New tools for epilepsy

Electricity powers homes, computers and even the human brain. In varying levels of intensity, electrically charged signals form the basis of communication between neurons within brain circuits. Although neuroscientists have learned much about brain structures, they don't fully understand the way individual neurons and neural circuits operate, especially within the temporal lobe.

Sanjay Kumar, biomedical sciences researcher, has received a $1.6 million grant from the National Institute of Neurological Disorders and Stroke to identify components of underlying epilepsy-causing neural circuits within three key temporal lobe areas: the presubiculum, the parasubiculum and the entorhinal area.

"We record neurons' electrical activity and manipulate circuits in different regions of the brain to see if activity can be altered," said Kumar, associate professor in the Department of Biomedical Sciences. "Although the temporal lobe structures are interconnected, the precise details of that connectivity are still unknown."

The temporal lobe region is responsible for turning sensory information into meaningful visual memories, language comprehension and emotion association. Temporal lobe epilepsy — the most common form in adults — is not improved with anti-epileptic medications. Kumar and his electrophysiology lab want to gather precise details for better treatment.

"The only way to get to therapeutic avenues for treatment is to understand what happens to the circuits and the neurons," Kumar said. "A hallmark of temporal lobe epilepsy is the loss of a vulnerable population of neurons in a particular region called the entorhinal area."

That region stores memories temporarily. During preliminary studies, Kumar and his team wanted to know why neurons there are overstimulated and die during an epileptic seizure.

"For a long time we looked for answers within the entorhinal area itself," he said, "and it dawned on us that perhaps the circuits that drive these neurons to become overactive are in two surrounding regions: the presubiculum and parasubiculum. These regions were not being studied, and nobody knew what was happening in these structures during epilepsy."

In studying the structure and function of neurons in these surrounding regions, Kumar and his lab characterized seven types of neurons. One became hyperexcitable during epilepsy and projected to two areas at the same time: the entorhinal area and the hippocampus, which are responsible for learning and memory.

"This was a new discovery," Kumar said.

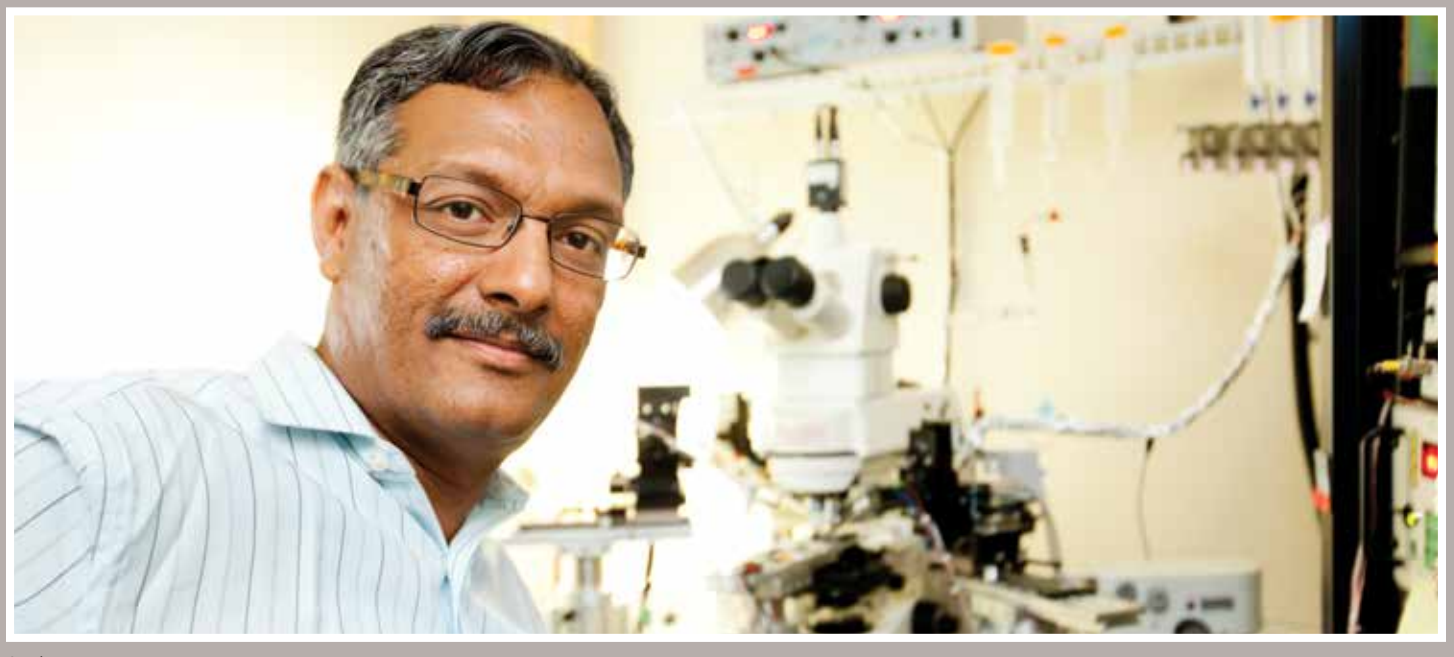
With this information, and with the new grant, the lab is now ready to look for additional culprit neurons and neural circuits.

Kumar hopes his research will lay the groundwork for neuroscientists developing new methods of treatment, such as replacing lost and/or hyperexcitable neurons with stem cells or using optogenetics.

"By differentiating stem cells into particular types of neurons, implanting them back into the region, making them proliferate and integrate into circuits, stem cell researchers are suppressing epilepsy," he said. "Optogenetics uses a light stimulus to activate or suppress specific populations of neurons, including inhibitory neurons that directly alter excitability."

Kumar believes his research will help advance such therapies for temporal lobe epilepsy.

"In both of these approaches, you need to know which cell types become hyperexcitable and which circuits are responsible for bringing about epileptic seizures," he said. "Our study will allow us to get new tools to intervene in people with temporal lobe epilepsy."



Sanjay Kumar