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Cognitive Neuroscience: Navigating Human Verbal Memory

Arne D. Ekstrom[1,2,3]

[1]Center for Neuroscience, University of California, Davis, 1544 Newton Court, Davis, CA 95618

[2]Department of Psychology, University of California, Davis,1 Shields Ave, Davis, CA 95616

[3]Neuroscience Graduate Group, University of California, Davis, 1 Shields Ave. Davis, CA 95616

SUMMARY

A recent study in humans shows that the same neurons that represent location during spatial navigation also code elements of verbal recall. This study thus provides a critical missing link between two previously unconnected functions of the hippocampus.

Decades of work have helped to establish the importance of neurons called place cells to spatial navigation [1-5]. A separate literature, largely based on neuropsychological and brain imaging studies of human verbal memory, demonstrates the importance of the hippocampus for remembering specific events (termed episodic memory) [6, 7]. Yet whether place cells, which are primarily located in the hippocampus, are part of a broader network of cells subserving episodic memory, is not known. A recent study by Miller and colleagues [8] shows that hippocampal place cells respond in the absence of spatial cues when spatial context is nonetheless retrieved during verbal free recall.

One of the most striking findings from rodent electrophysiology is the place cell, first noted by O'Keefe and Dostrovsky [1]. These neurons, located primarily in the hippocampus, increase firing rate at specific spatial locations. The collection of place cells in an environment provides a fairly accurate "map" of a rat's position within the environment [2]. The prevalence of place cells within the hippocampus, paired with findings that lesions to the hippocampus severely impair the ability of a rat to navigate using external-referenced landmarks [9], initially argued for a primary role of the hippocampus in spatial navigation [2, 3]. More recently, neurons in the medial entorhinal cortex, which show regularly spaced "grid-like" firing patterns [10, 11], argue for a more general role for the hippocampal complex (hippocampus and surrounding entorhinal and parahippocampal cortices) in spatial navigation.

Patients with damage to medial temporal lobe, which includes the hippocampus, demonstrate severe impairments in the ability to verbally recall recently experienced events, termed "episodic memories" [12]. Fueled by this critical advance, much subsequent work in humans focused on the role for the medial temporal lobe in episodic memory retrieval [13, 14]. Episodic memory is thought to involves representation of object-related information (e.g., a "jar") in surrounding perirhinal cortex and binding of this information with specific contextual details in the hippocampus [6]. Benchmark findings in this literature have demonstrated greater hippocampal involvement when participants must remember the location or color of a recently learned word compared to simply indicating whether the word was studied before [6, 7].

This binding process, whereby event-details are combined with object representations in the hippocampus, is thought to be a fundamental function of the hippocampus in humans [6]. Yet given the verbal nature of many human episodic memory paradigms, exactly how and in what manner contextual representations emerge in the first place remains unknown. Several studies have suggested that context representation could emerge from the posterior parahippocampal cortex [6], which shows unusual sensitivity when people view scenes compared to other objects [15]. In this way, context-related and object-specific responses could arrive in the hippocampus through separate yet parallel streams involving medial and lateral entorhinal cortex [16]. Yet the specific nature of contextual representations in the hippocampus and its relation to object coding, particularly during verbal memory retrieval, remains unclear.

Capitalizing on a rare situation involving epilepsy patients with electrodes implanted for surgical monitoring, Miller and colleagues recorded single neurons directly from the medial temporal lobes. This allowed Miller and colleagues to observe directly how neurons changed their firing rate as a function of spatial context during both navigation and verbal memory retrieval. Building on past studies that have employed virtual reality with humans and non-human primates to identify place responsive neurons [4, 5, 11], Miller and colleagues had patients explore a virtual environment by searching for certain stores. Upon locating a specific store, an object appeared (either visually or auditorily) at that store. Thus, if the patient delivered to the store “Pickle Store,” a jar might appear when the patient found that store; other stores involved different object pairings. Analyzing patient trajectories, Miller and colleagues demonstrated that significant numbers of medial temporal lobe neurons increased their firing rate at specific spatial locations within the virtual environment, consistent with past work in humans and non-human primates [4, 5, 11].

Yet the crucial innovation introduced by Miller and colleagues occurred following exploration of the spatial environment when patients freely verbally recalled objects from the environment. Critically, when participants recalled an object such as a jar, place cells that were nearby where this object was dropped off were more active than cells further from that location. Additionally, cellular firing rate patterns during free recall of objects more closely resembled those of place cells near that object compared to place cells further away from the object. Together, these findings suggest that when we recall objects from environments we have recently visited, place cells representing areas at or nearby the locations at which we encountered these objects are also active.

These findings thus help resolve an important debate about the function of the hippocampus. Consistent with theories positing a role for the hippocampus (across species) in spatial navigation [2, 3], the authors show neurons coding specific spatial locations during virtual exploration. Importantly, the authors demonstrate that these cells are also active during verbal recall such that they provide information about the spatial context that participants retrieve. These findings thus demonstrate that the neural machinery of the hippocampus, of which place cells are thought to be fundamental, are also active during verbal tasks that involve retrieval of that spatial context. These findings thus suggest that the spatial functions of the hippocampus play a more general role in episodic memory processes.

As with any important advance like the Miller et al. study, it also raises several novel and important research questions for future consideration. First, given the importance of object representations within the medial temporal lobe, how exactly does the activity of cells representing specific objects and stores activated during recall [17, 18] relate to place cell activity [16, 18, 19]? Second, given the potential importance of separate streams of input for object and spatial context into the hippocampus, how exactly is this information combined from perirhinal and parahippocampal cortices [16]? One intriguing possibility is that CA1 subfield of the hippocampus, which receives input both perirhinal and parahippocampal cortex (via entorhinal cortex) as well as subfield CA3, may play a role in integrating this information [20]. Third, to what extent are place cells and spatial context part of a more a general contextual coding apparatus, such as temporal or emotional context [6]? These issues pertaining to object and contextual representation are critical next steps to better decoding how memory is represented within the medial temporal lobes and further bridging the gap between research on rodents and humans.

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