New drug offers relief for treatment-resistant epilepsy patients, clinical trial finds

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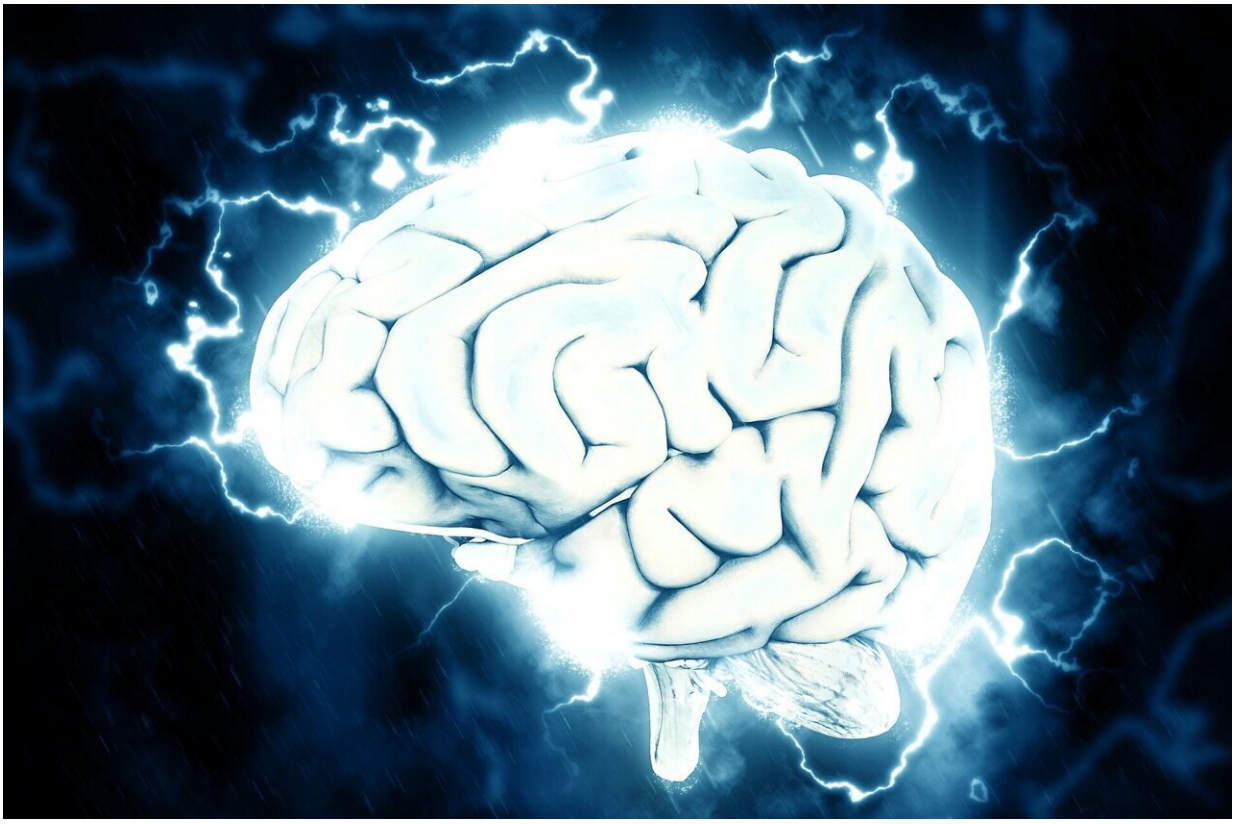

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In cases where standard therapies fail, a medication called XEN1101 reduces seizure frequency by more than 50% in some patients and sometimes eliminates them altogether, a new study shows. Unlike several

treatments that must be started at low doses and slowly ramped up, the new drug can safety be taken at its most effective dose from the start, the authors say.

Focal seizures, the most common type seen in epilepsy, occur when nerve cells in a particular brain region send out a sudden, excessive burst of electrical signals. Along with seizures, this uncontrolled activity can lead to abnormal behavior, periods of lost awareness, and mood changes. While many available therapies control or reduce seizures, they fail to stop seizures in about one-third of patients and may cause harsh side effects, experts say.

Led by researchers at NYU Grossman School of Medicine, a new clinical trial found that patients who added XEN1101 to their current antiseizure treatments saw a 33% to 53% drop in monthly seizures, depending on their dose. By contrast, those given a placebo had on average 18% fewer seizures during the treatment phase of the trial, which lasted eight weeks.

Most patients then volunteered to extend the trial, with about 18% of those treated with the new drug remaining entirely seizure free after six months, and about 11% having no seizures after a year or longer.

"Our findings show that XEN1101 may offer a swift, safe, and effective way to treat focal epilepsy," said study lead author, neurologist Jacqueline French, MD. "These promising results offer hope for those who have struggled for decades to get their symptoms under control."

French, a professor in the Department of Neurology at NYU Langone Health, notes that XEN1101 was well tolerated by the study participants, who reported side effects similar to other antiseizure treatments, including dizziness, nausea, and fatigue, and the majority felt well enough to continue the regimen. Another benefit of the drug, she adds, is

that it takes more than a week to break down, so levels in the brain remain consistent over time.

This steadiness allows the treatment to be started at full strength and helps to avoid dramatic spikes that worsen side effects, and dips that allow seizures to return. This lengthy breakdown time also allows for a "grace period" if a dose is accidentally skipped or taken late.

XEN1101 is part of a class of chemicals called potassium-channel openers, which avert seizures by boosting the flow of potassium out of nerves, stopping them from firing. French notes that while other drugs of this kind have been explored for epilepsy patients in the past, such treatments were taken out of use because the compounds were later found to gradually build up in the skin and eyes, prompting safety concerns, the researchers say.

Meanwhile, XEN1101 combines the effectiveness of potassium-channel openers with the safety of more traditional drugs, says French, who is also a member of NYU Langone's Comprehensive Epilepsy Center. A report on the trial was published in the journal *JAMA Neurology*.

For the study, which included 285 men and women with epilepsy and ran from January 2019 to September 2021, the research team recruited adults with epilepsy who had already tried and stopped taking an average of six drugs that failed to treat their focal seizures.

Patients in the trial had to have experienced at least four episodes a month despite ongoing treatment to qualify. The patients were randomly provided either a daily oral capsule of XEN1101 (in doses of 10 milligrams, 20 milligrams, or 25 milligrams) or an inert placebo tablet that appeared identical to the real drug.

Among the results, the trial revealed no signs of dangerous side effects

such as heart problems, allergic reactions, or concerning skin discolorations. However, French says that the research team plans to expand the number of patients exposed to the drug and monitor for potential issues that could arise in the long term, or include specific groups of people, such as pregnant women.

In addition, the team also intends to explore XEN1101 for other types of seizures, including those that broadly affect the brain at the same time (generalized seizures).

"Our study highlights the importance of finding as many therapeutic options as possible for those who suffer from seizures," says French. "Since everyone responds differently, treating epilepsy cannot be a one-size-fits-all approach."

More information: Jacqueline French et al, Efficacy and Safety of XEN1101, a Novel Potassium Channel Opener, in Adults With Focal Epilepsy: A Phase 2b Randomized Clinical Trial, *JAMA Neurology* (2023). DOI: 10.1001/jamaneurol.2023.3542

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