From brouhaha to coordination: Motor learning from the neuron's point of view

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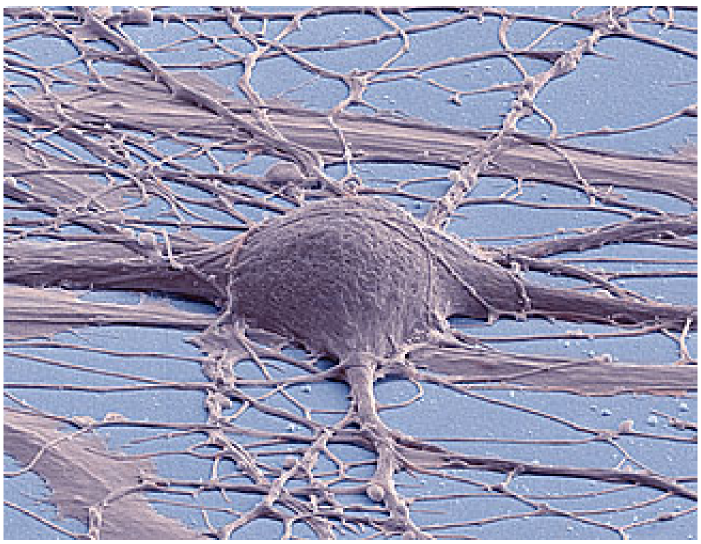

This is a scanning electron micrograph (false color) of a human induced pluripotent stem cell-derived neuron. Credit: Thomas Deerinck, UC San Diego

When starting to learn to play the piano, there is much hesitation and hitting the wrong keys. But with training, the movements of the player become more fluid and accurate. This motor improvement begins in the brain, but how do the involved neurons manage to organize themselves in order to identify and consolidate the neural circuits that best allow for such a fine motor control?

An international team of neuroscientists, from the Champalimaud Centre for the Unknown (CCU), in Lisbon, Portugal, and the University of California Berkeley, has begun "dissecting" the evolution of the patterns of neural activity associated with the learning of motor tasks by animals. Their results, which are published in the journal *Neuron*, could make it possible to improve the performance of brain-machine interfaces (BMI), the devices that can allow paralyzed patients to literally control robotic arms with the "power of the mind".

Motor learning goes through an initial phase of trial and error and a final phase of movement consolidation. "When learning a novel motor skill, animals initially have to explore different movements" says Vivek Athalye, first author of the study, who divides his time between Berkeley and the CCU. "And, as they observe the consequences of their movements, they shape those movements and consolidate the ones that lead to rewarding outcomes."

But Athalye wants to know more. "We want to know how the brain explores and consolidates the neural activity patterns which underlie these behavioral changes", he emphasizes.

To do that, together with Rui Costa - a neuroscientist at Champalimaud Research -, Athalye used, in the present study, data obtained in 2009 by the two other co-authors of the paper, José Carmena and Karunesh Ganguly, at Berkeley. "The data was already available", says Rui Costa. And he adds, as an aside: "Which goes to show that, in this era of Big Data, new insight does not always come from doing new experiments".

Carmena and Ganguly had performed their experiments on two animals, each of them with electrodes implanted in their motor cortex and connected to a BMI. The electrodes simultaneously recorded the activity of about a dozen motor cortex neurons, and the animals had learned to move a cursor on a computer screen through the activity of those few neurons.

"The animals quickly realize, in about one day, that they can move the cursor with their brain activity", explains Costa. And again, after an initial exploration phase, the animals' behavior evolved towards a consolidation of the cursor movements. "At the end of 15 training sessions, the animals became proficient", he says.

For their part, Athalye and Costa - and various other independent teams - had observed changes in motor cortex neural activity during animal learning of other motor tasks.

"In the motor cortex, activity is highly variable at the beginning and then becomes consistent, not so variable - it crystallizes", says Costa. "So Vivek wanted to know: 'Can we devise a way to see how the brain does this?'"

One of the aspects that were unclear was whether neurons varied their activity independently from each other (the authors call this activity "private") or jointly (shared activity). "How do the neurons coordinate over learning? Does each neuron explore and acquire activity patterns independently, or do the neurons coordinate to search for and acquire activity patterns?", asks Athalye. To answer this question, we developed statistical models" based on the animal experimental data.

"Vivek developed an algorithm to separate the two components - the private and the shared", Costa further explains. "And he found that, early on in the learning process, the activity of the animal neurons is mainly private, while at the end, when the animals have become very skillful at the motor task, the activity becomes mainly coordinated. Like musical instruments that start by playing separately and end up forming an orchestra."

"We found that, in the beginning, as the cursor explored the computer screen, each neuron explored independently. This suggests that the brain has a lot of flexibility in finding activity patterns to produce behavior", adds Athalye. "Then, over learning, the neurons began to coordinate to skillfully control the cursor."

An implication of these results, Carmena says, is that they make it possible to develop, in the future, better BMIs for medical applications such as the use of robotic arms by paralyzed patients. In theory, this could be done by extracting, from the "noise" made by countless neurons, the activity of only those neurons which are relevant to the skillful performance of the motor task at hand - and then sending only those relevant signals to the robotic arm.

The experimental settings of this study are obviously much simpler than natural motor learning, in which the muscles are the ones making the movements under the control of the brain. But, as Costa says, "in natural movement, we don't know which exact neurons control the muscles". In the experiments with the animals, on the other hand, only the neurons that are connected to the BMI can be doing the job.

This doesn't prevent the authors to speculate by saying that a similar process might also be at work in natural motor learning. "As crazy hypotheses go, I think our results could explain many learning processes", says Costa with a smile.

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