Building momentum toward neural prostheses

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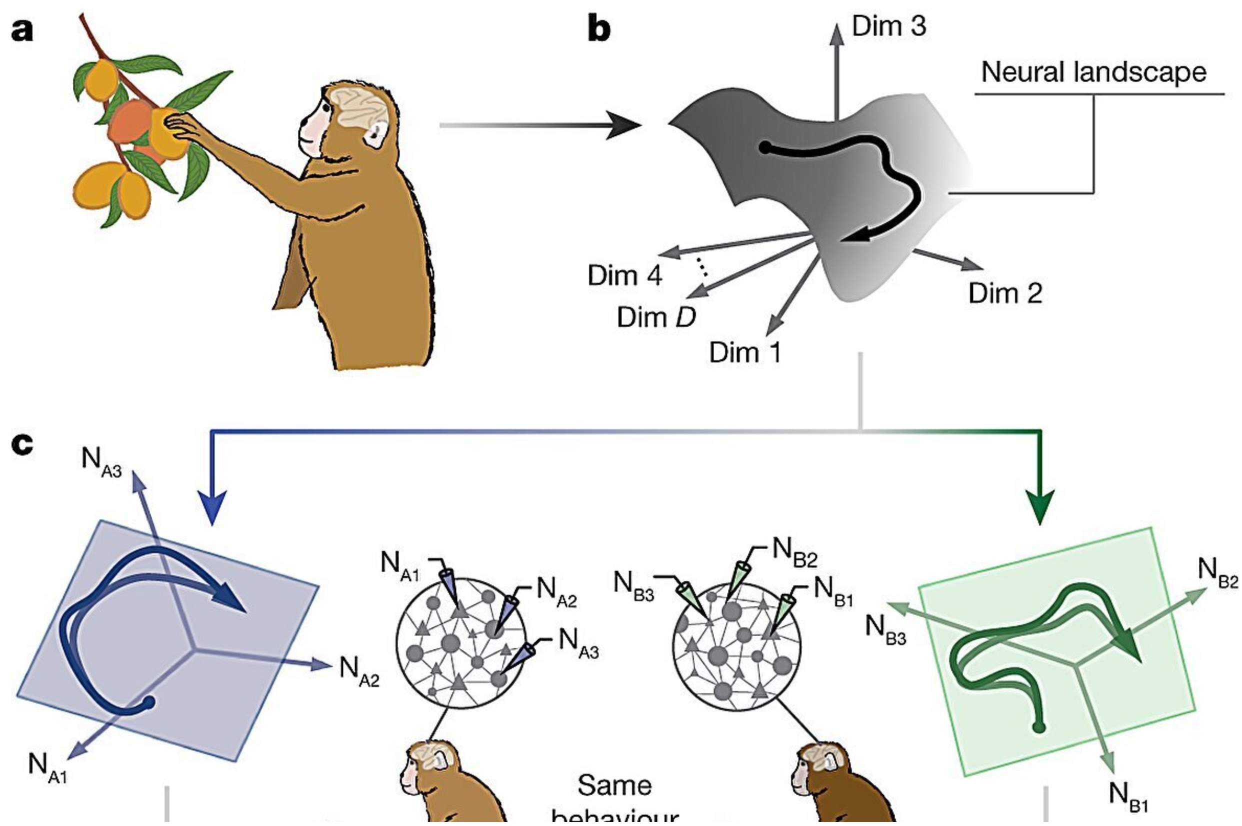

a,**b**, Different individuals from the same species performing the same behavior will generate preserved neural population latent dynamics by instantiating a species-wide 'neural landscape' embedded in *D* dimensions (Dim) of neural activity. **c**, These preserved latent dynamics can be revealed by 'aligning' the latent dynamics estimated from neural population recordings of each individual ($N_{A1–3}$ and $N_{B1–3}$ illustrate three neurons recorded from monkey A and monkey B, respectively). Credit: *Nature* (2023). DOI: 10.1038/s41586-023-06714-0

It's estimated that 42 million people in the U.S. live with some form of movement disorder springing from a neurological issue, according to the National Institutes of Health, and that number is projected to rise further as life expectancy increases.

Despite the prevalence of these conditions, treatments are sparse and very little is understood about the dysfunctional neurons underlying the disorders.

Lee Miller, '90 Ph.D., professor of Neuroscience, Physical Medicine and Rehabilitation and of Biomedical Engineering, has been involved in three recent collaborative studies that have shed light on the complex nature of neuronal communication and the evolution of mammalian brains that may aid scientists as they develop treatments and assistive devices for debilitating movement disorders in humans.

"When we study the brain, whether as neuroscientists or neural engineers, we are faced with a problem as diverse and multi-faceted as any I know of," Miller said. "Success requires that we collaborate broadly, which these studies nicely illustrate."

Within and across animal species, certain tasks elicit similar brain activity

In a recent study published in *Nature*, animals of the same species exhibited remarkably similar brain activity while performing the same tasks, even in very different species, a discovery that may help scientists better understand how mammalian brains initially evolved.

The findings also illustrate the complex neurological activity underlying animal behavior and may inform future research on neuroprosthetics, an emerging class of assistive devices which are controlled by brain activity working in harmony with computers.

"The brain is built from neurons; nearly as many as there are stars in the milky way," said Miller, who was a co-author of the study. "Yet at least in the parts of the brain that control our movements, these vast number of neurons work closely together, to produce a tiny number—perhaps 10— of independent, movement-specific related 'latent' signals. This study compared how these latent signals vary across individuals."

In the study, investigators recorded the activity from many neurons of several mice trained to perform different upper limb tasks to receive a reward. They then computed the latent signals underlying these neurons. Similar experiments were then conducted with other, more complex animal species. Different animals from the same species all exhibited similar latent activity when they perform the same movement, according to the study.

"We had this broad hypothesis: although we have different neurons by necessity because we have different brains that are different physical things in this world, the types of behaviors we evolved to do are very similar," said Matthew Perich, '17 Ph.D., a former student in the Miller laboratory who is now an assistant professor of Neuroscience at the Université de Montréal and was co-corresponding author of the study.

Because the study found similar brain activity not only across members of a species performing a given activity but even members of different species, the same could be true for humans, Perich said. This could open the door for assistive devices utilizing a brain-computer interface—anything from robotic limbs to computer cursors controlled by a paralyzed person's brain signals—to be developed and made available more widely.

"With this study, we now have this very fundamental scientific insight that provides a theoretical basis for why you could use data from different individuals to aid in the creation of a brain-computer interface for somebody who's paralyzed," Perich said.

The findings also add to the field's understanding of how brains evolved and function, said Juan Gallego, Ph.D., a senior lecturer of Bioengineering at Imperial College London, who was a former post-doctoral fellow in the Miller laboratory and is co-corresponding author of the study. Mostafa Safaie, Ph.D., and Joanna Chang, students in the Gallego lab, were co-leading authors of the study.

"Since all of our brains have a similar structure and all our hands have a similar structure, it follows that the way the brain controls the hand may be similar across individuals, which is what we found," Gallego said. "This finding also implies that we should think about the brain as this collective activity of neurons, instead of the individual activity of each neuron. It's more about the orchestra than the individual players."

Moving forward, both Miller and Gallego hope to validate the findings in humans in collaboration with clinical and industrial partners. Because the current study only looked at one specific activity, more research is needed to understand if neural activity is conserved across animals performing a wider variety of tasks, he added.

Decoding signals between the brain's motor and sensory hubs

In the human brain, the primary motor and somatosensory cortices play critical roles in motor control: one causing movement, and the other monitoring it. In ongoing experiments conducted at the University of Chicago and the University of Pittsburgh, signals recorded from the motor cortex of a person with a spinal cord injury can be used to grasp, squeeze and transport objects in virtual reality.

When participants attempt to move their paralyzed fingers and hands, their motor cortical activity was mapped to a VR hand which carried out the task. In order to provide the vital sense of touch when the participant's VR hand "touched" the object, electrodes in areas of the participants' somatosensory cortex that represent the hands were electrically stimulated, causing an artificial sense of touch that improved their task performance.

Despite this correlation, exactly how the communication from the somatosensory to the motor cortex occurs is not well understood.

In a second study, recently published in *Nature Communications*, investigators at the University of Chicago led by Sliman Bensmaia, Ph.D., recorded the activity of neurons in the primary motor cortex of people who had paralyzed hands as they received intracortical microstimulation in the area of their somatosensory cortex associated with touch sensation from the hand.

Miller, who was a co-author of the study, and his collaborators found that stimulating this area of the somatosensory cortex activated many of the neurons in the primary motor cortex which were being used to control hand and arm movement through the brain-computer interface (BCI). The findings highlight the complex nature of brain communication and how sensory input guides movement, Miller said.

"This paper describes the effects on the motor cortex when we stimulate the somatosensory cortex, which is useful as we begin to understand the impact of those effects on our BCI," Miller said. "We found two types of connections from the somatosensory cortex to the motor cortex. There's what appear to be very direct synaptic connections, and there are also more indirect connections with more complicated properties."

While the direct responses in the motor cortex had fairly predictable, short-lasting consequences, the indirect effects were not only longer-lasting, but they also depended on what the person was trying to do. Miller and his colleagues found that this stimulation activated different parts of the motor cortex depending on what task was being carried out, suggesting that communication between the motor and somatosensory cortices varies by task and is highly dynamic, Miller said.

"Because the effect of stimulation on the motor cortex depends on what the person was doing, this becomes a new problem for us to try to work out," Miller said. "There seems to be no one-size-fits all algorithm for BCIs with touch feedback. For future brain-computer interfaces, this is a warning."

Developing battery-free implants for spinal cord stimulation

Electrical stimulation of the spinal cord and muscles by neuroprostheses holds promise as an emerging strategy for controlling BCIs and treating neurological movement disorders, but powering these devices remains a significant challenge.

This situation led Miller and other collaborators at Feinberg and the University of Arizona to develop an implant capable of delivering therapeutic electrical stimulation to the spinal cord of rats through a wireless energy source, a process detailed in a third study, also published in *Nature Communications*.

"This is a device that harvests energy wirelessly, communicates wirelessly, and if scaled up to humans could be a fully implanted device that would facilitate spinal and muscle stimulation to restore movement, ideally under the control of a brain-computer interface," Miller said.

By utilizing electrical stimulation to replace dysfunctional neural signaling, these devices may also be capable of accelerating rehabilitation following a spinal cord injury, said Miller, who was a co-author of the study.

In the study, which was led by Philipp Gutruf, Ph.D., assistant professor of Biomedical Engineering at the University of Arizona in collaboration with Miller and Matthew Tresch, Ph.D., chair of Biomedical Engineering in the McCormick School of Engineering, professor of Physical Medicine and Rehabilitation and co-corresponding author of the publication, investigators optimized the wireless power component with a passive resonator, enabling the implant to harness 500 percent more power compared to previous experimental devices.

"Previous devices required batteries that need frequent replacement or cables to supply power, especially for stimulation of muscles which requires high voltages and currents," Tresch said. "The device created by the Gutruf lab in this work is capable of stimulating at a wide range of voltages and currents, enabling it to activate either muscles or neural sites such as the spinal cord."

Although more research is needed to test the device in humans, the results are encouraging, Tresch said.

"The device enables us to evaluate strategies for long-term rehabilitation involving electrical stimulation," Tresch said. "The device would make it possible to evaluate these strategies in freely behaving animals, continuously and over multiple days or weeks, in order to potentially achieve greater rehabilitation outcomes after injury."

The new approach to wireless power could also be applied to other assistive devices in the future, Miller said.

"If you've got a bunch of electrodes implanted in the muscles and nerves of your forearm you can turn those on and make your hand open or close. But that currently requires wires going through the skin and into muscles," Miller said.

"This new device was born from the desire to be able to put a device in the body that's fully implanted and works wirelessly, not only to stimulate muscles, but also to stimulate the spinal cord. A device like this could dramatically improve our opportunity for translation of the underlying stimulation methods to humans."

More information: Mostafa Safaie et al, Preserved neural dynamics across animals performing similar behaviour, *Nature* (2023). DOI: 10.1038/s41586-023-06714-0

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