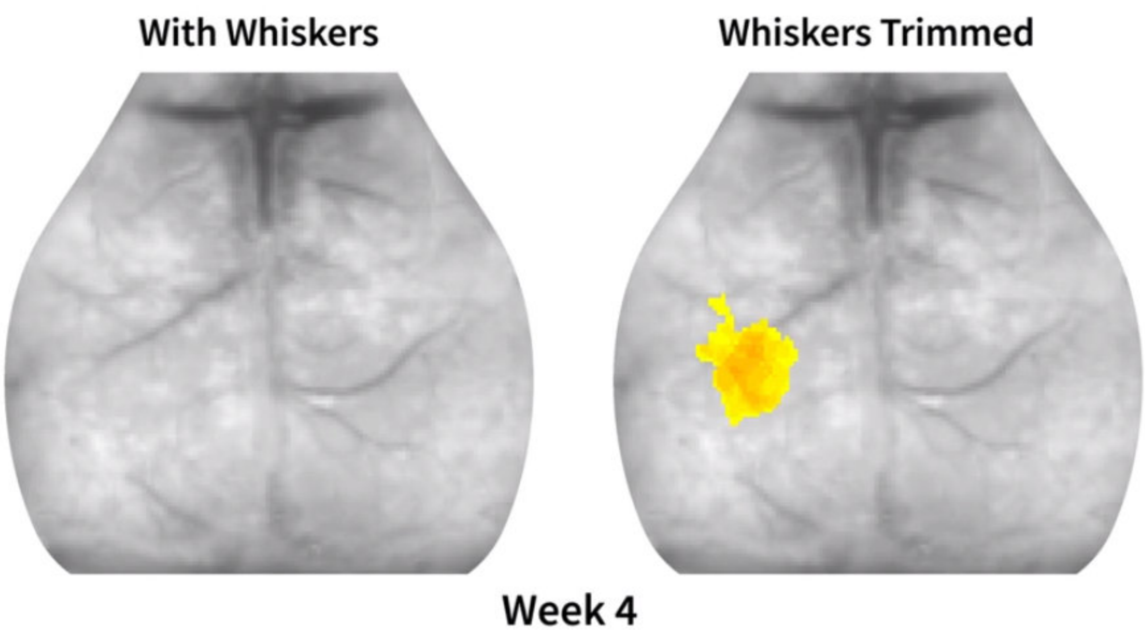
Stroke recovery improved by sensory deprivation, mouse study shows

January 31 2018



Credit: Washington University School of Medicine

Temporarily shutting off neuronal signals to a healthy part of the brain may aid stroke recovery, according to new research in mice.

The findings, from researchers at Washington University School of Medicine in St. Louis, are published Jan. 31 in *Science Translational Medicine*.

Mice that had experienced strokes were more likely to recover the ability to use a front paw if their whiskers were clipped following a stroke. Trimming the whiskers deprives an area of the mouse's brain from receiving sensory signals from the animals' whiskers. And it leaves that area of the brain more plastic - or receptive to rewiring to take on new tasks.

"We may have to rethink how we do stroke rehabilitation," said senior author Jin-Moo Lee, MD, PhD, the Norman J. Stupp Professor of Neurology at the School of Medicine. "Stroke rehab often focuses on trying to train patients to compensate for disability caused by the stroke, but this strategy has limited effectiveness. Our findings suggest that we may be able to stimulate recovery by temporarily vacating some brain real estate and making that region of the brain more plastic. One way to do that might be by immobilizing a healthy limb."

About 450,000 people survive strokes every year. Because the brain is adaptable, people typically recover a limited amount of function naturally. For example, a person who is unable to move his arm the day after a stroke sometimes can wiggle his fingers a week later. Brain imaging on such people shows that control of the fingers shifts from the stroke-damaged area of the brain to a neighboring undamaged area, a process known as remapping. How thoroughly a person recovers correlates with how well his or her brain rewires and moves functions from injured to uninjured areas.

But this adaptability also means there's a constant battle for control over the brain's real estate. Normally, if neuronal signaling to one area gets cut off - by sensory deprivation or limb amputation, say - neighboring functions will spread into that unused area.

Lee, first author Andrew Kraft, an MD/PhD student at Washington University, and colleagues reasoned that shutting off signals to an uninjured area near the site of stroke damage would promote remapping into that area by generating vacant real estate.

The researchers triggered, in mice, a stroke in the part of the brain that controls the right forepaw. Then, they trimmed whiskers in half of the mice to induce sensory deprivation in a brain region near the stroke and left the whiskers of the other mice intact. Mice rely on their whiskers, which are rich with nerve endings, to sense the location of objects in their environment.

The researchers measured recovery by comparing right and left forepaw use. Immediately after the strokes, both groups of mice favored their left forepaws. But by four weeks after the strokes, those with clipped whiskers had begun using their right forepaws again, and by eight weeks, they were back to using both equally. In contrast, mice whose whiskers were not clipped showed no improvement at four weeks and only partial recovery at eight weeks.

The researchers then mapped the mice's brains to find the exact area that controlled the right forepaw. In each mouse with trimmed whiskers, the locus of forepaw control had taken over part of the area that usually receives whisker sensation. In the mice with intact whiskers, the locus of forepaw control had moved to any of several spots adjoining the site of injury.

The researchers kept the mice's whiskers trimmed for eight weeks, until they had fully recovered from the strokes and were back to using both forepaws equally. Then, they allowed the whiskers to grow back. Four weeks later, whisker control had reclaimed part of its former real estate in the brain. Still, forepaw control remained in a corner of the area. The mice continued to have full use of their paws.

Lee and colleagues do not know whether allowing the forepaw to take over part of the area normally devoted to governing whisker movement caused the mice to lose some control over their whiskers. But it is possible for a brain function to reach into another function's territory without any apparent ill effects, they said.

"The part of the brain that controls fine finger movements is unusually large in musicians, and the part for navigation is enlarged in taxi drivers," Lee said. "Developing those skills doesn't cause musicians and taxi drivers to lose any other abilities. They are probably just using their brains more efficiently."

The neurological areas that govern the parts of the body are mapped out in the brain in the same order they exist in reality: The part of the brain that directs the arm is next to the area that controls the shoulder, and so on. If brain injury causes a person to lose control of her arm, then immobilizing her shoulder would shut off neuronal signaling to the adjacent brain area, opening up space for remapping.

"Maybe we need to start thinking about improving outcomes by enhancing plasticity in targeted regions of the brain," Lee said. "This study shows that it's possible to do that, and it could lead to improved recovery."

More information: A.W. Kraft el al., "Sensory deprivation after focal ischemia in mice accelerates brain remapping and improves functional recovery through Arc-dependent synaptic plasticity," *Science Translational Medicine* (2018). stm.sciencemag.org/lookup/doi/ … scitranslmed.aag1328

Provided by Washington University School of Medicine