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Remembering goal locations

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Spatial navigation encompasses the capability to compute various paths leading to one's goal. In order to achieve such a feat, a navigation system must also have access to the animal's current location. Although the latter is well documented with over forty years of research devoted to hippocampal place cells, how the goal location is coded and kept in memory is a much more debated issue. Here, we review evidence that such processing occurs within a small network of structures involving at the very least the hippocampus and the frontal cortex. Indeed, growing evidence suggests that path planning relies on a much more extended neural network, with each of its subcomponent ensuring a specific role in the overall process. We suggest that understanding how goal location is remembered can only be achieved through a better characterization of the time-defined events during path planning at both neural and behavioral levels.

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Introduction

The ability to navigate efficiently in space is crucial for the survival of most species. The last four decades have provided increasing evidence that the hippocampus and its place cells carry out fundamental computations involved in spatial navigation [1]. Place cells are hippocampal pyramidal neurons that fire only when a rat is in a particular location within an environment, thereby allowing self-localization (reviews in [2,3]). They therefore provide ideal building blocks for implementing the capability to navigate since they may support a representation of both the environment layout and the animal's current location in that environment. However, for an animal to solve a complex spatial problem, it must also know where to go and how to get there. Behavioral performance observed during the water-maze navigation task is the best demonstration of this capability. Current evidence indicate that rats may rapidly store new goal locations under certain circumstances and that hippocampal activity is involved in this memory both during online [4,5] and offline episodes [6,7].

In spite of this behavioral evidence, how a rat remembers the location of a goal and plans a path to this location is still poorly understood [2,8]. In particular, while place cells are clearly involved in self-localization, their role in the memory of the goal location faces a logical difficulty [9,10]. Indeed, if place cells support both mapping and planning functions of a navigation system, the code conveyed by their firing activity would become ambiguous. Following this idea, place cells would fire whenever the rat has to process goal information, which presumably can happen everywhere in navigation space, and so would not be expected to display a precise firing field. Because firing fields are usually well defined even during navigation behavior, it is therefore unlikely that place cells carry direct information about the goal.

Nevertheless, recent research has revealed a number of alternative solutions through which hippocampal place cell activity may carry indirect information about goal locations. In addition, place cells themselves need not directly signal information about the goal, if 'goal' (or 'critic') cells, located elsewhere, receive input from place cells together with reward information so as to signal goal direction during navigation. In this hypothesis, these cells would have firing clustered at the goal locations whereas place cells need not [11,12]. With regard to this possibility, a number of extra-hippocampal regions have been reported to be involved one way or another in the coding and storage of goal information. Here we review the current literature data about how goal locations may be coded and remembered. A central aspect of such processing is that remembering goal location is required only during a specific phase of spatial navigation, namely when making a decision as to which direction to take to reach a goal location and/or planning a path to that goal location. We therefore also address recent data that show neural activities to be influenced by the location of the goal during decision making, thereby suggesting that remembering a goal location might be embedded into a more global process.

Memory of goal location in the hippocampus

As mentioned above, even though the spatial function of place cells is hardly disputable, their direct involvement in remembering goal locations is controversial, at least in

terms of field accumulation at the goal location. Although no simple representation of goal within the hippocampus has yet been found, several valuable observations have been reported.

The first is that firing field distributions may be biased during performance of goal-related tasks. Thus, field accumulation at the goal was seen while rats swam in an annular water maze in which an escape platform could be raised at a fixed location [13]. These results suggest that the hippocampus somehow over-represents behaviorally significant regions of space. Another study, in which place cells were recorded from rats trained to take fixed trajectories to obtain intracranial stimulation rewards at two specific locations in a cylinder, found that some cells changed their firing patterns as the rat learned the task and displayed excess firing at the two rewarded locations [14]. This finding was confirmed more recently in a food rewarded spatial learning task, in which CA1 firing fields were reorganized to represent newly learnt goal locations [15•]. These new representations reemerged during subsequent memory recall. Their stabilization and their retrieval were seen to depend on reactivations associated with sharp wave/ripple network oscillations, thus supporting the hypothesis that memory for goal locations was encoded in the assembly firing patterns within the hippocampus (see also [16]). Changes in firing field density that occur when fields shift location in a goal-directed manner have been suggested to carry enough information about goal direction for successful navigation [10].

In contrast to these reports of excess place cell fields numbers at goals, other studies failed to see any such tendency during spatial tasks. For instance, place cells were recorded while rats performed a continuous place navigation task (see Figure 1a) in which they had to enter an unmarked circular goal zone in a cylindrical arena and stay there for two seconds to release a food pellet at a random location in the environment; then, they had to leave the goal zone to find and eat the pellet [17,18]. Thus, the task required the rat to make target-directed movements to an unmarked goal while preserving the undirected foraging behavior necessary for sampling unit activity everywhere in the apparatus. In addition, the reward location was consistently dissociated from the constant goal zone, thus making it possible to disentangle the goal value of places from their reward value. Lastly, as navigation paths started from the last reward location which varied randomly, rat's trajectories also varied considerably across trials. Under these circumstances, no clustering of firing fields was seen at the goal location [17].

Although this could be a result of dissociating the goal zone from the variable reward site, several studies in which the goal and reward sites were coincident also failed to see firing field accumulation at the goal [19,20], or to see fields undergo systematic changes when the goal was moved [19–22]. It is therefore possible that idiosyncratic characteristics of behavioral tasks impact the hippocampal representation so that fields over-represent specific places. For example, the existence of fixed trajectories such as those observed when both rat's starting point and goal locations are constant [13,15•] may increase place cell excitability when the rat gets close to the goal location along the navigation path.

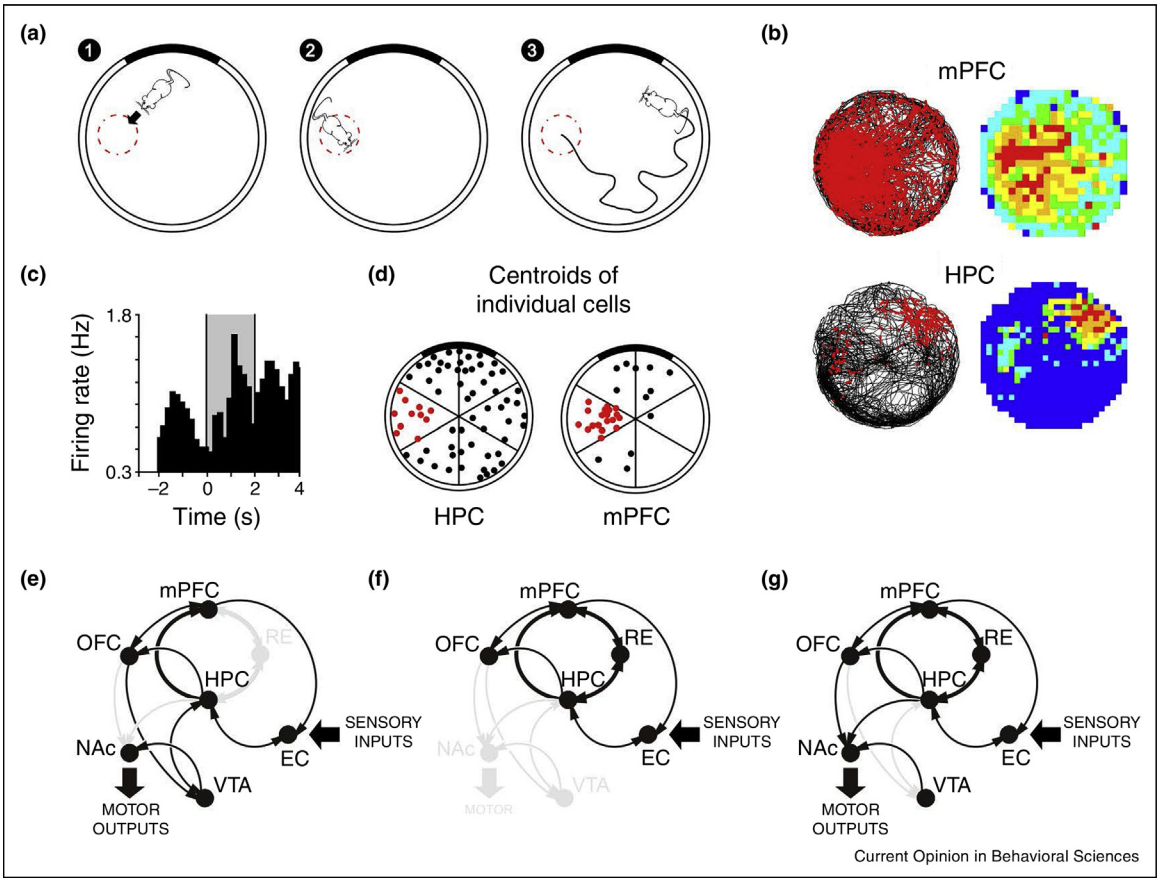
In support of the last hypothesis, two interesting findings need be mentioned here. First, moving the platform to a new location in the annular water maze was observed to induce excess firing at the new location, but this excess firing vanished rapidly as the rat learned the new goal [23]. So it cannot be excluded that field accumulation at a goal may be a transient phenomenon observed under certain conditions.

Second, field accumulation at a goal may also instead reflect excess goal firing of place cells with a field elsewhere in space as observed both in rats [17] and in mice [24]. For example, in the continuous place navigation task described above, most place cells discharged a few spikes out of their primary firing field when the rat was at the goal location (see Figure 1b). A further observation was that such extra-firing at the goal was not associated with increased occurrence of sharp wave ripple activity [25,26], thus making it unlikely that it reflected replay of a trajectory that ended at the goal location [17]. In addition, even hippocampal pyramidal cells that were silent or had no clear-cut field in the apparatus were seen to display goal-related firing. Although this firing was weak at the single cell level, it was remarkably coherent at the population level, therefore suggesting that place cells provide a consistent signal when the rat is at the goal. This population signal is so precisely defined in the time domain that it could reflect the rat's awareness that it is at the correct location (see Figure 1c). This awareness could rely on several processes such as online maintenance of the goal representation, comparisons of the current panorama with a memory template of the goal panorama, or a simple temporal estimation of the time spent at the goal. Alternatively, this signal could represent expectancy of upcoming reward [27]. At this time, whether place cell goal-related firing is caused by identification of the goal location rather than a reward-modulated signal is still unclear. Nonetheless, this reward-modulated activity could explain, at least partly, the discrepancies about the influence of the goal location on the changes affecting firing fields in goal-directed spatial tasks [13,14,15•,17,19,20].

Memory of goal location in extra-hippocampal structures

The lack of a clear-cut place cell representation of goal locations suggests that such a representation may exist in

Figure 1



A model network for goal-coding. **(a)** Sketch of the continuous navigation task. The rat must enter an unmarked goal zone (1, red dashed circle) and stay there for two seconds to release a food pellet from an overhead feeder (2). To find and eat the food pellet, the rat has to forage around the cylinder (3) before initiating a new navigation path to the goal. **(b)** Trajectory (left) and firing rate (right) maps of one medial prefrontal cortex cell (mPFC) and one hippocampal place cell (HPC) recorded in the continuous navigation task. Red dots in the trajectories indicate the rat's location when the cell is active. The mPFC cell has a large firing field that roughly overlaps the goal zone. In contrast, the HPC place cell has its main firing field away from the goal though it fires a few additional spikes at the goal location. **(c)** Cumulative PETH for all HPC place cells recorded from rats tested in the continuous navigation task. The 2 s goal period (0–2 s) is bracketed by vertical lines (200 ms bins). Note that the mean peak activity is delayed by ~1 s during the goal period. **(d)** Distribution of firing field centroids for both HPC and mPFC cell populations. While HPC fields are widely and homogenously distributed, mPFC fields are clustered in the goal zone (red dots). **(e–g)** A model network for goal-coding. In this highly speculative model, mPFC neurons provide coarse coding of goal locations independent of whether the animal is actually engaged in navigation [30]. HPC cells provide a population signal when the rat is at the goal, possibly indicating correct goal localization [17]. mPFC and HPC are connected to each other through various pathways, including one pathway passing through the thalamic nucleus reuniens (RE) [36]. This circuit is assumed to be crucial for how goal locations are remembered on the long term (panel f). (e) During acquisition: sensory inputs from the entorhinal cortex (EC) and place information from HPC are associated with reward value from the ventral tegmental area (VTA) [31,50] so that the goal location is represented in mPFC [30]. This representation is further reinforced by reward expectancy through activation of a set of structures including VTA [50], orbitofrontal cortex (OFC) [48] and ventral striatum (NAc) [49]. (f) During retrieval of goal location from long-term memory: sensory inputs (EC) enable mPFC goal representation through a hippocampo-fronto-thalamic loop (involving RE) [37] supplemented by OFC reward expectancy signal [48,49]. (g) During navigation: mPFC-dependent short-term (working) memory of goal location triggers the selection of the strategy (RE) [40] leading to appropriate locomotor outputs from ventral striatum (NAc).

other brain structures. Here we briefly review some findings showing that the medial prefrontal cortex (mPFC) might have a special role in this function. Before doing so, however, it is worth noting that remembering a goal location can reflect two different memory processes, which roughly correspond to two distinct stages of spatial navigation. First, information about the goal location has to be retrieved from long-term memory before initiating any navigational trajectory. The primary aim of this short review is to address this long-term memory of the goal location. Nevertheless, to be useful, this information must also be kept in a temporary short-term working memory store to ensure that the appropriate trajectory is planned and executed. It is remarkable that the prefrontal cortex appears to be involved in these two aspects of goal memory.

Thus, cell discharge in mPFC has been shown to be associated with temporary storage of information in memory [28,29]. Indeed, the activity of mPFC neuronal ensembles changed in parallel with learning of a delayed alternation task and correctly allowed decoding of previous and future goal choices, showing therefore that working memory is robustly represented at ensemble level. In a similar vein, many mPFC neurons were seen to selectively 'tag' specific arms of a radial arm maze, according to both previous choices and reward expectancies [29]. Noticeably, although this tagging is essential for online maintenance of goal locations in working memory, hence for prospective coding and decision making during spatial navigation, it cannot be used for remembering goal locations on a longer term.

Nevertheless, another form of activity, compatible with a long-term memory of goal location, has also been documented. Medial prefrontal neurons were recorded while rats were performing the continuous place navigation task described above, in which they had go to a goal location to cause pellet release and then had to find the pellet. Roughly a quarter of them had clear spatial correlates (a result not seen when rats simply forage randomly), and their fields were clustered in the immediate vicinity of goal locations [30] (see Figure 1d). Since these goal locations were dissociated from eating locations, mPFC cells coded the motivational salience of these specific locations, independently of their primary reward properties. In addition, mPFC goal cell firing did not result from the occurrence of task-related specific behaviors. In sum, these cells appear to provide a reliable signal about the location of goals.

How might this signal be generated? There are many areas connecting the medial prefrontal cortex. Thus, mPFC receives direct input from the ventral hippocampus, whose pyramidal cells provide a low resolution positional signal (in particular to the prelimbic area of mPFC), as well as from the ventral tegmental area which may be the source of information about the reward value of different locations in the environment [31]. In addition, the ventral hippocampus would selectively route goal-related information to mPFC [32,33•], thus targeting neurons that label locations of high motivational significance. Interestingly, integrity of ventral hippocampal function is required for goal-directed navigation performance and for coherent mPFC goal coding [34], as well as for updating the value of a goal location [35].

In return, the medial prefrontal cortex connects back to the hippocampus through several indirect pathways. One of these pathways passes through nucleus reuniens, a ventral midline thalamic nucleus whose some collaterals project to both the mPFC and hippocampus, thus making it a key structure in the communication between the mPFC and hippocampus [36]. Since damage to nucleus reuniens specifically abolishes long-term memory of the goal location in a modified version of the water maze task [37], it appears that this communication is crucial for remembering as well as rapid encoding of goal locations [38,39] and more generally for spatial navigation [40].

How could mPFC goal cells be useful for spatial navigation? Several models have been proposed which fall into two classes. The first considers that navigation is achieved through the specification of a sequence of places to traverse to reach the goal. In this view, mPFC goal signals would be retro-propagated from the goal location to the rat's current location so as to activate the set of places that minimize the overall path to the goal [41,42]. The second class stipulates that navigation is achieved through the determination of the vector between the current and goal locations [43]. Although such computations are speculated to involve entorhinal grid cells [44,45], they would require a strong signal to mark the grid cell node corresponding to the goal location. There are connections from mPFC to the entorhinal cortex that are susceptible to convey goal information but it is currently unknown if these connections influence grid cell activity in any manner. However, it is also possible that reciprocal connections between the hippocampus and entorhinal cortex are sufficient to 'mark' the grid cell nodes to the goal location through place cell goal-related signals, which would make unnecessary a direct connection from mPFC to the entorhinal cortex. Finally, we note that the two mechanisms of goal-directed spatial navigation by vector representation and path computation are seen to operate flexibly and in parallel in humans and to activate the hippocampal formation [8,46••].

Conclusion

Key aspects from the current state of research on goal-oriented navigation highlight the central role of the hippocampus and medial prefrontal cortex in this process. However, these structures are likely just components of a more distributed neural network that necessarily combines the sensory and reward aspects of goal locations. Such network would therefore include the orbitofrontal cortex [47,48], the ventral striatum [49] and the ventral tegmental area [50] (see Figure 1e–g). Keeping a goal location in memory therefore requires activation of a widespread brain network.

As a final note, we would like to stress the possibility that remembering goal locations may be supported by dynamic coding and retrieval of information at certain stages of navigation such as when planning a path or making a decision at waypoints. Accumulating evidence strongly support the existence of various forms of prospective signals in the discharge of hippocampal place cells during these stages both in animals [51–53,54•] and humans [55••]. It is still unclear if such prospective firing codes a representation of the goal location [56] or a route

to that goal [57]. The possibility also exists that place cells encode a vectorial representation of the goal as recently shown in bats [58], even though similar evidence in rats is lacking so far. Whatever the alternative, however, the existence of prospective firing suggests that goal memory results from the activity of neuronal assemblies involved in path planning. Such assemblies are shaped during learning so that important places are embedded in a topological representation of space from which possible sequences of places or actions can be derived to perform efficient navigation. Thus, understanding how goal locations are remembered could ultimately rely on understanding how path planning is achieved.

Conflict of interest statement

Nothing declared.

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- • of special interest
- •• of outstanding interest

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