Mind-readers: Scientists crack a piece of the neural code for learning and memory (Update)

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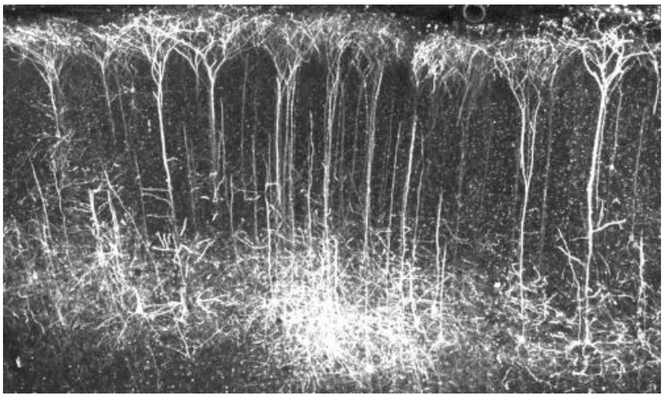

Scientists mapped and read sound memories in rat brains. Credit: Dr. Zador, Cold Spring Harbor Laboratory, N.Y.

Lights, sound, action: we are constantly learning how to incorporate outside sensations into our reactions in specific situations. In a new study, brain scientists have mapped changes in communication between nerve cells as rats learned to make specific decisions in response to particular sounds. The team then used this map to accurately predict the rats' reactions. These results add to our understanding of how the brain processes sensations and forms memories to inform behavior.

"We're reading the memories in the brain," said Anthony Zador, M.D., Ph.D., professor at Cold Spring Harbor Laboratory, New York, and senior author of the study, published in *Nature*. The work was funded by the National Institutes of Health and led by Qiaojie Xiong, Ph.D., a former postdoctoral researcher in Dr. Zador's laboratory.

"For decades scientists have been trying to map memories in the brain," said James Gnadt, Ph.D., a program director at the National Institute of Neurological Disorders and Stroke (NINDS), one of the NIH institutes that funded the study. "This study shows that scientists can begin to pinpoint the precise synapses where certain memories form and learning occurs."

The communication points, or synapses, that Dr. Zador's lab studied were in the striatum, an integrating center located deep inside the brain that is known to play an important role in coordinating the translation of thoughts and sensations into actions. Problems with striatal function are associated with certain neurological disorders such as Huntington's disease in which affected individuals have severely impaired skill learning.

"Insights from this work on central synaptic plasticity help us understand how auditory learning can be triggered and maintained, with potential implications for even very complex skills like learning language," said Christopher Platt, Ph.D., program director at National Institute of Deafness and Other Communications Disorders (NIDCD), another NIH institute that funded the study.

Hearing begins with hair cells in the ear that transform sounds into nerve cell signals sent to the brain where they are processed by the auditory cortex. Most cortical regions, including the auditory cortex, have neurons that send signals down long thin axons to make synaptic connections on neurons in the striatum. The striatum is part of a multiple relay circuit that processes information from multiple cortical areas and returns it back to the cortex. This circuit is critical in skill learning.

Petr Znamenskiy, Ph.D., a former graduate student in Dr. Zador's laboratory, previously demonstrated that neurons in the auditory cortex, which code for specific sound frequencies send signals to striatal neurons which in turn drive behavioral decisions during performance of an auditory discrimination task. Some striatal cells were tuned to high frequency sounds and others to low frequency tones.

In the current study, Dr. Zador's team found that training rats to learn directional movements in response to low frequency sounds increased the strength of the synaptic connections between the auditory cortex and the striatum.

To study these signals, the scientists recorded electrical responses in the striatum to high and low frequency tones. The recordings were made in the rat's left striatum, which is responsible for rightward movements. Some synapses were found to respond to high frequency tones and others low frequency tones, giving the scientists a tonotopic map of the left striatum of each rat.

The scientists also injected the auditory cortex cells with light-sensitive molecules that enabled them to directly stimulate the axons from the auditory cortex in response to flashes of light rather than sound.

Then the scientists trained the rats. They put the rats in front of three doors. In the first set of experiments, they trained the rats to find food behind the right-side door in response to low frequency tones and behind the left-side door in response to high frequency sounds. Over the course of four training sessions the performance dramatically improved. As a result of learning the relationship between specific sounds and the food location, they were able to find the food faster after each session.

Before each training session, Dr. Zador's team recorded synaptically generated electrical signals in the left striatum in response to stimulating the axons from the auditory cortex with laser flashes. They found that as the rats performed better, the synapses in the left striatum, which are tuned to low frequency tones and lead to rightward movement, became progressively stronger. In contrast, the strength of the high frequency synapses did not change. Training the rats to respond to visual cues also had no effect on the synaptic strength, confirming the changes were strictly due to hearing low frequency tones and not other sensations.

"We literally watched the synapses listen and learn to respond to very specific sounds over the course of the training," said Dr. Zador.

The scientists then mapped the synapses by dissecting slices of the left striatum from the trained rats and then inducing axonal activity in different parts of the slices with light flashes. They found that training rats to associate low frequency tones with food behind the right door strengthened communication at synapses near the inside border of the striatum, and the effects decreased as recordings moved toward the outer surface of the striatum.

Next the scientists reversed the training and flipped the map. They taught the rats to find food behind the right-side door for high frequency tones. In this case the synapses toward the outside border of the left striatum, which are responsive to high frequencies and turning toward the right, were strengthened by the training. The results demonstrate that the circuits for learning have specificity for the exact conditions of the task.

These studies suggest that selective strengthening of certain connections between cortex and striatum provides a general mechanism of how sensory representations guide the selection of motor responses.

"This study is a great example of how the brain can turn senses - sights, sounds, smells - into meaning," said Dr. Zador.

More information: "Selective corticostriatal plasticity during acquisition of an auditory discrimination task" appears online in *Nature* on March 2, 2015: DOI: 10.1038/nature14225

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