

Parkinson's Researchers Develop Treatments Through Neural Circuits

By Kasra Zarei

kasra-zarei@uiowa.edu

Several University of Iowa Researchers study Parkinson's Disease with the goal of making new treatments to help patients.

Parkinson's Disease has long been understood to affect how people move. A chemical substance called dopamine helps control the brain's reward and pleasure systems, but its deficiency has been known to result in Parkinson's.

Recently, researchers led by Nandakumar Narayanan, assistant professor of Neurology, have been uncovering how Parkinson's can affect how people think.

"We know a lot about Parkinson's disease in that it involves dopamine neurons and the basal ganglia, but we don't know why a loss of dopamine in Parkinson's impairs patients' ability to think," Narayanan said.

The brain uses stereotyped electrical signals to process all the information it receives and analyzes. Neurons, cells that make up the brain, form individual circuits that are specialized for each of the brain's different subsystems.

"Through mapping circuits, we try to localize a specific activity not just to a specific area of the brain, but to a specific group of neurons in an area of the brain," Narayanan said.

Narayanan and his team are studying Parkinson's disease through understanding the detailed mappings of the circuits of the brain.

"Essentially, we can stimulate and inhibit these circuits in real time so we can ask questions about what specific populations of neurons do, and how dopamine affects them," Narayanan said.

Narayanan is particularly interested in an area called the prefrontal cortex, the part of the brain that controls flexible behavior and cognitive processing.

"Our goal is to be able to identify where cognitive information converges in the brain, so we can potentially manipulate it," Narayanan said. "Then, we can hopefully develop new treatments for Parkinson's."

Narayanan's lab recently discovered that dopamine in the prefrontal cortex is required for low frequency brain rhythms that can be picked up with electroencephalogram (EEG) and potentially be used to diagnose Parkinson's or general cognitive dysfunction.

“We found that these low frequency rhythms are an index of a healthy frontal cortical function. You see them in anyone who is able to guide their behavior or even inhibit inappropriate behavior,” Narayanan said.

This dopamine-dependent low frequency rhythm behaves like an oscillation, and is present in humans and animal models studied by Narayanan.

“Essentially these oscillations set the neurons in motion, and we can study how these oscillations engage specific neurons that express a particular type of dopamine receptor,” Narayanan said. “This is important because we have no drugs that target these dopamine receptors, so that’s an incredible opportunity for treatment.”

This work epitomizes Narayanan’s scientific motivation to pin very specific dysfunction in Parkinson’s to localized circuits.

“If we map the circuits and know how they are dysfunctional, then we can think about how to intervene,” Narayanan said.

Narayanan and his colleagues already rectify deficient circuits in advanced Parkinson’s patients, and have sights set on improving stimulation treatments.

Right now current treatments deliver constant deep brain stimulation, essentially shocks to reduce tremors, in Parkinson’s patients. However, these solutions are not adaptive and do not appropriately respond to the brain’s signals leading to undesirable side effects in patients.

“You don’t need stimulation all the time, so there is a need for delivering the maximally effective treatment,” Narayanan said.

To address this clinical need, Narayanan and two collaborators, Soura Dasgupta and Raghuraman Mudumbai, University of Iowa professors of electrical and computer engineering (ECE), seek to develop powerful new tools to provide highly personalized, real-time brain stimulation for movement disorders.

“The idea of adaptive stimulation is relatively new. We wish to formulate new adaptive brain stimulation techniques to rectify cognitive impairments in the most effective way,” Dasgupta said.

The idea could help Parkinson’s patients after proof-of-principle is established in mice, and also generalize brain stimulation to behavioral disorders like anxiety disorder.

According to Er-Wei Bai, ECE professor and departmental executive officer, “This interdisciplinary research is a hall mark of the ECE department, including a range of active healthcare related projects funded by National Institutes of Health.”