Abstract 388.8 Summary

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Small Groups of Neurons Evoke Complex Memories

Animal study shows stimulation of specific cell groups recalls past learning

Complex memories can be triggered by activating a tiny fraction of brain cells, according to new animal research. After specific groups of neurons — those associated with memory — were stimulated in mice, the animals froze in fear as they recalled frightful memories. The findings were presented at Neuroscience 2009, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

Exactly how the brain retrieves memories from its circuits is a long-explored topic of research. While there has been great progress in understanding memory retrieval, researchers still know little about how events from our past can be recalled under the right conditions.

In this case, scientists used two genetic tools to find how brain circuits are involved in memory recall. One was a gene that highlighted the particular cells associated with recent brain activity, such as learning something new. The second was a gene that produced a light-sensitive protein taken from algae that responds to blue laser light. The researchers used the first gene to mark recently active neurons, while the second gene (expressing the light-sensitive protein in the same neurons) made it possible for them to be activated by blue light.

"These tools allowed us to perform a powerful experiment: We could reactivate specific groups of cells and test whether this 'spark' was enough to recall the memory the animal had learned," said senior author Michael Hausser, PhD, at the Wolfson Institute for Biomedical Research in London.

The authors discovered that stimulating neurons in the hippocampus made mice freeze with fear because they remembered prior fearful experiences. When cells unassociated with learning and memory were stimulated, the mice did not appear fearful. Results also showed that activation of only a tiny fraction of neurons in the learning brain area were needed to recall memories.

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388.8, Memory recall driven by optical stimulation of functionally identified sub-populations of neurons
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TECHNICAL ABSTRACT: The mammalian brain is capable of storing information in sparse populations of neurons encompassing several brain areas. Immediate recall of this information is possible upon presentation of a cue or context. Most aspects of this process remain unresolved: are the cells involved in information storage also responsible for its recall? What portion of this distributed circuit needs to be reactivated, in order to achieve successful recall? To answer these questions we selectively expressed a genetically encoded optogenetic probe (Boyden et al., 2005) in neurons engaged during the learning of a specific association. A plasmid encoding channelrhodopsin-2 and EGFP under an immediate early gene promoter (c-fos-ChR2-IRES-EGFP) was electroporated in vivo into granule cells (GCs) of the dorsal dentate gyrus of anaesthetized C57BL/6 mice. Mice were allowed to recover, and then underwent classical delay fear conditioning (consisting of 10-20 pairings of a 5 second auditory tone and a 2 second footshock). An optic fiber was implanted intra-cranially to allow optical stimulation of transfected neurons. Light stimulation (λ = 530 nm; 5 Hz) successfully induced recall of the fear memory, measured as freezing behaviour (n = 27 animals). Post-hoc analysis of the transfected tissue revealed that a remarkably small subpopulation of GCs (<~100 cells) was sufficient to cause this effect. We then tested whether any, comparatively sized, subset of GCs could be equally effective. We transfected neurons with a plasmid encoding ChR2 expression under a general promoter (pCAG-ChR2) to obtain ChR2 expression in a random population of cells. Interestingly, optical stimulation of this population was insufficient to induce memory recall (population data: n=30). Our results therefore suggest that recall of a learned association, sparsely stored in neuronal circuits distributed over several brain areas, can be achieved by the simple reactivation of a very small subset of neurons involved in learning this association. Furthermore, our strategy may also be useful for dissecting the complexities associated with memory storage and recall.