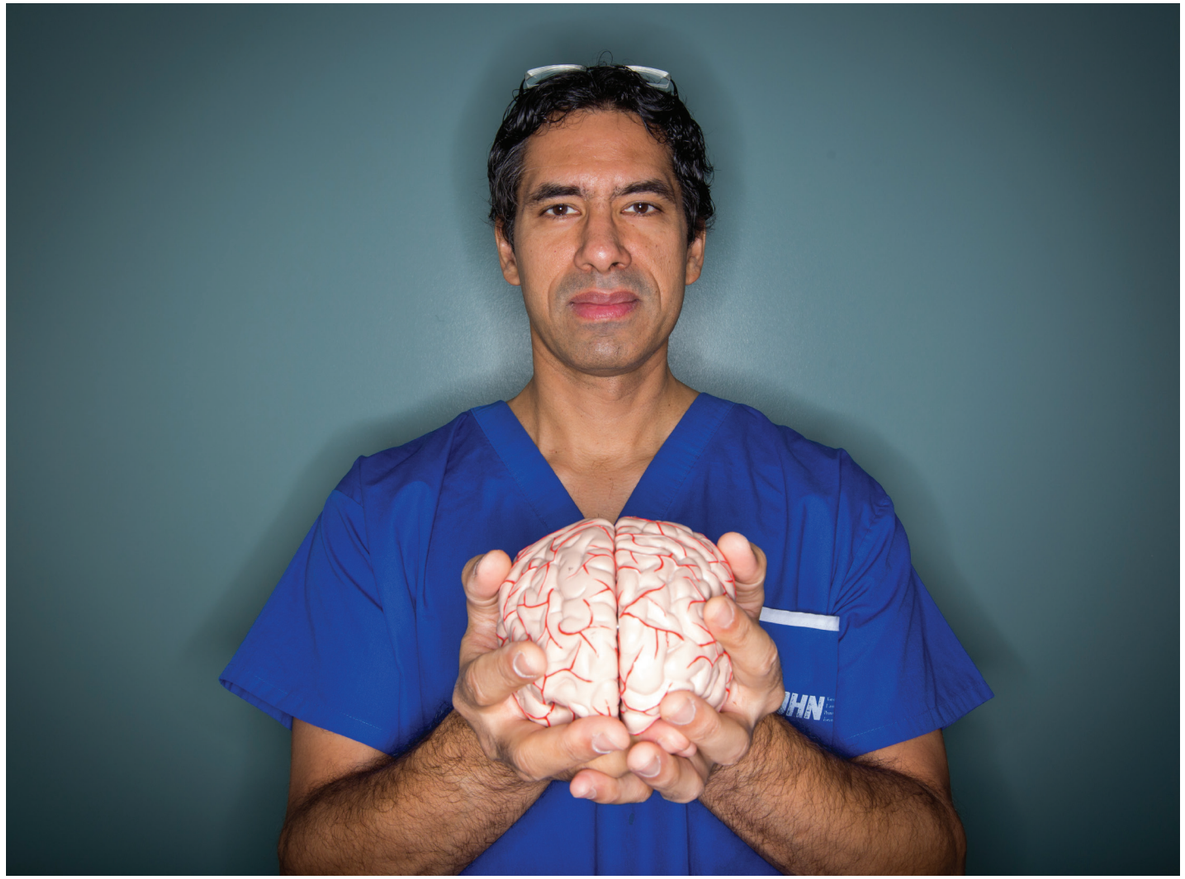

The ‘Holy Grail’ of epilepsy research

Neurosurgeon Dr. Taufik Valiante thinks an implanted electronic device could sense and stop seizures

Shelley White

As tech-savvy citizens of the world, we’ve become accustomed to the idea of a tiny computer chip controlling the functions of a sophisticated device, whether it’s a mobile phone, a laptop or an automobile. But what if an especially “smart” computer chip could control activity in the most sophisticated machine of all – the human brain?

Dr. Taufik Valiante, scientist at the Krembil Research Institute and neurosurgeon at Toronto Western Hospital, is working toward what he calls the “Holy Grail” of epilepsy research – an electronic device implanted in the brain that could monitor brain activity, sense a coming seizure and prevent it from happening, all without the patient’s awareness.

It’s an innovation that offers new hope for people living with epilepsy, a neurological condition that can be especially debilitating when seizures cannot be controlled by medication. For the 30 per cent of those who have an intractable (drug-resistant) form of epilepsy, brain surgery is often their only treatment option. But Dr. Valiante’s research could offer a less-invasive alternative. In collaboration with colleagues at the University of Toronto’s Faculty of Engineering, Dr. Valiante is building and testing an implanted electronic device that would reduce the need to remove a part of the brain.

“The idea is that can we actually change brain function, so that if a person is starting to have a seizure, we can push the brain out of that seizure state,” he says.

Dr. Valiante’s innovative device works through a process called neuromodulation – the targeted delivery of a stimulus to the brain. Electrodes on the device monitor electrical signals in the brain. That information is processed in real time with the purpose of detecting a developing seizure. Then the device delivers a pulse to influence the neurons that participate in seizure development in such a way that the seizure is avoided.

And while there are currently devices on the market that deliver electrical stimulation to the brain (to treat diseases like Parkinson’s, for example), they do so without a precise picture of what is going on in the brain, says Dr. Valiante.

“When the device becomes sentient, when it’s measuring something, it [stimulates] meaningfully in the context of what it’s sensing,” he says. “It [becomes] a closed-loop system.”

The key to creating a platform that has the capacity to record, interpret and respond to an individual patient’s brain activity is machine-learning, says Professor Roman Genov, director of the Intelligent Sensory Microsystems Laboratory at the University of Toronto and a collaborator on Dr. Valiante’s neuromodulation project. Prof. Genov says that there is a class of algorithms that can be trained to learn as they function, so that the device can adapt to individual patients.

Brain activity data collected from patients with epilepsy would be used to develop a set of features that the chip could recognize and respond to.

“It would be patient-tailored, where depending on the signals that are generated by the brain of this given patient, the algorithm would, over time, learn to detect or anticipate seizures [in that individual] better than you could do otherwise,” says Prof. Genov. “What the device learns could indeed be different for every patient it’s used for.”

Another priority for the researchers is to create a system that can remain implanted, operating independently, for a significant amount of time.

“We study how we can implement machine-learning algorithms on a small electronic microchip that uses very little energy,” says Prof. Genov. “The reason it needs to be energy-efficient is because you would like the battery that powers it to run for the longest possible time, and that the heat that is generated as a by-product of its operation is minimal.”

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– Dr. Taufik Valiante

The device wouldn’t have to be limited to delivering an electrical pulse to prevent a seizure, says Dr. Valiante. It could deliver a pharmacological agent to the brain at the right time or even deliver light.

Dr. Valiante is exploring the potential of optogenetics in neuromodulation – light-sensitive proteins that can be expressed in cells, so that they are turned on or off with light. Compared with using an electrical current, optogenetics allows for greater precision over which cell types are controlled, he says.

“It’s an incredible tool because you can turn on specific cells, depending on their genetic composition. So for example, you can turn on a pyramidal cell or turn it off; you can turn on an interneuron or turn it off.” Pyramidal neurons are found in regions of the forebrain (such as the cerebral cortex, hippocampus and amygdala) and are thought to play a key role in advanced cognitive functions; interneurons are nerve cells that connect sensory and motor pathways during a reflex response.

After successfully testing his neuromodulation platform on laboratory models in collaboration with Toronto’s Hospital for Sick Children, Dr. Valiante and his colleagues are starting clinical testing at Krembil involving human subjects. While the machine-learning aspect of the device is still in the development stage, they are currently evaluating the platform’s ability to monitor brain activity and prevent seizures with a well-timed electrical pulse.

The test subjects are patients with intractable epilepsy, and Dr. Valiante says he’s found they are more than willing to take part in the research. The patients, like him, are hopeful this work someday leads to a better quality of life for people with epilepsy.

“If you look at the statistics, people with epilepsy have the lowest quality of life among all people with self-reported chronic conditions in Ontario, so it’s devastating from a biological, physiological and social point of view,” says Dr. Valiante.

“When [patients] are asked about participating, they’ll say, ‘If this could help somebody else, absolutely,’ and that’s incredible to me. They hope nobody else would have to experience what they experience.” ■

Genetic research leads to better treatment for epilepsy

For most people with epilepsy, medication is the primary mode of controlling seizures. But when someone is diagnosed, it can be a lengthy, difficult process to find the right medication.

“The way we treat epilepsy today is by using general guidelines for the use of the antiepileptic drugs. But we know each patient is different. So it often ends up being a matter of trial and error,” says Dr. Danielle Andrade, medical director of the epilepsy program at University Health Network (UHN).

While some medications may work, others may be ineffective or may even make seizures worse, which can be “distressing, tiring and anxiety-causing for the family and for the patient,” says Dr. Andrade. “[They wonder], ‘Why am I having this? What is going to be the next step?’”

Dr. Andrade is on the front-line of researchers identifying the genetic roots of different types of epilepsy and using that information to treat patients more effectively.

“Forty years ago, a small portion of epilepsies were thought to be genetic,” she says. “Now we know that around 70 per cent of epilepsies are genetic,” as opposed to epilepsy caused by brain tumours, injury or illness. “What we can do with genetics is tailor the treatment better.”

As an example, Dr. Andrade points to the discovery of the gene responsible for Dravet syndrome, a severe form of epilepsy that causes both generalized and partial onset seizures. It’s a condition that is normally treated by a combination of medications, with varying degrees of efficacy. But when researchers identified the Dravet syndrome gene as a “sodium channel” gene, they realized that certain commonly used medications that block that sort of channel were actually making the seizures worse.

Identifying genes can also help researchers repurpose drugs – find new medications for epilepsy that might already be on the market to treat other illnesses or conditions.

Although all the genes that cause epilepsy haven’t yet been identified, Dr. Andrade and her colleagues have already identified some. They are also working with the Ontario Brain Institute in the hopes of compiling the genetic data of epilepsy patients throughout the province to gain even more insight.