New Algorithm Using Scalp Electrodes Predicts Seizures

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ARTICLE IN BRIEF

A software program, based on a mathematical model, detects patterns in the EEG output that correlate with a high risk of seizure within the coming hours. A "correct" prediction was one followed by a seizure within 2.5 hours.

BALTIMORE—Predicting seizures by using scalp electrodes to monitor brain activity has met with little success. Now, results from a test in over fifty patients suggest that a new computer algorithm that monitors scalp electrode output can predict 95 percent of seizures in selected patients, with relatively few false positives, a record one expert called "amazing."

The research was described in a poster here at the annual meeting of the American Neurological Association.

The study enrolled 51 patients with medically intractable partial seizures who had been admitted to an epilepsy monitoring unit for presurgical evaluation. Scalp electrodes were attached in standardized positions, and EEG data were analyzed by software developed by a team of investigators at Optima Neurosciences of Alachua, FL —Deng-Shan Shiau, PhD, vice president of scientific affairs, and J. Chris Sackellares, MD, chief scientific officer.

> 'I'd like to see a lesser number of false positives, and this needs to be retested in a separate population, but the size of the sample is good enough in my view that there is some signal here.'

The software detects patterns in the EEG output, Dr. Sackellares explained, that correlate with a high risk of seizure within the coming hours. For this study, a "correct" prediction was one followed by a seizure within 2.5 hours.

The 51 patients spent an average of 48 hours being monitored, during which there were a total of 159 seizures. The software correctly predicted 95 percent of the seizures, with a false positive about once every eight hours. The authors compared this to a random predictor, with a fixed mean interval between predictions. As the interval shortened, the number of correct predictions increased, but so did the false positives. With an interval that correctly predicted at least 80 percent of seizures, there was a false positive every two hours. The false positive rate could be reduced by increasing the mean interval between predictions, but only at the cost of lowering the number of correct predictions. The superiority of the software detection program over the random predictor was significant at the $p<0.001$ level.

A MATHEMATICAL MODEL

The detection program uses a formula called the "pattern match regularity statistic," developed by Dr. Shiau, a mathematician, to compare outputs from multiple electrodes to determine how similar in appearance they are. As the similarity increases, the risk for seizure rises. "We don't know why this signal coherence triggers a seizure," Dr. Sackellares said, although he and his colleagues do have an intriguing model to explain it.

Their work traces back to chaos theory, a branch of mathematics that analyzes the behavior of complex systems. In the 1980s, he said, "some people had proposed that epilepsy may actually be a self-organizing behavior in a complex, chaotic system," namely the human brain. "We wanted to explore that," he said.

Early attempts to map chaos theory onto the workings of the brain met with limited success, but the group continued to explore how the "mathematics of complexity" could be used to understand epilepsy.

The theory they are working with, which Dr. Sackellares said is just speculation for now, is that the coherence pattern seen just before the seizure is an "attractor" state, an alternative stable state to the brain's normal electrical activity pattern. "Part of the speculation is that the seizure is the brain's way out of the attractor; it's a resetting mechanism. A lot of people think we are crazy. But people in engineering don't. It makes sense when you think of it from a mathematical perspective."

He thinks it is likely that the false positives occur when the brain approaches the attractor state, but then finds another way out of it. "We don't know that yet, though."

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CLINICAL APPLICATIONS

The clinical applications of an accurate prediction program are potentially far-reaching, he said. "The problem in presurgical evaluation is that you don't know when the seizure will happen," requiring a high investment in time and resources for a patient who, during most of the evaluation, doesn't need them. A better predictor may be able to reduce those expenditures while maintaining good patient surveillance. Additionally, it could aid in epilepsy imaging studies, such as SPECT or PET, which require injecting labile imaging agents just before a seizure occurs.

It might even be used for seizure prophylaxis, providing a warning in time to administer powerful anticonvulsants. Further in the future might be electrical stimulation to shut down the seizure pattern, a technique that has some support in animal studies, Dr. Sackellares said. "But we are decades behind" similar work in cardiac arrhythmia, he added.

The investigators are also exploring the development of an "index of susceptibility," rather than to try to predict individual seizures, to provide patients information about their long-term susceptibility to seizure, outside of an intensive monitoring situation.

Dr. Sackellares said a more widespread immediate use might be in intensive care units or emergency rooms, where many patients without epilepsy are at risk for nonconvulsive seizures due to head injury, stroke, central nervous system infections, or other causes. "In the ICU, you get an EKG, a blood pressure monitor, a pulse oximeter; you get everything monitored but your brain," he said. An inexpensive and noninvasive monitor might change that.

EXPERTS COMMENT

"The remarkable thing about this protocol is that Dr. Sackellares was able to predict seizure onset with high sensitivity with external electrodes," according to Jose Cavazos, MD, PhD, associate professor of neurology at the University of Texas Health Sciences Center in San Antonio, and director of the Epilepsy Center at the Audie L. Murphy Veterans Administration Hospital, also in San Antonio. "That's honestly amazing."

"The biggest problem for patients with seizures is the unpredictability," he said. While a patient may experience seizures for only minutes per month, he or she may be disabled every day by not knowing when to expect one.

"I'd like to see a lesser number of false positives, and this needs to be retested in a separate population," he said, "but the size of the sample is good enough in my view that there is some signal here." •

REFERENCE:

- Sackellares JC. Seizure prediction. *Epilepsy Curr* 2008: 8(3):55-59.