



Helping Epilepsy Patients to “Pre-empt” Their Seizures

Once patients have the tools needed to predict seizure occurrence, AED treatment can be better timed. Here’s how it can work.

For most patients with epilepsy, one of the most disturbing aspects of the disorder is the fact that seizures are unpredictable.¹ A person with epilepsy may begin an ordinary activity such as a trip to the store and wake up in an emergency room, having had a seizure on the street. While nearly all persons with epilepsy take preventive medications, approximately 40 percent continue to experience seizures.² If there were a reliable method to predict seizures before they occurred, this would open the door to “pre-emptive” therapy, in which treatment could be taken during a period of high risk for seizure.

Do Seizures Occur Randomly?

If seizures occur randomly, then by definition they cannot be predicted. However, there is ample evidence that seizure occurrence is not always random. Patterns of seizures have been reported as early as 1901 by Gowers, who commented on relation to menstruation and time of day.³ Well-documented seizure cycles include ultradian or circadian patterns, such as nocturnal (*i.e.*, autosomal dominant nocturnal frontal lobe epilepsy), or early morning (juvenile myoclonic epilepsy), as well as monthly cycles associated with menstruation.^{4,5} Further proof of nonrandomness is the fact that trigger factors such as sleep deprivation appear to be significant precipitants, as discussed below.

Seizures may also deviate from randomness when they occur in clusters. If

seizures are truly random, then the occurrence of one seizure does not increase or decrease the likelihood of a subsequent one. However, studies have shown that seizures that occur in clusters do deviate from a random (Poisson) process.⁶ Thus, we begin our discussion with the concept that seizures may not in fact occur randomly, and thus prediction may be possible.

Researchers have taken different approaches to attempt to predict seizures. Many studies have concentrated on the analysis of EEG changes preceding a seizure. Other studies have focused on clinical symptoms and triggers that patients report prior to seizure occurrence. In a recent diary study discussed below, we directly examined patients’s ability to predict their own seizures.⁷

Predicting Seizures with EEG

There are many studies in progress that examine seizure prediction using electroencephalographic (EEG) data.^{8,9} This approach examines EEG changes that precede a seizure by days, hours or seconds. These studies rely on complex linear and nonlinear analysis methods, and are typically performed on EEG obtained during intracranial monitoring. If electrophysiologic seizure prediction is feasible, it may be possible to develop devices that deliver medication or stimulation directly to the brain when a seizure is predicted.¹⁰ To date, these studies remain outside of clinical practice, although a clinical trial of an implanted stimulation device is in process.¹¹

Predicting Seizures Clinically

Predicting seizures based on triggers and pre-seizure symptoms (premonitory features) is an area that is currently more directly applicable to patient care. Many patients report either premonitory features, trigger factors or both. A trigger factor is a factor whose presence is associated with an increased probability of seizure over a brief time period. Premonitory features are symptoms that a patient reliably recognizes as preceding a seizure. Unfortunately, few prospective studies have been performed to confirm that premonitory features or triggers do indeed reliably predict an upcoming seizure.

Seizure triggers. Ninety percent of patients with epilepsy identify at least one specific seizure precipitant, or trigger.¹²⁻¹³ Frequently reported seizure triggers include sleep deprivation, emotional stress and menstruation, among others (see Table 1 on the following page).¹⁴⁻¹⁶ For some patients, identification of triggers is reliable enough to lead to treatment options. For example, women who typically experience seizures before or during menstruation (catamenial seizures) may take additional or specific medications peri-menstrually. For most patients however, triggers often occur without subsequent seizures, and seizures often occur without preceding triggers.

Helping patients understand and identify their unique triggers is very important in epilepsy treatment. Trigger management can reduce seizure frequency, and increase self-efficacy. On the other hand, there are striking indi-



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Table 1: Commonly Reported Seizure Triggers/Precipitants

- Sleep deprivation
- Menstruation
- Medication non-compliance
- Intercurrent illness
- Stress and stressful life events
- Anxiety
- Alcohol
- Weather
- Cyclical (i.e. time of year)
- Diet

Table 2: Commonly Reported Premonitory Features

- Irritability
- Headache
- Depression
- Difficulty concentrating
- Confusion
- “Funny feeling”
- Elation
- Speech disturbance
- Epigastric sensation

vidual differences in triggers, and misidentification of triggers for a particular patient may lead to unnecessary changes in lifestyle. Furthermore, instructing a patient to adjust their medications to prevent a seizure when they experience seizure triggers is not recommended, as there are no clinical trials to support this practice, and taking additional anti-epileptic medication may lead to toxicity. This is where seizure diaries, discussed below, may be very helpful.

Premonitory symptoms. Some patients also report subjective feelings before a seizure, or “premonitory symptoms” (see Table 2 above). Drowsiness, headache, irritability or difficulty concentrating are among the premonitory features frequently reported similar to the prodrome of migraine,¹⁷⁻²⁰ although occurring less commonly than in migraine. For patients who regularly experience premonitory features, the appearance of these symptoms may reliably herald an upcoming seizure. Consider recommending seizure precautions to patients during this high-risk period; traveling with a companion is an example.

Strategies for Patient Self-Prediction

In response to the observation that many patients with epilepsy feel that

they can predict when they will have a seizure, we investigated this concept in a large seizure diary study.⁷ Patients answered the following question, completed on a daily basis: “Do you think you will have a seizure in the next 24 hours?” Response options included extremely likely, somewhat likely, somewhat unlikely and extremely unlikely. We also collected data on potential triggers, such as hours of sleep, medication compliance, menstruation, stress, anxiety and alcohol use.

Seventy-one subjects in our study returned a total of 15,635 detailed diary days. Fifty-seven subjects had experienced at least one seizure during the follow-up period. Overall, 1,488 seizure days occurred, of which 31.9 percent had been positively predicted (sensitivity). For 13,691 seizure-free days, 83 percent had been rated “somewhat unlikely” or “extremely unlikely” (specificity). The adjusted odds ratio for positive prediction was 2.25 (1.91-2.65) indicating that seizures were twice as likely in the 24 hours following a positive prediction.

In the cohort, we identified a subgroup of 21 percent of patients who were significant “predictors.” This group correctly predicted 37 percent of their seizures, and correctly identified seizure-free days 90 percent of the time. For this group, a positive prediction

yielded a 3.2 times increased risk of seizure in the next 24 hours.

Sleep deprivation, stress and anxiety were all significant triggers for seizures.²¹ Much of the self-prediction appeared to be based on stress and anxiety levels. When the predictors experienced increased stress and anxiety, they were more likely to positively predict a seizure. This study was a paper diary study, so the patient answers were not time stamped. We are currently repeating this study with electronic diaries, and with attention to premonitory symptoms as well as an expanded list of triggers.

If some patients can indeed reliably predict their seizures, this may lead to clinical trials to investigate the use of pharmacologic or behavioural interventions during periods of increased risk.

Using a diary. Diaries can play an important role in epilepsy care. Most patients with epilepsy are very accustomed to recording their seizures in a calendar or diary that they bring to their appointments. Studies have indicated that seizure diaries are reliable,²² and in our study, compliance with the detailed daily diary was high.

While seizure frequency is an important aspect of diaries, other information can be included as well. If patients note specific seizure triggers, they can record and monitor these in relation to actual seizure occurrence. Medication compliance may increase if a medication check-off is included.

We believe that maintaining a diary allows patients with epilepsy to feel a sense of control over a disorder that frequently removes their control. While diaries have traditionally been paper, a number of online/electronic database seizure diaries have recently become available for patient use. For more information, see the online resources available at:

- www.neomedsoft.com/epitrax
- www.epilepsy.com

Conclusions

Future research concerning EEG and clinical seizure prediction is promising. One day, perhaps an implantable device will allow for precisely targeted therapy. For now, helping patients develop the skills needed to predict their seizures offers the potential for improved safety, self-efficacy and seizure control.

Ask patients about the seizure triggers and premonitory features they have observed, as these are quite common. Recommend that all epilepsy patients maintain a seizure diary, as diaries provide them with a more active role in their own care, and may offer potential therapeutic interventions. For patients who do demonstrate reliable triggers and/or premonitory features, specific precautions may be indicated during periods of high risk. **PN**

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