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Review

Hippocampal–cortical interaction in decision making

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ABSTRACT

When making a decision it is often necessary to consider the available alternatives in order to choose the most appropriate option. This deliberative process, where the pros and cons of each option are considered, relies on memories of past actions and outcomes. The hippocampus and prefrontal cortex are required for memory encoding, memory retrieval and decision making, but it is unclear how these areas support deliberation. Here we examine the potential neural substrates of these processes in the rat. The rat is a powerful model to investigate the network mechanisms underlying deliberation in the mammalian brain given the anatomical and functional conservation of its hippocampus and prefrontal cortex to other mammalian systems. Importantly, it is amenable to large scale neural recording while performing laboratory tasks that exploit its natural decision-making behavior. Focusing on findings in the rat, we discuss how hippocampal–cortical interactions could provide a neural substrate for deliberative decision making.

1. Deliberation in the rat

Behavioral observations in naturalistic settings demonstrated that the brown rat, *Rattus norvegicus*, has remarkable spatial memory (Calhoun, 1963; Telle, 1966). Individuals can remember locations of food sources, paths, predators and competitors in an environment and use this information for efficient foraging. Moreover, natural environments are complex and change over time. The rat needs to adapt to any changes it encounters, such as the presence of predators and obstacles on its foraging routes. As a result, relying solely on reflexive or habitual routines is insufficient for successful foraging in the long term. Memory, in particular the ability to learn spatial relationships and to modify stored representations when the world changes, is therefore critical for a foraging rodent to obtain food while avoiding danger.

Making navigational decisions based on stored memories requires planning and evaluation of potential trajectories from information about past foraging experiences. This representation of the external world stored in memory has been referred to as the "cognitive map" (Tolman, Ritchie, & Kalish, 1946; Tolman, 1948). Navigational decision making can therefore be seen as an internal deliberation process whereby different routes through the animal's cognitive map are evaluated. In this type of decision making, the animal considers the action and consequences of multiple options, weighing up the pros and cons in order to decide on the most suitable option.

We expect that this type of deliberation is most important during the learning of new routes and following changes to the environment. In these situations, no single option stands out as being correct and therefore many alternatives need to be considered. Many aspects of natural foraging behavior are captured in laboratory behavior paradigms that require a rat to find food rewards by navigating along defined paths or in an arena. Thus, these paradigms are well suited to investigate deliberation in a spatial context that is ethologically relevant. Indeed, a rat performing a laboratory task that requires a choice between different arms of a maze pauses briefly at maze choice points and turn its head back and forth to scan the possible routes before choosing one, a behavior termed vicarious trial and error (Muenzinger & Gentry, 1931; Tolman, 1938; Johnson & Redish, 2007). This behavior is most frequent in the learning phase of the task when the rat is still unsure of the rules.

2. Neural signatures of deliberation

The processes of deliberation include the initial formation of memory, its subsequent recall to provide the options for deliberation and the comparison and evaluation of these options. These processes depend on a number of brain regions, including the hippocampus and the prefrontal cortex (PFC). While patterns of activity important for memory formation have been identified in the

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hippocampus, the neural substrates and patterns of activity that support the recall and evaluation of choice options based on memory remain somewhat unclear. We will review findings in the fields of memory and decision making and propose candidate neural mechanisms in the hippocampus and PFC to support these steps of deliberation.

To find the pattern of neural activity and mechanisms mediating different steps of deliberation, we need to identify the prerequisites necessary to support deliberation. Since deliberation is more important during learning, we expect the pattern of activity to be more prominent during this period. The pattern of neural activity also needs to occur at locations where deliberation is important. These locations are where a rat needs to plan its next trajectory, which include the starting point and subsequent choice points. The content of the pattern of activity should also contain information useful for the decision. In the case of navigational decisions, the pattern of activity should contain spatial representations not limited to the current location but instead representations of extended trajectories or remote locations of interest. Lastly, the pattern of activity must be required for decisions that require deliberation. Having these requirements in mind, we will explore various patterns of neural activity in the hippocampus and the PFC and determine if they are likely candidates for deliberation.

3. Hippocampal contribution to deliberation

If experience is to be used in the future for making decisions, it must be encoded and stored. Strong neural correlates of memory encoding processes can be found in the hippocampus across species (Squire, 1992). In the rat, the hippocampus forms representations of experience that are expressed through the sequential firing of unique ensembles of pyramidal neurons as the animal explores an environment. The pyramidal neurons are often active at specific spatial locations in the environment, giving rise to their name: "place cells" (O'Keefe & Dostrovsky, 1971). The location in which a place cell fires is called its "place field". However, place cells represent much more than place. Numerous studies have shown that these neurons can respond to a complex combination of spatial and non-spatial information including external sensory stimuli and aspects of task relevant behaviors (Wible et al., 1986; Eichenbaum, Kuperstein, Fagan, & Nagode, 1987; Wiener, Paul, & Eichenbaum, 1989; Sakurai, 1996; Frank, Brown, & Wilson, 2000; Wood, Dudchenko, Robitsek, & Eichenbaum, 2000; Ferbinteanu, Ray, & McDonald, 2003; Pastalkova, Itskov, Amarasingham, & Buzsaki, 2008; MacDonald, Lepage, Eden, & Eichenbaum, 2011). Taking account of these findings, the ensemble activity of "place cells" in the hippocampus is perhaps best described as encoding a moment by moment representation of different dimensions of experience (Eichenbaum, Dudchenko, Wood, Shapiro, & Tanila, 1999).

4. Theta oscillations

Physiologically, hippocampal information processing can be characterized as a continuum of states that appears to reflect the relative dominance of processed sensory input and stored representations (Kemere, Carr, Karlsson, & Frank, 2013). During periods of active exploration, processed sensory input drives coordinated neuronal activity in the hippocampus and is associated with synchronous oscillation in the 7–10 Hz range, termed theta (Buzsaki, 2002; Hasselmo & Stern, 2013). Theta oscillations are most prominent during locomotion and less so during pauses in activity.

During bouts of theta oscillations, each place cell fires at a preferred phase of each period. As the animal traverses the place field of a place cell, the phase at which spikes fire gradually shifts earlier with each theta cycle, a phenomenon called theta precession (O'Keefe & Recce, 1993; Skaggs & McNaughton, 1996). Thus, the activity of place cells during theta oscillations seems well suited to encode information about the rat's current location and a local trajectory on a rapid timescale. Having a representation of the current location is necessary for the animal to determine if it is in a place where a decision needs to be made. This information could also be used by other brain areas to monitor if the current course of action matches the choice made in the original decision.

With respect to deliberation, we expect to observe representations of potential trajectories beyond the current location of the rat. Representations of locations ahead of the rat during theta have been reported at trajectory choice points and correspond with vicarious trial and error behavior (Johnson & Redish, 2007; Gupta, van der Meer, Touretzky, & Redish, 2012). This study suggests theta oscillations during pauses at a choice point is a period when place cells momentarily encode non-local representations and could reflect the exploration of future trajectories. Further work will be required to determine the characteristics of these sequences in other circumstances.

5. Sharp-wave ripples

At low movement speeds and when a rat is not actively exploring, another network pattern of hippocampal activity known as sharp-wave ripples (SWRs) becomes prominent. SWRs are brief high frequency oscillations, between 150 and 250 Hz (Buzsaki, 1986) originating from the CA3 region and propagating to the CA1 region of the hippocampus (Buzsaki, 1986; Csicsvari, Hirase, Mamiya, & Buzsaki, 2000). During this period, ensembles of pyramidal neurons become briefly reactivated (Wilson & McNaughton, 1994; Skaggs & McNaughton, 1996; Kudrimoti, Barnes, & McNaughton, 1999; Foster & Wilson, 2006; Jackson, Johnson, & Redish, 2006; Diba & Buzsaki, 2007; Davidson, Kloosterman, & Wilson, 2009). Cells whose activity would span many seconds as the animal explores, during theta oscillations, are reactivated within a few hundred milliseconds. Importantly, ensemble firing on this fast time scale often preserves the original temporal relationship between cells. Relating the sequence of firing of individual cells and their place fields in an environment reveals representations of actual trajectories traversed by the animal (Lee & Wilson, 2002; Foster & Wilson, 2006; Diba & Buzsaki, 2007). These observations provide strong evidence that during SWRs the hippocampus reactivates a time-compressed version of past experiences.

SWR replay events have been linked to the offline strengthening of cortical representations of memory through repeated activation of cortical ensembles during sleep or inactivity (Buzsaki, 1996; Frankland & Bontempi, 2005; Diekelmann & Born, 2010; O'Neill et al., 2010; Girardeau & Zugaro, 2011). Since the first reports of hippocampal replay during sleep, replay has subsequently been observed to occur frequently during active behavior (Kudrimoti et al., 1999; Foster & Wilson, 2006; Jackson et al., 2006; Diba & Buzsaki, 2007; Davidson et al., 2009; Karlsson & Frank, 2009; Dupret, O'Neill, Pleydell-Bouverie, & Csicsvari, 2010). On a network level, the reactivation of memory sequences during SWRs could provide a convenient mechanism to quickly recall memories during the awake state (Carr, Jadhav, & Frank, 2011).

The dynamics of SWRs and the behavioral correlate of deliberation, vicarious trial and error, are similar: both are initially more frequent and then decrease with learning (Muenzinger, 1938; Jadhav, Kemere, German, & Frank, 2012). When a rat is first exposed to a novel task, SWRs are prevalent. As the animal learns and becomes familiar with the task, the number of SWRs gradually decreases (Cheng & Frank, 2008; O'Neill et al., 2008; Singer & Frank, 2009). When a change in the task is introduced, such as exposing the rat to a second novel environment, an increase in the number of

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