Hippocampal and prefrontal cortical mechanisms for goal-directed and memory-guided behavior.

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ABSTRACT:

Mechanisms of memory-guided behavior were analyzed in a simulation of the hippocampus and prefrontal cortex which guided movements of a virtual rat in a virtual delayed spatial alternation task, in which correct turning response depended upon the previous episode. At the choice point, both possible episodes were retrieved in entorhianl cortex and temporal context from dentate gyrus and region CA3 allowed selection of one episode in CA1. Episodic retrieval allowed selection of correct goal-directed movement by prefrontal cortex circuits. Network activity replicates current source density during theta rhythm, as well as theta phase precession and context sensitivity of place cells.

SUMMARY:

Lesions of the hippocampus cause impairments in memory guided tasks including delayed spatial alternation, delayed match to position and the 8-arm radial maze (Markowska et al., 1989; Ennaceur et al., 2002, see Eichenbaum and Cohen, 2001). Many models have addressed hippocampal memory function, but few have explicitly modeled the actions of a virtual rat in these types of tasks. Ongoing research in the Hasselmo laboratory uses the MATLAB program and the CATACOMB simulation package (Cannon et al., 2002) to analyze cortical mechanisms involved in memory guided behavior in these tasks.

A number of models have addressed memory-guided behavior, but do not simultaneously address neurophysiological phenomena such as theta rhythm (Sharp et al., 1996; Redish and Touretzky, 2000). Recent models from the Hasselmo lab have addressed the role of theta rhythm in memory guided behavior (Hasselmo et al., 2002b, 2002c). However, several new features have been addressed in the models to be presented at CNS 2004. In particular, previous models from this lab used an interaction of a reverse spread of activity from the goal and forward retrieval activity to select next desired destination in the form of region CA1 activity. However, general goal-directed behavior is spared by hippocampal lesions, and appears to involve prefrontal cortical circuits. Therefore, we now use a model of prefrontal cortical circuitry to address the interaction of goal and current state, to obtain selection of the next action. This network implementation of goal directed function has features resembling aspects of temporal difference learning and action selection in reinforcement learning (Sutton and Barto, 1998). The hippocampal simulation interacts with this representation of prefrontal cortex.

In addition, the new simulations address context-dependent retrieval of full sequences of activity, which is necessary for memory-guided behavior in spatial alternation. This requires both encoding of the sequential associations between elements of an episode, as well as encoding of temporal context analogous to that described by Howard and Kahana (Howard and Kahana, 2002; Howard et al., 2004). Activity necessary for both aspects can be provided by sustained activity in entorhinal cortex due to cholinergic activation of intrinsic regenerating cation currents (Klink and Alonso, 1997; Fransen et al., 2002). As described in previous models (Jensen and Lisman, 1996; Hasselmo et al., 2002c), these currents allow slow behavioral transitions to cause sequential spiking which falls within the window of spike timing dependent synaptic plasticity (Levy and Steward, 1983; Bi and Poo, 1998). In addition, gradual decay of these representations allows formation of associations between a gradually changing temporal context (Howard and Kahana, 2002) and individual behavioral events.

Previous simulations of the hippocampus have demonstrated forward retrieval of individual sequences (Levy, 1996; Jensen and Lisman, 1996; Lisman, 1999). The simulation presented here addresses the additional problem of selective episodic retrieval without interference from other episodes. In the new simulations, sequential retrieval of all possible previous episodes occurs due to associations within the circuit. Selection of a single current episode without interference from other episodes involves the convergence of sequential retrieval with temporal context in region CA1 of the simulation. This utilizes dynamical interactions during theta rhythm which match features of the physiological data on theta rhythm obtained with current source density analysis (Brankack et al., 1993). The sequential read out of previous episodes resembles theta phase precession (Skaggs et al., 1996), but has the additional feature of context-dependent retrieval, which matches evidence for place cell responses specific to prior or future responses in spatial alternation (Wood et al., 2000). As before, the model requires separate phases of encoding and retrieval, such that synaptic modification for encoding occurs on one phase of theta rhythm (Holscher et al., 1997; Huerta and Lisman, 1993; Hyman et al., 2003), whereas retrieval occurs on a separate phase of theta rhythm (Hasselmo et al., 2002a).

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