Medical Xpress

Scientists identify a neural circuit involved in translating premotor planning into active movement

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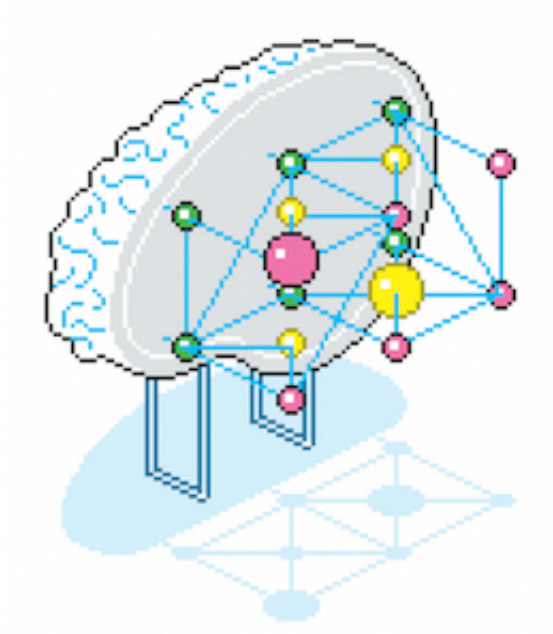

With half a second's planning, an animal's brain prepares it to quickly and precisely execute complex movements. Scientists at Howard Hughes Medical Institute's Janelia Research Campus have identified a neural circuit that transforms the flurry of activity that occurs during this preparatory period into commands that direct muscle movements.

The research by the Janelia scientists explains why injuries that disrupt the brain's ability to carry out movement planning typically impair a person's ability to make movements on just one side of his or her body. Janelia group leader Karel Svoboda and his colleagues reported their findings in the February 26, 2014 issue of the journal *Nature*.

Neurons in the brain's premotor cortex are active during the planning period that occurs a fraction of a second before a person or other primate initiates a movement. Those neurons do not directly receive sensory input, nor do they directly stimulate movement of the body. Instead, Svoboda says, their activity represents a cognitive phenomenon. "You can actually read out from the neurons what the animal will do in the future," he says. "In humans, you can record this activity with an EEG electrode and read out in coarse terms when and how a person will move, before he or she is aware of where they will move."

Still, Svoboda says, there had been no direct evidence that the brain translated this pre-movement signaling into motor commands. Furthermore, seemingly conflicting observations about how the left and right side of the premotor cortex affect movement had left scientists puzzled.

Most of what is known about the premotor cortex comes from observations of patients and experiments with primates. Patients whose premotor cortex is damaged during a stroke lose the ability to plan movements on the side of the body opposite the injured side of the brain. "So when a person has a lesion on one side, there is a strongly lateralized effect. But the dynamics of the neurons that people have found in neurophysiology experiments really don't jibe with that," Svoboda says.

Scientists had found about an equal number of cells on both sides of the

premotor cortex whose activity was associated with movement to the left side of the body; the same was true for neurons associated with movement to the right side of the body. "It looks like the planning activity is completely distributed for both sides in both hemispheres," Svoboda says.

About a year ago, Svoboda's team identified a region in the brains of mice that behaves like the premotor cortex in humans and other primates. That, he says, opened the opportunity for more precise experiments.

To learn more about how neuronal activity during this preparatory period affect movements, the team used a technology called optogenetics, in which a light-sensitive protein is genetically introduced into neurons so that experiments can switch the cells on or off with a laser pulse. Postdoctoral researchers Nuo Li and Zengcai Guo developed a behavioral task in which they trained mice to respond to a sensory cue – a pole whose position an animal could detect with its whiskers – by licking to either the right or the left, following a delay of 1.3 seconds to allow for movement planning.

Li then silenced neurons on either side of the premotor cortex-like part of the mouse brain, known as the anterior lateral motor cortex. Optogenetics allows for millisecond precision, so Li could silence the neurons specifically during the movement-planning period. Silencing neurons on the right side impaired the animals' ability to lick towards the left, whereas silencing neurons on the left side impaired their ability to lick toward the right. But just as other scientists had observed in primates and humans, when Li monitored neural activity in the animals' anterior lateral motor cortex, about the same number of neurons on each side fired in advance of movements toward either side of the body.

Many types of cells wend their way through this part of the brain and

previous experiments were unable to sort out different neurons in the mix. By applying new optogenetics tools to examine activity in specific cell types, the team found a small group of neurons whose activity was associated only with future movements on the opposite side of the animal's body. These were pyramidal tract neurons, which extend to the motor centers that produce movement. Research specialist Tsai-Wen Chen used imaging to follow the activity of the pyramidal tract neurons, and found the same relationship with movements on the opposite side of the body.

"In the cortex, we have neurons that project to half a dozen different brain areas," Svoboda says. "These output neurons are a small minority of cells in this region, so if you record indiscriminately from all neuron types, they get washed out," Svoboda says. "To understand how the brain works, we really have to study the neural code at the level of defined neural populations."

The scientists found that they could influence the direction of an animal's licking response by stimulating the pyramidal tract neurons. "If we stimulate these neurons during motor preparation, seconds before movement, this causes the animal to move into the contralateral [opposite side] direction much more often than it would otherwise," Svoboda says. "This really shows these brain areas and these neurons are causally related to planning these movements."

"So a very simple picture arises," Svoboda says. "The motor plan is distributed across both hemispheres, which talk strongly to each other. Activity is widely distributed, involving neurons that interact with sensory areas. Just before movement, this motor plan is effectively downloaded into the pyramidal tract neurons. And it's in these neurons that we see strongly lateralized population activity."

With a new understanding of the circuit that connects motor planning to

movement, Svoboda's team is eager to begin investigating how that planning activity is generated, how the motor cortex participates in decision making, and how information about the plan is stored until a movement is executed. "You cannot write a computer program to generate this based on what we know about neurons," he says. "There are real mysteries there."

More information: "A motor cortex circuit for motor planning and movement." *Nature* (2015) DOI: 10.1038/nature14178

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