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Review article

Flexible weighting of diverse inputs makes hippocampal function malleable

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HIGHLIGHTS

- The hippocampus contributes to many domains of cognition beyond long-term memory.
- This results from a diversity of anatomical inputs and the flexibility of their weighting.
- A core set of computations performed on these weighted inputs support its broad role.

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ABSTRACT

Classic theories of hippocampal function have emphasized its role as a dedicated memory system, but recent research has shown that it contributes broadly to many aspects of cognition, including attention and perception. We propose that the reason the hippocampus plays such a broad role in cognition is that its function is particularly malleable. We argue that this malleability arises because the hippocampus receives diverse anatomical inputs and these inputs are flexibly weighted based on behavioral goals. We discuss examples of how hippocampal representations can be flexibly weighted, focusing on hippocampal modulation by attention. Finally, we suggest some general neural mechanisms and core hippocampal computations that may enable the hippocampus to support diverse cognitive functions, including attention, perception, and memory. Together, this work suggests that great progress can and has been made in understanding the hippocampus by considering how the domain-general computations it performs allow it to dynamically contribute to many different behaviors.

Contents

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1. Introduction

The brain is hierarchically organized along multiple dimensions, including space, time, and features. For example, spatial receptive fields are smallest in primary visual cortex and increase in size throughout the ventral visual stream [1]. Likewise, primary visual cortex responds to simple features such as oriented edges, whereas downstream areas are driven by more complex feature combinations, such as shapes, objects, faces, and scenes, as well as information from other modalities [1–3]. Finally, information from the current environment is preferentially represented in early sensory areas, whereas information integrated over the past several seconds or minutes is represented in higher-order areas in posterior medial cortex [4].

The brain also contains a more abstract hierarchy of "malleability" – the extent to which neural function is fixed and immutable vs. influenced by other processes and variable across tasks. The retina is perhaps the least malleable: light signals are passed ballistically along a fixed route from photoreceptors to bipolar cells to ganglion cells; this pathway supports a very specific function (transduction of light and transmission to visual areas in the brain); and the direction that information is routed and what function it performs are unaffected by abstract factors such as memories, motivations, or goals.

Early visual cortex is relatively more malleable. On one hand, neurons respond to specific features and locations in a standard and reliable way that can be described by a unidimensional tuning curve. On the other hand, this tuning can be modulated by top-down or feedback processes such as expectation, reward, and attention [5–9].

The hippocampus is perhaps at the apex of this hierarchy of malleability, along with other regions like prefrontal cortex (which is beyond the scope of this paper, but will be discussed briefly in Section 4). For example, unlike cells in early visual cortex, individual hippocampal cells can have mixed selectivity, responding to multiple dimensions such as object identities, object positions, spatial contexts, and rewards [10,11]. Such mixed selectivity means that hippocampal cells can change how they respond as a function of task demands or goal states. By definition, this is a key aspect of malleability as we discussed above. The hippocampus is also malleable in that it contributes broadly to many cognitive domains (including attention, perception, working memory, long-term memory, and decision making), and does so in a manner influenced by our goals and motivational states [11–16].

We propose that the malleability of hippocampal processing is tied to the *diversity* and *flexibility* of its inputs: the myriad types of information it receives from other brain areas, and how flexibly the weights on those inputs can change as a function of behavioral goals. We argue that the hippocampus, far from being a dedicated memory system, can be configured to contribute to many functions, and that future progress will come by considering how these functions load on different computations implemented in the hippocampus (Fig. 1).

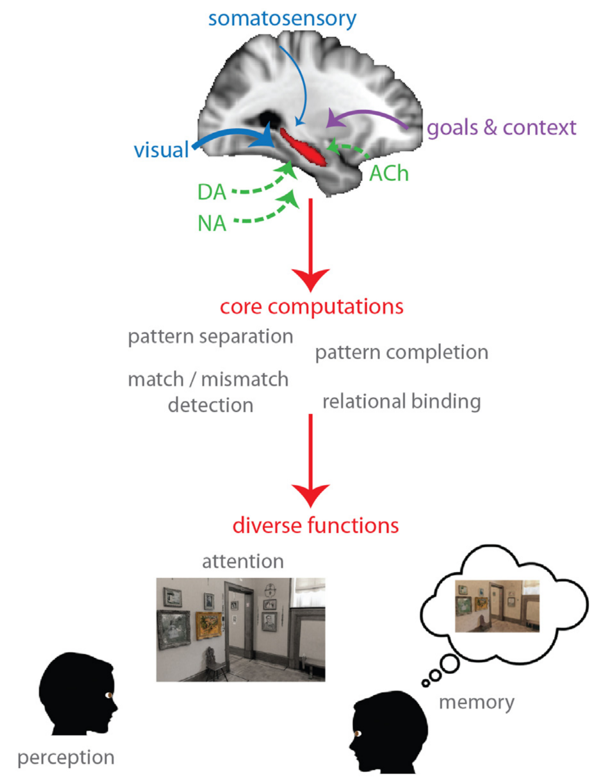

Fig. 1. *Top*: Multiple sensory modalities, including vision, audition, somatosensation, and olfaction, converge on the hippocampus. These inputs can be flexibly weighted based on behavioral goals and task context, which themselves are represented elsewhere, such as in frontoparietal cortex. In this example, visual signals are up-weighted (thicker arrow) while somatosensory signals are down-weighted (thinner arrow). Neuromodulatory systems, including dopaminergic (DA), cholinergic (ACh), and noradrenergic (NA) systems, can bias this flow of information and local processing. *Middle*: The hippocampus performs a core set of domain-general computations. *Bottom*: Flexibly weighted inputs, combined with some or all of these computations, enable the hippocampus to contribute to various cognitive functions.

2. Diversity of input: what features can the hippocampus represent?

The hippocampus receives indirect input (via medial temporal lobe cortex) from multiple sensory modalities, including vision, audition, somatosensation, and olfaction [1,3]. It also receives input from prefrontal cortex (e.g., information about goals, task rules, and contexts), both directly [17], and indirectly via the nucleus reuniens of the thalamus [18,19] and medial temporal lobe cortex [3]. Furthermore, it is modulated by the dopaminergic, cholinergic and noradrenergic systems [20–24]. Given this diversity of anatomical inputs and neuromodulation, it is no surprise that the hippocampus has been identified as a hub in brain networks [25–27].

The multiplicity of information relayed to the hippocampus makes it difficult to identify what "features" it represents. One dominant perspective – especially from the rodent literature – is that the hippocampus forms an allocentric (i.e., world-centered) representation of space, and its contribution to different domains of cognition can be understood via its role in representing spatial context [2,28–30]. An alternative, but complementary, perspective is that the hippocampus is fundamentally relational, and thus the "features" it represents are the associations between objects, locations, spatial and temporal contexts, rewards, and actions [11,13,16,31]. Thus, the hippocampus integrates multiple types of information, perhaps forming a conjunctive representation that subsumes all input features [25,32,33], enabling the retrieval of associatively related information and reinstatement of episode-specific patterns of activity that were present during encoding [34–37].

These two views – purely spatial vs. conjunctive/relational – have been compared in detail elsewhere [14,31]. In the current paper, we consider both spatial and (non-spatial) relational representations in the hippocampus.