Howard Eichenbaum 1947–2017

Marc Howard, Chantal E Stern & Michael E Hasselmo

Howard Eichenbaum, the Warren Professor in the Department of Psychological and Brain Science and the Director of the Center for Memory and Brain at Boston University, died 21 July 2017 during recovery from spinal surgery. A leader in the field of memory research, Howard Eichenbaum performed creative and innovative studies for decades. His work changed our understanding of the neurobiological basis of memory and in particular the role of the hippocampus in supporting long-term declarative memory.

A prolific writer and gifted speaker, Howard Eichenbaum's career illuminated the role of the hippocampus in both spatial and non-spatial memory, bridging between human and animal memory. While in his first faculty position at Wellesley College, and subsequently at the University of North Carolina, State University of New York at Stony Brook, and Boston University, Howard Eichenbaum and his lab members performed a series of groundbreaking studies using olfactory stimuli in rodents that illuminated the role of the hippocampus in memory. By the 1980s, the importance of the hippocampus in human episodic memory had been dramatically illustrated by Brenda Milner and Suzanne Corkin in studies of the famous amnesia patient H.M. By that time, research in rodents demonstrated that hippocampal lesions cause impairments of spatial memory, consistent with the discovery of hippocampal neurons that coded for the animal's current location in space, 'place cells'. However, initial results did not show clear behavioral deficits from hippocampal lesions in non-spatial tasks in rodents. Work in the Eichenbaum lab showed that the hippocampus was essential for learning complex relationships between stimuli. Neurophysiological work during this period showed that the hippocampus did not code only for spatial location, but also for nonspatial stimuli and combinations of spatial and nonspatial material. Together with human amnesia studies showing deficits in memory for the relations among stimuli, whether spatial or nonspatial, these findings provided evidence for an influential theory of the role of the hippocampus in relational memory. According to this view, developed with long-time friend and collaborator Neal Cohen, the hippocampus, rather than being exclusive to spatial memory, constructs a general 'memory space', supporting memory for relationships among all the constituent elements of an event.

In reflecting on his work during this period, Howard often noted that the methodological breakthrough was the use of olfactory stimuli during freely moving exploration of an environment. Because this approximated natural rat behavior, these methods led to relatively rapid learning and allowed the animal to demonstrate subtle behavioral effects that would be invisible in other, less natural behavioral models. "The problem with rats," Howard remarked in an early article about the Center for Memory and Brain, "is that I can't ask them if they remember what they had for breakfast. My ability to carry on a discussion with them about their memory is somewhat limited. I would like to relate my research to what's happening in humans, and the way to do that is to carry out parallel studies in

Marc Howard, Chantal E. Stern and Michael E. Hasselmo are at the Center for Memory and Brain, Department of Psychological and Brain Sciences, Boston University, Boston, Massachusetts, USA.

e-mail: hasselmo@bu.edu

Photograph taken at the 2003 founding of Boston University's Center for Memory and Brain. From left, Howard Eichenbaum, Denise Parisi, Michael Hasselmo and Chantal Stern.

Vernon Doucette

people that are inspired by studies in animals." He also felt strongly that neurophysiology was most effective when informed by consideration of the cognitive and psychological processes supporting behavior.

In his position at Boston University, Howard Eichenbaum's more recent research was centered on the neural mechanisms of episodic or declarative memory, which enables the retrieval of a specific event in a particular spatiotemporal context. His work showed that the hippocampus was an essential node in a network of regions responsible for episodic recollection (but not familiarity) in the rat. He coined the term 'time cells' to describe individual neurons within a population that each fire at different sequential time points during the delay period of memory experiments. Analogous to place cells, which fire when the animal is in a specific region of space, individual time cells fire during a specific period of time before or after a memorable event. Howard's work demonstrated that both time cells and place cells encode temporal and spatial relationships between stimuli. For instance, to learn the relationship "three minutes after the button on the coffee-maker is pressed, coffee becomes available," one could form an association between a time cell that fires three minutes after the button press to another cell that fires to signal the presence of the coffee reward. Similarly, place cells would enable encoding and recovery of spatial relationships, such as "the coffee maker is two meters from the north wall of the kitchen." In this framework, episodic recollection of a particular event corresponds to the reinstatement of the set of temporal and spatial relationships that were experienced as part of that event.

Recent neurophysiological work at Boston University in the Eichenbaum lab explored the role of the hippocampus in coding abstract contextual relationships. In these studies, the animal experiences odors with reward contingencies that vary with the spatial and/or behavioral context. Under these circumstances the hippocampus codes for all of these variables in a conjunctive hierarchical code that is shared among many brain regions, including the entorhinal cortex, prefrontal cortex and orbitofrontal cortex. This work places the hippocampus within a larger

network of regions that all feature mixed selectivity, responding to a mixture of task-relevant features.

All of us who had the honor of working with Howard knew the challenge of keeping up with his quick and energetic pace. One person whom Howard knew he could rely on to keep up with him was Denise Parisi. Denise worked tirelessly with Howard both at Boston University and for the journal *Hippocampus*. Paper drafts and manuscript reviews were returned within a day or two; many an evening e-mail would be returned by 6 a.m. A natural mentor, Howard Eichenbaum fostered the careers of numerous students, postdoctoral fellows and junior faculty in his laboratory. Moreover, he also founded and led undergraduate and graduate

training programs at Boston University that affected the training of an even wider set of students. He guided the field as editor-in-chief of the journal *Hippocampus* and as a member of the Council for the Society for Neuroscience and the National Advisory Mental Health Council of the US National Institute of Mental Health. Howard was also a fellow of the Association for Psychological Science, the American Academy of Arts and Sciences and the American Association for the Advancement of Science.

Howard Eichenbaum's work established essential principles of neural coding and memory that have influenced generations of researchers working in animal models and human cognitive neuroscience. This influence will certainly continue for many generations to come.