'Time cells' bridge the gap in memories of event sequences

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The hippocampus is a brain structure that plays a major role in the process of memory formation. It is not entirely clear how the hippocampus manages to string together events that are part of the same experience but are separated by "empty" periods of time. Now, new research published by Cell Press in the August 25 issue of the journal *Neuron* finds that there are neurons in the hippocampus that encode every sequential moment in a series of events that compose a discrete experience.

"The hippocampus is critical for remembering the flow of events in distinct experiences and, in doing so, bridges gaps between events that are separated by periods of time," explains senior study author, Dr. Howard Eichenbaum from the Center for Memory and Brain at Boston University. "We were interested in investigating how hippocampal neurons represent the temporal organization of extended experience and, more specifically, how they bridge the gaps between events that are discontiguous, that is, they do not occur in an immediate sequence."

Dr. Eichenbaum and colleagues developed an innovative task that required rats to distinguish sequences of two events that were separated by a time delay. The task required the rats to remember the initial event in order to respond appropriately to the second event and receive a reward. The researchers recorded hippocampal neural activity as the rats completed the tasks. "Our paradigm provided the opportunity to examine whether hippocampal neurons encode sequential events and to explore how the activity of hippocampal neurons bridges and disambiguates an

identical empty delay in time between events in the task sequence," explains Dr. Eichenbaum.

The researchers observed that activity in the hippocampus robustly represented sequential memories and that certain cells became activated at successive moments during the empty gap that occurred between the two events. "Each cell by itself provided a detailed 'snapshot' of the experience, and only at specific moments. But together, the activity from all of the cells filled in the gap," said coauthor Dr. Christopher MacDonald. The appropriately named "time cells" that were active have much in common with previously described "place cells" that are active when animals are at particular locations in space. The time cells were able to adjust, or "retime," when the duration of the delay period was altered.

Importantly, the activity of hippocampal neurons also signaled the timing of key events in the sequences and could differentiate between the different types of sequences. "Our findings suggest that hippocampal neurons segment temporally organized memories much the same as they represent locations of important events in spatially defined environments," concludes Dr. Eichenbaum. "Place cells and time cells may reflect fundamental mechanisms by which hippocampal neurons parse any spatiotemporal context into discrete units of where and when important events occur."

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