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Temporal and Rate Coding for Discrete Event Sequences in the Hippocampus

Highlights

- CA1 neurons exhibited nonspatial event-specific elevated firing activities
- These "event cells" displayed transient theta phase precession at event onset
- Transient phase precession was followed by phase locking to early theta phases
- Theta sequences of CA1 neurons for event sequences had discrete representations

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In Brief

Terada et al. investigated the neuronal representations of nonspatial event sequences in the hippocampus and demonstrate that discrete event sequences are encoded by theta sequences of CA1 cell assemblies similar to space encoding.

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Temporal and Rate Coding for Discrete Event Sequences in the Hippocampus

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SUMMARY

Although the hippocampus is critical to episodic memory, neuronal representations supporting this role, especially relating to nonspatial information, remain elusive. Here, we investigated rate and temporal coding of hippocampal CA1 neurons in rats performing a cue-combination task that requires the integration of sequentially provided sound and odor cues. The majority of CA1 neurons displayed sensory cue-, combination-, or choice-specific (simply, "event"-specific) elevated discharge activities, which were sustained throughout the event period. These event cells underwent transient theta phase precession at event onset, followed by sustained phase locking to the early theta phases. As a result of this unique single neuron behavior, the theta sequences of CA1 cell assemblies of the event sequences had discrete representations. These results help to update the conceptual framework for space encoding toward a more general model of episodic event representations in the hippocampus.

INTRODUCTION

The hippocampus is fundamental for the neuronal encoding of episodic memory and spatial navigation (O'Keefe and Nadel, 1978; Tulving and Markowitsch, 1998; Burgess et al., 2002; Leutgeb et al., 2005), both of which consist of sequential representations of events or locations. These sequences involve both rate and temporal coding of information across the ensembles of active neurons. Rate coding takes the form of receptive fields of locations (i.e., place fields; O'Keefe and Dostrovsky, 1971), items (Wood et al., 1999; Quiroga et al., 2005), or time (Pastalkova et al., 2008; MacDonald et al., 2011; Kraus et al., 2013), while temporal coding can be seen in the phases of spike sequences on concurrent theta cycles, which shift as a function of distance relative to the center of the receptive field (i.e., phase precession; O'Keefe and Recce, 1993; Huxter et al., 2003; Buzsáki, 2002). With these two forms of coding, hippocampal cell assemblies generate sequential structures across single theta cycles, termed theta sequences, which compressively represent sequences of past, current, and future positions (Skaggs et al., 1996; Dragoi and Buzsáki, 2006; Foster and Wilson, 2007). However, the mechanisms of theta sequence formation remain largely unknown (Mehta et al., 2002; Harvey et al., 2009; Royer et al., 2012; Wang et al., 2015; Feng et al., 2015; Middleton and McHugh, 2016).

Recent studies demonstrated that hippocampal theta sequences can reflect optic-flow signals (Terrazas et al., 2005; Cei et al., 2014), motion speed information (Geisler et al., 2007), and intentions of goal-directions (Wikenheiser and Redish, 2015; Pastalkova et al., 2008). Further, theta phase precession can be observed even in the absence of spatial movement (Harris et al., 2002; Pastalkova et al., 2008; Lenck-Santini et al., 2008; Takahashi et al., 2014). These observations indicate that theta sequences during spatial navigation might reflect the dynamic integration of multiple types of information including external cues, locomotion, and internal metrics of the animal (Feng et al., 2015). This predicts that information integration is essential for updating internal models of the current situation and reorganizing the temporal structure of cell assemblies within theta cycles (Tsodyks et al., 1996; Lisman, 2005; Hasselmo, 2005; McNaughton et al., 2006; Foster and Knierim, 2012). To test this hypothesis, it is crucial to control the timing of information updating. However, in spatial navigation or time perception tasks, this is difficult due to the continuous nature of space and time.

To address this, we developed a decision-making task that requires the integration of nonspatial information. In this task, the rat's correct response is determined by a combination of two sensory cues (sound and odor). The key feature of this task is precise control of the timing of information updating by isolating two unique external inputs and sequencing the periods of the stimuli and choice actions. We found that many CA1 neurons showed stimulus-specific firing activities mostly sustained during the stimulus presentation period. Stimulus-specific cells demonstrated transient theta phase precession following stimulus onset but then became locked to early theta phases during the remainder of the stimulus presentation period. In consequence, the theta sequences of stimulus-specific cells had segmented and discrete representations. Our results indicate that information updating is essential for theta sequence

