New Stanford-led program aims to produce insights into brain injury, recovery

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Researchers at four institutions, led by Stanford University and Brown University, have begun an effort with more than $14 million of federal funding to learn both how the brain and its microcircuitry react to sudden physiological changes and what can be done to encourage recovery from injury.

"This program is about conducting the fundamental neuroscience and developing the neurotechnology to ultimately enable an entirely new class of brain injury therapeutics," said Krishna Shenoy, an associate professor of electrical engineering and of bioengineering at Stanford.

"Using new tools like optogenetics, which enables us to interact with, and even temporarily turn off, active brain circuits in animals with pulses of light, our team can harmlessly simulate injuries and therefore learn more about how the brain responds when an injury occurs.

"The understanding of brain function that we create will help pave the way to new approaches to mitigating the effects of injury."

The project will yield new brain implant technologies that can both sense the brain's electrical signals and deliver optogenetic light pulses to neural tissue.

"To access and truly understand the operation of brain microcircuits and their function, the team will pursue a new generation of implantable optogenetic microdevices, with the ultimate aim of achieving a clinically useful, two-way communication link with the brain," said Arto Nurmikko, a professor of electrical engineering and physics at Brown.

Shenoy is the principal investigator of the REPAIR project (for Reorganization and Plasticity to Accelerate Injury Recovery), for which the Defense Advanced Research Projects Agency (DARPA) is providing $14.9 million for two years with an option to increase the project's scope to $28.8 million and four years.

Stanford and Brown (with Nurmikko as the co-lead) are working with the University of California-San Francisco and University College London. Collectively, the team composed of 10 professors and their research teams has expertise ranging from neuroscience, neurology and psychiatry to semiconductors, optoelectronics, statistical signal processing, machine learning and brain modeling.

About 1.7 million people experience traumatic brain injuries of varying severity in the United States each year, including many returning war veterans, according to the Centers for Disease Control and Prevention. Of those, about 3 percent, or 52,000 are fatal.

New technologies

Optogenetic techniques allow researchers to genetically engineer specific types of cells in brain circuits that will turn on or off in response to pulses of a specific color of light delivered to brain tissue via an implant. The light is flickered as fast as 1,000 times a second, the frequency at which neurons operate. Optogenetics has only recently become usable in primates.

In REPAIR, the researchers will use optogenetics to produce completely reversible "injuries" in the brains of research animals, by temporarily turning off specific parts of the brain. They will then study how the brain might rewire itself to deal with that tissue becoming unavailable, said Karl Deisseroth, associate professor of bioengineering and of psychiatry and behavioral sciences at Stanford, who pioneered optogenetics.

"There are many advantages to using optogenetics instead of drugs or lesions," Deisseroth said. "You are in no way injuring the animals, because as soon as you turn the light off they are back to normal, and it is also a lot cheaper, easier and more precise to use."

Reading and writing neural signals

As the team's researchers learn more about brain function in normal operation and during a simulated injury, Shenoy says, they hope to gain a better understanding of how to encourage the brain to rewire itself further. Or, in instances when the brain's ability to heal itself reaches a limit, the researchers may find other ways to restore function.

For instance, Shenoy said, the team hopes to develop a new model of the flow of information around the brain and how each part generates the signals needed by other parts. That kind of insight could help lead to the development of prosthetic computer chips that mimic and replace the computational role of injured regions of the brain. These chips might be miniaturized versions of the implants developed in the REPAIR project, which are capable not only of reading neural-electrical signals but also of generating optical-neural signals for use by brain cells.

"Ultimately, this is aimed at trying to help people who've suffered a brain injury, in an entirely new way," said Shenoy.

Provided by Stanford University