

Functions of the Primate Hippocampus in Spatial and Nonspatial Memory

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In this article I consider the functions of the primate hippocampus, as shown by investigations in macaque monkeys. I consider whether the primate hippocampus is involved in nonspatial as well as spatial functions, the types of spatial information for which the hippocampus is required, how spatial information is represented by neuronal activity in the primate hippocampus, and the types of memory function to which hippocampal neuronal networks appear suited. More detailed analyses and references are provided by Rolls (1990).

DAMAGE TO THE HIPPOCAMPAL SYSTEM AND SPATIAL FUNCTION

Damage to the hippocampus or to some of its connections, such as the fornix in monkeys, produces deficits in learning about the places of responses and about the places of stimuli. For example, fornix lesions impair conditional left-right discrimination learning, in which the visual appearance of an object specifies whether a response is to be made to the left or the right (Rupniak and Gaffan, 1987). A comparable deficit is found in humans (Petrides, 1985). Fornix-sectioned monkeys are also impaired in learning which object to choose on the basis of a spatial cue (e.g., if two objects are on the left, choose object A, but if the two objects are on the right, choose object B) (Gaffan and Harrison, 1989a). Similarly, macaques and humans with damage to the hippocampus or fornix are impaired in object-place memory tasks in which not only what objects are seen, but where they were seen, must be remembered (Smith and Milner, 1981; Gaffan and Saunders, 1985; Parkinson et al., 1988). Such object-place tasks require a whole scene or snapshot-like memory in which spatial relations in a scene must be remembered.

Monkeys with fornix damage are also impaired in using information about their place in an environment. For example, Gaffan and Harrison (1989b) found learning impairments when the monkey had to choose between two or more objects, depending on the position of the monkey in the room.

NONSPATIAL ASPECTS OF THE FUNCTION OF THE HIPPOCAMPUS IN PRIMATES: ITS ROLE IN MEMORY

Damage to the hippocampal system or the perirhinal and entorhinal cortices in primates can produce impairments in recognition memory tasks (Gaffan, 1974; 1977; Zola-Morgan et al., 1989). The impairment is much less clear if delayed nonmatch-to-sample methods are used than if delayed match-to-sample methods are used (Gaffan et al., 1984). The impairment is also less severe if the monkeys are trained initially

with the long (and, therefore, difficult) intervals between stimuli with which they are tested later (Gaffan et al., 1984). The implication is that the deficit produced by the fornix section is not simply due to an inability to distinguish novel from familiar stimuli, but is due perhaps just as much to a difficulty these lesioned animals have in altering their response strategies. The deficit may be partly due to inability to apply a special rule (e.g., pick the familiar object) in one context (that is, in the testing situation).

Another nonspatial impairment produced by fornix section in monkeys is a deficit in learning the unnatural instrumental response rule "Choose the object not previously paired with reward" (sometimes called a win-shift rule) (Gaffan et al., 1984). (Fornix section did not impair use of the natural instrumental rule "Choose the object previously associated with reward," sometimes called the win-stay rule) (Gaffan et al., 1984.)

RELATION BETWEEN SPATIAL AND NONSPATIAL ASPECTS OF HIPPOCAMPAL FUNCTION

One way of relating the impairment of spatial processing to other aspects of hippocampal function is to note that this spatial processing involves a snapshot type of memory, in which one whole scene must be remembered. This memory may then be a special case of episodic memory, which involves an arbitrary association of a set of events that describe a past episode. Further, the nonspatial tasks impaired by damage to the hippocampal system may be impaired because they are tasks in which a memory of a particular episode, rather than of a general rule, is involved. Thus, the learning of tasks with nongeneral rules, such as "choose the object not previously rewarded" (i.e., win-shift, lose-stay) may be impaired because to solve them the particular pairing in the particular context (of performing with this special rule) must be remembered in order to choose the correct object later. (The natural rule, which will in the natural environment usually lead to reward, is to choose the object previously associated with reward.) Another example is that choosing familiar rather than novel objects in a recognition memory task may be particularly difficult for monkeys with damage to the hippocampal system because it involves a special rule: choose the familiar object in this task, rather than the novel object; it may be a more general tendency to choose the novel object. The latter rule is what normally guides behavior, as this rule is more likely to lead to reward for objects without an explicit reward association already in the natural environment.

I suggest that the reason why the hippocampus is used for the spatial and nonspatial types of memory described above, and the reason that makes these two types of memory so analogous, is that the hippocampus contains one stage, the CA3 stage, that acts as an autoassociation memory, in the way described below. (More detailed evidence, and the structure, operation, and properties of autoassociation memories, are described elsewhere by Rolls, 1989a; 1989b; 1990). The suggestion is that an autoassociation memory implemented by the CA3 neurons equally enables whole (spatial) scenes or episodic memories to be formed, with a snapshot quality that depends on the arbitrary associations that can be made

and the short temporal window that characterizes the synaptic modifiability in this system.

THE COMPUTATIONAL SIGNIFICANCE OF THE FUNCTIONAL ARCHITECTURE OF THE HIPPOCAMPUS

The internal connections of the hippocampus, and the learning rules implemented at its synapses, have led to ideas about how its neuronal networks contribute to memory; these are described much more completely elsewhere (Rolls, 1989a; 1989b; 1990). A major feature of hippocampal neuronal networks is the recurrent collateral system of the CA3 cells, which enables CA3 cells to have approximately a 4% probability of contacting any other CA3 cell. Given that the synaptic modification rule for these synapses is probably Hebbian, it is suggested that the CA3 cells form a single association network. Given that it has been shown in primates that connections reach the hippocampus (via the entorhinal cortex and parahippocampal gyrus) from high-order areas of cerebral cortex, such as inferior temporal visual cortex, superior temporal auditory cortex, parietal cortex, and frontal cortex, it is suggested that the CA3 system would enable events received from any of these high-order areas to be linked associatively in the CA3 system to concurrent events received from other areas. This would enable, for example, the sight of an object, represented by firing in the inferior temporal cortex, to be linked associatively to its place in space, represented by firing in the parietal cortex. This autoassociation system would thus instantiate an episodic memory, used in this case to remember where a particular object was seen. Each episode would be defined by a conjunction of a set of events, and each episodic memory would consist of the association of one set of events (such as where, with whom, and what one ate at lunch on the preceding day).

Computational ideas on how the dentate granule and CA1 stages contribute to the processing being performed by the CA3 system are developed elsewhere (Rolls, 1989a; 1989b; 1990).

THE INFORMATION REPRESENTED BY THE FIRING OF CELLS IN THE PRIMATE HIPPOCAMPUS

The information processing performed by the primate hippocampus while it is performing the functions for which lesion studies have shown it is needed has been investigated in studies in which the activity of single hippocampal neurons has been analyzed during the performance and learning of these (and related) tasks.

In an object-place memory task (and similar tasks), in which monkeys had to remember not only which visual stimuli had been seen before, but the positions on a video monitor in which they had been seen, Rolls et al. (1989) found that 9% of neurons recorded in the hippocampus and parahippocampal gyrus had spatial fields; they responded whenever there was a stimulus in some but not in other positions on the screen. Two point four percent of the neurons responded to a combination of spatial information and information about the object seen; they responded more the first time a particular image was seen in any position. Six of these neurons

showed this combination even more clearly. For example, they responded to only some positions, and only the first time a particular stimulus had appeared there. Thus, not only is spatial information (probably originating from the parietal cortex) processed by the primate hippocampus, but it can be combined, as shown by the responses of single neurons, with information about which stimuli have been seen before (probably originating from the inferior temporal visual cortex) (Rolls et al., 1989), consistent with the points made above.

These "space" neurons (Rolls et al., 1989; Cahusac et al., 1989) may be compared with "place" cells recorded in the rat hippocampus (McNaughton et al., 1983; O'Keefe, 1984). The "place" cells that have been described in the rat respond when the rat is in a particular place in the environment, as specified by extra-maze cues, whereas the cells described here respond to particular positions in space, or at least when stimuli are shown in particular positions in space (Feigenbaum and Rolls, 1991). In current experiments, we are analyzing the distinction further by investigating the responses of cells when macaques are moved in a small chair on wheels to different places in a cue-controlled testing environment. Many cells with spatial responses are being found. For a number of cells, it was possible to show that firing rate depended on where in space the monkey looked, and not on the place in the environment of the monkey, or head direction. Cells that respond according to the location of the monkey and independently of local view and head direction have not yet been found, but testing is continuing.

These studies showed that some hippocampal neurons in primates have spatial fields. In order to analyze further how space is represented in the primate hippocampus, Feigenbaum and Rolls (1991) investigated whether the spatial fields use egocentric or some form of allocentric coordinates. This was investigated by locating a neuron with a space field and then moving both the monitor screen and the monkey relative to each other to different positions in the laboratory. For 7% of the spatial neurons, the responses remained in the same position relative to the monkey's body axis when the screen was moved or the monkey was rotated or moved to a different position in the laboratory. These neurons thus represented space in egocentric coordinates. For 61% of the spatial neurons analyzed, the responses remained in the same position on the screen or in the room when the monkey was rotated or moved to a different position in the laboratory. These neurons thus represented space in allocentric coordinates. Evidence for two types of allocentric encoding was found. In the first type, the field was defined by its position on the monitor screen independently of the position of the monitor relative to the monkey's body axis and of the position of the monkey and the screen in the laboratory. These neurons were called "frame-of-reference" allocentric, in that their fields were defined by the local frame provided by the monitor screen. The majority of the allocentric neurons responded in this way. In the second type of allocentric encoding, the field was defined by its position in the room, and was relatively independent of position relative to the monkey's body axis or to position on the monitor screen face. These neurons were called "absolute" allocentric, because their fields were defined by position in the room.

Cahusac et al. (1989) found that the majority of the neurons

that responded in the object-place memory task did not respond in a delayed spatial response task. Instead, a different population of neurons (5.7% of the total) responded in the delayed spatial response task, with differential left-right responses in the sample, delay, or match periods. Thus, this latter population of hippocampal neurons had activity that was related to the preparation for or initiation of a spatial motor response.

In another type of spatial task for which the primate hippocampus is needed—conditional spatial response learning—the monkeys had to learn associations between visual stimuli and spatial responses; 14% of hippocampal neurons responded to particular combinations of stimuli and responses (Miyashita et al., 1989). Further, during such conditional spatial response learning, 22% of this type of neuron altered their responses so that they became differential to the two stimuli when the monkey learned to make different responses to the two stimuli (Cahusac et al., 1986; Rolls et al., 1991). These results are consistent with the theory described above in which part of the mechanism of this learning involves associations between visual stimuli and spatial responses learned by single hippocampal neurons.

The activity of hippocampal neurons in nonhuman primates has also been analyzed during the performance of nonspatial tasks for which the hippocampus is needed, such as recognition memory tasks (Rolls et al., 1991). It has been found that in the macaque hippocampus, some neurons do respond differently to novel and familiar stimuli in a serial recognition memory task; those that did respond differentially typically responded more to novel than to familiar visual stimuli. The proportion of hippocampal neurons that responded in this way was small (2.3%), but this is not inconsistent with the hypothesis that the hippocampus is involved in episodic memory.

SYSTEMS LEVEL THEORY

These computational and systems level analyses suggest that the hippocampus is specialized to detect the best way in which to store information. By its return paths to the cerebral cortex it may direct memory storage there. A key hypothesis is that the CA3 autoassociation system is ideal for remembering particular episodes and their context, for, perhaps uniquely in the brain, it provides a single autoassociation matrix that receives from many different areas of the cerebral association cortex. Impairment of this ability to remember episodes by using the CA3 autoassociation matrix memory may underlie many of the memory deficits produced by damage to the hippocampal system. For example, conditional spatial response learning (Miyashita et al., 1989) may be impaired by hippocampal damage because a monkey or human cannot make use of the memory of the episode of events on each particular trial for which a particular stimulus and response were made and reward was received. Similarly, object-place memory tasks require associations to be made between particular locations and particular objects—again, a natural function for an autoassociation memory. Further, the difficulty with memory for places produced by hippocampal damage (Barnes, 1988) may be because a place is normally defined by a conjunction of a number of features or environmental

cues or stimuli; this type of conjunction is normally made by the autoassociation memory capability of the hippocampus.

The empirical and theoretical analyses of hippocampal function described here are thus consistent with the hypothesis that the hippocampus is important for certain types of spatial and nonspatial memory because it contains a single network that provides a special capability to enable events to be linked associatively to form episodic memories. According to this hypothesis, spatial computation *per se*, as required for navigation by performing vector operations involving, for example, bearings and distances from known objects to compute present location or desired trajectories, would not take place in the hippocampus. Instead, such spatial computation would take place in the parietal cortex, damage to which does impair spatial computation, as in visuospatial agnosia (McCarthy and Warrington, 1990).

It should be noted that this theory is not inconsistent with the possibility that the hippocampus provides a working memory; in the present theory the hippocampus sets up a representation using Hebbian learning that is useful in determining how information can best be stored in the neocortex, and this representation could provide a useful working memory.

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