Gene therapy for epilepsy could stop seizures

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(Medical Xpress) -- Sparking production of a hormone in the brain that people with epilepsy often lack could prevent debilitating seizures, University of Florida researchers have discovered.

The researchers used gene therapy in rats to stimulate production of somatostatin, a seizure-stopping chemical that naturally occurs in the brain. The study was published in the February issue of the journal *Neuroscience Letters*.

More than 3 million people in the United States have epilepsy, according to the Centers for Disease Control and Prevention. This lifelong disease is characterized by uncontrollable seizures and can keep people from living independently or holding jobs, particularly if they do not respond to seizure-controlling medication. Finding novel ways to prevent these seizures could help people with epilepsy live more normal, symptom-free lives, said Dr. Paul Carney, chief of the division of neurology in the UF College of Medicine department of pediatrics and senior author of the study.

“For years people have focused only on treating the disease, not preventing the disease,” Carney said. “The mantra is no seizures, no side effects.”

People with epilepsy tend to have lower levels of the hormone somatostatin, as do people with Alzheimer’s disease. Although somatostatin, which belongs to a group of protein-like molecules called

neuropeptides, is present in the brains of people with epilepsy, scientists have shown that its levels decrease during seizures, said Rabia Zafar, the lead author of the paper and a former postdoctoral associate in Carney's lab.

To test whether they could prevent seizures by bolstering levels of this hormone, the researchers administered a dose of the gene that triggers somatostatin expression. A harmless virus transported the gene safely through the body.

"There is some somatostatin in the brain anyway, because it's a neuropeptide, but there was a dramatic increase after the injection," Zafar said.

Boosting somatostatin levels led to weaker and shorter seizures, and none of the subjects that received the injection suffered the highest level of seizure. Better yet, the treatment did not result in unwanted side effects. The only side effect was positive: subjects learned better after the treatment.

"Being able to restore somatostatin up to normal levels allows the brain to heal itself and that is the idea here," Carney said. "We're putting something back in that is normally there and allowing the brain to pick it up as part of its normal machinery. We're not putting in a drug."

In addition to epilepsy, studies have shown that somatostatin may play a role in aging and neurodegenerative disorders such as Alzheimer's disease, Carney said. Somatostatin is a neuromodulator, which means it can alter how nerve cells behave.

In this study, the researchers focused on temporal lobe epilepsy, the most common form of the disease. Although medication helps control seizures in most people with this type of epilepsy, about 30 percent of patients do

not respond to therapy, Carney said.

“We need better, more effective treatments for a large population of children and adults who don’t respond to conventional treatments,” he said. “Gene therapy, as well as other forms of treatment, are emerging, and there is the hope and promise they will offer more effective and novel treatments for people with drug-resistant epilepsy.”

But the researchers caution that this study is just a first step. Additional research is needed before the technique can be attempted in humans. Researchers are particularly focused on ensuring the treatment does not cause inflammation and discovering the best way to administer it, either be injection to the brain or a less invasive intravenous infusion.

“What effect a compound is going to have partly depends on where in the seizure circuit that new compound or gene is being placed. You could put the same chemical in two places and get two different results,” said Dr. Edward Bertram III, a professor of neurology at the University of Virginia, who was not involved in the study. “That is going to be the issue as they try to develop this: Where should we be putting this to have the best effect? On the promising side, they put (the gene) in a restricted area and had an effect. That is a great first step.”

Provided by University of Florida