How Seizure Detection by Continuous Electroencephalographic Monitoring Affects the Prescribing of Antiepileptic Medications

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Objective: To assess the effect of continuous electroencephalographic monitoring on the decision to treat seizures in the inpatient setting, particularly in the intensive care unit.

Design: Retrospective cohort study.

Setting: Medical and neuroscience intensive care units and neurological wards.

Patients: Three hundred consecutive nonelective continuous electroencephalographic monitoring studies, performed on 287 individual inpatients over a 27-month period.

Main Outcome Measures: Epileptiform electroencephalographic abnormalities and changes in antiepileptic drug (AED) therapy based on the electroencephalographic findings.

Results: The findings from the continuous electroencephalographic monitoring led to a change in AED prescribing in 52% of all studies with initiation of AED therapy in 14%, modification of AED therapy in 33%, and discontinuation of AED therapy in 5% of all studies. Specifically, the detection of electrographic seizures led to a change in AED therapy in 28% of all studies.

Conclusions: The findings of continuous electroencephalographic monitoring resulted in a change in AED prescribing during or after half of the studies performed. Most AED changes were made as a result of the detection of electrographic seizures.

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Seizures occur frequently in patients in intensive care units (ICUs), particularly in the neurological ICU, and most of these are nonconvulsive or clinically subtle. Uncontrolled seizures result in neuronal injury and clinical morbidity. Acute symptomatic seizures, particularly when convulsive, are associated with increased morbidity and mortality in acute brain injury, particularly as a result of intraparenchymal hemorrhage, subarachnoid hemorrhage, cerebral hypoxic injury, head injury, and ischemic stroke. Patient mortality increases with delay in diagnosis of seizure activity and in sustained status epilepticus (SE). The evidence that nonconvulsive seizures (NCS) and nonconvulsive SE (NCSE) lead to significant tissue injury and clinical morbidity is less compelling and, hence, the subject of ongoing debate. Nevertheless, many clinicians treat NCS and NCSE in the same manner as clinically overt seizures and SE. Increasing recognition of the difficulty in clinical detection of seizures as well as the realization that untreated SE probably results in added morbidity and mortality will likely lead to increased use of the continuous electroencephalogram (cEEG) in the care of neurologically ill patients.

Timely interpretation of long periods of EEG recording has been made increasingly available to the treating physician through digital EEG and Intranet access. Despite the undoubted ability of cEEG to detect electrographic seizure, the effect of cEEG on patient management and clinical outcome remains unclear. This study attempts to objectively quantify the effect that cEEG monitoring had on patient care by evaluating the effect of cEEG data on antiepileptic drug (AED) prescribing by the treating physician.

Methods

Study Population

We reviewed the clinical and cEEG data of 300 emergent cEEG studies of 287 consecutive adult and pediatric inpatients in both the ICU and...
non-ICU at Massachusetts General Hospital, Boston. Attention was paid to clinical decision making before, during, and after the cEEG studies. Information was obtained from the Electronic Medical Record, Electronic Prescribing Log, and, where necessary, clinician interview.

**cEEG RECORDING**

Three hundred nonelective cEEG studies were performed in our hospital for varying indications over a 27-month period. All cEEG studies were reviewed and reported by a fellow in epilepsy (R.D.K. or D.J.C., among others) and a board-certified neurophysiologist (K.H.C., among others). Primary cEEG data and formal reports were reviewed in detail. Where a prior routine EEG was performed, these results were noted. Only those studies with interpretable EEG data were included in this study. Electroclinical or presurgical cEEG studies were excluded from the study. Continuous EEG studies were performed in the ICU and non-ICU setting. The nonelective nature of these studies was defined by an urgent request by a treating physician for cEEG monitoring. The stated indications were divided into 3 groups as defined by the clinician request: (1) the diagnosis of clinically uncertain events or screening for possible seizure activity, (2) the management of suspected electrographic seizure activity and assistance in monitoring of AED therapy, and (3) therapeutic drug monitoring in the management of raised intracranial pressure.

**EEG PARAMETERS AND DEFINITIONS**

Patient demographics, clinical diagnosis, location (ICU or non-ICU), and duration of study were all noted. Continuous EEG findings were defined as (1) normal, (2) containing background rhythm abnormalities without epileptiform abnormality, (3) containing epileptiform abnormality (local or generalized) without electrographic seizure(s) and (4) containing electrographic seizures (local or generalized). For this study, on a scalp-derived EEG recording, an electrographic seizure was defined as a paroxysm of entrained rhythmic EEG activity distinctly different from the ambient background EEG activity with some or all of the following characteristics: (1) artifactual origin excluded by appropriate considerations of the EEG pattern (eg, configuration of activity, potential field, no association with physiological sources of artifact [eg, respiratory activity or ballistocardiogram], and no association with extraneous sources of artifact [respiratory activity, electrical pumps, and others]); (2) temporospatial evolution with an initial buildup of regularly repetitive sharp wave or rhythmic sinusoidal activity of gradually increasing frequency and amplitude, progressing to a slowing in frequency and a more irregular appearance; (3) transient postictal disorganization and slowing in the same region where the original electrographic seizure arose, (4) of sufficient duration to disrupt normal cortical activities in the involved region, arbitrarily set at 10 seconds, or of sufficient duration to cause clinical impairment (5) usually repetitive in nature and highly stereotypic (Figure 1). An electroclinical seizure was defined as an electrographic seizure with stereotypic and paroxysmal clinical manifestations. When deciding if atypical EEG patterns represent electrographic seizure activity, we included special circumstances in which the designation of a particular EEG pattern as an electrographic seizure arose from the observation of consistent, linked clinical and EEG phenomena. This particularly applies to EEG patterns that may not be particularly striking but are associated with stereotypical clinical manifestations, for example, abrupt electrodecremental responses associated with tonic posturing. This assessment was dependent on bedside clinical assessment or review of videotape accompaniment, which was available in 92 of 300 studies performed. Periodic epileptiform discharges (PEDs) were defined as repetitive monotonous sharp transients occurring throughout the recording, typically every 1 to 3 seconds with some irregularity in the interval between discharges, without entraining into discrete electrographic seizures. PEDs may be unifocal (PLEDs), bifocal or multifocal (Bi-PEDs), or generalized (GPEDs). We did not categorize PEDs as electrographic seizures but view them as an interictal pattern, often associated with discrete electrographic seizures in the same cEEG recording.

**AED FACTORS**

Particular attention was paid to the administration of AED therapy for seizure prevention or control. The presence of prior AED therapy before the hospitalization or onset of a given study was noted. Any decision to subsequently change (initiate new AED therapy, modify the current AED regimen, or discontinue AED therapy) treatment (1) prior to the initiation of the cEEG study, (2) during the cEEG study, or (3) after the completion of cEEG monitoring were all investigated. Bolus dosing, AED dose changes, and AED substitution were all noted and were considered an active clinical decision and change in medical management.

**PATIENT DEMOGRAPHIC AND cEEG STATISTICS**

Three hundred nonelective cEEG studies were performed during the 27-month study period on a total of 287 individual patients. Thirteen patients had second cEEG studies. Of the monitored cases, 154 were male patients (51.3%) and 146 were female patients (48.7%). The mean age of monitored patients was 41.5 years (median age, 46 years; age range, 1 day to 90 years). Two hundred forty studies were performed on adults (≥18 years old) while 60 studies were performed on pediatric patients, of which 36 (12% of total, and 60% of the pediatric cohort) were performed in the first year of life. One hundred eighty-nine of the 300 nonelective cEEG studies were performed in the ICU. Ninety-two of the 300 nonelective cEEG monitoring studies performed were carried out using video. The duration of studies varied from 2 to 432 hours, with a mean duration of 51.5 hours (median, 24 hours). The duration of the cEEG studies are shown in Figure 2.

**STUDY INDICATIONS**

The indication for cEEG monitoring was determined by physician request at the time of study initiation. In 200 of the 300 studies (66.6%), the stated reason for cEEG monitoring was for diagnostic monitoring, that is, surveying the background EEG for event detection. Ninety-one of 300 studies (30.3%) were requested to monitor strongly suspected seizure activity and specifically to assist in monitoring AED therapy. A further 9 of the 300 cEEG studies (3.0%) were requested solely for the purpose of monitoring the effects of ongoing drug therapies (in the setting of burst suppression treatment for raised intracranial pressure) and not for the expressed intention of surveying for ongoing seizure activity.
cEEG FINDINGS

Interpretable EEG data were obtained in all studies. Normal EEG findings were present in 57 (19.0%) and background abnormalities without epileptiform abnormality were seen in 92 (30.6%) of 300 cEEG studies. Epileptiform abnormalities without seizure activity were seen in 67 (22.3%), and electrographic seizures were detected in 84 (28.0%) of all 300 cEEG studies. Generalized background slowing was the most common abnormality present, seen in 132 of all 300 cEEG studies performed. Focal background slowing was evident in 61 studies. Of the 84 cEEG studies during which electrographic seizures were detected, 82 showed focal onset seizures, 1 showed only generalized onset seizures, and 1 showed focal and generalized onset seizures.

Figure 1. Example of a focal electrographic seizure, arising from the left hemisphere, on a bipolar “double banana” montage at a sensitivity of 10 µV/mm (electroencephalogram samples are sequential from A to B). ECG indicates electrocardiogram.
THERAPEUTIC DECISION MAKING FOLLOWING SEIZURE DETECTION

Antiepileptic drug therapy had not been administered to the patients at onset of recording prior to 101 of the 300 cEEG studies (34%) performed. Seizures were detected in 20 of these 101 studies (6.7% of 300 studies) and AED therapy was subsequently administered to all 20 patients. Prior to the remaining 199 of the 300 cEEG studies performed, patients were treated with AED therapy. During or after 99 of these cEEG studies, patients had a subsequent change in their AED regimen, and in 15 patients AED therapy was discontinued. During or after the remaining 85 cEEG studies in which patients received AED therapy prior to study onset, there was no change in prescribed AED therapy.

Therefore, of the 300 cEEG monitoring studies performed, 13.7% (n = 41) were associated with AED initiation, 33.0% (n = 99) were associated with AED modification, and following 5.0% of monitored studies, patients had AED therapy discontinued. Hence, 52.0% (n = 155) of all studies performed resulted in a change in prescribing of AED therapy. Forty-eight percent (145 of 300) of studies were not associated with AED changes. This decision making is summarized in Figure 3.

THERAPEUTIC DECISION MAKING INDEPENDENT OF SEIZURE DETECTION

One hundred one studies were performed on patients who were not treated with an AED prior to cEEG study, of these, 41 patients were subsequently prescribed AED therapy. Prior to 199 of the cEEG studies performed, patients were prescribed AED therapy. During or after 99 of these cEEG studies, patients had a subsequent change in their AED regimen, and in 15 patients AED therapy was discontinued. During or after the remaining 85 cEEG studies in which patients received AED therapy prior to study onset, there was no change in prescribed AED therapy.

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COMMENT

Continuous EEG monitoring is a well-established tool used for detecting electrographic seizure activity and for studying paroxysmal clinical phenomena. However, to date it remains uncertain how the information obtained by longer-term EEG recording, which is labor intensive and costly, influences clinical decision making and how decisions made based on the findings of cEEG study affect the patient outcome. In this retrospective study of 300 consecutive nonelective cEEG studies, we report significant changes in medical management based on the findings of longer-term EEG recording. To our knowledge, this is the first study to evaluate the effect of cEEG on
clinical decision making, with particular reference to AED prescribing.

In this study, as expected, the most common reason for a change in AED therapy was the detection of electrographic seizures that might otherwise not be detected by direct clinical observation or by short-term (<1 hour) routine EEG studies, particularly in patients in the ICU. While concurrent videotape recording certainly helps in determining if EEG abnormalities are artifactual, we do not believe that the lack of videotape recording significantly affects decision making although we did not study this in detail. Almost two-thirds of these longer-term EEG recordings were performed in the ICU, of which two-thirds were longer than 24 hours in duration. Continuous EEG monitoring was associated with AED therapy initiation in 13.7% (n = 41), modification of preexisting AED therapy in 33.0% (n = 99), and discontinuation of AED therapy in 5.0% (n = 15) of 300 studies.

We examined the decisions made by clinicians to treat patients with AED therapy, when seizures are suspected as defined by a request for cEEG monitoring. In the majority of patients (n = 199 [66%]) who underwent this non-elective investigation the decision to administer AED therapy had been made prior to commencement of cEEG monitoring. Some of these patients were receiving chronic AED therapy while others received AED therapy on admission, prior to the cEEG. Nevertheless, in these patients when cEEG detected seizures (n = 63, 21.0% of all studies), AED therapy was modified, either by changing the dose of the preexisting AED or by adding a new AED. When the clinical index of suspicion was sufficient to prompt cEEG investigation but not initiate AED therapy prior to the cEEG monitoring (n = 99, 33.0% of all studies), a significant proportion of them (n = 20, 6.7% of all studies) were found to have seizures, and in all of these cases AED therapy was prescribed. As a result, in 27.7% (n = 83) of all cEEG studies, the detection of electrographic seizures led to an active change in AED prescribing by the treating clinician. Furthermore, the AED continued to be prescribed at the time of discharge from hospital in all but one of these patients. Among the 199 studies in which the patients were prescribed an AED prior to the cEEG recording, 15 studies confirmed an alternate diagnosis, and AED therapy was discontinued (5.0% of total).

The changes in AED prescribing were significant, primarily starting, stopping, or giving boluses of either maintenance AED or infusion therapy. One could argue that AED prescribing, particularly dose modification, was governed by factors other than cEEG data, such as drug levels. However, 56 cEEG studies (19% of total) were associated with AED therapy initiation or discontinuation, likely due to detection, or lack thereof, of electrographic seizures. Ninety-nine studies (33% of total) were associated with AED therapy modification and it is possible that in this subset of patients factors other than the cEEG findings affected clinical decision making. The retrospective nature of this study makes it difficult to know with certainty what informed the treating physician’s decision to modify AED therapy. However, during or after 52% of all cEEG studies performed there was a significant change in medical management.

In this study we paid careful attention to categorizing and defining the cEEG findings, as cEEG is prone to misinterpretation. Our study reports a similar prevalence of seizure activity to prior studies with 28% of monitored studies found to have seizure activity in most cases, the seizures were nonconvulsive in nature. The high proportion of cEEG performed in the ICU and the high rate of detection of electrographic seizures are indicative of the extent of neurological illness in this cohort. While we did not consider PEDs (PLEDs, BiPEDs, and GPDs) to represent electrographic seizures, their detection likely prompted a change in AED prescribing given their tendency to be associated with electrographic seizures if one performs extended EEG recording.

As seen with other studies, this study highlights the potential utility of cEEG in preventing inappropriate AED prescribing, particularly when interpreted and acted on by experienced EEG readers. Continuous EEG monitoring provides an opportunity to determine the need for an AED and the effect of prescribed AED therapy in real time. The information obtained from cEEG monitoring not only increases clinician understanding of a given patient’s illness presentation but also affects treatment decisions. This study supports the hypothesis that cEEG monitoring has a significant effect on clinical decision making. It remains to be seen if decisions informed by cEEG improve clinical outcomes, reduce duration of ICU stay, and lessen iatrogenic morbidity.

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Author Contributions: Each author had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Kilbride. Acquisition of data: Kilbride and Costello. Analysis and interpretation of data: Kilbride, Costello, and Chiappa. Drafting of the manuscript: Kilbride. Critical revision of the manuscript for important intellectual content: Kilbride, Costello, and Chiappa. Administrative, technical, and material support: Kilbride, Costello, and Chiappa. Study supervision: Chiappa.

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REFERENCES