three-dimensional stimuli and to their spatial location. Furthermore, there are cells that respond preferentially to locations and the presence of objects in a particular location during conditional place discrimination tasks.

Tamura et al. (1992) reported that 10% of cells in the hippocampal formation responded differentially to the presentation of three-dimensional objects, some of which had been conditioned to rewarding (2.7%) or aversive (1.5%) stimuli. In a follow-up study, they showed 61% of object-responsive cells tested in the same apparatus varied their response as a function of the location of the stimulus in egocentric or allocentric space. More importantly for the present discussion, hippocampal units have been recorded from primates while they performed on the paradigmatic relational task, delayed match, or non-match to sample. On these tasks, the animal must signal whether two successive stimuli separated by an interval are the same or different. Recognition tasks of this sort were originally thought to depend on the integrity of the hippocampus but are now known to depend on the perirhinal/parahippocampal cortices and only minimally (Alvarez et al., 1995) or not at all (Murray and Mishkin, 1998) on the hippocampus itself. In keeping with (and anticipating) the lesion results, it has been found that only a very small number of cells show a differential response to the familiarity of the stimuli (0% Riches et al., 1991; 0.8% Tamura et al., 1992; 2.3% Rolls et al., 1993; 0.6% table 1 in Brown and Xiang, 1998). In contrast, Wilson et al. (1990) found that 40.2% of their hippocampal cells in this task correlated with the response, signalling whether the animal was reaching to the left or right position in their task. In contrast and in keeping with the lesion results, there is evidence that cells in the rhinal cortex are involved in familiarity judgments. Brown and Xiang (1998) reported that 24.2% of cells in the rhinal cortex and area TE showed a decreased response to the second presentation of the stimulus in a delayed match to sample task.

Rolls and his colleagues (1993) have tested monkeys on object recognition tasks and compared unit responses to object familiarity with those to object location. Only a small percentage (2.3%) of cells responded to familiar objects (see above). In contrast, they reported that about 9% of cells in the hippocampal region responded differentially to the location of the stimulus on a display screen. This group has also looked for spatially coded cells in the hippocampus of monkeys free to move around the environment. They have not found place cells but have found spatial view cells (Rolls et al., 1997) and whole body motion cells

(O'Mara et al., 1994). Spatial view cells respond selectively when the animal looks at particular locations in the testing room irrespective of where the animal was situated in the room when it looked at that location. On the other hand, Ono and his colleagues (1993) have found place-coded neurons in the hippocampal formation of monkeys that could visit different locations in an environment while performing different tasks. The monkeys were trained to sit in an enclosed cart that they could move to 9 different locations in the testing environment by pressing a lever. About 13% of the cells fired more when the animal was at one location than when it was in other locations. In a subsequent task, (Eifuku et al., 1995), the animals were required to perform an object-in-place discrimination. The cart was moved to a particular location and the view window was opened, allowing the animal a sight of an object at that location. About a quarter of cells responded when objects were shown to the animal in this task. A subset of these (5% of the total) were object-in-place cells that responded differentially when the animal was shown an object in a particular location and not in other locations. These cells were also not interested in a different object in the preferred location. They appear to have similar properties to the place and misplace cells described in the rat. Further evidence that the cells are appropriately described as place cells comes from an experiment by Nishijo et al. (1997) in the same laboratory. Here the animal in the cart was moved backwards as well as forwards through the environment and the cells continued to fire at the same location. This manipulation reverses the cues in egocentric space but leaves unchanged allocentric cues. It is still not clear how similar or different the spatial cells in the monkey hippocampus are from those found in the rat.

Conclusion

The relational theory of Cohen and Eichenbaum (1993) claims that the hippocampus is implicated in the memory for a class of non-spatial as well as spatial relationships between stimuli. The theory aspires to incorporate the cognitive map theory as a specific example of this more general relational theory. The success of the relational theory depends on its ability to sharply delineate the boundary between those relations that are and those that are not dependent on the hippocampus, and the identification of a body of experiments that support a role for the hippocampus in non-spatial relational processing. Despite considerable effort, it has been difficult to give anything other than a vague specification of the class of non-spatial relations for which the hippocampus is essential. The most concrete of these is the most recent one (Wallenstein et al., 1998), which states that only relations between discontinuous stimuli require the hippocampus. A detailed analysis of the results of single unit experiments in the hippocampus of freely-moving animals suggests that many responses that appear to be non-spatial may, on closer analysis, reflect the second order correlates of the place cells, signalling either the speed of movement in the place field or the presence or absence of a stimulus in the place field (misplace cell).

A comparison of the results of single unit experiments with the effect of lesions on comparable or similar tasks shows that they

rarely, if ever, provide support for each other. In trace conditioning of the NMR, few single units show the response properties required to support the motor response learning. Rather, the evidence suggests that the hippocampus may play a background contextual role. Lesion experiments offered in support of relational deficits have typically used fornix lesions to disconnect rather than destroy the hippocampus. These lesions may affect retrohippocampal areas as well as hippocampal ones. To my knowledge, only the social-olfactory learning task has been studied with neurotoxic lesions and here it has been found necessary to lesion both hippocampus and subiculum in order to achieve a deficit. In unpublished experiments (Burton and O'Keefe, unpublished data), our group has consistently failed to reproduce these results in three separate replications. The cognitive map theory still provides the best explanation for the pattern of unit and lesion results.

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