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MEMORY MACHINE

What happens in our brains when we learn and remember? Are memories recorded in a stable physical change, like writing an inscription permanently on a clay tablet? Prof. Yadin Dudai, Head of the Weizmann Institute's Neurobiology Department, and his colleagues are challenging that view. They recently discovered that the process of storing long-term memories is much more dynamic, involving a miniature molecular machine that must run constantly to keep memories going. They also found that jamming the machine briefly can erase long-term memories. Their findings, which appeared today in the journal *Science*, may pave the way to future treatments for memory problems.

Dudai and research student Reut Shema, together with Todd Sacktor of the SUNY Downstate Medical Center, trained rats to avoid certain tastes. They then injected a drug to block a specific protein into the taste cortex – an area of the brain associated with taste memory. They hypothesized, on the basis of earlier research by Sacktor, that this protein, an enzyme called PKMzeta, acts as a miniature memory "machine" that keeps memory up and running. An enzyme causes structural and functional changes in other proteins: PKMzeta, located in the synapses – the functional contact points between nerve cells – changes some facets of the structure of synaptic contacts. It must be persistently active, however, to maintain this change, which is brought about by learning. Silencing PKMzeta, reasoned the scientists, should reverse the change in the synapse. And this is exactly what happened: Regardless of the taste the rats were trained to avoid, they forget their learned aversion after a single application of the drug. The technique worked as successfully a month after the memories were formed (in terms of life span, more or less analogous to years in humans) and all signs so far indicate that the affected unpleasant memories of the taste had indeed disappeared. This is the first time that memories in the brain were shown to be capable of erasure so long after their formation.

"This drug is a molecular version of jamming the operation of the machine," says Dudai. "When the machine stops, the memories stop as well." In other words, long-term memory is not a one-time inscription on the nerve network, but an ongoing process which the brain must continuously fuel and maintain. These findings raise the possibility of developing future, drug-based approaches for boosting and stabilizing memory.

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