Watching neurons learn

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What happens at the level of individual neurons while we learn? This question intrigued the neuroscientist Daniel Huber, who recently arrived at the Department of Basic Neuroscience at the University of Geneva. During his stay in the United States, he and his team tried to unravel the network mechanisms underlying learning and memory at the level of the cerebral cortex.

What's the role of individual neurons in behavior? Do they always participate in the same functions? How do their responses evolve during learning?" asks the professor. One way to address these questions is to follow the activity of a large set of neurons while the subject learns a novel task. The goal is to link the behavioral changes with the changes in neuronal representations.

It's currently impossible to follow the activity of a large number of individual neurons in humans, but the team of researchers quickly realized that mice are excellent subjects for such studies. "We were surprised by capacities of these small rodents. They learn novel associations quickly and are able to focus for hours on complex behavioral tasks. However, it is important to keep them motivated by rewarding them accordingly. They are very similar to us in that way."

The behavioral task of the mice consisted in sampling the area in front of their snout with their whiskers to search for a small object. The object was presented either within reach and out of reach of their whiskers. Each time the object was detected with the whiskers, the mouse had to respond by licking to a reward spout. The correct choices were rewarded with a drop of liquid. "In this task different sensory and motor circuits have to interact in order to establish a novel association, leading to better and better performance".

Remained the problem of how to follow the activity of the large number of neurons across many days of learning. The researchers replaced a small part of the bone overlying motor cortex with a tiny glass window. The neurons underneath the window were genetically modified to express a fluorescent marker which changes its intensity according to the activity of the neurons. This window into the brain allowed the researches around Daniel Huber to use two-photon microscopy to record the activity of the same set of 500 neurons during days of learning.

"We then correlated the activity of the individual neurons with the different actions of the mouse, such as moving the whiskers, touching the object or licking at the right moment. It's like synchronizing the soundtrack with the images in a movie" adds the neuroscientist. The researchers analyzed this data using a series of computational approaches to establish a link between the neuronal activity and the different sensory and motor features of the task. This allowed them to build algorithmic models that can predict different motor outputs by solely monitoring the neuronal activity. Decoding the neuronal activity allowed the researchers then to construct functional maps of the recorded neurons and quantify each neuron's link with the different aspects of the behavior.

These functional maps revealed several fundamental findings: "Although the movements of the whiskers became more and more precise and targeted to search for the object during the learning, their relative neuronal representation remained relatively stable. In contrast, the representation of licking to respond and collect the rewards became more and more pronounced". Taken together, only selected aspects of the learned behavior induced changes it the neuronal representation in the cortex. The scientists also found that different sensory and motor representations are spatially intermingled in the rodent brain.

Other analysis revealed that individual neurons remain stably linked to a given behavioral function, but they have a flexibility to remain silent on a given day. This functional stability despite a flexibility to join (or not) a given representation was actually suggested by different theoretical work on learning.

"If these characteristics are limited to the motor cortex or if these are more general rules that are apply across the cerebral cortex remains open" says Daniel Huber. That in fact this is one of the questions we are currently investigating in my lab in Geneva".

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