

Spatial Memory and Hippocampal Function: Where are we now?

Mark Good*

Cardiff University

The main aim of this paper is to provide an overview of current debates concerning the role of the mammalian hippocampus in learning with a particular emphasis on spatial learning. The review discusses recent debates on (1) the role of the primate hippocampus in recognition memory and object-in-place memory, (2) the role of the hippocampus in spatial navigation in both rats and humans, and (3) the effects of hippocampal damage on processing contextual information. Evidence from these lines of research have led many current theories to posit a function for the hippocampus that has as its organizing principle the association or binding of stimulus representations. Based on this principle, recent theories of hippocampal function have extended their application beyond the spatial domain to capture features of declarative and episodic memory processes.

The hippocampus has maintained a central position in the development of psychological theories of normal and abnormal human and animal memory for the last 40 years or so. In 1984, Nestor Schmajuk provided a comprehensive review of then current psychological theories of hippocampal function and highlighted over 20 theories. A theme that emerged from Schmajuk's review was that the hippocampus contributed to memory processes and particularly to spatial memory. The aim of this paper is to examine what progress has been made in understanding the contributions of the hippocampus to learning and memory and to spatial learning in particular. An examination of the role of the hippocampus in memory is best appreciated in its historical context. Therefore, the first section of the paper provides a summary of findings from studies of human temporal lobe amnesia, and is then followed in the second section by an overview of recent primate studies of memory. The third section summarises recent research concerning the role of the hippocampus in spatial navigation and refers to both animal and human studies of navigation. The fourth section summarises recent animal work examining the role of the hippocampus in processing contextual information.

* School of Psychology, Cardiff University, Cardiff CF10 3YG, United Kingdom. This paper was supported by a grant from the BBSRC.

The last section briefly describes two recent theories of hippocampal function that represent recent attempts to bridge the gap between theories of human temporal lobe amnesia and the spatial processing functions of the hippocampus in animals.

1. The development of a neural theory of memory

In 1957 Scoville and Milner presented the case of HM who had severe anterograde amnesia following bilateral medial temporal lobe resection. The lesion in HM included the anterior two thirds of the hippocampus, the hippocampal gyrus, amygdala and periamygdaloid cortex. Formal memory testing of HM and 9 other patients with less extensive bilateral medial temporal lobe removal led to the view that damage to the hippocampus was responsible for the amnesia. That is, memory impairments were observed whenever the hippocampus and the hippocampal gyrus were damaged bilaterally (Milner, 1972). While he was severely amnesic for every day events, HM was able to recall certain types of material. For example, HM possessed normal perceptual, cognitive and linguistic abilities. HM could remember remote biographical details of his childhood and showed normal primary or short-term memory, unless he was distracted from rehearsing the information (Sidman et al., 1968; Cohen 1984)

The pattern of impaired and spared memory functions displayed by HM prompted a now commonly acknowledged characterisation of the temporal lobe amnesic syndrome. A general consensus is that damage to the medial temporal lobe in humans disrupts declarative memory processes and more specifically episodic memory functions (e.g., Tulving, 1972; Kinsbourne & Wood, 1975; Eichenbaum, Otto and Cohen, 1992; Squire, 1992; Mishkin et al., 1997; Tulving & Markowitsch, 1998; Tulving 2002). Declarative memories are those available to conscious recollection as information about facts, events or specific stimuli. Declarative memories have been further divided into episodic and semantic components. Episodic memory is concerned with conscious recall of specific episodes, and semantic memory with the storage of factual information. The contribution of the hippocampus and related cortical temporal lobe structures to semantic memory remains controversial but there is general agreement that the hippocampus contributes to the encoding and storage of episodic memories (see Griffiths et al., 1999; Mishkin et al., 1997; Tulving & Markowitsch 1998 for further discussion). The memory functions that are spared in temporal lobe amnesia have been referred to collectively as nondeclarative (Squire, 1992) or procedural memories (Cohen & Eichenbaum, 1993). Examples of procedural memories include associative learning, word priming, perceptual learning, stimulus-response habits and motor learning (Squire & Zola, 1996). Nondeclarative or procedural memory processes are thought to operate automatically and do not include information about where or when an event or learning experience took place. As well as receiving support from lesion studies in humans, the declarative/nondeclarative distinction has also received support from recent neuroimaging studies of hippocampal activation (for recent reviews see

Schacter & Wagner, 1999; Cohen et al., 1999; Tulving et al., 1999; Maguire, 2001; Mayes & Montaldi, 2001; see also Tulving 2002). Beyond this basic distinction between impaired and spared memory systems in human temporal lobe amnesia, however, there remain a number of controversies, e.g., the involvement of the hippocampus in (1) semantic memory (see for example Squire, 1992; Vargha-Khadem, et al., 2001), (2) familiarity – versus context-based recognition memory (Reed & Squire, 1997; Duzel, Varga-Khadem, Heinze & Mishkin, 2001) and the extent of retrograde amnesia following temporal lobe damage (e.g. Clark et al., 2002; Spiers et al., 2001). A discussion of these issues is, however, beyond the scope of the present paper (the reader is referred to Spiers et al., 2001, for further information).

From a historical perspective, the pattern of memory deficits in humans with temporal lobe damage prompted two questions: (1) What were the temporal lobe regions involved in the amnesic syndrome and (2) what role did the hippocampus play in memory? The first question instigated research with non-human primates with the specific aim of identifying medial temporal lobe brain structures responsible for amnesia. As we shall see, the central issue in primate research has changed over recent years from understanding the anatomical locus of amnesia to examining the role of the hippocampus in recognition memory processes.

2. Primate models of human amnesia

To address the question of which temporal lobe brain structures were important for memory in monkeys, behavioural tasks were required that were similar to tasks used with amnesic patients. Early psychological characterisation of the human amnesic syndrome (Talland, 1965; Warrington and Weiskrantz, 1970) suggested that amnesic patients were deficient specifically in recognition memory (a component of the declarative/episodic memory system)--- that is, “the ability to assign to a certain action in a certain context a value of familiarity-unfamiliarity” (Gaffan, 1972, p 328). Gaffan (1974) examined recognition memory in monkeys using a matching-to-sample procedure (DMTS). In this task, a trial was compromised of two stages. In the first stage, the monkey was shown a junk object (the sample stimulus) and was rewarded for displacing the object. In the subsequent, comparison, trial, the same (previously rewarded) object was presented again together with a novel object. The monkey was rewarded for displacing the familiar object. Animals with fornix lesions (a major input/output pathway of the hippocampus) performed as well as control animals when a short delay (10 sec) was interpolated between the sample and comparison stimuli, but were impaired when longer delays (70 and 130 sec) were used. The results seemed to support the view that the hippocampus in primates was important for recognition memory. A view that was reinforced by evidence that human amnesic patients showed a similar deficit on a DMTS task (e.g., Sidman et al., 1968).

Subsequent developments of this task included a delayed non-matching-to-sample (DNMTS) version of the procedure (Mishkin, Prockop

and Rosvold, 1962; Mishkin and Delacour, 1975). In this version of the task, the animal was rewarded for choosing the novel stimulus in the comparison stage of a trial. The first indication that temporal structures were important for DNMTS was provided by a study conducted by Mishkin (1978). Monkeys with damage to the hippocampus (H), the amygdala (A) and the surrounding cortex (referred to as the H+ A+ lesion) were severely impaired on the DNMTS task. This finding appeared to confirm that conjoint damage to the hippocampus and amygdala was sufficient to produce an amnesic syndrome in monkeys (e.g., Zola-Morgan et al., 1982). However, this conclusion was limited by the fact that additional damage to adjacent cortical tissue was caused by the surgical approach (i.e., damage extended to the entorhinal and perirhinal cortex). Further refinement of the hippocampal lesion procedure resulted in a reduction of the damage to the adjacent cortex (e.g., Mahut, Zola-Morgan & Moss, 1982; Alvarez-Royo, Clower, Zola-Morgan & Squire, 1991; Alvarez et al., 1995). More recently, selective neurotoxins (such as ibotenic acid) have been used to produce fibre-sparing lesions in which cell loss is limited to the hippocampal formation (Murray & Mishkin, 1998; Beason-Held et al., 1999; Zola et al., 2000). As lesions of the hippocampus have become more selective, however, the magnitude of the deficits on DNMTS task in lesioned monkeys has become smaller. Although cell loss limited to the hippocampal formation in monkeys has revealed memory impairments in the majority of studies, the DNMTS deficit is unmistakably greater following bilateral damage to cortical regions adjacent to the hippocampus (Squire & Zola-Morgan, 1991; Zola-Morgan et al., 1989; see also Suzuki, et al., 1993; Malkova et al., 2001). Furthermore, recent studies have shown striking DNMTS deficits in monkeys with lesions restricted to the perirhinal/ entorhinal cortex that leave the hippocampus intact (Meunier et al., 1993; Malkova et al., 2001, see Aggleton, 1999; Aggleton & Brown, 1999, for discussion). A similar pattern of results has also been revealed in studies of object recognition memory in rats (see Mumby, 2001 for a review).

Although it is widely accepted that the entorhinal and perirhinal cortices are important for recognition memory, the role of the hippocampus in this type of memory remains controversial (see, Clark, West, Zola & Squire, 2001; Dudchenko et al, 2000; Wan et al., 1999). One proposal for resolving the controversy has been put forward recently by Aggleton & Brown (1999). These authors suggested that the DNMTS task can be solved in at least two ways – either by *recollecting* the stimulus or the event (i.e., by episodic recognition memory) or by detecting stimulus *familiarity*. According to Aggleton & Brown, the hippocampus supports episodic recognition (i.e. context dependent aspects of recognition) and the surrounding cortex (entorhinal and perirhinal cortex) supports familiarity-based recognition. This hypothesis has received some support from studies of scene-specific memory in primates. Gaffan (1994) developed an analogue of human memory tests for monkey in which the animal remembered the unique context (an artificial scene constructed on a computer-driven visual display) in which an object was rewarded. Gaffan has argued that many of the tasks that revealed deficits in human amnesic patient involved episodic memory about a complex event –

that is the memory included information about the scene or context in which an event took place. Standard tests of object recognition memory in monkeys (i.e., the DNMTS procedure), in contrast, had previously used apparatus with only a single background scene or context. Memory for the context in which an object was seen was therefore irrelevant. Consistent with previous research using overtly spatial tasks (e.g., Mahut, 1972; Murray et al., 1989) Gaffan reported that monkeys with hippocampal lesions were impaired in learning place discriminations in scenes and were severely impaired in learning an object-in-place memory task in which each unique scene contained a correct and incorrect object (typographic characters). In contrast, monkeys with hippocampal lesions were as accurate as control animals in learning object discriminations when the background scenes varied between trials. Under these conditions scene-specific object memory was irrelevant. The object-in-place test may represent a more accurate analogue of episodic memory tests in humans Gaffan (Gaffan, 1991, 1994; see also Gaffan & Parker, 1996). These findings suggest that a fundamental role for the hippocampus in forming a representation of the spatial organization of a scene that may be critical for episodic memory processes.

A critical role of the hippocampus in forming object-in-place representations has also been revealed in studies with rats and humans. For example Mumbey et al. (2002) reported that rats with hippocampal lesions explored a novel object in an open-field arena to the same degree as control animals, but failed to explore a familiar object when it was presented either in a novel place in a familiar test arena or in a different context. Control rats, on the other hand, showed a preference for exploring a familiar object when it was presented in a novel place or in a novel context. A similar finding has been reported in a patient with selective hippocampal damage. Holdstock et al., (2002) reported that a patient with restricted hippocampal damage showed normal forced-choice object recognition performance but impaired forced-choice object-location associations (see also Mayes et al., 2002; Manns & Squire, 1999). Taken together these results indicate that hippocampal damage in rats, primates and humans disrupts the memory for the spatial layout of a context where an object was recently experienced.

In summary, recent evidence indicates that the contribution of the primate hippocampus to the standard DNMTS test of recognition memory is limited and that damage to underlying cortical regions (entorhinal/perirhinal cortex) results in a severe impairment on this task. However, these findings do not rule out the possibility that the hippocampus may contribute to recognition memory processes. More specifically, recent research has suggested that the hippocampus is important for scene or context-specific object memories. The evidence that the hippocampus in non-human mammals encodes information about the place or context in which an object is experienced provides an apposite link between deficits in overtly spatial navigation tasks in animals and impairments in declarative/episodic memory in humans. However, we shall return to the issue of whether the hippocampus contributes to forming a representation of the spatial layout of a scene/context or to context-dependent memory retrieval in a discussion of context processing in rats. Before doing

so, the next section will consider recent evidence that suggests that rats with hippocampal lesions are able to learn place information.

3. Spatial learning and hippocampal lesions in rodents

One of the most important theories of hippocampal function to emerge over the last 20 years or so has been the cognitive mapping theory proposed by O'Keefe & Nadel (1978). The primary impetus for the cognitive mapping theory was the discovery that the firing rate of hippocampal neurons was correlated with the location of the animal in a test environment (these cells are referred to as place cells; O'Keefe & Dostrovsky, 1971; O'Keefe, 1976; O'Keefe & Conway, 1978) and the wealth of lesion data at the time that revealed spatial learning deficits in animals with hippocampal damage (O'Keefe & Nadel, 1978, for a review). In brief, O'Keefe and Nadel proposed that learning and memory was supported by two systems. The *locale* system was dependent upon an intact hippocampus and supported cognitive mapping. Cognitive mapping refers to learning about the spatial relationships between cues. The second learning system (referred to as the *taxon* system) was not reliant upon the hippocampus and supported stimulus-response learning or habit learning. Over the years since its inception, there has been considerable support for the cognitive mapping theory from lesion studies and unit recording studies. For example, rats with hippocampal lesions are impaired in learning the radial arm (Olton et al., 1979; Jarrard 1983), the T-maze (e.g., Rawlins and Olton, 1982; Bannerman et al., 2001; see also, Murray et al., 1989.) and the Morris water maze, where lesioned rats are impaired in swimming to a hidden, but not to a visible, platform (Morris et al., 1982; Morris et al., 1986; see also Pearce et al., 1998). There is a large body of evidence showing that the activity of hippocampal neurons in both rats and primates reflects information about the spatial organisation of an animal's environment (for a recent review of hippocampal unit recording studies see Hippocampus 9, 1999: Special issue on Place Cells). A role for the hippocampus in spatial learning appears to generalize across species. For example, damage to the anatomical homologue of the hippocampus in birds (the hippocampus and area parahippocampalis; see Macphail current volume) and the hippocampus in humans disrupts spatial learning. Indeed, recent neuroimaging studies in humans have provided evidence that the hippocampus becomes active during spatial navigation and that hippocampal morphology can be affected by reliance upon spatial navigation skills. Before briefly discussing recent studies of spatial navigation in humans, the next section will consider current research that suggests the hippocampus in rats may contribute to more than one type of spatial navigation.

Hippocampus and spatial learning: Knowing where or getting there?

Path integration is a form of navigation in which an animal integrates self-movement cues (i.e., vestibular information) to locate its present position or to return to a starting location. This ability has been shown in different species including gerbils (Mittelstaedt and Mittelstaedt, 1980), house mice

(Alyan and Javander, 1994), rats (e.g., Maaswinkel et al., 1999), insects (Wehner and Srinivasan, 1981) and humans (Mittelstaedt and Mittelstaedt, 2001). A view that has emerged recently is that the hippocampus may contribute to path integration processes – according to one class of theory the path integrator lies within the hippocampus (McNaughton et al., 1996; Whishaw, 1998) and according to a second class of theory the path integrator lies outside the hippocampus (see, O'Keefe, 1976; Redish and Touretzky, 1997, Redish, 2001; Cho & Sharp, 2001; Sharp et al., 2001).

Support for the role of the hippocampus in path integration comes from both electrophysiological and lesion studies in rats. Electrophysiological evidence indicates that hippocampal place cells in rats are sensitive to vestibular and visual motion cues (Sharp et al., 1995) and that the subiculum (a region adjacent to the hippocampus) contains cells that are sensitive to the direction of the animals' head (Taube, 1998). Furthermore, recent research has shown that temporary inactivation of the vestibular inputs to the hippocampus disrupts the location-specific firing of place cells and the direction specific discharge of subicular head direction cells (Stackman et al., 2002). The electrophysiological data suggest, therefore, that the hippocampal neuronal representation of space is strongly influenced by vestibular information.

The principal behavioural evidence in support of a role for the hippocampus in path integration comes from lesions studies carried out by Whishaw and colleagues. Whishaw (1998) proposed that the hippocampus is “dedicated to monitoring cues generated by self-movement and that it is part of a directional system that provides information to an *extrinsic* location system.” (P. 218). That is, the hippocampus was thought to support path integration and other brain regions supported place learning. One source of evidence in favour of this proposal comes from studies that purport to show that rats with hippocampal damage are able to acquire place responses. For example, Whishaw et al., (1995) reported that, like control animals, lesioned rats were able to reduce swim speeds as they approached the spatial location of a submerged platform in a watermaze. Whishaw et al., interpreted this as evidence that control rats and rats with damage to the fornix anticipated the location of the platform. In contrast, however, Hollup et al., (2001) reported that rats with hippocampal lesions failed to slow down their approach to a platform in an annular watermaze when its location was specified by extramaze cues. When a salient intramaze landmark identified the position of the platform, rats with hippocampal lesions reduced the speed of their approach to the platform as effectively as control animals. The reasons for the discrepancy between these two studies are unclear, but may reflect differences in the apparatus, type and/or extent of pretraining or lesion technique. Nevertheless, it would seem that rats with hippocampal lesions are able to identify the location of the platform using extramaze cues under some conditions. However, this could reflect an ability of lesioned rats to use an individual (salient) cue to modify their behaviour.

Subsequent studies by Whishaw and colleagues have provided a more direct test of the role of the hippocampus in path integration. Whishaw and

Maaswinkle (1998) studied path integration using a foraging task on an elevated circular maze. The rats were trained to climb out on to the maze from a home cage that was located beneath the table at the periphery of the maze. The rats were trained to find a food pellet and to then return with the food pellet to the home cage beneath the table to consume the reward. In the first experiment, the rats were pretrained as normal animals to forage for food and to return to a fixed home cage start location. Following pretraining, the rats received either a lesion to the fimbria-fornix (hippocampus) or a sham operation. During post-operative testing, in which a novel home cage location was used, control animals initially returned to the old home cage location used during pretraining. However, as training continued, control rats were increasingly more likely to return to the new location from which they had recently emerged. Rats with fimbria fornix lesions, however, adopted a very strong perseverative strategy and returned to the pretrained home cage location.

In a second experiment, Whishaw and Maaswinkle (1998) trained rats postoperatively on the table top foraging task. Following acquisition, the rats received two types of probe trials, both using a novel home cage start location. In Probe 1, the rats were tested with access to the visual cues around the maze. In Probe 2, the rats were blindfolded, thus excluding the visual extramaze cues. The removal of the visual extramaze cues in Probe 2 was designed to force the animals to rely upon a path integration strategy to return to the home cage. During acquisition training, when the visual extramaze cues were available, rats with fimbria fornix lesions learned the foraging task as effectively as control animals. On the first probe trial, in which the extramaze cues were available, the control rats initially returned with their food reward to the old training location. When they discovered that the home cage location had been changed, all of the control rats went to the new home cage location. The rats with lesions of the hippocampus, however, continued to return to the old home cage location. In Probe 2, the blindfold probe trial, significantly more of the control rats returned to the new home cage location than rats with hippocampal lesions. When naïve control and hippocampal lesioned rats were trained on the foraging task wearing blindfolds, lesioned rats failed to return to their home cage as accurately as control animals. Two conclusions can be drawn from these results. First, rats with hippocampal lesions were able to use a cue or cues outside the maze to guide their return journeys to the home cage, second, in the absence of visual extramaze cues rats with hippocampal damage were impaired in navigating by path integration (see also Whishaw & Gorny, 1999; Whishaw et al., 2001; Wallace et al., 2002).

The pattern of results from these (and other) studies supports Whishaw and colleagues view that rats with hippocampal lesions are able to use extramaze cues but are impaired in adopting a path integration strategy. However, it is not clear from these studies how rats with hippocampal lesions are using extramaze cues. It is not clear whether the representation of extramaze cues formed by lesioned rats differed from that formed by control animals. For example, rats with hippocampal lesions are able to find a hidden platform in the watermaze if they are always started from the same location

(Eichenbaum et al., 1990), or if they are trained with a platform that reduces in size over the course of training (Day et al., 1999) or if a cue is available from which they can generate a heading vector (Pearce et al., 1998). Such examples of apparent place learning may be supported by a number of different strategies, for example simple conditioned approaches to a salient landmark. Thus these results do not provide conclusive evidence that rats with hippocampal lesions are able to encode the spatial relationship between extramaze cues. Nevertheless, the results from Whishaw and colleagues are certainly consistent with the view that the hippocampus contributes to navigation by path integration

An alternative view to Whishaw and colleagues path integration hypothesis of hippocampal function is that the path integration system lies outside the hippocampus (see Redish 2001, and Redish & Turetzky, 1997). Evidence in support of view is that rats with hippocampal lesions are able to navigate by path integration at least under some conditions. Alyan and McNaughton (1999) showed that rats with hippocampal lesions navigated as accurately as control animals in the dark on a circular table top task, similar to that used by Whishaw and colleagues. Furthermore, Alyan & McNaughton also showed that various manipulations that disrupted path integration in control rats, also disrupted performance in rats with hippocampal lesions (for discussion of these finding see Maaswinkel et al., 1999). If the path integration system lies outside the hippocampus then what are the likely brain areas that might support such a navigation system? There are several candidate regions. McNaughton et al., (1996) suggested that the posterior parietal and retrosplenial cortex may contribute to path integration and an idea supported recently by Cooper and Mizumori (2001). Sharp (2001) has proposed a role for the mammillary bodies, dorsal tegmental nuclei and subiculum in path integration. Redish and Touretzky (1997) have suggested that the path integration is accomplished by an anatomical loop that includes the hippocampus, the subiculum, the parasubiculum and the entorhinal cortex.

As described earlier, place cell activity is clearly influenced both by extramaze landmarks and vestibular information (for a recent review see Best et al., 2001). What role might the interaction between these two types of information in the hippocampus play in spatial navigation? One proposal (e.g., Stackman et al., 2002) is that vestibular information is used to accurately represent the animals' moment-to-moment spatial location in a familiar environment and its directional heading. Thus, the hippocampus may associate information from internal (path integration) and external, i.e., landmark-based, sources. An interaction of this type could provide an error correction mechanism during navigation, by using external cues that have been associated with the internal navigation system, to accurately update representations of the animals' location in a *familiar* environment (see also, McNaughton et al., 1996).

In summary recent evidence has shown that the hippocampus receives vestibular information that may be important for navigation by path integration. One of the key issues that remains to be resolved is the precise contribution of the hippocampus to path integration and what role other

closely-related brain regions, such as the subiculum, play in path integration. In addition, if the hippocampus does contribute to navigation by path integration, then further work is required to understand how this function may be related to (episodic) memory processes supported by this structure (for recent discussions on this issue see Gaffan, 1998; Redish, 2001).

The human hippocampus and spatial learning

The important role assigned to the hippocampus in spatial learning in animals has prompted examination of the role played by the human hippocampus in spatial navigation. Along with traditional studies of brain damaged patient, insights into the role of the human hippocampus in spatial learning has been greatly enhanced by the development of neuroimaging techniques such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). This next section will consider recent findings from neuroimaging studies of human navigation.

Maguire et al., (1996) measured regional cerebral blood flow while subjects watched and memorised film footage depicting navigation in an urban area (referred to as topographical memory). In a control condition, subjects were exposed to similar footage, but the camera remained stationary while people and cars moved past the viewer. Maguire et al., argued that in the latter condition it was not possible for the subject to construct an internal spatial map of the environment. An analysis of the changes in rCBF between the two conditions showed increased activation of the right medial parietal region, parahippocampal cortex and hippocampus on and the left parahippocampal cortex during topographical navigation. Aguirre et al., (1996) used fMRI and a computer simulation of a maze-like environment to examine topographical learning. These authors also reported activation of the hippocampal formation (parahippocampus), the medial parietal region and cingulate cortex. Other studies, however, have failed to find activation of the hippocampus using relatively simple computer generated environments (Maguire et al., 1998). Maguire has argued, however, that navigation in simple environments may be insufficient to detect activation of the hippocampus against background noise and that more complex, large-scale environments may be more likely to reveal hippocampal activation. In support of this idea, increased hippocampal activation has been observed when participants navigate through more complex virtual environments (Maguire et al., 1996; Maguire et al., 1997; see Aguirre and D'Esposito 1999; Maguire, 1999, for further discussion).

Maguire et al., (1997) examined the neural substrates of long-term topographical memory using official London taxi drivers. The aim of the study was to test subjects on their knowledge of complex routes, where all subjects were tested on the same familiar stimuli, and where no encoding of new environmental information occurred during performance of the task. To provide a comparison condition, Maguire et al., examined subjects during the retrieval of landmark knowledge *per se*, that is, landmark information that did not include knowledge about the large scale spatial context of the landmarks. Comparison of PET scans made during route recall with scans taken during

landmark recall revealed activation of the parietal lobe, cingulate cortex, parahippocampal region and activation of the right hippocampal formation. Comparison of the landmark task with baseline scans revealed no activation of the right hippocampus. The results from this study again confirmed activation of the right hippocampus during retrieval of spatial memories.

The main conclusion that can be drawn from these studies is that the right hippocampus in humans appears to participate in both the encoding and the retrieval of topographical memory (Maguire et al., 1998). A number of lesion studies have also provided support for the view that structures within the right temporal lobe support spatial or topographical memory. For example, patients with right temporal lobe damage are impaired in their ability to remember the location of objects on a table top (Smith & Milner, 1981, 1989, Nunn et al., 1999), in a scene (Pigott & Milner, 1993), and spatial information in a virtual town (Spiers et al., 2001). Interestingly, right temporal lobe damage has been shown to affect performance on procedures that mimic rodent spatial learning tasks, e.g., navigation in a room (Bohbot et al., 1998; Worsley et al., 1999). In many of these studies, patients with left temporal damage performed at levels that were similar to control subjects. This begs the question of what role the left temporal lobe (hippocampal) region might play in memory? One interesting suggestion that requires further investigation is that the context-dependent aspects of episodic memory may be preferentially mediated by left medial temporal lobe structures (see Spiers et al., 2001; Maguire, 2001, and Aguirre and D'Esposito, 1999 for discussion).

Increased hippocampal volume relative to brain and body size has been reported in birds that engage in spatial behaviour, e.g., in food storing birds (Lee et al., 1998, see also Lee et al., 2001). A recent study by Maguire et al., (2000) investigated whether morphological changes could be detected in human brain with participants whose work was associated with extensive experience of spatial navigation. Intriguingly, Maguire et al., (2000) found that the posterior hippocampi of experienced official London taxi drivers were significantly larger relative to control subjects. Furthermore, hippocampal volume was positively correlated with the amount of time spent as a taxi driver. One interpretation of this study is that morphological changes may take place in the posterior region of the hippocampus in people with a high dependence on spatial navigational skills. Whether other types of navigation skills, e.g., those that might rely more on path integration, result in similar changes in hippocampal volume has yet to be addressed.

In conclusion, there is a growing body of evidence to suggest that the hippocampal formation in humans contributes to the encoding and retrieval of spatial (topographical) information. The findings from imaging and lesion studies of navigation in humans correspond well with rat and primate studies in showing that a robust and enduring deficit in spatial navigation results from hippocampal damage. Although the role of the human hippocampus in navigation by path integration processes has not been studied extensively, a recent report by Worsley et al., (2001) showed that humans with right temporal lobectomy (i.e. damage that included the hippocampus) were impaired in navigating by path integration. However, the precise anatomical

substrate of the temporal lobe impairment in path integration in humans needs to be examined further before a role in path integration can be ascribed to the human hippocampus. In general, however, the results from navigation studies in humans are in broad agreement with animal studies and suggest an important role for the hippocampus in processing landmark and perhaps self-movement related spatial information.

4. Place learning revisited: the role of the hippocampus in processing contextual cues.

One of the distinguishing features of episodic memory processes is the ability to encode and retrieve the rich temporal and spatial context of an event. Recent studies with primates have suggested that the hippocampus may encode the spatial relationship between components of a scene or context and that in the absence of this representation, animals with hippocampal lesions are unable to form object-place configurations important for episodic memory (e.g., Gaffan, 1998; Mizumori et al., 1999). The term context refers to the ambient cues that together define the place, situation or location in which an organism is present and in which learning occurs. As described above there is a wealth of evidence from rats and primates that the activity of hippocampal neurons reflects spatial information about the animal's environment (e.g., Best et al., 2001; Rolls, 1999; see also de Araujo et al, 2001). This section will consider recent controversies concerning the role of the rodent hippocampus in processing contextual information and will focus on two main questions: (1) Does the hippocampus contribute to the formation of a representation of context? (2) Is the hippocampus involved in the contextual retrieval of information?

Before addressing these questions, I will first consider the role of context in learning from the perspective of animal learning theory. Learning theorists have proposed that context may influence learning and performance of animals in a number of ways. One view of context is that, like any other conditioned stimulus (or CS), a representation of context cues can enter into direct associations with reinforcement (unconditioned stimulus or US; Rescorla & Wagner, 1972) and other discrete CSs, such as a tone (Wagner, 1981). An alternative view is that the context may set the occasion for relationships between other (CS and US) events that occur within them (referred to as occasion setting; Holland 1993). There is considerable evidence to support this view (see, Holland 1993). For example, Bouton (1993) has reviewed evidence showing that several associative learning phenomena rely at least in part upon contextual cues to select or retrieve appropriate CS-US relationship. Bouton concludes that retrieval function of the context appears is most readily apparent when contextual cues disambiguate the meaning of a stimulus.

Research concerning the role of the hippocampus in processing contextual information has revolved around the issue of whether damage to this structure disrupts the formation of a context representation (c.f., Anagnostaras, Gale and Fanselow 2001; Gaffan, 1994) or the contextual

retrieval of information (c.f., Hirsh, 1974; Honey & Good, 1993; Maren & Holt, 2000). These views will be considered in the following section.

The hippocampus and context memories.

A commonly held view is that the formation of a representation of a context requires the integration of the multiple cues that comprise a context into a unified (often referred to as configural or conjunctive) representation -- a process that has been allied to the formation of a spatial memory (Nadel, & Willner, 1980; Gaffan, 1994; Sutherland & Rudy, 1989; Anagnostaras et al., 2001). During conditioning a configural context representation can enter into direct associations with other stimuli and/or act as a retrieval cue for other associative relationships. Context fear conditioning has become a popular task to evaluate the effects of lesions (including genetic manipulations; e.g., Crawley, 1999) on context memories. In the basic procedure, animals are exposed to a novel conditioning context and then presented with either signalled (e.g., a tone) or unsignalled footshock. As result of these pairings, control animals display a well-characterised freezing response to presentations of the context and/or the conditioned stimulus (CS). Several studies have reported that animals with lesions of the hippocampus showed impaired freezing elicited by contextual cues but displayed normal levels of freezing to a standard CS e.g., a tone (for a review see Maren et al., 1998). This pattern of results has been taken to indicate that the hippocampus is required for the formation of a context representation. Other evidence is also consistent with this view. For example, prior exposure to a context before hippocampal surgery protects the animals against a contextual freezing deficit (Young et al., 1994). According to Young et al., the exposure to a context before the hippocampus is damaged allows the context representation to be formed in the hippocampus and then stored elsewhere (e.g., cortex). After a hippocampal lesion, the intact context representation is then able to enter in to an association with a US. Consistent with this view, other studies have shown that the role of the hippocampus in context processing is temporally graded. Rats that have received pairings of a context with shock, either 1, 7, 28, or 100 days prior to hippocampal surgery show impaired context freezing when surgery was conducted 1 day after training. In contrast, freezing elicited by a context in rats with hippocampal lesions was comparable to control animals when the surgery was conducted 28 days after training (Kim & Fanselow, 1992; or 100 days after training, (Maren et al., 1997).

Although evidence in favour of the context representation account appears compelling, there are reports of normal context learning in rats with hippocampal lesions. For example, Maren et al., (1997) found that neurotoxic lesions of the dorsal hippocampus did not disrupt the acquisition of contextual fear (see also Phillips and LeDoux, 1994; Cho et al. 1999). A recent report by Richmond et al (1999) has suggested that contextual fear conditioning and spatial navigation may have different neural substrates. These authors reported that lesions to the ventral hippocampus, but not the dorsal hippocampus, disrupted fear conditioning. In contrast, it is reasonably

well established that damage to the dorsal, but not to the ventral, hippocampus disrupts navigation in the Morris watermaze (Moser et al., 1995; Hock & Bunsey, 1998; see also Cho et al., 1999). One explanation that has been offered for those instances in which hippocampal damage does not influence contextual fear conditioning is that lesioned animals may have formed associations between individual salient features (or elements) of the context and shock (see Anagnostaras, et al., 2001). At the very least what this explanation suggests, however, is that a better test of context memory is required. This is further illustrated by a performance account of the contextual freezing impairment in rats with hippocampal lesions.

According to the performance account, hippocampal lesions in rats result in hyperactivity (Teitelbaum & Milner, 1963; Douglas & Isaacson, 1964; Good & Honey, 1997). Rats with lesions of the hippocampus may fail to exhibit normal freezing simply because the tendency to be active interferes with the expression of contextual fear (Good & Honey, 1997; McNish et al., 1997). In addition, the performance account assumes that stimuli, such as a tone conditioned stimulus, that usually elicit higher levels of fear, are less susceptible to the activity-related disruption in performance. One issue that remains to be addressed is whether the lesion-induced changes in activity level can explain the time-limited retrograde amnesia for context fear in hippocampal rats.

At the very least, the performance account has raised an important issue concerning the impact of changes in activity levels following hippocampal lesions on conditioned freezing. Do alternative measures of context learning support the context memory theory of hippocampal function? McNish et al (1997) reported that rats with hippocampal lesions acquired a context fear-potentiated startle response as well as control rats. Interestingly, the same lesioned animals, nevertheless, showed impaired freezing to contextual cues. Similarly McNish et al., (2000) showed that blocking (Kamin, 1969) by a context of conditioning to a CS was intact in rats with hippocampal lesions. These studies show that, at least some, alternative measures of context learning do not support the proposal that the hippocampus contributes to forming a representation of a context.

In summary, contextual fear conditioning paradigms alone are not sufficient to demonstrate a role for the rodent hippocampus in forming a representation of a context (see Holland & Bouton, 1999; Gewirtz et al., 2000, Anagnostaras et al., 2001, for further discussion). What is required is a more direct test of the nature of the representations that are formed during exposure to a context. The development of behavioural tests that reveal whether a configural or elemental process has been used to encode information about a context will advance our understanding of the role of the rodent hippocampus in context learning.

The contextual retrieval of memories.

There is a long history of research showing that the expression of memories depends upon the context in which a memory is retrieved (Tulving & Thomson, 1973; Spear, 1973; Bouton, 1993). In 1974, Richard Hirsh proposed that the hippocampus participated in a process of contextual retrieval of information. Hirsh proposed two learning systems, a contextual retrieval system, that was dependent upon the hippocampus, and a performance line system that was independent of the hippocampus. Hirsh's view of context included the ambient cues of the environment and interoceptive cues that were associated with hunger, thirst, etc. According to Hirsh, contextual cues can "refer to but are not described within the information to be retrieved" (Hirsh, 1974). Examples of procedures that encourage contextual retrieval include conditional learning such as occasion setting. According to Hirsh, information that is retrieved from memory by contextual stimuli is placed into a performance system referred to as the "performance line". When independent of contextual retrieval processes, the learning supported by the performance line system reflected simple stimulus-response associations and was relatively inflexible. According to Hirsh, learning supported by the contextual retrieval system was much more flexible. For example, intact rats could use contextual retrieval cues to rapidly store and adjust to changes in the reinforcement contingencies experienced in an environment. Rather than overwriting a learning experience, an animal could store an experience using a unique contextual tag for later retrieval, should similar environmental events be encountered in the future. In the absence of the contextual retrieval system (following hippocampal damage), Hirsh proposed that performance was governed simply by the summation of the current and previous reinforcement history of stimuli. More specifically, Hirsh (1974) proposed that animals with hippocampal lesions were unable to apply different contextual labels to different sets of reinforcement contingencies. One consequence of hippocampal damage, according to Hirsh's view, is that lesioned rats should be impaired in learning conditional discriminations.

Although there is now evidence that hippocampal lesions do not severely disrupt conditional learning of the type predicted by Hirsh (e.g., Deacon et al., 2001), there is evidence that hippocampal lesions may disrupt contextual retrieval of associative information under some conditions (see also O'Reilly & Rudy, 2001). For example, rats with hippocampal lesions fail to show contextual specificity of some forms of learning, e.g., latent inhibition. Latent inhibition refers to the retardation in conditioning that is associated with non-reinforced exposure to a CS (Lubow, 1973). A hallmark of latent inhibition is that it is reduced or abolished if the exposure and conditioning stages of latent inhibition are carried out in different contexts. In addition, latent inhibition can be renewed after the CS has been exposed and conditioned in different contexts, if the CS is tested in the preexposure context (see, Maren and Holt, 2000). One account of latent inhibition is that the poorer conditioned responding to a preexposed CS results from the (contextual) retrieval of conflicting memories of the CS. For example, when preexposure and conditioning occur in the same context, the context may activate conflicting

memories of the CS – a memory of the CS paired with nothing and another of the CS paired with reinforcement. However, changing the context between the preexposure and conditioning phases of LI will reduce the impact of the preexposure memory on performance to the CS during conditioning (see, Holland & Bouton 1999).

To examine the effects of hippocampal lesion on contextual specificity of latent inhibition, Honey and Good (1993) exposed rats to two different CSs, each CS in a different context (e.g., stimulus x in context A and stimulus y in context B). Both stimuli were then paired with food in the same context (i.e., stimulus x and stimulus y were paired with food separately in context A). For control animals, the CS that was conditioned in the same context as exposure (e.g., stimulus x in context A in our example) acquired conditioned responding at a slower rate than the CS exposed and conditioned in a different context (stimulus y in context A). However, rats with hippocampal lesions did not show this pattern of responding. They responded at a lower rate to both of the stimuli, that is they showed latent inhibition to both CSs regardless of the context in which they were conditioned. Honey and Good (1993) also showed that rats with hippocampal lesions were able to discriminate as quickly as control animals between the two contexts when free-food was presented in one context but not the other. This pattern of results along with other studies (e.g., Good & Honey, 1991; Good and Bannerman, 1997; Good et al., 1998; but see, Fox and Holland, 1998 and Frohardt et al., 2000) support the view, first proposed by Hirsh (1974), that the hippocampus contributes to the contextual retrieval of associative information.

One limitation of the lesion method is that the disruption to hippocampal function is present throughout training and is not confined only to the retrieval stage of testing. A recent study by Holt and Maren (1999) has over come this limitation by using a drug (muscimol) that, when injected directly in to the hippocampus, temporally suspends neural transmission. Holt and Maren (1999) examined the context specificity of the expression of latent inhibition using a fearconditioning paradigm. They first exposed rats to a tone CS in one context and simply the animal to a second context (i.e., stimulus x in context A; nothing in context B). After exposure, rats then received conditioning trials in which the CS was followed by foot shock in a third novel context (stimulus x paired with shock in context C). Before testing, subgroups of animals were infused either with muscimol or saline into the dorsal hippocampus. During testing, rats infused with saline showed lower levels of freezing to the tone when it was tested in the same context as exposure (i.e., stimulus x in context A), that is they expressed latent inhibition. However, rats that had received infusion of muscimol into the hippocampus during testing, showed the same low levels of freezing to the CS regardless of whether it was tested in the same or a different context to that of exposure. That is, rats with a temporary inactivation of the hippocampus during retrieval showed latent inhibition regardless of the context in which the CS was tested. Holt and Maren, excluded the possibility that rats treated with muscimol were unable to discriminate between the contexts at test. Rats first received unsignalled footshock in one context and no shock in a second context. The rats then

received an extinction test following infusion of either saline or muscimol into the dorsal hippocampus. The infusion of muscimol into the dorsal hippocampus had no detrimental effect on the context discrimination. More recently, Corcoran and Maren (2001) have also shown that the context specific expression of extinction is also disrupted by infusion of muscimol into the dorsal hippocampus. Taken together these studies provide compelling evidence that hippocampal inactivation impairs the contextual retrieval of associative information.

In summary, the contribution of the rodent hippocampus to forming a representation of the context remains controversial. Even if one acknowledges that rats with hippocampal lesions are able to form only elemental representations of a context, it nevertheless remains the case that a high-order retrieval process is impaired by hippocampal dysfunction in rats. In order to resolve the debate between the contextual representation and contextual retrieval views of hippocampal function in rats, new behavioural tests are required that reveal the nature of representations formed during context learning (see also, O'Reilly & Rudy, 2001). Nevertheless, there is converging evidence from studies using rats and primates that the hippocampus contributes to processing information about contexts and the events that are associated with them.

5. Events, contexts, space and the hippocampus.

The evidence reviewed above has shown that the hippocampus contributes to processes supporting episodic recognition memory, spatial navigation and context dependent retrieval processes. In attempting to capture the mechanism(s) that might be central to these forms of learning, a common principle has emerged in many recent theories of hippocampal function. That is, that the hippocampus plays a fundamental role in integrating representations. This view is prevalent in many psychological and computation theories of hippocampal function (e.g., Burgess et al., 2001; Eichenbaum, 2001; Gluck & Myers, 1993; Morris, 2001). Thus, the majority of recent theories of hippocampal function have at their core the organizing principle that representations of objects/ events and their spatiotemporal context are integrated together (or indeed separated) from each other in a neural network instantiated in the hippocampal formation. A comprehensive review of all these theories is beyond the scope of this paper (for a recent summary of computational models, see *Hippocampus*, 6, 1996, Special Issue: Computational Models of Hippocampal Function in Memory, and Gluck & Myers, 1997). Instead I will conclude with a brief overview of two recent theories that have stimulated a great deal of empirical interest and that represent the organising principles of several recent theories of hippocampal function.

The hippocampus and configural representations.

One of the most influential non-spatial psychological theories of hippocampal is the configural learning theory proposed by Sutherland & Rudy (1989; see also Rudy and Sutherland, 1995). According to the configural theory, learning is supported by two separate systems. One system, that is independent of the hippocampus, forms association between simple or elemental stimuli, e.g., a CS and reward. An elemental association is one that develops between cue elements of one stimulus and cue elements of another stimulus. The ability of a CS to activate a representation of another event depends upon the associative strengths of the individual elements of the stimulus and the associative strength of other stimuli present on a trial. The second learning system proposed by Sutherland and Rudy, is the configural learning system and is dependent upon the hippocampus. A configural representation is a unique representation of the joint occurrence or conjunction of two or more stimuli. Sutherland & Rudy (1989) proposed that rats with hippocampal damage are unable to learn non-linear conditional problems, such as negative patterning (stimulus x and stimulus y are followed by food but the compound cue comprising of x and y is non reinforced) that require configural representations. An important feature of these discriminations is that they cannot be solved by the combination of the individual associative strengths of the component stimuli. Unfortunately, a large literature has amassed that shows that rats with hippocampal lesions are able to acquire at least some nonlinear discriminations, such as negative patterning (e.g., Davidson et al., 1993; see also Good et al., 1998).

In response to these negative findings, O'Reilly and Rudy (2001) reconfigured the configural theory and suggested that two separate systems contribute to forming conjunctive (i.e., configural) representations. The first is a cortical system that can form configural representations and thus support the learning of nonlinear discriminations, such as negative patterning, and the second is a hippocampal system that is capable of *rapidly* forming conjunctive representations during *incidental* learning tasks. A characteristic of the cortical learning system is that it develops conjunctive representations over a relatively large number of trials when conjunctive representations are explicitly required for the solution of the task. The cortical system is therefore driven by task contingencies and is capable of forming complex representations when given sufficient training. O'Reilly and Rudy suggest that non-linear discriminations such as negative patterning (or ambiguous cue problems) are not ideal tasks to reveal the contribution of the hippocampus to configural learning. Instead, it is suggested that the hippocampus contributes to processing incidental configural or conjunctive representations. Examples of tasks in which hippocampal incidental conjunctive representations contribute to performance include, spatial learning, habituation (Save t al., 1992), the contextual specificity of conditioning and latent inhibition (Good & Honey, 1991; Good & Bannerman, 1997; Honey & Good, 1993; Good et al., 1998), contextual fear conditioning (Phillips & LeDoux, 1994) and the detection of associative mismatches (Honey et al., 1998; Honey & Good 2000). Interestingly, O'Reilly and Rudy also predict that rats with hippocampal lesions should be

unable to form incidental sensory-sensory associations. However, Honey & Good (2000; see also Good et al., 1998) and Ward-Robinson et al (2001) have shown recently that rats with hippocampal lesions are able to form (incidental) sensory-sensory associations using serial habituation and sensory preconditioning tasks, respectively. Nevertheless, the view that the hippocampus processes or forms configural representations is expressed, albeit in different ways, in a number of theories of hippocampal function (e.g., de Araujo et al., 2001; Anagnostaras et al., 2001; Gaffan, 1998; Gluck & Myers, 1993; McNaughton & Morris, 1987; Schmajuk & Buhusi, 1997)

Relational memory

Eichenbaum and colleagues (e.g., Eichenbaum et al., 1992; Eichenbaum, 2001) suggest that the hippocampus plays a critical role in declarative memory for both episodic and semantic information. More specifically, Eichenbaum and colleagues propose that declarative memories are expressed through conscious recollection of events and may be used to solve novel problems by making inferences based upon retrieval of declarative memories. Thus, relationships between items or events that have never been directly trained or experienced together can be inferred by reference to the hippocampal relational network.

Eichenbaum and colleagues have examined the effects of hippocampal lesions on relational learning using a number of non-navigation tasks, such as transitive inference. For example, Dusek & Eichenbaum (1997) trained rats on a series of pair-wise odour discrimination problems; e.g., stimulus A was followed by food when paired with stimulus B, stimulus B was followed by food when paired with stimulus C, stimulus C was followed by food when paired with D, and finally stimulus D was followed by food when paired stimulus E. The test for transitive inference examined the preference for items that had never been directly paired together i.e., B and D. Rats with fornix lesions or lesions of the entorhinal cortex acquired the initial discrimination of the odour stimuli at the same rate as control animals. During the transitive inference test control animals selected B over D. This preference was thought to reflect a representation of the orderly relationships amongst the stimuli, i.e., stimulus B was preferred over stimulus C and C preferred over stimulus D, the preference for stimulus B should be greater than for stimulus D. In contrast, rats with hippocampal lesions did not show this pattern of results. The rats also received a test with stimulus A and stimulus E. In this case, stimulus E had never been paired directly with food and should therefore possess lower associative strength than stimulus A. Control rats and rats with hippocampal lesions both preferred stimulus A over stimulus E. Thus, while rats with hippocampal lesions were able to acquire stimulus-stimulus associations, Eichenbaum argues that these associations are hyper specific to the trained events. According to Eichenbaum (2001), the control rats in Dusek & Eichenbaum study were able to encode the odour discrimination as distinctive experiences and flexibly express the orderly relations among the items during the test of stimulus B and D.

Eichenbaum has extended the relational model to capture certain features of spatial learning. In the Morris watermaze for example, training involves releasing the animal from different start locations at the periphery of the pool and encourages the rat to adopt different routes to the hidden platform. According to Eichenbaum (2001), the training trials can be viewed as different trial episodes containing common information, e.g., the landmarks the location of the platform. However, individual landmarks may be used differently on any given trial (e.g., on some trials a rat will swim to the left of a landmark on another it may swim away from a landmark). According to Eichenbaum (2001), the differences in the distinct views that a rat is exposed to during learning is reconciled by “constructing a spatial organization.” (p 204) of trial events. Control rats are then able to use the spatial organization of trial episodes to make spatial inferences to navigate to the hidden platform from novel start locations. The central principle in Eichenbaum and colleagues theory, in common with other theories, is the linking or binding of episodic memories by their common events and places that results in a capacity to move among related memories in a network.

Although the studies carried out by Eichenbaum and his colleagues have succeeded in drawing attention to the contribution of the hippocampus to non-spatial learning, some of their behavioural findings are open to alternative interpretation. For example, an alternative explanation for the performance shown by control animals on the B vs. D test in the transitive inference paradigm described above is that the associative strength of B is simply greater than that of D. The associative strength of B may be greater than that of D by nature of its own association with food and by its association with A (see Couvillon & Bitterman, 1992; Hall, 1996; and Zentall, 2001, for discussion). If this analysis were correct then it would suggest that damage to the hippocampus disrupts a higher-order associative learning process.

Where are we now?

The last 10-20 years have certainly seen important developments in characterisation of the hippocampal damage in animals. Advances have been made in understanding the contribution of (1) the primate hippocampus to recognition memory, (2) the human hippocampus to spatial navigation (3) the rodent hippocampus to different types of spatial navigation and context processing. The current memory theories of hippocampal function possess a common organizing principle -- that the hippocampus contributes to the binding together of memories of events and their spatiotemporal context (see O'Reilly and Rudy for discussion). This has led to a reinterpretation of a range of behavioural deficits in animals with hippocampal damage in terms of declarative/episodic versus procedural memory processes (e.g., Gaffan, 1998; Eichenbaum 2001; O'Reilly & Rudy 2001). However, there is a danger in over generalising the performance of animals (in both spatial and non-spatial tasks) to episodic or declarative memory processes. Many tasks that are claimed to capture aspects of episodic (or episodic-like) memory processes are open to interpretation in terms of simpler (associative and non-associative)

processes (see Honey & Good, 2000; Griffiths et al., 1999 for discussion). As Tulving (2001) has noted “evolution is an exceedingly clever tinkerer who can make its creatures perform spectacular feats without necessarily endowing them with sophisticated powers of conscious awareness.” (p1513). A goal for the future is to develop more sophisticated behavioural tasks for animals that engage specific processes that are thought to underlie episodic memory, e.g., what, where and when an event took place, and that permit evaluation of hippocampal cell loss on memory processes in a tractable fashion (see Morris, 2001 for further discussion).

There remains one indisputable fact concerning hippocampal function – the hippocampus clearly plays an important role in spatial navigation. The advocates of the spatial mapping theory continue to press home this fact and, further, propose that this characterisation remains the best explanation for both experience-dependent patterns of hippocampal neuronal activity and the outcomes of lesions studies (O’Keefe, 1999). Perhaps one way to approach the issue of the memory functions of the hippocampus is to continue our efforts to understand the principles governing spatial learning. A better understanding of the conditions, the nature of the representations and the mechanism(s) by which spatial learning (in all its forms) takes place (Dickinson, 1980) will provide important clues to the role of the hippocampus in memory.

REFERENCES

- Aggleton, J.P. (1999) Mapping recognition memory in the primate brain: Why it’s sometimes right to be wrong. *Brain Res Bull* 50, 447-448.
- Aggleton, J.P., & Brown, M.W., (1999) Episodic memory, amnesia and the hippocampal-anterior thalamic axis. *Behav. Brain Sci.*, 22, 425-489.
- Aguirre, G.K., Detre, J.A., Alsop, D.C. and D’Esposito, M. (1996) The parahippocampus subserves topographical learning in man. *Cerebral cortex*, 6, 823-9.
- Aguirre G.K. and D’Esposito, M. (1999) Topographical disorientation: a synthesis and taxonomy. *Brain*, 122, 1613-28.
- Alvarez, P., Zola-Morgan, S., and Squire, L.R. (1995) Damage limited to the hippocampal region produces long-lasting memory impairment in monkeys. *J Neurosci.* 15, 3796-807.
- Alvarez-Royo, P., Clower, R.P., Zola-Morgan, S., and Squire, L.R. (1991) Stereotaxic lesions of the hippocampus in monkeys: determination of surgical coordinates and analysis of lesions using magnetic resonance imaging. *J Neurosci Methods.* 38, 223-32.
- Alyan, S.H., and Jander, R. (1994) Short-range homing in the mouse *Mus musculus*: Stages in the learning of directions. *Anim Behav*, 48, 285-298.
- Alyan, S. and McNaughton, B.L. (1999) Hippocampectomised rats are capable of homing by path integration. *Behav Neurosci*, 113, 19-31.
- Anagnostaras, S.G., Gale, G.D., and Fanselow, M.S. (2001) Hippocampus and contextual fear conditioning: recent controversies and advances. *Hippocampus*, 11, 8-17.

- Bannerman, D.M., Yee, B.K., Lemaire, M., Wilbrecht, L., Jarrard, L., Iversen, S.D., Rawlins, J.N., and Good, M.A. (2001) The role of the entorhinal cortex in two forms of spatial learning and memory. *Exp Brain Res*.141, 281-303.
- Best, P.J., White, A.M., & Minai, A. (2001) Spatial processing in the brain: the activity of hippocampal place cells. *Annu Rev Neurosci.*, 24, 459-86.
- Biegler, R. & Morris, R.G.M., (1993) Landmark stability is a prerequisite for spatial but not discrimination learning. *Nature*, 361, 631-633.
- Biegler, R., & Morris, R.G. Blocking in the spatial domain with arrays of discrete landmarks. (1999) *J Exp Psychol Anim Behav Process*. 25, 334-51.
- Beason-Held, L.L., Rosene, D.L., Killiany, R.J., Moss, M.B. (1999) Hippocampal formation lesions produce memory impairment in the rhesus monkey. *Hippocampus*. 9, 562-74.
- Bohbot, V., Kalina, M., Stepankova, J., Spackova, N., Petrides, M., and Nadel, L. (1998) Spatial memory deficits in patients with lesions to the right hippocampus and to the right parahippocampal cortex. *Neuropsychologia*, 36, 1217-38.
- Bouton, M.E. (1993) Context, time, and memory retrieval in the interference paradigms of Pavlovian learning. *Psychol Bull*.114, 80-99.
- Bunsey, M., Eichenbaum, H. (1995) Selective damage to the hippocampal region blocks long-term retention of a natural and nonspatial stimulus-stimulus association. *Hippocampus*. 5, 546-56.
- Burgess, N., Becker, S., King, J.A., and O'Keefe, J. (2001) Memory for events and their spatial context: models and experiments. *Philos Trans R Soc Lond B Biol Sci.*, 356, 1493-503.
- Cho, Y.H., Friedman, E., and Silva, A.J., (1999) Ibotenate lesions of the hippocampus impair spatial learning but not contextual fear conditioning in mice. *Behav Brain Res*, 98, 77-87.
- Cho, J., and Sharp, P.E. (2001) Head direction, place, and movement correlates for cells in the rat retrosplenial cortex. *Behav Neurosci* 115, 3-25.
- Cohen, N.J. (1984) Preserved learning capacity in amnesia: Evidence for multiple memory systems. In L.R. Squire & N. Butters (Eds.). *The neuropsychology of memory* (pp. 83-103). New York: Guilford Press.
- Cohen, N.J. & Eichenbaum, H. (1993). *Memory, amnesia and the hippocampal system*. Cambridge: MIT Press.
- Cohen, N.J., Ryan, J., Hunt, C., Romline, L., Wszalek, T. (1999) Hippocampal System and declarative (relational) memory: Summarizing the data from functional neuroimaging studies. *Hippocampus*, 9, 83-98.
- Cooper, B.G., & Mizumori, S.J. (2001) Temporary inactivation of the retrosplenial cortex causes a transient reorganization of spatial coding in the hippocampus. *J Neurosci*. 21, 3986-4001.
- Corcoran, K.A., & Maren, S. (2001) Hippocampal inactivation disrupts contextual retrieval of fear memory after extinction. *J Neurosci*.21, 1720-6.
- Couvillon, P.A., and Bitterman, M.E. (1992) A conventional conditioning analysis of transitive inference in pigeons. *J Ebptal Psychol: Animal Behav Proc*, 18, 308-310.
- Crawley, J.N. (1999) Behavioral phenotyping of transgenic and knockout mice: experimental design and evaluation of general health, sensory functions, motor abilities, and specific behavioral tests. *Brain Res*. 835, 18-26.
- Davidson, T.L., McKernan, M.G., Jarrard, L.E. (1993) Hippocampal lesions do not impair negative patterning: a challenge to configural association theory. *Behav Neurosci*. 107, 227-34.
- Day, L.B., Weisend, M. Sutherland, R.J., Schallert, T. (1999) The hippocampus is not necessary for a place response but may be necessary for pliancy. *Behav Neurosci*, 113, 914-24.

- Deacon, R.M., Bannerman, D.M., Rawlins, N.P. (2001) Conditional discriminations based on external and internal cues in rats with cytotoxic hippocampal lesions. *Behav Neurosci.*, 115, 43-57.
- de Araujo, I.E., Rolls, E.T., and Stringer, S.M. (2001) A view model which accounts for the spatial fields of hippocampal primate spatial view cells and rat place cells. *Hippocampus*, 11, 699-706.
- Dickinson, A. (1980) *Contemporary animal learning theory*. Cambridge University Press: Cambridge
- Douglas, R.J. and Isaacson, R.L. (1964) Hippocampal lesions and activity. *Psychonomic Sci*, 1, 187-188.
- Dusek, J.A., Eichenbaum, H. (1997) The hippocampus and memory for orderly stimulus relations. *Proc Natl Acad Sci U S A*. 94, 7109-14.
- Duzel, E., Vargha-Khadem, F., Heinze, H.J., & Mishkin, M. (2001) Brain activity evidence for recognition without recollection after early hippocampal damage. *Proc Natl Acad Sci U S A*, 98, 8101-6.
- Eichenbaum, H. (2001) The hippocampus and declarative memory: cognitive mechanisms and neural codes. *Behav Brain Res*.127, 199-207.
- Eichenbaum, H., Otto, T., Cohen, N.J. (1992) The hippocampus--what does it do? *Behav Neural Biol.*, 57(1):2-36.
- Eichenbaum, H., Stewart, C. and Morris, R.G.M. (1990) Hippocampal representations in place learning. *J Neurosci*, 10, 3531-42.
- Fox, G.D., Holland, P.C. (1998) Neurotoxic hippocampal lesions fail to impair reinstatement of an appetitively conditioned response. *Behav Neurosci*.112, 255-60.
- Frohardt, R.J., Guarraci, F.A., Bouton, M.E. (2000) The effects of neurotoxic hippocampal lesions on two effects of context after fear extinction. *Behav Neurosci.*;114, :227-40.
- Gaffan, D. (1972) Loss of recognition memory in rats with lesions of the fornix. *Neuropsychologia*, 10, 327-341.
- Gaffan, D. (1974) Recognition impaired and association intact in the memory of monkeys after transection of the fornix. *J Comp Physiol Psychol* 86, 1100-1109.
- Gaffan, D. (1994) Scene-specific memory for objects : a model of episodic memory impairment in monkeys with fornix transection. *J Cogn Neurosci*, 6, 305-320.
- Gaffan, D. (1998) Idiopathic input into object-place configuration as the contribution to memory of the monkey and human hippocampus: a review. *Exp Brain Res*. 123, 201-9.
- Gaffan, D. (1991) Spatial organization of episodic memory. *Hippocampus*. 1, 262-4.
- Gaffan, D., & Parker, A. (1996) Interaction of perirhinal cortex with the fornix-fimbria: memory for objects and "object-in-place" memory. *J Neurosci*.16, 5864-9.
- Gallistel, C.R. (1990) *The organization of learning*. Cambridge, MA: MIT Press.
- Gewirtz, J.C., McNish, K.A., Davis, M. (2000) Is the hippocampus necessary for contextual fear conditioning? *Behav Brain Res.*, 110, 83-95.
- Gluck, M.A. and Myers, C.E. (1997) Psychobiological models of hippocampal function in learning and memory. *Annu Rev Psychol.*, 48, 481-514.
- Gluck, M.A. and Myers, C.E. (1993) Hippocampal mediation of stimulus representation: a computational theory. *Hippocampus*, 3, 491-516.
- Good, M., Bannerman, D. (1997) Differential effects of ibotenic acid lesions of the hippocampus and blockade of N-methyl-D-aspartate receptor-dependent long-term potentiation on contextual processing in rats. *Behav Neurosci*.111, 1171-83.
- Good, M., de Hoz, L., Morris, R.G. (1998) Contingent versus incidental context processing during conditioning: dissociation after excitotoxic hippocampal plus dentate gyrus lesions. *Hippocampus*, 8,147-59.

- Good, M. and Honey, R.C. (1997) Dissociable effects of selective lesions to the hippocampal subsystems on exploratory behavior, contextual learning and spatial learning. *Behav Neurosci*, *111*, 487-493.
- Griffiths, D., Dickinson, A., Clayton, N. (1999) Episodic memory: what can animals remember about their past? *Trends Cogn Sci.*, *3*, 74-80.
- Hall, G. (1996) Learning about associatively activated stimulus representations: Implications for acquired equivalence and perceptual learning. *Anim Learn & Behav*, *24*, 233-255.
- Healey, A.N., Gaffan, E.A. (2001) Configural learning without configural training. *J Exp Psychol Anim Behav Process*, *27*, 373-93.
- Hirsh, R. (1974) The hippocampus and contextual retrieval of information from memory: a theory. *Behav Biol*, *12*, 421-444.
- Hock, B.J. Jr., and Bunsey, M.D. (1998) Differential effects of dorsal and ventral hippocampal lesions. *J Neurosci*, *18*, 7027 – 7032.
- Holland, P.C. (1993) Cognitive aspects of classical conditioning. *Curr Opin Neurobiol.*, *3*, 230-6.
- Holland, P.C. and Bouton, M.E. (1999) Hippocampus and context in classical conditioning. *Curr Opin Neurobiol.* *9*, 195-202.
- Hollup, S.A., Kjelstrup, K.G., Hoff, J., Moser, M.B., & Moser, E.I. (2001) Impaired recognition of the goal location during spatial navigation in rats with hippocampal lesions. *J Neurosci.*, *21*, 4505-13.
- Holt, W., & Maren, S. (1999) Muscimol inactivation of the dorsal hippocampus impairs contextual retrieval of fear memory. *J Neurosci.* *19*, 9054-62.
- Honey, R.C. and Good, M. (1993) Selective hippocampal lesions abolish the contextual specificity of latent inhibition and conditioning. *Behav Neurosci*, *107*, 23-33.
- Honey, R.C., & Good, M. (2000a) Associative modulation of the orienting response: distinct effects revealed by hippocampal lesions. *J Exp Psychol Anim Behav Process.* *26*, 3-14.
- Honey, R.C., & Good, M. (2000b) Associative components of recognition memory. *Curr Opin Neurobiol.* *10*, 200-4.
- Honey, R.C., Watt, A., & Good, M. (1998) Hippocampal lesions disrupt an associative mismatch process. *J Neurosci.* *1998 18*, 2226-30.
- Jarrard, L.E. (1983) Selective hippocampal lesions and behavior: Effects of kainic acid lesions on performance of place and cue tasks. *Behav Neurosci* *97*: 873-889
- Jarrard, L.E. (1989) On the use of ibotenic acid to lesion selectively different components of the hippocampal formation. *J Neurosci Methods* *29*: 251-259.
- Kesner, R.P., Bolland, B.L., Dakis, M. (1993) Memory for spatial locations, motor responses, and objects: triple dissociation among the hippocampus, caudate nucleus, and extrastriate visual cortex. *Exp Brain Res.* *93*, 462-70.
- Kim, J.J., Fanselow, M.S. (1992) Modality-specific retrograde amnesia of fear. *Science.*, *256*, 675-7.
- Kinsbourne, M & Wood, F. (1975) Short-term memory processes and the amnesic syndrome. In *Short-term memory* (ed., D. Deutsch & J.A. Deutsch), pp.258-291. New York: Academic Press.
- Lee, D.W., Miyasato, L.E., Clayton, N.S. (1998) Neurobiological bases of spatial learning in the natural environment: neurogenesis and growth in the avian and mammalian hippocampus. *Neuroreport.*, *9*, 15-27.
- Lee, D.W., Smith, G.T., Tramontin, A.D., Soma, K.K., Brenowitz, E.A., Clayton, N.S. (2001) Hippocampal volume does not change seasonally in a non food-storing songbird. *Neuroreport.* *12*, 1925-8.
- Lubow, R.E. (1973) Latent inhibition. *Psychol Bull*, *82*, 276-98.

- Maaswinkel, H., Whishaw, I.Q. (1999) Homing with locale, taxon, and dead reckoning strategies by foraging rats: sensory hierarchy in spatial navigation. *Behav Brain Res.* 99, 143-52.
- Maaswinkel, H., Jarrard, L.E., Whishaw, I.Q. (1999) Hippocampectomised rats are impaired in homing by path integration. *Hippocampus*, 9, 553-561.
- Maguire, E.A. (1999) Hippocampal and parietal involvement in human topographical memory: evidence from functional neuroimaging. In *The hippocampal and parietal foundations of spatial cognition* (Burgess, N Jeffery, KJ and O'Keefe J Eds). Oxford University Press.
- Maguire, E.A. (2001) Neuroimaging studies of autobiographical event memory. *Philos Trans R Soc Lond B Biol Sci.* 356:1441-51.
- Maguire, E.A., Frackowiak, R.S., Frith, C.D. (1996) Learning to find your way – a role for the human hippocampal region. *Proc Royal Soc Lond: Biol Sci*, 263, 1745-50.
- Maguire, E.A., Frackowiak, R.S., Frith, C.D. (1997) Recalling routes around London: activation of the right hippocampus in taxi drivers. *J Neurosci*, 17, 7103-10.
- Maguire, E.A., Frith, C.D., Burgess, N., Donnett, J.G. and O'Keefe, J. (1998) Knowing where things are: parahippocampal involvement in encoding object locations in virtual large-scale space. *J Cog Neurosci*, 10, 61-76.
- Maguire, E.A., Gadian, D.G., Johnsrude, I.S., Good, C.D., Ashburner, J., Frackowiak, R.S., & Frith, C.D. (2000) Navigation-related structural change in the hippocampi of taxi drivers. *Proc. Natl. Acad. Sci., U S A.*, 97, 4398-403.
- Mahut, H., & Zola, S.M. (1973) A non-modality-specific impairment in spatial learning after fornix lesions in monkeys. *Neuropsychologia*, 11, 244-269.
- Mahut, H., Zola-Morgan, S., & Moss, M. (1982) Hippocampal resections impair associative learning and recognition memory in the monkey. *J Neurosci.* 2, 1214-20.
- Malkova, L., Bachevalier, J., Mishkin, M., Saunders, R.C. (2001) Neurotoxic lesions of perirhinal cortex impair visual recognition memory in rhesus monkeys. *Neuroreport*. 12, 1913-7.
- Maren, S., Aharonov, G., Fanselow, M.S. (1997) Neurotoxic lesions of the dorsal hippocampus and Pavlovian fear conditioning in rats. *Behav Brain Res.* 88, 261-74.
- Maren, S., Anagnostaras, G., Fanselow, M.S. (1998) The startled seahorse: is the hippocampus necessary for contextual fear conditioning? *Trends Cogn Sci*, 2, 39-42.
- Maren, S., Holt, W. (2000) The hippocampus and contextual memory retrieval in Pavlovian conditioning. *Behav Brain Res.* 110, 97-108.
- Mayes, A.R., & Montaldi, D. (2001) Exploring the neural bases of episodic and semantic memory: the role of structural and functional neuroimaging. *Neurosci Biobehav Rev.*, 25, 555-73.
- McDonald, R.J., and White, N.M. (1994) Parallel information processing in the watermaze: Evidence for independent memory systems involving dorsal striatum and hippocampus. *Behav Neural Biol* 61, 260-270.
- McNaughton, B.L., and Nadel, L. (1990) Hebb-Marr networks and the neurobiological representation of action in space. In *Neuroscience and connectionist theory* (Gluck, MA, Rumelhart, DE, eds) pp 1-63, Hillsdale, NJ: Lawrence Erlbaum.
- McNaughton, B.L., Barnes, C.A., Gerrard, J.L., Gothard, K., Jung, M.W., Knierim, J.J., Kudrimoti, H., Qin, Y., Skaggs, W.E., Suster, M., Weaver, L. (1996) Deciphering the hippocampal polyglot: The hippocampus as a path integration system. *J Exp Biol*, 199, 173-186.
- McNish, K.A., Gewirtz, J.C., Davis, M. (1997) Evidence of contextual fear after lesions of the hippocampus: a disruption of freezing but not fear-potentiated startle. *J Neurosci*. 17, 9353-60.

- McNish, K.A., Gewirtz, J.C., Davis, M. (2000) Disruption of contextual freezing, but not contextual blocking of fear-potentiated startle, after lesions of the dorsal hippocampus. *Behav Neurosci*, 114, 64-76.
- Meunier, M., Bachevalier, J., Mishkin, M., Murray, E.A., (1993) Effects on recognition memory of combined and separate ablations of the entorhinal and perirhinal cortex in rhesus monkeys. *J. Neurosci.*, 13, 5418-5432.
- Milner, B. (1972) Disorders of learning and memory after temporal lobe lesions in man. *Clin. Neurosurg.* 19:421-46.
- Mishkin, M. (1978) Memory in monkeys is severely impaired by combined but not by separate removal of amygdala and hippocampus. *Nature*, 273, 297-298.
- Mishkin, M., and Delacour J. (1975) An analysis of short-term visual memory in the monkey. *J. Exp. Psychol*, 1, 326-334.
- Mishkin, M., Prockop, E.S., and Rosvold, E. (1962) One-trial object discrimination learning in monkeys with frontal lesions. *J Comp Physiol Psychol.*, 33, 178-181.
- Mishkin, M., Suzuki, W.A., Gadian, D.G., & Vargha-Khadem, F. (1997) Hierarchical organization of cognitive memory? *Phil. Trans. R. Soc. Lond.* 356, 1461-1467
- Mittelstaedt, M.L. and Mittelstaedt, H. (1980) Homing by path integration in a mammal. *Naturwissenschaften*, 67, 566-567.
- Mittelstaedt, M.L. and Mittelstaedt, H. (2001) Ideothetic navigation in humans : estimation of path length. *Exp Brain Res*, 139, 318-332.
- Mizumori, S.J., Ragozzino, K.E., Cooper, B.G., & Leutgeb, S. (1999) Hippocampal representational organization and spatial context. *Hippocampus*. 9,444-51.
- Morris, R.G.M., Garrud, P., Rawlins, J.N.P., O'Keefe, J. (1982) Place navigation impaired in rats with hippocampal lesions. *Nature* 297: 681-683
- Morris, R.G.M. (1983) An attempt to dissociate "spatial mapping" and "working memory" theories of hippocampal function. In: W Seifert (ed) *The neurobiology of the hippocampus*. Academic Press, London. pp. 405-432
- Morris, R.G.M. (2001) Episodic-like memory in animals: psychological criteria, neural mechanisms and the value of episodic-like tasks to investigate animal models of neurodegenerative disease. *Phil. Trans. R. Soc. Lond. B*, 356, 1453-1465
- Morris, R.G., Anderson, E., Lynch, G.S., Baudry, M. (1986) Selective impairment of learning and blockade of long-term potentiation by an N-methyl-D-aspartate receptor antagonist, AP5. *Nature*, 319, 774-6.
- Moser, M.B., Moser, E.I., Forrest, E., Andersen, P. and Morris, R.G.M. (1995) Spatial learning with a minislab in the dorsal hippocampus. *Proc Natl Acad Sci (USA)*, 92, 9697-9701.
- Mumby, D.G. (2001) Perspectives on object-recognition memory following hippocampal damage: lessons from studies in rats. *Behav Brain Res*, 127, 159-181.
- Mumby, D.G., Gaskin, S., Glenn, M.J., Schramek, T.E., & Lehmann, H. (2002) Hippocampal damage and exploratory preferences in rats: memory for objects, places, and contexts. *Learn Mem.* 9, 49-57.
- Murray, E.A., & Mishkin, M. (1998) Object recognition and location memory in monkeys with excitotoxic lesions of the amygdala and hippocampus. *J Neurosci.* 1998 18, 6568-82.
- Murray, E.A., Davidson, M., Gaffan, D., Olton, D.S., & Suomi, S. (1989) Effects of fornix transection and cingulate cortical ablation on spatial memory in rhesus monkeys. *Exp. Brain Res.* 74, 173-86.
- Nadel, L. and Willner (1980) Context and conditioning: a place for space. *Physiol. Psychol*, 8, 218-228
- Nunn, J.A., Graydon, F.J., Polkey, C.E., & Morris, R.G. (1999) Differential spatial memory impairment after right temporal lobectomy demonstrated using temporal titration. *Brain.* 122, 47-59.

- O'Keefe, J. (1976) Place units in the hippocampus of freely moving rat. *Expl Neurol.*, 51, 78-109.
- O'Keefe, J. (1999) Do hippocampal pyramidal cells signal non-spatial as well as spatial information? *Hippocampus*, 9, 352-64.
- O'Keefe, J., and Conway, D.H. (1978) Hippocampal place units in the freely moving rat: why they fire where they fire. *Expl Brain Res*, 32, 573-590.
- O'Keefe, J. and Dostrovsky, J. (1971) The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Res*, 34, 171-175.
- O'Keefe, J. and Nadel, L. (1978) *The hippocampus as a cognitive map*. Oxford University Press.
- O'Keefe, J. and Speakman, A. (1987) Single unit activity in the rat hippocampus during a spatial memory task. *Exp Brain Res.*, 68, 1-27.
- O'Reilly, R.C., Rudy, J.W. (2001) Conjunctive representations in learning and memory: principles of cortical and hippocampal function. *Psychol Rev.* 108, 311-45.
- Olton, D.S., Becker, J.T., Handelmann, E. (1979) Hippocampus, space and memory. *Behav Brain Sci*, 2, 313-366.
- Pearce, J.M., Roberts, A.D., & Good, M. (1998) Hippocampal lesions disrupt navigation based on cognitive maps but not heading vectors. *Nature*, 396, 75-77.
- Pearce, J.M., Ward-Robinson, J., Aydin, A., Good, M., & Fussell, C. (2001) Influence of a beacon on spatial learning based on the shape of the test environment. *J Exp Psychol: Animals Behav Processes*, 27, 329-344.
- Pigott, S., and Milner, B. (1993) Memory for different aspects of complex visual scenes after unilateral temporal- or frontal-lobe resection. *Neuropsychologia*, 31, 1-15.
- Phillips, R.G., LeDoux, J.E. (1994) Lesions of the dorsal hippocampal formation interfere with background but not foreground contextual fear conditioning. *Learn Mem.* 1:34-44.
- Rawlins, J.N.P., Olton, D.S. (1982) The septohippocampal system and cognitive mapping. *Behav Brain Res* 5: 331-358.
- Redish, A.D. and Touretzky, D.S. (1997) Cognitive maps beyond the hippocampus. *Hippocampus*, 7, 15-35.
- Redish, A.D. (2001) The hippocampal debate: are we asking the right questions? *Behav Brain Res.* 127, :81-98.
- Reed, J.M., & Squire, L.R. (1997) Impaired recognition memory in patients with lesions limited to the hippocampal formation. *Behav Neurosci.* 111, 667-75.
- Rescorla, R.A. and Wagner, A.R. (1972) A theory of Pavlovian conditioning: variations in the effectiveness of reinforcement and nonreinforcement. In AH Black & WF Prokasy (Eds.), *Classical conditioning II: current research and theory*. New York, Appleton-Century-Crofts.
- Richmond, M.A., Yee, B.K., Pouzet, B., Veenman, L., Rawlins, J.N., Feldon, J., & Bannerman, D.M. (1999) Dissociating context and space within the hippocampus: effects of complete, dorsal, and ventral excitotoxic hippocampal lesions on conditioned freezing and spatial learning. *Behav Neurosci.*, 113, 1189-203.
- Rolls, E.T. (1999) Spatial view cells and the representation of place in the primate hippocampus. *Hippocampus*. 9, 467-80.
- Rudy, J.W., Sutherland, R.J. (1995) Configural association theory and the hippocampal formation: an appraisal and reconfiguration. *Hippocampus*. 5, 375-89.
- Save, E., Poucet, B., Foreman, N., Buhot, M.C. (1992) Object exploration and reactions to spatial and nonspatial changes in hooded rats following damage to parietal cortex or hippocampal formation. *Behav Neurosci.* 106, 447-56.
- Schacter, D.L., and Wagner, A.D. (1999) Medial temporal lobe activations in fMRI and PET studies of episodic encoding and retrieval. *Hippocampus*, 9, 7-24

- Schmajuk, N.A. (1984) Psychological theories of hippocampal function. *Physiol Psychol*, 12, 166-183.
- Schmajuk, N.A., & Buhusi, C.V. (1997) Stimulus configuration, occasion setting, and the hippocampus. *Behav Neurosci.*, 111, 235-57.
- Scoville, W.B. & Milner, B. (1957) Loss of recent memory after bilateral hippocampal lesions. *J Neurol, Neurosurg Psychiatry*, 20, 11-21.
- Sharp, P.E. (1999) Comparison of the timing of hippocampal and subicular spatial signals: implications for path integration. *Hippocampus*, 9, 158-72.
- Sharp, P.E., Blair, H.T., & Cho, J. (2001) The anatomical and computational basis of the rat head-direction cell signal. *Trends Neurosci.* 24, 289-94.
- Sharp, P.E., Blair, H.T., Etkin, D., Tzanetos, D.B. (1995) Influences of vestibular and visual motion information on the spatial firing patterns of hippocampal place cells. *J Neurosci*, 15, 173-189.
- Sidman, M., Stoddard, L.T. & Mohr, J.P. (1968) Some additional quantitative observations of immediate memory in a patient with bilateral hippocampal lesions. *Neuropsychologia*, 6, 245-254.
- Smith, M.L. and Milner, B. (1981) The role of the right hippocampus in the recall of spatial location. *Neuropsychologia*, 19, 781-95.
- Smith, M.L. and Milner, B. (1989) Right hippocampal impairment in the recall of location: encoding deficit or rapid forgetting? *Neuropsychologia*, 27, 71-82.
- Spear, N.E. (1973) Retrieval of memory in animals. *Psychol Rev*, 80, 163-94.
- Spiers, H.J., Burgess, N., Maguire, E.A., Baxendale, S.A., Hartley, T., Thompson, P.J., O'Keefe, J. (2001) Unilateral temporal lobectomy patients show lateralized topographical and episodic memory deficits in a virtual town. *Brain*. 124, 2476-2489.
- Spiers, H.J., Maguire, E.A., & Burgess, N. (2001) Hippocampal amnesia. *Neurocase*, 7, 357-82.
- Squire, L.R. (1992) Memory and the hippocampus: a synthesis of findings with rats, monkeys, and humans. *Psychol Rev*, 99, 195-231.
- Squire, L.R., Zola, S.M. (1996) Structure and function of declarative and nondeclarative memory systems. *Proc Natl Acad Sci U S A*. 93, 13515-22.
- Squire, L.R., Ojemann, J.G., Miezin, F.M., Petersen, S. E, Videen, T.O., Raichle, M.E. (1992) Activation of the hippocampus in normal humans: A functional anatomical study of memory. *Proc. Natl. Acad. Sci USA*. 89, 1837-1841.
- Squire, L.R., Zola-Morgan, S. (1991) The medial temporal lobe memory system. *Science*, 253, 1380-6.
- Sutherland, R.J. and Rudy, J.W. (1989) Configural association theory: The role of the hippocampal formation in learning, memory and amnesia. *Psychobiology*, 17, 129-144.
- Suzuki, W.A., Zola-Morgan, S., Squire L.R., Amaral, D.G. (1993) Lesions of the perirhinal and parahippocampal cortices in the monkey produce long-lasting memory impairment in the visual and tactual modalities. *J Neurosci*. 13, 2430-51.
- Talland, G.A. (1965) *Deranged memory* Academic Press, New York.
- Taube, J.S. (1998) Head direction cells and the neurophysiological basis for a sense of direction. *Prog Neurobiol*. 55, :225-56.
- Teitelbaum, H. and Milner, P. (1963) Activity changes following partial hippocampal lesions in rats. *J Comp Physiol Psychol*, 56, 281-289.
- Tolman, E.C., (1932) *Purposive behavior in animals and men*. New York: Century
- Tolman, E.C. (1948) Cognitive maps in rats and men. *Psychol. Rev.*, 55, 189-208.
- Tulving, E. (1972) Episodic and semantic memory. In *Organization of memory* (ed. E. Tulving & W. Donaldson), pp. 381-403. New York: Academic Press.

- Tulving, E. (2001) Episodic memory and common sense: how far apart. *Phil. Trans. R. Soc. Lond.* 356, 1505-1515.
- Tulving, E., Habib, R., Nyberg, L., Lepage, M., McIntosh, A.R. (1999) Positron emission tomography correlations in and beyond medial temporal lobes. *Hippocampus*, 9, 71-82.
- Tulving, E. and Thompson, D.M. (1973) Encoding specificity and retrieval processes in episodic memory. *Psychol Rev*, 80, 352-73.
- Tulving, E. & Markowitsch, H.J. (1998) Episodic and declarative memory: a role of the hippocampus. *Hippocampus*, 8, 198-204.
- Vargha-Khadem, F., Gadian, D.G., Mishkin, M. (2001) Dissociations in cognitive memory: the syndrome of developmental amnesia. *Philos. Trans. R. Soc. Lond. B Biol Sci.*, 356, 1435-40.
- Wagner, A.R. (1981) SOP: A model of automatic memory processes in animal behavior. In NE Speers & RR Miller (Eds.) *Information processing in animals: Memory mechanisms*. Hillsdale, NJ: Erlbaum.
- Ward-Robinson, J., Coutureau, E., Good, M., Honey, R.C., Killcross, A.S., and Oswald, C.J.P. (2001) Excitotoxic Lesions of the Hippocampus Leave Sensory Preconditioning Intact: Implications for Models of Hippocampal Function. *Behav Neurosci*, 115, 1357-1362.
- Warrington, E.K., and Weiskrantz, L. (1970) Amnesic syndrome: consolidation or retrieval? *Nature*, 228, 628-630.
- Whener, R. and Srinivasan, M.V. (1981) Searching behavior of desert ants, genus *Cataglyphis* (Formicidae, Hymenoptera). *J Comp Physiol A*, 142, 315-338.
- Whishaw, I.Q. (1998) Place learning in hippocampal rats and the path integration hypothesis. *Neurosci Biobehav Rev*, 22, 209-20.
- Whishaw, I.Q., Cassel, J.C., Jarrad, L.E. (1995) Rats with fimbria-fornix lesions display a place response in a swimming pool: a dissociation between getting there and knowing where. *J Neurosci*, 15, 5779-88.
- Whishaw, I.Q., Hines, D.J., Wallace, D.G. (2001) Dead reckoning (path integration) requires the hippocampal formation: evidence from spontaneous exploration and spatial learning tasks in light (allothetic) and dark (idiothetic) tests. *Behav Brain Res* (127, 49-69)
- Whishaw, I.Q., and Maaswinkel, H. (1998) Rats with fimbria-fornix lesions are impaired in path integration: a role of the hippocampus in sense of direction. *J Neurosci*, 18, 3050-8.
- Whishaw, I.Q., and Gorny, B. (1999) Path integration absent in scent-tracking fimbria-fornix rats: Evidence for hippocampal involvement in sense of direction and sense of distance using self-movement cues. *J. Neurosci*, 19, 466-4673.
- Worsley, C.L., Recce, M., Spiers, H.J., Marley, J., Polkey, C.E., Morris, R.G. (2001) Path integration following temporal lobectomy in humans. *Neuropsychologia*, 39, 452-64.
- Young, S.L., Bohenek, D.L., & Fanselow, M.S. (1994) NMDA processes mediate anterograde amnesia of contextual fear conditioning induced by hippocampal damage: immunization against amnesia by context preexposure. *Behav Neurosci*, 108, 19-29.
- Zentall, T.R. (2001) The case for a cognitive approach to animal learning and behavior. *Behav Processes*, 54, 65-78.
- Zola-Morgan, S., Squire, L.R., Amaral, D.G., & Suzuki, W.A. (1989) Lesions of perirhinal and parahippocampal cortex that spare the amygdala and hippocampal formation produce severe memory impairment. *J Neurosci*, 12, 4355-70.
- Zola-Morgan, S., Squire, L.R., Clower, R.P., & Rempel, N.L. (1993) Damage to the perirhinal cortex exacerbates memory impairment following lesions to the hippocampal formation. *J Neurosci*, 13, 251-65.

- Zola-Morgan, S., Squire, L.R., & Mishkin, M. (1982) The neuroanatomy of amnesia: amygdala-hippocampus versus temporal stem. *Science*, 24;218, 1337-9.
- Zola, S.M., Squire, L.R., Teng, E., Stefanacci, L., Buffalo, E.A., & Clark, R.E. (2000). Impaired recognition memory in monkeys after damage limited to the hippocampal region. *J Neurosci*, 20, 451-63.