Forecasting method may help people with epilepsy predict their seizures

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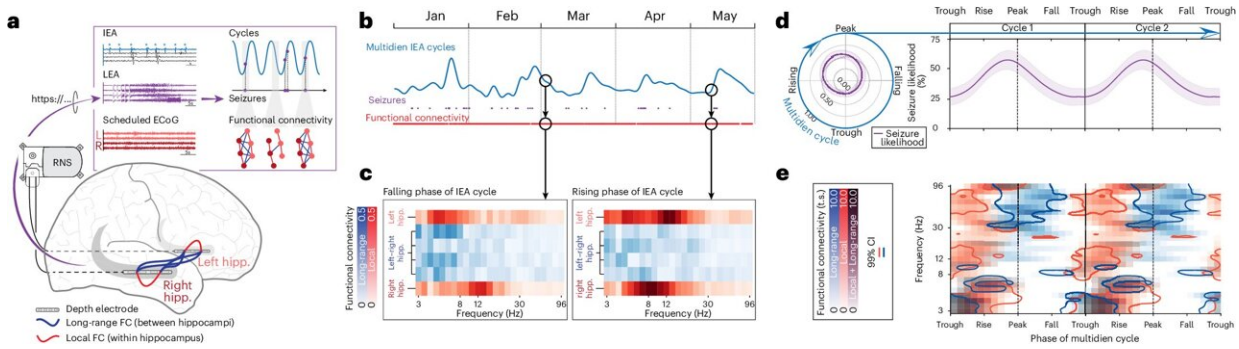

Mapping network connectivity to cycles of seizure likelihood. Credit: *Nature Medicine* (2024). DOI: 10.1038/s41591-024-03149-6

A team of epilepsy specialists at UC San Francisco has developed a method to predict 24-hour seizure risk. The discovery, which may be scalable to large numbers of patients, could help to improve the quality of life for the 2.9 million Americans living with the daily uncertainties of epilepsy.

The researchers, led by Vikram Rao, MD, Ph.D., a Distinguished Professor in Neurology, showed that the storm of brain activity characterizing a seizure is presaged by abnormal communication between specific areas of the brain. By analyzing just 90 seconds of these aberrant brain signals, the researchers could forecast seizure risk.

"Until now, the changes in brain activity and the sequence of events leading up to a seizure have been largely unknown," Rao said. "By identifying one of those events, we can offer patients information that can reduce one of the most stressful aspects of epilepsy: the unpredictability of seizures."

The results appear in *Nature Medicine*.

A storm in the brain

The effort to predict seizures isn't new, but current methods need to gather data over long periods of time, which can be burdensome for patients. Accuracy varies widely, based on the specifics of the person's condition, the quality of the data and the algorithm that is used.

Some people with epilepsy who don't respond to anti-seizure medications have a device implanted that can monitor brain activity and try to prevent it with electrical stimulation when it recognizes the sign of a seizure.

These responsive neurostimulation systems, or RNS devices, sometimes respond too late to fend off the seizure. But Rao's technology can predict seizures.

Rao collaborated with Ankit Khambhati, Ph.D., an assistant professor of neurosurgery who studies brain circuits associated with epilepsy, in the hopes of identifying a pattern of changes in how parts of the brain communicate with each other that could more easily and accurately foreshadow an oncoming seizure.

"Patients aren't always having seizures, but their epilepsy never goes away," Khambhati said. "We wanted to find a signature of how patients' brains are operating long before an event, while the disease is there in

the background but they're not having an episode."

Rao recruited 15 volunteers whose seizures arise from the hippocampus, which is found on both sides of the brain and plays a role in most types of epilepsy. These patients all had RNS devices that had recorded months of brain activity, which the researchers scanned for clues.

They found a cycle of activity several days long that was associated with seizures. Within it was evidence of a change in communication between the two hippocampi.

When the risk of a seizure was low, the right and left hippocampus operated independently, in a normal, healthy way. But signs of seizure risk increased when the two sides began to communicate, slowly synchronizing.

Whatever mechanism had kept them from communicating with each other was breaking down, Khambhati explained, likening the result to the onset of stormy weather.

"Before a storm, the clouds come in and the wind picks up, and you know that soon, the thing will really get going."

Snapshot seizure forecasting

In the brain of a person living with epilepsy, the time between sunny skies and the storm striking ranges from minutes to hours, but the indicators are there up to a day before.

To see these indicators, Rao's team had patients download and transmit data from their RNS devices to the researchers, who then run the data through their algorithm.

The researchers found that as little as 90 seconds of data was sufficient to spot the pattern and assess the likelihood of a seizure occurring in the next 24 hours, a process they call "snapshot seizure forecasting." It gives the person time to take precautions, like avoiding driving or making sure they have a caregiver with them.

The forecasting pattern was similar for virtually all the 15 study participants, increasing the likelihood that the approach will work for other people with this form of epilepsy.

Rao and Khambhati plan to test the approach on a much larger number of patients, including those with different types of epilepsy. They also hope to develop a method for gathering the data in a noninvasive way that doesn't require a brain implant.

Surveys of people with epilepsy show that up to 70% of them would use a forecasting system to help plan the following day, Khambhati said, adding that patients find it just as helpful to know when their seizure risk is low as when it is high.

"People with epilepsy often live in so much fear of having an unpredictable event that they avoid doing things they'd like to do," Khambhati said. "These forecasts can give them confidence that they can just go out and have a normal day."

More information: Ankit N. Khambhati et al, Hippocampal network activity forecasts epileptic seizures, *Nature Medicine* (2024). DOI: 10.1038/s41591-024-03149-6

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