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Editorial

New perspectives on the hippocampus and memory

Memory research underwent a renaissance after the groundbreaking report of severe amnesia following resection of the hippocampus and medial temporal lobe cortex by Scoville and Milner in 1957 [1]. Milner's case reports on H.M., and her subsequent studies of amnesic patients, launched an entire field of research on the role of the hippocampus and surrounding medial temporal lobe cortex in the formation and retention of memories, and research on this topic grew exponentially over the next 60 years.

Over time, the myth of H.M. came to overshadow the complexities of the neurobiology and cognitive sequelae of amnesia. The majority of neuroscience and cognitive psychology textbooks now ascribe to the hippocampus and medial temporal lobe cortex a specialized role in episodic or declarative memory, to the exclusion of other functions, such as perception, working memory, and implicit memory. Moreover, brain areas outside of the medial temporal lobe are given limited consideration for their role in episodic memory.

Modern research, however, has shattered many of the myths described in the textbooks. It is still clear that the hippocampus is involved in, and critical for, episodic memory, but its role appears to be more nuanced than we initially thought. It is also clear that episodic memory depends on a network that extends beyond the hippocampus. Moreover, accumulating evidence suggests that the hippocampus contributes to many cognitive domains beyond long-term memory. These findings have prompted many of us to question long-held dogmas about the hippocampus, along with the idea that memory is an ability that can be separated from other forms of cognition.

The goal of this special issue is to call attention to new perspectives on the functions of the hippocampus, how it performs these functions, and how future research can address outstanding controversies and better characterize the hippocampus and the networks with which it interacts.

A great deal can be understood about the hippocampus by taking a phylogenetic perspective. Murray, Wise, and Graham [2] take such an approach, and they delve into how the functions of the hippocampus might have developed over the course of evolution. Specifically, the development of foveal vision in primates enabled our ancestors to forage in an extensive spatial environment, and make decisions at a distance based on information in the visual scene. The authors argue that these developments enabled specialization of the primate hippocampus in the representation of visual scenes, as well as more abstract spatial representations. They suggest that these basic functions of the hippocampus are recruited to represent temporal and spatial information that supports perception, implicit memory, and explicit memory.

The claim that the hippocampus plays a role in perception is a hotly contested one. But it is just one of many recent discoveries that the hippocampus, far from being a dedicated memory system, makes important contributions to many different cognitive domains. Aly and Turk-Browne [3] try to answer the question of how, and why, the hippocampus plays a broad role in cognition. They argue that the hippocampus can play a role in many different functions because it is particularly malleable, with such malleability due to its diverse anatomical inputs and the flexible weighting of those inputs with different behavioral goals. They suggest that a core set of hippocampal computations, alongside this malleability, enable the hippocampus to contribute broadly to cognition, including attention, perception, and memory.

Moving from attention and perception to more abstract knowledge, Elward and Vargha-Khadem [4] examine the literature on developmental amnesia, and they ask in what ways early hippocampal damage affects episodic memory and the emergence of semantic memory. Despite deficits in episodic and autobiographical memory, individuals with developmental amnesia can learn semantic knowledge in the real world, suggesting that such knowledge can be learned via cortical routes independent of the hippocampus. Nevertheless, these individuals are slower to acquire new semantic information in laboratory settings, showing that hippocampally dependent episodic memory might be used to bolster semantic learning, at least initially.

Mack, Love, and Preston [5] further consider how the episodic memory functions of the hippocampus can enable the formation of new conceptual knowledge. Focusing on computational models and neuroimaging, they show how hippocampal memory integration, attentional modulation, and prediction can be leveraged to elucidate how integrated knowledge structures can arise from individual, elemental memories. Thus, this work bridges the gap between the traditional perspective of the hippocampus as an episodic memory system, with new work showing its importance in building conceptual knowledge that is abstracted over many experiences.

That episodic memory can be used in the service of forming new semantic memories suggests that episodic memories might be transformed into memories that are context-independent and schematic. Indeed, episodic memories are not static, but change over their lifetime. Sekeres, Winocur, and Moscovitch [6] assess how detailed episodic memories can be transformed over time into memories that lack detail and contextual specificity, while nevertheless maintaining the gist of the initial memory (or its schematic features). They propose a differential representation of these aspects of an episodic memory, with posterior hippocampus and posterior neocortex forming a network that represents the detailed perceptual, spatial, and temporal components of

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an episodic memory; anterior hippocampus and anterior neocortex representing the gist of an episode; and medial prefrontal cortex representing the schematic aspects of events that are relevant to many different episodic memories. They argue that with memory transformation over time (i.e., as details are lost, but gist and schema maintained), there is a shift from the posterior network to the anterior network. By broadening their memory transformation model to accommodate new findings, their proposal poses a significant challenge to traditional models of systems consolidation.

Hardt and Nadel [7] further discuss memory consolidation and transformation, focusing on recent technological innovations that have enabled researchers to test memory consolidation in animal models. They highlight the ambiguity of such research, because this work often does not measure the quality of the memory and how it may be changed from recent to remote time points. Like Sekeres et al., Hardt and Nadel suggest that systems consolidation involves transformation of memories. Consequently, they argue, it is necessary to perform careful behavioral assessments of the quality of the memory in order to clarify how different neural systems support recent vs. remote memories.

Much progress in memory research has come by considering how the brain can recognize or recall events that have taken place previously. However, there is a long tradition of research on the opposite question of how the brain identifies and processes novel information and events. Kafkas and Montaldi [8] tackle this issue, and they challenge the simple notion that novelty is simply the flip side of memory. Instead, they highlight evidence suggesting that there are important differences between "absolute novelty" vs "contextual novelty". Thus, just as memory for prior events can be subdivided — e.g., into item vs relational or contextual memory — one can distinguish between corresponding processes in novelty detection, and these processes may depend on different kinds of neuromodulation in the hippocampus.

Reagh and Ranganath [9] expand on the role of extra-hippocampal structures in episodic memory by exploring the larger-scale networks of which the hippocampus is a part. They argue that memory is not a function of specific localized regions but rather the dynamic interaction of many regions distributed throughout the brain. The different representations in medial temporal lobe structures (e.g., contextual information in the hippocampus and parahippocampal cortex; item information in the perirhinal cortex) are argued to be best understood in terms of the broader networks of which they are a part: a posterior medial network that represents knowledge that is used to generate situation models or contextual information, and an anterior temporal network that represents semantic and perceptual information about items, objects, and people. The hippocampus is part of both networks, thus enabling its diverse and essential role in episodic memory as well as other cognitive functions. Reagh and Ranganath describe how this framework can potentially shed light on themes, phenomena, and controversies in cognitive psychology.

A great deal of converging evidence reviewed in the above papers — from human neuropsychology, human neuroimaging, and animal models — suggests that the hippocampus is critical for representing the context in which events occurred, and either discriminating between or generalizing across similar contexts to support unique vs integrated memories, respectively. Although many theories emphasize the role of the hippocampus in context representation, Stark, Reagh, Yassa, and Stark [10] confront the challenges involved in defining and operationalizing context. Stark et al. propose three tenets for operationalizing context that can be used to direct future research (see [11] for a similar perspective). They argue that, by adopting a shared definition of context, considerable progress can be made in understanding exactly what aspects of context are key players in hippocampal memories, and whether and how other brain regions are critical for representing certain kinds of contextual details.

Taking an even broader perspective, Eichenbaum [12] questions assumptions about how neurons in the hippocampus and neocortex represent memories for past experiences. He points out that much of the literature on the hippocampus (e.g., studies of place cells) is based on the premise that neurons serve as feature detectors that respond maximally to different kinds of inputs (e.g., items, rewards, locations, etc). Eichenbaum contrasts this assumption with Hebb's proposal [13] that memories are encoded by populations of neurons called "cell assemblies". The latter view implies that, even in the absence of cells that show clear featural selectivity, populations of cells with mixed selectivity can carry information about multiple aspects of experience. Consistent with the cell assembly hypothesis, Eichenbaum reviews evidence showing that, at the population level, neurons in inferotemporal cortex, hippocampus, and orbitofrontal cortex represent multiple different aspects of an experience in a hierarchical manner. This work raises questions about the existence of a qualitatively unique role for the hippocampus in memory, and instead suggests that many regions represent the same kinds of information, though the priority placed on each type of information may vary across brain areas.

Although the papers in this issue adopt different perspectives and address somewhat different questions, a common theme is that we have come a long way in understanding hippocampal function. Fifteen years ago, many of the ideas expressed here — the very idea that the hippocampus could play important roles in perception, working memory, attention, and implicit memory — would have seemed ridiculous. The papers in this issue demonstrate that these ideas are not only reasonable, but that they are compellingly supported by mechanistic theories of hippocampal function that focus on representations and computations, rather than domains of cognition.

The authors in this special issue represent only a subset of a large number of researchers who are advancing controversial perspectives about the functions of the hippocampus and the very nature of memory and cognition. Some ideas proposed here will fare better than others, but the important lesson to be gained from this special issue is that it is important to remain open to new ideas and pay attention to "odd" findings that fly in the face of dogma. A diversity of perspectives is necessary in order to advance science, and as a new generation of researchers takes on the hypotheses raised here, we can anticipate a number of breakthroughs and paradigm shifts in the coming years.

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We are grateful and honored that Howard Eichenbaum contributed to this special issue before he passed away on July 21, 2017. His work has had a tremendous influence in advancing the field of hippocampal research, evidenced by the numerous citations of his theories and discoveries in this special issue. We dedicate this issue to Howard, whose contributions will continue to extend over space and endure over time.

References

[1] W.B. Scoville, B. Milner, Loss of recent memory after bilateral hippocampal lesions, J. Neurol. Neurosurg. Psychiatry 20 (1957) 11–21.
[2] E.A. Murray, S.P. Wise, K.S. Graham, Representational specializations of the hippocampus in phylogenetic perspective, Neurosci. Lett. (2018), http://dx.doi.org/10.1016/j.neulet.2017.04.065 this issue.
[3] M. Aly, N.B. Turk-Browne, Flexible weighting of diverse inputs makes hippocampal function malleable, Neurosci. Lett. (2018), http://dx.doi.org/10.1016/j.neulet.2017.05.063 this issue.
[4] R.L. Elward, F. Vargha-Khadem, Semantic memory in developmental amnesia, Neurosci. Lett. (2018), http://dx.doi.org/10.1016/j.neulet.2018.04.040 this issue.
[5] M.L. Mack, B.C. Love, A.R. Preston, Building concepts one episode at a time: the hippocampus and concept formation, Neurosci. Lett. (2018), http://dx.doi.org/10.1016/j.neulet.2017.07.061 this issue.
[6] M.J. Sekeres, G. Winocur, M. Moscovitch, The hippocampus and related neocortical structures in memory transformation, Neurosci. Lett. (2018), http://dx.doi.org/10.

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1016/j.neulet.2018.05.006 this issue.
[7] O. Hardt, L. Nadel, Systems consolidation revisited, but not revised: the promise and limits of optogenetics in the study of memory, Neurosci. Lett. (2018), http://dx.doi.org/10.1016/j.neulet.2017.11.062 this issue.
[8] A. Kafkas, D. Montaldi, How do memory systems detect and respond to novelty? Neurosci. Lett. (2018), http://dx.doi.org/10.1016/j.neulet.2018.01.053 this issue.
[9] Z.M. Reagh, C. Ranganath, What does the functional organization of cortico-hippocampal networks tell us about the functional organization of memory? Neurosci. Lett. (2018), http://dx.doi.org/10.1016/j.neulet.2018.04.050 this issue.
[10] S.M. Stark, Z.M. Reagh, M.A. Yassa, C.E.L. Stark, What's in a context? Cautions, limitations, and potential paths forward, Neurosci. Lett. (2018), http://dx.doi.org/10.1016/j.neulet.2017.05.022 this issue.
[11] C. Ranganath, A unified framework for the functional organization of the medial temporal lobes and the phenomenology of episodic memory, Hippocampus 20 (2010) 1263–1290.
[12] H. Eichenbaum, Barlow versus Hebb: when is it time to abandon the notion of feature detectors and adopt the cell assembly as the unit of cognition? Neurosci. Lett. (2018), http://dx.doi.org/10.1016/j.neulet.2017.04.006 this issue.
[13] D.O. Hebb, The Organization of Behavior, John Wiley and Sons, New York, 1949.

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