

## Prediction of Seizures in Patients with Temporal Lobe Epilepsy, more than 30 minutes before onset

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*Dear Madam,* Around 52.5 million people worldwide suffer from the neurological illness known as epilepsy, which is frequently characterized by recurring seizures.<sup>1,2</sup> As epilepsy is a chronic disorder that can lead to cognitive deficits, sadness, and anxiety in sufferers, it has a considerable negative impact on individuals and society. The most common type of seizures, affecting around 61% of persons with epilepsy, are focal seizures, which raise the risk of injury and early death.<sup>2</sup> One of the most common forms of focal epilepsy, temporal lobe epilepsy (TLE), is characterized by recurring spontaneous seizures that begin in the temporal lobe(s).<sup>3</sup>

In the last two decades, many new antiseizure medications (ASMs) have been developed; however, about 40% of people with epilepsy may be drug-resistant, meaning ASMs are unable to control their seizures; therefore, despite the advent of new treatments, a high unmet need remains unaddressed.<sup>2</sup> Surgery is an alternate treatment, however, it cannot be used if larger areas of the brain are affected, in such cases, neuromodulation is a novel and successful therapeutic tool developed.<sup>4</sup> Conventionally, neural activity in epilepsy is categorized into interictal, and post-ictal states. With the help of continuous EEG, researchers have subdivided interictal state into a pre-ictal and pro-ictal state in temporal lobe epilepsy patients (which is the typical drug-resistant focal epilepsy targeted for interventions such as neuromodulation). The pre-ictal states indicate imminent seizure onset, while pro-ictal states reflect changes in neural activity that create a propensity for seizures over longer periods. The EEG-based pro-ictal state detection is critical to adaptive neuromodulation, with early detection of seizure allowing electrodes to be applied therapeutically to the brain's seizure onset zone and thalamus enabling treatment to be modified as per seizure risk.<sup>5</sup>

A prospective cohort study was conducted on adults with drug-resistant temporal lobe epilepsy at UHealth

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Houston, in which pro-ictal state – i.e., pathologic brain activities during periods of heightened seizure risk could be detected up to one-half hour prior to seizure onset. A classifier was developed that could reasonably accurately distinguish between physiological and pathologic brain states in temporal lobe epilepsy. Thalamocortical dynamics were used to identify pro-ictal states in each patient. As the limbic thalamus exerts a diverse influence on cortex activity, thalamocortical EEG was used for pro-ictal state detection as opposed to previous paradigms derived solely from cortical structures. The study design used two electrode contacts (one in the seizure onset zone and one in the thalamus), ensuring its compatibility with contemporary neuromodulation technologies.<sup>5</sup> Thus, this method of seizure onset prediction, can help create potent treatments enhancing the quality of life for epilepsy patients.

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