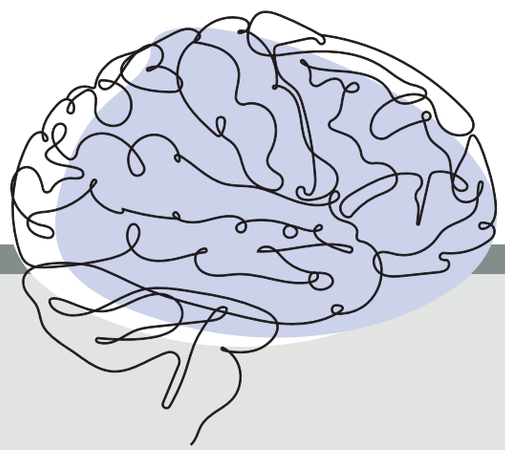

BASIC// DISCOVERY

EXCITING FINDINGS on EPILEPSY

Epilepsy, one of the most common neurological conditions, is characterized by recurrent seizures prompted by abnormal, excessively synchronous firing of neurons in the brain. It may be caused by abnormal brain connections, an imbalance of neurotransmitters or changes in signaling channels within brain cells. For about 70 percent of patients, seizures can be controlled with pharmaceutical treatments. But for many—especially those who experience prolonged seizures—current treatments are ineffective and epilepsy can be life-threatening.

Clinician-scientist **Michael Sperling, MD**, Baldwin Keyes Professor of Neurology, is internationally known for his work in epilepsy surgery and electrophysiology. He integrates clinical practice with research, trying to understand why certain patients benefit from available treatments—and to identify new, effective therapies for those who do not. Dr. Sperling founded and directs the **Jefferson Comprehensive Epilepsy Center**, noted for its basic science and clinical research on epilepsy's underlying mechanisms and on experimental therapeutics. Center researchers are using electrophysiology, structural MRI and functional MRI to map seizure spread within the brain, observe seizure effects on structures involved in cognition, memory and language and develop methods for preventing seizure onset.

Recently, Center researchers found that some seizures start after a burst from neurons that inhibit brain activity. In other words, neurons that dampen other neuronal activity may be key to starting the large-scale hypersynchrony that becomes a seizure. The study, which was part of the group's search for activation-and-resting patterns that correlate with more significant seizures, was the first time that the pre-seizure neural inhibition was seen in patients. In the study, performed in collaboration with neurosurgeons at Jefferson and University of California at Los Angeles, patients undergoing preparation for epilepsy surgery had electrodes placed in the brain to determine the exact location of seizure onset. The electrodes then captured signals from the individual excitatory and inhibitory neurons involved in the seizures. Analysis of cell signaling showed that inhibitory neurons fired immediately prior to the excessive discharge of excitatory neurons. This inhibitory burst may increase the likelihood of subsequent hypersynchronous firing that leads to a seizure.

Among the researchers' goals in leveraging these findings is to develop a way to use the pre-inhibition phenomenon as a biomarker for determining who will (and will not) respond to seizure-prevention therapy. Other biomarkers are also being investigated—in particular, functional MRI signals—in hopes of better predicting response to therapy and developing new methods of modifying abnormal neuronal firing. ■