Drug helps mouse and monkey brains recover from stroke

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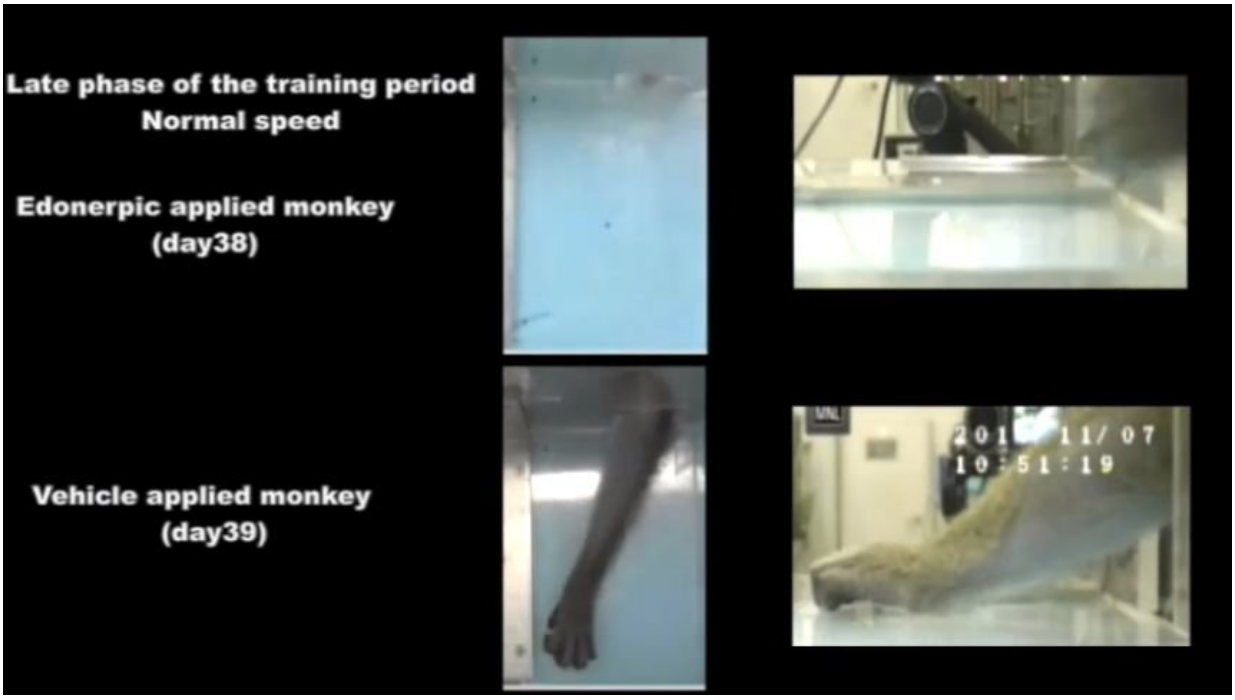

A team of researchers from several institutions in Japan has found that a certain drug in conjunction with physical therapy has resulted in improved recovery from a stroke in mice and monkeys. In their paper published in the journal *Science*, the group describes their study of the impact of the drug on mice and monkeys and what they found. Simon Rumpel with the University Medical Center of the Johannes Gutenberg

University Mainz in Germany offers a Perspectives piece on the work done by the team in the same issue, and also offers an outline on other therapies being developed to treat stroke victims.

A stroke occurs when the brain is damaged by lack of oxygen, either due to blockage or bursting of a blood vessel. The brain is unable to repair dead nerve cells, but some degree of function can be restored through physical therapy, which results in rewiring unharmed parts of the brain. But rewiring can only do so much. Thus, scientists continue to look for better therapies to help stroke victims. In this new effort, the researchers have found a drug that promotes brain rewiring, resulting in improved recovery of motor skills.

Prior research has shown that a protein called CRMP2-binding compound is involved in rewiring the brain. The researchers wondered if it might be possible to introduce a drug into the brain that would bind with CRMP2 and help it do its rewiring job better. Prior research had suggested that a drug called edonerpic maleate might do just that.

To test the drug, the researchers induced strokes in test mice and then gave them a dose of the drug a day later. Then, they put the rodents through physical therapy, testing them periodically to see how well motor function was being restored. They report significant improvements over mice administered a control drug. They note further that it was not enough just to give the mice the drug; the rodents still required physical therapy for motor improvement. Pleased with their results, the researchers conducted the same round of tests with monkeys and report similar results. They are now making plans for a clinical trial, as the drug has already been proven safe for use in humans.

More information: Hiroki Abe et al. CRMP2-binding compound, edonerpic maleate, accelerates motor function recovery from brain

damage, *Science* (2018). DOI: 10.1126/science.aao2300

Abstract

Brain damage such as stroke is a devastating neurological condition that may severely compromise patient quality of life. No effective medication-mediated intervention to accelerate rehabilitation has been established. We found that a small compound, edonerpic maleate, facilitated experience-driven synaptic glutamate AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic-acid) receptor delivery and resulted in the acceleration of motor function recovery after motor cortex cryoinjury in mice in a training-dependent manner through cortical reorganization. Edonerpic bound to collapsin-response-mediator-protein 2 (CRMP2) and failed to augment recovery in CRMP2-deficient mice. Edonerpic maleate enhanced motor function recovery from internal capsule hemorrhage in nonhuman primates. Thus, edonerpic maleate, a neural plasticity enhancer, could be a clinically potent small compound with which to accelerate rehabilitation after brain damage.