MEMORY

ZIPping erases memories

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The neocortex is presumed to be the ultimate repository of many types of long-term memory, but little is known about the mechanisms that underlie memory preservation. Dudai and colleagues have now demonstrated that inhibiting the enzyme protein kinase Mζ (PKMζ), which was previously shown to be crucial for maintaining hippocampal long-term potentiation (LTP) and spatial memory, rapidly and perhaps permanently erases a long-term memory in the rat neocortex.

The authors used a conditioned taste-aversion paradigm to test rats' long-term memory. Rats normally prefer to drink a diluted saccharine solution rather than water, but if they receive an injection of nausea-inducing lithium chloride shortly after consuming saccharine (the conditioning phase of the paradigm), they develop a 'taste aversion' for the sweetener, which can then be observed in a test phase.

A few days after the conditioning phase, when the memory was assumed to have been stored, rats received microinfusions of the PKMζ inhibitor ZIP into the insular cortex, which processes, among other things, taste information. ZIP-treated rats still drank saccharine when they were tested 1 week or 1 month later, indicating that ZIP causes a long-term loss of taste-aversion memory. ZIP infusion blocked the memory even when it was given several weeks after conditioning, and its effect was measureable as early as 2 hours after administration. The authors tested rats several times after a single ZIP treatment, and found that the rats' memory did not recover. Even when they tried to boost the rats' memory by giving them a reminder exposure to lithium chloride, the taste-aversion memory could not be re-instated.

ZIP administration was able to disrupt memory for two conditioned stimuli at a time, indicating that PKMζ is not specific for any particular type of memory. However, ZIP-treated rats were still able to acquire a taste aversion for a new flavour, which indicates that ZIP does not damage the cortex and that PKMζ is not involved in the encoding of new memories into the insular cortex.

This study suggests that long-term storage of memories in the cortex requires constant maintenance, in which PKMζ is crucial. It is possible that PKMζ activity sustains synaptic contacts, similar to its role in maintaining LTP in the hippocampus, and that disrupting this process may cause a memory to disappear. It will be difficult to show whether PKMζ inhibition in the insular cortex disrupts all established gustatory memories, and it remains to be determined whether PKMζ has a role in long-term memory maintenance in other parts of the cortex. Despite these caveats, the findings offer the possibility that PKMζ might be used to enhance or therapeutically eliminate long-term memories.

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