New medication offers hope to patients with frequent, uncontrollable seizures

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A new type of anti-epilepsy medication that selectively targets proteins in the brain that control excitability may significantly reduce seizure frequency in people whose recurrent seizures have been resistant to even the latest medications, new Johns Hopkins-led research suggests.

"Many other drugs to treat frequent seizures have been released in the last 10 years and for many people, they just don't work," says study leader Gregory L. Krauss, M.D., a professor of neurology at the Johns Hopkins University School of Medicine. "For a drug-resistant population that has run out of options, this study is good news. These are patients who are tough to treat and are fairly desperate."

Perampanel is the first in a new class of drugs that appears to blunt an excitatory response in the brain by inhibiting a specific form of glutamate receptor called an AMPA receptor and therefore reducing seizures without causing major side effects. Other drugs targeting all three forms of glutamate receptors in the brain have tended to make patients too sleepy to function, even putting them in comas, Krauss says. But this new medication, he says, may potentially offer relief not only to people with epilepsy, but to those struggling with drug addiction problems or the neurodegenerative disorder ALS.

"For years, people have been trying to modify glutamate receptors to cure disease," he says. "It's been a very difficult area to develop new drugs in."

In a multinational, blinded, placebo-controlled trial of more than 700 people with uncontrolled partial-onset seizures, roughly one-third of participants saw the frequency of their seizures fall by more than 50 percent when they were given 8 milligrams a day of perampanel. Partial-onset seizures — the most common form in epilepsy — begin in one part of the brain, occurring when there is an injury or abnormality in one of the brain's electrical networks. They can involve anything from the twitching of a limb to confusion to convulsions. Those in this trial typically had roughly 10 seizures a day at baseline.

One in 200 Americans have epilepsy and more than half have partial-onset seizures.

The participants in the study, being reported this week in the journal *Neurology*, were all taking one to three anti-epileptic drugs before adding perampanel (or a placebo) to their regimen. Krauss and his colleagues assigned each to receive a placebo, two milligrams, four milligrams or eight milligrams per day of the drug. The lowest effective dose was four milligrams per day and the higher the dose, they found, the better the results. Another trial is currently looking at a 12 milligram per day dose. The most common side effect was dizziness, Krauss says.

More information: The study was paid for by Eisai Inc., a New Jersey-based pharmaceutical firm. Krauss says he believes the U.S. Food and Drug Administration will review perampanel in the next year.

Provided by Johns Hopkins Medical Institutions