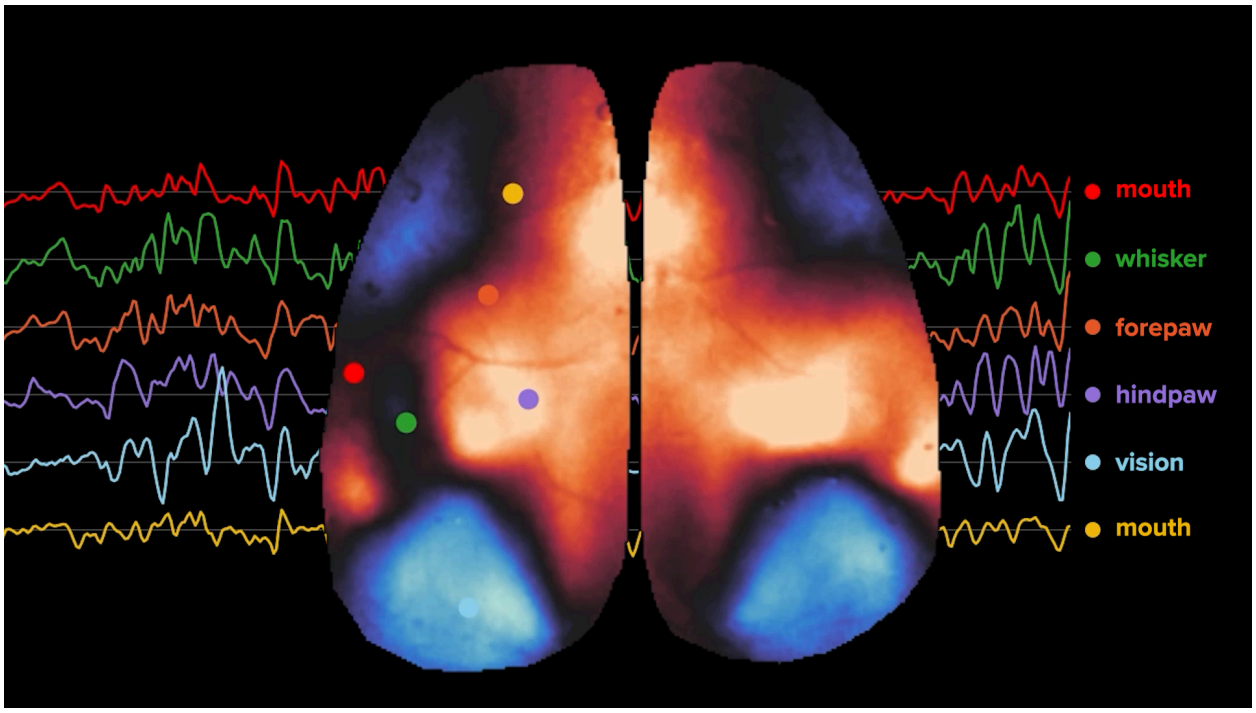
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New Body Map Traces Origins of Complex Movements in the Brains of Mice

Discovery of specific brain activity patterns in rodents at rest could shed light on the brain's ability to coordinate movements



Lines show activity at different locations in a mouse's brain (dots) associated with different body parts. (Weihao Xu / Columbia's Zuckerman Institute)

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IN BRIEF

- Researchers monitored activity across the surface of the brain while mice moved and rested.
- They discovered a body map in a brain region not thought to have one.
- This could help scientists study how the brain coordinates complex motions requiring multiple body parts.

NEW YORK, NY — A new biological blueprint of how the body of a mouse is represented in its brain could help scientists answer a fundamental question: how do we perform complex motions that use more than one body part, such as coordinating arm, hand, head and lips to sip a spoonful of soup? The study was published today in *Nature Communications*.

"Coordinating many body parts at once seems effortless for animals, but it's so complex that robots still struggle with it," said study lead author Weihao Xu, PhD, who carried out the research while a doctoral student and postdoctoral research scientist in the laboratory of Dr. Elizabeth Hillman at Columbia's Zuckerman Mind Brain Behavior Institute. This newfound map could help researchers understand key details about the dextrous movements that can be lost after brain injuries such as strokes, he added.

Dr. Xu and colleagues examined the brain area underlying voluntary movements, called the motor cortex. "Philosophers have been exploring the relationship between mind and body for centuries," Dr. Xu said. "Science is catching up as new tools let us revisit the question."

Studying the motor cortex is surprisingly difficult in mice, since even a well-trained rodent can't move one body part in isolation. In some cases, scientists have examined parts of the motor cortex by directly stimulating it and looking for the resulting movements. Such research revealed that part of the brain, called the primary motor cortex or M1, possesses sub-regions that control different body parts. For example, stimulating one spot in M1's map might lead a person's finger to twitch.

However, this method of mapping gave less clear results for the secondary motor cortex, or M2, leading researchers to think that M2 lacked the kind of body map seen in M1. Previous research had linked M2 with more complex combinations of motions, but interpreting its activity patterns in terms of body movements has proven especially challenging.

The new study took a different approach. Using high-speed wide-field optical brain imaging techniques developed in the Hillman lab, the researchers analyzed patterns of neural activity across the brain while mice moved. Unexpectedly, they realized that apparently random activity in the brain while the rodents rested was even more revealing. A closer look at this resting activity revealed small spots in M2 whose activity patterns were synchronized to regions of the sensory cortex, which interprets information from the senses and has a long-established map of the body.

"We put these small spots together, and found that they formed a body map hidden in the intrinsic chatter of M2, a part of the brain that wasn't supposed to have a body map," Dr. Xu said.

Dr. Xu spent three years testing the surprising results. With the help of Zuckerman Institute collaborators, he employed two-color wide-field optical mapping to distinguish the activity of corticospinal neurons that send signals down the spinal cord, which are most concentrated in M1, from other neurons. This analysis confirmed that the newfound map was not in M1 but in M2.

The team also checked the neural wiring connecting the sensory cortex with M2, confirming the synchronized sub-regions in each brain region were anatomically connected. The researchers then verified that different mouse movements activated the parts of M2 the new body map suggested they would. For instance, when a mouse raised both forepaws to its mouth and licked them, each corresponding point in the M2 map activated when those parts moved.

Importantly, these findings helped reveal a key role M2 plays. The researchers found that M2 activates strongly when multiple body parts work together, such as when a mouse raises its forepaws to its mouth and licks them, or when a person brings a cup to their lips.

"All of these features of M2 explain why understanding the activity patterns of M2 has been so challenging," said Dr. Elizabeth Hillman, corresponding author of the study who is now chair of the Department of Imaging Sciences at St. Jude Children's Research Hospital. "Confusingly, M2 chatters when the body is still, and cares more about complicated movements than simple ones." Dr. Hillman expects that these insights will help us to better interpret how the brain plans and coordinates movements from moment to moment, which could be useful for understanding movement disorders, and even how to build better robots.

Dr. Xu, now a data scientist in industry, noted that his training in computer science and machine learning at Columbia was essential to this study, complementing his courses in biomedical engineering and neuroscience. "Columbia encouraged me to take challenging courses and bring what I learned back to the project," Dr. Xu said. "I use these skills every day now."

"All in all, I hope that other researchers will leverage this discovery to further understand how activity in the brain becomes movement in the body, and how the brain's resting activity can reveal its hidden wiring," Dr. Xu said.

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