Neurobiology of Learning and Memory 92 (2009) 559–573

Contents lists available at ScienceDirect

Neurobiology of Learning and Memory

journal homepage: www.elsevier.com/locate/ynlme

A model of episodic memory: Mental time travel along encoded trajectories using grid cells

Michael E. Hasselmo *

Center for Memory and Brain, Department of Psychology and Program in Neuroscience, Boston University, 2 Cummington St., Boston, MA 02215, United States

ARTICLE INFO

Article history:
Received 13 February 2009
Revised 20 June 2009
Accepted 12 July 2009
Available online 15 July 2009

Keywords:
Episodic memory
Entorhinal cortex
Hippocampus
Postsubiculum
Grid cells
Place cells
Head direction cells
Trajectory
Spatial cognition

ABSTRACT

The definition of episodic memory includes the concept of mental time travel: the ability to re-experience a previously experienced trajectory through continuous dimensions of space and time, and to recall specific events or stimuli along this trajectory. Lesions of the hippocampus and entorhinal cortex impair human episodic memory function and impair rat performance in tasks that could be solved by retrieval of trajectories. Recent physiological data suggests a novel model for encoding and retrieval of trajectories, and for associating specific stimuli with specific positions along the trajectory. During encoding in the model, external input drives the activity of head direction cells. Entorhinal grid cells integrate the head direction input to update an internal representation of location, and drive hippocampal place cells. Trajectories are encoded by Hebbian modification of excitatory synaptic connections between hippocampal place cells and head direction cells driven by external action. Associations are also formed between hippocampal cells and sensory stimuli. During retrieval, a sensory input cue activates hippocampal cells that drive head direction activity via previously modified synapses. Persistent spiking of head direction cells maintains the direction and speed of the action, updating the activity of entorhinal grid cells that thereby further update place cell activity. Additional cells, termed arc length cells, provide coding of trajectory segments based on the one-dimensional arc length from the context of prior actions or states, overcoming ambiguity where the overlap of trajectory segments causes multiple head directions to be associated with one place. These mechanisms allow retrieval of complex, self-crossing trajectories as continuous curves through space and time.

1. Introduction

Episodic memory includes the capacity to internally re-experience the sequence of events that occurred at particular places and times, in what has been termed "mental time travel" (Eichenbaum & Cohen, 2001; Tulving, 2001, 2002). Episodic memory includes the capacity to mentally retrace trajectories through previously visited locations, including re-experiencing specific stimuli encountered on this trajectory, and the relative timing of events. For example, you can probably remember the route you followed when you left your home this morning, with a memory of the locations you visited and the time you spent in individual locations. You can use this memory to remember where you parked the car, who you saw on your trip, or where you left your car keys. This aspect of episodic memory requires some means by which neurons can code continuous trajectories through space with time intervals representing the original episode. This also requires some means for encoding the location and time of specific events or stimuli encountered along this trajectory.

Physiological data shows that hippocampal activity during REM sleep can replay the relative time intervals of spiking activity evoked by different spatial locations during waking (Louie & Wilson, 2001), indicating the capacity to replay spatiotemporal trajectories with the same time scale as actual behavior. Other experiments also show that spiking activity in the hippocampal formation can maintain information about the relative timing of events (Berger, Rinaldi, Weisz, & Thompson, 1983; Deadwyler & Hampson, 2006; Hoehler & Thompson, 1980).

Lesion data suggests that encoding and retrieval of previously experienced episodic trajectories involves the entorhinal cortex and hippocampus. In humans, lesions of these structures cause profound impairments of episodic memory, tested both qualitatively and with quantitative measures in verbal memory tasks (Corkin, 1984; Eichenbaum & Cohen, 2003; Graf, Squire, & Mandler, 1984; Rempel-Clower, Zola, Squire, & Amaral, 1996; Scoville & Milner, 1957). Impairments in formation of object-location associations occur with right hippocampal or parahippocampal lesions (Bohbot, Allen, & Nadel, 2000; Bohbot et al., 1998; Milner, Johnsrude, & Crane, 1997; Stepankova, Fenton, Pastalkova, Kalina, & Bohbot, 2004). In rats, hippocampal manipulations impair performance in tasks that can be solved using episodic retrieval

* Fax: +1 617 358 3296.
E-mail address: hasselmo@bu.edu

1074-7427/$ - see front matter © 2009 Elsevier Inc. All rights reserved.
doi:10.1016/j.nlm.2009.07.005

of specific recent trajectories, including the 8-arm radial maze (Bunce, Sabolek, & Chrobak, 2004), delayed spatial alternation (Ennaceur, Neave, & Aggleton, 1996), the Morris water maze with new platform location on each day (Buresova, Bolhuis, & Bures, 1986; Steele & Morris, 1999) and a task testing a sequence of spatial locations (Lee, Jerman, & Kesner, 2005). Spatial memory is also impaired by lesions of the entorhinal cortex (Steffenach, Witter, Moser, & Moser, 2005) and postsubiculum (Taube, Kesslak, & Cotman, 1992). Learning of spatial trajectories may be a special case of a general capacity for learning sequences within the hippocampus (Eichenbaum, Dudchenko, Wood, Shapiro, & Tanila, 1999), including the sequential order of sensory stimuli (Agster, Fortin, & Eichenbaum, 2002; Fortin, Agster, & Eichenbaum, 2002; Kesner, Gilbert, & Barua, 2002; Kesner & Novak, 1982).

Many previous models of hippocampal function focus on its role in spatial navigation to goals (Burgess, Donnett, Jeffery, & O'Keefe, 1997; Foster, Morris, & Dayan, 2000; Touretzky & Redish, 1996; Trullier & Meyer, 2000), but not on episodic retrieval of specific trajectories. Most previous hippocampal models that focus on encoding and retrieval of sequences (Hasselmo & Eichenbaum, 2005; Jensen & Lisman, 1996a, 1996b; Levy, 1996; McNaughton & Morris, 1987; Minai & Levy, 1993; Redish & Touretzky, 1998; Treves & Rolls, 1994; Tsodyks, Skaggs, Sejnowski, & McNaughton, 1996; Wallenstein & Hasselmo, 1997; Zilli & Hasselmo, 2008c) focus on encoding associations between discrete sequential states (items or locations). However, recent data on grid cell firing in the entorhinal cortex (Barry, Hayman, Burgess, & Jeffery, 2007; Hafting, Fyhn, Molden, Moser, & Moser, 2005; Moser & Moser, 2008; Sargolini et al., 2006) suggests a different approach (Hasselmo, 2008b) in which each individual state (place) is associated with an action (the velocity coded by speed-modulated head direction cells).

This model of the episodic encoding and retrieval of trajectories can use either of two main classes of grid cell models. One class of models generates grid cells based on interference patterns (Burgess, 2008; Burgess, Barry, & O'Keefe, 2007). This model could use mechanisms of membrane potential oscillations shown in entorhinal neurons (Alonso & Llinas, 1989; Giocomo & Hasselmo, 2008a, 2008b; Giocomo, Zilli, Fransen, & Hasselmo, 2007; Hasselmo, Giocomo, & Zilli, 2007), or could use mechanisms of stable persistent spiking (Egorov, Hamam, Fransen, Hasselmo, & Alonso, 2002; Fransén, Tahvildari, Egorov, Hasselmo, & Alonso, 2006; Hasselmo, 2008; Tahvildari, Fransen, Alonso, & Hasselmo, 2007). The other class of models uses attractor dynamics to generate grid cell activity (Fuhs & Touretzky, 2006; McNaughton, Battaglia, Jensen, Moser, & Moser, 2006). The first type of model is used here, but either or both types of models could be used, because both models update grid cell position with a velocity signal from head direction cells. As shown here, a circuit mechanism using grid cells provides a substrate for encoding and retrieval of trajectories defined on continuous dimensions of space and time.

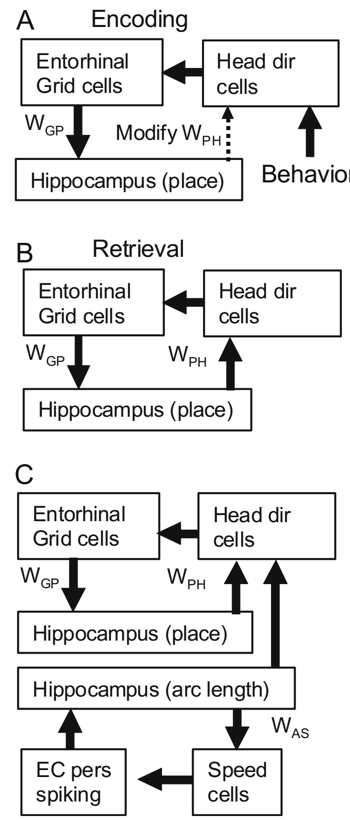

Fig. 1. Proposed circuit for episodic encoding of trajectories. (A) During encoding, head direction activity is driven by external behaviour. Head direction input updates grid cells in entorhinal cortex that drive place cell firing in the hippocampus. Associations between state (place) and action (speed and head direction) are formed by strengthening synapses between place cells and head direction cells W_{PH}. (B) During retrieval, place cells drive head direction cells via previously modified synapses W_{PH}. Head direction cells update grid cells that update place cells to complete the loop driving internal retrieval. (C) A parallel circuit generates arc length cells due to input from persistent spiking entorhinal neurons (EC pers spike) that fire near theta frequency and are modulated by input from cells coding rat movement speed (speed cells). Interference patterns generate cells that respond according to arc length along the one-dimensional trajectory. As shown in the figure, this parallel circuit also influences speed-modulated head direction cells to influence grid and place cells.

2. Materials and methods

2.1. Model of trajectory encoding and retrieval

The model presented here will consider encoding and retrieval of a trajectory of movement through the environment by an agent over time. The agent could be a human being or other mammal. The circuit model of encoding and retrieval is summarized in Fig. 1. The physiological data used to justify the model has primarily been obtained from the rat, including data on entorhinal grid cells (Fyhn, Hafting, Treves, Moser, & Moser, 2007; Hafting et al., 2005; Moser & Moser, 2008), head direction cells in structures such as postsubiculum (Sharp, 1996; Taube, 1998; Taube & Bassett, 2003; Taube, Muller, & Ranck, 1990a), hippocampal place cells (O'Keefe & Burgess, 1996, 2005), and context-dependent firing in hippocampus (Eichenbaum et al., 1999; Ferbinteanu & Shapiro, 2003; Griffin, Eichenbaum, & Hasselmo, 2007; Lee, Griffin, Zilli, Eichenbaum, & Hasselmo, 2006; Smith & Mizumori, 2006). Analogous neural responses have been demonstrated in non-human primates (Robertson, Rolls, Georges-Francois, & Panzeri, 1999; Rolls, Robertson, & Georges-Francois, 1997) and humans (Ekstrom et al., 2003). The following sections describe how the model uses representations of head direction activity, entorhinal grid cell activity, and hippocampal cell activity to perform episodic encoding and retrieval of trajectories.

2.2. Encoding associations between location and velocity

The model can encode the trajectory through the environment by encoding associations between location and velocity at each location. The two-dimensional location of an animal at one time can be represented with the row vector $\vec{x} = [x\ y]$. The trajectory through different locations over time can be represented by a sequence of vectors $\vec{x}(t)$. This representation can be obtained by integration of the velocity row vector $\vec{v}(t) = [dx/dt\ dy/dt]$. Integrating the velocity vector over time yields the current location vector $\vec{x}(t)$ at time t relative to the starting location vector $\vec{x}_0$, as follows: