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LEARNING AND MEMORY

It's all in the timing

Theta oscillations occur in the hippocampus during periods of learning and are thought to support synaptic plasticity and memory formation. However, it was not understood how these oscillations relate to single-neuron activity in response to a stimulus and to the formation of a memory of that stimulus. Schuman and colleagues now show that, in humans, spike timing in single hippocampal and amygdala neurons is phase-locked with theta oscillations and that the strength of this phase-locking predicts the strength of the memory being formed.

Study participants with electrodes implanted in the hippocampus and amygdala performed a memory task. They were shown 100 images during the learning session followed by a second set of 100 images, half of which were new, during the subsequent memory session. For each image in the memory session, the participants had to indicate whether they had seen it before and how confident they were about their response. The authors recorded both the local field potential and the activity of individual hippocampal and amygdala neurons during the task.

Although the firing of many neurons increased in response to images presented during the learning session, the firing rate — both of individual neurons and of populations of neurons — did not predict whether a memory would be formed for an image. Interestingly, however, about one-fifth of the recorded neurons were phase-locked to the ongoing theta oscillations measured in the local field potential, with the majority of these neurons firing in response to an image close to either the peak or the trough of the oscillation.

To investigate the functional relevance of this spike timing, the authors determined the relationship between the spikes of single neurons and the ongoing theta oscillation during learning. They found that the spike–field coherence (SFC) was greater for images that were subsequently remembered than for images that were not remembered. Further analysis revealed that the increased SFC in 'remembered' (compared with 'forgotten') learning trials was particularly evident ~500 ms before and ~500 ms after stimulus onset, suggesting that these times might represent receptive states.

The authors also examined whether phase-locking predicted the confidence of subjects about the accuracy of their memory decisions. They found that the SFC was higher in strongly remembered than in weakly remembered learning trials and was lowest in forgotten trials.

These findings suggest that memory formation is stronger when neurons fire synchronously and that the theta rhythm acts as an internal clock by which neurons can time their action potentials during learning. Future studies might discover the projections and neurotransmitters that regulate the learning-related timing of action potentials in the hippocampus and amygdala.

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ORIGINAL RESEARCH PAPER Rutishauser, U. *et al.* Human memory strength is predicted by theta-frequency phase-locking of single neurons. *Nature* 24 Mar 2010 (doi: 10.1038/nature08860)