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Review article

Prefrontal–hippocampal interactions for spatial navigation

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ABSTRACT

Animals have the ability to navigate to a desired location by making use of information about environmental landmarks and their own movements. While decades of neuroscience research have identified neurons in the hippocampus and parahippocampal structures that represent an animal's position in space, it is still largely unclear how an animal can choose the next movement direction to reach a desired goal. As the goal destination is typically located somewhere outside of the range of sensory perception, the animal is required to rely on the internal metric of space to estimate the direction and distance of the destination to plan a next action. Therefore, the hippocampal spatial map should interact with action-planning systems in other cortical regions. In accordance with this idea, several recent studies have indicated the importance of functional interactions between the hippocampus and the prefrontal cortex for goal-directed navigation. In this paper, I will review these studies and discuss how an animal can estimate its future positions correspond to a next movement. Investigation of the navigation problem may further provide general insights into internal models of the brain for action planning.

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1. Navigation behavior of animals

Spatial navigation is one of the most fundamental abilities of animals. All animals are required to explore from one location to another for survival. However, their navigation strategies are not necessarily the same – different animal species appear to develop their own strategy that is suitable for their living purpose, their environment, and functional features of their nervous system. For example, many animals, including insects, are known to have the ability to return to the nest location after a long period of exploration in their environment. Some animals, such as sea turtles, pigeons or bees, appear to use a special sensory system for the Earth's magnetic field or for sunlight polarization to estimate their home location (Wehner, 1984; Lohmann et al., 2008; Mehlhorn and Rehkamper, 2009). Other animals, such as desert ants, are good at using a navigation strategy called path integration, in which the animal accumulates its movement vectors from the beginning of the navigation so that the resultant vector should represent the direction and distance of the nest location from the animal's current position (Wehner and Wehner, 1986; Muller and Wehner, 1988; Wittlinger et al., 2006). These navigation strategies do not impose a large demand of memory, providing an efficient strategy for navigation when returning home.

However, the navigation strategies described above are not necessarily suitable when an animal is required to visit multiple

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destinations in the environment. In our daily life, it is often necessary to plan a route so that we can visit multiple destinations with a minimum travel distance. While one potential strategy may be to memorize all possible routes between spatial landmarks in the environment, this exhaustive strategy will require a huge capacity of memory. Furthermore, in such a strategy, animals will never be able to find a novel shortcut route because route planning is based on prior experiences. Here, map-based navigation provides a versatile strategy for navigation. The main idea of this navigation strategy is that the brain does not need to memorize individual routes, but instead, the brain makes direct use of a geometric structure of the environment, or a map, so that an appropriate route can be planned for each start–goal combination. While this strategy requires the brain to store the information about positional relationships in the environment, once it is completed, it allows the brain to estimate the direction and distance between any two locations. The strategy will further enable an animal to discover a novel shortcut route based on geometric relationships of positions, even if the animal has never experienced such routes before.

While humans appear to use a map-based navigation strategy by mentally visualizing a geometric structure of the environment during the route-planning process, are there any animals that can perform a similar map-based navigation? Edward Tolman has performed a series of behavioral experiments that support the idea that rats have the ability to perform map-based navigation (Tolman, 1948). For example, rats can find a novel shortcut route to a destination (Tolman et al., 1946) and can correctly estimate the direction and distance of a destination from different start positions (Morris, 1981; Eichenbaum et al., 1990) . These behavioral studies led to investigations of the rat nervous system in an effort to search for neural representations of the environmental geometry.

2. Hippocampus for spatial navigation

2.1. Spatial-representation system in the brain

While behavioral evidence suggests that rats can perform map-based navigation, how does the brain represent a geometric structure of the environment? One of the biggest breakthroughs was made by John O'Keefe and colleagues. They discovered neurons in the hippocampus called place cells that fire whenever an animal visits a particular location in space (O'Keefe and Dostrovsky, 1971). This led to the idea that place cells are the key elements of an internal map, also known as a cognitive map, in the brain (O'Keefe and Nadel, 1978). Place cells have several features distinct from neurons that were discovered prior to that time. First, while place cells exhibit a selective tuning to external features in the environment, these neurons were found in the hippocampus, a higher cortical region that is multiple synapses away from the peripheral sensory organs (e.g. Felleman and Van Essen, 1991). Second, while neurons in other brain areas sometimes exhibit activity preferences to the stimulus location, the spatial tuning of these neurons is typically based on a self-centered, egocentric coordinate, for example, bound to an animal's own eye or body position (Hubel and Wiesel, 1959; Andersen et al., 1985; Brotchie et al., 1995). The activity tuning of place cells is, in contrast, based on an allocentric coordinate that is bound to the external environment, which implies a requirement for additional computation to transform sensory inputs from an egocentric to an allocentric representation. Finally, a pair of place cells that share the place fields in one environment do not necessarily represent the same location in another environment (Muller and Kubie, 1987), suggesting that this representation is different from a 'map' observed in sensory cortices in which a pair of neurons maintain the same feature relationships across different stimuli. The hippocampus seems to create multiple independent orthogonal representations for each environment, which may be important to prevent overlaps of different experiences or memories.

How can place cells be formed in the brain? A particular spatial position may be determined by local landmarks, such as visual, tactile or olfactory sensory cues, but may also be estimated by idiothetic motion-related or proprioceptive cues. Experimental evidence suggests that both of these mechanisms are used to form place cells (Poucet et al., 2000). For example, while firing fields of place cells are influenced by the shift of sensory-cue locations, partial removal of cues can be compensated by the system so that place cells maintain the same firing fields (O'Keefe and Conway, 1978). The firing fields of place cells do not change in darkness (Quirk et al., 1990; Markus et al., 1994; McNaughton et al., 1996), and furthermore, place cells can be formed even if animals were blinded at a young age (Save et al., 1998), suggesting the importance of idiothetic information for the formation of location-specific firing in place cells. These studies indicate the necessity for an internal metric system to estimate a direction and distance relative to a particular location based on the animal's own movement. In accordance with this idea, grid cells in the medial entorhinal cortex, an upstream structure of the hippocampus, have multiple firing fields with equal-distance spacing in particular directions, which forms a metric system for spatial distance and direction (Hafting et al., 2005; Moser et al., 2014). A recent computational study has demonstrated that a population of grid cells, with different spacing sizes and spatial phases, are sufficient to extract information about the distance and direction between two positions (Stemmler et al., 2015). Furthermore, the existence of head-direction cells and speed cells in the medial entorhinal cortex (Sargolini et al., 2006; Kropff et al., 2015) supports the idea that this brain region implements integration of the animal's own running speed and direction to estimate the traveled distance and the direction after a move. Altogether, evidence suggests that the hippocampus and parahippocampal regions create an internal metric of space to represent spatial positions and their relationships in the environment.

2.2. Navigation problem and prospective activity in place cells

Significant progress has been made in understanding the brain's spatial representation system. Place cells and grid cells have been discovered in the human hippocampus and entorhinal cortex (Ekstrom et al., 2003; Jacobs et al., 2013), and damage in these structures has been shown to impair the ability for spatial navigation in both rats and humans (Morris et al., 1982; Bohbot et al., 1998; Spiers et al., 2001; Burgess et al., 2002; Steffenach et al., 2005). Place cells and grid cells constitute key elements for spatial navigation by representing an animal's instantaneous position in the environment (Moser et al., 2008). However, the information provided by these cells is not sufficient for goal-directed navigation. For an animal to plan a route to a destination, it is necessary for the animal to estimate its future state in space following a planned movement. This requires the brain to have relationships between the next movement and future positions. Several studies have reported place-cell activity that appears to reflect such relationships, indicating a possibility that the animal's future spatial state is represented in the hippocampus.

One of the potential mechanisms of future representation in the hippocampus is based on the temporal coding of spatial positions in place cells. Place cells are known to exhibit a systematic spike-phase shift relative to the local hippocampal theta rhythm (8–11 Hz) as the animal passes through the firing field of the cell – a phenomenon called phase precession (O'Keefe and Recce, 1993) (Fig. 1A). This indicates that place cells fire in accordance with the distance to their field center before an animal reaches there, implying the place-cell's representation of an animal's expected future position. David Redish and colleagues have tested this idea