Dynamics of Retrieval Strategies for Remote Memories.

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Public Summary:
Prevailing theory suggests that long-term memories are encoded via a two-phase process requiring early involvement of the hippocampus followed by the neocortex. Contextual fear memories in rodents rely on the hippocampus immediately following training but are unaffected by hippocampal lesions or pharmacological inhibition weeks later. With fast optogenetic methods, we examine the real-time contribution of hippocampal CA1 excitatory neurons to remote memory and find that contextual fear memory recall, even weeks after training, can be reversibly abolished by temporally precise optogenetic inhibition of CA1. When this inhibition is extended to match the typical time course of pharmacological inhibition, remote hippocampus dependence converts to hippocampus independence, suggesting that long-term memory retrieval normally depends on the hippocampus but can adaptively shift to alternate structures. Further revealing the plasticity of mechanisms required for memory recall, we confirm the remote-timescale importance of the anterior cingulate cortex (ACC) and implicate CA1 in ACC recruitment for remote recall.

Scientific Abstract:
Prevailing theory suggests that long-term memories are encoded via a two-phase process requiring early involvement of the hippocampus followed by the neocortex. Contextual fear memories in rodents rely on the hippocampus immediately following training but are unaffected by hippocampal lesions or pharmacological inhibition weeks later. With fast optogenetic methods, we examine the real-time contribution of hippocampal CA1 excitatory neurons to remote memory and find that contextual fear memory recall, even weeks after training, can be reversibly abolished by temporally precise optogenetic inhibition of CA1. When this inhibition is extended to match the typical time course of pharmacological inhibition, remote hippocampus dependence converts to hippocampus independence, suggesting that long-term memory retrieval normally depends on the hippocampus but can adaptively shift to alternate structures. Further revealing the plasticity of mechanisms required for memory recall, we confirm the remote-timescale importance of the anterior cingulate cortex (ACC) and implicate CA1 in ACC recruitment for remote recall.