Jorge R. Brotons-Mas
Instituto de Neurociencias de Alicante
Universidad Miguel Hernández-Consejo Superior de Investigaciones Científicas, San Juan de Alicante, Spain
and
Institute of Neuroscience
Trinity College
Dublin, Ireland

Shane O'Mara
Institute of Neuroscience
Trinity College
Dublin, Ireland

Maria V. Sanchez-Vives*
Instituto de Neurociencias de Alicante
Universidad Miguel Hernández-Consejo Superior de Investigaciones Científicas, San Juan de Alicante, Spain

Neural Processing of Spatial Information: What We Know about Place Cells and What They Can Tell Us about Presence

Abstract

Brain processing of spatial information is a very prolific area of research in neuroscience. Since the discovery of place cells (PCs)(O'Keefe & Dostrovsky, "The hippocampus as a spatial map," *Brain Research 34,* 1971) researchers have tried to explain how these neurons integrate and process spatial and non-spatial information. Place cells are pyramidal neurons located in the hippocampus and parahippocampal region which fire with higher frequency when the animal is in a discrete area of space. Recently, PCs have been found in the human brain. The processing of spatial information and the creation of cognitive maps of the space is the result of the integration of multisensory external and internal information with the brain's own activity. In this article we review some of the most relevant properties of PCs and how this knowledge can be extended to the understanding of human processing of spatial information and to the generation of spatial presence.

1 Introduction

Spatial navigation is a fundamental form of interaction with the environment. Animals and humans must move about in their environments in search of food, shelter, or a mate, actions that are basic for the survival of the individual and the species. The brain in different species has evolved in an effort to make individuals capable of navigating their environments in an efficient manner. The understanding of the brain mechanisms underlying the generation of internal maps of the external world, the storage (or memory) of these maps, and the use of them in the form of navigation strategies is the field of study of a large number of researchers in the neuroscience community. On the other hand, the study of navigation in real and virtual environments (VE) has been a broad field of study, including a diverse range of topics from model city design (Lynch, 1960) to the generation of VEs that successfully result in spatial presence and that are optimal for the transfer of spatial information between virtual and real worlds (Darken & Banker, 1998; Darken, Allard, & Achille, 1998).

In this paper we review data (including our own) on the neural basis of spatial navigation, mostly centered on hippocampal and parahippocampal neurons

Presence, *Vol. 15, No. 5, October 2006,* 485–499

---

*Correspondence to mavi.sanchez@umh.es

called “place cells” that are specialized in responding to spatial position. The functional properties of these neurons embody many aspects of human navigation that are well known from a behavioral point of view. It is our purpose to demonstrate that the understanding of the neuronal basis of spatial processing is relevant to the understanding and successful generation of spatial presence. Furthermore, we suggest that the similar activation of brain structures during navigation in virtual *compared to* real worlds can be in itself an objective measurement of presence. In other words, if place cells activation occurs in the same way in a VE as it does in a physical environment then this is one level of evidence, a very important one, that presence is occurring within that VE.

In Section 2 we review general mechanisms and strategies of navigation and the underlying brain structures that control them. We go on to center our attention on the best known structure that codes for spatial information (Section 3), the hippocampus and parahippocampal region. Its anatomical structure is briefly described, as well as the properties of one of the most prominent electrophysiological signatures of this region, the *theta* rhythm. This rhythm is important because it synchronizes activity within the hippocampal formation and it affects the firing of place cells. The theta rhythm has been repeatedly implicated in integrative functions related to the navigation tasks (e.g., sensory-motor integration), and therefore it is worth mentioning. Once the general framework for investigating place cells has been described, we go on to explain their specific functional properties, with an emphasis on the factors that determine their spatial firing fields (location, visual or other sensory cues, behavioral relevance of the area, etc.) and the involvement of other areas of the brain in relevant aspects of navigation, such as place significance or reward. These functional properties that are studied at the cellular level are the most feasible candidates so far to support many of the well known features of navigation and their understanding results in the knowledge of the elements that could induce spatial presence. Based on that knowledge, in Section 4 we review relevant aspects of place cells and we suggest how this information could be useful to the understanding on how the brain processes spatial information in VR. To expand on how this could be relevant to presence research, we suggest some empirical experiments and predictions based on observations made in place cells.

2 Spatial Navigation in Animals and Humans

Species varying from migratory birds to humans need to utilize different information to generate knowledge of environments to navigate successfully. O’Keefe and Dostrovsky (1971) suggested that the hippocampus was the central brain structure implicated in spatial navigation and the neuronal substrate in which a cognitive map of the external environment is created. A cognitive map is an internal representation of an environment that allows subjects to choose the best way to get to an objective by making calculations based on the relations between different environmental landmarks. Other strategies could be used by humans and animals in an effort to navigate such as egocentric navigation (see below), and these route or taxon-based strategies are also dependent on non-hippocampal brain systems.

Birds with hippocampal lesions can navigate during migration using a compass strategy, following a fixed direction, but they get lost in their local area because they are not capable of generating a cognitive map of the area (Bingman & Yates, 1992). Classic studies of migratory birds shed light on the strategies of these expert navigators to make use of different types of available information to orient themselves throughout long distances in their migratory flights or in their short trips in search for food. Watson and Lashley (1915) showed that if naïve migratory birds in their first flight were captured and transported in a perpendicular direction to that which they were directed they would miss the final destiny by the amount of kilometers they were transported. These birds were flying towards a fixed goal using a compass strategy (Griffin, 1955). On the other hand if the same procedure was implemented in experienced birds, these would correct the distance they were transported, successfully reaching the final goal. Experienced birds use a more elaborate approach to navigation involving knowledge of the environment. Therefore, cognitive mapping would depend on experience and learning, ruling out the possibility of instinctive knowledge of migratory routes. While using a compass strategy, birds can use three different sources of information: the sun, geomagnetism, and the stars (Keeton, 1974). Experiments that have manipulated the internal (circadian) clock of birds have demonstrated that they use the sun to orient themselves with respect to their internal clock (Bingman & Jones, 1994). Animals also use geomagnetism to orient themselves and by applying magnets in the head of the animals they can be redirected towards a specific direction if the skies are overcast. More recently, some studies have demonstrated that pigeons, while flying to their nests, can also use highways and their exits as cues using compass adjustment during the middle part of the fly and a cognitive map when approaching the loft area (Lipp et al., 2004).

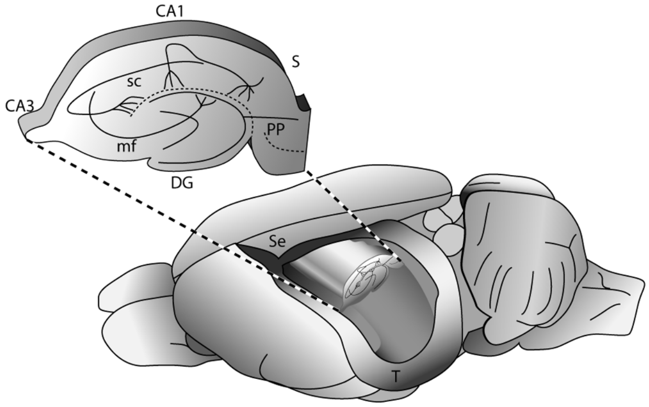

Figure 1. *Anatomy of the rat hippocampus. Towards the left is the frontal area of the brain and to the right, the cerebellum. CA1, CA3, S (subiculum), DG (dentate gyrus), mg (musgose fibers), sc (Schaffer collaterals), PP (perforant path), Se (septum), T (temporal lobe).*

No evidence has been found in the human brain of magnetic sensors contributing to spatial orientation. However, there are recent advances in the understanding of the cellular networks underlying human navigation by means of single neuron recordings in implanted patients (Ekstrom et al., 2003) and fMRI studies (Hartley, Maguire, Spiers, & Burgess, 2003) in virtual environments.

2.1 The Construction of the Cognitive Map

Whenever an animal or a person visits a new environment it is necessary to create a new internal representation of the new visited location. Since each spatial context is represented in a specific and individual way, each new location that is visited would generate the need for exploring and creating a new cognitive map (O'Keefe & Nadel, 1978). Two different informational processes seem to be involved in map generation. On one side *allocentric information* would enable humans and animals to generate an internal representational system based on the global coordinates of the environment and the relation between them. Thus, a topographical representation of the environment is generated by using multiple relevant landmarks of their surroundings and determining the different angular relations, distance, and so forth. This facilitates a precise navigation to specific goals even if those are not visible. For example it has been proved that rats are able to locate a hidden platform that allows them to escape from a pool (watermaze). To achieve this kind of successful navigation rats need to use multiple environmental cues available in the experimental room that allow them to generate a maplike representation of the environment enabling them to perform different calculations to find a nonvisible place (Morris, Garrud, Rawlins, & O'Keefe, 1982). Studies performed on experimental groups that were trained to navigate in the watermaze searching for the hidden platform while having different degrees of damage in the parahippocampal region (Schenk & Morris, 1985) revealed that rats with a strong degree of impairment were able to find the hidden platform, but not to carry out the visible platform version of the task. The results of these experiments would suggest that different structures of the parahippocampal complex and the hippocampus (Figure 1) are necessary for the allocentric navigation strategy (Morris, Schenk, Tweedie, & Jarrard, 1990). Similar evidence has been found in humans, whose hippocampus and parahipocampal region appeared activated in fMRI studies in which subjects navigated in a virtual environment (Aguirre, Detre, Alsop, & D'Esposito, 1996; Jordan, Schadow, Wuestenberg, Heinze, & Jancke, 2004). The activation of these structures followed a different pattern depending on the type of navigation, wayfinding or route following (Hartley et al., 2003).

The second process implies an *egocentric approach* and the use of other available information such as internal cues, motor and vestibular input, and directional information. All these sources of information allow the subject to calculate its present and its future position by integrating subsequent movements and turns, a process called *path integration* or *dead reckoning* in which the hippocampus and other areas such as the parietal cortex seem to be involved (Commins, Gemmell, Anderson, Gigg, & O'Mara, 1999; Whishaw, Hines, & Wallace, 2001; Save, Paz-Villagran, Alexinsky, & Poucet, 2005). This is also the case in humans while navigating in virtual environments using a route strategy (Wolbers, Weiller, & Buchel, 2004). For efficient map construction both types of information process must converge. The egocentrical representation must be coherent with the allocentric information. In this way motor input and directional information in relation to distal cues would be coordinated to generate the final cognitive map. These two strategies not only contribute to the generation of the cognitive map, they also are complementary approaches to solve navigational problems. Subjects can switch from one to the other depending on environmental conditions. For example animals can use an allocentric approach while navigating an illuminated maze and use an egocentric approach while navigating in the same apparatus in the dark (Whishaw et al., 2001). The complementarity of both processes in map generation can help us understand some of the transfer problems after training in virtual navigation.

3 Neuronal Substrates of Spatial Navigation

So far we have briefly described some of the neuronal basis of spatial navigation and the two basic strategies that are used during navigation. To better understand how the brain integrates spatial information it is necessary to briefly describe the anatomy of the hippocampus, its physiology, and the functionality of hippocampal place cells.

3.1 The Anatomy of the Hippocampus

A distinction between the hippocampus proper and the hippocampal region must be made. The hippocampus proper consists of two interlocked cell layers with the shape of a C consisting of the dentate gyrus and the cornus ammonis comprising areas CA1 and CA3, the two main subfields. The parahippocampal region comprises the entorhinal cortex, the periallocortical area of the perirhinal area, the subicular complex, presubiculum, parasubiculum, and subiculum (Witter, Groenewegen, Lopes da Silva, & Lohman, 1989) (Figure 1). The functional connections between these areas and their attributed functions are represented in Figure 2.

3.2 Electrophysiology of the Hippocampus

It has been suggested that the major electrophysiological activity involved in sensory and motor integration is hippocampal theta rhythm (for a review see Bland & Oddie, 2001). Theta activity is characterized by a regular sinusoidal activity between 4–8 Hz. Its modulation is directly related to sensory inputs reflecting changes in any sensory pathway and also changes in motor behavior (Whishaw & Vanderwolf, 1973; Kramis, Vanderwolf, & Bland, 1975; Bland et al., 2001). The fact that hippocampal PCs firing is related to the theta rhythm (O'Keefe and Recce, 1993) strengthens the idea that this sensory and motor integration process conveys at least some of the essential information required for spatial navigation. Theta rhythm has been detected in humans while navigating a virtual maze (Bischof & Boulanger, 2003), being related to the difficulty of the maze (Kahana, Sekuler, Caplan, Kirschen, & Madsen, 1999). This rhythm appears to be dissociated from other components of the task, being associated with navigation (de Araujo, Baffa, & Wakai, 2002). Nevertheless, some authors find an association of theta rhythm just with the motor act of exploring, but find no

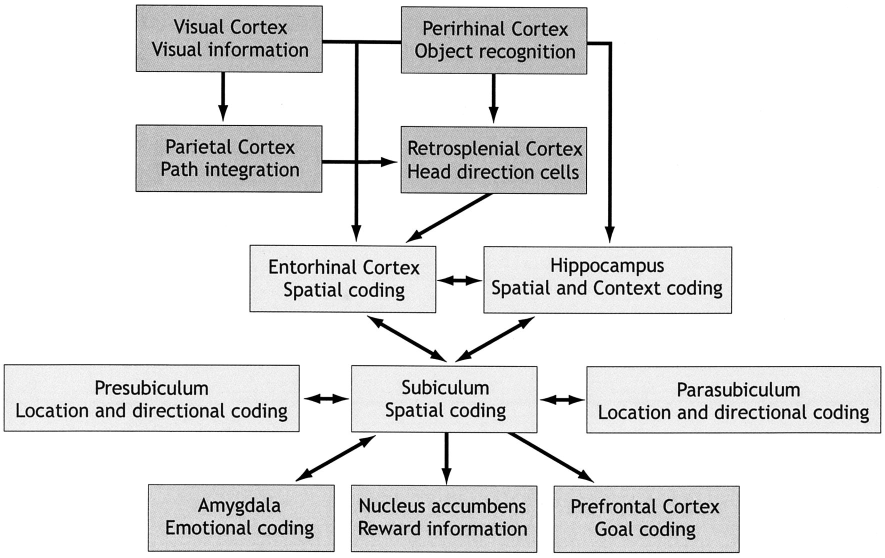

Figure 2. *Simplified anatomical afferent and efferent connections between the hippocampus and other brain areas relevant to spatial processing including some of their attributed functions.*

correlations between any theta characteristics and the cognitive demand of the tasks (Kelemen, Moron, & Fenton, 2005).

3.3 Place Cells

O'Keefe and Dostrovsky (1971) recorded single neurons in the hippocampus from chronically implanted rats foraging freely for food in a small arena. They described a group of cells whose firing increased whenever the animal was in a discrete location of the environment and this location was called the firing field (FF) of that particular neuron. The firing of these neurons seemed to be independent of other variables such as view, direction, or speed of movement; location or position was the best predictor of their firing (Poucet, Lenck-Santini, Paz-Villagran, & Save, 2003). Subsequent research has supported the original finding and PCs were seen as the first objective measurable neuronal basis of an advanced or higher-order cognitive process. The study of PCs has generated a broad body of investigation and research but initially they were only recorded in rodents, and proved difficult to detect in primates (O'Mara, Rolls, Berthoz, & Kesner, 1994; O'Mara, 1995) until recently (Ludvig, Tang, Gohil, & Botero, 2004). It was questionable if this same mechanism would be also present in the human brain. Lately, recordings from subcortical implanted electrodes in epileptic patients revealed that cells in the human hippocampus fire strongly in specific locations while the subject navigated a VE (Ekstrom et al., 2003), thus proving the existence of PCs in humans. Furthermore, it is evident that human hippocampal formation is strongly activated during virtual navigation and exploration using brain imaging (Hartley et al., 2003).

Standard methods for studying the spatial selectivity of hippocampal formation neurons require freely-moving rats to traverse mazes or open fields (sometimes foraging for food); neuronal activity is recorded and correlated with the rats' moment-to-moment position, from which color-coded contour maps are generated (representing normalized/averaged spike firing density at all points occupied by the rat; see Figure 3 discussed later in the paper. Different parameters have been studied to better understand how PCs code spatial information, among which we can highlight stability, directionality of PCs firing, sensory information, and cue control of PCs firing.

3.3.1 Place Cell Stability. Stability of place cells, or the opposite, plasticity of place cells, are relevant to the understanding of how space is represented when we enter a real or virtual space. How stable are the maps coded by PCs? PCs tend to fire in a stable manner if no spatial or other manipulation is implemented in the environment. Thompson and Best (1990) reported a neuron whose firing field was stable over 153 days of recording, using the same recording arena. Hill (1978) suggested that PCs FFs are generated as quickly as the animal explores the environment. Subsequent studies have demonstrated that PCs learn to code salient cues in the environment. Thus, hippocampal PCs can generate a progressive differential representation of two different arenas (Lever, Wills, Cacucci, Burgess, & O'Keefe, 2002). Although in this study firing patterns were similar in both arenas at the beginning this spatial representation, they diverged after repetitive exposure. This new representation was stable one month later for each of the environments. Therefore, although FFs can be stable for long periods of time they also reflect spatial and neuronal plasticity. Indeed, the blockade of NMDA receptors (involved in synaptic plasticity and memory) impaired PCs firing stability in new environments (Kentros et al., 1998). However, other authors (McNaughton, Barnes, Meltzer, & Sutherland, 1989; McNaughton et al., 1996) postulated that PCs firing depends not only on a learning process but it is relatively hardwired in the hippocampus during brain development, a view that is challenged by data showing the great plasticity of place cells under appropriate circumstances.

3.3.2 Directionality of Place Cells. Although it is clear that PCs fire in relation to the animals' location (McNaughton, Barnes, & O'Keefe, 1983) it was not clear if PCs also coded for the direction of the movement. It has been reported that the firing frequency of PCs was higher when the animal was running in an inward direction in a radial arm maze (Markus et al., 1995). Later research suggested that PCs directional firing was related to the physical characteristics of the maze and to the task's demands. Thus, directional firing of PCs was higher in the radial arm maze and also in an open field arena whenever the animal had to move in a linear track to retrieve a reward (Muller, Bostock, Taube, & Kubie, 1994). Taube et al. (Taube, Muller, & Ranck, 1990; Taube, 1995) described a type of cell whose firing coded for head direction firing only whenever the animal head it is oriented to a specific direction. These type of cells, head direction cells (HDC) are found in different structures of the parahippocampal complex as well as in other subcortical structures (Goodridge, Dudchenko, Worboys, Golob, & Taube, 1998). The firing of HDC conveys information about where the animal's head is pointing. They seem to use environmental cues to calibrate their directional firing and they depend on vestibular input, without which their firing disappears. A group of cells were found in the presubiculum with firing codes for location and direction (Cacucci, Lever, Wills, Burgess, & O'Keefe, 2004). This type of cell was also theta modulated; therefore it could be hypothesized that they could synthesize spatial information and direction information being the bridge between both systems.

Recently, neurons that represent the geometry of the space by integrating place, distance, and direction, have been discovered in the entorhinal cortex (Hafting, Fyhn, Molden, Moser, & Moser, 2005). These neurons, called grid cells, have firing fields that coincide with the vertex of a regular grid of equilateral triangles covering the surface of the environment and seem to be stable under different changes in the environment such as light-dark conditions.

3.3.3 Place Cells and Goal Navigation. It seems reasonable that a navigational system should be able to integrate the significance of a place in the cognitive map for spatial navigation. It is not enough to know where you are, you must know where you want to go (O'Mara, 1995). O'Keefe and Nadel (1978) suggested in their model that PCs do not code for goals or hedonics aspects of navigation. On the other hand some authors have suggested that place cells have to do with the meaning of a place (Breese, Hampson, & Deadwyler, 1989). Speakman and O'Keefe (1990) found that goal location changes did not affect the location of FFs in a radial arm maze, although prefrontal lesions do impair performance on this goal navigation task (Gemmell & O'Mara, 1999) which suggests that goal-related information might be located in the prefrontal cortex. On the other hand, when animals were trained to escape a watermaze using a hidden platform, a strong concentration of PCs near the escape platform was found, suggesting that areas of space of behavioral significance could be overrepresented by the hippocampus (Hollup, Molden, Donnett, Moser, & Moser, 2001).

Subiculum and nucleus accumbens cells firing predicted reward administration and also coded for spatial location (Martin & Ono, 2000). Similarly, PC firing changes due to task demands and those changes correlate with the efficiency of the performance (Kobayashi, Nishijo, Fukuda, Bures, & Ono, 1997). Gemmell and O'Mara (1999) have suggested that the prefrontal cortex might be the central structure involved in goal coding during navigation. Likewise, Hok, Save, Lenck-Santini and Poucet (2005) found cells in the rat prefrontal cortex that they suggested coded for a goal; and it has been proved that prefrontal cells are able to differentiate between high and low frequency rewarded arms in the radial arm maze (Pratt & Mizumori, 2001).

The amygdala is another structure involved in place preference learning (White & McDonald, 1993; Hollup et al., 2001). In humans, while hippocampal PCs code for location, neurons in the parahippocampal region as well as throughout the frontal and temporal lobes were found to respond to the subject's navigational goals and to conjunctions of place, goal, and view (Ekstrom et al., 2003). We could summarize that hippocampal place cells are susceptible to changes in navigational tasks by adapting to new demands in relation to reward location changes. Also, hippocampal place cells could overrepresent relevant areas of space. These changes could be due to integration of place significance in other areas of the brain such as the nucleus accumbens, amygdala, and prefrontal cortex, areas that are all strongly interconnected with the hippocampus.

3.3.4 What Does Affect the Firing of PCs?

Environmental cues help animals and humans to make navigational decisions, to locate themselves, and to calculate different trajectories to reach relevant goals (O'Mara, 1995). How does multisensory information affect position coding? Muller and Kubie (1987) introduced different manipulations of the recording arena to study the different effects on PCs. The recordings were carried out in a cylindrical arena with a cue card attached at the wall acting as a distal cue. Rotation of this visual cue produced a rotation of the FFs keeping the same angular relation as in the original configuration and removal of this cue card only produced FF rotation to unpredictable positions. However, manipulations of the cue card size did not affect FFs. Placing a small barrier over the location of previously recorded FFs was enough to make the FFs disappear. Doubling the size of the area and wall height produced the result that some cells expanded their FFs in relation to the new size (Sharp, 1999a) although most cells generated new FFs, producing what has been called remapping. In the same way if the arena shape was changed from a cylinder to a square, the cells also remapped.

The removal of existing cues has different effects depending on the proximity of the cues (Hetherington & Shapiro, 1997). It was found that removal of a cue proximal to the FF reduced the size of the FF, while removal of a distal cue would produce an enlargement of FF size. In Jeffery and O'Keefe (1999) a visual cue was manipulated either when the animal was present or before it was placed in the recording arena. PCs did not rotate their FF if the cue was moved in their presence but if the cue was rotated while away, then the FF would also be rotated. Rats learned to rely on egocentric information when the visual cue was not reliable demonstrating flexibility in the strategy used by the animal if environmental changes were implemented. Cressant, Muller, and Poucet (1997) placed objects centrally in the arena. They found that this configuration did not exert any control on the FF. On the contrary, if these objects were placed against the walls of the arena then they were capable of exerting control on the FF. In another experiment, proximal and distal cues were rotated in different directions inducing a rotation in the FFs that in some neurons was determined by the distal cues and in others by the proximal cues (Shapiro, Tanila, & Eichenbaum, 1997). Recordings in animals deprived of visual and auditory information revealed that the PCs of these animals were stable despite of the lack of sensory input (Quirk, Muller, & Kubie, 1990; Save, Cressant, Thinus-Blanc, & Poucet, 1998; Paz-Villagran, Lenck-Santini, Save, & Poucet, 2002). It is then clear that a mechanism other than allocentric information is being used by the animals. PCs would be using some sort of path integration or egocentric information to keep their firing stable (McNaughton et al., 1996).

PCs can strongly respond to features of the environment anchoring their firing around specific objects such as barriers. In this way cells called barrier cells, would generate their FF by the barrier during the first recording session and the FF would move with the barrier if this one was relocated during a second recording session exerting similar control if the animal was placed in a second new environment in which a barrier was present (Poucet et al., 2004).

Previous research found that the geometry of the arena exerts a quite strong control on PC firing (O'Keefe & Burgess, 1996; Anderson & Jeffery, 2003). Sharp hypothesized that hippocampal place cells would not only code spatial information but also contextual spatial information (Sharp, 1999b). Anderson and Jeffery proposed that place cells would be modulated by geometric and nongeometric changes in the environment. This would explain that subtle changes in context might generate extreme changes in the established firing field of a place cell and why sometimes geometric changes would not strongly affect FFs. They found a high heterogeneity in the remapping of place cells after specific contextual but not geometrical manipulation were implemented, leading to the conclusion that contextual information does not affect place cells in a whole block but in a fragmented way. Similarly, the fact that hippocampal PCs display different maps in different environments could be seen as evidence that the hippocampus is coding spatial and nonspatial aspects of the environmental context. On the contrary, subicular and entorhinal cortical PCs tend to represent different environments in similar ways (Sharp, 1999b). In our laboratory we recorded place cells in a square arena of 50 cm × 50 cm, with a 60 cm height wall. The animals were first trained to forage for food in the light and in the dark. We found that PCs in the hippocampus indeed show a larger heterogeneity regarding their stability under different light conditions in comparison with subicular place cells, whose FFs were more stable under different light conditions (Figure 3). Neurons that remap under different light conditions would be the ones that integrate visual information into their spatial coding.

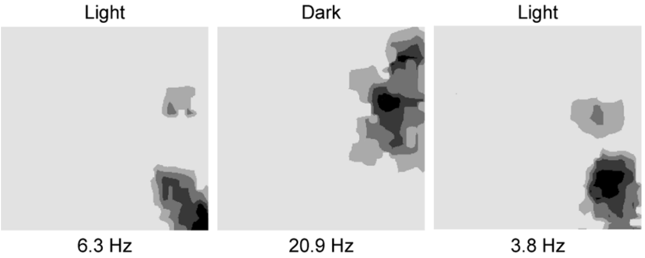

Figure 3. *Influence of visual information on spatial coding in place cells. Recordings were carried out under light-dark-light conditions for a minimum of 8 minutes each. In order to calculate a neuronal spatial firing field, the total number of spikes is divided by the dwelling time in each pixel. Then a matrix of 64 × 64 bins is constructed and firing frequencies of neuronal discharges are represented by different gray levels on steps of 20%. The black area represents the peak of neuronal firing and its value is given in the figure. The firing field of the cell is located in the upper center area of the arena, whose size was 0.5 × 0.5 m. Place cell recorded in CA1 (hippocampus). It shows how firing is affected by the presence of visual input: the firing field appears in the lower right area of the arena during the two illuminated conditions whereas it is displaced during the dark condition.*

It is clear that multiple factors are being encoded by the hippocampus and the parahippocampal region. Visual information influences PCs firing, but visual information is not enough to disrupt PCs firing fields, under all circumstances looked at experimentally. The fact that some PCs can keep their FFs in the darkness or after being blind is strong evidence that the animals are using other information to keep their representation. Also, 3D objects can produce an effect on PC firing if located distal from the center of the arena. PCs adapt in different ways when the size of the arena is manipulated but this adaptation seems to be different in different brain areas. It has been well described that the hippocampus would code more than spatial information while other areas of the region would be less sensitive to these aspects. Therefore it is of great interest to investigate how different areas of the parahippocampal region and the hippocampus code different aspects of the "where" experience as well as other elements of the context. Recent research has found that rats can learn to navigate in a VR environment (Holscher, Schnee, Dahmen, Setia, & Mallot, 2005) and this opens a new door to use VR as a valuable tool in the quest for the understanding of spatial processing.

4 Place Cells and Presence Research

Presence research and research on spatial processing are strongly interrelated. On the one hand, an understanding of the factors that most influence our sense of location in space and that induce the creation of internal cognitive maps of the space can be exploited to induce presence. On the other hand, the use of virtual environments is one of the fundamental tools to comprehend spatial processing.

We have reviewed in this paper the neuroscience literature devoted to spatial coding, concentrating mostly on hippocampal and parahippocampal place cells which comprise the best defined neuronal populations that participate in an internal representation of space.

What can we learn from how spatial information is processed in the brain that can be useful in the field of presence research? We follow the operational definition of presence that it is the successful substitution of real by virtual sensory data, where success is indicated by participants acting and responding to virtual sensory data in a VE as if it were real world sensory data, and where response is multi-level, from low level physiological responses all the way up to behavioral and cognitive (Sanchez-Vives & Slater, 2005). From this point of view, and since PCs code for particular locations in the space, we propose that if the firing of PCs during virtual navigation would correspond to the firing of these PCs in the equivalent real space, this would provide one component of a measure of presence based on brain activity. It has been shown that indeed PCs in humans respond to particular locations within VEs (Ekstrom et al., 2003). However, a systematic use of this tool to measure presence is so far unattainable since it is only rarely, in presurgical brain patients with deep implanted electrodes, that this type of single unit recordings can be obtained in humans. Otherwise, it would be appealing to test whether presence correlates with the appropriate firing of place cells in VEs under a variety of experimental conditions (differences in visual realism, frame rate, etc.), or to measure to what extent the pattern of PC activation was transferable from a real to a virtual representation of the same space and vice versa. Although the difficulties in carrying out these experiments are obvious, in theory they could provide a tool to better understand brain processing of spatial information both in real and VE. This theoretical consideration will still be valid if we consider that other methods of measuring brain activity such as brain imaging (fMRI) have already been used to detect the activation of neural structures during virtual navigation (Hartley et al., 2003). The limitations in this case are determined by the spatial resolution of the techniques (no single PCs can be detected). Another limitation is that the subject must navigate while remaining motionless, since fMRI cannot be performed on mobile subjects as of this writing. Therefore, it does not provide the means to compare human brain activity under real and virtual navigation. However, with the rapid transformation that brain recording techniques have experienced in recent decades, it is reasonable to think that all these limitations will only lessen over time.

So far, as we have presented in this review, most of the studies on the neural mechanisms underlying spatial navigation in real environments have been performed in animal models. Recently, the first really effective VE for rats has been described (Holscher et al., 2005). In this study a group of rats were trained to navigate to specific locations in order to obtain a series of rewards. A second experimental group was trained in the equivalent real environment, without significant differences in the learning process between them (Holscher et al., 2005). We could take this result as evidence of spatial presence in the VE. The obvious next step that has not been yet taken is to record from PCs in these animals in the equivalent real and VE and to try to correlate the stability of the PC firing fields with the successful transfer of information between both experimental conditions. According to our hypothesis and to the operational definition of presence, similar firing of PCs in both environments would underlie a similar processing of the spatial information and would reveal presence in the VE. The fact that hippocampal cells are very sensitive to spatial contextual changes could be used to measure how different a VE is perceived in relation to its corresponding real environment. It also provides the means to experiment on the impact that different streams of sensory information have on the brain processing of space, exploiting the possibility of disrupting sensory modalities in VEs that always appear together in real environments. Thus, in VEs, visual, vestibular, somatosensory, and auditory or propioceptive information could be dissociated, providing an excellent tool for the evaluation of their individual role on spatial processing.

Although some authors have described VEs as useful for acquiring spatial knowledge (Bliss, Tidwell, & Guest, 1997), these findings are not exempt from controversy (Darken & Banker, 1998); differences in the fidelity of the environments or the training methods can yield different behavioral results. We know that when cells learn to fire in order to code for a new space, this pattern of firing can be maintained for at least a month (Lever et al., 2002). Therefore, we should expect that if we learn to navigate in a virtual reconstruction of a city (i.e., virtual Madrid), once in Madrid we should be able to use this spatial information and navigate with the same level of proficiency as in virtual Madrid. This would imply that the cognitive map created in the virtual environment was accurate and stable and that it remained functional in the real world. This hypothesis could also be tested inversely, by evaluating the proficiency of subjects in navigating the VR version of their own towns or new cities learned in the real world. If transfer of learning to VR under these circumstances is better that for the opposite case, it would suggest that something is missing in the VE that is available in real world navigation and that is some critical element for the generation of internal spatial maps. Our suggestion is that the egocentric information is missing, since navigation in VEs is most often done from a static position. The mechanism of action of egocentric cues would implicate the theta oscillations in the hippocampus (see above). Synchronous activity of neurons in the theta range (4–8 Hz) has been related to sensory-motor integration. When comparing restrained versus free rats navigating a virtual environment it was found that restrained rats had both less specificity of place cells firing as well as less theta frequency in the EEG (Foster, Castro, & McNaughton, 1989). Recently, in a very elegant experiment Terrazas et al. (2005) studied the firing of place cells in a circular maze under three different conditions. In the CAR condition the animal was placed on a toy train that travelled between different points in the circular track. In the WALK condition, the animal had to walk freely in the same circular track; and in the WORLD condition the animal was placed in the same train, which remained still while the whole environment would be rotated, therefore dissociating motor, visual, and vestibular information. It was found that the theta rhythm was reduced in the two conditions where motor input was limited, the WORLD and CAR conditions. On the other hand, in the WALK condition, the firing of place cells was strongly modulated by theta, which power was correlated with speed of movement. Firing fields were enlarged during the no-movement condition and there was a loss of spatial specificity and information per spike. Therefore, self-motion cues are critical to regulate the spatial scale on which place cells work (Terrazas et al., 2005) and they are as well one of the most relevant determinants of theta generation. Self-motion, direction, and speed, would also be the internal source of information that would drive the firing of some recently discovered grid cells, modulated by theta activity (Hafting et al., 2005; Jeffery & Burgess, 2006). The firing of these neurons is distributed in space generating a grid in which their firing fields would act as nodes and where distance between nodes would be constant independent of the size of the arena. Therefore they seem to play an important role in the metrics of the brain, for which self-motion seems to play a key role. Taking all that into consideration, it appears that the lack of egocentric information, and thus a deficient theta rhythm while navigating without movement in a VE, could result in flawed maps due to the fact that one of the most basic neurophysiological mechanisms involved in producing spatial learning would be compromised. The lack of self-movement and theta rhythm would affect the correct generation of a map in different ways. If the spatial metrics over which cells generate their firing is altered, the generation of correct relationships between different landmarks could meddle with a correct estimation of distance which could be affected by a poor representation of spatial metrics in the brain. The calculation of distance between the subject and the environmental cues would be affected by the lack of self-movement, and therefore learning a map in a VE with restricted self-motion cues would compromise the whole map generation. Presence studies with humans in VR are in agreement with the importance of physical movement in the environment. A comparison of subjective and reported behavioral presence between subjects that navigated in a VR by a) using a mouse, b) walking in place, and c) really walking, revealed that both walking in place and really walking resulted in higher presence than using a mouse (Usoh et al., 1999). Both studies suggest that navigating by using a mouse or joystick, and therefore with a very limited motor activity, may share some aspects with the navigation of a restrained rat. In this sense, the lack of motor activity and of propioceptive information results in a weaker theta activity in the hippocampus and in a lack of specificity of the firing of place cells. In this regard, our hypothesis is that the realization of motor activity (walking in place or treadmill walking, static bike riding) during navigation in VR would generate a more stable cognitive map of space than navigation by means of a mouse or joystick. As a result, the success of transfer of spatial information from a virtual to a real environment would be more successful, having important consequences on tasks involving training. The success of this transfer could reflect the activation of the same network of PCs both in the virtual and the real environments and the contribution of the spatial metrics supplied by hippocampal theta during the learning period in a similar way to naturalistic learning conditions. We also suggest that the success of spatial information transfer could be taken as a surrogate for the stability of the map coded in the PCs and, furthermore, as a measure of spatial presence during virtual navigation. To what extent the generation of theta activity in the EEG during spatial navigation correlates with spatial presence and ultimately successful transfer of spatial information is a matter that requires further investigation. This correlation should also be explored if the lack of egocentric cues in virtual navigation could be compensated for, at least in part, by VEs enriched in visual, auditory, or haptic cues used for allocentric strategies.

At the same time that spatial mapping in place cells can be very stable, PCs are plastic and one observation that reveals this plasticity is the fact that areas of the space that are relevant from a behavioral point of view, have been reported to have larger representation in the hippocampal map (Martin et al., 2000). This means that if a particular area of the space goes on to increase its relevance for the subject, the number of neurons that code for that particular area of space increases. Based on this observation it seems reasonable to predict that those VEs with higher behavioral significance for the subject are going to induce higher spatial presence. Or, to put it another way, a relatively crude VE could induce high spatial presence if what is represented is behaviorally relevant for the subject.

5 Conclusions

Place cells in the hippocampus and parahippocampal formation create an internal cognitive map of the external space that integrates information about location derived from multisensory inputs and internal information (propioceptive, vestibular, etc.). Chronic recordings of PCs in animal experiments and eventually in humans have yielded valuable information about the functional properties of these neurons that we have reviewed. We believe that this information is relevant for presence research since these neurons constitute the roots of spatial presence, without underestimating the involvement of other areas of the brain (parietal, frontal cortex) in the process.

In this paper we suggest that if place cell activation operates in the same way in a VE as it does in the equivalent physical environment, then this is one level of evidence that presence is occurring within that VE. We propose that this similar activation of PCs in virtual and real spaces should have a behavioral correlation in a successful transfer of spatial information across both environments.

Acknowledgments

This work has been sponsored by PRESENCIA (European Union FET IST-2001-37927) and MEC (BFI2002-03643) to MVSV.

References

Aguirre, G. K., Detre, J. A., Alsop, D. C., & D'Esposito, M. (1996). The parahippocampus subserves topographical learning in man. *Cerebral Cortex, 6,* 823–829.

Anderson, M. I., & Jeffery, K. J. (2003). Heterogeneous modulation of place cell firing by changes in context. *Journal of Neuroscience, 23,* 8827–8835.

Bingman, V. P., & Jones, T. J. (1994). Sun compass-based spatial learning impaired in homing pigeons with hippocampal lesions. *Journal of Neuroscience, 14,* 6687–6694.

Bingman, V. P., & Yates, G. (1992). Hippocampal lesions impair navigational learning in experienced homing pigeons. *Behavioral Neuroscience, 106,* 229–232.

Bischof, W. F., & Boulanger, P. (2003). Spatial navigation in virtual reality environments: An EEG analysis. *CyberPsychology & Behavior, 6,* 487–495.

Bland, B. H., & Oddie, S. D. (2001). Theta band oscillation and synchrony in the hippocampal formation and associated structures: The case for its role in sensorimotor integration. *Behavioral Brain Research, 127,* 119–136.

Bliss, J., Tidwell, P., & Guest, M. (1997). The effectiveness of virtual reality for administering spatial navigation training to firefighters. *Presence: Teleoperators and Virtual Environments, 6,* 73–86.

Breese, C. R., Hampson, R. E., & Deadwyler, S. A. (1989). Hippocampal place cells: Stereotypy and plasticity. *Journal of Neuroscience, 9,* 1097–1111.

Cacucci, F., Lever, C., Wills, T. J., Burgess, N., & O'Keefe, J. (2004). Theta-modulated place-by-direction cells in the hippocampal formation in the rat. *Journal of Neuroscience, 24,* 8265–8277.

Commins, S., Gemmell, C., Anderson, M., Gigg, J., & O'Mara, S. M. (1999). Disorientation combined with bilateral parietal cortex lesions causes path integration deficits in the water maze. *Behavioral Brain Research, 104,* 197–200.

Cressant, A., Muller, R. U., & Poucet, B. (1997). Failure of centrally placed objects to control the firing fields of hippocampal place cells. *Journal of Neuroscience, 17,* 2531–2542.

Darken, R., & Banker, W. (1998). Navigating in natural environments: A virtual environment training transfer study. *Proceedings of the IEEE Virtual Reality Annual International Symposium,* 12–19.

Darken, R. P., Allard, T., & Achille, L. B. (1998). Spatial orientation and wayfinding in large-scale virtual spaces: An introduction. *Presence: Teleoperators and Virtual Environments, 7,* 101–107.

de Araujo, D. B., Baffa, O., Wakai, R. T. (2002). Theta oscillations and human navigation: A magnetoencephalography study. *Journal of Cognitive Neuroscience, 14,* 70–78.

Ekstrom, A. D., Kahana, M. J., Caplan, J. B., Fields, T. A., Isham, E. A., Newman, E. L., et al. (2003). Cellular networks underlying human spatial navigation. *Nature, 425,* 184–188.

Foster, T. C., Castro, C. A., & McNaughton, B. L. (1989). Spatial selectivity of rat hippocampal neurons: Dependence on preparedness for movement. *Science, 244,* 1580–1582.

Gemmell, C., & O'Mara, S. M. (1999). Medial prefrontal cortex lesions cause deficits in a variable-goal location task but not in object exploration. *Behavioral Neuroscience, 113,* 465–474.

Goodridge, J. P., Dudchenko, P. A., Worboys, K. A., Golob, E. J., & Taube, J. S. (1998). Cue control and head direction cells. *Behavioral Neuroscience, 112,* 749–761.

Griffin, D. (1955). Bird navigation. In A. Wolfson (Ed.), *Recent studies in avian biology* (pp. 154–197). Urbana: University of Illinois Press.

Hafting, T., Fyhn, M., Molden, S., Moser, M. B., & Moser, E. I. (2005). Microstructure of a spatial map in the entorhinal cortex. *Nature, 436,* 801–806.

Hartley, T., Maguire, E. A., Spiers, H. J., & Burgess, N. (2003). The well-worn route and the path less traveled: Distinct neural bases of route following and wayfinding in humans. *Neuron, 37,* 877–888.

Hetherington, P. A., & Shapiro, M. L. (1997). Hippocampal place fields are altered by the removal of single visual cues in a distance-dependent manner. *Behavioral Neuroscience, 111,* 20–34.

Hill, A. J. (1978). First occurrence of hippocampal spatial firing in a new environment. *Experimental Neurology, 62,* 282–297.

Hok, V., Save, E., Lenck-Santini, P. P., & Poucet, B. (2005). Coding for spatial goals in the prelimbic/infralimbic area of the rat frontal cortex. *Proceedings of the National Academy of Sciences USA, 102,* 4602–4607.

Hollup, S. A., Molden, S., Donnett, J. G., Moser, M. B., & Moser, E. I. (2001). Accumulation of hippocampal place fields at the goal location in an annular watermaze task. *Journal of Neuroscience, 21,* 1635–1644.

Holscher, C., Schnee, A., Dahmen, H., Setia, L., & Mallot, H. A. (2005). Rats are able to navigate in virtual environments. *Journal of Experimental Biology, 208,* 561–569.

Jeffery, K. J., & Burgess, N. (2006). A metric for the cognitive map: Found at last? *Trends in Cognitive Science, 10,* 1–3.

Jeffery, K. J., & O'Keefe, J. M. (1999). Learned interaction of visual and idiothetic cues in the control of place field orientation. *Experimental Brain Research, 127,* 151–161.

Jordan, K., Schadow, J., Wuestenberg, T., Heinze, H. J., & Jancke, L. (2004). Different cortical activations for subjects using allocentric or egocentric strategies in a virtual navigation task. *Neuroreport, 15,* 135–140.

Kahana, M. J., Sekuler, R., Caplan, J. B., Kirschen, M., & Madsen, J. R. (1999). Human theta oscillations exhibit task dependence during virtual maze navigation. *Nature, 399,* 781–784.

Keeton, W. T. (1974). The mystery of pigeon homing. *Scientific American, 231,* 96–97.

Kelemen, E., Moron, I., Fenton, A. A. (2005). Is the hippocampal theta rhythm related to cognition in a non-locomotor place recognition task? *Hippocampus, 15,* 472–479.

Kentros, C., Hargreaves, E., Hawkins, R. D., Kandel, E. R., Shapiro, M., & Muller, R. V. (1998). Abolition of long-term stability of new hippocampal place cell maps by NMDA receptor blockade. *Science, 280,* 2121–2126.

Kobayashi, T., Nishijo, H., Fukuda, M., Bures, J., & Ono, T. (1997). Task-dependent representations in rat hippocampal place neurons. *Journal of Neurophysiology, 78,* 597–613.

Kramis, R., Vanderwolf, C. H., & Bland, B. H. (1975). Two types of hippocampal rhythmical slow activity in both the rabbit and the rat: Relations to behavior and effects of atropine, diethyl ether, urethane, and pentobarbital. *Experimental Neurology, 49,* 58–85.

Lever, C., Wills, T., Cacucci, F., Burgess, N., & O'Keefe, J. (2002). Long-term plasticity in hippocampal place-cell representation of environmental geometry. *Nature, 416,* 90–94.

Lipp, H. P., Vyssotski, A. L., Wolfer, D. P., Renaudineau, S., Savini, M., Tröster, G., et al. (2004). Pigeon homing along highways and exits. *Currents in Biology, 14,* 1239–1249.

Ludvig, N., Tang, H. M., Gohil, B. C., Botero, J. M. (2004). Detecting location-specific neuronal firing rate increases in the hippocampus of freely-moving monkeys. *Brain Research, 1014,* 97–109.

Lynch, K. (1960). *The image of the city.* Cambridge, MA: MIT Press.

Markus, E. J., Qin, Y. L., Leonard, B., Skaggs, W. E., McNaughton, B. L., & Barnes, C. A. (1995). Interactions between location and task affect the spatial and directional firing of hippocampal neurons. *Journal of Neuroscience, 15,* 7079–7094.

Martin, P. D., & Ono, T. (2000). Effects of reward anticipation, reward presentation, and spatial parameters on the firing of single neurons recorded in the subiculum and nucleus accumbens of freely moving rats. *Behavioral Brain Research, 116,* 23–38.

McNaughton, B. L., Barnes, C. A., Gerrard, J. L., Gothard, K., Jung, M. W., Knierim, J. J., et al. (1996). Deciphering the hippocampal polyglot: The hippocampus as a path integration system. *Journal of Experimental Biology, 199,* 173–185.

McNaughton, B. L., Barnes, C. A., Meltzer, J., & Sutherland, R. J. (1989). Hippocampal granule cells are necessary for normal spatial learning but not for spatially-selective pyramidal cell discharge. *Experimental Brain Research, 76,* 485–496.

McNaughton, B. L., Barnes, C. A., & O'Keefe, J. (1983). The contributions of position, direction, and velocity to single unit activity in the hippocampus of freely-moving rats. *Experimental Brain Research, 52,* 41–49.

Morris, R. G., Garrud, P., Rawlins, J. N., & O'Keefe, J. (1982). Place navigation impaired in rats with hippocampal lesions. *Nature, 297,* 681–683.

Morris, R. G., Schenk, F., Tweedie, F., & Jarrard, L. E. (1990). Ibotenate lesions of hippocampus and/or subiculum: Dissociating components of allocentric spatial learning. *European Journal of Neuroscience, 2,* 1016–1028.

Muller, R. U., Bostock, E., Taube, J. S., & Kubie, J. L. (1994). On the directional firing properties of hippocampal place cells. *Journal of Neuroscience, 14,* 7235–7251.

Muller, R. U., & Kubie, J. L. (1987). The effects of changes in the environment on the spatial firing of hippocampal complex-spike cells. *Journal of Neuroscience, 7,* 1951–1968.

O'Keefe, J., & Burgess, N. (1996). Geometric determinants of the place fields of hippocampal neurons. *Nature, 381,* 425–428.

O'Keefe, J., & Dostrovsky, J. (1971). The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Research, 34,* 171–175.

O'Keefe, J., & Nadel, L. (1978). *The hippocampus as a cognitive map*. Oxford, UK: Clarendon Press.

O'Keefe, J., & Recce, M. L. (1993). Phase relationship between hippocampal place units and the EEG theta rhythm. *Hippocampus, 3,* 317–330.

O'Mara, S. M. (1995). Spatially selective firing properties of hippocampal formation neurons in rodents and primates. *Progress in Neurobiology, 45,* 253–274.

O'Mara, S. M., Rolls, E. T., Berthoz, A., & Kesner, R. P. (1994). Neurons responding to whole-body motion in the primate hippocampus. *Journal of Neuroscience, 14,* 6511–6523.

Paz-Villagran, V., Lenck-Santini, P. P., Save, E., & Poucet, B. (2002). Properties of place cell firing after damage to the visual cortex. *European Journal of Neuroscience, 16,* 771–776.

Poucet, B., Lenck-Santini, P. P., Hok, V., Save, E., Banquet, J. P., Gaussier, P., et al. (2004). Spatial navigation and hippocampal place cell firing: The problem of goal encoding. *Review of Neuroscience, 15,* 89–107.

Poucet, B., Lenck-Santini, P. P., Paz-Villagran, V., & Save, E. (2003). Place cells, neocortex and spatial navigation: A short review. *Journal of Physiology (Paris), 97,* 537–546.

Pratt, W. E., & Mizumori, S. J. (2001). Neurons in rat medial prefrontal cortex show anticipatory rate changes to predictable differential rewards in a spatial memory task. *Behavioral Brain Research, 123,* 165–183.

Quirk, G. J., Muller, R. U., & Kubie, J. L. (1990). The firing of hippocampal place cells in the dark depends on the rat's recent experience. *Journal of Neuroscience, 10,* 2008–2017.

Sanchez-Vives, M. V., & Slater, M. (2005). From presence to consciousness through virtual reality. *Nature Reviews Neuroscience, 6,* 332–339.

Save, E., Cressant, A., Thinus-Blanc, C., & Poucet, B. (1998). Spatial firing of hippocampal place cells in blind rats. *Journal of Neuroscience, 18,* 1818–1826.

Save, E., Paz-Villagran, V., Alexinsky, T., & Poucet, B. (2005). Functional interaction between the associative parietal cortex and hippocampal place cell firing in the rat. *European Journal of Neuroscience, 21,* 522–530.

Schenk, F., & Morris, R. G. (1985). Dissociation between components of spatial memory in rats after recovery from the effects of retrohippocampal lesions. *Experimental Brain Research, 58,* 11–28.

Shapiro, M. L., Tanila, H., & Eichenbaum, H. (1997). Cues that hippocampal place cells encode: Dynamic and hierarchical representation of local and distal stimuli. *Hippocampus, 7,* 624–642.

Sharp, P. E. (1999a). Subicular place cells expand or contract their spatial firing pattern to fit the size of the environment in an open field but not in the presence of barriers: Comparison with hippocampal place cells. *Behavioral Neuroscience, 113,* 643–662.

Sharp, P. E. (1999b). Complementary roles for hippocampal versus subicular/entorhinal place cells in coding place, context, and events. *Hippocampus, 9,* 432–443.

Speakman, A., & O'Keefe, J. (1990). Hippocampal complex spike cells do not change their place fields if the goal is moved within a cue controlled environment. *European Journal of Neuroscience, 2,* 544–555.

Taube, J. S. (1995). Head direction cells recorded in the anterior thalamic nuclei of freely moving rats. *Journal of Neuroscience, 15,* 70–86.

Taube, J. S., Muller, R. U., & Ranck, J. B., Jr. (1990). Head-direction cells recorded from the postsubiculum in freely moving rats. II. Effects of environmental manipulations. *Journal of Neuroscience, 10,* 436–447.

Terrazas, A., Krause, M., Lipa, P., Gothard, K. M., Barnes, C. A., & McNaughton, B. L. (2005). Self-motion and the hippocampal spatial metric. *Journal of Neuroscience, 25,* 8085–8096.

Thompson, L. T., & Best, P. J. (1990). Long-term stability of the place-field activity of single units recorded from the dorsal hippocampus of freely behaving rats. *Brain Research, 509,* 299–308.

Usoh, M., Arthur, K., Whitton, M. C., Bastos, R., Steed, A., & Slater, M., et al. (1999). Walking > walking-in-place > flying, in virtual environments. *Proceedings of the 26th Annual Conference on Computer Graphics and Interactive Techniques,* 359–364.

Watson J., & Lashley K. (1915). Homing and related activities of birds. *Carnegie Institute Publication, 211,* 1–104.

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. *Behavioral Brain Research, 127,* 49–69.

Whishaw, I. Q., & Vanderwolf, C. H. (1973). Hippocampal EEG and behavior: Changes in amplitude and frequency of RSA (theta rhythm) associated with spontaneous and learned movement patterns in rats and cats. *Behavioral Biology, 8,* 461–484.

White, N. M., & McDonald, R. J. (1993). Acquisition of a spatial conditioned place preference is impaired by amygdala lesions and improved by fornix lesions. *Behavioral Brain Research, 55,* 269–281.

Witter, M. P., Groenewegen, H. J., Lopes da Silva, F. H., & Lohman, A. H. (1989). Functional organization of the extrinsic and intrinsic circuitry of the parahippocampal region. *Progress in Neurobiology, 33,* 161–253.

Wolbers, T., Weiller, C., & Buchel, C. (2004). Neural foundations of emerging route knowledge in complex spatial environments. *Brain Research: Cognitive Brain Research, 21,* 401–411.