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Paradis' research could impact seizure treatment

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Assistant Professor Suzanne Paradis works in the lab with a student. Credit: Mike Lovett

(Medical Xpress)—Suzanne Paradis is interested in synapses, sites of cell-to-cell contact that help neurons communicate. She never planned to research a technique that could affect the treatment of epilepsy. She doubted her experiment to build synapses would work at all, let alone work fast enough to be a potential therapy for seizures.

But science – despite the determined efforts of scientists – doesn't always go according to plan.

Now Paradis, an assistant professor of biology, and her team have applied for a patent and are continuing research that could have implications for millions of people who suffer from epilepsy.

It started with a simple question: How are GABAergic synapses built?

Paradis, neuroscience PhD candidate Marissa S. Kuzirian, post-doctoral fellow Anna R. Moore and lab manager Emily K. Staudenmaier, found that a protein called Sema4D, was an essential building block.

There are two main types of synapses in the mammalian brain: excitatory, glutamatergic and inhibitory, or GABAergic. If neuronal connections are like roadways, carrying information in the brain, the synapses are the intersections. The glutamatergics synapses are the green lights triggering the movement of information. The GABAergic synapses are the red lights, stopping the information from proceeding to the next neuron.

The team discovered that when Sema4D was removed, neurons could no longer produce GABAergic synapses. It was Kuzirian who had the idea to test what happened if Sema4D was added to neurons.

Would cells build more GABAergic synapses?

"I thought it would never work," Paradis recalled with a laugh. "No way."

But she gave her student the go ahead and within 30 minutes the proof was under the microscope: dozens of new GABAergic synapses. Not only did it work, the Sema4D caused synapses to form much more quickly than Paradis and her team could have ever anticipated.

That's when they realized the ramifications Sema4D could have on

epilepsy. ?

Epileptic seizures are caused when there is too much excitation in the brain, when all the lights between neurons turn green and there is nothing to stop the onslaught of signals. This can be triggered by a variety of sources, including head trauma, genetic conditions or illness.

Building more GABAergic synapses would be like putting red lights on the autobahn.

To test this theory, the team used a "seizure in a dish" model of epilepsy, triggering seizure-like conditions in a slice of mammalian tissue. They treated the neurons with Sema4D and waited. Within two hours, the electrical output of the neurons was almost back to normal.

Last month the team published its initial findings in the *Journal of Neuroscience*.

Paradis is quick to caution that this research is in its very early stages. It has not been tested outside of a tissue culture dish or in human tissue and its long-term effects are unknown.

But, she says, the research highlights the value of academic inquiry at a time when many in Congress are questioning the importance of funding research through organizations like the National Institute of Health.

"We were not intending to study epilepsy, yet we discovered something we didn't know before," she said. "That's why funding basic research is so important. You never know where the next big, ground-breaking discovery is going to come from."

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