New connections between brain cells form in clusters during learning

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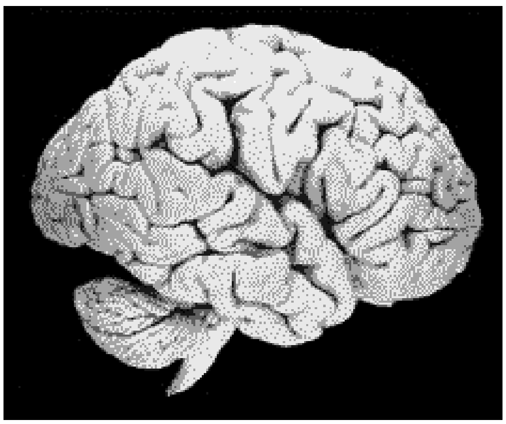

New connections between brain cells emerge in clusters in the brain as animals learn to perform a new task, according to a study published in *Nature* on February 19 (advance online publication). Led by researchers at the University of California, Santa Cruz, the study reveals details of how brain circuits are rewired during the formation of new motor memories.

The researchers studied mice as they learned new behaviors, such as reaching through a slot to get a seed. They observed changes in the motor cortex, the brain layer that controls muscle movements, during the learning process. Specifically, they followed the growth of new "dendritic spines," structures that form the connections (synapses) between nerve cells.

"For the first time we are able to observe the spatial distribution of new synapses related to the encoding of memory," said Yi Zuo, assistant professor of molecular, cell and developmental biology at UC Santa Cruz and corresponding author of the paper.

In a previous study, Zuo and others documented the rapid growth of new dendritic spines on pyramidal neurons in the motor cortex during the learning process. These spines form synapses where the pyramidal neurons receive input from other brain regions involved in motor memories and muscle movements. In the new study, first author Min Fu, a postdoctoral researcher in Zuo's lab, analyzed the spatial distribution of the newly formed synapses.

Initial results of the spatial analysis showed that one third of the newly formed synapses were located next to another new synapse. These clustered synapses tended to form over the course of a few days during the learning period, when the mouse was repeatedly performing the new behavior. Compared to non-clustered counterparts, the clustered synapses were more likely to persist through the learning sessions and after training stopped.

In addition, the researchers found that after formation of the second spine in a cluster, the first spine grew larger. The size of the spine head correlates with the strength of the synapse. "We found that formation of a second connection is correlated with a strengthening of the first connection, which suggests that they are likely to be involved in the same circuitry," Zuo said. "The clustering of synapses may serve to magnify the strength of the connections."

Another part of the study also supported the idea that the clustered synapses are involved in neural circuits specific to the task being learned.

The researchers studied mice trained first in one task and then in a different task. Instead of grabbing a seed, the mice had to learn how to handle a piece of capellini pasta. Both tasks induced the formation of clustered spines, but spines formed during the learning of different tasks did not cluster together.

The researchers also looked at mice that were challenged with new motor tasks every day, but did not repeat the same task over and over like the ones trained in seed-grabbing or capellini-handling. These mice also grew lots of new dendritic spines, but few of the new spines were clustered.

"Repetitive activation of the same cortical circuit is really important in learning a new task," Zuo said. "But what is the optimal frequency of repetition? Ultimately, by studying the relationship between synapse formation and learning, we want to find out the best way to induce new memories."

The study used mice that had been genetically altered to make a fluorescent protein within certain neurons in the motor cortex. The researchers used a special microscopy technique (two-photon microscopy) to obtain images of those neurons near the surface of the brain. The noninvasive imaging technique enabled them to view changes in individual brain cells of the mice before, during, and after learning a new behavior.

Provided by University of California - Santa Cruz

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