Commentary

How to Avoid Going Bump in the Night: Object and Place Representations in the Hippocampus

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The cognitive map theory has been a dominant influence over research into hippocampal function since the publication of O'Keefe and Nadel's *The Hippocampus as a Cognitive Map* in 1978 (now freely available at http://www.cognitivemap.net). The main premise of the theory is articulated in the book's first paragraph: "We shall argue that the hippocampus is the core of a neural memory system, providing an objective spatial framework within which the items and events of an organism's experience are located and interrelated" (O'Keefe and Nadel, 1978). The existence of "place cells" in the hippocampus—principal cells that fire selectively when the animal occupies restricted locations in an environment—is one of the primary pieces of evidence in support of the theory (O'Keefe and Nadel, 1978; Ekstrom et al., 2003). Early investigations of place cells characterized some of these cells as "misplace cells" (O'Keefe and Nadel, 1978), which fired in a specific location only when an unexpected object or reward was located in that place, or when an expected object or reward was missing. Thus, object-related influences on place cells were known from the very first investigations. Many subsequent experiments concentrated on the influences of distal landmarks on place cells, however (O'Keefe and Conway, 1978; but see Wible et al., 1986; Wiener et al., 1989). These experiments showed that place fields were controlled primarily by landmarks in the periphery of the environment, in that rotation of these landmarks caused place fields to rotate correspondingly. In contrast, rotation of the recording apparatus generally had no effect on the place fields. Thus, it became widely viewed that place cells were selective for spatial locations defined by the distances and angles to distal visual cues. Over the past decade, however, it has become clear that proximal, apparatus-based cues can control place cell firing if these cues are matched in salience to the distal landmarks (Young et al., 1994; Shapiro et al., 1997; Zinyuk et al., 2000; Knierim, 2002a). In addition, the importance of self-motion cues in updating the spatial representation in the hippocampus also has been demonstrated (McNaughton et al., 1996; Knierim, 2002b). It is clear that the location-specific firing of place cells arises from an interaction between proximal, distal, and self-motion cues, the details of which are still being debated.

Regardless of the eventual resolution of the question of how different types of cues interact to endow place cells with their spatial specificity, a fundamental question remains. What is the purpose of a cognitive map of space? A map is useful as a spatial framework only if it organizes and locates objects or places of importance within that space. A map of New York City would not be helpful if it did not incorporate the locations of potential destinations, such as the Empire State Building, the Statue of Liberty, or one's favorite Italian restaurant or dance club. Similarly, a cognitive map of one's bedroom is only useful if it incorporates objects of interest, such as the nightstand and bathroom door, allowing one to move directly to these locations and avoid obstacles even in total darkness. What happens, however, when the nightstand is moved to a new location? How does this new location become incorporated into the map, and what happens to the representation of the nightstand's old location?

In this issue, Rivard et al. (2004) provide physiological evidence that some place fields in the hippocampus are bound to objects in an environment; when the objects are rotated or translated to new locations in the environment, the place fields of these cells move with the object. Rats were trained to forage for food pellets in a cylindrical apparatus with a transparent barrier extending from the center of the cylinder to the 7:30 o'clock position at the edge of the cylinder. Place fields were characterized at locations near and far from the barrier. When the barrier was moved to new locations in the cylinder, the far place fields were unaffected. Place fields located near the barrier, however, tended to move along with the barrier, showing that they were bound to the movable object rather than to the stable framework of the cylinder. New place fields were formed to fill in the "hole" in the map created at the old barrier location. Further, the place fields that previously occupied the new barrier location tended to disappear, as if the cells that represent the object

took over the representation of that location in the environment.

These results are important demonstrations of how hippocampal cells represent both locations and objects occupying those locations (at least large objects like a barrier) in an apparently seamless manner. There are a number of remarkable aspects to these findings. First, the effects of the barrier appear to be local only to cells that fire near the barrier. Cells with place fields away from the barrier are largely unaffected by the barrier manipulations. This result is consistent with a number of previous studies. Muller and Kubie (1987) first demonstrated that addition of a barrier into the place field of a cell could cause the cell to cease firing. If the barrier was placed in a location away from the place field, the cell remained unaffected. Similar results were shown by Fyhn et al. (2002), who moved a learned goal platform to a new location in an annular water maze and saw that some place cells fired at the new location, whereas the place cells that represented the rest of the maze were unaffected. In addition, Fenton et al. (2000) showed that cells with place fields near two narrow cue cards on the wall of a cylindrical chamber were controlled by the nearest card when the cards were moved further apart from each other, while cells with place fields more distant from the cards were less affected by the manipulation of the cues.

Another important finding of Rivard et al. (2004) is that the place fields that were bound to the barrier in one environment also were bound to the same barrier in a completely different environment. Typically, if two environments are sufficiently distinct in their sensory landmarks or behavioral significance, the hippocampus creates two distinct representations of the two environments (i.e., the hippocampal representation "remaps" from one environment to the other; Muller and Kubie, 1987; Knierim, 2003). With a complete remapping, some cells have place fields in one of the environments and are completely silent in the other, whereas other cells have place fields in both environments but the locations of the fields are unrelated. In Rivard et al. (2004), most place fields located away from the barrier completely remapped two visually distinct environments. However, place cells that had fields near the barrier tended to fire near the barrier in the new environment as well. Thus, these cells did not partake in the remapping of the new environment, suggesting that they subserved a role related to the identification of the barrier rather than to the representation of the enclosed environment. This result is markedly different from that of Gothard et al. (1996), who demonstrated similar object/goal-related firing. In that study, rats were trained to leave a goal box and find food reward either at the end of a linear track (experiment 1) or near a movable beacon on a two-dimensional platform in a different environment (experiment 2). Gothard et al. (1996) found that in both experiments, some fields were bound to the movable box rather than to the static spatial cues in the environment. In contrast to the current findings, however, box-related fields in one environment were not necessarily box-related fields in the second environment. Gothard et al. (1996) suggested that both place-related and box-related cells were the same type of place cell, each tied to a different reference frame (the static environment vs. the dynamic box). The barrier cells of Rivard et al. (2004) seem to behave very differently, in that they are attached to the barrier even when the rest of the place fields undergo full remapping.

There are a number of intriguing questions that arise from these results. One question regards the extent to which the classic place cells and the barrier cells correspond to two distinct classes of neurons, as Rivard et al. (2004) argue. In any given environment, an estimated 33–40% of CA1 pyramidal cells are active and spatially selective, while the remaining cells are virtually silent (Wilson and McNaughton, 1993). In other environments, a different subset of the CA1 cells is active, with some degree of overlap between the active subsets in each environment. It thus has been argued that all pyramidal cells in CA1 of the dorsal hippocampus are potential place cells, just waiting for the right environment to demonstrate a place field. The question raised by these results is whether the barrier-selective cells will always be object related in all environments in which they are tested sufficiently, or whether they may act as classic place cells under other circumstances. The finding that they tend to maintain their firing relative to the barrier in a new environment, even though the rest of the hippocampal representation remaps, suggests that they may be a different class. This interpretation must be put to a more stringent test, however. It is possible that the barrier-related cells may become classic place cells in a new environment in which the barrier is not present. Because most models of hippocampal circuitry and function assume that CA1 pyramidal cells are a homogeneous class, a crucial question with profound implications for these models is whether some CA1 pyramidal cells are wired to represent the spatial locations in an environment while other cells are wired to represent the objects in that environment, or whether each cell is capable of representing either locations or objects depending on the particular environment or context.

It is also important to understand whether the object-related firing in the present study is somehow particular to the barrier used in this study. In a previous study in which a barrier inserted into a place field caused local disruptions, a smaller object (i.e., the stand that supported the barrier) did not affect the fields. Muller

and Kubie (1987) suggested that the object needed to cause changes to the animal's movement patterns in order to disrupt the spatial representation. In contrast, the finding of misplace cells by O'Keefe and Nadel (1978) and the goal platform results of Fyhn et al. (2002) suggest that smaller objects can indeed alter hippocampal firing. What factors determine whether an object will cause the local remapping phenomena described here and cause place fields to attach to the object? A number of clues come from other studies. Moita et al. (2003) showed that auditory conditioned stimuli can drive place cells in a restricted location when the animal is trained in a fear-conditioning task; before training, the auditory stimuli did not drive the cells. Fyhn et al. (2002) showed that place cells were more active at goal platforms only if the platform was in an unexpected location; moving the platform repeatedly from trial to trial, such that the animal presumably came to expect the goal instability, did not cause the place fields to fire more strongly at the platform. It is possible that high-order cognitive factors determine whether nonspatial stimuli are incorporated into the hippocampal representation of an environment. These factors may include expectancy (is an expected object missing or displaced or is an unexpected object present? [O'Keefe and Nadel, 1978]), behavioral contingency (does this object or sound predict a behaviorally relevant outcome? [Markus et al., 1995; Wood et al., 1999; Moita et al., 2003]), or attention (do I need to be paying attention to spatial cues or objects in the environment? [Kentros et al., 2004]). Perhaps a large barrier automatically captures an animal's attention in the task used by Rivard et al. (2004); even though the barrier is not explicitly related to reward contingencies, its presence requires the animal to alter its trajectories as it forages for the food scattered on the floor. Understanding the factors that control whether hippocampal cells explicitly represent an object or fail to incorporate it into its spatial representation is a critical question toward understanding hippocampal function.

A number of recent studies from rodents, primates, and humans have been converging on the notion that the hippocampus and related areas may be critically involved in creating object/item + place associations (Suzuki et al., 1997; Gaffan, 1998; Davachi et al., 2003; Ekstrom et al., 2003; Moita et al., 2003). In accordance with the cognitive map theory, these associations may provide the brain with an objective framework to organize and interrelate the items and events of the animal's experience. Such a framework might be crucial for supporting such phenomena as context-dependent learning, and may also provide a substrate for human episodic memory (i.e., conscious recollection of specific events in one's past, including their spatial and temporal context). The robust results of Rivard and

colleagues hold promise for deciphering how the hippocampus, together with its input and output structures, creates spatial representations of environments and incorporates the important objects and other discrete items or events that occur in that space to guide adaptive behavior in different contexts.

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