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Research Award Brief

A Rapid Neural Assay for Hippocampal Memory Formation (2014 - 2016)

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Research Question: How does the hippocampus support the creation of memories?

Interdisciplinary Approach: Our research combines neurophysiology with computational techniques to study neuronal patterns associated with memory formation in animals and humans.

Potential Implications of Research: We are exploring the development of a completely novel methodology for measuring replay activity, with wide application to both animal models and human patients.

Learning is fundamentally tied to our ability to form and retrieve memories. When learning occurs, a memory forms and corresponds to changes in the brain. While a great deal is known about changes at the molecular and cellular level in the brain, less is known about how neural activity patterns change. The hippocampus is a structure in the medial temporal lobe that is critical to the ability to form new memories, and in particular, memories of a certain kind. Remembering how to ride a bicycle is not dependent on the hippocampus, for example; instead the hippocampus is necessary for the kind of remembering that happens when someone asks you "What did you have for dinner yesterday evening?" or when you ask yourself "In which parking spot did I leave my car this morning?" The process happening in your mind when answering such questions has been called "mental time travel" by the psychologist Endel Tulving, who coined the term "episodic memory" for this kind of memory. Until recently, it has been difficult to understand how such a process might be supported by the neural circuitry of the brain.

Over the last decade, an understanding of how the hippocampus might support memory has begun to emerge from the study of how large numbers of cells in the hippocampus communicate with one another. By recording from the brains of freely behaving animals, it was found that collections of hippocampal cells would be activated together in brief bursts lasting about a tenth of a second, and occurring every second or so during periods of rest. While these bursts were first identified in sleep, it was later discovered that they occur also when animals were awake. Critically, the activity of cells during the bursts is far from random; rather, the activity represents speeded-up versions of the precise sequences of activity across different cells that have occurred previously during behavioral experience. For example, if a sequence of hippocampal cells responds in different places while an animal runs along a track, then the same sequence is "replayed" in temporally compressed form during rest-related population bursts. Our recent work examined these activity bursts in a spatial memory task; we found that the activity represented two-dimensional trajectories through space, generally starting from the current location and moving to the future location of the animal, predicting its behavior and reflecting the remembered location of a hidden chocolate reward in the task.

These findings suggest that sequenced activity across hippocampal cells might be a good candidate for the mechanism of episodic memory. However, a considerable technical challenge remains, since measuring sequenced activity requires recording from hundreds of well-isolated individual cells simultaneously in freely behaving organisms. Enormous time and care must be taken to position each of many recording electrodes in precisely the correct locations, and the resulting data sets take even longer to unpack and analyze, so that experiments take many years to complete.

In this project we are attempting to develop more efficient recording methods to obtain data from the population burst activity in the hippocampus. Specifically, we are developing a method for using local field potential recordings to recover information that corresponds to the encoding and retrieval of hippocampal memory. In collaboration with Dr. Stan Anderson of Johns Hopkins' Neurosurgery department, we plan to extend these methodologies to the human case, making use of recording technology used in human patients. We will build on essential previous animal studies to develop an electrophysiological assay for the formation of hippocampally dependent memories. We will ask whether the human brain exhibits the same signature of memory formation as we have found in our animal models, and whether this signature corresponds to the mental experience of memory you have when you remember where you parked your car.

For more information, please contact David Foster (david.foster@jhu.edu).