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Researchers to develop 'brain prosthesis' to help brain-injured patients recover memory

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The University of California, Los Angeles (UCLA), has been tapped by the Defence Advanced Research Projects Agency to spearhead an innovative project aimed at developing a wireless, implantable brain device that could help restore lost memory function in individuals who have suffered debilitating brain injuries and other disorders.



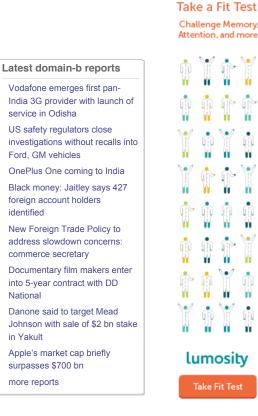
Illustration of memory-restoring device to be developed by UCLA researchers.

The four-year effort, to be led by UCLA's Program in Memory Restoration and funded by up to \$15 million from DARPA, will involve a team of experts

in neurosurgery, engineering, neurobiology, psychology and physics who will collaborate to create, surgically implant and test the new "neuroprosthesis" in patients.

Memory is the process by which neurons in certain brain regions encode information, store it and retrieve it. Various illnesses and injuries can disrupt this process, causing memory loss. Tramautic brain injury, which has affected more than 270,000 military members since 2000, as well as millions of civilians, is often associated with such memory deficits. Currently, no effective therapies exist to address the long-term affects of these injuries on memory.

"Losing our ability to remember past events and form new memories is one of the most dreaded afflictions of the human condition," said UCLA's lead investigator, Dr. Itzhak Fried, a professor of neurosurgery at the David Geffen School of Medicine at UCLA and a professor of



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psychiatry and biobehavioral sciences at the Semel Institute for Neuroscience and Human Behavior at UCLA.



Developing models of the brain's 'memory works'

The ambitious, first-if-its-kind project at UCLA builds on Fried's 2012 research - published in the New England Journal of Medicine with UCLA's Nanthia Suthana and colleagues - demonstrating that human memory can be strengthened by stimulating the brain's entorhinal cortex, a region involved in learning, memory and Alzheimer's disease. Considered the entrance to the hippocampus, which helps form and store memories, the entorhinal cortex plays a crucial role in transforming daily experience into lasting memories.

"The entorhinal cortex is the 'golden gate' to the brain's memory mainframe," Fried said.

"Every visual and sensory experience that we eventually commit to memory funnels through that doorway to the hippocampus. Our brain cells send signals through this hub in order to form memories that we can later consciously recall."

In a key part of the project, the research team will stimulate and record the activity of single neurons and of small neuronal populations in patients who already have brain electrodes implanted as part of epilepsy treatment. UCLA's Mayank Mehta, a professor of physics and neurobiology, and Harvard Medical School's Gabriel Kreiman will then work with Fried's group, using this information to develop computational models of the hippocampal—entorhinal system and determine how to intervene with electrical stimulation to help restore memory function.

Turning the models into a workable 'neuroprosthesis'

The models will be transformed into therapeutics using technology developed by researchers from UCLA's Henry Samueli School of Engineering and Applied Science. This group, led by associate professor of electrical engineering Dejan Markovic, will work with engineers from Lawrence Livermore National Laboratory and Stanford University to develop electronics for the implantable neuromodulation device. As part of the UCLA-led project, Lawrence Livermore will be awarded a separate \$2.5 million grant from DARPA to build the device, which will have the ability to record and stimulate neurons to help restore memory.

Markovic said the goal is to create miniature wireless neural sensors that are far more sophisticated - much smaller and with much higher resolution - than those that exist today. The sensors will track and modulate neural activity with very precise spatial and temporal resolution, allowing the device to continuously update and modulate precise patterns of stimulation to optimize therapy and restore memory function.

"We are developing ultra—low-power electronics in order to measure activity of specific areas of the brain, perform neural signal analysis and wirelessly transmit that information to an outside device in close proximity to the implants," Markovic said. "The implants and the outside device will talk to each other. The goals are to provide better therapy for people with neurological dysfunction and help those with epilepsy and brain injury to enhance and restore memory."

"Currently, there is no effective treatment for memory loss caused by a condition such as traumatic brain injury," said Lawrence Livermore project leader Satinderpall Pannu, director

Tools

of the lab's Center for Bioengineering, a facility dedicated to fabricating biocompatible neural interfaces. "This is a tremendous opportunity from DARPA to leverage Lawrence Livermore's unique capabilities to develop cutting-edge medical devices that will change the health care landscape."

Testing the new device in brain-injured patients

During the second phase of the program, Fried, using a minimally invasive procedure, will implant the neuromodulation device into the entorhinal area and hippocampus in patients with traumatic brain injury as part of a groundbreaking clinical trial.

The DARPA initiative aimed at developing these implantable brain devices, Restoring Active Memory (RAM), also involves the University of Pennsylvania. The program supports President Obama's BRAIN initiative. Under the terms of a cooperative agreement with DARPA, UCLA is slated to receive up to \$15 million for its work on the program, with full funding contingent on meeting a series of technical milestones.

The RAM program poses a formidable challenge reaching across multiple disciplines from basic brain research to medicine, computing and engineering," Fried said. "But at the end of the day, it is the suffering individual, whether an injured member of the armed forces or a patient with Alzheimer's disease, who is at the center of our thoughts and efforts."



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