Brain Dynamics of Memory Consolidation During Sleep

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ABSTRACT

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Most modern theories of memory formation and consolidation posit that initially labile memory traces are formed in the hippocampus, then stabilized in neocortex for long-term storage. A seminal mechanistic model proposed that hippocampal endogenous activity during high frequency oscillations (*ripples*) played a key role in this process. This idea received striking correlative support with the discovery of sleep replay in rats, whereby neural activity patterns experienced during exploration of a maze are endogenously reactivated during sleep ripples, as if the rats were *dreaming* of their exploration.

Yet, direct causal evidence that these patterns were involved in memory consolidation remained elusive for the following 20 years. Using a real-time, closed-loop perturbation approach, we first demonstrated that selective ripple suppression during sleep significantly impaired memory consolidation on a spatial reference memory task. In a subsequent study, we trained rats to learn but not remember a spatial reference memory task, and showed that boosting during subsequent sleep the precise temporal coupling between ripples, cortical delta waves and thalamo-cortical spindles, triggered functional changes in neocortical subnetworks which induced memory consolidation and resulted in perfect performance upon recall on the next day. This provided direct and causal evidence for the long-hypothesized hippocampo-cortical dialogue underlying memory consolidation. Finally, we have recently shown that the emergence of sleep replay

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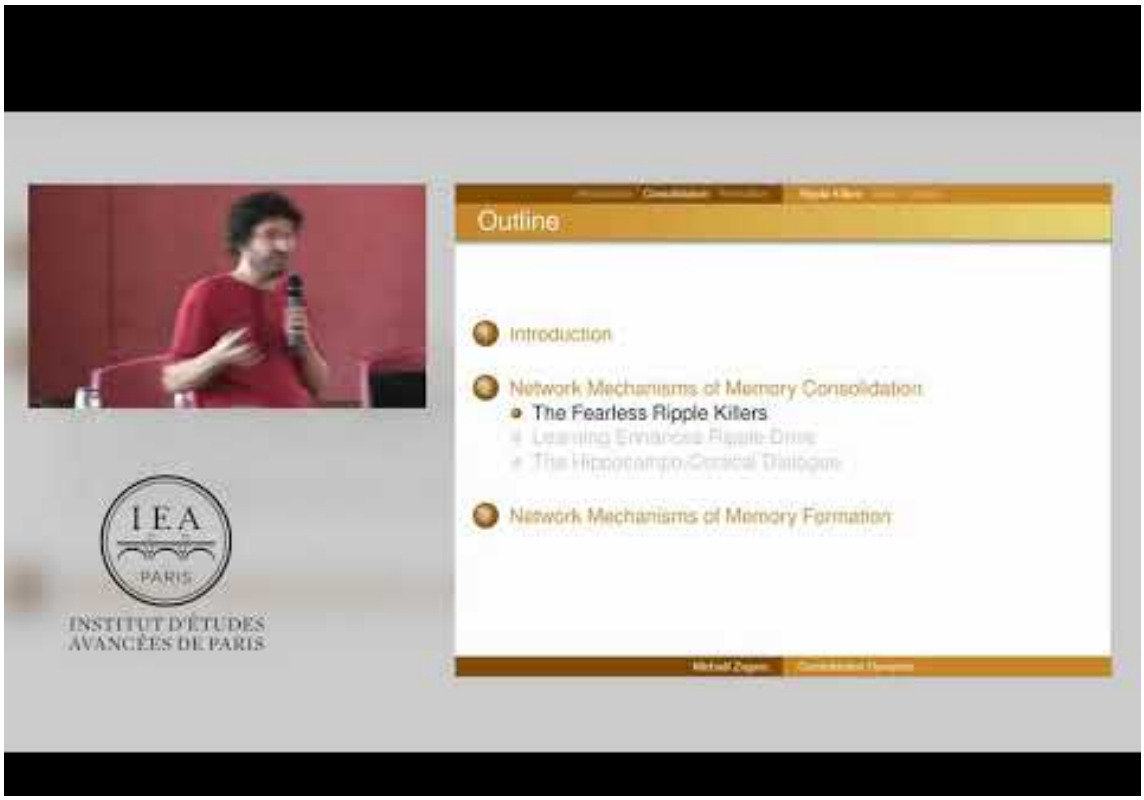
requires a delicate, fine timescale organization of hippocampal activity during previous behavior. This activity takes the form of fast sequences paced by ongoing theta oscillations, and are thus known as *theta sequences*. Our results show that theta sequences mediate the initial learning phase during

behavior. In summary, hippocampal sequences emerge during behavior, then endogenously reactivate during sleep ripples, finely coordinated with cortical rhythms. These network events mediate the formation and consolidation

of memory.



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