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Review

The form and function of hippocampal context representations

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ABSTRACT

Context is an essential component of learning and memory processes, and the hippocampus is critical for encoding contextual information. However, connecting hippocampal physiology with its role in context and memory has only recently become possible. It is now clear that contexts are represented by coherent ensembles of hippocampal neurons and new optogenetic stimulation studies indicate that activity in these ensembles can trigger the retrieval of context appropriate memories. We interpret these findings in the light of recent evidence that the hippocampus is critically involved in using contextual information to prevent interference, and propose a theoretical framework for understanding contextual influence on memory retrieval. When a new context is encountered, a unique hippocampal ensemble is recruited to represent it. Memories for events that occur in the context become associated with the hippocampal representation. Revisiting the context causes the hippocampal context code to be re-expressed and the relevant memories are primed. As a result, retrieval of appropriate memories is enhanced and interference from memories belonging to other contexts is minimized.

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1. Introduction

The context plays an undeniably profound role in memory. Learned information is bound to the learning context, and the context can be a remarkably potent retrieval cue (Smith, 1988). Anyone who has returned to their childhood neighborhood after decades away can attest to the striking experience of long lost memories that come flooding back in vivid detail. Empirical studies of contextual cueing of memory have a long history in psychology. Items learned in one context are better recalled when testing takes place in the same context (Godden and Baddely, 1975). The context can also serve as a disambiguating cue that allows subjects to retrieve information associated with one context without interference from items learned in other contexts. For example, subjects who learn two lists of items in distinct contexts exhibit better recall than those who learn both lists in the same context (for review see Smith, 1988). In fact, the association between context and memory is so strong that simply asking subjects to think about the learning environment is sufficient to improve recall (Smith, 1979).

The hippocampus has been known to be involved in processing contextual information since the 1970s (Hirsh, 1974). In the decades since, several theories of hippocampal context coding have been proposed. Several authors have noted the similarity between spatial mapping functions of the hippocampus and representations of the environmental context (Mizumori, 2007; Nadel et al., 1985). Another theory holds that the hippocampus binds the various components of the context into a complex multimodal configural cue

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(Sutherland and Rudy, 1989). Yet another theory suggests that context representations are a natural consequence of the relational memory encoding functions of the hippocampus (Cohen and Eichenbaum, 1994). Despite these theoretical accounts, detailed knowledge about the form of these hippocampal context representations has only recently become available, with the advent of large scale neuronal population recording and ensemble stimulation techniques. In this article, we review new findings about the nature of hippocampal context representations and present evidence that each context a subject encounters is encoded by a unique ensemble of hippocampal neurons. With experience, these hippocampal ensemble context codes become associated with the memories and behaviors that are appropriate for that context. When subjects revisit a familiar context, the hippocampal context code is automatically re-expressed, thereby priming the relevant memories and reducing the interference from memories associated with other contexts.

2. The hippocampus and context

In this article, we focus our discussion on the nature of hippocampal context representations and their functional significance for preventing interference. More general discussion of the hippocampal role in contextual memory can be found in several comprehensive reviews (Eichenbaum et al., 2012; Holland and Bouton, 1999; Lee and Lee, 2013; Maren et al., 2013; Mizumori, 2013; Mizumori et al., 1999; Rudy, 2009). Current ideas about the hippocampal role in context coding have come primarily from two parallel streams of research on conditioning and spatial navigation. Conditioning research has shown that learned behaviors are linked to the learning environment (i.e. the context) and that hippocampal lesions reliably disrupt contextual associations (for reviews see Anagnostaras et al., 2001; Maren, 2001; Myers and Gluck, 1994). The most well studied of these behaviors is contextual fear conditioning, in which rats quickly learn to fear an environment where foot shock occurs. Hippocampal lesions selectively impair conditioned fear responses to the context but do not impair fear responses to phasic cues, such as a tone or light (Kim and Fanselow, 1992; Phillips and LeDoux, 1992). Other studies have shown that subjects with hippocampal lesions are insensitive to changes in the context. For example, intact control subjects trained in one context showed reduced responding when tested in another context, but subjects with hippocampal or entorhinal cortical damage continued to respond as if they did not notice the context had changed (Freeman et al., 1997; Honey and Good, 1993; Penick and Solomon, 1991). Finally, the hippocampus is needed for the ability to match a learned behavior with the appropriate context (Good and Honey, 1991; Kim et al., 2012; Smith et al., 2004). In one study (Smith et al., 2004), intact controls were readily able to learn one auditory discrimination problem in one context and a different discrimination in another context. In contrast, subjects with fornix lesions were severely impaired and were only able to learn one discrimination problem at a time. These findings suggest that the context can directly elicit conditioned responses or prime the relevant behaviors so that when an appropriate cue is encountered retrieval is facilitated.

As a number of authors have noted, the well-known spatial firing properties of hippocampal neurons (i.e. place fields, O'Keefe and Nadel, 1978) are consistent with the idea of a hippocampal role in representing contexts (Mizumori et al., 2007; Nadel et al., 1985; Smith, 2008). Hippocampal neurons reliably change their activity patterns in response to changes in the spatial/environmental context (Anderson and Jeffery, 2003; Muller and Kubie, 1987). However, it is now apparent that hippocampal neurons are also highly sensitive to a variety of non-environmental aspects of the experimental situation. For example, small changes in the task demands, such as switching from a random foraging strategy to following an experimenter-defined path for rewards, cause large changes in hippocampal place fields (i.e. remapping, Markus et al., 1995). This kind of hippocampal sensitivity to task demands has been seen in a variety of experimental conditions (Eichenbaum and Cohen, 1988; Ferbinteanu and Shapiro, 2003; Smith and Mizumori, 2006b; Wood et al., 2000). Hippocampal firing is also influenced by other non-environmental aspects of the situation, including whether the subject plays an active or passive role in the task (Terrazas et al., 2005), the strategy needed to solve the task (Eschenko and Mizumori, 2007), expectations (Skaggs and McNaughton, 1998) and even the subject's motivational state (Kennedy and Shapiro, 2009).

These observations complicate how we should think about hippocampal context coding. The term 'context' can be problematic due to the difficulty in clearly defining a concept that has been used in many different ways. By convention, most conditioning studies have operationally defined the context as the continuously present background cues. However, this convention should not limit the way we think about the neural systems that encode contexts. The notion of context is necessarily broad because it refers to any situation defined by a coherent set of conditions, and meaningful contextual distinctions frequently occur within a single environment. For example, a staff meeting and the department holiday party are very different contexts even though they may occur in the same conference room. Animals also differentiate these kinds of abstractly defined contexts, as do their hippocampal neurons. We will use the term context to refer to any experimental situation that has a coherent set of expectations and appropriate behaviors. More importantly, when we refer to a hippocampal context code, we specifically mean a representation that can uniquely identify a given experimental situation, regardless of whether that situation is characterized by a particular environment or by more abstract features such as the task demands.

We examined the hippocampal role in encoding contexts in a series of neuronal recording studies in which rats learned to distinguish two different behavioral contexts (Fig. 1, Smith and Mizumori, 2006b). In this task, rats were trained to approach the east arm of a plus maze during the first block of fifteen trials of each session and to approach the west arm during the second block of trials, creating two distinct behaviorally-defined contexts. After learning, hippocampal neuronal firing was markedly different in the "go east" and "go west" contexts. Differential responses included changes in spatial firing as well as firing that occurred during the intertrial interval and firing associated with retrieving the reward. In short, hippocampal neurons responded to a variety of task events and stimuli and these responses were highly specific to each of the behavioral contexts. The context specific firing patterns developed as the rats learned and they did not develop in a control condition that did not involve a context manipulation. Moreover, muscimol inactivation of the dorsal hippocampus impaired learning, suggesting that differential firing patterns were necessary for the ability to distinguish the two contexts. These studies and other similar experiments (Eschenko and Mizumori, 2007; Ferbinteanu and Shapiro, 2003) suggest that hippocampal neurons respond to changes in behaviorally defined contexts in much the same way that they respond to changes in the spatial and environmental context, by generating a new representation.

On the basis of these results, we proposed the hypothesis that hippocampal firing patterns, when considered at the population level, could serve as a neural representation of the context (Smith and Mizumori, 2006a). However, although these studies recorded activity from dozens or hundreds of neurons, the basic unit of analysis was the individual neuron and population dynamics cannot readily be inferred from the activity of individual neurons. For