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Seizure Prediction and Monitoring

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Seizure Prediction and Monitoring Technology

The essential question as to what causes seizures to come and go remains unanswered. In 1988, Sackellares and Iasemidis initiated research to test the hypothesis that the transition from the interictal state to a seizure (ictal state) is similar to the state transitions that had been observed in chaotic systems (Iasemidis et al., 1988(a), (b); 1990; Iasemidis and Sackellares, 1990). In the course of these investigations, they found that the spatiotemporal patterns of the ictal states were consistently more ordered than that of the interictal and postictal states. Further, there was a significant change in measures of spatial order of EEG signals that precede seizures by periods on the order of an hour. Thus, by combining measures of temporal order, spatial order, and signal energy, it is possible develop devices that can predict as well as detect seizures.

Seizure prediction and seizure detection devices have a wide range of potential clinical applications which depend on the performance of the devices in terms of sensitivity and false prediction or detection rates. These applications include patient monitoring in venues such as epilepsy monitoring units, intensive care units, and emergency departments. They also may be incorporated into closed loop seizure control devices. Preliminary studies in the rodent chronic limbic epilepsy model indicate that the development of seizures, once detected, can be reversed by electrical stimulation of the brain, thereby delaying or even preventing seizure occurrence.

These scientific discoveries led to the development and testing of patented methods for automated seizure detection and prediction algorithms, and novel methods for use in implantable seizure control devices. The methods utilize spatio-temporal patterns derived from EEG dynamics, including linear and nonlinear, uni- and bi-variate EEG descriptors. An important finding is that the transition before a seizure occurrence (i.e., so called preictal transition) can be characterized by (1) progressive convergence of the mean Short Term Maximum Lyapunov exponents (STLmax) among specific anatomical areas (mean value entrainment), and (2) progressive phase locking of the STLmax profiles among various electrode sites (phase entrainment). In initial studies, preictal entrainment of EEG dynamics among electrode sites was detected by visual inspection of STLmax versus time plots. More recently, methods have been developed that provide objective criteria of pattern recognition for dynamical entrainment among electrode pairs (Iasemidis et al., 1998; 2000). Based on these findings, algorithms have been developed for the automatic detection of the preictal state for prediction of impending seizures (Iasemidis and Sackellares, 2001; Iasemidis et al., 2003; 2005; Sackellares et al., 2006).

Although the initial application of these methods was to intracranial EEG recordings, our research team also has developed a scalp EEG based automated seizure monitoring system that exhibits high seizure detection sensitivity with low false detection rate. The EEG features common to almost all seizure onsets are the abrupt changes in amplitude and organization caused by the sudden increase in neuronal synchrony. Hence, the detection algorithm uses measures of signal energy, frequency, and pattern regularity to capture these features (Sackellares and Shiao, 2007). Nonlinear techniques are used to detect seizures while linear

features are used to reject recording artifacts and normal physiological activities (e.g., sleep transients, muscle and chewing artifacts). The algorithm not only detects seizure events, but also recognizes onset patterns (i.e., left-unilateral, right-unilateral, or bilateral) based on the spatial distribution of the EEG dynamics.

Clinical Applications

Based on this technology, Optima Neuroscience is producing a line of brain monitoring products designed for use in hospital emergency rooms and intensive care units. In US emergency rooms, over 10 million patients are admitted every year due to acute brain injuries including head trauma, TIAs and stroke. Due to the limited availability of EEG diagnostics, an alarming percentage of these patients develop unrecognized seizure activity causing further neuronal damage and loss of function. Optima's monitors will help automate the process of EEG interpretation, reducing the current time delay to treatment and greatly improving the identification of subclinical seizures.

Optima's seizure detection and prediction technology will also be used to improve the efficiency of reviewing long-term EEG recordings. Our software marks the areas of interest (spike and seizures) with a higher sensitivity and lower false positive rate than commercially available products. This translates to a dramatic time savings for any neurologist or technician tasked with manually screening multiple days of EEG recordings. When used online in an Epilepsy Monitoring Unit, our software can help the attending physician discharge the patient sooner by notifying the staff as soon as the requisite number of events has been recorded.

Similar algorithms are being developed by our research team to detect a wide range of normal and abnormal brain wave patterns. These algorithms are applied to the detection of EEG patterns that occur during stroke, impending stroke, hypoxia, hypoglycemia, and other metabolic disorders that alter brain function. These algorithms will be incorporated in the same brain monitoring systems used to detect and predict seizures. The systems can be used in a variety of settings including special diagnostic and treatment units, intensive care units, emergency departments, postoperative recovery rooms, general care hospital beds, emergency vehicles, and even in the home.

Status of Development

Optima Neuroscience is nearing the completion of a clinical study demonstrating the high sensitivity and low false positive rate of our automated seizure detection algorithms. We are using a large sample of long-term EEG recordings and comparing the performance of our algorithm to commercially available products. Once cleared by the FDA, this technology will be available to EEG specialists as a software package to improve the efficiency of EEG review. Development is underway to design a clinically useful brain function monitor using the same core analysis techniques. Our unobtrusive, bedside monitor will enhance diagnostic capabilities, patient safety, and reduce personnel costs in hospitals. Designed for use in intensive care units, emergency rooms and epilepsy monitoring units, our portable stand alone monitor will increase the availability of EEG diagnostics. This system will record and monitor the brain's electrical activity and provide critical brain function information, including seizure warning and detection. In later generations, the system will include alerts and detections of other threatening brain conditions such as ischemia (reduced blood supply and impending stroke), hypoglycemia, and hypoxia, as well as monitor the effects of treatment with drugs such as anticonvulsants, sedatives, and anesthetics. The brain monitoring system will include easy-to-use disposable electrode arrays to be placed on patients by nursing staff with minimal training.

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