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Navigating Life

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Abstract

The discoveries of “place cells” in the hippocampus and “grid cells” in the entorhinal cortex are landmark achievements in relating behavior to neural activity, permitting analysis of a powerful system for spatial representation in the brain. The contributions of this work include not only the empirical findings but also the approach this work pioneered of examining neural activity in complex behaviors with real ecological validity in freely moving animals, and of attempting to place the findings in the larger context of how the neural representations of space are used in service of real-world behavior, namely what the Nobel committee described as permitting us to “navigate our way through a complex environment.” These discoveries and approaches have had far-ranging impact on and implications for work in human cognitive neuroscience, where we see (1) confirmation in humans that the hippocampus and overlying MTL cortex are critically engaged in supporting a relational representation of space, and that it can be used for flexible spatial navigation and (2) evidence that these regions are also critically involved in aspects of relational memory not limited to space, and in the flexible use of hippocampal memory extending beyond spatial navigation. Recent work, using tasks that emphasize the requirement for the active use of memory in online processing, just as spatial navigation has long placed such a requirement on rodents, suggests that the hippocampus and related MTL cortex can support the navigating of environments even more complex than what is needed in spatial navigation. It allows us to use memory in guiding upcoming actions and choices to act optimally in and on the world, permitting us to navigate life in all its beautiful complexity.

Keywords

hippocampus; navigation; relational memory; space

INTRODUCTION

This commentary, together with the others in this special issue of *Hippocampus*, celebrates the awarding of the 2014 Nobel Prize in Physiology or Medicine to John O’Keefe, May-Britt Moser, and Edvard Moser “for their discoveries of cells that constitute a positioning system in the brain.” The charge for this brief commentary is to offer some observations about the implications for work in human cognitive neuroscience of the discovery of “place cells” and

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“grid cells” in the hippocampus and entorhinal cortex, respectively, and the proposed roles of these neurons and these brain regions in spatial mapping and navigation.

There is much to celebrate! The discovery of neurons in the hippocampus whose activity was determined by the location of the animal moving freely in space, that is, neurons with “place fields” (O’Keefe and Dostrovsky, 1971), was a landmark in relating behavior to neural activity, and the conclusion that these neurons mediate the creation of cognitive maps of the environment and the use of these maps to navigate through the environment (articulated more fully in O’Keefe and Nadel, 1978) has and continues to have an enormous impact on theoretical and empirical work in neuroscience. Its impact flows not just from the basic empirical findings themselves, but from (1) the success of the paradigm of examining neural activity in complex behaviors with real ecological validity in freely moving animals, and (2) the commitment to place the findings in the larger context of how the proposed representations of space by the hippocampus are used in service of the real-world behaviors being observed—navigating through space. The recording of neuronal activity in animals moving freely in the course of navigating one or another spatial environment has come to dominate research in this area of neuroscience, and has set the stage for numerous theories and models of the brain mechanisms of spatial navigation. The subsequent discovery and characterization of neurons in the neighboring entorhinal cortex that fired at multiple locations arrayed in a hexagonal grid pattern (Hafting et al., 2005; Moser et al., 2008) provided the necessary evidence concerning the mechanistic foundation for such theories and models. It pointed to neural networks that, operating together with hippocampal place cells and entorhinal head direction cells and boundary cells, can mediate the powerful spatial representation system that the Nobel committee cited as “a comprehensive positioning system, an inner GPS, in the brain” that permits us to “navigate our way through a complex environment.”

RELATIONSHIP TO HUMAN COGNITIVE NEUROSCIENCE

One of the most powerful features of research on memory and the brain is that memory can be studied in both humans and animals, and examined with a multitude of methods, aimed at one or another of multiple levels of brain organization, from cellular and molecular mechanisms, to single neurons, to circuits, networks, and systems. One of the great challenges, of course, is to be able to bridge the levels, to connect the phenomena across these various levels all the way to cognition and behavior. For the purposes of this commentary, we consider the relationship and some implications of the above discoveries specifically for human cognitive neuroscience, focusing particularly on the study of patients.

THE HIPPOCAMPUS, SPATIAL MEMORY, AND NAVIGATION

The hippocampus has long enjoyed a special place within the field of cognitive neuroscience, ever since the report of profound amnesia following bilateral medial temporal lobe resection, including a large portion of the hippocampus, in the patient H.M. (Scoville and Milner, 1957), who was the subject of intensive study for the ensuing five decades (see Corkin, 1984, 2002). The body of work with this patient and others with amnesia resulting from damage to the hippocampus has illuminated the critical role this structure plays in

memory, and in turn has energized many lines of neuroscientific investigations into hippocampus and memory.

With the discoveries relating hippocampal and entorhinal neuronal activity to spatial representation and navigation, several lines of cognitive neuroscience research on memory have focused on space. The memory deficits in hippocampal amnesia certainly include spatial or topographical memory (Milner et al., 1968; Ryan et al., 2000; Hannula et al., 2006, 2007; Maguire et al., 2006; Hartley et al., 2007; Konkel et al., 2008; Watson et al., 2013). For patients with Alzheimer's Disease, whose brain pathology includes entorhinal cortex and hippocampus relatively early in the disease process, wandering and getting lost is a well-known and particularly troublesome symptom, so much so that the Alzheimer's Association in collaboration with MedicAlert runs a 24-hour nationwide Safe Return program. Finally, patients with damage to MTL cortical areas, including parahippocampal and retrosplenial cortex, have deficits in topographic memory and/or spatial navigation (Aguirre and D'Esposito, 1999; Epstein et al., 2001).

Neuroimaging work has also addressed the involvement of hippocampus and MTL cortex in spatial memory and navigation. One particular well-known finding is that the volume of the posterior hippocampus in London taxi drivers was greater the more years of experience they had navigating through that large, very complex city, an effect not seen in London bus drivers with similar years of service (Maguire et al., 2006), strongly consistent with the idea that the hippocampus is involved in updating and using spatial representations for navigation. Functional neuroimaging work, likewise, has demonstrated the engagement of hippocampus and related areas of MTL cortex, as part of larger brain networks, in spatial navigation in humans (e.g., Maguire et al., 1998; Spiers and Maguire, 2007, 2008; Epstein, 2008; Howard et al., 2014; Zhang and Ekstrom, 2013); other commentaries in this issue will discuss such findings in more detail.

THE HIPPOCAMPUS AND MEMORY

An even more extensive literature in human cognitive neuroscience shows that spatial memories are not the only ones supported by the hippocampus, and spatial navigation is not the only application of memory dependent on hippocampal involvement. Patients with hippocampal amnesia have well established deficits in memory that are domain- and material-general, severely impairing declarative memory, the ability to learn and remember everyday facts and events (Cohen and Squire, 1980; Cohen and Eichenbaum, 1993). With regard to memory for events, or episodic memory (Tulving, 1972), such patients have profound deficits, critically, not just with regard to the where of events, but also with regard to the who, what, and when of events (e.g., Giovanello et al., 2003; Hannula et al., 2006; Konkel et al., 2008). One view of this is of an impairment in the binding in memory of the (spatial and non-spatial) relations among the constituent elements of events or of scenes, a deficit in relational memory (Cohen and Eichenbaum, 1993; Eichenbaum and Cohen, 2001, 2014; Konkel and Cohen, 2009). For example, one study of amnesia documented impaired memory not only for which objects had been studied where in space (spatial relations), but also which objects went when (temporal or sequential relations), and which objects were associated by having been studied together in the same trial, independent of spatial location

or temporal position (associative relations), all tests sampling different aspects of memory for the same complex study events (Konkel et al., 2008).

Likewise, functional neuroimaging studies implicate the hippocampus not only in spatial but also non-spatial memory (e.g., Davachi, 2006; Staresina and Davachi, 2009), with one particularly interesting line of work showing hippocampal activity related to temporal memory, paralleling work on hippocampal neuron coding of temporal relations in rats (see Eichenbaum, 2013; Eichenbaum and Cohen, 2014). Finally, while the volume of the hippocampus has been shown to be related to years of spatial navigation through the streets of London (Maguire et al., 2006), it has also been shown to be related to performance on a set of relational memory tasks differing in response modalities, stimulus modalities or cognitive domains (verbal, visual, and spatial), and delay intervals (from 4 s to 30 min; Monti et al., 2015).

Critically, while these findings from human cognitive neuroscience emphasize aspects of memory that extend beyond space and spatial navigation, the view that the hippocampus supports a fundamentally relational system (Cohen and Eichenbaum, 1993; Eichenbaum and Cohen, 2001, 2014; Eichenbaum, 2004) is also a central feature of the cognitive mapping view of hippocampus, albeit there specific to spatial relations (O'Keefe and Nadel, 1978). Thus, it was shown early on by O'Keefe (O'Keefe and Conway, 1978) and others (e.g., Muller and Kubie, 1987) that the place fields of hippocampal neurons were sensitive to, indeed controlled by, the relations among the set of environmental cues, just as those cues collectively define for the animal where it is in space (O'Keefe and Speakman, 1987; Shapiro et al., 1997). The cognitive mapping view holds that the hippocampus constructs representations of the topographic relations among elements of the environment, and the resulting allocentric representation of space—the cognitive map—can be thought of as a spatial relational system that can be used to provide the animal with information about its location in space and to guide the animal's behavior. This provides a strong connection between the earlier work on space and the more recent cognitive neuroscience literature.

THE FLEXIBILITY AND FLEXIBLE USE OF HIPPOCAMPAL MEMORY

A central aspect of the cognitive mapping view is that the “map” supported by place cells, grid cells, and related brain mechanisms is a flexible representation of space, which, as pointed out by the Nobel committee in their citation for the 2014 Nobel Prize in Physiology or Medicine, can be used to “navigate our way through a complex environment.” It can be used not merely to retrace earlier steps but, more powerfully, to generate or derive novel paths or trajectories through the environment. This is demonstrated nicely in findings from the Morris water maze in which animals are placed into a circular pool filled with milky water, with a platform hidden below the surface onto which they can climb to escape (Morris et al., 1982). Intact animals could learn the location of the hidden platform across trials with variable start locations, generating short swimming paths even from novel start locations, but animals with hippocampal damage could not do so; animals with hippocampal damage approximated the performance of intact animals only on a variant of the task where all they needed to learn were inflexible routes from a constant start location to a constant hidden platform location (Morris et al., 1982; Eichenbaum et al., 1990).

The idea that hippocampal memory can be used flexibly so as to be useful even in novel situations is also seen clearly in the human cognitive neuroscience literature (see Cohen, 1984; Graf and Schacter, 1989; Tulving and Schacter, 1990; Cohen et al., 1997; Eichenbaum and Cohen, 2014; Rubin et al., 2014). Several examples using spatial memory or navigation nicely illustrate the flexibility that hippocampal memory affords. Following hippocampal damage, a marked impairment was seen in testing in a 3D virtual environment when successful performance in recognizing scenes required the patient to flexibly vary their viewpoint (King et al., 2002). Another amnesic patient was able to learn to drive a small number of routes from her home to each of a few destinations; but she could only navigate to each of these locations from her home—she could not flexibly navigate among these few destinations, and on any of the home-to-destination routes, if there was road construction or a detour she would turn around and go home (Duff et al., 2008). A related finding from neuroimaging comes from the work mentioned earlier, contrasting London taxi drivers and bus drivers (Maguire et al., 2006), in which the relationship between size of hippocampus and years of driving in London was seen for the taxi drivers but not the bus drivers. This result was obtained presumably because while taxi drivers were constantly being challenged to flexibly generate routes between many different start locations and destinations, bus drivers instead drove fixed routes.

More recent work in human cognitive neuroscience further extends these findings on the flexible use of memory. In the Introduction, we noted that one of the very significant contributions of the work by John O’Keefe and Ervard and May-Britt Moser was the commitment to understand how hippocampal and entorhinal representations of space are actually used in service of real-world behaviors, in this case navigating through space. Several recent threads in human cognitive neuroscience likewise has investigated which other real-world behaviors might depend upon hippocampal memory. This work has benefited from the use of tasks that emphasize the requirement for the active use of memory in online processing, just as spatial navigation has long placed such a requirement on rodents. What we find in reviewing this new literature is that just as the involvement of hippocampus in human memory is not limited to space, so too the flexible use of hippocampal memory extends beyond spatial navigation.

The hippocampus, interconnected with MTL cortices and a host of neocortical networks, seems to play a critical role in the generation, recombination, and flexible use of information of all kinds, as revealed by deficits in patients with damage to the hippocampus in tests sampling various domains, including memory-guided behavioral choice, future imagining and projection, creativity, advantageous decision making, social evaluation and social discourse, and language use (see Rubin et al., 2014). For example, patients with hippocampal amnesia were impaired at generating rich descriptions of imaginary and future events (Hassabis et al., 2007; Kwan et al., 2010; Race et al., 2013), findings supported by functional neuroimaging studies showing hippocampal activation in tasks requiring participants to create fictional mental scenarios (Buckner and Carroll, 2007; Hassabis et al., 2007; Schacter and Addis, 2007; Schacter et al., 2007; Addis and Schacter, 2012). Patients with hippocampal amnesia were impaired on well-validated, standardized measures (Torrance Tests of Creative Thinking) of verbal and figural creativity, failing to generate the quantity or quality of creative responses generated by comparison participants (Duff et al.,

2013). On a widely used decision-making task, the Iowa Gambling Task, patients with hippocampal amnesia failed to develop a preference for advantageous over disadvantageous decks of cards across trials, responding only to the most current outcome and employing the most simplistic ‘lose-shift’ strategy (Gupta et al., 2009). In a task encouraging active volitional control of what and how long to study various items in a to-be-remembered set of items, patients with hippocampal amnesia made less advantageous search/study choices and failed to benefit at all in the active condition over passive viewing of the stimuli; in comparison participants, active volitional control engaged the hippocampus as part of a larger brain network, the activity of which predicted the magnitude of the benefit of the active over the passive condition (Voss et al., 2011, 2012). Finally, damage to the hippocampus impaired aspects of social communication that require creative and flexible uses of language, for example, producing less, and less creative, reported speech (representing or reenacting words or thoughts from other times and/or places into current speech output) and verbal play (in which speakers play with the sounds and meanings of words) in their social interactions with others (Duff et al., 2007, 2009; Duff and Brown-Schmidt, 2012).

NAVIGATING LIFE

We join with the Nobel Committee in recognizing the achievements of John O’Keefe and May-Britt and Edvard Moser, in their discoveries of place cells and grid cells, and in their contribution to illuminating how we “navigate our way through a complex environment.” In this final section of the commentary, we note that the recent developments in the human cognitive neuroscience literature discussed in the previous section may suggest an even more ambitious agenda for the hippocampus and related MTL structures. That is, in concert with the larger brain networks of which they are part, the hippocampus and related MTL cortices might actually help us navigate environments even more complex than what is needed in spatial navigation.

Humans are active agents, engaging with the world, actively acquiring and representing information about the environment and people, and manipulating, updating, and using those acquired representations flexibly to meet current situational demands. We use hippocampal memory to guide upcoming actions and choices in order to optimally act in and on the world (Rubin et al., 2014; Eichenbaum and Cohen, 2014; Wang et al., 2015). Accordingly, the discoveries we honor in this special issue help move us on the path toward an understanding of how the hippocampus and the memory system of which it is a key part, are capable of helping us to navigate life in all its beautiful complexity.

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References

Aguirre GK, D’Esposito M. Topographical disorientation: A synthesis and taxonomy. *Brain*. 1999; 122:1613–1628. [PubMed: 10468502]

- Addis DR, Schacter DL. The hippocampus and imagining the future: Where do we stand? *Front Hum Neurosci.* 2012; 5:173. [PubMed: 22291625]
- Buckner RL, Carroll DC. Self-projection and the brain. *Trends Cogn Sci.* 2007; 11:49–57. [PubMed: 17188554]
- Cohen, NJ. Preserved learning capacity in amnesia: Evidence for multiple memory systems. In: Butters, N., Squire, LR., editors. *Neuropsychology of Memory.* San Diego, CA: Guilford Press; 1984. p. 83-103.
- Cohen, NJ., Eichenbaum, H. *Memory, Amnesia, and the Hippocampal System.* Cambridge: MIT Press; 1993.
- Cohen NJ, Squire LR. Preserved learning of pattern-analyzing skill in amnesia: Dissociation of “knowing how” and “knowing that”. *Science.* 1980; 210:207–210. [PubMed: 7414331]
- Cohen NJ, Poldrack RA, Eichenbaum H. Memory for items and memory for relations in the procedural/declarative memory framework. *Memory.* 1997; 5:131–178. [PubMed: 9156097]
- Corkin S. Lasting consequences of bilateral medial temporal lobectomy: Clinical course and experimental findings in H.M. *Semin Neurol.* 1984; 4:249–259.
- Corkin S. What’s new with the amnesic patient H.M.? *Nat Rev Neurosci.* 2002; 3:153–160. [PubMed: 11836523]
- Davachi L. Item, context and relational episodic encoding in humans. *Curr Opin Neurobiol.* 2006; 16:693–700. [PubMed: 17097284]
- Duff MC, Brown-Schmidt S. The hippocampus and the flexible use and processing of language. *Front Hum Neurosci.* 2012;6. [PubMed: 22375109]
- Duff MC, Hengst JA, Tranel D, Cohen NJ. Talking across time: Using reported speech as a communicative resource in amnesia. *Aphasiology.* 2007; 21:702–716.
- Duff MC, Wszalek TW, Tranel D, Cohen NJ. Successful life outcome and management of real-world memory demands despite profound anterograde amnesia. *J Clin Exp Neuropsychol.* 2008; 30:931–945. [PubMed: 18608659]
- Duff MC, Hengst JA, Tranel D, Cohen NJ. Hippocampal amnesia disrupts verbal play and the creative use of language in social interaction. *Aphasiology.* 2009; 23:926–939. [PubMed: 20300442]
- Duff MC, Kurczek J, Rubin R, Cohen NJ, Tranel D. Hippocampal amnesia disrupts creative thinking. *Hippocampus.* 2013; 23:1143–1149. [PubMed: 24123555]
- Eichenbaum H. Hippocampus: Cognitive processes and neural representations that underlie declarative memory. *Neuron.* 2004; 44:109–120. [PubMed: 15450164]
- Eichenbaum H. *Memory on time.* *Trends Cogn Sci.* 2013; 17:81–88. [PubMed: 23318095]
- Eichenbaum, H., Cohen, NJ. *From Conditioning to Conscious Recollection: Memory Systems of the Brain.* Oxford: Oxford University Press; 2001.
- Eichenbaum H, Cohen NJ. Can we reconcile the declarative memory and spatial navigation views on hippocampal function? *Neuron.* 2014; 83:764–770. [PubMed: 25144874]
- Eichenbaum H, Stewart C, Morris RGM. Hippocampal representation in spatial learning. *J Neurosci.* 1990; 10:331–339.
- Epstein RA. Parahippocampal and retrosplenial contributions to human spatial navigation. *Trends Cogn Sci.* 2008; 12:388–396. [PubMed: 18760955]
- Epstein R, DeYoe EA, Press DZ, Rosen AC, Kanwisher N. Neuropsychological evidence for a topographical learning mechanism in parahippocampal cortex. *Cogn Neuropsychol.* 2001; 18:481–508. [PubMed: 20945226]
- Giovanello KS, Verfaellie M, Keane MM. Disproportionate deficit in associative recognition relative to item recognition in global amnesia. *Cogn Affect Behav Neurosci.* 2003; 3:86–194.
- Graf P, Schacter DL. Unitization and grouping mediate dissociations in memory for new associations. *J Exp Psychol Learn Mem Cogn.* 1989; 15:930–940.
- Gupta R, Duff MC, Denburg NL, Cohen NJ, Bechara A, Tranel D. Declarative memory is critical for sustained advantageous complex decision-making. *Neuropsychologia.* 2009; 47:1686–1693. [PubMed: 19397863]
- Hafting T, Fyhn M, Molden S, Moser MB, Moser EI. Microstructure of a spatial map in the entorhinal cortex. *Nature.* 2005; 436:801–806. [PubMed: 15965463]

- Hannula DE, Tranel D, Cohen NJ. The long and the short of it: Relational memory impairments in amnesia, even at short lags. *J Neurosci*. 2006; 26:8352–8359. [PubMed: 16899730]
- Hannula D, Ryan JD, Tranel D, Cohen NJ. Rapid onset relational memory effects are evident in eye movement behavior, but not in hippocampal amnesia. *J Cogn Neurosci*. 2007; 19:1690–1705. [PubMed: 17854282]
- Hartley T, Bird CM, Chan D, Cipolotti L, Husain M, Vargha-Khadem F, Burgess N. The hippocampus is required for short-term topographical memory in humans. *Hippocampus*. 2007; 17:34–48. [PubMed: 17143905]
- Hassabis D, Maguire EA. Deconstructing episodic memory with construction. *Trends Cogn Sci*. 2007; 11:299–306. [PubMed: 17548229]
- Hassabis D, Kumaran D, Vann SD, Maguire EA. Patients with hippocampal amnesia cannot imagine new experiences. *Proc Natl Acad Sci USA*. 2007; 104:1726–1731. [PubMed: 17229836]
- Howard LR, Javadi AH, Yu Y, Mill RD, Morrison LC, Knight R, Loftus MM, Staskute L, Spiers HJ. The hippocampus and entorhinal cortex encode the path and euclidean distances to goals during navigation. *Curr Biol*. 2014; 24:1331–1340. [PubMed: 24909328]
- King JA, Burgess N, Hartley T, Vargha-Khadem F, O’Keefe J. The human hippocampus and viewpoint dependence in spatial memory. *Hippocampus*. 2002; 12:811–820. [PubMed: 12542232]
- Konkel A, Cohen NJ. Relational memory and the hippocampus: Representations and methods. *Front Neurosci*. 2009; 3:166–174. [PubMed: 20011138]
- Konkel A, Warren DE, Duff MC, Tranel D, Cohen NJ. Hippocampal amnesia impairs all manner of relational memory. *Front Hum Neurosci*. 2008; 2:15. [PubMed: 18989388]
- Kwan D, Carson N, Addis DR, Rosenbaum RS. Deficits in past remembering extend to future imagining in a case of developmental amnesia. *Neuropsychologia*. 2010; 48:3179–3186. [PubMed: 20561535]
- Maguire EA, Burgess N, Donnett JG, Frackowiak RS, Frith CD, O’Keefe J. Knowing where and getting there: A human navigation network. *Science*. 1998; 280:921–924. [PubMed: 9572740]
- Maguire EA, Nannery R, Spiers HJ. Navigation around London by a taxi driver with bilateral hippocampal lesions. *Brain*. 2006; 129:2894–2907. [PubMed: 17071921]
- Maguire EA, Woollett K, Spiers HJ. London taxi drivers and bus drivers: A structural MRI and neuropsychological analysis. *Hippocampus*. 2006; 16:1091–1101. [PubMed: 17024677]
- Milner B, Corkin S, Teuber HL. *Neuropsychologia*. 1968; 6:215–234.
- Monti JM, Cooke Gillian E, Watson PD, Voss MW, Kramer AF, Cohen NJ. Relating hippocampus to relational memory processing across domains and delays. *J Cogn Neurosci*. 2015; 27:234–245. [PubMed: 25203273]
- Morris RGM, Garrud P, Rawlins JNP, O’Keefe J. Place navigation impaired in rats with hippocampal lesions. *Nature*. 1982; 297:681–683. [PubMed: 7088155]
- Moser EI, Kropff E, Moser MB. Place cells, grid cells, and the brain’s spatial representation system. *Annu Rev Neurosci*. 2008; 31:69–89. [PubMed: 18284371]
- Muller RU, Kubie JL. The effects of changes in the environment on the spatial firing of hippocampal complex-spike cells. *J Neurosci*. 1987; 7:1951–1968. [PubMed: 3612226]
- O’Keefe J, Conway DH. Hippocampal place units in the freely moving rat: Why they fire where they fire. *Exp Brain Res*. 1978; 31:573–590. [PubMed: 658182]
- O’Keefe J, Dostrovsky J. The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Res*. 1971; 34:171–175. [PubMed: 5124915]
- O’Keefe J., Nadel, L. *The Hippocampus as a Cognitive Map*. New York: Oxford University Press; 1978.
- O’Keefe J, Speakman A. Single unit activity in the rat hippocampus during a spatial memory task. *Exp Brain Res*. 1987; 68:1–27. [PubMed: 3691688]
- Race E, Keane MM, Verfaellie M. Losing sight of the future: Impaired semantic prospection following medial temporal lobe lesions. *Hippocampus*. 2013; 23:268–277. [PubMed: 23197413]
- Rubin RD, Watson PDK, Duff MC, Cohen NJ. The role of the hippocampus in flexible cognition and social behavior. *Front Hum Neurosci*. 2014; 8:742. [PubMed: 25324753]

- Ryan JD, Althoff RR, Whitlow S, Cohen NJ. Amnesia is a deficit in relational memory. *Psychol Sci*. 2000; 11:454–461. [PubMed: 11202489]
- Schacter DL, Addis DR. The cognitive neuroscience of constructive memory: Remembering the past and imagining the future. *Philos Trans R Soc B*. 2007; 362:773–786.
- Schacter DL, Addis DR, Buckner RL. Remembering the past to imagine the future: The prospective brain. *Nat Rev Neurosci*. 2007; 8:657–661. [PubMed: 17700624]
- Scoville WB, Milner B. Loss of recent memory after bilateral hippocampal lesions. *J Neurol Neurosurg Psychiatry*. 1957; 20:11–21. [PubMed: 13406589]
- Shapiro ML, Tanila H, Eichenbaum H. Cues that hippocampal place cells encode: Dynamic and hierarchical representation of local and distal stimuli. *Hippocampus*. 1997; 7:624–642. [PubMed: 9443059]
- Spiers HJ, Maguire EA. A navigational guidance system in the human brain. *Hippocampus*. 2007; 17:618–626. [PubMed: 17492693]
- Spiers HJ, Maguire EA. The dynamic nature of cognition during wayfinding. *J Environ Psychol*. 2008; 28:232–249. [PubMed: 19325934]
- Staresina BP, Davachi L. Mind the gap: Binding experiences across space and time in the human hippocampus. *Neuron*. 2009; 63:267–275. [PubMed: 19640484]
- Tulving, E. Episodic and semantic memory. In: Tulving, E., Donaldson, W., editors. *Organization of Memory*. NY: Academic Press; 1972. p. 381-402.
- Tulving E, Schacter DL. Priming and human memory systems. *Science*. 1990; 247:301–306. [PubMed: 2296719]
- Voss JL, Gonsalves BD, Federmeier KD, Tranel D, Cohen NJ. Hippocampal brain-network coordination during volitional exploratory behavior enhances learning. *Nat Neurosci*. 2011; 14:115–120. [PubMed: 21102449]
- Voss JL, Warren DE, Gonsalves BD, Federmeier KD, Tranel D, Cohen NJ. Spontaneous revisitation during visual exploration as a link among strategic behavior, learning, and the hippocampus. *Proc Natl Acad Sci USA*. 2012; 108:E402–E409.
- Wang JX, Cohen NJ, Voss JL. Covert rapid action-memory simulation (CRAMS): A hypothesis of hippocampal-prefrontal interactions for adaptive behavior. *Neurobiol Learn Mem*. 2015; 117c:22–33.
- Watson PD, Voss JL, Warren DE, Tranel D, Cohen NJ. Spatial reconstruction by patients with hippocampal damage is dominated by relational memory errors. *Hippocampus*. 2013; 23:570–580. [PubMed: 23418096]
- Zhang H, Ekstrom AD. Human neural systems underlying rigid and flexible forms of allocentric spatial representation. *Hum Brain Mapp*. 2013; 34:1070–1087. [PubMed: 22786703]